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FACULDADE DE ENGENHARIA QUÍMICA

ÁREA DE CONCENTRAÇÃO
DESENVOLVIMENTO DE PROCESSOS QUÍMICOS

Modelagem Detalhada e Otimização de Processos de Cristalização

AUTORA: CALIANE BASTOS BORBA COSTA
ORIENTADOR: Prof. Dr. RUBENS MACIEL FILHO

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Prof. Dr. Rubens Maciel Filho (Orientador)

Profa. Dra. Aline Carvalho da Costa (Titular)

Prof. Dr. Marcelo Martins Seckler (Titular)

Prof. Dr. Osvaldir Pereira Taranto (Titular)

Prof. Dr. Roberto de Campos Giordano (Titular)

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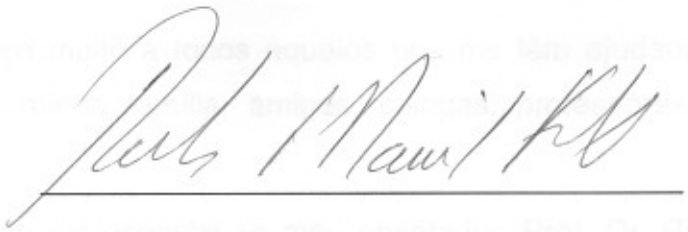

Prof. Dr. Rubens Maciel Filho (Orientador)

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Resumo

O foco de estudo neste trabalho é a cristalização, processo bastante utilizado industrialmente, principalmente na obtenção de produtos de alto valor agregado nas indústrias farmacêuticas e de química fina. Embora seja um processo de clássica utilização, seus mecanismos, sua modelagem e o real controle de sua operação ainda requerem estudos. A tese apresenta discussões e desenvolvimentos na área de modelagem determinística detalhada do processo e sua otimização, tanto por métodos determinísticos quanto estocásticos.

A modelagem é discutida detalhadamente e os desenvolvimentos presentes na literatura de métodos numéricos aplicáveis à solução do balanço de população, parte integrante da modelagem, são apresentados com enfoque nos processos de cristalização e nas principais vantagens e desvantagens.

Estudos preliminares de melhoria do processo de cristalização em modo batelada operada por resfriamento indicam a necessidade de otimização da política operacional de resfriamento. Uma vez que o método determinístico de otimização de Programação Quadrática Sucessiva se apresenta ineficiente para resolução do problema de otimização, a utilização de Algoritmo Genético, um método estocástico de otimização bastante estabelecido na literatura, é avaliada, para a busca do ótimo global deste processo, em um estudo pioneiro na literatura de aplicação dessa técnica de otimização em processos de cristalização. Uma vez que o uso de Algoritmos Genéticos exige que se executem sucessivas corridas com diferentes valores para os seus parâmetros no intuito de se aumentar a probabilidade de alcance do ótimo global (ou suas cercanias), um procedimento original, geral e relativamente simples é desenvolvido e proposto para detecção do conjunto de parâmetros do algoritmo de influência significativa sobre a resposta de otimização. A metodologia proposta é aplicada a casos de estudo gerais, de complexidades diferentes e se mostra bastante útil nos estudos preliminares via Algoritmo Genético. O procedimento é então aplicado ao problema de otimização

da trajetória de resfriamento a ser utilizada em um processo de cristalização em modo batelada.

Os resultados obtidos na tese apontam para a dificuldade dos métodos determinísticos de otimização em lidar com problemas de alta dimensionalidade, levando a ótimos locais, enquanto os métodos evolucionários são capazes de se aproximar do ótimo global, sendo, no entanto, de lenta execução. O procedimento desenvolvido para detecção dos parâmetros significativos do Algoritmo Genético é uma contribuição relevante da tese e pode ser aplicado a qualquer problema de otimização, de qualquer complexidade e dimensionalidade.

Abstract

This work is focused on crystallization, a process widely used in industry, especially for the production of high added-value particles in pharmaceutical and fine chemistry industries. Although it is a process of established utilization, its mechanisms, modeling and the real control of its operation still require research and study. This thesis presents considerations and developments on the detailed deterministic modeling area and the process optimization with both deterministic and stochastic methods.

The modeling is discussed in detail and the literature developed numerical methods for the population balance solution, which is part of the modeling, are presented focusing on crystallization processes and on the main advantages and drawbacks.

Preliminary studies on batch cooling crystallization processes improvement drive to the need of cooling operating policy optimization. Since the Sequential Quadratic Programming deterministic method of optimization is inefficient for the optimization problem, the use of Genetic Algorithm (GA), a stochastic optimization method well established in literature, is evaluated in the global optimum search for this process, in a pioneering literature study of GA application in crystallization processes. Since the GA requires that many runs, with different values for its parameters, are executed, in order to increase the probability of global optimum (or its neighborhood) achievement, an original, general and relatively simple procedure for the detection of the parameters set with significant influence on the optimization response is developed and proposed. The proposed methodology is applied to general case studies, with different complexities and is very useful in the preliminary studies via GA. The procedure is, then, applied to the cooling profile optimization problem in a batch cooling optimization process.

The results of the study presented in this thesis indicate that the deterministic optimization methods do not deal well with high dimensionality problems, leading to achievement of local optima. The evolutionary methods are

able to detect the region of the global optimum but, on the other hand, are not fast codes. The developed procedure for the significant GA parameters detection is a relevant contribution of the thesis and can be applied to any optimization problem (of any complexity and of any dimensionality).

Sumário

Capítulo 1 - Introdução

Existem muitas maneiras pelas quais a cristalização a partir de solução é conduzida, incluindo-se cristalização evaporativa, por adição de anti-solvente ou pelo resfriamento da solução. A operação de um cristalizador, seja em modo contínuo ou em modo batelada, deve satisfazer as especificações do cliente para a pureza do produto e para a distribuição de tamanhos de cristal e as necessidades da planta produtiva para uma produção econômica e livre de custos adicionais, como os decorrentes de complicações das operações posteriores à cristalização. A distribuição de tamanho de cristal gerada afeta também outras características, como a taxa de dissolução ou fluidez. De modo a garantir que os objetivos, tanto de processo quanto de produto, sejam alcançados, todas as variáveis que afetam o processo de cristalização devem ser controladas dentro de uma faixa aceitável, a qual é ditada pela natureza química do soluto, do solvente e de possíveis impurezas presentes. Para satisfazer as necessidades de melhoria de processo e melhor condução do mesmo, a modelagem detalhada do processo é necessária. Quando se trata de cristalizadores operados em modo batelada, a análise de processo é mais complicada do que aquela em cristalizadores em modo contínuo, principalmente devido às dificuldades encontradas em sistemas batelada: a massa e superfície dos cristais variam de modo complexo durante o processo, como função do tempo.

1.1 Objetivos

O objetivo desta tese é apresentar um estudo detalhado da cristalização, com abrangência sobre as etapas de modelagem determinística detalhada e sobre otimização de políticas operacionais. Dentre os objetivos, destacam-se:

- Estabelecimento do modelo determinístico detalhado do processo de cristalização;

- Levantamento dos métodos numéricos para resolução do balanço de população mais usuais na literatura, com considerações relativas aos seus principais aspectos positivos e negativos, tempo computacional de resolução e incoerências apresentadas, fundamentalmente quando esses métodos são aplicados a processos de cristalização.
- Elaboração de *software* para avaliação e melhoria de processos de cristalização;
- Identificação da influência das variáveis de processo;
- Avaliação de melhores políticas operacionais;
- Avaliação das potencialidades de algoritmos determinísticos e estocásticos de otimização no tratamento do problema de otimização de políticas operacionais na cristalização;
- Desenvolvimento de um procedimento baseado em estatística para detecção de parâmetros significativos do método estocástico de otimização.

1.2 Organização da Tese

O Capítulo 2 apresenta o processo de cristalização e discute tópicos relativos a seus mecanismos e sua modelagem. Fazem parte ainda do capítulo considerações acerca de problemas de otimização, aplicados a processos. O método determinístico de otimização por Programação Quadrática Sucessiva e o método estocástico Algoritmo Genético são apresentados e discutidos quanto à estrutura de funcionamento e seus parâmetros.

A modelagem determinística detalhada do processo de cristalização e estudos preliminares de melhorias de processo são apresentados no Capítulo 3, no qual o método de Programação Quadrática Sucessiva é utilizado para gerar informações de melhorias de processo em tentativas de otimização.

No Capítulo 4, o balanço de população é detalhadamente discutido, uma vez que sua equação é de tratamento matemático/numérico difícil e ela, indefectivelmente, faz parte de qualquer modelagem determinística de processos de cristalização.

O Capítulo 5 é responsável por apresentar a ferramenta computacional desenvolvida, utilizando-se da modelagem e de métodos de otimização, para estudos de desenvolvimento de processos orientados para especificações de produto. Segue-se a isso o estudo do perfil ótimo de temperatura em diversos sistemas solvente-soluto, de modo a se atingir a desejada especificação de produto, o que é determinado por sua aplicação.

A otimização do processo de cristalização do ácido adípico é então considerada no Capítulo 6, tanto por Programação Quadrática Sucessiva quanto por Algoritmo Genético, e os resultados obtidos por ambas as técnicas de otimização e o seu desempenho são discutidos.

A utilização do Algoritmo Genético mostrou que havia uma deficiência na literatura quanto a uma metodologia de detecção de seus parâmetros que apresentam influência significativa sobre o problema de otimização considerado e, portanto, no Capítulo 7, um procedimento inovador, geral e de fácil utilização é proposto e aplicado a diferentes casos de estudo de dimensionalidade e complexidade diversas.

O procedimento proposto é, então, no Capítulo 8, aplicado ao problema de otimização, por Algoritmo Genético, da política operacional de resfriamento da cristalização, em modo batelada, do ácido adípico.

Por fim, o Capítulo 9 apresenta as conclusões deste trabalho e sugestões para trabalhos futuros.

O fluxograma da Figura 1 ilustra de que forma a tese está organizada, com as inter-relações entre capítulos.

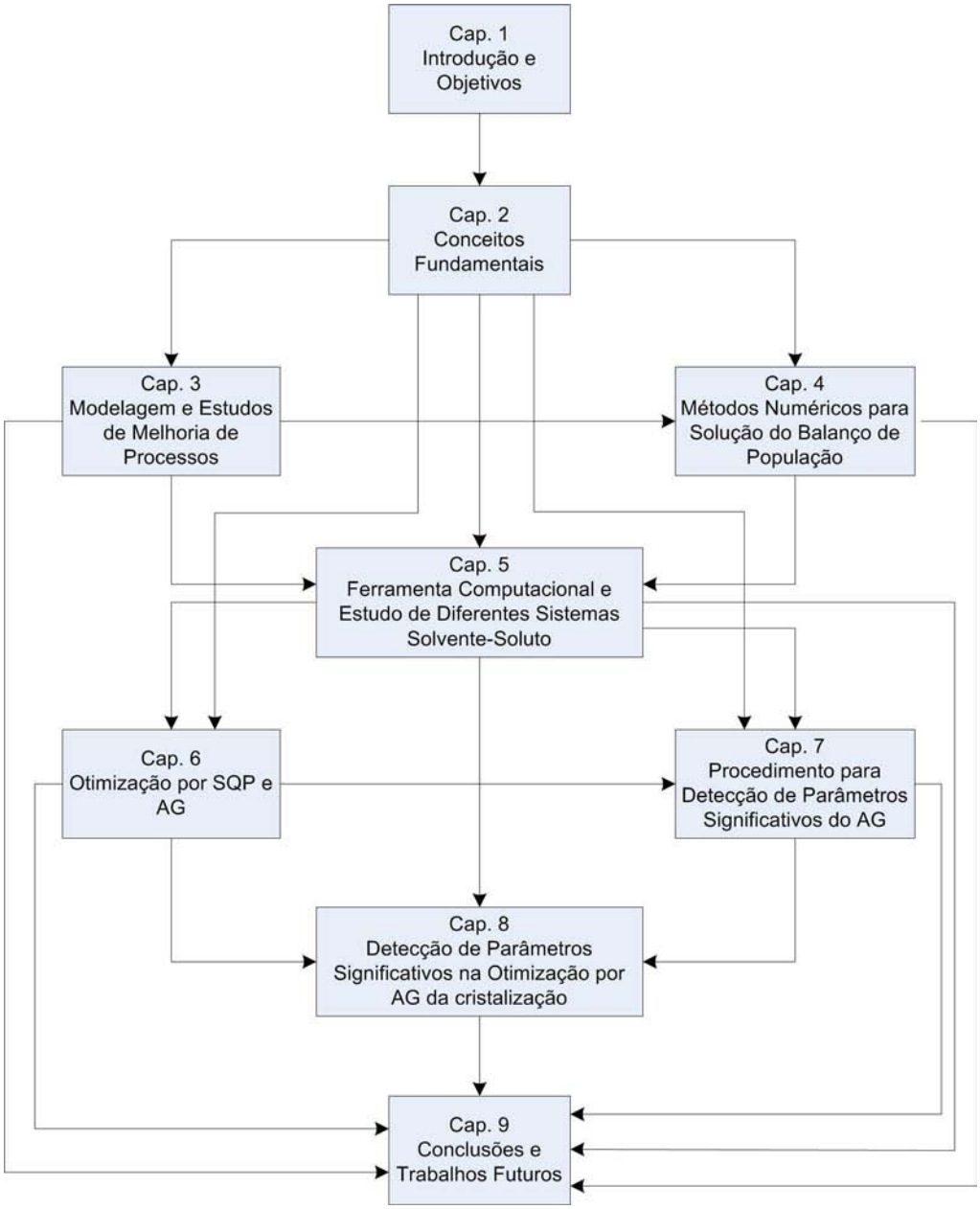

Figura 1: Fluxograma ilustrando as inter-relações entre capítulos da tese

1.3 Contribuições da Tese

Dentre as contribuições desta tese, destacam-se:

- Desenvolvimento de ferramenta computacional para avaliação, otimização e projeto de processos de cristalização;
- Avaliação do impacto dos parâmetros e estratégias operacionais no desempenho de processos de cristalização;

- Formulação dos procedimentos de otimização com a proposição e avaliação de diferentes funções objetivo;
- Avaliação do desempenho de Algoritmo Genético para solução do problema matemático de otimização de cristalização, em um trabalho pioneiro na literatura;
- Desenvolvimento e proposta de procedimento geral para identificação dos parâmetros do Algoritmo Genético de influência significativa em qualquer problema de otimização resolvido por esse método estocástico.

Capítulo 2 – Conceitos Fundamentais

2.1. Introdução

Cristalização é uma técnica de separação e purificação empregada na produção de uma ampla gama de materiais. Teoricamente, a cristalização pode ser definida como uma mudança de fase em que um produto cristalino é obtido a partir de uma solução (Myerson, 1993). Cristalizadores operados em batelada são usados na produção de cristais de química fina, especialidades e princípios ativos de fármacos, além de encontrar aplicações nas indústrias alimentícias, como alimentos funcionais, sendo muitas vezes a produção desses processos de baixa tonelagem, mas com alto valor agregado e com alta pureza (Mullin, 1988; McCabe et al., 1993; Rohani et al, 2005; Hojjati e Rohani, 2005). Para o estudo determinístico detalhado da modelagem e de otimização de políticas operacionais a que se propõe esta tese, este capítulo traz alguns conceitos fundamentais sobre a cristalização, sua modelagem, seu modo de operação e sobre problemas de otimização, por resolução determinística ou estocástica.

2.2. Aspectos gerais sobre cristalização

A força motriz para qualquer processo de cristalização é a supersaturação, que representa a distância da concentração do sistema em relação à concentração de saturação, também chamada de concentração de equilíbrio (representada pela curva de solubilidade do soluto no solvente como função da temperatura, Figura 1) e cuja geração no sistema pode-se dar de maneiras diversas. Dentre as diversas maneiras de se manipular a supersaturação durante o curso da batelada, inclui-se o resfriamento da solução (se a solubilidade do soluto aumenta fortemente com a temperatura), a evaporação do solvente e adição de anti-solvente.

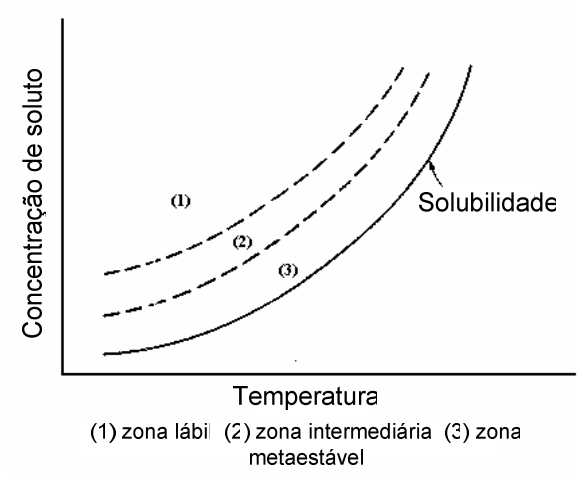

Figura 1: Regiões de supersaturação

Em um processo de cristalização, uma massa discreta de cristais, com determinada distribuição de tamanhos, é produzida. Os fenômenos cinéticos responsáveis pela retirada de soluto da solução e inclusão em rede cristalina são nucleação, que envolve nucleação primária e secundária, e crescimento dos cristais já existentes em solução. Além desses fenômenos, há que se atentar para a ocorrência de aglomeração entre cristais e quebra dos mesmos, uma vez que esses fenômenos, embora não retirem soluto da solução, modificam a distribuição de tamanho dos cristais (CSD – *Crystal Size Distribution*) já existentes.

Em qualquer processo de cristalização, as características das partículas formadas influenciam na seleção ou escolha de todas as operações unitárias posteriores, além de, incontestavelmente, determinar a qualidade e aplicabilidade do produto formado. O tamanho e forma das partículas em produtos particulados são importantes por muitas razões. A eficiência de qualquer processo de produção de material particulado depende de sua forma, de seu tamanho e sua distribuição: a forma do cristal de muitos fármacos influencia nas taxas de dissolução dos mesmos, o que leva a uma variação da biodisponibilidade para cristais de diferentes formas; um produto de tamanho médio muito pequeno é difícil de ser centrifugado, de lavar e ensacar; muitos produtos devem ser dissolvidos para uso subseqüente e uma faixa larga de tamanhos leva a uma variação no tempo necessário para a dissolução. De modo a satisfazer requisitos relacionados à qualidade do produto final, todas as variáveis que afetam o processo de cristalização devem ser controladas dentro

de uma faixa aceitável, através da manipulação de variáveis do processo em um esquema de controle automático, seja na forma de um controlador ótimo em malha aberta (determinação *offline*) ou um controlador *feedback* tradicional (PID) ou preditivo. A disponibilidade de um modelo matemático confiável para estudos do comportamento dinâmico é importante para fins de projeto, otimização e controle e é válido, portanto, o investimento em estudos aprofundados para desenvolvimento de modelo matemático detalhado do processo de cristalização.

2.3 Cinética e Mecanismos de Cristalização

A cinética de um processo de cristalização é caracterizada em termos de dois fenômenos principais: nucleação e crescimento do cristal. A nucleação consiste na formação de novos cristais, enquanto o crescimento é o processo através do qual os cristais já existentes se tornam maiores. A nucleação e o crescimento dos cristais são fenômenos competitivos, já que ambos consomem massa de soluto durante o processo de cristalização. Dois outros fenômenos podem se fazer presentes e, apesar de não consumirem massa de soluto da solução, alteram a distribuição de cristais nos diversos tamanhos de partícula (alteram a CSD): a aglomeração e a quebra de cristais.

2.3.1 Nucleação

A nucleação primária ou espontânea ocorre na ausência de cristais e está associada a altos níveis de supersaturação. Na nucleação primária homogênea, a formação de novas partículas não é influenciada por sólidos de qualquer tipo, incluindo as paredes do cristalizador ou as partículas submicroscópicas de substâncias estranhas, e a formação de uma nova fase se dá por colisão de partículas de soluto que se aglomeram. Na nucleação primária heterogênea, uma substância estranha constituída de partículas finas está presente na solução na qual ocorre a cristalização, catalisando um aumento da taxa de nucleação. A nucleação heterogênea ocorre em níveis de supersaturação significativamente menores do que os requeridos para a homogênea, mas, mesmo assim, freqüentemente esses níveis de supersaturação ainda são muito altos para a formação de cristais de boa qualidade (Rawlings et al., 1993). A nucleação secundária, por definição,

ocorre somente quando cristais do soluto em consideração já estão presentes. Como este é quase sempre o caso em cristalizadores, a nucleação secundária é o mecanismo dominante na maioria dos processos industriais. Ao contrário da nucleação primária, que requer supersaturações relativamente altas, a nucleação secundária já ocorre em valores de supersaturação de baixos a moderados, o que leva à formação de cristais de boa qualidade.

2.3.2 Crescimento

O crescimento de cristais em uma solução pode ser descrito de maneira simplificada como um processo em duas etapas, que envolve: (1) transferência de massa, por difusão ou convecção, do soluto do seio da solução para a superfície do cristal, seguida por (2) reação na superfície, na qual as unidades de crescimento são integradas à rede cristalina. Para compostos muito solúveis, a etapa de integração superficial em geral não é limitante. Para solutos pouco solúveis, a integração superficial é o passo limitante. Além da solubilidade, também o tamanho do cristal e o nível de supersaturação têm efeito sobre qual dos dois passos de crescimento é dominante. Para cristais muito pequenos e valores muito baixos de supersaturação, a integração superficial é sempre a etapa dominante no processo de crescimento. Para a maioria dos compostos, entretanto, ambas as etapas devem ser levadas em conta no cálculo da taxa de crescimento (Bermingham et al., 2001).

2.4 Cristalização em Modo Batelada Resfriada e suas Respostas a Diferentes Políticas Operacionais

Uma cristalização típica em batelada por resfriamento se inicia com a alimentação de uma corrente quente (temperatura dependente de cada problema específico de cristalização) de uma solução não saturada a um tanque agitado, dotado de sistema de resfriamento (jaqueta / serpentina). A Figura 2 ilustra um cristalizador industrial dotado de jaqueta, agitador e chicanas. A supersaturação é criada por resfriamento, levando à ocorrência dos diversos mecanismos cinéticos (nucleação, crescimento, aglomeração e quebra).

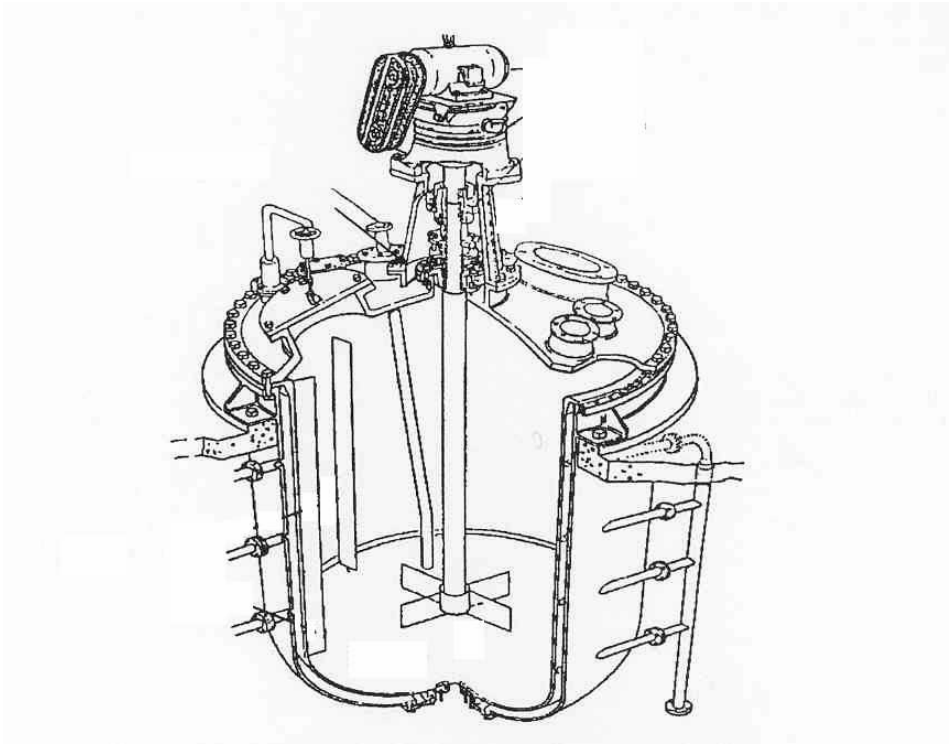

Figura 2: Cristalizador industrial

Enquanto houver supersaturação, os fenômenos cinéticos da cristalização se fazem presentes. No entanto, a magnitude de cada mecanismo é função da sua dependência em relação à supersaturação, dependência esta explicitada na expressão matemática de cada fenômeno. A CSD obtida ao final da batelada depende, portanto, do perfil de supersaturação seguido durante o curso do processo, evidenciando a importância da taxa de resfriamento empregada (Mullin, 1993).

Na política operacional de resfriamento natural, o qual consiste em se passar fluido refrigerante a uma temperatura e vazão fixas pelo sistema de resfriamento, um grande pico de supersaturação é gerado nos instantes iniciais do processo de cristalização, devido ao alto gradiente de temperatura entre a solução e o fluido refrigerante, como mostrado na Figura 3. Esse pico se deve a uma queda muito rápida da temperatura da solução nos estágios iniciais da batelada. Isto faz aumentar a taxa de nucleação logo no início da batelada e o resultado deste tipo de operação são cristais pequenos com uma larga CSD ou ainda a obtenção de uma CSD final bimodal, caso tenha havido semeadura.

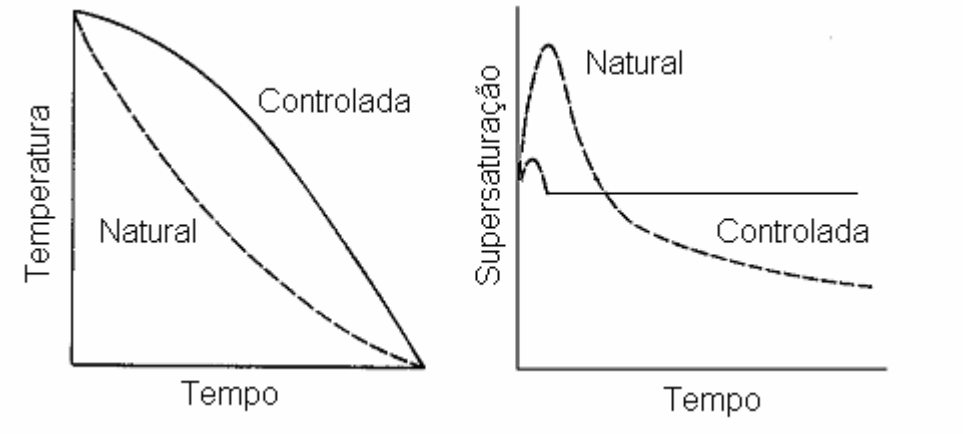

Figura 3: Resfriamento natural e controlado em cristalização em modo batelada por resfriamento: perfis de temperatura e de supersaturação.

A diminuição do pico de supersaturação melhora significativamente o desempenho do processo. Para geração de um pico pequeno de supersaturação, que leva à nucleação não excessiva, e para a posterior manutenção da supersaturação em nível praticamente constante e relativamente baixo, uma política de resfriamento controlado deve ser aplicada. No resfriamento programado, o nível de supersaturação é calculado de forma tal que se mantenha dentro do limite da zona metaestável em toda a batelada, o que minimiza a taxa de nucleação primária. Neste tipo de operação, a curva de resfriamento cai lentamente nos estágios iniciais e mais rapidamente no final (Mullin, 1993), conforme ilustra a Figura 3.

Na presença de sementes de cristal, a nucleação secundária pode ser suprimida. Aumentando-se a carga de semeadura, reduz-se a supersaturação em todos os modos de resfriamento (Figura 4). Em cristalização semeada, a magnitude da supersaturação deve ser controlada de tal maneira que o mecanismo necessário prevaleça: se a taxa de crescimento prevalece sobre a taxa de nucleação secundária, uma CSD estreita e unimodal, com um tamanho médio de cristal grande é obtida. Estes objetivos podem ser alcançados com o resfriamento e semeadura adequados. A quantidade de sementes necessárias para superar a nucleação secundária depende do tamanho médio, da quantidade e da qualidade das sementes, assim como da política operacional (Hojjati e Rohani, 2005).

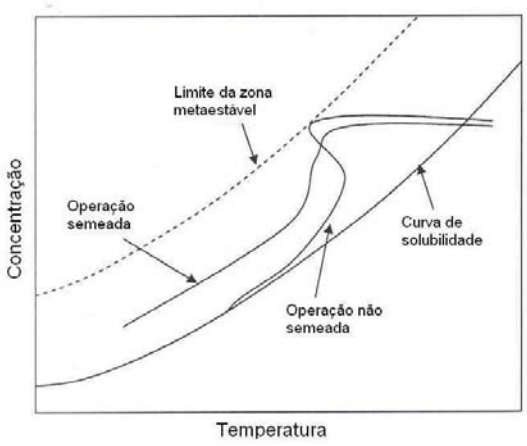

Figura 4: Diferentes curvas de operação em cristalização semeada e não semeada

2.5 Modelagem Matemática da Cristalização

A modelagem completa de um processo de cristalização envolve balanço de massa (uma massa de soluto deixa a solução e se transforma em cristais, seja na forma de novos núcleos cristalinos, seja incorporando-se a estruturas cristalinas já existentes), balanço de energia (no processo de resfriamento, calor é retirado da solução pela passagem de um fluido refrigerante pela camisa / jaqueta que envolve o cristalizador) e balanço de população (que descreve de que forma os cristais se distribuem em diversos tamanhos de partícula, durante o curso do processo). No balanço de população, todos os fenômenos cinéticos responsáveis pela geração e distribuição de cristais em tamanhos variados são levados em consideração. São estes fenômenos cinéticos que caracterizam o andamento de um processo de cristalização, sendo a supersaturação existente a força motriz significante que desencadeia a sua ocorrência.

Não somente a cristalização se utiliza do balanço de população: qualquer processo que envolva formação, crescimento, aglomeração ou quebra de entidades, sejam elas cristais, bolhas ou células, lança mão dessa abordagem. Uma das grandes dificuldades nesses processos, no entanto, é que, embora a estrutura teórica de abordagem para sua modelagem determinística (o balanço de população) esteja já bastante estabelecida, a solução do modelo resultante é inexistente em forma analítica na grande

maioria dos casos. A equação do balanço de população (PBE – *Population Balance Equation*) é diferencial parcial hiperbólica e nenhum método numérico geral foi desenvolvido de modo a produzir uma solução eficiente e precisa para uma ampla classe de processos, sendo que a escolha do melhor método é dependente do caso de estudo em que se vai aplicar a PBE.

A equação referente ao balanço de população geral quando aplicada a processos de cristalização em que se desconsideram variações espaciais é apresentada na Equação (2.1)

$$\frac{\partial n}{\partial t} + \frac{\partial (Gn)}{\partial L} + n\frac{\partial V}{V\partial t} + D(L) - B(L) + \sum_k \frac{\dot{V}_i \cdot n_i}{V} = 0 \qquad (2.1)$$

O termo $\partial n / \partial t$ fornece a mudança da densidade em número com relação ao tempo em um cristalizador (regime transiente). A expressão $\partial (Gn) / \partial L$ descreve a diferença entre cristais crescendo para dentro ou para fora do intervalo dL, devido à taxa de crescimento de cristal G = dL/dt. O termo n($\partial V / V\partial t$) considera mudanças no volume em relação ao tempo (por exemplo, o decréscimo de volume em cristalizadores evaporativos operados de modo batelada devido à evaporação do solvente). Os parâmetros D(L) e B(L) representam as taxas de desaparecimento e aparecimento, respectivamente. Esses eventos incluem aglomeração, nucleação e quebra. Finalmente, o termo $\sum_k (\dot{V}_i \cdot n_i / V)$ fornece a soma de todos os fluxos de partículas entrando e saindo do cristalizador.

No caso de cristalização batelada operada por resfriamento, o balanço populacional se reduz a:

$$\frac{\partial n}{\partial t} = -\frac{\partial (Gn)}{\partial L} - D(L) + B(L) \qquad (2.2)$$

Como a PBE é uma equação diferencial parcial com relação ao tempo e ao tamanho de partícula (n(L,t)), são necessárias uma condição inicial e uma condição de contorno para sua resolução (Bermingham et al., 2001):

$$n(0,t) = \left[\frac{dN}{dL}\right]_{L=0} = \left[\frac{dN}{dt}\right]\left[\frac{dt}{dL}\right]_{L=0} = \frac{B_0(t)}{G_L(0,t)} \qquad (2.3)$$

$n(L,0) =$ distribuição inicial (2.4)

Na Equação (2.3), o termo $B_0(t)$ indica taxa de aparecimento de partículas de tamanho zero e $G_L(0,t)$ representa a taxa de crescimento de cristais de tamanho zero.

A modelagem da cristalização, portanto, envolve equações integro-diferencias (na grande maioria das vezes, os termos relativos à aglomeração e quebra na PBE são representados por equações integrais sobre o tamanho das partículas). A evolução, durante o tempo da batelada, da CSD, da concentração de soluto e da temperatura do cristalizador pode ser completamente descrita pela solução das equações do modelo determinístico (os balanços de massa, energia e população). No entanto, a solução simultânea da equação parcial hiperbólica que compõe o balanço de população e das equações diferenciais ordinárias representativas dos balanços de massa e energia pode ser uma tarefa extraordinária e a literatura apresenta uma série de trabalhos dedicados a desenvolver métodos numéricos de resolver a PBE em um estudo caso a caso (Sarkar et al., 2006). O Capítulo 4 desta tese faz um levantamento de vários métodos da literatura e discute-os, com enfoque em processos de cristalização.

2.6 Políticas Operacionais e Otimização Matemática Aplicada a Processos de Cristalização

Uma solução supersaturada não está em equilíbrio e, de modo a alcançar o equilíbrio, a solução supersaturada cristaliza. O processo de incorporação de soluto, que deixa a solução, a uma rede cristalina ocorre fundamentalmente, como já exposto, por dois mecanismos cinéticos: nucleação e crescimento. Apesar de serem mecanismos competitivos, uma vez que ambos retiram soluto da solução e aumentam a massa cristalina, suas cinéticas são bastante diferentes, principalmente no que concerne à dependência da força motriz do processo, a supersaturação. Além desses dois mecanismos fundamentais, a aglomeração e quebra de cristais podem se fazer presentes e afetar a distribuição de partículas cristalinas nos diversos tamanhos ao longo do curso do processo. Uma vez iniciada a cristalização, portanto, a supersaturação pode ser consumida por uma combinação dos seus

mecanismos cinéticos. É essa relação entre nucleação, crescimento, aglomeração e quebra que controla a distribuição de tamanho de cristais do produto obtido e é, portanto, um aspecto crucial de processos de cristalização industrial.

Uma série de trabalhos na literatura lida com o problema de otimização de cristalização em modo batelada operada por resfriamento. O trabalho pioneiro foi o de Mullin e Nyvlt (1971), seguido dos de Jones (1974) e Jones e Mullin (1974), que o apresentaram tanto teórica quanto experimentalmente.

A etapa de otimização do processo de cristalização em modo batelada operado por resfriamento envolve geralmente a determinação da trajetória ótima de resfriamento (ou conjuntamente, da semeadura ótima) a ser usada em um esquema de controle integrado ao problema de otimização, devido ao fato de que a CSD obtida ao final da batelada depende do perfil de supersaturação (e da semeadura) seguido durante o curso do processo. Em cristalizadores operados por resfriamento em modo batelada, uma das maneiras mais usadas na indústria, a otimização tem sido tratada tradicionalmente com relação ao perfil de resfriamento e características da semeadura, de modo a manter a supersaturação em nível ótimo durante a operação (Sarkar et al., 2006). A determinação da trajetória ótima é feita pela resolução de um problema matemático de otimização. Seu cálculo é feito objetivando minimizar ou maximizar um critério de desempenho pré-determinado. A definição do critério de desempenho, a chamada função objetivo, é feita baseada em termos da necessidade ou metas de produção da planta ou qualidade do produto. Os objetivos de otimização em processos de cristalização em modo batelada são definidos usualmente como função da CSD final ou de propriedades a ela relacionadas. Normalmente, deseja-se minimizar a nucleação e maximizar o crescimento do cristal, além de obter uma CSD final com baixo desvio padrão de distribuição. A Equação (2.5) é uma exemplificação de um possível problema de otimização em um processo de cristalização. Nessa equação, n representa a função de distribuição, os índices n e s representam, respectivamente, CSDs provenientes de cristais nucleados e de sementes, L representa o tamanho característico dos cristais e T é a temperatura.

$$\min_{T}\left[\frac{\int_0^{\infty} n_n(L)L^3 dL}{\int_0^{\infty} n_s(L)L^3 dL}\right]$$

$$\text{sujeito a : } \begin{array}{l} 1)\ \text{modelo do cristalizador} \\ 2)\ \text{restrições de processo} \\ 3)\ \text{restrições de projeto} \end{array} \qquad (2.5)$$

O problema de otimização matemática do processo de cristalização é, portanto, postulado em termos de minimização ou maximização de características da CSD, estando sujeito ao modelo do processo (os balanços de massa, energia e população), e a possíveis restrições de processo e projeto (tais como taxa máxima possível de resfriamento, imposição de perfis decrescentes de temperatura e produtividade mínima aceitável da planta). Tal tipo de abordagem para a otimização do processo de cristalização se enquadra dentro da teoria de controle ótimo, uma técnica na qual o sinal de controle otimiza um certo índice de avaliação. Em um problema de controle ótimo, tendo-se as equações dinâmicas do processo e o critério de desempenho, o problema de otimização é formulado matematicamente de modo a minimizar (maximizar) a função objetivo, sujeitas às restrições dinâmicas/de processo, admitindo-se o conhecimento dos valores iniciais das variáveis de estado e estando livres seus valores finais.

Para a solução do problema de otimização, a literatura apresenta uma série de métodos, os quais se dividem fundamentalmente, segundo a teoria clássica da literatura, em métodos determinísticos e métodos estocásticos de otimização, conforme descrito no item a seguir.

2.7 Métodos Determinísticos e Estocásticos para Resolução de Problemas Matemáticos de Otimização

Em qualquer problema matemático de otimização, deseja-se minimizar ou maximizar uma determinada função objetivo, sujeita a restrições de igualdade e desigualdade, conforme descrito na Equação (2.6), em que se deseja minimizar a função $f(x)$, que está sujeita a m restrições de igualdade e n restrições de desigualdade.

$$\begin{aligned} &\min\ f(x) \\ &sujeito\ a:\ \ h_i(x) = 0 \qquad i = 1,2,...,m \\ &\qquad\qquad g_j(x) \geq 0 \qquad j = 1,2,...,n \end{aligned} \tag{2.6}$$

Uma solução de um problema de otimização deve ser factível, isto é, deve obedecer às restrições do problema matemático. A solução ótima, por outro lado, deve, além de satisfazer às restrições do problema, fornecer o valor ótimo para a função que está sendo otimizada. Esta solução pode ser única ou não (Edgar e Himmelblau, 1989).

Classicamente, a literatura classifica os métodos para se encontrar a solução de um problema de otimização em métodos determinísticos ou estocásticos. Os métodos determinísticos de resolução de problemas de otimização se utilizam de características matemáticas da própria função objetivo e exigem que ela seja contínua e diferenciável, bem como suas restrições. Assim, funções não diferenciáveis ou cuja diferenciação não se dá de forma analítica não permitem, a princípio, a utilização de métodos determinísticos, a menos que se lance mão de diferenciação numérica. Funções multimodais, que são caracterizadas por apresentarem mais de um mínimo (máximo) local, isto é, diversos ótimos locais e um ótimo global, dificultam ainda mais a aplicação de métodos determinísticos, pois se passa a depender da estimativa inicial.

Um método determinístico bastante utilizado para a solução de problemas matemáticos de otimização não linear é a Programação Quadrática Sucessiva (*Sequential Quadratic Programming*, SQP). Neste método, a função objetivo é aproximada localmente por uma função quadrática e as restrições são aproximadas por funções lineares, de modo que a programação quadrática pode ser usada recursivamente. Programação quadrática é o nome atribuído ao procedimento que minimiza funções quadráticas de muitas variáveis sujeitas a restrições lineares de desigualdade ou igualdade, ou de ambos os tipos (Edgard e Himmelblau, 1989).

As dificuldades associadas ao uso de otimização matemática em problemas de engenharia em larga escala contribuíram para o desenvolvimento de soluções alternativas (não determinísticas). Os métodos estocásticos não

usam, nas suas etapas internas de busca pelo ótimo global, nenhuma informação de derivadas da função objetivo ou das restrições. Pode-se, inclusive, utilizar um modelo não matemático como função objetivo. Via de regra, os métodos estocásticos são bastante robustos pela independência da(s) estimativa(s) inicial (is), operam com uma população de soluções individuais (exceto no Recozimento Simulado – *Simulated Annealing*) e geralmente simulam ou mimetizam a evolução biológica natural e/ou o comportamento social das espécies, apresentando um balanço notável entre aproveitamento de melhores soluções e exploração de espaço de busca. No entanto, são geralmente de cálculo mais lento do que os métodos determinísticos.

Uma corrente de pesquisadores defende a classificação dos métodos de otimização em métodos locais ou globais, em oposição à classificação entre métodos determinísticos e estocásticos. Isso é motivado pelo fato de que os chamados métodos determinísticos são dependentes da estimativa inicial (tornando-os locais) e nem todos os métodos classicamente classificados como estocásticos se utilizam de aleatoriedade, mas todos os chamados métodos estocásticos têm maior capacidade de varredura do espaço de busca que os métodos locais, não sendo levados para o ótimo local mais próximo à estimativa inicial (daí a denominação de globais).

O Algoritmo Genético (AG), técnica estocástica baseada em evolução, muito referenciada na literatura, foi concebido em analogia ao princípio da evolução das espécies de Darwin, segundo o qual o indivíduo mais apto sobrevive e tem maior probabilidade de propagar seus genes ao longo das gerações. Baseada em sua reconhecida habilidade em atingir soluções próximas ao ótimo em problemas de larga escala, o AG é muito aplicado em engenharia (Elbeltagi et al., 2005). Neste método, a solução para um dado problema é representada na forma de um cromossomo, que é formado por genes. Cada cromossomo representa uma solução, por conter valores codificados para cada variável de otimização. Uma população aleatória de soluções (cromossomos) é iniciada e o grau de adaptação de cada solução é avaliado de acordo com uma função objetivo e com as restrições do problema. De modo a simular o processo natural de sobrevivência dos mais aptos, os

melhores cromossomos trocam informações através do operador cruzamento, produzindo uma nova geração de cromossomos. No entanto, todos os indivíduos estão sujeitos a mutações aleatórias, geralmente empregadas com baixa probabilidade de ocorrência. Essa nova geração é novamente avaliada e usada para levar a população a evoluir (seqüência de passos de avaliação, cruzamento e mutação). O Algoritmo Genético requer que alguns parâmetros internos ao método tenham seus valores estipulados no início de uma corrida de otimização. Estes parâmetros incluem as probabilidades de cruzamento, de mutações, tamanho da população, mecanismos de seleção de indivíduos, semente para geração da população inicial e o número máximo de gerações a serem avaliadas. É importante, em problemas de otimização resolvidos por Algoritmo Genético, que se analise de que maneira esses parâmetros influenciam a resposta final obtida, isso é, o ótimo encontrado. Embora apresente etapas não determinísticas em seu desenvolvimento, o Algoritmo Genético não é um método de busca puramente aleatório, pois combina variações aleatórias com seleção polarizada pelos vetores de adequação atribuídos a cada indivíduo.

É bom que se ressalte que o Algoritmo Genético faz parte das técnicas estocásticas de otimização, especificamente daquelas que se baseiam em técnicas evolutivas. No entanto, nada tem a ver com a chamada Operação Evolutiva (EVOP – *Evolutionary Optimization*). A EVOP consiste em uma metodologia para a melhoria de processos contínuos ou descontínuos e trata-se de uma ferramenta estatística para a busca de melhoria da qualidade, produtividade e capacidade de plantas químicas. Foi desenvolvida estudando-se as respostas, após variações dos fatores (variáveis) relevantes do processo, constituindo-se em uma variação do Planejamento Fatorial. Através de métodos estatísticos pode-se chegar a informações não previstas pela teoria ou modelos determinísticos utilizados nos estudos de projeto e otimização de unidades. A técnica destina-se a buscar melhores pontos de operação durante o próprio curso do processo, através de medidas de saídas do processo provocadas por pequenas alterações em duas ou três variáveis. Um dos objetivos da técnica é buscar substituir uma operação estática comum pela contínua investigação, através de uma operação evolucionária. O sucesso de

implementação desta metodologia depende da busca constante de melhorias, que não deve ser uma atividade isolada do processo. A operação evolutiva, que efetivamente busca novas condições de operação, deve ser uma atividade do cotidiano das pessoas responsáveis por um conjunto de unidades de produção (Stinghen, 1998).

Neste trabalho, a otimização da política operacional a ser adotada em um processo de cristalização em modo batelada operado por resfriamento é feita tanto por SQP quanto por Algoritmo Genético. O desempenho de ambos os métodos é avaliado e discutido.

Capítulo 3 – Modelo Matemático de Cristalização e Estudos Preliminares de Melhoria de Processo

3.1. Introdução

Com o intuito de propor maneiras de melhorar o desempenho de processos de cristalização, este capítulo se dedica a apresentar o modelo matemático determinístico detalhado do processo de cristalização, em modo batelada do ácido adípico, e a fazer análises preliminares de melhorias de processo. O caso de estudo selecionado é representativo de muitos sistemas industriais e a supersaturação necessária para os cristais aparecerem e crescerem é gerada pelo resfriamento da solução.

A modelagem aqui abordada engloba os mecanismos cinéticos de nucleação, crescimento e aglomeração. Esta última é desconsiderada em muitos trabalhos da literatura. No entanto, muitos sistemas solvente-soluto são caracterizados por aglomeração marcante, como é o caso do sistema ácido adípico-água, de modo que a aglomeração não poderia aqui ser negligenciada. Contudo, a sua consideração aumenta significantemente a não-linearidade do modelo, o que, como será exposto, dificulta grandemente o estudo de busca por melhores políticas operacionais. O balanço de população é resolvido neste capítulo com o uso do Método das Classes, desenvolvido originalmente por Marchal et al. (1988). Trata-se de um método de solução relativamente simples e geral, amplamente usado na literatura até a atualidade (detalhes acerca de suas principais vantagens e desvantagens, quando comparado a outros métodos desenvolvidos na literatura para a solução da equação do balanço de população, são discutidos no Capítulo 4).

A análise preliminar de influência das variáveis de processo e de como se pode melhorá-lo apresentada neste capítulo é fundamental porque fornece evidências do papel e magnitude de cada variável, assim como da sua interação no desempenho do processo. A otimização é considerada, formulada em termos de se buscar a trajetória ótima de resfriamento através da teoria de controle ótimo. O estudo de otimização envolve etapas de como se deve

postular o problema, levando-se em consideração as restrições e qual o melhor critério de desempenho a ser utilizado. O problema é postulado com o uso de programação não-linear e é resolvido por Programação Quadrática Sucessiva (*Sequential Quadratic Programming*, SQP) e com discretização da variável de controle.

3.2. Desenvolvimento

O desenvolvimento deste capítulo é apresentado a seguir, no artigo intitulado *Mathematical modeling and optimal control strategy development for an adipic acid crystallization process*, publicado no periódico internacional *Chemical Engineering and Processing* (v. 44, p. 737 – 753, 2005).

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Mathematical modeling and optimal control strategy development for an adipic acid crystallization process

Caliane B.B. Costa*, Aline C. da Costa, Rubens Maciel Filho

Faculty of Chemical Engineering, State University of Campinas (UNICAMP), CP 6066, Campinas, CEP 13081-970, SP, Brazil

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Abstract

The aim of this work is to propose ways to improve crystallization processes performance, choosing the batch crystallization of adipic acid as a case study. In this process, representative of many industrial systems, the supersaturation necessary for the crystals to appear and grow is generated by the cooling of the solution. The proposed approach involves the process modeling and its further optimization in a real-time fashion. The modeling of the crystallization process is presented and it takes into account the contribution of agglomeration. The influence of the process variables on the final crystal size distribution (CSD) and on the quantity of solids is analyzed. This analysis is fundamental because it gives evidence of the role and magnitude of each variable as well as their interaction in the process performance. The optimization of the process is then considered, and it can be focused on finding the optimal cooling trajectory through optimal control theory. A study of the best way to postulate the problem is considered, taking into account the constraints and which is the best performance criterion to be used. The problem is postulated as a non-linear programming problem, which is solved through sequential quadratic programming (SQP). The non-linearity feature of the problem is strongly increased by the agglomeration contribution. The results have shown that the developed mathematical model is a good representation of the process, able to reproduce results from the literature. The optimization problem has shown to be strongly non-linear and difficult to postulate. Nevertheless, the solutions obtained through the optimization study, though the global optimum may not be guaranteed, lead to a substantial improvement of the end product quality, expressed in terms of the mean size and the variation coefficient.

Keywords: Crystallization; Mathematical modeling; Optimization; Dynamic behavior; SQP

1. Introduction

Crystallization is an ancient unit operation and is widely used, since solids of high purity can be obtained. Batch crystallization is specially used in the production of high-value-added products, such as pharmaceuticals, photo materials and fine chemicals, mainly because it offers flexible and simple processing steps for plants with frequently changing recipes and product lines [1,2]. For this kind of material, product purity and crystal size distribution (CSD) are of prime importance. Furthermore, the crystals produced through a crystallization process have a decisive influence on the downstream processing, and therefore, the CSD should be reproducible in each operation and as regular as possible [3]. Bearing this in mind, it is important that the variables that affect the crystallization process be known and controlled so as to be kept within an acceptable range, in order to satisfy the requirements concerning the final product quality and the production demand [2].

The main purpose of this work is to propose and analyze ways to improve the performance of batch crystallization processes. The batch cooling crystallization of adipic acid is chosen as a case study, since it is typical of many processes of industrial interest and some data are available from literature. In a well-mixed batch crystallizer, the final crystal

* Corresponding author. Tel.: +55 1937883971; fax: +55 1937883910.
E-mail address: caliane@lopca.feq.unicamp.br (C.B.B. Costa).

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product is determined by the supersaturation profile, the initial seed mass, and the seed crystal size distribution [3]. The supersaturation evolution in time, during batch crystallization processes, determines the magnitude of the many kinetic phenomena of the process. Since in cooling crystallization processes, the supersaturation magnitude is determined mainly by the cooling rate during the process, the optimization of the cooling trajectory is indispensable to the improvement of the process performance and a substantial research activity has been devoted to the computation of optimal temperature trajectories [4]. According to Zhang and Rohani [1], many studies have been recently focused on the solution of optimization problems aiming to find the best operating profiles in batch crystallization processes. Lewiner et al. [4] stress that the control of industrial crystallizers or at least the optimization of operating conditions is of potentially great importance, mainly to avoid or to reduce the production of solids with low quality and the differences in CSD from batch to batch. Nevertheless, no work in the open literature has been devoted to study optimizing cooling trajectories in crystallization when agglomeration is present.

Seeding is frequently applied to avoid a supersaturation peak at the beginning of the process [5]. This occurs because the supersaturation values sufficient for crystal growth are lower than the necessary ones for spontaneous nucleation. So, if the system could be kept at a region in the metastable zone with not so high supersaturation values and with addition of seeds, just seed growth will occur. Hence, in the cooling crystallization, the optimal purpose of the heat exchange is to obtain a supersaturation level that favors the maximum growth rate and suppresses nucleation of new crystals in order to obtain crystals with a suitable CSD [6,7].

In this work, the mathematical modeling of the adipic acid crystallization process was derived in order to implement optimal trajectories, looking at the process improvement. The agglomeration mechanism is not neglected in the modeling, which increases the non-linearity of the problem. A software (written to be used in real-time implementations) was developed to simulate the process and to identify the role of the several process variables in the final product, as well as to analyze the impact of the optimal cooling trajectory on the product quality. The computation of optimal cooling trajectories is done through optimal control theory and its complexity is increased due to the agglomeration contribution.

2. Mathematical modeling

In order to completely model a crystallization process, mass balance, energy balance and a description of the crystal size distribution are necessary. This description is required because the process produces a mass of particles, the description of size distribution being crucial to its characterization. The models used in this description are denominated population balance models. According to Puel et al. [8], the population balance modeling is firmly established as a basic theoretical framework for all particulate processes.

Two phenomena dominate the crystallization kinetics, i.e. nucleation and crystal growth. Both phenomena produce the desired material during the crystallization process and are, therefore, competing mechanisms. They are different in the way they produce material: nucleation involves the formation of new crystals while in crystal growth the crystals become larger with the deposition of material onto the already existing crystals [9]. Apart from nucleation and growth, other phenomena such as agglomeration and breakage may occur during the process, making it difficult to carry out reliable predictions. Neglecting agglomeration may result in poor representation of reality, especially when the crystallizing substance is classically known as having an agglomerating behavior.

Zhang and Rohani [1] emphasize that one of the advantages of the process modeling over heuristic approaches is that it makes possible the calculation of further on-line optimal operating policies.

2.1. Population balance – the method of classes

The population balance equation (PBE) is a hyperbolic partial differential equation, which involves all the crystallization kinetic phenomena. Being strongly non-linear, the PBE do not possess an analytical solution in most cases, requiring the development and adaptation of numerical techniques. According to Wulkow et al. [10], in the present state of PBE studies, no standard numerical method has been established for population balance models and none of the presently available methods produce an efficient and accurate solution for a broad class of models. In the literature, the techniques are mainly one of three families: method of moments, discretization techniques and finite elements methods [8]. Discretization sizing techniques appear to be robust. Marchal et al. [11] developed the method of classes, a method that transforms the partial differential equation into an ordinary differential equations system by discretizing the range of variation of the variable L, related to the crystal size. The obtained differential equations are then no longer written with population density functions but with absolute numbers of crystals in each class [12]. Nallet et al. [12] used the method of classes for solving salicylic acid batch precipitation model. In a recent work, Puel et al. [8] also used the method of classes to solve the population balance equation, but they extended the method to consider two characteristic dimensions. This was necessary because they dealt with crystallization of organic products (in particular, hydroquinone) presenting anisotropic morphologies that sometimes vary during the process. This is not the case of the present study, and so the original development of Marchal et al. [11] (monodimensional PBE) was used as a base to the proposed solution procedure.

In the method of classes, the particles sizes are defined as $L_0, L_1, L_2, \ldots, L_N$, where L_0 is the size of the nuclei and L_N

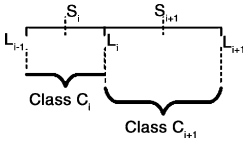

Fig. 1. Division of classes.

is the size of the largest crystals. These sizes determine the existence of N granulometric classes C_i, whose widths are defined by $\Delta C_i = L_i - L_{i-1}$ and whose characteristic size is $S_i = (L_{i-1} + L_i)/2$ (see Fig. 1).

The population of crystals is described by the number density function $\Psi.\Psi(L, t)\mathrm{d}L$ is the number of crystals with a size between L and $L + \mathrm{d}L$ per unit volume at time t [12]. $N_i(t)$ is the number of crystals per unit of volume in the ith class (C_i) at time t and is given by:

$$N_i(t) = \int_{L_{i-1}}^{L_i} \psi(L, t)\,\mathrm{d}L \tag{1}$$

The model assumes that the number density function is constant at each granulometric class. The assumptions make possible the transformation of the population balance equation into a set of ordinary differential equations, as represented in (2).

Scarlett [13] suggested that mass was used as the distribution parameter in order to make the consistency of mass balance easier. However, in the present work, the classical formulation based on crystal number density function was used. In the development of the software for the crystallization simulation, the method of classes was chosen, because it is an efficient method widely tested in literature [1,8,11,12,14].

$$\begin{cases} \dfrac{\mathrm{d}N_1}{\mathrm{d}t} + \dfrac{1}{V_{\mathrm{susp}}}\dfrac{\mathrm{d}V_{\mathrm{susp}}}{\mathrm{d}t}N_1 + \dfrac{Q_{\mathrm{s}}N_1 - Q_{\mathrm{e}}N_{1\mathrm{e}}}{V_{\mathrm{susp}}} + \dfrac{G(L_1)}{2\Delta C_2}N_2 + \dfrac{G(L_1)}{2\Delta C_1}N_1 = r_{\mathrm{N}} + R_{A,1} - R_{B,1} \\ \dfrac{\mathrm{d}N_i}{\mathrm{d}t} + \dfrac{1}{V_{\mathrm{susp}}}\dfrac{\mathrm{d}V_{\mathrm{susp}}}{\mathrm{d}t}N_i + \dfrac{Q_{\mathrm{s}}N_i - Q_{\mathrm{e}}N_{i\mathrm{e}}}{V_{\mathrm{susp}}} + \dfrac{G(L_i)}{2\Delta C_{i+1}}N_{i+1} + \dfrac{G(L_i) - G(L_{i-1})}{2\Delta C_i}N_i \\ -\dfrac{G(L_{i-1})}{2\Delta C_{i-1}}N_{i-1} = R_{A,i} - R_{B,i} \\ \dfrac{\mathrm{d}N_N}{\mathrm{d}t} + \dfrac{1}{V_{\mathrm{susp}}}\dfrac{\mathrm{d}V_{\mathrm{susp}}}{\mathrm{d}t}N_N + \dfrac{Q_{\mathrm{s}}N_N - Q_{\mathrm{e}}N_{N\mathrm{e}}}{V_{\mathrm{susp}}} + \dfrac{-G(L_{N-1})}{2\Delta C_N}N_N \\ -\dfrac{G(L_{N-1})}{2\Delta C_{N-1}}N_{N-1} = R_{A,N} - R_{B,N} \end{cases} \tag{2}$$

In the development of particulate system modeling, the great challenge is the correct specification of the many mechanisms occurring in the crystal population evolution, which requires a detailed understanding of the transport and kinetic events taking place [2]. The main mechanisms that are present in the crystallization processes are nucleation, growth, agglomeration and breakage. Except for the last one, all other mechanisms are involved in the model.

2.1.1. Growth mechanism

The expression for the growth rate developed by Marchal et al. [11] is based on the film model and may be written as:

$$G = \frac{\mathrm{d}L}{\mathrm{d}t} = \frac{k_{\mathrm{a}}\mathrm{MM}k_{\mathrm{c}}}{3\rho_{\mathrm{c}}k_{\mathrm{v}}}\eta_{\mathrm{r}}(c - c^*)^{j'} \tag{3}$$

The effectiveness factor, η_{r}, is found by the solution of the following expression:

$$\left[\frac{k_{\mathrm{c}}}{k_{\mathrm{d}}}(c - c^*)^{j'-1}\right]\eta_{\mathrm{r}} + \eta_{\mathrm{r}}^{1/j'} - 1 = 0 \tag{4}$$

The effectiveness factor expresses the diffusional limitations in crystal growth, causing a distribution at the growth rates among the classes.The mass transfer coefficient, k_{d}, is found by the following expression for Sherwood number:

$$Sh = \frac{k_{\mathrm{d}}L}{D} = 2.0 + 0.47\left[\frac{L^{4/3}\varepsilon^{1/3}}{\nu}\right]^{0.62}\left[\frac{\mathrm{Diam}}{\mathrm{Diam}_T}\right]^{0.17}\left[\frac{\nu}{D}\right]^{0.36} \tag{5}$$

From the previous equation, it is possible to note that each granulometric class has a value for the mass transfer coefficient, which means that the growth rate is size dependent.

The solubility data of adipic acid in water were extracted from Postnikov and Nalivaiko [15] and are presented in Table 1 (units as in Nomenclature):

2.1.2. Nucleation mechanism

The nucleation occurs in two distinct mechanisms, normally referenced as primary and secondary. When nucleation from a clear solution takes place, it is known as primary homogeneous nucleation. In industrial practice, this type of nucleation seldom occurs because solutions usually contain foreign particles that act as substrates for nucleation, known as primary heterogeneous nucleation. When a supersaturated solution is in contact with particles of the crystallizing compound, secondary nucleation occurs [5]. Secondary nucleation is the dominant mechanism for producing new crystals in most seeded batch crystallizers [3]. Both primary and secondary nucleations are inserted into the developed model.

Table 1
Solubility data of adipic acid

T	c	T	c
283.0	74.10	311.0	306.52
285.0	82.84	313.0	335.52
287.0	92.47	313.8	347.74
289.0	103.04	313.8	345.09
291.0	114.64	315.0	370.92
293.0	127.34	317.0	417.67
295.0	141.23	319.0	469.35
297.0	156.40	321.0	526.36
299.0	172.94	323.0	589.08
301.0	190.94	325.0	657.92
303.0	210.51	327.0	733.26
305.0	231.74	329.0	815.51
307.0	254.74	331.0	905.03
309.0	279.63	333.0	1002.19

The expressions for these mechanisms are based on the work of Marchal et al. [11] and are given by Eqs. (6) and (7):

$$r_{N_1} = A \exp\left[-\frac{B}{\ln^2([HR]/[HR]^*)}\right] \tag{6}$$

$$r_{N_2} = k_N^{'}([HR] - [HR]^*)^{i'} C_s^{k'} \tag{7}$$

2.1.3. Agglomeration mechanism

The agglomeration is considered as a chemical reaction between particle m and particle n, leading to the formation of a crystal of size q. A model for the agglomeration mechanism is proposed in literature, where only the agglomeration of two particles is considered. The pseudo-chemical reaction describing the agglomeration can be schematically shown as:

$$a\,(m) + a\,(n) \longrightarrow b\,(q) \tag{8}$$

A particle of class m agglomerates with a particle of class n, generating an agglomerate in the class q. Since in the agglomeration mechanism, the total volume of crystalline mass is preserved, $b/a = ({S_m}^3 + {S_n}^3)/{S_q}^3$ and the class q, where the agglomerate fits, is found by the relation: $L_{q-1} < ({S_m}^3 + {S_n}^3)^{1/3} \leq L_q$. Considering the reaction:

$$(m) + (n) \longrightarrow \nu\,(q) \tag{9}$$

$\nu_{est} = \nu = ({S_m}^3 + {S_n}^3)/{S_q}^3$ may be considered as its stoichiometric coefficient.

All possible agglomerations between two particles (m and n, $n \geq m$) can be arranged in a series and each one has its position in its series represented by the rank $l_{m,n}$. For N granulometric classes, $N(N+1)/2$ different binary agglomerations are present and the series are represented by (1,1), (1,2), ..., (1,N), (2,2), (2,3) ... (m, n) ... (N, N). The position $l_{m,n}$ of the agglomeration of a particle m with a particle n is found by the relation:

$$l_{m,n} = N(m-1) - \frac{m(m-1)}{2} + n \tag{10}$$

This agglomeration will affect class i, only if i equals m, n (in both cases, $\nu_{est} = -1$) or q (with $\nu_{est} = ({S_m}^3 + {S_n}^3)/{S_q}^3$). In this way, an overall stoichiometric coefficient of class i, with respect to agglomeration of rank l can be computed, as follows:

$$\nu_{est\,l,i} = \left(\frac{S_m^3 + S_n^3}{S_q^3}\right)\delta_{i,q} - (\delta_{i,m} + \delta_{i,n}) \tag{11}$$

where $\delta_{ij} = 1$ if $i = j$ and $\delta_{ij} = 0$ if $i \neq j$.

The net rate of particle production by agglomeration in the ith class is calculated by the following expression:

$$R_{A,i} = \sum_{l=1}^{N(N+1)/2} \nu_{est\,l,i}\, r(l) \tag{12}$$

where $r(l)$ is the intrinsic rate of agglomeration of rank l. The intrinsic rate of agglomeration is a function of the number of collisions per volume per time as well as of the supersaturation.

David et al. [16] proposed an expression for the calculation of the intrinsic rate of agglomeration, based on phenomenological and fluid mechanical considerations, taking into account the concentration of particles, the supersaturation, the power dissipation per mass unit, the crystallizer size as well as of the crystals being agglomerated. Based on these assumptions, expression (Eq. (13)) was developed and allows the agglomeration contribution computation:

$$r = k_A^{'} S_m \left(1 + \frac{S_n}{S_m}\right)^2 N\,\mathrm{Diam}\, f\left(\frac{S_n}{S_m}\right)\left[1 - \frac{(S_n + S_m)^2}{\lambda_e^2}\right] \times k_d^{'}(c - c^*) \times N_n N_m (S_m - \delta) H(\lambda_e - S_n - S_m) \tag{13}$$

where $H(x) = 1$ for $x \geq 0$ and $H(x) = 0$ for $x < 0$. The coefficient $k_d^{'}$ is calculated by the same expression as for k_d (Eq. (5)), but the size of crystal considered must be the size of the agglomerate ($S_m + S_n$). The f function represents a relative shape function of both crystals. Considering both particles as spheres, the f function can be written as:

$$f\left(\frac{S_n}{S_m}\right) = \frac{4\left((1 + S_n/S_m - \sqrt{(S_n/S_m)^2 - 1})\right)}{1/3 + S_n/S_m - \sqrt{(S_n/S_m)^2 - 1} - \left((S_n/S_m - \sqrt{(S_n/S_m)^2 - 1})\right)^2 \times \left(2(S_n/S_m)/3 + \left(\sqrt{(S_n/S_m)^2 - 1}\right)/3\right)} \tag{14}$$

λ_e is defined as Lagrangian microscale, which is taken as having the same magnitude as the Taylor microscale, calculated by [16]:

$$\lambda_e = 0.3\pi N\,\mathrm{Diam}\left(\frac{60\nu}{10\varepsilon}\right)^{1/2} \tag{15}$$

It is interesting to stress that the calculation of further on-line optimal operating policies takes an advantage with the inclusion of agglomeration into the model, compared to most batch optimization studies found out in literature. Most of them neglect agglomeration and consider just nucleation and growth, which may be a poor consideration, as is the case with adipic acid, a substance known to agglomerate during crystallization processes.

2.2. Mass balance – batch crystallizer

The material balance of the solute is made based on the fact that changes in the solution concentration results in alterations of the mass of crystals per volume unit.

Since the crystallizer is operated in a batch mode, there is no entrance of fluid (or solute) into the system after $t = 0$. The solute present in the solution in the beginning of the batch is the whole mass of adipic acid available for crystallization. The mass balance is made using the dissociation constant of adipic acid, considered as a monoacid: the concentration of solid in the suspension can be connected with the concentration of protons in the solution [11]:

$$V_0 C_0 = \frac{(H^+)^2}{K}\left[1 + \frac{K}{[H^+]}\right] V_0 + \frac{V_0}{1 - (\mathrm{MM}/\rho)C_s} C_s \quad (16)$$

2.3. Energy balance

The energy balance must take into account the differences in enthalpy of the streams in and out, the heat of crystallization and the heat removed by the cooling system. For batch crystallization, the energy balance equation is:

$$\rho C_p V \frac{dT}{dt} = -\Delta H_c 3\rho_c k_v V_{susp} \int_0^\infty nL^2 G dL - UA_c(T - T_c) \quad (17)$$

Using the method of classes, the integral present in the previous equation is substituted by a summation over all granulometric classes.

According to Postinikov and Nalivaiko [15], the heat of crystallization of adipic acid is 37.2 kJ/mol for temperatures lower than 313.8 K and 50.7 kJ/mol for higher ones.

The specific heat of the slurry is considered to be not so different from that of water, since the process considered is the crystallization from solution, with not so high concentrations of solids.

3. The software development

In the development of the model, it was assumed that no breakage occurs during the process and that the crystallizer is well-mixed, so that there is no spatial dependence of the solution properties within the crystallizer. This is a reasonable assumption since usually low density and viscosity occur in most of the systems to be processed [2].

The solution procedure of the model equations consists of solving Eq. (16) to find out the concentration of solution, the supersaturation calculation, the nucleation rates (Eqs. (6) and (7)), the mass transfer coefficient for each class through Eq. (5), the effectiveness factor for each class through Eq. (4) and the growth rate in each granulometric class (Eq. (3)). The agglomeration rates are also calculated (Eqs. (11–13)). With all kinetic contributions, the system (Eq. (2)) can be solved, followed by the solution of the energy balance (Eq. (17)). Taking into account the proposed solution procedure, a software in Fortran 90 language was developed. The structure of the developed software can be delineated as follows (Fig. 2):

- the initial data are supplied to the software (characterization of the system, the batch and the particle analyzer);
- the time is counted from zero till the maximum batch time through the time step. At each time, mass balance, population balance (with the computation of nucleation rate, growth rate in each class and agglomeration rates) and energy balance are solved; and
- the output files are generated at the end of the batch time.

At the first part of this work (influence of the process variables on the final CSD as well as on the quantity of solids), the ordinary differential equations system (population balance) was solved using a Runge–Kutta routine (subroutine DIVMRK of the IMSL Fortran electronic library) and the energy balance was solved using first-order finite difference (Euler). This was done, primarily, for the sake of simplicity of software development. Furthermore, the solution of the energy balance through Euler brings not significant divergences compared to the solution via Runge–Kutta, as shown in item 6.

4. Model validation

In order to validate the model, results from the literature were reproduced. The results of Marchal et al. [11] are

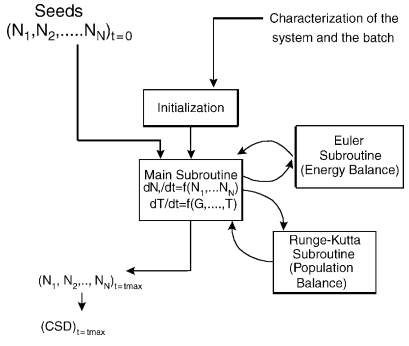

Fig. 2. Structure of the developed software.

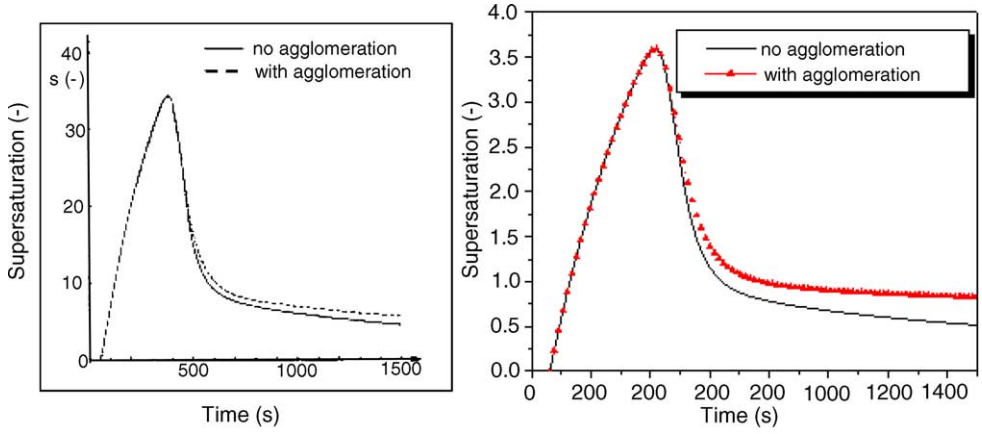

Fig. 3. Comparison between results from Marchal et al. [11] (left) and those obtained from the developed software (right) for the evolution of the relative supersaturation during the crystallization.

compared with the ones generated through the developed software.

Marchal et al. [11] analyzed the influence of agglomeration, presenting results from a semi-batch crystallization both with and without agglomeration. The same data were used as an input to the developed software in order to compare the original results with the predictions. The plots presented in the original work are here reproduced and placed together with the analogous results from the software developed in the present work (Figs. 3–7).

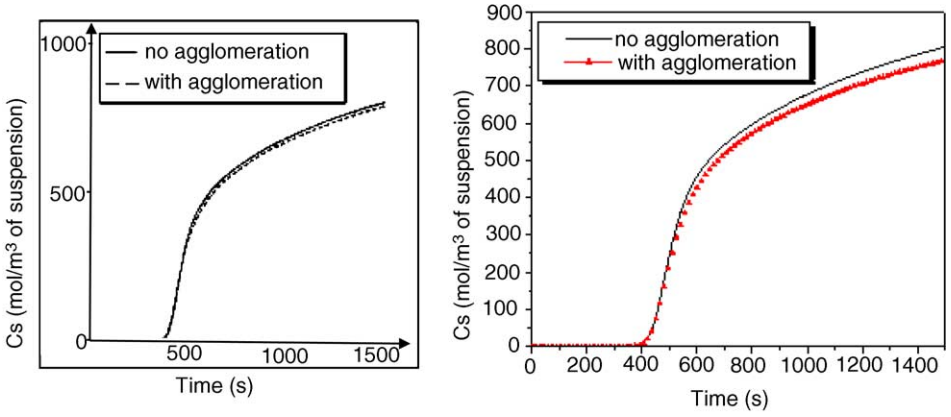

Fig. 4. Comparison between results from Marchal et al. [11] (left) and those obtained from the developed software (right) for the evolution of the concentration of solid during the crystallization.

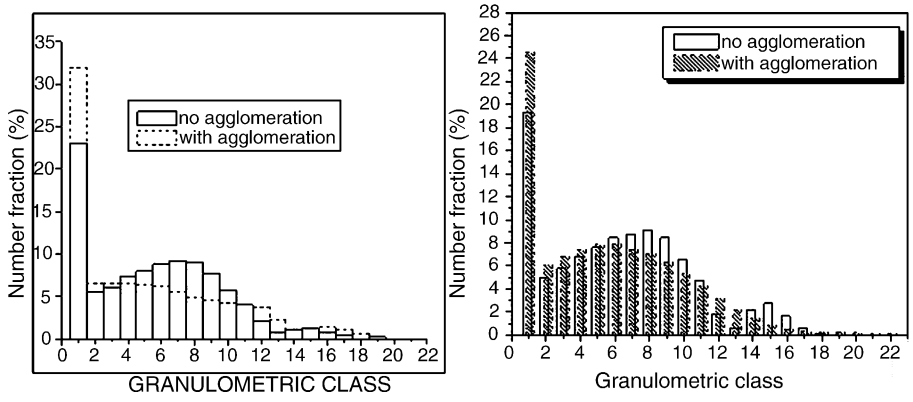

Fig. 5. Comparison between results from Marchal et al. [11] (left) and those obtained from the developed software (right) for the crystal size distribution at the end of the crystallization (number fraction).

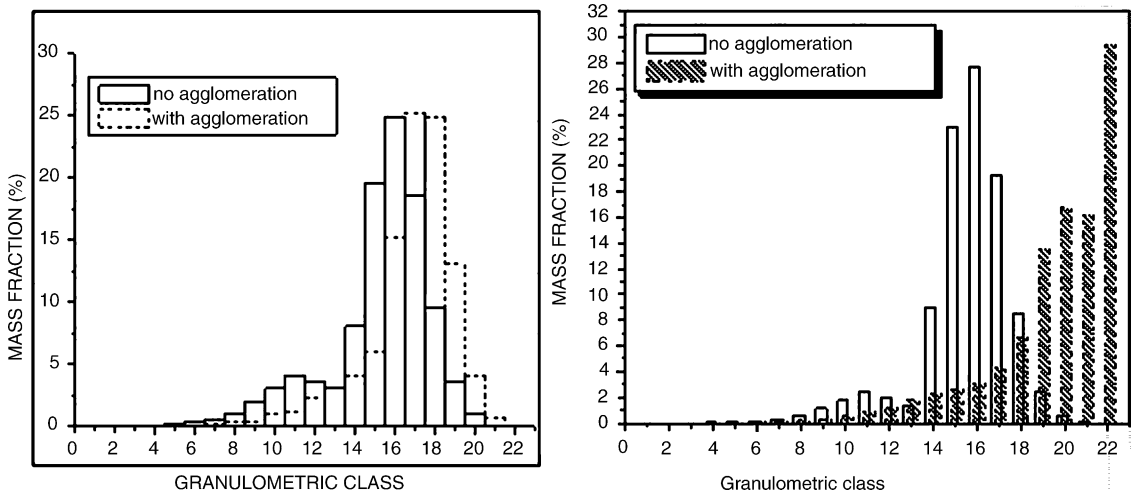

Fig. 6. Comparison between results from Marchal et al. [11] (left) and those obtained from the developed software (right) for the crystal size distribution at the end of the crystallization (mass fraction).

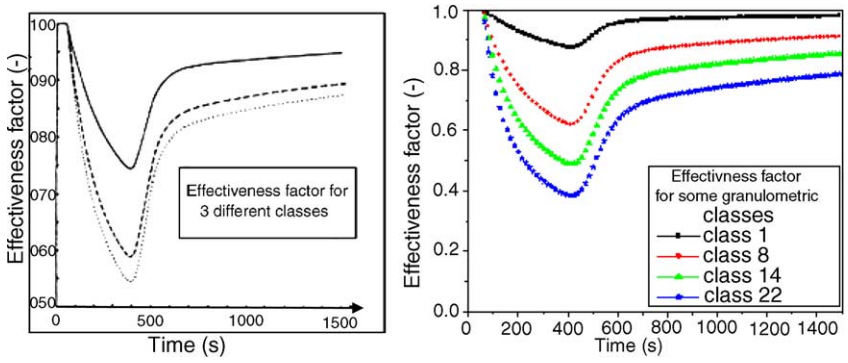

Fig. 7. Comparison between results from Marchal et al. [11] (left) and those obtained from the developed software (right) for the effectiveness factor for some granulometric classes without agglomeration.

When the results presented by Marchal et al. [11] are compared to the ones generated through the developed software, it states that they are identical in the following:

- evolution of relative supersaturation (Fig. 3);
- evolution of the concentration of solids (Fig. 4); and
- effectiveness factor (Fig. 7) – here just the curve shape can be analyzed, since there is no information on which three classes were chosen in the original article.

Nevertheless, the results of CSD at the end of the batch (both number and mass fraction) generated via the developed software are slightly different form the ones presented by Marchal et al. [11] (Figs. 5 and 6). This point reveals the impact that some design/process variables have on the crystal size distribution. The original work of Marchal et al. [11] did not publish all input data, including the power dissipation rate per unit mass, and so the absent data were arbitrarily decided. The impact of the power dissipation on the final CSD is confirmed in the study of process variables influence (Fig. 14, next section).

5. Simulations – process variables influence

Some simulations were made in order to evaluate the influence of several process variables. The variables studied were seeding, global heat transfer coefficient, coolant temperature profile, batch time, power dissipation, rotation speed, impeller diameter, tank diameter and initial concentration of the solution.

The input and output data of the simulations presented in this section are shown in Appendix A.

The main results of this study are presented here. These results are concerned with seeding, cooling rate, influence of the global heat transfer coefficient and the role of the power dissipation.

The first result is the influence of the seeding on the crystallization process. In order to analyze the influence of this variable, the results from Figs. 8–10 are presented. They show the results of operation trajectories (Fig. 8), solution temperature evolution (Fig. 9) and supersaturation evolution (Fig. 10) for two batches that differ each other only in the seeding: the first one (Simu18) has insignificant amount of seeds, while

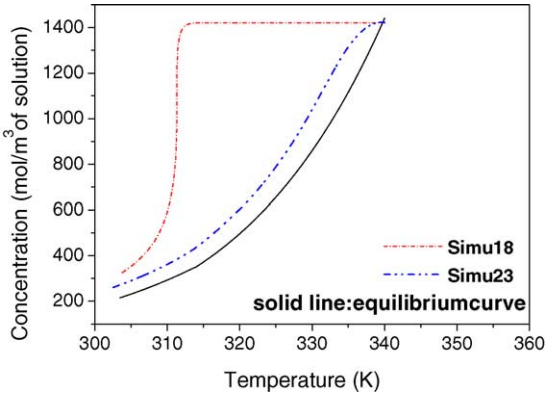

Fig. 8. Operation curve for a non-seeded (Simu18) and a seeded (Simu23) batch crystallization.

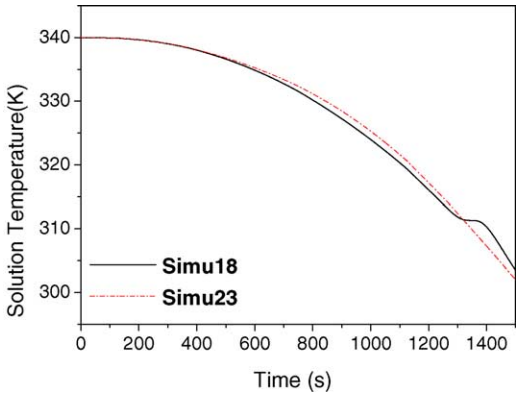

Fig. 9. Evolution of the solution temperature for a non-seeded (Simu18) and a seeded (Simu23) batch crystallization.

the second one (Simu23) has a considerable mass of crystals working as seeds. For these two simulations, a parabolic profile of coolant temperature, with negative second derivative, was employed (see Appendix A). The operation trajectories presented in Fig. 8 are formed by the pairs of values of solution concentration and temperature followed during the batch time. The difference in the path followed during the process in the two simulations is extremely visible. When no seeds are added to the crystallization process (Simu18), the solution is cooled with constant concentration until the metastable zone limit is probably reached. An enormous quantity of crystals is generated by nucleation, releasing great amount of heat of crystallization (exothermic reaction), making the solution temperature to rise (Simu18 in Fig. 9) – which means that the cooling system was unable to remove all the heat released. As a consequence of the operation curve, a great peak of supersaturation is noted (Simu18 in Fig. 10).

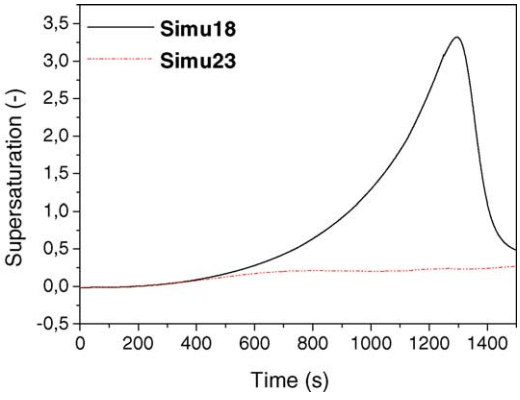

Fig. 10. Evolution of the supersaturation for a non-seeded (Simu18) and a seeded (Simu23) batch crystallization.

On the other hand, if the crystallization is conducted in the same way, except for the addition of seeds (Simu23), the cooling of the solution happens softly, while the concentration of adipic acid in solution decreases (Fig. 8), probably keeping the operation far from the metastable zone limit. It is kept at a reasonable distance from the equilibrium line [9]. Not so high values of supersaturation are reached in the process (Fig. 10) and the nucleation is disfavored. There is no great release of heat of crystallization, and so there is no increase of solution temperature (Fig. 9).

Apart from the influence of the seeding, other important factor in the crystallization performance is the rate of cooling during the whole process. According to Mullin [6], the use of natural cooling is not the best choice. By natural cooling, one understands that the coolant is passed through the exchange device at both constant temperature and constant flow rate. If natural cooling is used, the temperature inside the crystallizer decreases exponentially, making the supersaturation to increase very fast at the first moments of the process, favoring nucleation. As a result, at the end of the batch, small crystals and a large CSD are obtained. On the other hand, if the cooling profile is characterized to have a soft decrease at the early stages and a more pronounced one at the end of the process, the growth of crystals is favored [6].

Two seeded simulations that differ in the coolant temperature profile illustrate this feature appropriately. In the first one (Simu26), natural cooling is simulated (coolant temperature and flow rate are both constant). In Simu20 (the second one), the same amount of seed is used, but a parabolic profile of coolant temperature, with negative second derivative, is employed. This last cooling rate is characterized to have a soft decrease at the early stages and a more pronounced one at the end of the process. The results of the two simulations can be observed in Figs. 11–13 (evolution of solid concentration, CSD in number at the end of the batch and evolution of the supersaturation). When natural cooling is employed, a large number of fines is obtained (Fig. 12). A great peak of supersaturation occurs at the early stages of the crystallization process (Fig. 13), which causes the appearance of thousands of nuclei. The concentration of solids in the suspension increases too fast in the first moments (Fig. 11). Except for the disadvantage of the great number of fines, this kind of cooling has the advantage of being able to extract a great amount (mass) of solute from the solution, bringing them into crystal form (see output in Appendix A).

When a negative parabolic temperature profile is employed (Simu20), a much smaller number of fines is obtained

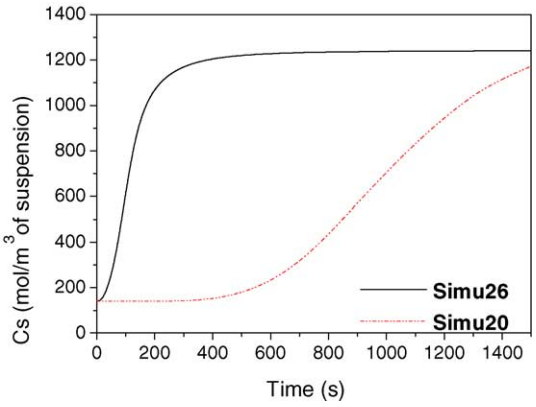

Fig. 11. Evolution of solid concentration in a seeded crystallization with natural cooling (Simu26) and with a negative parabolic coolant temperature profile (Simu20).

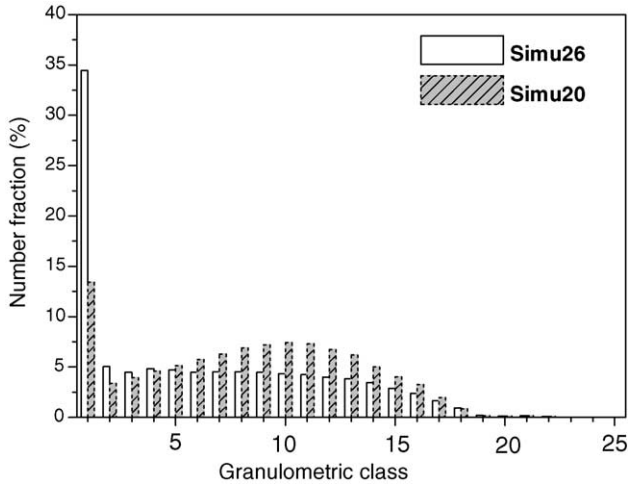

Fig. 12. CSD in number at the end of the batch in a seeded crystallization with natural cooling (Simu26) and with a negative parabolic coolant temperature profile (Simu20).

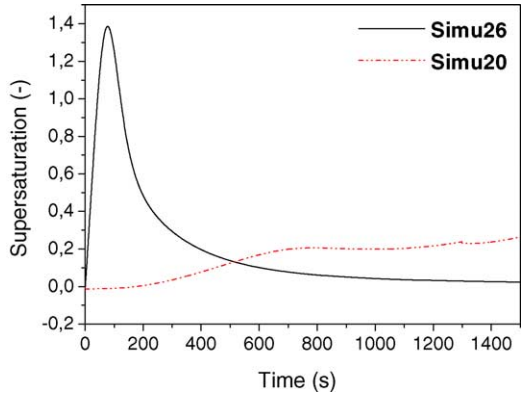

Fig. 13. Evolution of supersaturation in a seeded crystallization with natural cooling (Simu26) and with a negative parabolic coolant temperature profile (Simu20).

(Fig. 12) and the solid concentration evolves softly (Fig. 11), with seeds growth and less fines being generated. This is a consequence of the evolution of the supersaturation during the batch (Fig. 13), showing that it is desirable to avoid supersaturation peaks, in order to favor growth. This confirms the results from literature [9], indicating that the optimum temperature profile would produce no peak in supersaturation at all, being almost flat. However, the slow evolution of the process in Simu20 implies less extraction of solute from the solution (less mass is obtained compared to natural cooling) – see output in Appendix A.

Concerning the study of the influence of the global heat transfer coefficient, its variation results from a variation in the coolant flow rate: the greater the value of the global heat transfer coefficient, the greater the coolant flow rate. The study showed that an increase in the fluid flow rate would be advantageous only in cases where the coolant temperature profile decreases slowly in early stages and sharper latter in time (like the cooling rate used in Simu20), which means to pass the coolant fluid with lower temperature and higher flow rate as the batch time passes. In this way, more mass is obtained in the process. The simulations Simu04 and Simu18 (whose data are presented in Appendix A) illustrate this situation.

The role of the power dissipation is evaluated in the present work and this variable has shown itself to be important in the distribution of crystals into the various classes (Fig. 14). It is an expected result, since the power dissipation is present in the mass transfer coefficient expression, which influences the growth rate in each class, as well as the intrinsic rate of agglomeration. It has shown to be not so important in the amount (mass) of crystals obtained.

6. Optimization study

The main purpose of the optimization study was the evaluation of the problem and its optimization through the use of the sequential quadratic programming (SQP) algorithm. Lang et al. [9], have studied the dynamic optimization of a batch

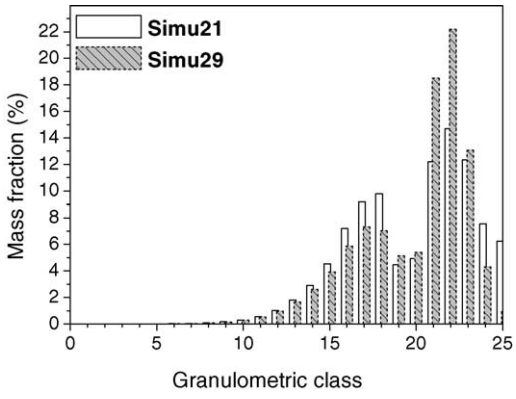

Fig. 14. CSD in mass at the end of the batch in Simu21 ($\varepsilon = 0.02$) and in Simu29 ($\varepsilon = 1.00$).

cooling crystallization process, treating the optimization of the coolant profile. A good analogy may be traced between the present work and the work of Lang et al. Both works deal with modeling and optimization of crystallizing processes, differing by the method used to solve the model. There, the model was discretized using collocation on finite elements, while in the present work the method of classes was used. Another point of distinction between the two works is the inclusion of agglomeration into the modeling of the present work.

According to Rawlings et al. [7], optimizing crystallizer batch problems means finding the optimal supersaturation versus time profile, a problem the solution of which is difficult and expensive to compute. The mean size and the variation coefficient provide a reasonable description of the final CSD [1].

As it was observed from the simulations results presented in this work and as it was published in literature [9], the cooling trajectory of crystallization processes is crucial for process improvement. It is interesting to keep the cooling trajectory in a part of the metastable zone that suppresses nucleation and enhances growth. This means to keep the operating trajectory as close as possible to the stable zone.

The natural cooling brings the largest cooling rate in the initial period of the process, causing a large degree of supersaturation at early times, leading to excessive nucleation and smaller final crystals. In contrast, if the supersaturation can be adjusted to maintain a constant level of nucleation,

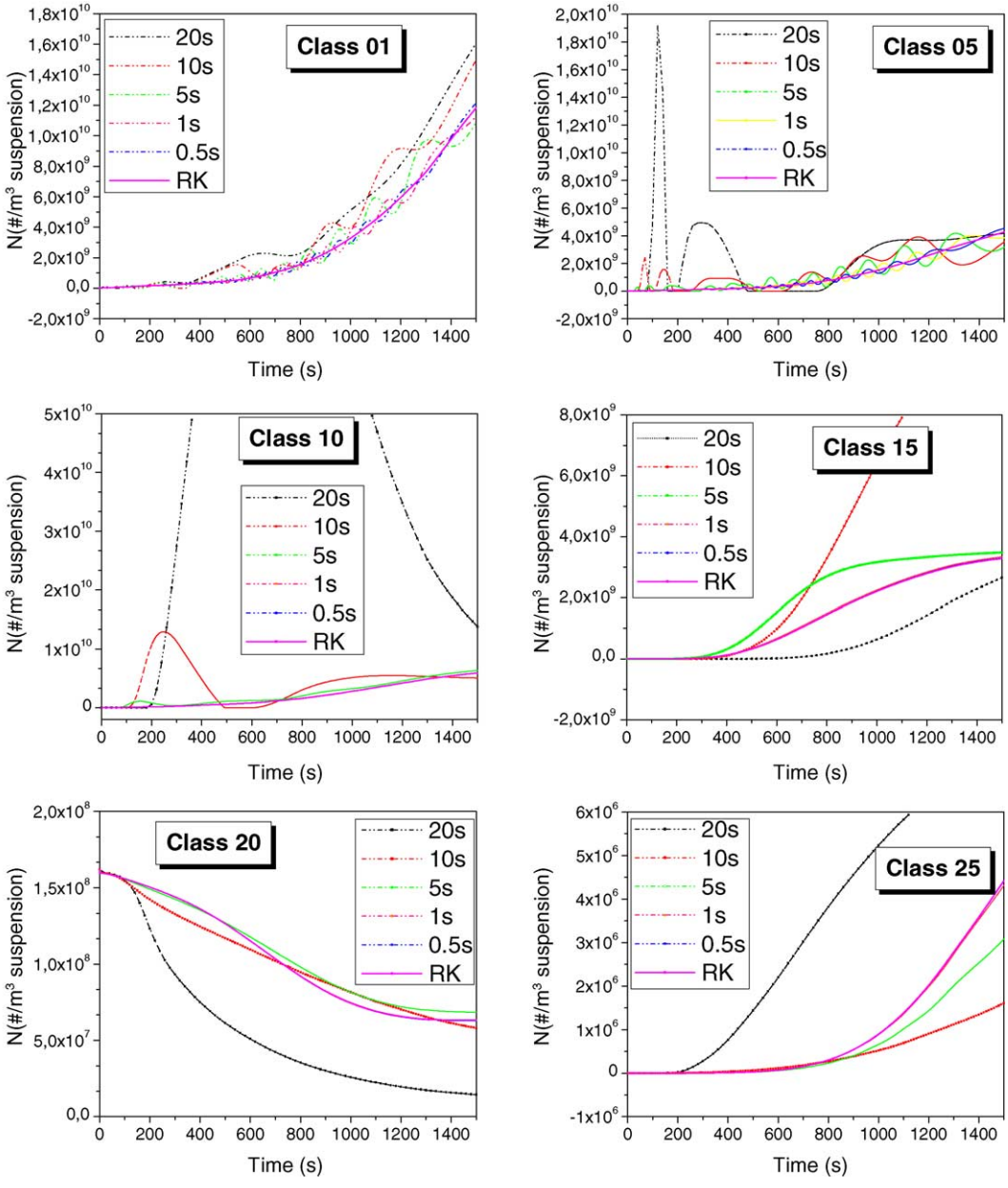

Fig. 15. Evolution of the number of particles per unit volume of suspension for the classes 01, 05, 10, 15, 20 and 25.

the crystal size is increased and the CSD variance can be improved [2].

Before the presentation of the results, it is interesting to discuss two points: the discretization (in time) method used and the set of objective function, control variable and the constraints imposed in the optimization problem formulation.

6.1. Discretization in time

In the dynamic optimization problem, the model must be discretized in time and a study of the proper method of discretization between Runge–Kutta and Euler was done. In this study, the system simulated was the same as the one used in item 5. The data used in the simulations are presented in Appendix A.

The energy and population balance equations were solved using Runge–Kutta with a time step of 0.5 s in a 1500 s batch. Other five simulations of the process were done with the differential equations being solved through Euler method. These five simulations differ in the value of the time step used: 20, 10, 5, 1 and 0.5 s.

The evolution of the number of crystals per unit volume of suspension in classes 1, 5, 10, 15, 20 and 25 were plotted, as well as the evolution of the solution temperature inside the crystallizer. These results can be seen in Figs. 15 and 16.

The study brings another contribution of the present work, showing that the Euler method is too inaccurate for solving the population balance ordinary differential equations, especially with larger time steps and at the smallest granulometric classes. The divergence, compared to the solution via Runge–Kutta, is insignificant for the solution of the energy balance (Fig. 16), which makes evident that the Euler method could be used to the solution of the energy balance in the optimization studies, but is not satisfactory to solve the population balance. It is an important point, since the choice of an inappropriate method could cause serious errors in crystallization calculations. In this way, the Runge–Kutta was chosen as the method for solution of both the energy and population balances in the optimization problem and the time step used was of 0.5 s.

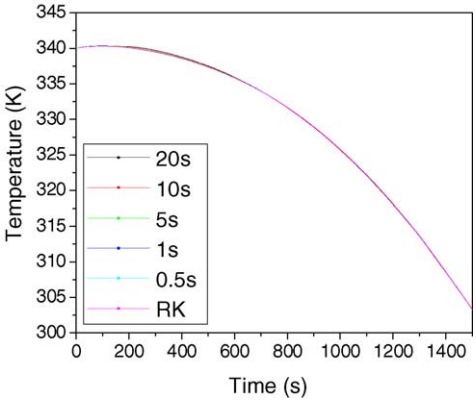

Fig. 16. Evolution of the solution temperature.

6.2. Objective function, control variable and constraints

In the optimization study, several tests were made in order to evaluate the function of the optimizer (the SQP algorithm) and the sensitivity of the problem: tests of control variable, objective function and constraints.

In the present work, as control variable, the coolant temperature and the temperature of the solution inside the crystallizer were tested. It is important to mention that, when the temperature inside the crystallizer was tested as control variable, it was not necessary to compute the energy balance, because studying the crystallizer temperature profile implies disregarding the heat released by the crystallization itself and the heat changed with the cooling device. In this case, the optimization study conducts to the optimum profile of the temperature inside the crystallizer and an extra investigation would be necessary to determine which coolant temperature (or flow rate) profile would lead to the optimum crystallizer temperature. In this extra investigation, the crystallization and heat exchange through the cooling device must be considered.

It is found in Rawlings et al. [2] that it would be desirable to determine the optimal operating policy that maximizes mean particle size and minimizes CSD variance in minimum time. Here, three objective functions were tested: minimization of the standard deviation of the crystal number distribution at the end of the batch, minimization of the variation coefficient of this distribution and minimization of the summation of the nucleation rates at all discretization points of the batch.

As constraints, during the study, some were imposed:

- The control variable should decrease or be kept constant during the batch (after all, the crystallizer should be cooled);
- The mass obtained at the end of the batch should be larger than a stipulated value;
- The supersaturation should be below a stipulated value;
- The cooling rate should be below a stipulated value.

So, for an optimization trial, the objective function of which has been set as the minimization of the standard deviation of the crystal number distribution at the end of the batch and for which the minimum mass to be obtained is 50 g, the optimization problem can be stated as:

Minimize $\sigma_{t_f}(\mathbf{T}_C)$

Subject to: model equations (Eqs. (2–7), (12) and (13))

$$\begin{aligned} &T_c(i) - T_c(i+1) \geq 0.0 \\ &\text{Mass of crystals } (t_f) \geq 50.0 \\ &1.0 - (c - c^*)/c^* \geq 0.0 \\ &T_c(i+1) - T_c(i) + 1/60 \geq 0.0 \end{aligned} \tag{18}$$

For the optimization problem represented by Eq. (18), the supersaturation has been limited to the unity and the cooling rate to 1 K/min.

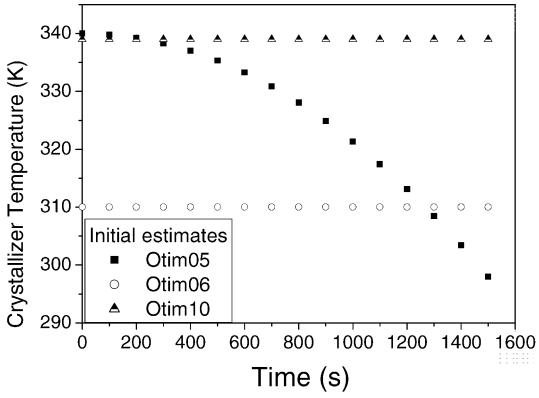

Fig. 17. Initial estimates for three different optimization trials (standard deviation of the number distribution as objective function).

6.3. Results of the optimization study

All input data concerned to the simulations presented in this item are detailed in Appendix A.

The subroutine DNCONF of the IMSL Fortran electronic library was used. This subroutine solves a general non-linear programming problem using the sequential quadratic programming (SQP) algorithm and a finite difference gradient.

The conducted study showed that the crystallization problem is a very non-linear one. The initial estimate provided to the optimizer has shown itself to be a very important item to the correct convergence of the SQP algorithm. The objective function seems to be very complex, with many local minimums, what causes the SQP algorithm to lead to the minimum nearest to the initial estimate.

This dependence on the initial estimate can be seen in Figs. 17 and 18. They show three optimization studies, with the same data supplied to the software, except for the initial estimate. In this part of the study, the standard deviation of the number distribution was set as objective function. As can be seen, the 'optimum point' found, i.e., the optimum profile

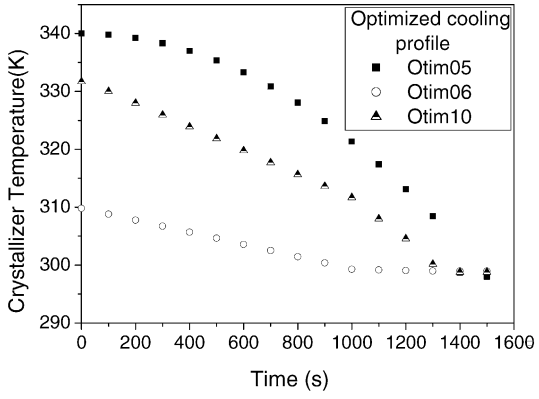

Fig. 18. Optimizer results for three different optimization trials (standard deviation of the number distribution as objective function).

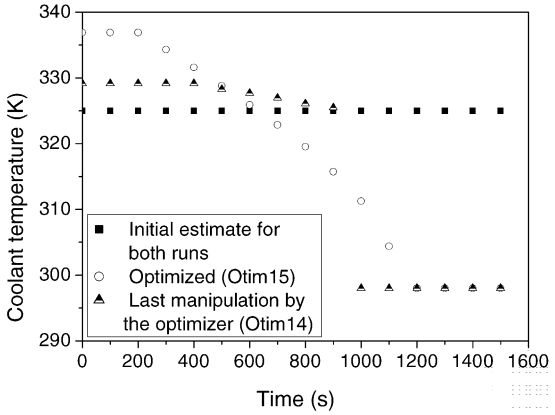

Fig. 19. Two optimization runs illustrating the difficulty of the optimizer for dealing with more granulometric classes when the variation coefficient of the CSD is set as objective function.

of the crystallizer temperature during the batch, was different in each one of the three cases.

It is interesting to note that in Otim05 the optimized profile is very close to the provided initial estimate, differing only in the final times of the batch. Probably, the final time differences are due to the minimum mass constraint. The initial estimate provided to Otim05 was one that has a smooth cooling in the early stages of the process, favoring growth, instead of nucleation. This type of cooling is vastly referred to in literature [1] as the best one. Really, the CSD properties of the optimized cooling of Otim05 are the best presented in Appendix A.

Another point of interest in the optimization study is the evaluation of different objective functions. The variation coefficient of a distribution is defined as the ratio of its standard deviation to its mean crystal size. In this way, the variation coefficient was thought to be the best objective function: while the standard deviation could be minimized, the mean crystal size could be maximized. But all the attempts to use the variation coefficient as objective function were not successful. The only positive result was obtained when just five

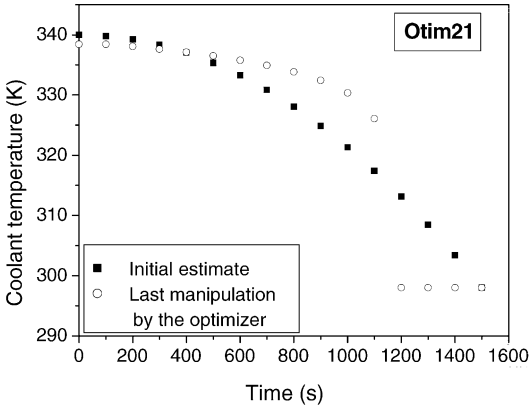

Fig. 20. Initial estimate and the last manipulation of the crystallizer temperature by the optimizer when the variation coefficient of the CSD is set as the objective function (10 granulometric classes).

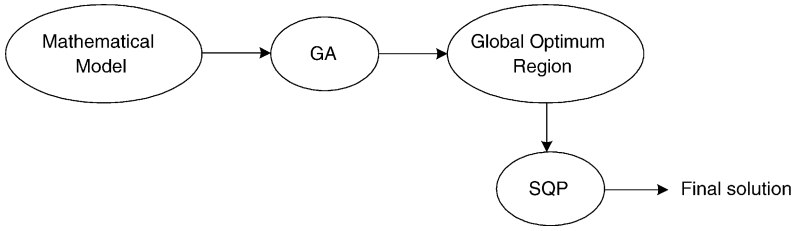

Fig. 21. Alternative way to face the optimization problem.

granulometric classes were used (Otim15 – Fig. 19). It seems that the optimizer is unable to deal with many granulometric classes. When more granulometric classes are used, the execution is terminated because the line search takes more than five function calls (Otim14 – Fig. 19). Figure 20 depicts another attempt to use the variation coefficient as objective function, with 10 granulometric classes, but with an initial estimate believed to be nearest to the global optimum (based on results illustrated in Fig. 18). Once more, the execution was terminated without coming to the optimum. The search seems to be close to the optimum, as can be seen by the last manipulation of the control variable by the optimizer in Figs. 19 and 20, but the execution is terminated because it comes to a stop criterion (line search takes more than five function calls).

The control variable has shown itself to be not the reason for not getting optimization convergence. When the optimizer did not come to an optimum profile, it was not because of the control variable being used, but due to extra reasons, such as objective function or the size of the problem (number of granulometric classes).

No success was obtained when the objective function was set as the summation of the nucleation rates at all discretization points of the batch.

The results of the optimization study suggest that a global optimization technique, such as genetic algorithm (GA), should be used to find out the region of the global optimum. Choong and Smith [17] present the first attempt in literature to use stochastic optimization in optimizing highly non-linear batch cooling crystallization systems. According to them, stochastic optimization strategies such as simulated annealing and genetic algorithm have been known to solve a large class of non-linear problems to global optimality. In their work, the effectiveness of the simulated annealing technique in preventing the optimization from being trapped in local optima has been demonstrated. Furthermore, this technique eliminates the traditional shortcoming of deterministic optimization methods, the optimization results of which are highly dependent on the initial estimate. In this way, a scheme such as the one depicted in Fig. 21 should be tried in future works, in order to obtain the correct convergence. Although GA is a computational time-demanding technique, its use may be an interesting alternative to define the region where the global optimum is located. The SQP may then be used, but limited to this region to achieve the global optimum.

7. Conclusions and further investigations

In this work a crystallization model is developed, which includes nucleation, growth and agglomeration phenomena. The inclusion of agglomeration in the model increases its non-linearity and brings a novelty of the present work when the optimization is considered, since no work deals with optimizing cooling trajectories when agglomeration is taken into account.

The developed model proved to be a good one, expressing representative results of the process. Literature results were satisfactory reproduced from the available information. The predictions generated by the model allow to analyze the impact of the process variables on the system behavior. The power dissipation has shown to have a great impact on the crystal distribution into the various classes. This means that this is a variable to which attention should be paid.

The optimization subroutine used in this study does not seem to be the most suitable for the solution of the problem, because this latter is extremely non-linear. The objective function has a lot of local minima and, as the SQP is unable to scan the whole objective function surface, the optimizer brings about local optima (minima). However, even so, the found solutions are better than the original ones.

The variation coefficient seems to be the most proper objective function, since it relates two features of the CSD. Nevertheless, the complexity of this objective function hampers its use.

An interesting approach to the problem that was not considered in this work is the imposition of the constraint of minimum mean crystal size at the end of the batch and the optimization of two control variables (32 values), to know, the coolant temperature and flow rate profiles. It is worthwhile mentioning that this latter approach would be advantageous only if one could express the global heat transfer coefficient as a function of the coolant fluid flow rate. The use of a global optimization technique, coupled with the SQP may be an interesting alternative to face the optimization problem, especially when the user is not familiar to the process.

Acknowledgements

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Appendix A

This appendix brings all data used in the simulations presented in this article. This appendix is separated according to the items in this article.

Item 5

The total number of simulations that were made to evaluate the influence of the process variables in the developed work was 36 (Simu01 to Simu36). But just those that were most significant were presented in this article (Simu04, Simu18, Simu20, Simu21, Simu23, Simu26 and Simu29). In each simulation made, one or two process variables were changed from those set in the standard simulation (Simu01). In this appendix, the input data to Simu01 (Tables 2 and 3) and the input and output data of Simu04, Simu18, Simu20, Simu21, Simu23, Simu26 and Simu29 (Table 4) are presented.

The seeding in Simu01 was insignificant: it was made just in the 21st class and the number of crystals per unit volume of suspension was $N_0(21) = 338$. No other granulometric class was seeded.

Item 6.1

The input data used in the study of the differential equations discretizations were the same as those used in Simu01 (see item 9.1), except for the seeding, which was 1.62×10^8 crystals at the 20th granulometric class.

Item 6.4

In the optimization study, many trials were made, changing objective function, imposed constraints, control variable and number of granulometric classes. Again, just the most relevant results (or of interesting analyses) were presented in this article (Otim05, Otim06, Otim10, Otim14, Otim15, Otim21).

Table 3
Interval boundaries and classes characteristic sizes

I	L_i (μm)	S_i (μm)	i	L_i (μm)	S_i (μm)
0	0.01	–	13	125.00	112.11
1	7.81	3.91	14	157.49	141.25
2	9.84	8.83	15	198.42	177.95
3	12.40	11.12	16	249.99	224.21
4	15.63	14.02	17	314.97	282.48
5	19.69	17.66	18	396.84	355.91
6	24.80	22.25	19	499.99	448.42
7	31.25	28.03	20	629.95	564.97
8	39.37	35.31	21	793.93	711.94
9	49.61	44.49	22	1000.24	897.09
10	62.50	56.06	23	1255.83	1128.04
11	78.75	70.63	24	1562.13	1408.98
12	99.21	88.98	25	1735.25	1648.69

The input data used in the characterization of the system were the same used in Simu01, except when something opposite is stated in the summary below. When the number of granulometric classes used was less than 25, the intervals boundaries were the same used in Simu01 until the number of the corresponding class.

Otim05

Number of granulometric classes	5
Objective function	Minimization of σ
Constraints	Control variable must decrease or remain constant during the batch; crystallized mass should be at least 50 g
Control variable	Crystallizer solution temperature
Initial estimate	$T = -0.000018666t^2 + 340$ K
$\bar{L}_{num}$	17.64 μm
σ	0.34 μm
VC	1.92%

Table 2
Values used in Simu01

Data	Value	Unit	Data	Value	Unit
V_0	0.3×10^{-3}	m^3	Time step	0.5	s
$Diam_T$	0.05	m	K	4.4	–
Diam	0.02	m	A	2.0×10^{15}	# m^{-3} s^{-1}
N (stirring speed)	13.6	s^{-1}	B	40	–
ε	2.107×10^{-2}	Wkg^{-1}	k'_N	1	# m^6 mol^{-3} s^{-1}
U	600	$W m^{-2}$ K^{-1}	I'	1	–
Ac	236.0×10^{-4}	m^2	k'	2	–
k_v	$\pi/6$	–	k_c	1×10^{-7}	m^4 mol^{-1} s^{-1}
k_a	π	–	j'	2	–
C_0	1500	mol m^{-3}	k'_a	1×10^{-6}	m^4 mol^{-1}
Batch time	1500	s	T_0	340	K
N (number of granulometric classes)	25	–	T_c	300	K

Table 4
Simulations data

Name	Change compared to Simu01	Seed mass (μg)	Crystallized mass (g)
Simu04	$T_c = -0.000018666t^2 + 340$	26	43.1
Simu18	$T_c = -0.000018666t^2 + 340$ $U = 600$ if $0 < t < 375$ $U = 650$ if $375 < t 750$ $U = 700$ if $750 < t < 1125$ $U = 800$ if $1125 < t < 1500$	26	44.7
Simu20	$T_c = -0.000018666t^2 + 340$ $N_0(20) = 1.62 \times 10^8$ (only seeded class)	6.4×10^6	51.4
Simu21	$T_c = 0.000018666t^2 - 0.056t + 340$ $N_0(20) = 1.62 \times 10^8$ (only seeded class)	6.4×10^6	54.4
Simu23	$T_c = -0.000018666t^2 + 340$ $N_0(20) = 1.62 \times 10^8$ (only seeded class) $U = 600$ if $0 < t < 375$ $U = 650$ if $375 < t < 750$ $U = 700$ if $750 < t < 1125$ $U = 800$ if $1125 < t < 1500$	6.4×10^6	52.0
Simu26	$N_0(20) = 1.62 \times 10^8$ (only seeded class)	6.4×10^6	54.4
Simu29	$T_c = 0.000018666t^2 - 0.056t + 340$ $N_0(20) = 1.62 \times 10^8$ (only seeded class) $\varepsilon = 1.0$	6.4×10^6	54.4

Otim06

Number of granulometric classes	5
Objective function	Minimization of σ
Constraints	Control variable must decrease or remain constant during the batch; crystallized mass should be at least 50 g
Control variable	Crystallizer solution temperature
Initial estimate	$T = 310$ K
$\bar{L}_{num}$	17.42 μm
σ	1.39 μm
VC	7.99%

Otim14

Number of granulometric classes	25
Objective function	Minimization of VC
Constraints	Control variable must decrease or remain constant during the batch; crystallized mass should be at least 50 g
Control variable	Coolant temperature
Initial estimate	$T = 325$ K
$\bar{L}_{num}$	69.40 μm
σ	81.43 μm
VC	117.38%

This trial did not came to the optimum. The execution was terminated without coming to it (line search took more than five function calls).

Otim10

Number of granulometric classes	5
Objective function	Minimization of σ
Constraints	Control variable must decrease or remain constant during the batch; crystallized mass should be at least 50 g
Control variable	Crystallizer solution temperature
Initial estimate	$T = 339$ K
$\bar{L}_{num}$	17.64 μm
σ	0.37 μm
VC	2.09%

Otim15

Number of granulometric classes	5
Objective function	Minimization of VC
Constraints	Control variable must decrease or remain constant during the batch; crystallized mass should be at least 50 g
Control variable	Coolant temperature
Initial estimate	$T = 325$ K
$\bar{L}_{num}$	17.66 μm
σ	0.17 μm
VC	0.94%

Otim21

Number of granulometric classes	10
Objective function	Minimization of VC
Constraints	Control variable must decrease or remain constant during the batch; crystallized mass should be at least 50 g
Control variable	Coolant temperature
Initial estimate	$T = -0.000018666t^2 + 340$ K
$\bar{L}_{num}$	48.340 μm
σ	8.73 μm
VC	18.06%

This trial did not came to the optimum. The execution was terminated without coming to it (line search took more than five function calls).

Nomenclature

A	pre-exponential factor (primary nucleation) ($m^{-3}\ s^{-1}$)
A_c	heat transfer area (m^2)
B	kinetic parameter of the primary nucleation law
c	solute molecules concentration in solution (mol m^{-3} of solution)
c^*	solute molecules concentration in solution at supersaturation (mol m^{-3} of solution)
C_i	granulometric class of rank i
ΔC_i	width of class C_i
C_p	slurry specific heat ($J\ kg^{-1}\ K^{-1}$)
C_S	solid concentration in the suspension (mol m^{-3} of suspension)
C_0	initial concentration of adipic acid (mol m^{-3} of solution)
D	diffusivity of the solute ($m^2\ s^{-1}$)
Diam	stirrer diameter (m)
$Diam_T$	tank diameter (m)
G	growth rate ($m\ s^{-1}$)
$[H^+]$	concentration of protons in solution (mol m^{-3} of solution)
H_k	enthalpy of stream k ($J\ m^{-3}$)
ΔH_C	heat of crystallization ($J\ mol^{-1}$)
[HR]	concentration of molecular adipic acid in solution (mol m^{-3} of solution)
$[HR^*]$	concentration of molecular adipic acid in solution at saturation (mol m^{-3} of solution)
i'	kinetic order of the secondary nucleation law
j	kinetic order of the integration growth law
K	modified acidity constant of adipic acid (mol m^{-3} of solution)
k'	exponent to the solid concentration in secondary nucleation law
k_a	surface shape factor
k_a'	agglomeration rate constant in the diffusional growth regime (s)
k_c	kinetic constant of the integration law ($m^{3j'-2}\ mol^{1-j'}\ s^{-1}$)
k_d	mass transfer coefficient ($m\ s^{-1}$)
k_d'	mass transfer coefficient in agglomeration process ($m^4\ mol^{-1}\ s^{-1}$)
k_N'	kinetic constant of the secondary nucleation law ($m^{3(i'+k')-3}\ mol^{-i'-j'}\ s^{-1}$)
k_v	volumetric shape factor
$l_{m,n}$	rank of the lth agglomeration of particle m with particle n
L	characteristic size of crystals (m)
L_i	upper limit of class of number i (m)
$\bar{L}_{num}$	mean size of the number distribution (m)
m, n, q	granulometric classes involved in the agglomeration reaction
MM	molecular weight of the crystal ($kg\ mol^{-1}$)
n	number distribution density (population) per unit volume of suspension (m^{-4})
N	number of granulometric classes
N	stirring speed (s^{-1})
$N_i(t)$	number of crystals per unit volume of suspension in granulometric class C_i at time t (m^{-3} of suspension)
Q_k	flow rate of stream k ($m^3\ s^{-1}$)
r_N	net rate of nucleation ($m^{-3}\ s^{-1}$)
r_{N1}	primary rate of nucleation ($m^{-3} s^{-1}$)
r_{N2}	secondary rate of nucleation ($m^{-3}\ s^{-1}$)
$r(l)$	intrinsic rate of agglomeration of rank $l_{m,n}$ ($m^{-3}\ s^{-1}$)
$R_{A,i}$	net rate of agglomeration in the granulometric class C_i ($m^{-3}\ s^{-1}$)
$R_{B,i}$	net rate of breakage in the granulometric class C_i ($m^{-3}\ s^{-1}$)
S_i	characteristic size of the crystals of granulometric class C_i (m)
Sh	Sherwood number
t	time (s)
t_f	final batch time (s)
T	crystallizer solution absolute temperature (K)
T_c	coolant absolute temperature (K)
$\mathbf{T}_c$	vector with the values for the coolant temperature at all optimizer discretization points
U	global heat transfer coefficient ($J\ m^{-2}\ s^{-1}\ K^{-1}$)
V	solution volume (m^3)
V_{susp}	suspension volume (m^3)
VC	variation coefficient of the number distribution ($=\sigma/\bar{L}_{num}$)
V_o	initial volume of the solution in the crystallizer (m^3)

Greek letters

ε	power dissipation per unit of mass ($W\ kg^{-1}$ ($m^2\ s^{-3}$))
η_r	effectiveness factor
λ_e	Lagrangian microscale (m)
ν	kinematic viscosity ($m^2\ s^{-1}$)

ν_{est} stoichiometric coefficient of a general agglomeration reaction
$\nu_{estl,i}$ stoichiometric coefficient of class i in agglomeration of number l
ρ slurry density (concentration) (kg m^{-3} of slurry)
ρ_c crystal density (kg m^{-3} of crystal)
σ standard deviation of the number distribution (m)
ψ number density function (m^{-1} m^{-3})

Subscripts
0 initial value
e,s inlet and outlet streams
i, j granulometric classes

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3.3. Conclusões

Os resultados apresentados neste capítulo mostram que o modelo matemático desenvolvido representa bem o processo, sendo capaz de reproduzir os resultados da literatura. O problema de otimização se mostrou altamente não-linear e difícil de ser postulado. No entanto, as soluções obtidas com o estudo de otimização, embora não haja garantia de que o ótimo global tenha sido encontrado, levam a uma melhora substancial da qualidade do produto final, expresso em termos de tamanho médio de cristal e do coeficiente de variação da distribuição de tamanhos.

A análise preliminar do efeito de variáveis de processo mostra que a semeadura é um fator importante em processos de cristalização em que se deseje evitar formação de muitos finos (via nucleação). Forte influência exerce também a taxa de resfriamento empregada durante a batelada. Trajetórias de resfriamento que apresentam taxas de decréscimo de temperatura pequenas no início do processo e mais acentuadas próximas ao final da batelada favorecem o crescimento das sementes adicionadas, devido à ausência de grandes picos de supersaturação.

O estudo de otimização mostra que o SQP é altamente dependente da estimativa inicial, especialmente em problemas que apresentam muitos ótimos locais. Além do mais, problemas altamente não-lineares, como o abordado neste trabalho, não se adequam de maneira geral ao método determinístico de otimização utilizado.

No próximo capítulo será apresentada uma breve revisão dos principais métodos numéricos já propostos na literatura para resolver o balanço de população, com enfoque em problemas de cristalização, visto que a PBE é uma equação diferencial parcial hiperbólica, cuja solução deve ser alcançada por métodos numéricos. O método numérico de solução selecionado traz consigo vantagens e desvantagens que terão influência direta na modelagem do processo de cristalização, uma vez que o balanço de população é parte integrante deste modelo, e consequentemente, faz-se presente na sua aplicação em estudos de otimização e controle.

Capítulo 4 – Solução do Balanço de População Aplicado a Problemas de Cristalização

4.1. Introdução

Em processos de cristalização, a necessidade de melhorar a qualidade de produto e minimizar os custos de produção requer um entendimento e a otimização para obtenção de uma distribuição apropriada de tamanhos de cristal. Para se alcançar esse objetivo, um modelo do processo é necessário e a distribuição de partículas deve ser representada, o que é feito pelo balanço de população. O balanço de população é representado por uma equação diferencial parcial hiperbólica altamente não linear e, na maioria dos casos, uma solução analítica não é possível. A ausência de soluções analíticas requer o desenvolvimento e adaptações de técnicas numéricas para que a equação do balanço de população seja útil para fins de modelagem, otimização e controle. Este capítulo se dedica a apresentar a estrutura original do balanço de população e a analisar os aspectos positivos e negativos de alguns métodos numéricos escolhidos como ferramenta no tratamento da equação do balanço de população (PBE) em processos de cristalização. São discutidos problemas de ordem numérica oriundos da transformação da equação diferencial parcial (especialmente quando todos os mecanismos cinéticos se fazem presentes – nucleação, crescimento, aglomeração e quebra) e o esforço computacional, bem como a predição incorreta do número total de partículas e/ou erros no balanço de massa da fase dispersa.

4.2. Desenvolvimento

O desenvolvimento deste capítulo é apresentado a seguir, no artigo intitulado *Considerations on the crystallization modeling: Population Balance Solution*, a ser publicado no periódico internacional *Computers and Chemical Engineering* em 2007 (v. 31, p. 206-218).

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Considerations on the crystallization modeling: Population balance solution

Caliane Bastos Borba Costa *, Maria Regina Wolf Maciel, Rubens Maciel Filho

Laboratory of Optimization, Design and Advanced Control (LOPCA), School of Chemical Engineering, State University of Campinas (UNICAMP), Cidade Universitária Zeferino Vaz, Caixa Postal 6066, CEP 13081-970 Campinas, SP, Brazil

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Abstract

In crystallization processes, the need to improve the product quality and to minimize production cost requires understanding and optimization on how to obtain an appropriate particle-size distribution. In order to achieve this goal, a model of the process is necessary and the distribution of particles must be represented, which is made through the population balance. This latter constitutes a strongly nonlinear hyperbolic partial differential equation and, in most cases, an analytical solution is not possible, requiring the development and adaptation of numerical techniques. In the present work, it is proposed to analyze the positive and negative aspects of some methods chosen as a tool in the treatment of the population balance equation in crystallization processes. Numerical problems arising from transformation of the partial differential equation, computational effort, as well as the incorrect prediction of the total number of particles and/or no mass conservation of the dispersed phase are discussed.

Keywords: Crystallization; Population balance; Numerical methods; Computer simulation

1. Introduction

Population balance is a well established approach as the mathematical framework for dealing with particulate systems. These kinds of processes involve formation of entities, growth, breakage or aggregation of particles, as well as dispersion of one phase in another one, and are, therefore, present in a large range of applications, like polymerization, crystallization, bubble towers, aerosol reactors, biological processes, fermentation or cell culture. Such mathematical approach in any of these systems follows the number of entities, such as solid particles, bubbles or cells in such way that their presence or occurrence may dictate the behavior of the system under consideration (Puel, Févotte, & Klein, 2003a; Ramkrishna & Mahoney, 2002). The theoretical treatment covered by the population balance, nevertheless, encounters a practical barrier in most applications, since it represents a hyperbolical partial differential equation with analytical solutions in just few cases. In others, numerical methods must be applied to calculate the system response, or even to optimize existing processes or to design new ones. A large number of numerical methods have been proposed in the open literature, but many of them have their applicability restricted to some special cases/processes, while others are of more general application.

Some applications of the model numerical solution demand fast and efficient codes, as in model-based control algorithms, in which the model must be solved in real time. The control objectives for many processes are different and the selection of a numerical method must look to it. In continuous crystallization problems, for example, the concern is in stabilization of a frequently oscillating operation, while, in batch mode, stability is not the issue. Here, the pressing question is whether the crystal size distribution (CSD) can be tailored to user specifications by applying an optimal manipulated variable trajectory to the system and by periodically on-line computing to correct noise and process disturbances (Rawlings, Witkowski, & Eaton, 1992).

Bearing the exposed in mind, the present paper presents the original population balance framework, the hyperbolic partial differential equation and reviews the main numerical methods already proposed to solve it. The methods are, then, analyzed and the advantages and drawbacks for application in crystallization processes are discussed, focusing on possible numerical problems, on the computational effort and on the correctness of prediction of the total number of particles and of mass conservation. The idea is not to present a formal organization of numerical methods based on any criteria, but, as mentioned,

* Corresponding author. Tel.: +55 19 3788 3971; fax: +55 19 3788 3965.
E-mail address: caliane@lopca.feq.unicamp.br (C.B.B. Costa).

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Nomenclature

$b\ (\varepsilon)$	breakage rate of a particle of size ε
b_k	defined as $b(x_k)$
B	birth rate using length as internal coordinate
B'	birth rate using volume as internal coordinate
$\bar{B}$	mean birth rate using length as internal coordinate
B_0	nucleation rate
C_i	ith granulometric class
D	death rate using length as internal coordinate
D'	death rate using volume as internal coordinate
$\bar{D}$	mean death rate using length as internal coordinate
f	mesh function
G	growth rate
h	net rate of production of particles
k_v	volume shape factor
L	characteristic length of the particles
L_a	lower limit of a subdomain
L_b	upper limit of a subdomain
$L_{\max}$	maximum length of the particles in a truncated domain
m	number of properties of particles used in the PBE
n	number density function using length as internal coordinate
n'	number density function using volume as internal coordinate
N	number of particles per suspension volume unit
NE	number of subdomains
p_i	properties of particles used in the PBE
$p\ (v/\varepsilon)$	fraction of daughter particles with size between v and $v + \mathrm{d}v$ generated from breakage of particles of size ε
Q_k	volumetric rate of kth stream
R	residual in the weighted residuals methods
R_A	net rate of agglomeration in C_i granulometric class ($=B_{\mathrm{agg}} - D_{\mathrm{agg}}$)
R_B	net rate of breakage in C_i granulometric class ($=B_{\mathrm{br}} - D_{\mathrm{br}}$)
$\mathbf{S}$	state vector
t	time
u_b, v_b, w_b	components of the particle velocity vector $\mathbf{v}_b$
$\mathbf{v}_b$	particle velocity vector
V	suspension volume
w_i	weighting functions
$\mathbf{x}$	vector of internal coordinates
x_i	representative volume of the ith size range, also the ith grid point
x, y, z	spatial coordinates

Greek letters

ΔC_i	width of ith class
$\beta\ (L, \lambda)$	agglomeration kernel using length as internal coordinate
$\beta'\ (v, \varepsilon)$	agglomeration kernel using volume as internal coordinate
$\beta'_{j,k}$	agglomeration kernel for sizes x_j, x_k ($=\beta'\ (x_j, x_k)$)
δ	Dirac Delta function
$\gamma\ (\varepsilon)$	number of daughter particles in the breakage of a particle of size ε
μ_j	moment j of a distribution
μ_{ij}	cross-moment ij of a distribution
ψ_i	basis functions used in the weighted residuals methods

Subscripts

agg	aggregation
br	breakage
nucl	nucleation

to stress the positive and negative features of methods in the solution of crystallization problems. Cooling crystallization is a process in which the mechanisms of nucleation, growth and aggregation occur in a competitive fashion and, so, a numerical method suitable for solving PBE in crystallization problems should deal with the three mechanisms with acceptable accuracy.

The paper is organized as follows. The population balance approach is first introduced, with discussions in its area of application and analytical solution limitations. Then the formal complete population balance equation and some definitions are presented, and some important issues are raised. Section 3 discusses in a general manner the three main groups in which the specific methods for solving the population balance equation may be classified, while Section 4 presents specific methods, with their applications in literature, advantages, drawbacks and applicability in crystallization systems. The next section presents other methods, which cannot be classified in none of the three main groups of Section 3. As an exemplification of a method application in a crystallization process, Section 6 gives some numerical results and points out the notable drawbacks and advantages. Finally, the last section provides the concluding remarks.

2. The general population balance equation

The population balance framework considers space as the physical one, as well as any important system property, which changes due to the intrinsic mechanisms and external influences to the system. Concerning to the physical space, the state vector coordinates refer to spatial coordinates, like (x, y, z), and are denoted as external coordinates. The coordinates corresponding to the properties (internal coordinates) are the ones of relevance to the process and may be composed, for example, by any important dimension of the particle or its age in the system (Hounslow, 1998; Randolph & Larson, 1971). The state vector $\mathbf{S}$ can be, then, expressed by $\mathbf{S} = [x, y, z, t, L, (p_i)_{1\le i\le m}]$, where L is the characteristic dimension of the particles, besides m other properties and t corresponds to time. The number density function $n[\mathbf{x}, t, L, (p_i)_{1\le i\le m}]$ can then be used to make a balance in the particles

population, composing the population balance equation, PBE (Pilon & Viskanta, 2003):

$$\frac{\partial n}{\partial t} + \frac{\partial}{\partial x}(u_b n) + \frac{\partial}{\partial y}(v_b n) + \frac{\partial}{\partial z}(w_b n) + \frac{\partial}{\partial L}(\dot{L} n) + \sum_{i=1}^{m} \frac{\partial}{\partial p_i}(\dot{p}_i n) = h \quad (1)$$

where u_b, v_b and w_b are the components of the particle velocity vector $\mathbf{v}_b$, $\dot{L}$ is the time rate of change of the characteristic dimension, while $\dot{p}_i$is the time rate of change of the other properties. The net rate of particles production of a particular state at time t is denoted by h, which comprises death and birth mechanisms.

The main reason for the unavailability of analytical solutions to the PBE is that the birth and death terms corresponding to breakage and agglomeration are expressed as integral functions. Apart from that, the density function may vary in multidimensional space and may depend on external variables. These two last complications to the solution of the PBE are normally neglected in most applications, by assuming perfectly mixed tank. In this way, the external coordinates are normally not considered and the PBE is expressed only with the internal coordinates. An interesting work presented in literature dealing with imperfect mixing is the one of Ma, Tafti, and Braatz (2002). The effect of spatial variation is evaluated using a compartmental model, which may require the use of parallel computations, if the number of considered compartments is large, in order to have shorter simulation times.

The hyperbolic differential operator of the PBE is the divergence term, composed by all derivatives with respect to the coordinates, which is divided into two parts. The divergence concerning to external coordinates expresses the change in population in a particular volume due to the particles passing through that volume with velocity $\mathbf{v}_b$. The second divergence term represents the change in population due to particle property, p_i. If the property is the particle size, then the divergence term represents the growth (represented by G) or shrinkage of the particles (Verkoeijen, Pouw, Meesters, & Scarlet, 2002).

The kinetic mechanisms present in particulate processes are growth (commonly associated with the rate of change of the characteristic dimension), nucleation (appearance of new entities), agglomeration and breakage. In crystallization field, nucleation and crystal growth are dominant, but in many systems, agglomeration and breakage are present to a certain extent, that must be considered into the modeling.

2.1. Expressions to birth and death terms

The birth (B) and death (D) terms represented in Eq. (1) by h correspond to breakage and agglomeration mechanisms, which are commonly expressed as integral functions.

Aggregation results from the binary collision of mother particles and the sticking by growth of crystalline bridges between particles. Bearing aggregation in mind, the birth and death terms, using volume as internal coordinate are given, respectively, by Eqs. (2) and (3):

$$B'_{\mathrm{agg}}(v) = \frac{1}{2}\int_0^v \beta'(v-\varepsilon,\varepsilon)n'(v-\varepsilon,t)n'(\varepsilon,t)\,\mathrm{d}\varepsilon \quad (2)$$

$$D'_{\mathrm{agg}}(v) = n'(v,t)\int_0^\infty \beta'(v,\varepsilon)n'(\varepsilon,t)\,\mathrm{d}\varepsilon \quad (3)$$

The agglomeration kernel, $\beta'(v,\varepsilon)$, is a measure of the frequency of collisions between particles of volumes v and ε which produces a particle of volume $v+\varepsilon$, being a function of the size domains of mother particles and of the agglomerate and the hydrodynamic conditions.

It is frequently easier to write the growth rate with length as internal coordinate, and, therefore, a modification in the birth and death rate terms, based on length, is necessary:

$$B_{\mathrm{agg}}(L) = \frac{L^2}{2}\int_0^L \frac{\beta[(L^3-\lambda^3)^{1/3},\lambda]n[(L^3-\lambda^3)^{1/3},t]n(\lambda,t)\,\mathrm{d}\lambda}{(L^3-\lambda^3)^{2/3}} \quad (4)$$

$$D_{\mathrm{agg}}(L) = n(L,t)\int_0^\infty \beta(L,\lambda)n(\lambda,t)\,\mathrm{d}\lambda \quad (5)$$

David, Paulaime, Espitalier, and Rouleau (2003) divide agglomeration in three levels, to know, Brownian, laminar and turbulent agglomeration and develop the expressions for the agglomeration kernel for each one of them.

According to Verkoeijen et al. (2002), the birth and death terms in the PBE express the transfer of particles from one size class to the other by breakage or by agglomeration and, since they are not rate processes, cannot be differentiated with respect to time.

A different perspective in the modeling of agglomeration was proposed by Marchal, David, Klein, and Villermaux (1988), considering this mechanism as chemical reactions between species in the many particle sizes. The final agglomeration rate expression per size domain is based on an intrinsic rate, function of the number of collision per time and volume unit and of supersaturation.

Equations analogous to Eqs. (2) and (3) can be formulated to express the birth and death terms due to the breakage mechanisms, as given by Eqs. (6) and (7):

$$B'_{\mathrm{br}}(v) = \int_v^\infty \gamma(\varepsilon)b(\varepsilon)p\left(\frac{v}{\varepsilon}\right)n'(\varepsilon,t)\,\mathrm{d}\varepsilon \quad (6)$$

$$D'_{\mathrm{br}}(v) = -b(v)n'(v,t) \quad (7)$$

where $\gamma(\varepsilon)$ is the number of daughter particles generated from the breakup of a particle of size ε, $b(\varepsilon)$ is the breakup rate of a particle with size ε and $p(v/\varepsilon)$ is the fraction of daughter particles with size between v and $v+\mathrm{d}v$, generated from breakup of particles of size ε.

2.2. Internal coordinate and density function considerations

Verkoeijen et al. (2002) present reasons why the population balance should be expressed with particle volume as the basic particle-size parameter. They argue, using the agglomeration mechanism, that when length is used to express size, consistency with the mass balance cannot be achieved. However, as pointed out by Mahoney and Ramkrishna (2002), singularity in the number density may occur in certain treatments. In precipitation systems, the length based growth rate is usually finite at small particle sizes. This corresponds to a volumetric growth rate that approaches zero at $L=0$, and a consequent singularity in the volume based number density. The singular behavior creates very steep gradients in the solution that are difficult to capture with a discrete representation, besides being difficult to scale the solution, even if $v=0$ is not included in the domain. These problems are avoided by the formulation in length, with the drawback that evaluation of aggregation kernel becomes considerably more complex.

Another point discussed by Verkoeijen et al. (2002) is the proposal that the basic population distribution should be the mass distribution of particle, instead of the common practice of expressing the distribution of the particle size as a number distribution. The reason is posed in terms that the number of particles is not conserved, since the particles may break or agglomerate, being the total mass of particles the amount that is conserved. As a result, the basic PBE should be expressed in terms of the mass distribution, or the volume distribution if the density is constant, so the mass in the system is automatically conserved. Nevertheless, the authors deal with the description of grinding and aerosol processes. Conservation of total particles mass is not the case for crystallization process, where the extraction of solute from solution can occur with the growth of existing crystals or with the nucleation of new entities. So, this argument is not valid for a crystallization application and, historically, the number distribution has been the preferred approach, as exposed by Puel et al. (2003a).

2.3. Moments of the distribution

The moment j of the number distribution n is defined as in Eq. (8):

$$\mu_j = \int_0^\infty L^j n(L,t)\,\mathrm{d}L \tag{8}$$

For the number distribution based on volume as internal coordinate, the moment j is given by Eq. (9):

$$\mu_j = \int_0^\infty v^j n'(v,t)\,\mathrm{d}v \tag{9}$$

The zeroth moment ($j=0$) represents the total number of particles present in the system, while the total volume of particles is inferred from the third moment ($j=3$) defined by Eq. (8) or from the first moment ($j=1$) defined by Eq. (9).

When more than one crystal dimension is considered, cross-moments can be defined. For example, for two dimensions in a distribution based on the width (L_1) and the length (L_2), the cross-moments can be defined as in Eq. (10):

$$\mu_{ij} = \int_0^\infty \int_0^\infty L_1^i L_2^j n(L_1, L_2, t)\,\mathrm{d}L \tag{10}$$

The total number is given by μ_{00}, while μ_{10} is the total width and μ_{01} is the total length. The average width of crystals is μ_{10}/μ_{00} and the average length is μ_{01}/μ_{00}.

Some methods for solving the PBE appeal to the moments of the distribution in order to manipulate the original partial differential equation. Special attention to these methods will be given in next section.

3. Numerical methods for PBE solution

The methods for solving the PBE can be classified into three main groups: the method of moments, the discretization of the size domain interval and the weighted residuals.

The method of moments is one of the oldest ones and transforms the PBE into a set of ordinary differential equations (ODEs) by multiplying the population balance equation by L^j (in a length based PBE) and integrating it, giving equations in terms of moments (Randolph & Larson, 1971). The solution of the set of equations gives the moments of the distribution as function of time, considering size independent growth and mean birth and death terms:

$$\int_0^\infty L^j \left[\frac{\partial n}{\partial t} + \frac{\partial}{\partial L}(Gn) + D - B\right] = 0 \tag{11}$$

$$\begin{aligned}
\frac{\mathrm{d}\mu_0}{\mathrm{d}t} &= B_0 + \bar{B} - \bar{D} \\
\frac{\mathrm{d}\mu_1}{\mathrm{d}t} &= \mu_0 G + \bar{B} - \bar{D} \\
\frac{\mathrm{d}\mu_2}{\mathrm{d}t} &= 2\mu_1 G + \bar{B} - \bar{D} \\
\frac{\mathrm{d}\mu_3}{\mathrm{d}t} &= 3\mu_2 G + \bar{B} - \bar{D}
\end{aligned} \tag{12}$$

In the set of Eq. (12), B_0 is the nucleation rate. When only nucleation and growth are being considered, the moments can be generated by the ordinary differential equation given by Eq. (13):

$$\frac{\mathrm{d}\mu_j}{\mathrm{d}t} = 0^j B_0 + jG\mu_{j-1} \tag{13}$$

It is easy to derive the ODEs when PBE is a two-dimensional one:

$$\frac{d\mu_{00}}{dt} = B_0$$
$$\frac{d\mu_{ij}}{dt} = iG_1\mu_{(i-1)j} + jG_2\mu_{i(j-1)} \quad i+j>0 \tag{14}$$

The great disadvantage of the method is the mathematical complication in the equations when the growth rate is a size dependent mechanism. In this case, an alternative method of solution is to use the moments and an orthogonal polynomial to simulate the population density function. When aggregation and/or breakage are included, the reduction to moment equations is impossible. Apart from this drawback, reconstructing the real distribution from its moments is numerically unstable (Nallet, Mangin, & Klein, 1998; Rigopoulos & Jones, 2003). This last disadvantage can represent a serious problem in certain model applications. Many times, as in certain optimal control evaluations, the entire particle size distribution may be necessary, which prevents the use of the method of moments (Ma et al., 2002).

The discretization technique, which is also referred to as discretization sizing technique, discretize the spectrum of the independent variable into a number of intervals and subsequently use the mean-value theorem to transform the continuous PBE into a series of equations in terms of either number or average population density in each class. The method turns the PBE in the so-called discretized population balance (DPB) and the resulting set of ODEs has so many equations as the number of granulometric classes.

The computational effort for the numerical solution can be severely reduced if the grid assumes a geometric progression—the number of combinations of particles that must be considered to evaluate the aggregation terms is substantially reduced (Rigopoulos & Jones, 2003). Furthermore, coarse discretization methods are particularly amenable to process control applications because of the speed with which solutions can be obtained especially when fronts and discontinuities are not present (Ramkrishna & Mahoney, 2002).

Two drawbacks can be cited. Conservation of both number of particles and mass is only guaranteed in the limit of infinite resolution and a discontinuity can arise along the separatrix, which is the curve that divides states deriving from initial conditions from those arising from boundary conditions. A sharp discontinuity can be created, which quickly broadens by numerical diffusion in simulation (Mahoney & Ramkrishna, 2002).

The weighted residuals comprise methods that retrieve the distribution by approximating the solution with a series of trial functions, whose coefficients are to be determined so that their sum will satisfy the PBE. They are divided in weighted residuals with global functions and finite element (FE) methods. Weighted residual methods with global functions were among the first to be tried in PBE numerical solution. It was soon realized, however, that global functions cannot capture the features of an arbitrarily shaped distribution, especially if it exhibits sharp changes and discontinuities. If a priori knowledge of the shape of the resulting distribution is available, the trial functions can be tailored to accommodate it; in that case, the method converges and may even be computationally attractive. Finite element methods approximate the solution with piecewise low-order polynomials that are only locally nonzero, and are, thus, flexible and capable of capturing highly irregular solutions. (Rigopoulos & Jones, 2003). According to Rawlings, Miller, and Witkowski (1993), the computational time for the model solution with the weighted residuals method is modest, turning possible to consider it in an on-line control scheme.

In global methods, the population density function is approximated as a linear combination of chosen basis function, $\Psi_i(L)$:

$$n(L,t) = \sum_{i=1}^{\infty} a_i(t)\Psi_i(L) \tag{15}$$

The unknown a_i's are determined by substituting the previous equation into the population balance to define a residual, $R(L, t)$. The sense in which the residual is made small determines the type of weighted residual method used. The idea of weighted residuals is to find the a_i's that force the residual to be orthogonal to a chosen set of weighting functions, $w_i(L)$:

$$\int_0^{\infty} w_i(L)R(L,t)\,dL = 0 \tag{16}$$

Possible choices of the weighting functions include Dirac's delta functions, resulting in collocation methods, or the basis functions themselves (possibly weighted), resulting in Galerkin's techniques (Mahoney & Ramkrishna, 2002).

In FE methods, the infinite domain is truncated to a finite one, $L = [0, L_{max})$. This truncated domain is then partitioned into NE discrete subdomains. For all $L \in (L_a, L_b]$, a subdomain, the solution to the PBE will be approximated as a linear combination of interpolation functions:

$$n(L) \approx n_h^e(L) = \sum_{j=1}^{n_c} n_j^e \Psi_j^e(L) \qquad \forall L \in (L_a^e, L_b^e] \tag{17}$$

where n_c is the number of nodes in element e, n_j's are the nodal values of the density distribution and the $\Psi_j(L)$'s are the basis polynomials of order $n_c - 1$ (Nicmanis & Hounslow, 1996).

The truncation results in an underestimation of the integrals of the death term due to agglomeration and breakage. In most practical applications, the density distribution asymptotes towards zero at sufficiently large particle sizes, so a maximum size can be selected to be sufficiently large that underestimation is negligibly small. However, care must be taken to avoid selection of unnecessarily large values of the upper limit, since tail regions can be difficult and/or computationally expensive to converge, because of the very small values they can attain at large particle sizes (Nicmanis & Hounslow, 1998).

In orthogonal collocation on finite elements (OCFE), the residual is made small by forcing it to vanish at selected L_i locations, called the collocation points. The choice of these locations is vital, since they control the density of the collocation points in the overall size domain. Thus, in regions with steep changes

a higher density of collocation points is usually required. The domain partition into finite elements can be performed either based on previous knowledge about the shape and characteristics of the distribution or based on the satisfaction of a certain error criterion (Krallis et al., 2004).

The choice of the basis functions, both in collocation and Galerkin's methods, must be suitable to the specific problem, either in global or FE applications. Laguerre polynomials are relevant for continuous flow crystallizers, since the steady-state solution is exponential in the range $[0, +\infty)$ and the cyclic behavior frequently present can be satisfactorily represented (Puel et al., 2003a; Rawlings et al., 1992).

Advantages are convergence properties on the entire distribution and the availability of adaptive mesh techniques. Major drawbacks include the inability to capture discontinuities, as may arise along the separatrix, and the computational overhead arising from double integral evaluations in Galerkin's formulations. Furthermore, the number of system states required to represent the solution grows exponentially with the number of dimensions (Mahoney & Ramkrishna, 2002). Here, DPBs are much easier and more robust to be extended in a second (or third, if necessary) dimension (Puel et al., 2003a).

The major advantages of FE numerical solutions are their robustness, easier convergence and open scale of the size domain. Apart from that, FE method does not incur any truncation errors at the lower volume range and uses significantly smaller amounts of memory when solving the PBE as well as CPU time needed to convergence than some DPB methods (Nicmanis & Hounslow, 1998).

The large number of schema that must be evaluated for a given system, as well as the difficulty to implement varying grid resolutions are possible disadvantages of the FE approach, although existing theory makes extension to multiple internal coordinates reasonably straightforward. Under conditions of excessive nucleation, the stiffness characteristics of the OCFE can cause integration problems (Immanuel & Doyle III, 2003).

Summarizing, a comparison of the DPB techniques with FE methods reveals that, although the latter are more difficult to implement and computationally demanding, they are very general and flexible, coping with any possible formulation, like size-dependent growth and different aggregation kernels. However, it is interesting to note that, when mechanisms of aggregation and breakage are present, DPBs are a more natural choice, since these mechanisms are essentially discrete. DPBs are, on the other hand, methods easy to use and computationally efficient, but less general, driven to specific problems, and may incur in severe errors of certain distribution moments.

4. Application of numerical methods in literature

4.1. Method of moments

As already exposed, this method, although providing a simple manipulation of the PBE, has a lot of restrictions and drawbacks. One of the most recent papers in crystallization area that uses this method is the one of Ma and Braatz (2003). The main proposal was an approach for robust identification and control of batch and semibatch processes and the two-dimensional crystallization was used to demonstrate it. The authors appealed to the cross-moments in order to reduce the PBE, with only nucleation and size-independent growth, to a set of ODEs.

4.2. Discretized population balances

Marchal et al. (1988) introduced the Method of Classes, applicable to a general case, making possible to consider agglomeration, breakage and length-dependent growth rate. The method discretizes the size domain interval in a free of choice grid, generating granulometric classes or bins (C_i). The mean size in each class is assumed as the characteristic size for all particles belonging to that class. The model assumes a constant value for the density function in each bin (zero order method).

$$\begin{cases} \dfrac{dN_1}{dt} + \dfrac{1}{V}\dfrac{dV}{dt}N_1 + \dfrac{Q_{out}N_1 - Q_{in}N_{1e}}{V} + \dfrac{G(L_1)}{2\Delta C_2}N_2 + \dfrac{G(L_1)}{2\Delta C_1}N_1 = B_0 + R_{A,1} - R_{B,1} \\ \dfrac{dN_i}{dt} + \dfrac{1}{V}\dfrac{dV}{dt}N_i + \dfrac{Q_{out}N_i - Q_{in}N_{ie}}{V} + \dfrac{G(L_i)}{2\Delta C_{i+1}}N_{i+1} + \dfrac{G(L_i) - G(L_{i-1})}{2\Delta C_i}N_i - \dfrac{G(L_{i-1})}{2\Delta C_{i-1}}N_{i-1} = R_{A,i} - R_{B,i} \\ \dfrac{dN_{NE}}{dt} + \dfrac{1}{V}\dfrac{dV}{dt}N_{NE} + \dfrac{Q_{out}N_{NE} - Q_{in}N_{NE_{in}}}{V} + \dfrac{-G(L_{NE-1})}{2\Delta C_{NE}}N_{NE} - \dfrac{G(L_{NE-1})}{2\Delta C_{NE-1}}N_{NE-1} = R_{A,NE} - R_{B,NE} \end{cases} \quad (18)$$

In their original work, Marchal et al. (1988) solved the formed set of ODEs (Eq. (18)) with a fourth order Runge–Kutta code and considered the mechanisms of nucleation, length dependent growth and agglomeration. The Method of Classes was vastly used in literature to solve the PBE in crystallization and precipitation field, for simulation of experimental results, determination of kinetic parameters, modeling of process or optimization of operation conditions (Blandin, Mangin, Nallet, Klein, & Bossoutrot, 2001; David & Bossoutrot, 1996; David et al., 2003; David, Villermaux, Marchal, & Klein, 1991; Frank, David, Villermaux, & Klein, 1988; Matthews, Miller, & Rawlings, 1996; Matthews & Rawlings, 1998; Miller & Rawlings, 1994;

An approach also used, which differs from the deterministic approach of the population balance considered so far, is the probabilistic Monte Carlo method. In this technique, the solution is determined using the Markov conditional probability, which is the probability of a particular state proceeding to any other state. Besides predicting the ensemble average properties, it also predicts the fluctuations. This technique solves more complex multi-dimensional population balance models (Immanuel & Doyle III, 2003).

Monnier, Févotte, Hoff, & Klein, 1996; Monnier, Févotte, Hoff, & Klein, 1997; Nallet et al., 1998; Puel et al., 2003a; Puel, Févotte, & Klein, 2003b).

The major drawback of the Method of Classes is its dependency of the number or density functions on the adopted grid. Since the number of discretized equations increases with the number of classes, high computational times can be necessary for the solution of a fine grid. Self-adaptive discretization has already been proposed in order to reduce the number of differential equations, without affecting the results. Another disadvantage of the method is that the feasibility of the computation is, likely, strongly dependent on the complexity and location of individual birth and death processes.

Numerical problems described in literature arise from the possible loss of crystals, leading to an unbalanced mass balance during the crystal growth. In coagulation (aggregation) processes, the method conserves particle mass, but underestimates the number of entities (Kostoglou & Karabelas, 1994).

Kumar and Ramkrishna (1997) stress that the discretization equations for the Method of Classes have the potential to produce negative values for the number of particles in each class and that the results from this technique oscillate about the analytical solution, apart from the fact that the numerical solutions around the location of a discontinuity are highly diffused, turning the method not adequate to include growth. This is quite natural for finite-difference-type approximation as they have an infinite velocity of propagation for the signal.

Puel et al. (2003a) extended the Method of Classes to a bi-dimensional population balance, arguing that some organic systems can not be represented solely by one characteristic dimension, being necessary the consideration of two particle dimensions. The bi-dimensional Method of Classes predicts the time-variation of the crystal habit, which must be a point of concern in some applications. They suggest the implementation of an adaptive bi-dimensional algorithm to improve the computation. In order to speed it up, the LSODAR was adopted to solve the resulting ODEs. In order to cope with possible unbalanced mass balance, the area of the each class in the grid was reduced, requiring an enormous number of classes (6×10^5 classes), which would prevent the use of this model for use in real time applications.

Hounslow, Ryall, and Marshall (1988) have devoted many works in the modeling of kidney stones formation, a process in which only growth and aggregation are involved. The method developed by them discretize the particle-size domain in a fixed geometric progression ($L_{i+1}/L_i = \sqrt[3]{2}$, which is equivalent to $v_{i+1}/v_i = 2$) and is also a zero order method, that is, the particle-size density is considered constant in each bin. The discretization is chosen to prevent the high computational complexity associated with the aggregation term. The authors identified four types of aggregation interactions that can change the total population in a size range and derived expressions for each one of them separately. The derived discretized expressions for the number of particles due to the mechanisms of aggregation, growth and nucleation are given, respectively, by Eqs. (19)–(21). When the three mechanisms are present in the process, Eqs. (19)–(21) must be combined in order to compute the evolution of the number of particles in each size range during time.

$$\left(\frac{dN_i}{dt}\right)_{agg} = N_{i-1}\sum_{j=1}^{i-1} 2^{j-i+1}\beta_{i-1,j}N_j + \frac{1}{2}\beta_{i-1,i-1}N_{i-1}^2 - N_i\sum_{j=1}^{i-1} 2^{j-i}\beta_{i,j}N_j - N_i\sum_{j=i}^{\infty}\beta_{i,j}N_j \tag{19}$$

$$\left(\frac{dN_i}{dt}\right)_{growth} = \frac{2G}{(1+r)L_i}\left(\frac{r}{r^2-1}N_{i-1} + N_i - \frac{r}{r^2-1}N_{i+1}\right), \quad \text{where } r = \frac{L_{i+1}}{L_i} = \sqrt[3]{2} \tag{20}$$

$$\left(\frac{dN_1}{dt}\right)_{nucl} = B_0 \tag{21}$$

The set of equations derived was internally consistent with regard to mass and total numbers (zeroth and, ultimately, third moments, in a length basis).

The DPB proposed by Hounslow et al. (1988) was extended by Litster, Smit, and Hounslow (1995) in order to permit the use of an adjustable discretization with the form $v_{i+1}/v_i = 2^{1/q}$, $q \geq 1$, integer. The expression for the contribution of aggregation with the adjustable discretization is given by Eq. (22).

$$\begin{aligned}\left(\frac{dN_i}{dt}\right)_{agg} = &\sum_{j=1}^{i-S(q)-1}\beta_{i-1,j}N_{i-1}N_j\frac{2^{(j-i+1)/q}}{2^{1/q}-1} + \sum_{k=2}^{q}\sum_{j=i-S(q-k+2)-k+1}^{i-S(q-k+1)-k}\beta_{i-k,j}N_{i-k}N_j\frac{2^{(j-i+1)/q}-1+2^{-(k-1)/q}}{2^{1/q}-1} \\ &+ \frac{1}{2}\beta_{i-q,i-q}N_{i-q}^2 + \sum_{k=2}^{q}\sum_{j=i-S(q-k+2)-k+2}^{i-S(q-k+1)-k+1}\beta_{i-k,j}N_{i-k+1}N_j\frac{-2^{(j-i)/q}+2^{1/q}-2^{-(k-1)/q}}{2^{1/q}-1} \\ &- \sum_{j=1}^{i-S(q)}\beta_{i,j}N_iN_j\frac{2^{(j-i)/q}}{2^{1/q}-1} - \sum_{j=i-S(q)+1}^{\infty}\beta_{i,j}N_iN_j\end{aligned} \tag{22}$$

where $S(q) = \sum_{s=1}^{q} s$.

The numerical solution is as more accurate as greater the value of q, but this demands more computational time.

The major drawback to the application of the method proposed by Litster et al. (1995) is its limitation in combined growth and aggregation mechanisms at large times, although nucleation problems can be successfully solved with such method.

Kumar and Ramkrishna (1996a) propose a discretization method for the PBE solution for breakage and agglomeration mechanisms, in which the size (volume) domain is divided into sections of arbitrarily scales and a representative volume (pivot) is chosen in each section. The main feature is not an attempt to approximate the continuous number density function on a suitably fine scale, but rather to target calculation of properties of the population of specific interest to an application without seeking the complete number density function resulting from the process events. In the method, called fixed-pivot (FP) technique, events among particles that lead to the formation of particles of sizes other then the pivot ones are incorporated in the set of discretized equations, in such a way that the properties corresponding to two moments of interest are exactly preserved. The moments to be preserved determine the two values of j in Eq. (9), here assigned to ζ and ξ. These last two variables determine the value of η in Eq. (23), used in Eq. (24), which computes the evolution of number of particles in each section.

$$\eta = \begin{cases} \dfrac{v^{\zeta}x_{i+1}^{\zeta} - v^{\xi}x_{i+1}^{\zeta}}{x_i^{\zeta}x_{i+1}^{\xi} - x_i^{\xi}x_{i+1}^{\zeta}}, & x_i \le v \le x_{i+1} \\ \dfrac{v^{\zeta}x_{i-1}^{\zeta} - v^{\xi}x_{i-1}^{\zeta}}{x_i^{\zeta}x_{i-1}^{\xi} - x_i^{\xi}x_{i-1}^{\zeta}}, & x_{i-1} \le v \le x_i \end{cases} \tag{23}$$

$$\frac{\mathrm{d}N_i}{\mathrm{d}t} = \sum_{j,\,k}^{j\ge k} \left(1 - \frac{1}{2}\delta_{j,k}\right) \eta\beta'_{j,k}N_jN_k \quad x_{i-1} \le (x_j + x_k) \le x_{i+1} - N_i\sum_{k=1}^{M}\beta'_{j,k}N_k + \sum_{k=1}^{M} n_{i,k}b_kN_k - b_iN_i \tag{24}$$

Kotoulas and Kiparissides (2004) and Krallis et al. (2004) used the FP technique for the numerical solution of the PBE applied to polymerization reactors. Stork, Tousain, Wieringa, and Bosgra (2003) also used the FP technique with a geometric grid of factor 1.2, but in a process of emulsification.

The main advantages of the method lie in the feature of preserving any two free of choice properties of the distribution and in the possibility of varying the coarseness of discretization. Furthermore, for appropriate values of involved parameters, it produces solutions that are exactly identical to those of Hounslow et al. (1988) and Litster et al. (1995) with less computation time. Nevertheless, the method is restricted to aggregation and breakage events, which makes the method useful in polymerization–depolymerization and aerosol dynamics problems (and indeed a lot of work which uses this numerical method is found in the open literature), but not in crystallization ones. Apart from that, according to Kumar and Ramkrishna (1996a), over prediction is always present with the discretized equations for pure aggregation, unless special effort is made to prevent it.

Due to this over prediction, Kumar and Ramkrishna (1996b) developed a technique that accounts for the variation of number density in a size range, proposing the definition of the pivots in such a way that their location in size range $\{v_i, v_{i+1}\}$ reflects the variation of the relevant density in the ith size range. In this way, if the density in a section changes from steeply decreasing to nearly uniform due to the particulate process, the pivot moves from the lower end of the section to the middle. Eq. (25) expresses the movement of the pivots in each section and Eq. (26) computes the evolution of the number of particles.

$$\frac{\mathrm{d}x_i}{\mathrm{d}t} = \frac{1}{N_i}\sum_{j,\,k}^{j\ge k} v_i \le (x_j + x_k) < v_{i+1} \times \left[1 - \frac{1}{2}\delta_{j,k}\right]\left[(x_j + x_k) - x_i\right]\beta'_{j,k}N_jN_k - \frac{1}{N_i}\sum_{j\ge i} b(x_j)N_j\left[\bar{B}_{i,j}^{(v)} - x_i\bar{B}_{i,j}^{(1)}\right] \tag{25}$$

$$\frac{\mathrm{d}N_i}{\mathrm{d}t} = \sum_{j,\,k}^{j\ge k} \left[1 - \frac{1}{2}\delta_{j,k}\right]\beta'_{j,k}N_jN_k \quad v_i \le (x_j + x_k) < v_{i+1} - N_i\sum_{k=1}^{M}\beta'_{j,k}N_k + \sum_{j\ge i} b(x_j)N_j\bar{B}_{i,j}^{(1)} - b(x_i)N_i \tag{26}$$

where $\bar{B}_{i,j}^{(v)} = \int_{v_i}^{v_{i+1}} v\beta(v, x_j)\,\mathrm{d}v$.

The new technique, called moving-pivot (MP) technique, shows that the correct discrete representation of the birth term due to the coalescence of smaller entities (which determines the movement of the front) is crucial for the accuracy of the numerical solutions.

The disadvantage of the two previous techniques of not including nucleation and growth terms was overcome with the work of Kumar and Ramkrishna (1997), which combines the developed discretized technique with the method of characteristics. The scale boundaries move with the growth rate of the particles belonging to the respective interval (Eqs. (27) and (28)). The presence of nucleation poses a new difficulty because a situation arises when some or all of the nuclei become smaller than the smallest particle size represented in the bins, due to the bins movement. This problem is overcome by adding new bins, one at a time (Eqs. (29) and (30)), with zero population at the small size end at regular intervals and the renumber of the old bins as increasing sequence of integers. The number of equations that need to be solved increases very rapidly, making the technique computation-intensive. The effectiveness is restored by eliminating some of the pivots to make the grid coarser in larger sizes and assigning them to the adjoining pivots in a way that the desired properties of the population at the pivot in question are preserved. Eq. (31) provides for the calculation on the number of particles in each section.

$$\frac{\mathrm{d}v_i}{\mathrm{d}t} = G(v_i) \tag{27}$$

$$\frac{dv_{i+1}}{dt} = G(v_{i+1}) \tag{28}$$

$$\frac{dv_1}{dt} = \frac{dv_0(t)}{dt} \tag{29}$$

$$\frac{dx_1}{dt} = \frac{1}{2}\left(\frac{dv_1}{dt} + \frac{dv_2}{dt}\right) \tag{30}$$

$$\frac{dN_i(t)}{dt} = \sum_{x_{i-1}\le(x_j+x_k)\le s_{i+1}}^{i\ge j\ge k} \left(1 - \frac{1}{2}\delta_{j,k}\right)\eta\beta'_{j,k}N_j(t)N_k(t) - N_i(t)\sum_{k=1}^{M}\beta'_{j,k}N_k(t) + \int_{v_i}^{v_{i+1}} B_0\,dv \tag{31}$$

An adaptive mesh method is proposed by Lee et al. (2001) to be used combined with the technique of Kumar and Ramkrishna (1997), conserving crystal number and mass during mesh adaptation, being able to handle stiff nucleation problems of the characteristic method. For the decision tolerance to adapt meshes, the authors use the mesh function based on the first derivative of the solution, as in Eq. (32).

$$f(v,t) = \sqrt{(\Delta v)^2 + (\Delta v N_v)^2} = \Delta v\sqrt{1+N_v^2} = \Delta v\sqrt{1+\left(\frac{\partial N}{\partial v}\right)^2} \tag{32}$$

The meshes will be adapted to equidistribute the mesh function. Therefore, the meshes having mesh function values larger than the tolerance defined in Eq. (33) or in Eq. (34), a relative equation in order to consider the size range where density function are very small, will be refined.

$$\mathrm{TOL} = \frac{\sum_{i=1}^{M}\Delta v_i\sqrt{1+N_{v,i}^2}}{M} \tag{33}$$

$$\mathrm{TOL}_{\mathrm{rel}} = \frac{\sum_{i=1}^{M}\Delta v_i\sqrt{(1/v_{\mathrm{ref}})^2 + (N_{v,i}/N_{\mathrm{ref}})^2}}{M} \tag{34}$$

The idea is to eliminate meshes when the mesh function of the solution is much smaller than the tolerance, in order to reduce the calculation time. Mesh elimination, for conservation of both number and mass, is made through Eqs. (35) and (36).

$$N_{i-1}^{\mathrm{new}} = \frac{\sum_{k=i-1}^{i+1}N_k^{\mathrm{old}}\left[k_v\left(x_i^{\mathrm{new}}\right)x_i^{\mathrm{new}} - k_v\left(x_k^{\mathrm{old}}\right)x_k^{\mathrm{old}}\right]}{k_v\left(x_i^{\mathrm{new}}\right)x_i^{\mathrm{new}} - k_v\left(x_{i-1}^{\mathrm{new}}\right)x_{i-1}^{\mathrm{new}}} \tag{35}$$

$$N_i^{\mathrm{new}} = \frac{\sum_{k=i-1}^{i+1}N_k^{\mathrm{old}}\left[k_v\left(x_k^{\mathrm{old}}\right)x_k^{\mathrm{old}} - k_v\left(x_{i-1}^{\mathrm{new}}\right)x_{i-1}^{\mathrm{new}}\right]}{k_v\left(x_i^{\mathrm{new}}\right)x_i^{\mathrm{new}} - k_v\left(x_{i-1}^{\mathrm{new}}\right)x_{i-1}^{\mathrm{new}}} \tag{36}$$

The study adopted the strategy of keeping the mass ratio in the nuclei mesh to all meshes under a pre-specified constant. In this way, a new mesh is added when the mass in the nuclei mesh is no longer negligible compared to the total mass. The populations of new ith and $(i+1)$th meshes should satisfy Eqs. (37) and (38).

$$N_i^{\mathrm{new}} = \frac{k_v\left(x_{i+1}^{\mathrm{new}}\right)x_{i+1}^{\mathrm{new}} - k_v\left(x_i^{\mathrm{old}}\right)x_i^{\mathrm{old}}}{k_v\left(x_{i+1}^{\mathrm{new}}\right)x_{i+1}^{\mathrm{new}} - k_v\left(x_i^{\mathrm{new}}\right)x_i^{\mathrm{new}}}N_i^{\mathrm{old}} \tag{37}$$

$$N_{i+1}^{\mathrm{new}} = \frac{k_v\left(x_i^{\mathrm{old}}\right)x_i^{\mathrm{old}} - k_v\left(x_i^{\mathrm{new}}\right)x_i^{\mathrm{new}}}{k_v\left(x_{i+1}^{\mathrm{new}}\right)x_{i+1}^{\mathrm{new}} - k_v\left(x_i^{\mathrm{new}}\right)x_i^{\mathrm{new}}}N_i^{\mathrm{old}} \tag{38}$$

The adaptive mesh method was applied to a potassium sulfate crystallization system, showing that the method is suitable for the simulation of crystallization processes.

Simultaneity of nucleation, growth and aggregation of particles is essential to characterize processes such as precipitation and crystallization, among others, and the possibility of modeling this processes are one of the advantages of the method. Furthermore, the presence of moving discontinuities, which is unavoidable due to the hyperbolic nature of the governing equation, is addressed with no additional difficulty.

The developments of Kumar and Ramkrishna (1996a, 1996b, 1997) allow the density function (particle distribution) evaluations as a consequence of distribution moments calculations. This fact makes the procedure interesting to broader applications. For example, in many processes, like polymerization, crystallization and aerosol, the control of the full particle-size distribution (PSD) may be necessary, due to the strong dependence of the physico-chemical and mechanical properties of products on the characteristics of the corresponding PSD (Kalani & Christofides, 2002). In order to control these processes, great effort is made to determine off-line and on-line state variables values that lead to the achievement of a target distribution. These calculations, which include optimization and control, require a system model able to predict the full PSD.

Nopens, Beheydt, and Vanrolleghem (2005) compared the methods of Hounslow et al. (1988), the FP technique and the MP technique applied to activated sludge flocculation, a process in which only aggregation and breakage mechanisms have significant dynamics. The authors concluded that when both mechanisms are present, the MP technique with a geometric grid of factor 2 is the most accurate method. A finer grid in the FP technique leads to an improvement in accuracy, but it is still worse than the one provided by the MP technique.

4.3. Method of weighted residuals

Rawlings et al. (1992) used the global orthogonal collocation for continuous crystallizers and orthogonal collocation on finite elements for batch mode. All simulations in this work were carried out using Petzold's differential–algebraic equation solver DASSL. Collocation and Galerkin FE algorithms were used by Nicmanis and Hounslow (1996, 1998) to solve the steady state population balance equation, using Lagrange cubic interpolation polynomials and evenly spaced nodes within each element. Simulations were performed for a large range of indices of aggregation, and included, besides aggregation, breakage, nucleation and particle growth. The algorithms were found to be able to accurately predict the number density with

reasonably small numbers of elements and the collocation and Galerkin methods made almost identical predictions and converged in similar numbers of iterations. The Galerkin algorithm, however, requires additional integrations that make this method computationally much more expensive than collocation method. The authors claim that the FE method proves to be able to predict two orders of magnitude more accurate than the results of the DPB developed by Litster et al. (1995) and that a mixed collocation-Galerkin formulation can be used to avoid the ill-conditioned matrices associated with growth problems.

The OCFE was also used by Crowley, Meadows, Kostoulas, and Doyle III (2000), Immanuel et al. (2002) and Doyle III, Harrison, and Crowley (2003), applied to the emulsion polymerization field, using Lagrange and Legendre interpolation polynomials.

Mahoney and Ramkrishna (2002) improved two refinements in the Galerkin's method on FE for the solution of PBEs for precipitation systems, in order to reduce the traditional drawbacks of this method: the time required for computation of the two-dimensional integrals arising from the aggregation integrals and the difficulty in handling discontinuities that often arise in simulations of seeded crystallizers. Linear basis functions were chosen. Computational costs were enormously reduced with the careful arrangement of invariant integrals of separable aggregation models. The discontinuities are proposed to be specifically tracked by the method of characteristics. It is found that the computation speed may be sufficient for dynamic online optimization.

A FE scheme was used by Rigopoulos and Jones (2003) with collocation linear elements and an upwind propagation of growth term. The method is claimed to be computationally much faster than higher-order FE collocation methods, such as cubic splines, or integral FE schemes, such as the Galerkin's.

5. Alternative numerical methods for solving the PBE

This section deals with some alternative methods to solve the PBE that are not included in the general classification of method of moments, discretization and weighted residual methods.

5.1. Integral method

A different approach in the modeling of particulate processes was made by Wynn and Hounslow (1997) by following the progress of particles since their insertion (through the feed flow or generation as nuclei) and computing their contribution to the eventual crystal size distribution (CSD). This approach leads to integrals from earlier times and smaller sizes until the present time and size, opposing to the traditional treatment of derivatives. It reduces to the characteristics method for a batch case, without nucleation and with length-dependent growth: particles in an interval are described by their characteristic curve, defined by the growth rate equation. Due to the differences in the growth rates between the lowest and the highest interval boundaries, the interval width changes, while the number of particles remains unchanged.

The integral approach can have more applications and it is easier to understand, having intuitive derivation in many cases. It can be employed to any residence-time distributions in continuous operations. Furthermore, it does not require the evaluation of the CSD in each time step, which can mean great computational time saving in applications where the detailed CSD is not needed in each instant.

The great disadvantage of this approach lies in its difficulty to cope with more complicated phenomena, like agglomeration.

5.2. Kinetics decomposition

Immanuel and Doyle III (2003) proposed other different approach based on employing individual rates of nucleation, growth and coagulation to update the PSD in a hierarchical framework, with a semi-analytical solution in the coagulation kernel, which reduces the computational requirement. Stiffness is claimed to be eliminated by the decomposition of the fast and the slow kinetics. The algorithm follows a two step strategy—one to calculate the individual rates of nucleation, growth and coagulation, and the other to update the PSD based on these individual rates. The method discretizes the size particle domain, but the proposed approach turns the method a completely different mathematical perspective other than a strictly DPB.

The method is applied to emulsion polymerization, but can be extended to other PBE systems. According to the authors, efficacy of the method in on-line feedback applications is guaranteed from a computational standpoint, while not losing any process information. In addition to this advantage, the current code is very robust to a variety of operating conditions that one might encounter in industrial practice, including very high nucleation rates.

5.3. Closed-form solution with the method of characteristics

Lee, Lee, Yang, and Mahoney (2002) used a closed-form of solution of the PBE, when the growth rate takes on a separable form of $G_t G_L$ in which G_t is the time-dependent part of the growth rate and G_L is the size-dependent part. The solution involves an integral along the characteristic curve and the analytical solution is given by the set of Eq. (39):

$$\begin{aligned} n(L,t) &= \frac{V(t_0)}{V(t)} n_{t_0}(L_b) \frac{G_L(L_b)}{G_L(L)} \quad \text{for} \quad L_b(L,t) \geq 0 \\ n(L,t) &= \frac{V(t_b)}{V(t)} n_{L_0}(t_b) \frac{G_L(0)}{G_L(L)} \quad \text{for} \quad t_b(L,t) \geq t_0 \end{aligned} \tag{39}$$

where t_0 is the start time of growth reaction. L_b and t_b are the birth size and birth time of the particle of size L at time t, respectively, and can be obtained by solving the following Eqs. (40) and (41):

$$\int_{L_b}^{L} \frac{1}{G_L(l)} \, \mathrm{d}l = \int_{t_0}^{t} G_t(t') \, \mathrm{d}t' \tag{40}$$

$$\int_{0}^{L} \frac{1}{G_L(l)} \, \mathrm{d}l = \int_{t_b}^{t} G_t(t') \, \mathrm{d}t' \tag{41}$$

This method is limited to absence of aggregation and breakage and to a separable form of the growth rate. The simulations are managed quickly and accurately, turning possible its use in on-line model-based control.

5.4. Parallel parent and daughter classes (PPDC)

A novel approach has been suggested by Bove, Solberg, and Hjertager (2005), but the technique is still limited to breakage and agglomeration problems, although the authors promise to extend it to include nucleation and growth in order to be applicable to wider classes of processes in which PBE is used.

The name of the technique comes from the generation of several distinct grids, parallel in the internal coordinate domain, each grid depending on the specific mechanism (aggregation, breakage). Breakage daughter classes are also parallel in the internal coordinate domain. In the PPDC method, the PBE is discretized in time using an explicit Eulerian time marching method and the density function is approximated by a finite set of Dirac's functions in order to assign function values just in the pivot sizes in each bin of the partition domain.

The advantages are the need to track very few classes, a better closure of the agglomeration processes and the improvement of the breakage mechanism accuracy with the increase in the number of breakage daughter classes.

6. Numerical results with the method of classes

This section is devoted to present a case study as an exemplification of a method application, in order to outline its numerical issues. The Method of Classes was selected, for its ease of implementation, and a FORTRAN code was written in order to simulate the batch cooling crystallization of adipic acid. Details about the code structure and the system features can be found in Costa, da Costa, and Maciel Filho (2005).

In order to test the numerical ability, many runs were made, which allowed acquisition of skill at the method. Some remarks may be, then, outlined about a few numerical issues.

As already pointed out by Kumar and Ramkrishna (1997), the set of ODEs produced with the Method of Classes (Eq. (18)) has the potential to produce negative values of the number of crystals in each class, when the kinetics that drives crystals out of a specific granulometric class is greater than the one responsible for the appearance of them. This is a point of concern that was not made clear in the development of the method. In the developed code (Costa et al., 2005), it was dealt merely by setting negative values of number of particles to zero. Apart from this point, the set of ODEs constitutes a very stiff-nonlinear system, which can cause oscillation in the numerical solution. It was already remarked in Costa et al. (2005) that some integrators are not suitable for the system solution. Fig. 1 illustrates this feature, showing the evolution of the number of crystals during batch time in the first and in the 25th granulometric classes in a run with 25 granulometric classes. The results were generated with the Euler method with three different time steps and with Runge–Kutta. The Euler integrator produces a lot of oscillation in the solution and this oscillation is more pronounced

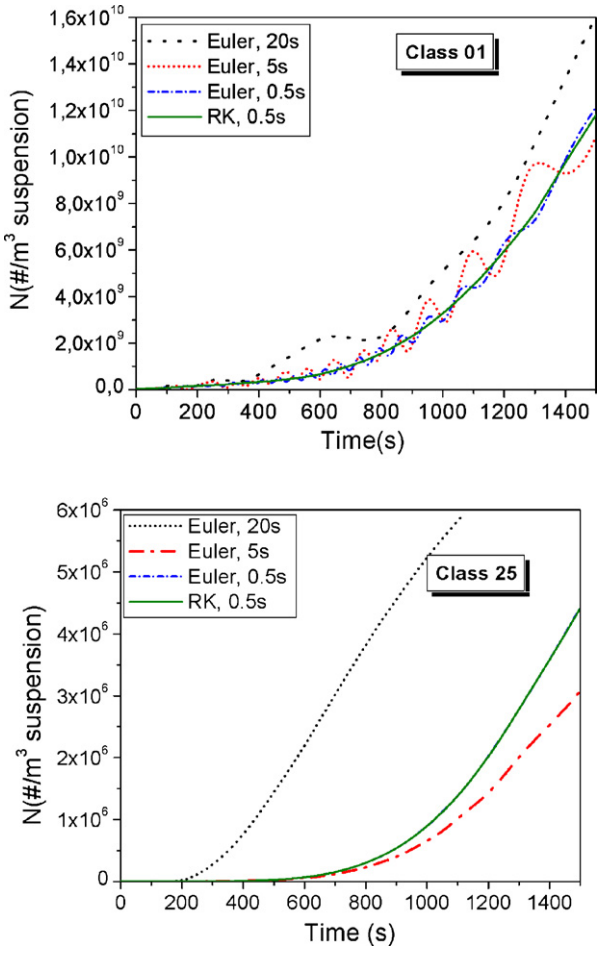

Fig. 1. Evolution of the number of particles per volume unit of suspension for the first and last classes.

with larger time steps and at the smallest granulometric classes. In the 25th granulometric class, the oscillation is of the order of 10^3 times smaller than the ones in the 1st class. Furthermore, for a time step of 0.5 s, there is no noticeable difference between the Euler and the Runge–Kutta solution (results are superimposed). It is evident, therefore, that the choice of an inappropriate integrator method could cause serious errors in crystallization calculations. The Fortran LSODAR code, developed by Petzold and Hindmarsh, is even better than the Runge–Kutta technique, since the former is a solver for ODEs with automatic method switching for stiff and nonstiff problems and with root-finding. Details about the solver can be found in Petzold (1980).

In order to evaluate the influence of the number of granulometric classes on the numerical result, the same system was simulated, with the same range of crystal size (from 0.01 to 1735.25 μm) and with the same amount (in mass) and size of seeds, but differing in the chosen number of classes (and, as a consequence, in the values of the characteristic sizes in each class). The set of ODEs was solved using LSODAR. Fig. 2 depicts the final CSD, both in mass and number percentage, for 5, 25 and 50 classes. The particle size in the right graphic of Fig. 2 was presented only up to 600 μm in order to increase its visualization in the smaller sizes range. It is clear that the number of classes is a key variable in the correct representation

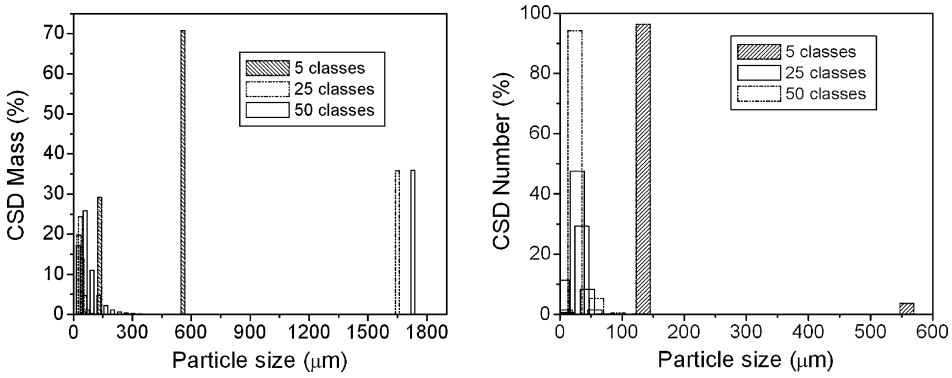

Fig. 2. Final CSD for different number of classes.

of the system. As the number of considered classes increases in the same size range, the solution is more accurate. The solutions with 25 and 50 classes are closer to each other than that of just 5 granulometric classes, but, since they are not superimposed, 50 classes is still not a enough number of classes for the method convergence. The main idea in the selection of optimal number of granulometric class is to increase it to the limit that produces no more change in the results (system minimization realization). Furthermore, the greater the number of granulometric classes, the better is the accuracy in the mass balance, a fact easily observed with the application of the Method of Classes.

Though the previous remarks represent disadvantages observed in the applicability of the method, it is easy to be implemented, leading to a very fast code, which took approximately 35 s to simulate a batch with 3000 time iterations in a AMD XP 2.4 GHz Processor with 50 granulometric classes. This is an important feature for on-line applications.

7. Conclusions

The present paper made a brief review in the numerical solution of the population balance model, discussing the difficulty in solving it, particularly when a complete set of mechanisms (nucleation, growth, agglomeration and breakage) is present, like in crystallization systems. Some important numerical methods developed in the literature in DPBs and in weighted residuals methods, besides different approaches, were presented and the major advantages and drawbacks were raised. Attention was given to the issues of numerical problems, computational effort and the correctness of prediction of the total number of particles and mass conservation. The discussion of the most used numerical methods and their limitations intends to be useful for the reader dealing with crystallization problems.

DPBs are a more natural choice when aggregation and breakage are included in the PBE. Notable developments are the ones of Kumar and Ramkrishna (1996a, 1996b, 1997), which allow to a free choice of grid and preserve two properties of interest (moments). Their method that includes nucleation and growth requires an adaptive grid and Lee et al. (2001) proposed an adaptive mesh method able to handle stiff nucleation problems, being able to deal with crystallization problems.

The weighted residuals methods are of more difficult implementation and are computationally demanding, but have the great advantage of being general and able to handle any formulation of the PBE. The computational burden was improved in the work of Mahoney and Ramkrishna (2002), turning the computational speed sufficient for dynamic online optimization.

As other presented methods, the integral approach has its limitations in the comprised kinetic mechanisms. The integral approach can save great computational time when detailed CSD is not needed in each instant, but cannot easily handle with agglomeration and breakage.

Acknowledgments

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4.3. Conclusões

Neste capítulo foi discutida a dificuldade de solução da PBE, especialmente em problemas de cristalização, em que os mecanismos cinéticos de nucleação, crescimento, aglomeração e, possivelmente, quebra estão presentes. A discretização do balanço de população é a escolha mais natural quando a aglomeração e quebra devem ser consideradas. Por outro lado, os métodos de resíduos ponderados têm a vantagem de ser mais gerais e capazes de lidar com qualquer formulação da PBE, embora sejam de implementação computacional mais difícil e dispendiosa.

Tendo sido apresentados a modelagem do processo de cristalização, a problemática de solução do balanço de população e um estudo preliminar de melhoria de processo, o capítulo seguinte apresenta a ferramenta desenvolvida para estudos de desenvolvimento de processos orientados a especificações de produto. A ferramenta faz uso da modelagem tanto para avaliar processos existentes quanto para buscar políticas operacionais que levem à obtenção de produtos com características definidas. Subseqüentemente, a ferramenta é utilizada para estudo de maneiras para alcançar CSDs desejadas em diferentes sistemas solvente–soluto.

Capítulo 5. Procedimento para Desenvolvimento de Processos Orientados para Especificações de Produto

5.1. Introdução

A área de projeto de produto aplicada à área de particulados demanda não mais somente pureza, mas também que o produto apresente CSD e morfologia específicas. Na área de projeto de processo, por outro lado, abordagens baseadas em modelo devem ser capazes de conduzir o processo para a máxima produtividade e para a redução de tempos e custos de retrabalho e limpeza. Neste capítulo, é apresentada uma ferramenta de engenharia de processos assistida por computador que foca em uma perspectiva ampla no projeto, tanto de processo quanto de produto, em uma operação de cristalização em modo batelada operado por resfriamento. A ferramenta abrange módulos para avaliação de processos, para projeto de política operacional ótima, em uma perspectiva dual processo-produto e para ajuste de modelo (estimativa de parâmetros). Alguns tópicos relacionados a cada módulo são discutidos, como os métodos disponíveis para a solução do modelo e para a otimização, assim como os desafios na área de projeto de produtos particulados.

Em seguida, um estudo é apresentado, em modo de engenharia reversa, que analisa a distribuição de cristais produzida ao final de uma batelada de cristalização operada por resfriamento em diversos sistemas solvente-soluto, submetidos a uma série de trajetórias de resfriamento previamente determinadas. A taxa de resfriamento utilizada durante a batelada determina os valores de supersaturação alcançados, o que delimita a extensão dos mecanismos cinéticos. Assim, diferentes sistemas solvente-soluto, representados por diferentes cinéticas de cristalização, são utilizados, de modo a permitir que seja determinado o efeito das taxas de resfriamento em diferentes sistemas sobre a distribuição final de tamanhos de cristal obtida. Este último estudo é bastante relevante segundo a ótica de projeto de produto,

uma vez que, a depender da cinética inerente a cada sistema, certas características de CSD são naturalmente favorecidas, como será exposto.

5.2. Desenvolvimento

O desenvolvimento deste capítulo é apresentado a seguir, nos artigos intitulados *Cooling Crystallization: a Process-Product Perspective* e *Achieving desired crystal size distributions by the properly manipulation of temperature profile in batch cooling crystallization processes*, publicados nos anais, respectivamente, do *ESCAPE 16 – 16th Europeran Symposium on Computer Aided Process Engineering* (v. 21A, p. 967-972, 2006) e do *ICheaP-7 – The 7th Italian Conference on Chemical and Process Engineering* (v. 6, p. 401-406, 2005).

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Cooling Crystallization: a Process-Product Perspective

Caliane Bastos Borba Costa, Rubens Maciel Filho

LOPCA, Chemical Engineering School (FEQ), UNICAMP, CP 6066, CEP 13081-970, Campinas – SP, Brazil

Abstract

This paper presents a CAPE tool that focus on a wide perspective to the process and product design in a batch cooling crystallization operation. The tool comprises modules for process evaluation, design of optimal operation policy, in a process-product perspective, and the adjustment of modeling (parameter estimation). Some issues concerned to each module are discussed, like the available methods for modeling solution and the optimization, as well as the challenges in the particulate product design field.

Keywords: crystallization, product design, process simulation, optimization, modeling

1. Introduction

The fast demanding market requires the development and increasing research in the area of product design, which devotes efforts in the design of specific products, for very specific purposes, such as drugs with controlled release of active ingredients or functional feed, in which additives may stimulate imune system or help in the cholesterol level control. In the particulate area, massively present in the high-value added chemicals and pharmaceutical industry, the product design nowadays demands not just purity, but also specific particle size distribution (PSD), particle shape and morphology, which represents an increase in the chemistry complexity (Ng, 2001). In the process design, on the other hand, model-based approaches must necessarily be able to drive to process designs that maximize productivity and reduce reprocessing/clean-up costs and time. Efforts should be driven to integrate both process and product requirements. In this scenario, the present paper presents a computer-aided tool to integrate process and product design for batch cooling crystallization, dealing with the issue of modeling and optimization as well as of the understanding of the product-process complexities.

2. Crystallization: Process and Product Design Concerns

The process design concerns the determination of the operating conditions (cooling rate, seeding policy and mixing) to produce the crystals, given the identity of the crystallizing product and the required yield. But the crystallization system does not exist in isolation and it does have an influence on the downstream processing system in which crystals are separated from solution and dried. Bearing the exposed in mind, not just yield is required, but also crystals features that are satisfactory for the downstream processing. In the present work, the process design is solved with CAPE methods, which integrate energy, mass and population balances, composing first principles understanding of materials and process to assure correct process representation

(modeling). Mathematical programming problems are formulated and solved in order to determine operating conditions that drive to achievement of required process yield.
On the other hand, the product design requires a look backwards in the process, in order to produce crystals with very specific features for the active ingredient to work properly (e.g. controlled release). In a lot of applications, PSDs often need to be maintened in specific ranges to ensure good quality indices. The proper PSD is, therefore, essential in product desings, being the critical link between the product quality indices and the operating process variables. Indeed, the achieved crystal-size distribution (CSD) in crystallization processes controls the end product quality and influences significantly the necessary liquid-solid separation. The population balance used in the modeling of the process can be used to accurately describe, analyze and control the CSD (Shi et al., 2006).
However, when a product is being designed from the beginning, a product is sought to meet a market need and then ideas are generated. The product must have a good performance (fulfill market need) and be convenient (ease of handling, minimal environmental impact) (Gani, 2004). If the product is a crystal, however, neither population balance nor mass and energy balances are able of predicting, for example, particle morphology when different solvents are used or the important solubility dependence on temperature. This sort of problem can be solved with molecular modeling, a research area of increasing interest, able of predicting product properties. It is still a challenge to integrate product and process design in a complex and complete CAPE tool (multi-level modeling tool), which could not only design a process to meet required yield and CSD of known properties, but also design the crystals properties. According to Gani (2004), the CAPE community has been an user/implementer of property models in various computer-aided application tools. For the current and future products, however, it is necessary to develop a new class of computer-aided methods and tools that is systematic but flexible, that is simple but accurate and most important, that can "create" the necessary models for a given problem.
In the present work a powerful and useful tool is presented, which itegrates the process and product designs of a crystal with known properties (solubility data, crystal morphology, and so on). Molecular issues are not covered by the tool; the properties are supplied as input data. The tool is able to cover various product-process crystallization design problem formulations, and to identify methods and policies to drive to optimal product design, constrained to economical or process/product issues.

3. Crystallization Modeling and Inter-relations in a Batch Crystallizer

The modeling of the process involves mass, energy and population balances. For a batch crystallization, these balances are represented by Eq. (1)-(3) respectively:

$$\frac{dC}{dt} = -3\rho_c k_v \int_0^\infty G(L,t)n(L,t)L^2 dL \tag{1}$$

$$\rho C_p V_{susp} \frac{dT}{dt} = -\Delta H_c 3\rho_c k_v V \int_0^\infty nL^2 G dL - UA_c\left(T - T_j\right) \tag{2}$$

$$\frac{\partial n}{\partial t} = -\frac{\partial\left(Gn\right)}{\partial L} - D(L) + B(L) \tag{3}$$

where *D(L)* and *B(L)* denote death and birth phenomena rate, which include agglomeration and breakage of existing crystals and nucleation of new ones. *G(L,t)* represents the growth rate. A_c is the heat transfer area, *C* the solute concentration, C_p represents the specific heat capacity, k_v the volume shape factor; *L* is the particle characteristic dimension, *n* is the density distribution of particles, *T* and T_j stand for the crystallizer and coolant temperatures, respectively. *U* denotes the global heat transfer coefficient, *V* and V_{susp} are the particle and suspension volumes, ΔH_c is the crystallization heat and ρ and ρ_c represent respectively suspension and particle densities. Among the kinetic mechanisms taking place in the crystallization process, nucleation and growth are the dominant ones, but in many systems, agglomeration and breakage are present to a certain extent, that must be considered into the modeling.
The developed CAPE tool deals with nucleation, growth and agglomeration. Fig. 1 depicts the general framework for the batch crystallization evolution.

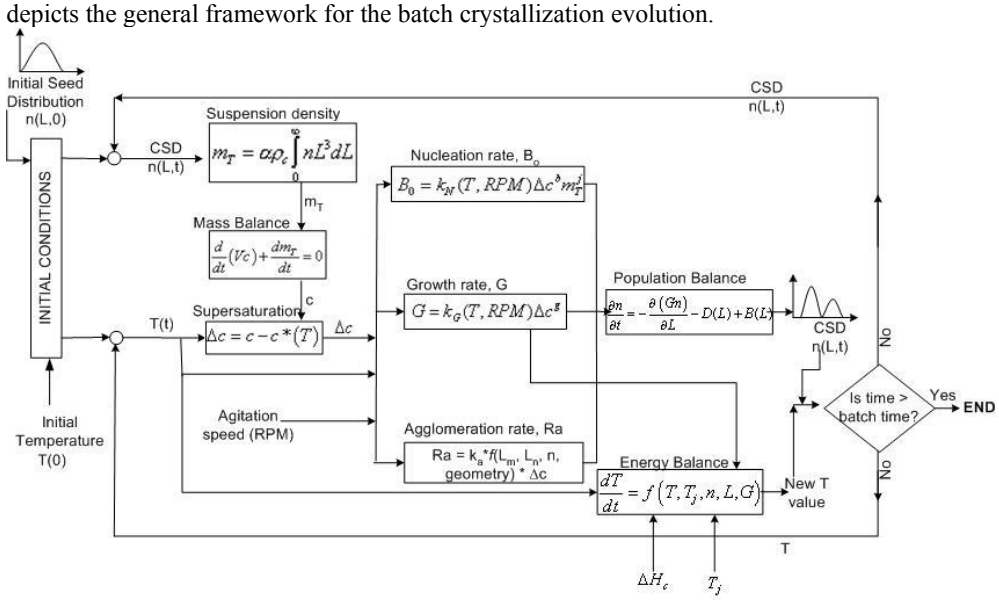

Fig. 1: General framework for the inter-relations among the conservative equations in a batch crystallizer.

Mass and energy balances are easily handled by numerical methods of ODEs solution. The population balance equation (PBE), Eq. (3), however, is a partial hyperbolic differential equation, with no analytical solution and requires development and adaptation of numerical techniques. The developed CAPE tool makes use of the Method of Classes (Marchal et al., 1988; David et al., 2003) and the vastly known Orthogonal Collocation Method to solve the PBE. Both methods transform the partial differential equation in a set of ODE, solvable by public recognized codes, like DASSL.

4. CAPE Tool for Batch Crystallization

The process-product design integration is achieved in the developed CAPE tool by incorporating the stages of both process and product problems into one integrated structure. It turns possible also cooling crystallization processes evaluation, i.e., perform an analysis of the present operating conditions and trial of new alternatives in order to improve sustainability indices based on product design.

The optimal process design, defined in terms of product feature requirements, may be obtained through optimization in terms of minimizing (or maximizing) both single or a multiparametric performance function. The step of optimizing a product design to meet a set of requirements of diferent production stages is an increasing area of interest and research, which is supported by CAPE tools development. Good understanding of the target product properties is essential to achieve optimal design.
Optimizing crystallization process, with focus on the integration of process-poduct design, is dealt in the developed CAPE tool both with Successive Quadratic Programming (SQP) and Genetic Algorithms (GAs). The latter is very attractive in simultaneously evaluating extremely different process conditions, in order to detect the region of global optimum operation. Fig. 2. brings, in a schematic way, the working structure of the CAPE tool, with three main modules: Process Evaluation, Process-Product Perspective, Modeling Adjustment. Due to the limitation of pages, it is not possible to get into details of each module unit. The code for each module is independent but make use of common sub-routines, like the one that contains the process modeling or the optimization codes

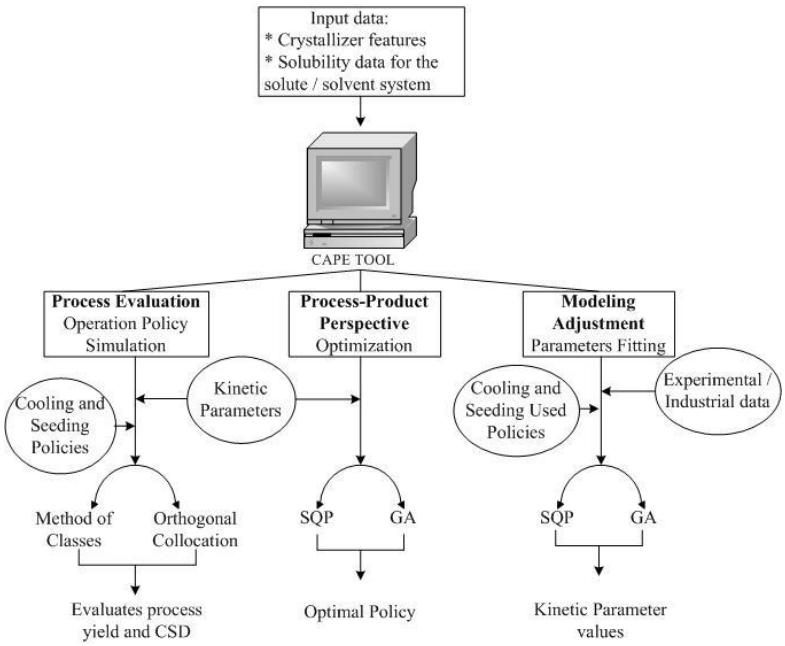

Fig. 2: Crystallizer CAPE tool and its modules structure.

Both modules of Process-Product Perspective and of Modeling Adjustment make use of optimization methods, that is, the problems covered by these modules are translated into optimization ones. For example, looking through a process-product perspective, the optimization is formulated with an objective function (actually, it is possible to define just one objective function, characterizing a single objective problem, or two or more objectives, composing a multi-objective optimization problem) that translates both product and process goals (for example, minimization of the coefficient of variation of the CSD and maximization of the mean crystal size). This objective function is constrained to a set of equality and inequality constraints related to process design

specification (such as physical operation ones and minimum acceptable yield) and a set of equality constraints representing the process model equations (mass, energy and population balances).

Process-product design problems may become too complex to solve if the model is highly non-linear and discontinuous, although in principle, a global solution could be obtained. Actually, this is the case of models dealing with PBE. Generally, optimization problems can be solved through deterministic and heursitic methods. The developed tool makes use of both of them, with Successive Quadratic Programming, SQP, (deterministic method) and Genetic Algorithms, GA, (an evolutionary algorithm, part of the heuristic procedures). Fig. 3, in which *maxgen* stands for the maximum number of generations, brings the main steps in each one of these methods. SQP is an iterative procedure, which makes use of the objective function and its derivatives in order to generate a new (better) solution. On the other hand, GA initializes a population of possible solutions and evolves the individuals with the genetic operators (selection, crossover, mutation) during some generations in order to get "fitter" solutions.

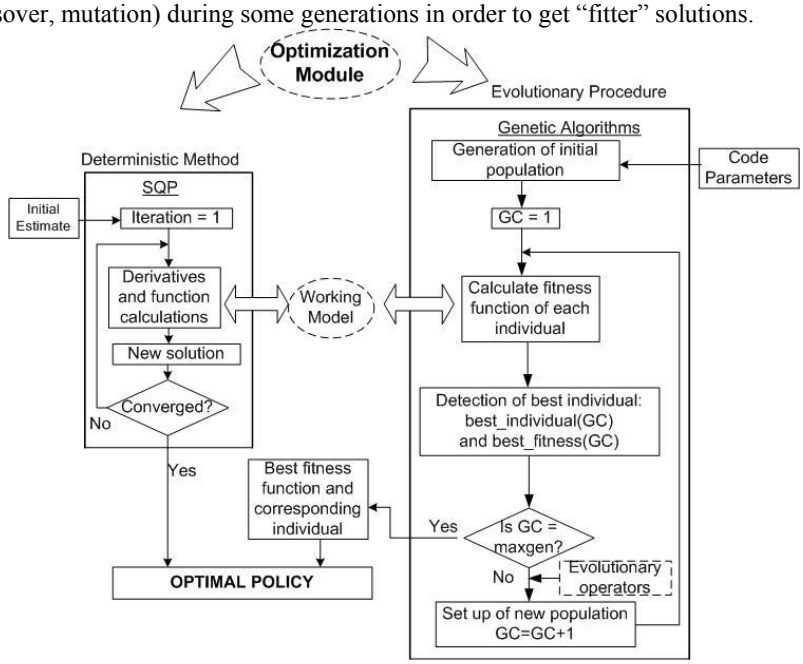

Fig. 3: Optimization Module, used both in Process-Product Perspective and in Modeling Adjustment Modules.

The developed tool provides evaluation of existing processes, understanding of the product-process complexities, evaluation of obtained products features (CSD) in extremely different kinetic systems with different operating policies, as well as optimizing both product and process in order to obtain the optimal policy to be implemented in the batch process. Fig. 4 brings examples of modules responses. On the left, two optimal cooling profiles are presented (for minimizing the coefficient of variation of the final CSD), as well as the non-optimized cooling policy. It is an illustrative example of two optimal responses from the Process-Product Perspective Module, each one using one type of method (deterministic and heuristic ones). The SQP response is dependent on the initial estimate and the optimal policy for the two methods were different. The CSDs depicted on the right of Fig. 4 illustrates how the system can

produce completely different responses, reflected in terms of final obtained CSDs, depending on the employed cooling policy. As a last powerful option, the user can obtain the kinetic parameters of a solute-solvent crystallizing system, given the employed policies and the the system response (experimental / industrial data).

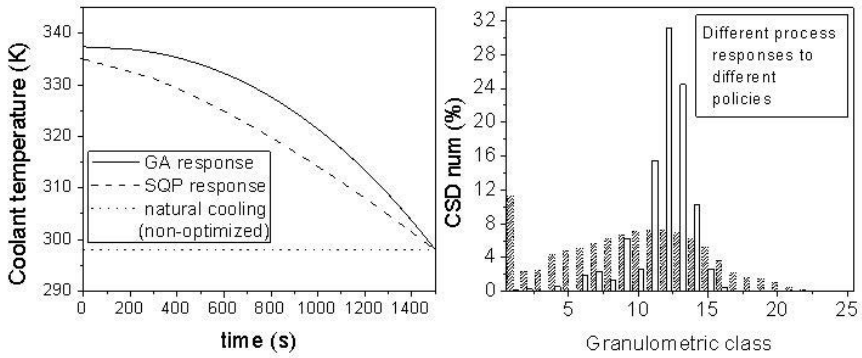

Fig. 4: CAPE tool response for two different problems: optimization of product-process (left) and processes simulations (right) in order to evaluate obtainable CSDs with different cooling and seeding policies.

5. Conclusions

The development of tools for process-product design integration is essential to carry out extensive evaluations so that decisions can be taken in an early stage of design leading to robust and relatively easy to operate process. Bearing this in mind, in this work it was developed a computer-aided tool able to integrate process and product design for batch cooling crystallization, dealing with the issue of modeling and optimization taking into account the product-process interactions. This was achieved through the incorporation of the stages of both process and product problems into one integrated structure. To do so, the process design is solved with CAPE methods, which integrate energy, mass and population balances and mathematical programming problems are formulated and solved in order to determine operating conditions that drive to achievement of required process yield. The product quality specifications are considered trough the particle size distribution maintained in specific ranges to ensure good quality indices.

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Achieving desired crystal size distributions by the properly manipulation of temperature profile in batch cooling crystallization processes

C.B.B. Costa, R. Maciel Filho
Chemical Engineering School, State University of Campinas (UNICAMP)
Cidade Universitária Zeferino Vaz, CP 6066, CEP 13081-970, Campinas- SP, Brazil

The present work proposes to study the crystal size distribution produced at the end of a batch cooling crystallization as a consequence of the imposition of different temperature profiles, as well as of the different kinetic features of the system. The rate of cooling used during the batch determines the values of supersaturation achieved, which characterize the extent of the kinetic mechanisms. Nucleation and growth are the most dominant phenomena in the crystallization process. Apart from them, other phenomena, such as agglomeration and breakage, may occur. Neglecting agglomeration may result in poor representation of reality, especially when the crystallizing substance is classically known as having an agglomerating behavior.

In this way, different systems, expressed by different crystallization kinetics, are studied with the imposition of very different temperature profiles in order to provide analyses of the effect of the cooling rates in different systems on the final crystal size distribution obtained. The optimal temperature profile depends on the desired application of the product, since it can favor the production of more fines or greater crystals. Systems characterized by having strong growth kinetics naturally disfavour nucleation, while strong secondary nucleation tend to produce many fines. Stronger agglomeration kinetics leads to the production of more particles with larger sizes.

1. Introduction

Batch crystallization is the preferred process in pharmaceutical, specialty and fine chemicals industries for obtaining their products, due to the purity achieved and to the flexibility of operation offered by batch operation (Choong and Smith, 2004; Ma et al., 2002). Nevertheless, the operation employed in the crystallizer during the batch determines the final crystal size distribution. Depending on the further processing of the crystallized material and on its application, the optimal crystal size distribution may exhibit different features: in industrial crystallization of an intermediate, it may be interesting to produce large crystals, with a small standard deviation of the particle distribution. In pharmaceuticals applications, otherwise, it may be desirable to have a large amount of very small crystals. Optimal operation is then important to improve the efficiency of the overall process and this optimum must be determined in terms of the extent, in each batch instant, of the kinetic phenomenon that governs the extraction of solute from solution and its deposition into crystal lattice (Zhang and Rohani, 2003).

The driving force for these phenomena is the supersaturation, which, in batch cooling crystallization, is achieved through the cooling of the solution (Choong and Smith, 2004).

In order to determine the optimal operation, it is, therefore, important to know the system response to different temperature profiles. Furthermore, depending on the system to be processed, different kinetics responses may be present and, hence, different crystal size distribution (CSD) responses are to be expected. The present study analyses the influence of both different imposed temperature profiles and different system kinetics on the final CSD.

2. Kinetic Phenomena and their Mathematical Equations

The model comprises the phenomena of primary and secondary nucleation (Rn_1 and Rn_2, respectively), growth (G) and binary agglomeration (R_A). The proposed mathematical expressions to represent these mechanisms rates are the empirical equations (1) to (7).

$$\mathrm{Rn}_1 = A\exp\left[-\frac{B}{\ln^2\left[\frac{(HR)}{(HR)*}\right]}\right] \tag{1}$$

$$\mathrm{Rn}_2 = \mathrm{k_n}\left[(HR)-(HR)*\right]^{j} C_s^{\mathrm{k}} \tag{2}$$

$$G = \frac{k_a MM \quad k_c}{3\rho_c k_v}\eta_r (c-c^*)^{j} \tag{3}$$

$$R_{A,i} = \sum_{l=1}^{\frac{N(N+1)}{2}} \nu_{est\ l,i}\, r(l) \tag{4}$$

$$\nu_{est\ l,i} = \left(\frac{S_m^3 + S_n^3}{S_q^3}\right)\delta_{i,q} - \left(\delta_{i,m} + \delta_{i,n}\right) \tag{5}$$

$$r = k_A S_m \left(1+\frac{S_n}{S_m}\right)^2 \cdot N \cdot \mathrm{Diam} \cdot f\left(\frac{S_n}{S_m}\right)\cdot\left[1-\frac{\left(S_n+S_m\right)^2}{\lambda_e^2}\right]\cdot k_D (c-c^*)\cdot N_n \cdot N_m \cdot H(S_m-\delta)\cdot \cdot H\left(\lambda_e - S_n - S_m\right) \tag{6}$$

$$f\left(\frac{S_n}{S_m}\right) = \frac{4\left(1+\frac{S_n}{S_m}-\sqrt{\left(\frac{S_n}{S_m}\right)^2-1}\right)}{\frac{1}{3}+\frac{S_n}{S_m}-\sqrt{\left(\frac{S_n}{S_m}\right)^2-1}-\left(\frac{S_n}{S_m}-\sqrt{\left(\frac{S_n}{S_m}\right)^2-1}\right)^2\left(\frac{2\frac{S_n}{S_m}}{3}+\frac{\sqrt{\left(\frac{S_n}{S_m}\right)^2-1}}{3}\right)} \tag{7}$$

In the adjustment of the kinetic expressions to the physical crystallizing system, the kinetic parameters must be estimated. These parameters are A and B for primary nucleation, kn', i' and k' for secondary nucleation, kc and j' for growth and ka' for agglomeration. During this study, the values for these parameters were varied, in order to simulate systems characterized by different kinetics of crystallization.

3. Analyzed Systems and Temperature Profiles

In order to study the influence of the imposition of different temperature profiles, eight different coolant temperature profiles were selected. The choice of the imposed cooling profile was made arbitrarily, with the restriction that it could vary only between 340K and 298K (due to the solubility curve imposed and operating conditions). It was imposed only decreasing temperature profiles, due to the need for cooling the crystallizer solution for the beginning and progress of the process. The eight imposed temperature profiles are illustrated in Figure 1.

The eight different imposed temperature profiles were selected in order to analyse different temperature rates during the process. In this way, the first temperature profile represents natural cooling (constant coolant temperature), while the second represents a linear decrease of temperature. The third and fourth profiles are arbitrarily strictly concave curves. Strictly convex curves are described by the fifth and sixth profiles. Finally, the seventh and eighth curves are composed part by convex and part by concave curves.

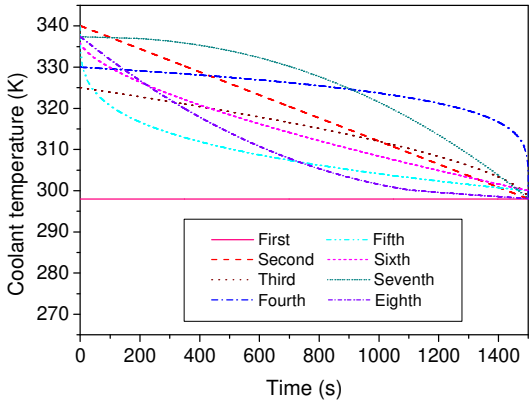

Figure 1: Coolant temperature profiles imposed during the study.

The simulation of different systems, characterized by different rates of nucleation, growth and agglomeration were made through the variation of some parameters values. A standard system was adopted, and the variations were made, accelerating or slowing down a particular mechanism. Table 1 brings the values of the standard parameters and of the parameters with variation in kinetics. Just secondary nucleation, and not primary nucleation as well, had a strong kinetics tested during the present study, because

primary nucleation hardly ever occur in industrial practice. Primary nucleation only happens when there is a complete absence of the solute crystals in the solution, a situation nearly impossible to happen in real practice.

Table 1: Parameters values in each case studied

Parameter	Standard	Strong secondary nucleation	Strong growth	Weak growth	Strong agglomeration
A	2.0×10^{15}	2.0×10^{15}	2.0×10^{15}	2.0×10^{15}	2.0×10^{15}
B	40.0	40.0	40.0	40.0	40.0
kn'	1.0	**2.0**	1.0	1.0	1.0
i'	1.0	**1.5**	1.0	1.0	1.0
k'	2.0	**4.0**	2.0	2.0	2.0
kc	1.0×10^{-7}	1.0×10^{-7}	$\mathbf{1.0 \times 10^{-7}}$	$\mathbf{1.0 \times 10^{-7}}$	1.0×10^{-7}
j'	2.0	2.0	**4.0**	**0.5**	2.0
ka'	1.0×10^{-6}	1.0×10^{-6}	1.0×10^{-6}	1.0×10^{-6}	$\mathbf{1.0 \times 10^{-3}}$

4. Results

In order to analyze just the influence of the different temperature profiles, the eight system responses to them were compared using the standard system kinetics. The first temperature profile is the one that produces the greatest coefficient of variation of the final crystal size distribution and produces the largest amount of fines among all profiles. It is also the profile that causes the most mass extraction from solution. This is somewhat expected, since the large temperature difference between the solution inside the crystallizer and the coolant just in the beginning of the process causes a sharp solution temperature decrease and, consequently, great supersaturation, favouring nucleation, instead of growth. The largest crystals – more than the double of the mean crystal size of the first temperature profile - and smallest coefficient of variation of the distribution are produced with the fourth profile, which is characterized by very smooth coolant temperature decrease during the most part of the process, with a sharp decrease at the final instants of the batch. This causes disfavouring of nucleation, letting the added seeds to grow. Nevertheless, this slow evolution of the process leads to only around 16% of the mass extraction achieved with the first temperature profile. The seventh profile produces an interesting result, extracting considerable mass of crystals (around 83% of the one produced with the first profile), with crystals around 42% greater than the mean crystal size of the first temperature profile and with the smallest coefficient of variation among all profiles (except by the one corresponding to the fourth temperature profile). It can be observed that the seventh temperature profile, as the fourth one, but not so marked, is characterized by having smaller first derivative of temperature at the beginning of the batch and increasing one with the advance of the process. In this way, depending on the application desired, the optimal temperature profile may be characterized by having the features as in the 4^{th} /7^{th} ones or the 1^{st}/5^{th}/6^{th} ones. Figure 2 exhibits the final crystal size distributions obtained with the imposition of the eight temperature profiles.

The different system kinetics may deviate the system response towards a particular direction, due to a marked kinetic contribution of any mechanism. With the purpose of evaluating kinetics' influence, the response to different kinetics is here evaluated.

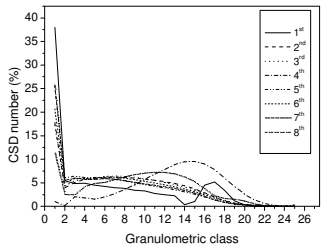

Figure 2: Final CSDs in the standard kinetics sytem with the 8 temperature profiles

Systems characterized by having strong growth kinetics naturally disfavour nucleation, leading to final CSD with a great improvement in the coefficient of variation of the distribution (smaller values) and move up of the CSD towards greater sizes, regardless of the imposed temperature profile. An inverse analogy may be traced when the system is characterized by having weak growth rate. The imposed temperature profiles cause similar influences as already discussed in previous paragraph. Figure 3 brings a comparison between the final CSD with a standard kinetics and with a strong growth rate for two temperature profiles.

The marked secondary nucleation in crystallizing systems tends to produce very large amount of small particles, no matter which temperature profile is imposed. Figure 4 brings the final CSD with a standard kinetics and with a strong secondary nucleation rate for some temperature profiles.

The influence of the agglomeration behavior was evaluated, by increasing the kinetics of agglomeration and comparing the final CSD. Figure 5 brings the result of the final CSD for the seventh temperature profile, both for standard kinetics and with accelerated agglomeration behavior. It can be observed that the agglomeration tends to produce more particles with larger sizes, due to the joining of particles.

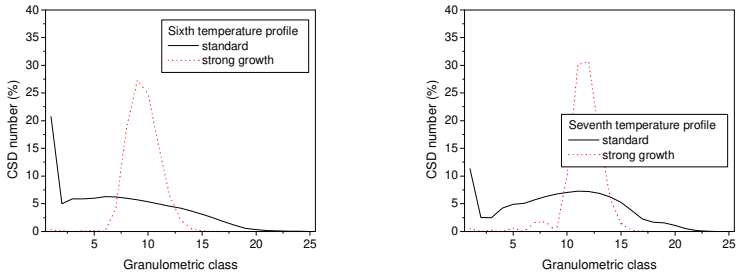

Figure 3: Final CSDs with standard kinetics and with strong growth.

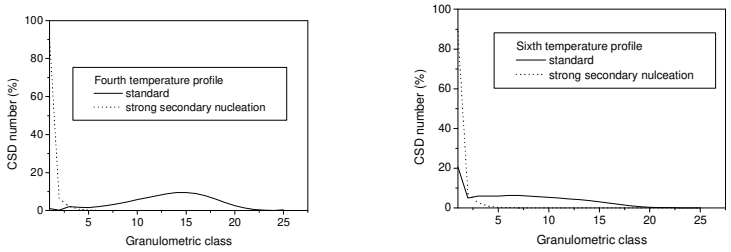

Figure 4: Final CSDs with standard kinetics and with strong secondary nucleation rate.

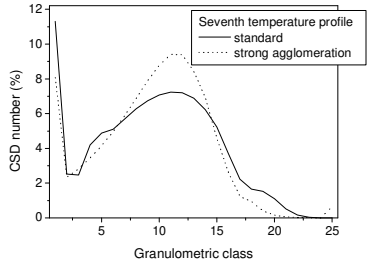

Figure 5: Final CSDs with standard kinetics and with strong agglomeration rate.

5. Concluding remarks

The present study analysed the influence of different temperature profiles and of different system kinetics on final responses of batch cooling crystallization systems. The choice of the best temperature profile is a matter of the desired application of crystals produced, as well as of the downstream processing of the particles, since it can favour the production of more fines or larger particles. Nucleation is disfavoured naturally if the system presents strong growth kinetics, while it is extremely difficult to produce larger particles if the system is characterized by having strong secondary nucleation kinetics. As it is expected, the more pronounced the agglomeration, the greater the number of particles with larger sizes produced.

6. References

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5.3. Conclusões

Este capítulo apresentou uma ferramenta computacional para integrar projeto de produto e processo de cristalização em modo batelada operado por resfriamento. A ferramenta envolve módulos de avaliação de processos, de projeto de processo–produto e de ajuste de parâmetros do modelo. As especificações de qualidade do produto foram consideradas através da distribuição de tamanho de partículas em extensões específicas. O estudo do perfil ótimo de temperatura mostrou que este depende da aplicação desejada do produto, uma vez que ela pode favorecer a produção de mais finos ou de maiores cristais. Sistemas caracterizados por ter cinéticas de crescimento fortes desfavorecem naturalmente a nucleação, enquanto cinéticas de nucleação secundária fortes tendem a produzir maiores finos. Aglomeração marcada por forte cinética leva à produção de mais partículas de tamanhos maiores. Dessa forma, o exato perfil de temperatura (supersaturação) que seja solução de um problema de otimização dependerá dos valores dos parâmetros do modelo, que são particulares para cada sistema solvente-soluto, e da função objetivo.

O capítulo a seguir se dedica a fazer um estudo criterioso da otimização da trajetória de resfriamento empregada na cristalização batelada de ácido adípico. Uma vez que o estudo preliminar de otimização apresentado no Capítulo 3, que se utilizava de discretização da variável de controle e do método determinístico SQP de otimização, demonstrou que a abordagem utilizada não possuía a habilidade necessária para lidar com o problema, a utilização de um método estocástico de otimização (especificamente o Algoritmo Genético) e a parametrização da variável de controle são avaliadas.

Capítulo 6. Otimização de Cristalização por Métodos Determinísticos e Estocásticos

6.1. Introdução

A otimização matemática de um processo de cristalização em modo batelada operado por resfriamento é o foco deste capítulo, que tem como objetivo minimizar o desvio padrão da distribuição final de tamanho de cristal (CSD final), o que é requerido em muitos processos industriais. Devido aos resultados preliminares obtidos no Capítulo 3, que demonstram ser o método SQP altamente dependente da estimativa inicial (característica de métodos de busca local, dentro dos quais se enquadra o SQP) e incapaz de lidar apropriadamente com a alta dimensionalidade e alta não-linearidade do problema, o Algoritmo Genético (AG), método estocástico de otimização bastante estabelecido na literatura, é avaliado conjuntamente com a parametrização da variável de controle. Essa parametrização é também acoplada ao SQP para verificação de seu desempenho. Os resultados obtidos com a variável de controle parametrizada, tanto com a utilização do método determinístico quanto com o método estocástico, são comparados com os resultados obtidos no Capítulo 3 (utilização de SQP conjuntamente com discretização da variável de controle).

6.2. Desenvolvimento

O desenvolvimento deste capítulo é apresentado a seguir, no artigo intitulado *Evaluation of optimisation techniques and control variable formulations for a batch cooling crystallization process*, publicado no periódico internacional *Chemical Engineering Science* (v. 60, p. 5312 – 5322, 2005).

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Evaluation of optimisation techniques and control variable formulations for a batch cooling crystallization process

Caliane B.B. Costa*, Rubens Maciel Filho

Chemical Engineering School, State University of Campinas (UNICAMP) Cidade Universitária Zeferino Vaz, CP 6066, CEP 13081-970 Campinas-SP, Brazil

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Abstract

The mathematical optimisation of a batch cooling crystallization process is considered in this work. The objective is to minimize the standard deviation of the final crystal size distribution (CSD), which is an important feature in many industrial processes. The results with the problem written as a nonlinear programming and solved with the successive quadratic programming (SQP) coupled with the discretization of the control variable are compared with those obtained when SQP coupled with the parameterisation of the control variable is applied. Also it is proposed the implementation of the genetic algorithm (GA) coupled with parameterisation of the control variable. Extensive evaluations show that the SQP method is sensitive both to the parameterisation formulation and to the initial estimate. The solution with GA provided the control variable profile that leads to the minimum standard deviation of the final CSD. Nevertheless, it is a very time-consuming technique, which hampers its utilization in real time applications. However, its feature of global searching suggests its suitability in solving offline problems, in order to provide initial setup profiles. Bearing this in mind, it is proposed an algorithm which allows for the implementation of GA solution in a real time fashion, taking advantage of its robustness to find out the optimal solution.

Keywords: Batch; Crystallization; Dynamic simulation; Genetic algorithm; Optimisation; Successive quadratic programming

1. Introduction

Crystallization is a very important unit operation, used in many processes mainly because it leads to the formation of particulate material with high purity. This can be carried out either in a continuous or batch operation mode. Batch operation offers the flexibility required when there are many simple steps to be executed, with changing recipes. In this way, batch crystallization is the preferred process in pharmaceutical, specialty and fine chemicals industries for obtaining their products. Nevertheless, the operation employed in the crystallizer during the batch influences all the subsequent processes (downstream processing), since the solids produced constitutes a mass of particulate material, which may exhibit an infinite number of different features, like habit, crystal size distribution (CSD) or solvent hindering (Ma et al., 2002). Optimal operation is then important to improve the efficiency of the overall process and, in the batch crystallization field, this optimum must be determined in terms of the extent, in each batch instant, of the kinetic phenomena that governs the extraction of solute from solution and its deposition into crystal lattice. The driving force for these phenomena is the supersaturation, which, in batch cooling crystallization, is achieved through the cooling of the solution. Therefore, many optimisation studies in batch cooling crystallization are focused on finding the optimal cooling profile in order to improve the process performance (Costa et al., 2005; Lewiner et al., 2002; Zhang and Rohani, 2003). In fact, the cooling profile is a dominant item in terms of operational policy and two questions arise at this point,

* Corresponding author. Tel.: +55 19 3788 3971; fax: +55 19 3788 3965.
E-mail address: caliane@lopca.feq.unicamp.br (C.B.B. Costa).

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to know, how to find out a suitable and feasible to implement cooling profile and how adequate are the design features, which may be a limitation to practical implementation in real situations.

The solution of an optimisation problem can be found through either a deterministic or a stochastic approach. The former composes the traditional optimisation methods (direct and gradient-based methods) and have the disadvantages of requiring the first and/or second-order derivatives of the objective function and/or constraints. This implies that such approach is not efficient in non-differentiable or discontinuous problems. Furthermore, the deterministic methods, such as Successive Quadratic Programming (SQP), are dependent on the chosen initial solution (da Costa and Maciel Filho, 2004; Deb, 1999). The stochastic methods, such as Genetic Algorithms (GA), do not possess these drawbacks. GAs are part of the so-called evolutionary algorithms and compose a search and optimisation tool with increasing application in scientific problems (Deb et al., 2004; Hanai et al., 2003; Immanuel and Doyle, 2002; Sarkar and Modak, 2003, 2004; Upreti, 2004). They do not need to have any information about the search space, just needing an objective/fitness function that assigns a value to any solution. Details about the working principle of GAs can be found elsewhere (Deb, 1998, 1999; Fühner and Jung, 2004).

The main objective of the present work is the evaluation of deterministic (SQP) and stochastic (GA) optimisation algorithms applied to a batch cooling crystallization system, coupled with different formulations of the problem in the dynamic optimisation, concerning the control variable. This is an important point to be dealt with, since it has impact on the numerical procedure performance as well as on the equipment design. The control functions in a dynamic optimisation problem can be discretized or parameterised and it is necessary to access the advantages and drawbacks of each approach. In the present work, the optimisation of the batch cooling crystallization of adipic acid (Costa et al., 2005) is addressed, which is typical of many processes of industrial importance. The objective is to minimize the standard deviation of the final crystal size distribution. Costa et al. (2005) optimized the same process using SQP coupled with discretization of the control variable (coolant temperature). Although this optimizing method is less time consuming than the evolutionary algorithms, it is highly dependent on the initial estimate, as exposed by Costa et al. (2005).

In the present study, the dynamic optimisation is considered with a parameterisation of the control variable and the optimisation is solved both by SQP and GA. These results are compared with the best result obtained through the discretization of the control variable coupled with optimisation by SQP (Costa et al., 2005). As the GA methods are usually not suitable for real time implementation, in this work an algorithm to deal with this matter is proposed.

2. Theoretical fundamentals

2.1. Batch cooling crystallization

In a batch cooling crystallization operation, the solution is cooled in order to create a supersaturation into the system, which is the driving force for the kinetic mechanisms. The nucleation and growth are the most dominant phenomena. Apart from them, other phenomena, such as agglomeration and breakage, may occur during the process, making it difficult to carry out reliable predictions. Neglecting agglomeration may result in poor representation of reality, especially when the crystallizing substance is classically known as having an agglomerating behaviour (Costa et al., 2005). Fig. 1 shows a scheme of the batch cooling crystallization. Figs. 2 and 3 bring the CSD at the end of the batch, both in mass and number fractions, for the same batch cooling crystallization system, differing each other in the inclusion or not of the agglomeration mechanism. It is clear from both figures the importance of not neglecting the agglomeration mechanism when it is of real occurrence, since its presence (and extent) alters significantly the final CSD obtained.

The modelling of the process involves mass, energy and population balances. This latter is a general approach and constitutes a complex partial differential equation, which accounts how the kinetic phenomena alter the population density both in size and time. Eq. (1) is the general form of the population balance equation for a well-mixed crystallizer, where $B(L)$ and $D(L)$ represent the birth and death rates, in which the effects of abrasion, breakage, agglomeration and dissolution are accounted; $\mathbf{v}_i$ is the internal velocity vector, orientated according to an internal orientation system; and $\dot{V}_i$ represents inlet and outlet streams particle volumetric rates.

$$\frac{\partial n}{\partial t}+\nabla \mathbf{v}_i n+n\frac{\partial V}{V\partial t}+D(L)-B(L)+\sum_k \frac{\dot{V}_i\cdot n_i}{V}=0. \quad (1)$$

A lot of work in literature (Kiparissides, 2004; Puel et al., 2003; Rawlings et al., 1993) reviews the many techniques

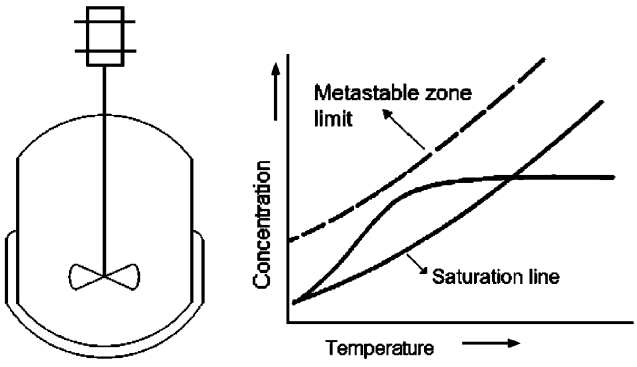

Fig. 1. Schematic drawing of the batch cooling crystallizer and the concentration versus temperature curve, showing a hypothetical cooling profile.

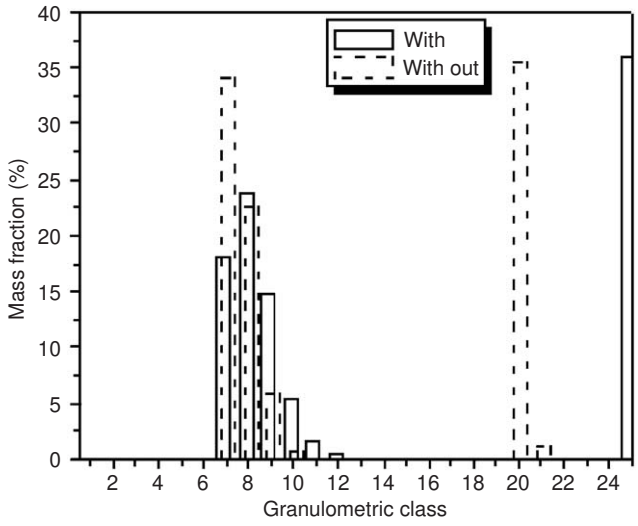

Fig. 2. Mass fraction in each particle size for the same system with and without inclusion of agglomeration into the model.

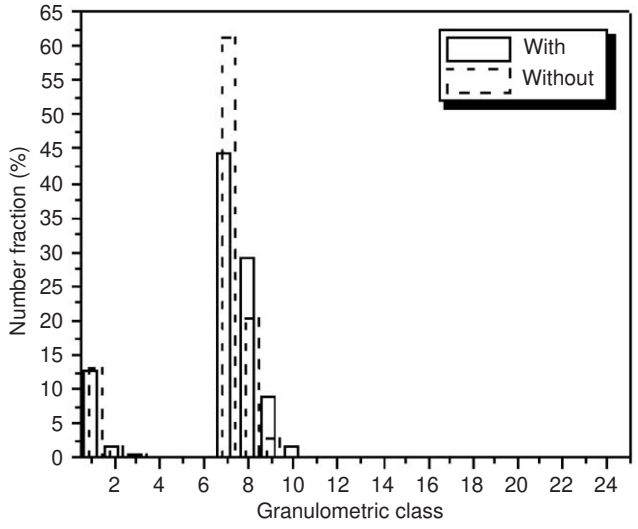

Fig. 3. Number fraction in each particle size for the same system with and without inclusion of agglomeration into the model.

and methods used to solve the population balance equation (PBE). In the present work, the Method of Classes (Costa et al., 2005; Marchal et al., 1988; Nallet et al., 1998; Puel et al., 2003) is used to solve the population balance equation. It is worth mentioning that the model of the process is highly nonlinear. The mean model equations are composed by Eqs. (2)–(4), which represent, respectively, the population, mass and energy balances, coupled with the kinetic equations for the growth, nucleation and aggregation mechanisms, Eqs. (5)–(8). More details about the model used, its validation and resolution can be found in Costa et al. (2005)

$$\begin{cases} \frac{dN_1}{dt} + \frac{1}{V_{susp}}\frac{dV_{susp}}{dt}N_1 + \frac{G(L_1)}{2\Delta C_2}N_2 \\ \quad + \frac{G(L_1)}{2\Delta C_1}N_1 = r_N + R_{A,1} - R_{B,1}, \\ \frac{dN_i}{dt} + \frac{1}{V_{susp}}\frac{dV_{susp}}{dt}N_i + \frac{G(L_i)}{2\Delta C_{i+1}}N_{i+1} \\ \quad + \frac{G(L_i)-G(L_{i-1})}{2\Delta C_i}N_i - \frac{G(L_{i-1})}{2\Delta C_{i-1}}N_{i-1} \\ \quad = R_{A,i} - R_{B,i}, \\ \frac{dN_N}{dt} + \frac{1}{V_{susp}}\frac{dV_{susp}}{dt}N_N + \frac{-G(L_{N-1})}{2\Delta C_N}N_N \\ \quad - \frac{G(L_{N-1})}{2\Delta C_{N-1}}N_{N-1} = R_{A,N} - R_{B,N}, \end{cases} \tag{2}$$

$$V_0C_0 = \frac{(H^+)^2}{K}\left[1 + \frac{K}{(H^+)}\right]V_0 + \frac{V_0}{1 - \frac{MM}{\rho}C_s}C_s, \tag{3}$$

$$\rho C_p V\frac{dT}{dt} = -\Delta H_c 3\rho_c k_v V_{susp}\int_0^\infty nL^2 G\,dL - UA_c(T - T_c), \tag{4}$$

$$G = \frac{dL}{dt} = \frac{k_a MM\ k_c}{3\rho_c k_v}\eta_r(c - c^*)^{j'}, \tag{5}$$

$$r_{N1} = A\exp\left[-\frac{B}{\ln^2\left[\frac{(HR)}{(HR)^*}\right]}\right], \tag{6}$$

$$r_{N2} = k'_N[(HR) - (HR)^*]^{i'}C_s^{k'}, \tag{7}$$

$$R_{A,i} = \sum_{l=1}^{\frac{N(N+1)}{2}} v_{est\ l,i}r(l). \tag{8}$$

2.2. Optimising batch cooling crystallization processes

The rate of cooling used during the batch determines the values of supersaturation achieved, which characterize the extent of the kinetic mechanisms. The favouring of nucleation over growth leads to a large crystal size distribution, with many small crystals, thanks to a great peak of supersaturation at the early stages of the crystallization process. Since the dependence of the nucleation rate upon the supersaturation is much larger than that of the growth rate, a great peak of supersaturation favours nucleation, consuming a large amount of solute and transforming it into a lot of nuclei. In batch crystallization, a large mean size and a narrow distribution are desired. According to literature, a cooling profile characterized as having a soft decrease in the beginning and a more pronounced one at the end of the process makes the supersaturation to evolve softly, without peaks, leading to a narrower CSD, due to the favouring of growth

(Choong and Smith, 2004; Costa et al., 2005; Mullin, 1993). In face of the importance of the final CSD in the downstream processes and in product applications, the objectives of the optimisation in crystallization problems are normally chosen according to features related to product quality and market specifications. The most common objective functions in crystallization optimisation problems are maximization of the mean crystal size at the end of the batch, minimization of the standard deviation (σ) of the final CSD or minimization of its coefficient of variation (CV), and sometimes minimization of the batch time.

The optimisation of the process can, then, be done selecting one of the previous objective functions, characterizing a single objective optimisation problem, or two (or even more) objective functions, which leads to a multi-objective optimisation problem (MOOP). These objectives are usually conflicting ones, that is, the improvement of one objective damages the quality of another one. There is in MOOPs no single optimal solution. The less robust Pontryagin principle is often recommended for handling MOOPs in the field of traditional optimisation. In evolutionary algorithms as GA, the approach usually employed yields a family of solutions called Pareto optimal set. Many fronts are identified in the population, each one formed by non-dominated solutions. A solution is said to dominate a second one if it is not worse than the second solution in all objectives and is strictly better in at least one objective. Thus, the non-dominated solutions in one front are superior to other solutions in fronts of inferior levels, but comparatively good among themselves. The upper front is the Pareto optimal front and any solution belonging to it is an acceptable solution (Deb et al., 2004; Mitra et al., 2004; Silva and Biscaia Jr., 2003; Suman, 2004).

There are fundamentally two ways to formulate a problem in dynamic optimisation: the control functions may be discretized or parameterised. The former is the most used in dynamic optimisation problems, and in this case the control variables are discretized by a piecewise constant or linear function (Costa et al., 2005). Nevertheless, the accuracy of the optimal control profile in this method is dependent on the number of discretizations and the computational effort increases with the number of discretizations. Furthermore, different discretization levels are needed to ensure that the discretized profile is a satisfactory approximation of the true continuous optimal profile (Choong and Smith, 2004). Bearing this in mind, these authors propose a new parameterisation framework for the control variable profile, able to produce all types of continuous curves. It consists of two distinct profiles, named Types 1 and 2, described by the following mathematical equations:

$$\textit{Type } 1 : X = X_F - (X_F - X_0)\left[1 - \frac{t}{t_{\text{total}}}\right]^{A_1}, \tag{9}$$

$$\textit{Type } 2 : X = X_0 - (X_0 - X_F)\left[\frac{t}{t_{\text{total}}}\right]^{A_2}. \tag{10}$$

In these equations, X is the instantaneous value of any control variable at time t. X_0 is the initial value and X_F is the final value. t_{total} is the total batch time. The whole control variable profile is composed by a combination of Types 1 and 2 functions, each one present in a batch period. The proposed framework for the control variable parameterisation makes possible the representation of any concave, convex or a combination of both types of functions.

This framework is interesting due to the reduction in the dimensionality of the problem, since it leads to only six adjustable variables: the initial and the final control variable values, two exponential constants, the intermediate time and its corresponding intermediate value of the control variable (there is the constraint for the whole function, composed by Types 1 and 2 functions, to be continuous). This proposed framework is chosen in the formulation of the dynamic problem in the present work, with the coolant temperature as the control variable, since it is desired to find out an optimal cooling profile.

The formulated optimisation problem presents some constraints that must be imposed to the optimisation algorithm. The first constraint is necessary in order to dispose of the so-called trivial solutions and, so, it is imposed a constraint of minimum acceptable yield of particles. Furthermore, as mentioned in the previous paragraph, the control variable must have a continuous profile and the intermediate value of the control variable of both types functions (Eqs. (9) and (10)) must be constrained to have the same value at the intermediate time.

Once the optimisation is formulated, the next step is to find out a solution procedure which is at the same time robust and precise. Two procedures are discussed, to know, the SQP and GA.

2.3. Successive quadratic programming (SQP)

The SQP method is a classically known deterministic optimisation method, based on iterative formulation and on the solution of quadratic programming subproblems. The subproblems are obtained using quadratic approximation of the Lagrangian and by linearizing the constraints. The augmented Lagrangian is the objective function less the sum of the active constraints multiplied by their respective estimated Lagrange multipliers. The Hessian of the augmented Lagrangian and the Jacobian of the active constraints compose a linear system, whose solution determines the search direction (line search) and then the new point (cooling profile).

The method is vastly used in optimisation problems, but it is also known that it depends on the initial estimate (Costa et al., 2005; da Costa and Maciel Filho, 2004). Furthermore, the high nonlinearity of the crystallization problem (Choong and Smith, 2004; Costa et al., 2005) imposes a severe complication to the solution. The derivatives of the system variables cannot be computed, making necessary the use of numerical ones.

In this work, SQP implementation was done using the routine DNCONF of the IMSL math library of FORTRAN.

2.4. Genetic algorithms (GA)

Genetic Algorithms have proven very adaptable to a great variety of different optimisation tasks (Fühner and Jung, 2004).The algorithms work with a population of possible solutions, which suffers evolution during the generations, an analogy borrowed from the Darwin's Evolutionary Theory. Each solution is coded as a collection (chromosome) of binary or real strings, each string representing a variable in the solution. The evolution is achieved by some genetic operators as reproduction, crossover and mutation. The survival of the fittest is achieved by the assignment of a fitness function, usually defined as the objective function for an unconstrained optimisation problem, or a combination of the objective function and a penalty function for constrained optimisation (Deb, 1998, 1999).

The set of solutions (i.e., the population) per iteration (generation) is fixed. In each iteration, pairs of individuals are selected randomly and are recombined into new solutions (crossover operator). A random change on the offspring generation is optionally applied (mutation operator). The newly created solutions are evaluated according to the fitness function (Fühner and Jung, 2004).

In a search for the optimum through the use of GA, it is necessary to set the population size, the maximum number of generations allowed during the search, the number of children in the offspring generation per pair of parents and the crossover, jump mutation and creep mutation probabilities. The definitions of the mutation and crossover (single-point, two-point or uniform crossover) types can be found elsewhere in literature. Niching and micro-GA technique are interesting tools, respectively, in multiple optimal solutions and in unimodal/simple problems. The features and details of both alternatives can be found in Deb (1999).

The imposition of constraints in GAs is normally made with penalty functions. Nevertheless, its use may require a lot of refinement, in order to find the most suitable penalty parameters needed to guide the search towards the constrained optimum, in a case fashion. Deb (2000) proposed a different constraint handling method, exploiting the feature of the GAs algorithm of pairwise comparison in tournament selection. Penalty parameters are not needed in the proposed method because, in any scenario of comparison between two solutions, they are never compared in terms of both objective function and constraint violation information, but, in fact, are analyzed separately. When two feasible solutions are compared, the one with better objective function value is chosen; when one feasible and one infeasible solutions are compared, the feasible solution is chosen; and when two infeasible solutions are compared, the one with smaller constraint violation is chosen. The proposed fitness function is formulated in the following manner (for a minimization problem), where infeasible solutions are compared based only on their constraint violation:

$$F(\vec{x}) = \begin{cases} f(\vec{x}) & \text{if } g_j(\vec{x}) \geqslant 0 \\ & \forall j = 1, 2, \ldots, m, \\ f_{\max} + \sum_{j=1}^{m} \langle g_j(\vec{x}) \rangle & \text{otherwise,} \end{cases} \tag{11}$$

where the parameter $f_{\max}$ is the objective function value of the worst feasible solution in the population

In this work, the GA used was basically the FORTRAN Genetic Algorithm Driver by David Carroll, version 1.7a (Carroll, 2004), with some modifications. The code initializes a random sample of individuals with different parameters (variables). The selection scheme used is tournament selection with a shuffling technique for choosing random pairs for mating. The individuals are coded in binary manner and the routine can apply jump mutation, creep mutation and single-point or uniform crossover. The routine is used coupled with the crystallization model (Eqs. (2–8)) in order to optimise the cooling profile parameterised as given by Eqs. (9) and (10). The constraint handling method proposed by Deb (2000) was implemented to the original Carroll's code in order to perform the needed constrained optimisation of the cooling profile.

During the optimisation with Carroll's GA code, it was set two children per pair of parents, niching and single-point crossover.

3. Methodology

The problem was formulated in order to compare parameterisation of the coolant temperature function with its discretization. This later formulation of the control variable, in the form of piecewise constant, was chosen in the work of Costa et al. (2005). In that work, the Method of Classes, with five granulometric classes, was used to solve the PBE in the process model coupled with SQP in order to minimize the standard deviation of the final CSD. The best result of that work is here referred to as SQP+discretization.

The optimisation problem formulated can be written as:

$$\begin{aligned} &\text{Minimize } \sigma_{\text{tf}}(\mathbf{T_c}) \\ &\text{Subject to : model equations (Eqs. (2–8))} \\ &\qquad T_c(i) - T_c(i+1) \geqslant 0.0, \\ &\qquad \text{mass of crystals } (t_f) \geqslant 50.0. \end{aligned} \tag{12}$$

It is worth noting that, in order to compare parameterisation of the coolant temperature with the discretization results obtained in the work of Costa et al. (2005), the same objective function is chosen, characterizing a single objective problem. A multi-objective optimisation problem would be an interesting task, addressing maximization of mean crystal size at the end of the batch, minimization of the standard deviation of the final CSD and, possibly, minimization of batch time, but it is beyond the scope of the present paper.

The parameterisation given by Eqs. (9) and (10) makes the optimisation problem formulation to be different: Costa et al. (2005) looked for the optimal coolant temperature values at the discretization points, and in this work the problem is formulated in order to find the best parameters of Types 1 and 2 equations (Eqs. (9) and (10)). Furthermore, the optimisation search should investigate whether it is best to have Type 1+Type 2 or Type 2+Type 1. The authors devised two ways of formulating the search with the proposed parameterisation of the control variable:

(A) *First parameterisation formulation*: five *searching variables*

The first variable sign determines whether the control variable is represented by Type 1+Type 2 or Type 2+Type 1 functions. The second variable determines X_0, the third X_F, the fourth the intermediate time, where the two type functions have an interception, and the fifth variable determines the exponential constant of the function in the first interval (before the intermediate time). The other exponential constant (of the function prevailing after the intermediate time) is found by mathematical manipulation of the two type function equations, since they must have the same X value at the intermediate time.

In this way, letting $\vec{x}$ be the vector containing all the searching variables, $x(1)$ is allowed to vary from -1 to $+1$. If it assumes a negative value, Type 1+Type 2 function is determined, otherwise, Type 2+Type 1 function is stipulated. $x(2) = X_0$, $x(3) = X_F$, $x(4) = t_{\text{intermediate}}$. Supposing $x(1)$ assumes a negative value, $x(5) = A_1$ and A_2 is calculated by Eq. (13):

$$A_2 = \frac{\log\left[1 - \left(1 - \dfrac{t_{\text{intermediate}}}{t_{\text{total}}}\right)^{A_1}\right]}{\log\left(\dfrac{t_{\text{intermediate}}}{t_{\text{total}}}\right)}. \tag{13}$$

An equation similar to Eq. (13) may be written to find out the value of A_1, if $x(1)$ assumes a non-negative value, when $x(5) = A_2$.

In this parameterisation formulation, the optimisation problem can be written as:

$$\begin{aligned} &\text{Minimize } \sigma_{\text{tf}}(\vec{x}) \\ &\text{Subject to : model equations (Eqs. (2–8))} \\ &\qquad \text{mass of crystals } (t_f) \geqslant 50.0. \end{aligned} \tag{14}$$

(B) *Second parameterisation formulation: six searching variables*

The first variable sign determines whether the control variable is represented by Type 1+Type 2 or Type 2+Type 1 functions. The second variable determines X_0, the third X_F, the fourth the intermediate time, where the two type functions have an interception, the fifth variable determines the A_1 exponential constant (Type 1 function) and the sixth the A_2 exponential constant (Type 2 function). This formulation, however, asks for the imposition of another constraint to the problem: both functions must have an interception at the intermediate time, that is, the X value calculated by the Type 1 function minus the X value calculated by the Type 2 function must equal zero (equality constraint). This equality constraint was handled transforming it in an inequality constraint with the use of a tolerance, set to 10^{-4}.

In this way, with this parameterisation formulation, the optimisation problem is written as:

$$\begin{aligned} &\text{Minimize } \sigma_{\text{tf}}(\vec{x}) \\ &\text{Subject to : model equations (Eqs. (2–8))} \\ &\qquad \text{mass of crystals } (t_f) \geqslant 50.0. \\ &\qquad \Big|X_F - X_0 - (X_F - X_0) \\ &\qquad\quad \times \left[1 - \frac{t_{\text{intermediate}}}{t_{\text{total}}}\right]^{A_1} + (X_0 - X_F) \\ &\qquad\quad \times \left[\frac{t_{\text{intermediate}}}{t_{\text{total}}}\right]^{A_2}\Big| \leqslant 10^{-4}. \end{aligned} \tag{15}$$

Both parameterisation formulations were tested in the present work.

It is worth stressing that the process model was developed in order to simulate a cooling crystallization process, not having any modelling of dissolution. This means that the coolant temperature (the control variable) that serves as input to the model could not have a positive derivative with respect to time. This constraint was posed in the lower and upper boundaries of the searching variables, and with the imposition that X_F could not be greater than X_0. It is important to point out that is worthwhile to consider a lack of dissolution modelling, since in many practical situations, especially in industrial plants, it is hard to have all the needed information to describe adequately a dissolution model. One of the strong reasons is the impurities presence in the crystals.

In order to compare the results generated with the parameterisation coupled both with SQP and GA with the results generated with SQP+discretization, the Method of Classes with five granulometric classes was also used in the present work. It is convenient to say that the choice of such number of granulometric classes was due to its capability to represent well experiment data in a suitable computer time. Also it has to be pointed out that, depending on the solution procedure, such number of classes may be a limitation (Costa, 2003).

4. Results and discussion

The study showed that the optimisation with GA was not sensitive to the parameterisation formulation: the best individual found with the same initial population was the same if five or six searching variables were used. This was

Table 1
Set-up of GA parameters for the best result in the GA+parameterisation study

Type of crossover	Single-point
Niching?	Yes
Number of children per pair of parents	2
Number of individuals per generation	50
Maximum number of generations	200
Jump mutation probability	0.05
Creep mutation probability	0.04
Crossover probability	0.8

Table 2
Initial estimates provided to SQP in the SQP+parameterisation study

Variable	Initial estimate that leads to the best result	Initial estimate that leads to a local minimum
Function combination ($x(1)$)	−0.5 (Type 1+Type 2)	0.5 (Type 2+Type 1)
X_0 ($x(2)$)	335.0	335.0
X_F ($x(3)$)	298.0	298.0
$t_{\text{intermediate}}$ ($x(4)$)	300.0	300.0
A_1 ($x(5)$)	0.6	0.6
A_2 ($x(6)$)	1.5	1.5

not observed with the SQP technique. In fact, with this optimizer it was not possible to conduct optimisation if five variables were used. In this case, the optimum was presented as the initial estimate, independently of which one it was. The reason to this fact should be located in the non-suitability of the SQP method in treating non-convex problems, converging to the initial estimate itself or to a point very near it. With the five searching variables parameterisation formulation, the second exponential constant is found exactly by mathematical manipulation (Eq. (13)). In this way, being the initial estimate feasible and the objective function surface extremely non-convex, the line search cannot find any downhill direction and the SQP algorithm identifies the point as the optimal. With the six searching variables parameterisation, the SQP optimizer executed the search but, as expected, the solution has shown to be dependent on the provided initial estimate. The six searching variable parameterisation formulation allows the SQP algorithm to move in the search for the optimal, since both exponential constants are searching variables, constrained to the imposition of continuous cooling profile to be obtained.

An extensive evaluation concerning the GA parameters was carried out and the best result is here presented, named GA+parameterisation. For this optimisation, the parameters input to the GA were the ones presented in Table 1.

The best result of this work with the SQP technique, named SQP+parameterisation, is showed to be compared to GA+parameterisation. The initial population provided to the optimizer in this situation is presented in Table 2. Table 3 brings the standard deviation of the three studies: SQP+discretization (Costa et al., 2005), SQP+parameterisation and GA+parameterisation.

Table 3
Standard deviation of the final CSD (σ_{tf}) for the optimal response in each optimisation study

Optimisation	σ_{tf} (μm)
SQP+discretization (Costa et al., 2005)	0.337
SQP+parameterisation	0.180
GA+parameterisation	0.165

Table 4
Optimal parameters, according to GA+parameterisation and SQP +parameterisation studies

Variable	GA+parameterisation	SQP+parameterisation
Function combination ($x(1)$)	−0.4755 (Type 1+Type 2)	−0.5 (Type 1+Type 2)
X_0 ($x(2)$)	337.3699	334.9994
X_F ($x(3)$)	298.0822	298.0006
$t_{\text{intermediate}}$ ($x(4)$)	197.4110	300.0
A_1 ($x(5)$)	0.0783	0.4847
A_2 ($x(6)$)	2.2233	1.4153

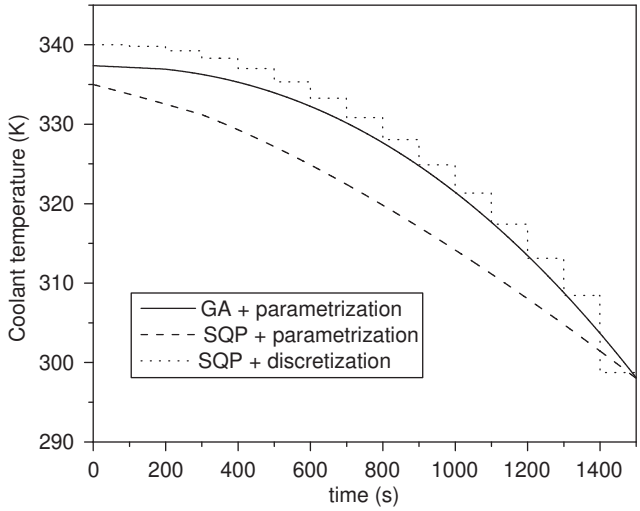

Fig. 4. Optimal coolant temperature profiles for the three optimisation studies.

It can be seen, from Table 3, that the genetic algorithm was the technique that allowed to find out the control variable profile that produced the minimum of the objective function. Nevertheless, it is a very time consuming technique, which could not be used in real time applications. The SQP+parameterisation formulation has provided a profile with a standard deviation better than the one found by the formulation SQP+discretization. However, the SQP was dependent on the initial estimate. Table 2 brings an example of an initial estimate that conducted to a local optimum, characterized by a standard deviation of $\sigma_{\text{tf}} = 0.185\,\mu\text{m}$.

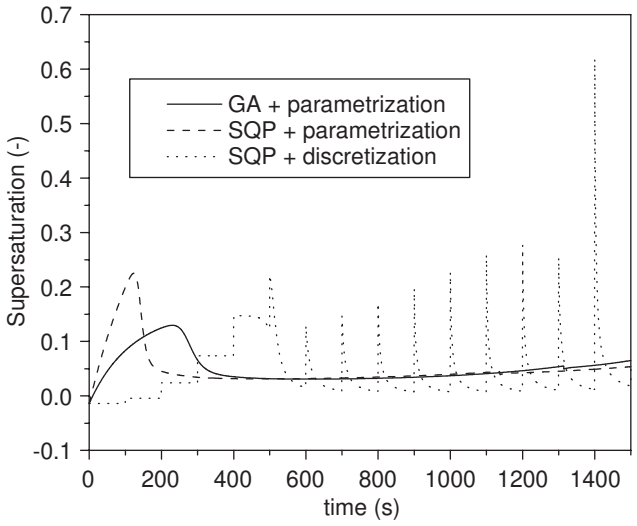

Fig. 5. Evolution of the supersaturation during the batch for the optimal profiles.

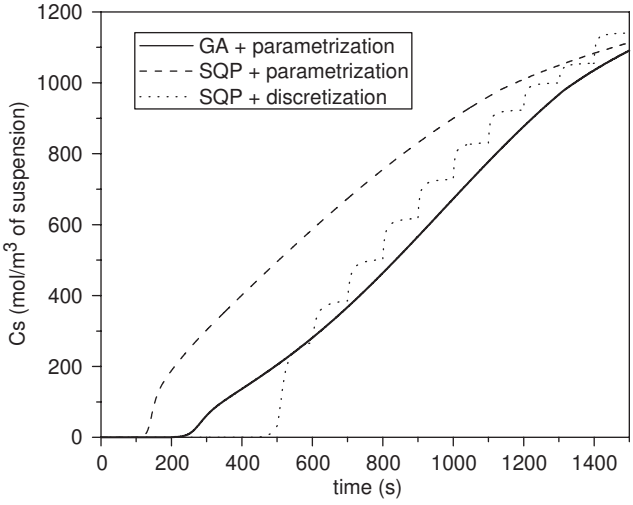

Fig. 6. Evolution of the solids concentration during the batch for the optimal profiles.

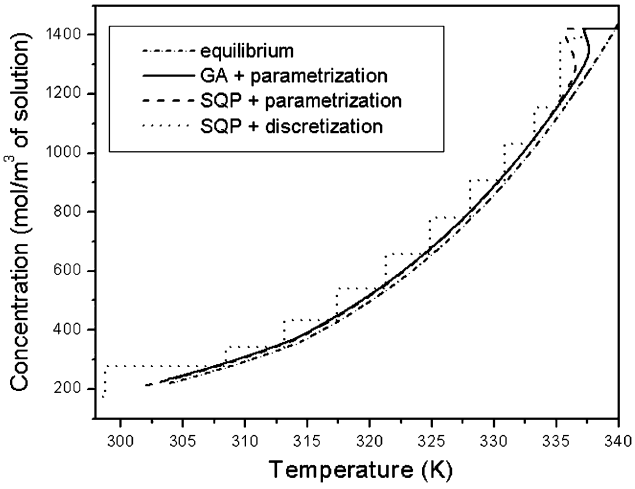

Fig. 7. Operation curve followed during the batch for the optimal profiles.

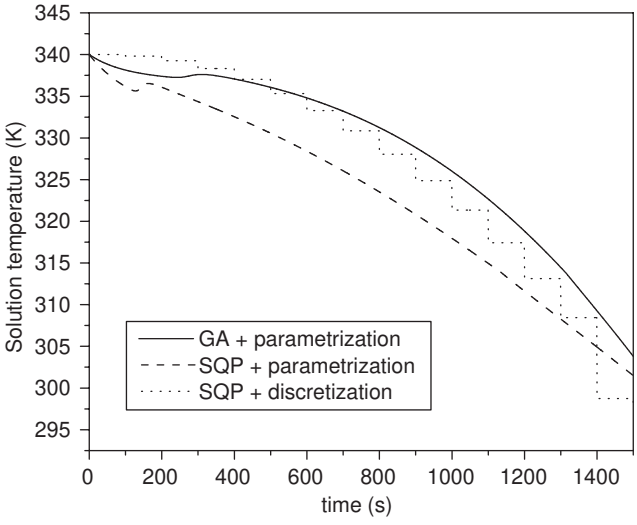

Fig. 8. Evolution of solution temperature during the batch for the optimal profiles.

The best profiles presented by the GA+parameterisation and SQP+parameterisation studies are determined by the best values found for the searching variables, Types 1 and 2 parameters. These best parameters are presented in Table 4.

The main graphical comparisons among the three optimisation approaches are presented from Figs. 4–8 . An interesting and important point of discussion is the real application of a discretized profile, as the one considered in the work of Costa et al. (2005). This type of profile is easy to calculate but hard to be implemented in practice. As pointed by Choong and Smith (2004), a discretized profile must be an approximation of the true optimal profile, but the instantaneous decrease of the coolant temperature depicted in Fig. 4 is not possible to carry out. A much more realistic approach to solve the problem is parameterise the control variable, and imposing, if necessary, additional constraints on the value of derivatives of the control variable with respect to time, due to physical and design constraints. In this way, the results presented in the present work (GA+parameterisation and SQP+parameterisation) are easier to follow in real process implementations.

Fig. 5 confirms the unrealistic feature of the results from SQP+discretization. In this case, the supersaturation during batch time is characterized by many peaks: the supersaturation reaches a high value and comes to nearly zero, due to solute consumption by the solid phase. The driving force for crystallization is almost none until the next discretization point in time for the coolant temperature is reached and the temperature is decreased to the next value, leading to the appearance of another supersaturation peak. The process evolves in this way successively. As a consequence, the

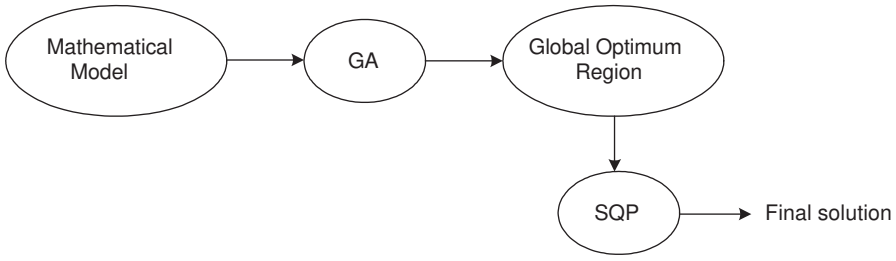

Fig. 9. Schematic diagram for the optimisation approach for real-time applications.

solids concentration (Fig. 6) for SQP+discretization presents periods of sharp increase, due to the supersaturation peaks at the discretization points, followed by soft evolution, when the supersaturation is small.

Fig. 6 shows the solids concentration evolution during the batch. GA+parameterisation profile is the one with softer increase, due to the prevailing of growth upon nucleation. Nevertheless, the soft increase of solids concentration during the same batch time makes this profile to generate less mass of solids at the end of the batch, as can be checked by the observation of the final values of solids concentration in Fig. 6: GA+parameterisation profile possesses the smallest one.

Fig. 7 depicts the operating trajectories for the three optimal profiles. The operation trajectories are formed by the pairs of values of solution concentration and temperature followed during the batch time. According to literature (Costa et al., 2005; Lang et al., 1999; Mullin, 1993), in cooling crystallization systems, it is interesting to keep the operation at a region in the metastable zone with not so high supersaturation values, since growth can occur with smaller driving force, while nucleation demands larger values of supersaturation to take place. This means to keep the operating trajectory as close as possible to the stable zone, for crystals with suitable CSD to be obtained. It is clear from Fig. 7 that the GA+parameterisation profile is the one kept nearest to the equilibrium line, leading to the smaller supersaturation values, as shown in Fig. 5. This confirms the results from literature, indicating that the optimum temperature profile would exhibit less values of supersaturation and corroborates the results presented in Table 3.

An important point to be considered is the noticeable difference between the GA+parameterisation and SQP+parameterisation profiles (Fig. 4), as well as the solution temperature profiles in both cases (Fig. 8). Nevertheless, as it was already pointed out, SQP is a method dependent on the initial estimate. It is clear that the profile presented by the GA study is the best (Table 3 results) and this profile can be used as the initial set point to be followed in real applications. Since GA is a very time-consuming technique, for real-time applications, in which online optimisation calculations are needed, the SQP can be used for optimisation calculations, since the region where the process may be operated would be near the global optimum region, thanks to the initial set point stipulated by the GA global searching technique. In this way, the schematic approach shown in Fig. 9 is proposed in order to deal with real-time applications. The use of GA is necessary to determine the region where the global optimum is located. The SQP is then used, but limited to this region to achieve the global optimum.

5. Conclusions

In this work an original study in batch crystallization optimization problems is carried out, with the comparison of results from deterministic and stochastic methods coupled with different control variable formulations. The study showed that parameterisation of the control variable profile is a much more realistic situation. Concerning to the chosen deterministic method, its sensitivity to problem formulation and initial estimate was clear. The genetic algorithm provided the best result. The procedure showed to be robust and efficient to find out the optimal conditions. However, due to its time-consuming feature, it is not recommended for real-time applications. Bearing this in mind, a shared procedure is proposed, which works with both optimisation methods. The results provided by this technique may be used as the initial set-point and deterministic methods may be used for online optimisation calculations.

Notation

$\langle\ \rangle$	indicates absolute value of the operand, if it is negative and zero value otherwise
A	pre-exponential factor (primary nucleation), $\mathrm{m}^{-3}\,\mathrm{s}^{-1}$
A_1	exponential constant of Type 1 function
A_2	exponential constant of Type 2 function
A_c	heat transfer area, m^2
B	kinetic parameter of the primary nucleation law
$B(L)$	birth rate, $\mathrm{m}^{-4}\,\mathrm{s}^{-1}$
c	solute molecules concentration in solution, $\mathrm{mol}\,\mathrm{m}^{-3}$ of solution
c^*	solute molecules concentration in solution at supersaturation, $\mathrm{mol}\,\mathrm{m}^{-3}$ of solution

C_i	granulometric class of rank i
ΔC_i	width of class C_i
C_p	slurry specific heat, $J\,kg^{-1}\,K^{-1}$
C_s	solid concentration in the suspension, $mol\,m^{-3}$ of suspension
C_0	initial concentration of adipic acid, $mol\,m^{-3}$ of solution
CV	coefficient of variation of the crystal size distribution, %
$D(L)$	death rate, $m^{-4}\,s^{-1}$
$f(\vec{x})$	objective function
f_{max}	objective function value of the worst feasible solution in the population
$F(\vec{x})$	fitness function
$g(\vec{x})$	inequality constraints
G	growth rate, $m\,s^{-1}$
ΔH_c	heat of crystallization, $J\,mol^{-1}$
(HR)	concentration of molecular adipic acid in solution, $mol\,m^{-3}$ of solution
(HR*)	concentration of molecular adipic acid in solution at saturation, $mol\,m^{-3}$ of solution
(H+)	concentration of protons in solution, $mol\,m^{-3}$ of solution
i	counter to discretization points
i'	kinetic order of the secondary nucleation law
j	counter to the number of constraints
j'	kinetic order of the integration growth law
k	total number of inlet and outlet streams
k'	exponent to the solid concentration in secondary nucleation law
k_a	surface shape factor
k_c	kinetic constant of the integration law, $m^{3j'-2}\,mol^{1-j'}\,s^{-1}$
k'_N	kinetic constant of the secondary nucleation law, $m^{3(i'+k')-3}\,mol^{-i'-j'}\,s^{-1}$
k_v	volumetric shape factor
K	modified acidity constant of adipic acid, $mol\,m^{-3}$ of solution
L	characteristic size of crystals, m
L_i	upper limit of class of number i, m
m	number of constraints
MM	molecular weight of the crystal, $kg\,mol^{-1}$
n	number distribution density (population) per unit volume of suspension, m^{-4}
N	number of granulometric classes
$N_i(t)$	number of crystals per unit volume of suspension in granulometric class C_i at time t, m^{-3} of suspension
r_N	net rate of nucleation, $m^{-3}\,s^{-1}$
r_{N1}	primary rate of nucleation, $m^{-3}\,s^{-1}$
r_{N2}	secondary rate of nucleation, $m^{-3}\,s^{-1}$
$r(l)$	intrinsic rate of agglomeration of rank $l_{m,n}$, $m^{-3}\,s^{-1}$
$R_{A,i}$	net rate of agglomeration in the granulometric class C_i, $m^{-3}\,s^{-1}$
$R_{B,i}$	net rate of breakage in the granulometric class C_i, $m^{-3}\,s^{-1}$
t	instantaneous time, s
$t_{intermediate}$	intermediate time, where Types 1 and 2 functions have the same value, s
t_f	final time, s
t_{total}	total batch time, s
T	crystallizer solution absolute temperature, K
$\mathbf{T_c}$	vector with the values for the coolant absolute temperature at all discretization points, K
U	global heat transfer coefficient, $J\,m^{-2}\,s^{-1}\,K^{-1}$
$\mathbf{v}_i$	internal velocity vector, orientated according to an internal orientation system
V	solution volume, m^3
V_{susp}	suspension volume, m^3
V_0	initial volume of the solution in the crystallizer, m^3
$\dot{V}_i$	inlet and outlet streams particle volumetric rates, $m^3\,s^{-1}$
$\vec{x}$	vector containing the optimizing (adjustable) variables
X	control variable
X_0	control variable initial value
X_F	control variable final value

Greek letters

η_r	effectiveness factor
$v_{est\ l,i}$	Stoichiometric coefficient of class i in agglomeration of number l
ρ	slurry density (concentration), $kg\,m^{-3}$ of slurry
ρ_c	crystal density, $kg\,m^{-3}$ of crystal
σ	standard deviation of the CSD
σ_{tf}	standard deviation of the final CSD

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6.3. Conclusões

Os resultados obtidos neste capítulo mostram que o método SQP é sensível tanto à formulação da parametrização quanto à estimativa inicial dada para a variável de controle (seus valores discretos, quando discretização é utilizada, ou os parâmetros da equação de parametrização, quando esta é utilizada). Já a solução obtida pelo AG demonstrou ser este realmente um método de busca global, levando a um ótimo bastante melhor do que os indicados pelo SQP. Porém, este método de otimização demanda muito tempo computacional de cálculo, o que impede a sua utilização pura e simples em aplicações em tempo real.

Como os resultados bastante promissores obtidos com o uso de AG indicam sua característica de busca global, sugere-se sua adequação para resolver problemas *offline*, para que sejam calculados os *setups* inicias de processo. No entanto, é sabido que qualquer estudo com Algoritmo Genético exige que sejam feitas diversas corridas de otimização, em que se variem os valores dos seus parâmetros (tais como probabilidade de mutação, probabilidade de cruzamento, tamanho de população, etc.) a fim de se garantir, ou ao menos, ter maior probabilidade de alcance do ótimo global (ou suas vizinhanças). Em face dessa característica do AG e da inexistência de um procedimento padrão na literatura de como se deve fazer a abordagem para variação desses parâmetros, o capítulo a seguir propõe um procedimento geral e original para detecção dos parâmetros do AG significativamente relevantes para um problema de otimização em que se vá utilizar o AG para detecção do ótimo global.

Capítulo 7. Procedimento Geral para Investigação dos Efeitos dos Parâmetros para Otimização por Algoritmo Genético

7.1. Introdução

Este capítulo propõe um procedimento geral e original a ser adotado em uma análise *a priori* em problemas de otimização a serem resolvidos com a utilização de algoritmos genéticos. Não há na literatura nenhum procedimento sistemático que determine qual o conjunto dos melhores parâmetros do algoritmo genético e que possa ser aplicado a qualquer problema (de qualquer dimensão e complexidade). Nesse sentido, aqui se apresenta uma sistemática significativa e de uso relativamente simples. O procedimento proposto consiste na aplicação do Planejamento Fatorial, uma técnica estatística bastante estabelecida, para que sejam identificadas as informações mais significativas relativas às influências dos fatores em um problema de otimização. O planejamento fatorial serve, portanto, como uma ferramenta suporte de identificação dos parâmetros do algoritmo genético que possuem efeito significativo sobre o problema de otimização. Essa abordagem é bastante útil em estudos *a priori*, uma vez que possibilita a separação dos parâmetros de efeitos significativos dos não-significativos, no processo de busca evolutiva do ótimo. Uma vez que qualquer estudo de otimização por algoritmos genéticos exige que se execute o algoritmo diversas vezes variando-se seus parâmetros de modo a se ter maiores chances de se alcançar o ótimo global (ou suas proximidades), a identificação dos parâmetros significativos reduz o tempo e a carga computacional em estudos de otimização evolucionária por descartar variações em parâmetros não significativos.

O procedimento proposto é detalhado neste capítulo e sua aplicação em casos de estudo gerais é apresentada. Os casos de estudo aqui selecionados exemplificam a aplicação da abordagem proposta em problemas gerais, desde problemas matemáticos simples a problemas não-lineares de engenharia. Todos os casos de estudo, no entanto, foram selecionados focando-se aplicações de engenharia, como, por exemplo, ajuste de funções polinomiais a dados. Além do

mais, exceto pelo primeiro, os casos de estudo selecionados possuem vários ótimos locais, situação típica dos problemas de engenharia e que os tornam difíceis de serem otimizados por métodos determinísticos (locais), tais como o SQP.

7.2. Desenvolvimento

O desenvolvimento deste capítulo é apresentado a seguir, no artigo intitulado *Prior Detection of Genetic Algorithm Significant Parameters: coupling Factorial Design Technique to Genetic Algorithm*, submetido ao periódico internacional *Chemical Engineering Science* e atualmente em fase de revisão.

Prior Detection of Genetic Algorithm Significant Parameters: coupling Factorial Design Technique to Genetic Algorithm

Caliane B. B. Costa*, Elmer A. C. Rivera, Rubens Maciel Filho

Chemical Engineering School, State University of Campinas (UNICAMP)

Cidade Universitária Zeferino Vaz, CP 6066, CEP 13081-970 Campinas-SP, Brazil

Abstract

This work proposes an original and general procedure to be adopted as a prior analysis in optimisation problems to be solved using genetic algorithm (GA). No systematic approach to establish the best set of GA parameters for any problem was found in literature and a relatively easy to use and meaningful approach is proposed. The proposed approach consists on applying factorial design, a well established statistical technique to identify the most meaningful information about the influences of factors on a specific problem, as a support tool to identify the GA parameters with significant effect on the optimisation problem. This approach is very useful in conducting further optimisation works, since it discharges GA parameters that are not statistically significant for the evolutionary search for the optimum, saving time and computation burden in evolutionary optimisation studies.

Keywords: Factorial Design, Genetic Algorithm, Optimisation, Numerical Analysis, Parameter Identification, Computation

1. Introduction

Genetic Algorithms (GAs) are part of the so-called evolutionary algorithms and compose a search and optimisation tool with increasing application in scientific problems (to cite just a few: Fühner and Jung, 2004; Laquerbe et al., 2001; Leboreiro and Acevedo, 2004; Silva and Biscaia Jr., 2003, Summanwar et al., 2002). They do not need to have any information about the search space, just

* Corresponding author. Tel.: +55 19 3788-3971; Fax: +55 19 3788-3965
E-mail address: caliane@lopca.feq.unicamp.br

needing an objective/fitness function that assigns a value to any solution. This makes the optimisation procedure to be very robust and attractive for the solution of large scale nonlinear systems. Deterministic procedures tend to fail for such problems and heuristic methods are difficult to be used without a relatively sophisticated knowledge basis. Details about the working principle of GAs can be found elsewhere (Deb, 1998, 1999; Fühner and Jung, 2004; Goldberg, 1989).

In order to use GAs, setting up a relatively large number of parameters is required. A quick view leads to about six to nine parameters to be established before running a typical GA algorithm. Since GAs are evolutionary algorithms, whose history of advance in the evolution is part provided at random and part by the values of their parameters, it is recommended in an optimisation search by GAs to perform a lot of runs to increase the chance to obtain the global optimum. The task of parameter tuning is an obscure one and many results of GAs are reported in literature without many explanations on the choice made. In fact, few attention has been given to a suitable parameter choice. However, Eiben et al. (1999) stress that the values of the parameters for each component (representation, crossover, mutation, selection mechanism and so on) greatly determine whether the algorithm will find a near-optimum solution and in an efficient way. The performance of the GA will depend, to a great extent, on the values of the parameters that govern these genetic operators, and some studies have been presented to determine suitable values (Leboreiro and Acevedo, 2004). The choice of the suitable parameter values is a time consuming task, normally made by hand in a try and error basis, which is not easy to cope, since specific problem requires specific GA setups. An interesting alternative, instead of tuning fixed values for the natural parameters, is the control (adaptation) of them during the evolutionary process, which is normally made in mutation parameter and penalty parameters in fitness function. Control of parameters includes any change of any of the parameters that influence the action of the evolutionary algorithm. The majority of applications control only one parameter, or a few parameters that relate to a single operator of the code, mainly because the exploration of capabilities of adaptation is done experimentally (Eiben et al., 1999).

The need for good parameter tuning methods is justified by the “optimal parameter” dependence on the problem type and by the often interaction of them in a complex way, which would require an enormous amount of runs in simultaneous tuning of GA parameters (Eiben et al., 1999).

Since a lot of parameters must be set in a GA in order to perform an optimisation study, factorial design, a well-known technique for the selection of the variables with the most meaningful effects on a response, is proposed to be applied in optimisation problems solved through GA. The selection of the GA parameters with significant effect on the optimisation response is dependent on the problem being considered. The present work aims to propose a methodology, coupling GA to a statistical technique, to compose a simple and systematic procedure to be adopted for identification of which GA parameters affect significantly the optimisation of particular problems. No systematic approach to establish the best set of parameters for GA in optimisation problems was found in literature, leading the proposed approach to be a simple and meaningful novel contribution. The proposed approach is an important analysis to be conducted prior to the optimisation trials through GAs, since it discharges GAs parameters that are not statistically significant for the evolutionary search. In a previous work, Costa et al. (2005) have detected the significant parameters in GA evolutionary search for the batch cooling crystallization. In present work, the proposed systematic procedure is presented as a general one and applied in some case studies, covering a broad class of problems.

The prior detection of significant parameters is an important point to be considered in optimisation studies through GA, particularly in engineering problems, which is characterized to be complex, nonlinear and, many times, implicit in the optimising variables. Furthermore, this kind of problems involves a detailed model of the process being analyzed and whose optimisation trials are very time consuming tasks. The proposed approach detects the significant GA parameters to be extensively varied, or on which control actions should be applied, saving human and computational effort in making variations to parameters not statistically significant.

2. Optimisation Problems and Genetic Algorithm

The general objective in optimisation problems is to choose a set of variables values subject to the various constraints that will reach the optimum response for the chosen objective function. Genetic Algorithms (GAs) are part of the optimisation evolutionary algorithms and work with a collection (population) of possible solutions. Each solution (chromosome) is composed by random values to each optimising variable (gene). The chromosome, also called individual, is usually codified through a series of bits (0-1), although it may also be represented by real values. The random initial population is evolved with three basic genetic operators: selection, crossover, and mutation (Leboreiro and Acevedo, 2004). The survival of the fittest is achieved by the assignment of a fitness function, usually defined as the objective function for the unconstrained optimisation problem, or a combination of the objective function and a penalty function for constrained optimisation (Deb, 1998, 1999). Detailed explanations on the GA technique and its operators may be found in Goldberg (1989).

GA may be particularly useful in practical engineering problems that have "black-box" functions or get aid of modular simulators, in which the model of each unit is only available in an implicit form. The use of such modules is common in chemical and related industries. Furthermore, modules external to optimisation subroutines are often black-box-like. (Jeżowski et al., 2005; Leboreiro and Acevedo, 2004).

Laquerbe et al. (2001) have used both simulated annealing and genetic algorithm in the problem of structural and parametric identification of models for residence time distribution. GA was applied with a set of parameters, according to the authors, 'quite unusual for a GA implementation', and whose values have been obtained after numerous numerical trials in order to obtain 'good' convergence. The authors performed a parameter sensitivity analysis of the GA through the ratio of exploration of search space. Their study showed that without mutation, the exploration ratio remained equal to 5%, showing that mutation clearly introduces diversity. Apart from that, the GA implemented in that case study appeared sensitive to essentially the number of generations, i.e., choosing the number of generations, and with the other GA parameters fixed to classical values, one could determine a fixed percentage of exploration of the search space. The authors concluded that the set of parameters of a

simulated annealing (SA) is easier to determine than the set of parameters of a GA (population size, mutation probability, percentage of crossover and number of generations) but a GA might give better solutions when its set of parameters was well suited to the problem under consideration. This claims for the need of tuning methods and of a procedure to prior identify in which GA parameters tuning methods should be applied.

Leboreiro and Acevedo (2002) analyse the effect of the parameters of the GA in its performance in a series of typical process engineering problems, solved with explicit mathematical models or using simulators. The results indicated that mutation is a governing factor in the performance of the GA, being the best values for the probability of the jump mutation between 0.005 and 0.01, while creep mutation was very dependent of the number and type of variables. Uniform crossover was preferred over single-point, with 0.6 as the best value for the crossover probability. The authors also proposed the use of group elitism, passing from 10 to 15% of the individuals directly from one generation to the next. The study of GA parameters effects was made using factorial design, though the paper did not detail the conducted procedure and did not establish a systematic procedure to be used in general problems. A possible way to attack the problem of finding the best set of GA parameters is through some statistical tool, since it may provide a comprehensive basis to analyse their impact on the algorithm performance. Bearing this is mind, it is proposed in this work the use of factorial design as a support tool in the definition of the best set of GA parameters.

3. Factorial Design

The factorial design is a well-known technique based on statistical considerations that brings the most meaningful information about the influences of factors on a specific problem, including the effects of interactions among variables. It evaluates at the same time all process (or any focus of study) variables in order to determine which ones really exert significant influence on the final response, which gives a better analysis of the response (Kar *et al.,* 2002). All variables are called factors and the different values chosen to study the factors are called levels (Barros Neto *et al.*, 2003; Box *et al.*, 1978).

In a complete factorial design, all possible combinations of the selected levels for the factors are made, but this procedure may be too time-consuming. On the other hand, the most common factorial designs are the two levels ones, which bring enough information for the purpose of this work. Important trends may be observed with these factorial designs and the effects of each independent variable, on the dependent one are estimated. The values of the resulting first order effects indicate the more sensitive parameters applied to the case studied and consequently which ones are more important in the seeking procedure. It is worth mentioning that the obtained results depend strongly on the case study to which the methodology is being applied (Rodrigues *et al.*, 2002).

When a relatively large number of factors is evaluated, the total number of combinations may be too large and, hence, time consuming to be evaluated. Furthermore, the high order interactions (third, fourth or superior) are usually small, when compared to first and second order effects, and may be mixed with the standard deviation of the effects. In this case, it is advisable and convenient to use a fractional factorial. The number of combinations is diminished and the most important effects are statistically determined (Barros Neto *et al.*, 2003).

In the interpretation of the results generated by a complete or fractional factorial design, it is necessary to decide which calculated effects are significantly different from zero. The usual practice is use the concept of statistical significance (generally 95% of confidence).

When analysing the results of a factorial design, two statistic parameters are of relevance, to know, the t-statistics and p-level. The t-statistics of a factor is obtained by the division of its effect by its error. This statistic parameter is dependent on the freedom degree, which is calculated by the subtraction of the number of calculated effects from the total number of experiments/trials available. The higher the t-statistics, the higher is the significance of the corresponding factor. On the other hand, the p-level, which represents the probability of error that is involved in accepting the effect as valid, is a decreasing index of the reliability of a result. The higher the p-level, the less one can believe that the observed relation between factor and effect is reliable. The common practice is to consider 95% of confidence in a result, so that, for an effect to be considered statistically significant, its p-level must be less than 0.05.

The two levels evaluated in a factorial design are coded by (+) and (-), representing the upper and lower levels, respectively.

4. A Novel Proposal: Coupling Factorial Design to GA Parameters to Identify Significant Effects

Since the GA technique itself has a lot of parameters that should be varied in many trials in order to drive so many possible evolutionary paths that the achievement of the specific problem global optimum can be more assured, the simple and original approach proposed in this work offers a plan of action (statistically guided orientation) to select in which ones of these GA parameters efforts should be concentrated in optimisation trials of the particular problem. Costa et al. (2005) proposed an approach in order to evaluate the most significant GA parameters in the search for the best cooling profile in a crystallization process. It proposes that efforts should be concentrated only in those parameters that have shown statistical significance on the problem response. In an optimisation problem through GA, the problem response is the best value of the objective function / fitness function among all individuals at the end of the evolutionary search. In this way, the proposed approach analyzes the effects that the GA parameters have on the fitness function. This proposed approach can be applied to any GA optimisation problem as well as for any kind of GA algorithm. This meaningful approach discharges many trials that would make variations to GA parameters that do not show to have any statistical effect on the problem response, saving time and computation burden in evolutionary optimisation studies. Optimisation trials without prior knowledge of on which GA parameters attention should be drawn could be a great waste of time and human and computational effort. This may have significant relevance for the development of real-time process integration procedures using GA as optimisation tool.

The proposed approach is based on the general structure of GA (Fig. 1), with its inputs and output. All features of GA compose the universe set of characteristics that must be defined in order to run an evolutionary search. This universe is subdivided into two subsets: the GA parameters and the GA settings and the elements of each subset are determined based only on the information whether if the particular feature for which the element stands for will have,

respectively, its influence on the GA response analysed or not. In this way, features such as type of crossover, use of niching, elitism, number of children per pair of parents, crossover probability, number of individuals selected in elitism or any other characteristic of GA may be part of the subset GA settings (if the characteristic is set to be fixed and not varied during the influence analysis) or GA parameters (if their values should be varied in many different optimisation trials).

The input data that must be supplied to GAs is composed by:

- GA settings: any characteristic feature fixed. Since these settings are fixed, they are not part of the so-called GA parameters, whose effects on the optimisation response are object of study in the detection of statistical significance.
- Problem variables minimum and maximum allowed variables: the decision on which are these minimum and maximum allowed variables is dependent on the specific problem being considered.
- GA parameters: these parameters must be varied in many GA trials (or a control action may be applied to them) in order to drive so many possible evolutionary paths that the achievement of the specific process global optimum can be more assured. Examples of GA parameters could be mutation probability, population size, crossover probability, selection mechanisms for selecting parents and survivors and initial population.

The problem model that figures in Fig. 1 is necessary for the evaluation of both the objective function and constraints violation (in constrained problems). GC and IC are only counters (respectively generation counter and individual counter) used by the algorithm to make calculations for each individual of each generation. The vectors **best_fitness** and **best_individual** are responsible for recording the best fitness function and the corresponding best individual in each generation.

As can be seen by the structure outlined in Fig. 1, given a set of values of the GA parameters, the GA optimisation code executes the evolutionary search and gives as output the best fitness function. The outer box of Fig. 1, which encloses all the sequence of steps for Genetic Algorithms, can be seen as a

black-box: given an input (GA settings, minimum and maximum allowed values and GA parameters values), for a particular problem model, the black-box gives an output. Since the problem is fixed, the minimum and maximum allowed values are fixed. The GA settings are also fixed. In this way, the only variables able to be varied in the input are the GA parameters. The proposal is, then, to use factorial design in the identification of the significant GA parameters in optimisation problems, i.e., parameters that really exert significant influence on the output. The proposed approach should be seen as a prior and important analysis to be conducted in optimisation trials through GAs in order to discharge GAs parameters that are not statistically significant for the evolutionary search in the specific problem. As already pointed out by Eiben et al. (1999), the choice of the suitable parameter values is a time consuming task, and the literature does not offer a conclusive procedure to identify the truly significant parameters, for which suitable values must be set or, alternatively, an adaptation should be imposed during the evolutionary process.

A step-by-step description of the proposed approach may be outlined as follows:

1. Define the case study/ problem and formulate it mathematically (process model) or design it in modular simulators;
2. Define the objective function;
3. Define the constraints of the problem;
4. Define the control variables (optimising variables), i.e., the variables that compose the individuals and that should suffer evolution in order to provide better fitness function values;
5. Stipulate the GA settings and the minimum and maximum allowed values of the control variables;
6. Stipulate the values of the upper and lower levels for the GA parameters to be used in the factorial design study;
7. Build the complete or fractional factorial design spreadsheet, with the many combinations of GA parameters levels that must be supplied to a GA to perform the evolutionary optimisation. For information on how to

build fractional factorial designs, the reader is referred to Barros Neto *et al.* (2003) and Box *et al.* (1978);

8. Perform the optimisation through GA for each combination of GA parameters in order to obtain the problem response to these GA parameters values;
9. Calculate effects of each GA parameters on the problem response, as well as their errors and statistical significance (p-level). Information on how to calculate the effects, its errors and p-levels is found in Barros Neto *et al.* (2003) and Box *et al.* (1978). Calculate, as well, the effects, errors and p-level for the interactions between factors (GA parameters);
10. The GA parameters that do not show statistical significance on the problem response may be discharged in further optimisation studies because, irrespective of which value is stipulated to these parameters, the problem response will not vary significantly, in statistical sense. The GA parameters that show effects statistically significant should be extensively varied in further optimisation works with this particular problem or should suffer a control action, as suggested by Eiben et al. (1999).

For multi-objective optimisation problems (MOOPs), for which a family of solutions (Pareto optimal set) is generated, the approach could also be applied. The Pareto optimal set is composed by solutions comparatively good among themselves and that dominate all other possible solutions. A solution is said to dominate a second one if it is not worse than the second solution in all objectives and is strictly better in at least one objective (Deb et al., 2004; Mitra et al., 2004; Silva and Biscaia Jr., 2003; Suman,2004). In this way, the statistically significant parameters would be those that cause a statistical change in the optimal values for all objectives.

5. Application of the proposed approach

In order to illustrate the proposed approach, it is here applied to four optimisation problems, with different levels of complexities concerning to the number of optimising variables, the presence of constraints, linearity and explicit dependence. This section is organized in the following manner. First, the

selected GA code is presented, with its features and restrictions. The manner in which the constraints are here dealt with in constrained problems is also explained. Then the four case studies are briefly introduced. Finally, the results for each case study are presented and discussed.

5.1 GA code

The GA used was basically the FORTRAN Genetic Algorithm Driver by David Carroll, version 1.7a (Carroll, 2005), with some modifications in order to deal with constraints. This code initializes a random sample of individuals with different genes (problem variables). This initial random sample of individuals is actually dictated by the value assigned to a GA parameter named *idum*: the same initial population is generated every time the code is run with the same value assigned to *idum*. The selection scheme used is tournament selection (Deb, 1999) with a shuffling technique for choosing random pairs for mating. The individuals are coded in binary manner and the routine can apply jump mutation, creep mutation and single-point or uniform crossover. Niching (sharing) and an option for the number of children per pair of parents are added. An option for the use of a micro-GA is also part of the code, as well as the possibility to use elitism, which consists of passing the best individuals, according to their fitness, from one generation to the next, without being modified by the genetic operators. However, the elitism in Carroll's code is restricted to just one individual. In all cases studied in this work, elitism was used.

It is interesting to stress here that the results extracted from the conducted studies are dependent on the selected code. If a real (not binary) code had been selected, the results would have been different. In fact, the specific GA parameters would have been different and so would their effects on the responses. Nevertheless, what is interesting to emphasize is that the proposed approach is general and important and meaningful results can be obtained with its application.

Carroll's code has the following variables to be set, in order to run the optimisation:

- *microga*: if set to 1, the micro-GA search is activated. In the conducted study cases, *microga* is set to 0 (deactivated)
- *npopsiz*: determines the number of individuals in each generation (iteration)
- *pmutate*: jump mutation probability
- *maxgen*: maximum number of generations to be accounted in the evolution
- *idum*: a parameter that determines the initial population of individuals; in the code *idum* is the initial random number seed for the GA run and it must equal a negative integer
- *pcross*: crossover probability
- *pcreep*: creep mutation probability
- *iunifrm*: 0 for single-point crossover; 1 for uniform crossover
- *iniche*: 0 for no niching, 1 for niching
- *nchild*: determines if the number of children per pair of parents is 1 or 2.

The code was modified in order to handle constraints as proposed by Deb (2000). The used approach exploits the feature of the GAs algorithm of pair-wise comparison during the selection of individuals with tournament selection operator. Penalty parameters are not needed in the proposed method because, in any scenario of comparison between two solutions, they are never compared in terms of both objective function and constraint violation information. The proposed fitness function is formulated in the following manner, where infeasible solutions are compared based only on their constraint violation (for a minimization problem):

$$F(\mathbf{x}) = \begin{cases} f(\mathbf{x}) & \text{if } g_j(\mathbf{x}) \geq 0 \quad \forall j=1,2,...,nc \\ f_{\max} + \sum_{j=1}^{m} \left\langle g_j(\mathbf{x}) \right\rangle & \text{otherwise} \end{cases} \tag{1}$$

The parameter f_{max} is the objective function value of the worst feasible solution in the population. In this way, when two feasible solutions are compared, the one with better objective function value is chosen; when one feasible and one

infeasible solution are compared, the feasible solution is chosen; and when two infeasible solutions are compared, the one with smaller constraint violation is chosen (Deb, 2000). The method makes the search initially focuse on finding feasible solutions, and later, when an adequate number of feasible solutions is found, the algorithm finds better feasible solutions by maintaining a diversity in solutions in the feasible region. In a number of test problems and in engineering design problem, this approach has shown to be able to find out constrained optimum solutions (Michalewicz et al., 2000).

5.2 Case studies

The characterization of any problem can be made according to many issues, like the number of linear constraints, the number of nonlinear constraints, the number of equality constraints, the ratio of sizes of feasible search space to the whole, number of variables, and number of local optima and the existence of derivatives of the fitness function (Michalewicz et al., 2000). The case studies selected to exemplify the application of the proposed approach goes from simply ones to nonlinear engineering problems. All case studies, however, were selected focusing engineering applications. For example, f_2 function (case study #2) can find application in fitting data to polynomial types. The majority of the selected case studies have numerous local optima, which cause serious problems for local optimisers.

5.2.1 Case study #1 (f_1)

The first case study is a very simple unconstrained problem, with no local optima and just one global optimum (Hatta et al., 1998). The optimisation problem for case study #1 is described in Eq. (2) and its global optimum is known to be located at (0,0) and with function value of zero.

$$\min_{\mathbf{x}} f_1 = \min_{\mathbf{x}} \sum_{i=1}^{2} x_i^2 \tag{2}$$

Fig. 2 brings the profile of f_1 for $5.12 \leq x_i \leq 5.12$, the interval in which the optimum is searched.

5.2.2 Case study #2 (f_2)

This case study is a typical benchmark GA test function and can be found in many references (Deb, 2000; Jeżowski et al., 2005; Michalewicz and Fogel, 2002). It possesses 13 variables and 9 linear constraints. Eq. (3) formulates mathematically the case study #2, which has a known minimum of -15.

$$\min_{\mathbf{x}} f_2 = \min_{\mathbf{x}} \left(5\sum_{i=1}^{4} x_i - 5\sum_{i=1}^{4} x_i^2 - \sum_{i=5}^{13} x_i \right)$$

$$\begin{aligned}
\text{subject to:} \quad & g_1 \equiv 2x_1 + 2x_2 + x_{10} + x_{11} \le 10 \\
& g_2 \equiv 2x_1 + 2x_3 + x_{10} + x_{12} \le 10 \\
& g_3 \equiv 2x_2 + 2x_3 + x_{11} + x_{12} \le 10 \\
& g_4 \equiv -8x_1 + x_{10} \le 0 \\
& g_5 \equiv -8x_2 + x_{11} \le 0 \\
& g_6 \equiv -8x_3 + x_{12} \le 0 \\
& g_7 \equiv -2x_4 - x_5 + x_{10} \le 0 \\
& g_8 \equiv -2x_6 - x_7 + x_{11} \le 0 \\
& g_9 \equiv -2x_8 - x_9 + x_{12} \le 0
\end{aligned} \tag{3}$$

The minimum and maximum allowed values for the optimising variables are $0 \le x_i \le 1$ for i=1, 2, …, 8, 9, 13 and $0 \le x_i \le 1000$ for i=10, 11, 12.

5.2.3 Case study #3 (f_3)

The case selected is a simple engineering optimisation problem, extracted from Summanwar et al. (2002). It is a heat exchanger network synthesis problem, requiring minimization of the total cost. There is only one optimising variable (T_1) and 12 constraints. The minimization problem can be described by the optimisation statement of Eq. (4).

$$\min_{T_1} f_3 = \min_{T_1}\left[2700\left(\frac{Q_1}{\Delta T_1}\right)+7200\left(\frac{Q_2}{\Delta T_2}\right)+240\left(\frac{Q_3}{\Delta T_3}\right)+900\left(\frac{Q_4}{\Delta T_4}\right)\right]$$

where: $Q_1 = 5.55(T_1 - 395)$

$Q_2 = 1000 - Q_1$

$T_2 = 398 + (Q_2 / 3.125)$

$Q_3 = 5.55(575 - T_1)$

$T_3 = 365 + (Q_3 / 4.545)$

$Q_4 = 3.125(718 - T_2)$

$T_4 = 358 + (Q_4 / 3.571)$

$\Delta T_1 = 0.5(T_1 - 305)$

$\Delta T_2 = 0.5(T_2 - 302)$

$\Delta T_3 = 0.5(T_1 - T_3 + 210)$

$\Delta T_4 = 0.5(T_2 - T_4 + 360)$

subject to:

$g_1 \equiv T_2 \geq 405$

$g_2 \equiv T_2 \leq 718$

$g_3 \equiv T_3 \geq 365$

$g_4 \equiv T_4 \geq 358$

$g_{j+4} \equiv \Delta T_i \geq 5, \quad j=1,..., 4$

$g_{j+8} \equiv Q_i \geq 0, \quad j=1,..., 4$ (4)

The minimum and maximum allowed values for the optimising variable are determined by $405 \leq T_1 \leq 575$ and the best solution, according to Summanwar et al. (2002), is a function value of 36,162.9886.

5.2.4 Case study #4 (f_4)

Case study #4 is an example of parameters estimate, a problem with which many engineers face, particularly those involved in the mathematical modelling of processes. These models frequently contain adjustable parameters that need to be determined from available experimental data. The process selected in this case study is batch ethanol fermentation from sugarcane molasses, for which the mass balance equations that describe microorganisms growth, substrate consumption and ethanol formation are:

$$\frac{dX}{dt} = r_X \tag{5}$$

$$\frac{dS}{dt} = -r_s \tag{6}$$

$$\frac{dP}{dt} = r_p \tag{7}$$

Atala et al. (2001) showed that, when *Saccharomyces cerevisiae* was used as yeast, cellular, substrate and product inhibitions are of importance. In this study, the cell growth rate, r_x, includes terms for such types of inhibitions, as expressed in Eq. (8):

$$r_x = \mu_{max} \frac{S}{K_s + S} \exp(-K_i S)(1 - \frac{X}{X_{max}})^m (1 - \frac{P}{P_{max}})^n X \tag{8}$$

Luedking-Piret expression (Lee et al., 1981) was used to account for the ethanol formation rate, r_p (Eq. 9), while the substrate (sugar) consumption rate, r_s, is given by Eq. (10), balancing cell mass and ethanol formation.

$$r_p = Y_{px} r_x + m_p X \tag{9}$$

$$r_s = (r_x / Y_x) + m_x X \tag{10}$$

According to Eq. (5)-(10), there are 11 parameters (μ_{max}, P_{max}, K_s, K_i, X_{max}, m, n, Y_x, m_x, Y_{px}, and m_p) that have to be estimated from experimental observations. Among them, some parameters are temperature-dependent: μ_{max}, P_{max}, X_{max}, Y_x and Y_{px}. The present case study is the estimate of these temperature-dependent kinetic parameters at 34ºC, based on experimental data (Atala et al., 2001). This parameter estimation, in fact, is part of a larger problem, which looks for the exact dependence of the five parameters on temperature. Nevertheless, the sub-problem of estimate of their values at 34°C is here selected as case study #4. The values of the non temperature-dependent parameters were extracted from Atala et al. (2001), which is referred to for detailed information on the process. These values are presented in Table 1.

The mathematical estimate of model parameters is made based on optimisation of a quantity that is a function of the kinetic parameters to be estimated. In the present case study, the least-squares error is considered as the chosen criterion to evaluate how close the computed profiles of the state variables (cell

mass, substrate and ethanol concentrations) is to the experimental observations (Wang et al., 2001). In this way, the optimisation problem of case study #4 can be described by Eq. (11):

$$\min_{\mathbf{x}} f_4 = \min_{\mathbf{x}} \left\{ \sum_{i=1}^{np} \left[\frac{(X_i - Xe_i)^2}{Xe_{\max}^2} + \frac{(S_i - Se_i)^2}{Se_{\max}^2} + \frac{(P_i - Pe_i)^2}{Pe_{\max}^2} \right] \right\} = \min_{\mathbf{x}} \left(\sum_{i=1}^{np} \varepsilon_i(\mathbf{x}) \right)$$

subject to: Model equations (5)-(10) (11)

In the objective function Xe_i, Se_i and Pe_i are the measured concentrations of cell mass, substrate and ethanol at the sampling time *i*. X_i, S_i and P_i are the concentrations computed by the model at the sampling time *i*. Xe_{max}, Se_{max} and Pe_{max} are the maximum measured concentrations and the term *np* is number of sampling points. Here $\varepsilon_i(\mathbf{x})$ is the error in the output due to the *i*th sample.

When one faces with the problem of parameters fitting, one of the major problems is the lack of information on the order of magnitude of the parameters, which, for this case study, implies a large range of searching values for the optimizing variables. The minimum and maximum allowed values for the temperature-dependent kinetic parameters were set so as to allow for a large range of values, since the order of magnitude of each parameter is supposed to be unknown. Table 2 brings the minimum and maximum allowed values for each one of the kinetic parameters. The values used at this table were chosen in a very large range to evaluate difficulties normally found in the definition of values for kinetic parameters. The aim in this study is to be able to evaluate the potential of the GA to work such adverse condition.

5.3 Results and Discussion

In order to estipulate a value for the population size at the zero level (central point), the scaling law suggested by Deb (1998) was used:

$$npoposiz = 1.65 \times 2^{0.21 \cdot \ell} \quad (12)$$

where ℓ is the total chromosome string length and corresponds, for each case study, to the total sum of each variable string length, ℓ_i:

$$\ell = \sum_{i=1}^{NV} \ell_i \tag{13}$$

Each variable string length is calculated based on the interval upon which the corresponding variable can vary and its required precision, as in Eq (14), where α_i denotes the required precision:

$$\ell_i = \log_2 \left(\frac{x_i^{\max} - x_i^{\min}}{\alpha_i} \right) \tag{14}$$

The estimate of the maximum number of allowed generations was set equal to the estimate of the population size.

The estimate of population size for the zero level was constrained to 225 individuals, since Eq. (12) is overkill, especially when there are many variables with a very tiny precision required in the problem.

Both jump and creep mutation probabilities were estimated at level zero with the scaling law of Eq. (15).

$$pcreep = pmutate = 1/\ell \tag{15}$$

Concerning to the crossover probability, the usual practice is to set at a large value (Deb, 1998). In all case studies, the crossover probability at level zero was set to 0.8. A variation of ±20% to the central point value of each factor was made in order to calculate the values for the upper and lower level values in each case study.

5.3.1 Case study #1

The string length for each problem variable is calculated as in Eq. (16), which leads to $\ell = 20$, and so npopsiz=30, by Eq. (12), and $pcreep = pmutate = 0.05$.

$$\ell_1 = \ell_2 = \log_2 \left(\frac{5.12 + 5.12}{0.01} \right) = \log_2 (1024) = 10 \tag{16}$$

For this first study case, 9 parameters of GA were selected as factors, in order to have their influence on the fitness function analyzed. Table 3 presents these factors and their corresponding values for each level. Some GA parameters of the used code allow only two possible values. This happens, for example, with

iunifrm: only 0 or 1 can be assigned to it, indicating, respectively, single-point and uniform crossover. Due to it, no central point can be calculated for the factorial design in this case study.

A fractional factorial design 2^{9-3} study was carried out. Table 4 depicts the combinations of GA parameters for the optimisations that were conducted for the fractional factorial design. The results for the fitness function of the best individual in the last generation generated by the GA in each case are presented in the final column. As case study #1 is an unconstrained one, F_1, the fitness function of this study case, is equal to f_1, its objective function.

The software STATISTICA (Statsoft, v. 6.0) was used to analyze the results. Table 5 presents the effect estimates of the GA parameters, calculated with 95% of confidence, with no interaction between the effects. Fig.3 brings the corresponding Pareto chart, used for identification of the most important factors. The 't' statistics that figures in Table 5 is presented with its freedom degree, which is 54, since there were 64 available runs and only 10 effects were calculated (the mean effect plus the effects for each factor). The values for the t-statistics are also indicated next to each bar in the Pareto chart.

As can be seen, two parameters, the jump mutation probability (expressed by *pmutate*) and the maximum number of generation allowed (expressed by *maxgen*) have significant effects on the search for a minimum of F_1.

The fraction factorial design was reduced by a factor of 8 from the complete factorial design and, so, some 2-way interaction effects cannot be estimated, since they are linear combination of other effects. In this way, the effects of (4) by (8) – maxgen *versus* pcross-, (4) by (9) – maxgen *versus* pmutate- and (8) by (9) – pcross *versus* pmutate- cannot be estimated. All estimable interaction effects are presented in Table 6.

Table 6 shows that no interaction effect is statistically important. Once again, factors (9) and (4) (jump mutation probability and maximum number of generations allowed) have shown a great effect on F_1 of the best individual generated by GA at the end of the evolution process.

5.3.2 Case study #2

The first 9 variables and the 13th one have string lengths calculated by Eq. (17), while string lengths for the 10th, 11th, and 12th variable are determined by Eq. (18).

$$\ell_i = \log_2\left(\frac{1-0}{0.001}\right) = \log_2(1000) \approx 10 \quad \text{for i=1,2,...,9 and i=13} \tag{17}$$

$$\ell_i = \log_2\left(\frac{10^3-0}{0.001}\right) = \log_2\left(10^6\right) \approx 20 \quad \text{for i=10,11,12} \tag{18}$$

The chromosome string is then $\ell = 10*10+3*20 = 160$. In this case, Eq. (12) is overkill (it would be necessary 7x10^9 individuals, according to Eq. (12)) and so npopsiz is set to 225. The mutation probability is $pcreep = pmutate = 1/160 = 6.25x10^{-3}$.

From study case #2 on, six GA parameters were selected as factors. In these three case studies (cases studies #2, #3 and #4), uniform crossover, 2 children per pair of parents and niching were set fixed in the code, i.e., *iunifrm*, *nchild* and *iniche* are part of the GA settings, with values fixed, respectively, to 1, 2 and 1.

Table 7 presents the analyzed GA parameters (factorial design factors) and corresponding values for each level, including the central point, while Table 8 presents the conducted optimisations for a 2^{6-1} fractional factorial design with a central point. F_2 that figures in the final column is the fitness function of the best individual in the last generation. Although this study case is a constrained optimisation problem, the way constraints were handled (Eq. (1)) led to feasible individuals, so that F_2 for the best individual is actually its value of f_2.

Table 9 and 10 present the effect estimates for, respectively, no interaction between the effects and with two-way interaction. Fig. 4 and 5 are the corresponding Pareto charts.

For case study#2, the crossover probability (*pcross*) and the maximum number of generations (*maxgen*) are GA parameters with the most significant effects on the response. Since the initial population, represented by *idum*, has an effect near the limit of significance, the analysis of interactions of factors (in couples) is conducted. In this second set of results (Table 10 and Fig. 5), the interaction

between the crossover probability and the initial population has shown to be of great significance. This result carries a great influence of the crossover probability, the most meaningful effect for this case study, but also shows that the initial population must be considered in further optimisations. The importance of the initial population effect is also corroborated by the significant (though the least one) effect it has on F_2 (Fig. 5)

5.3.3 Case study #3

The only problem variable determine the chromosome length, calculated by Eq. (19). The use of Eq. (12) leads to npopsiz ≈ 20 and $pcreep = pmutate = 1/17 = 0.0588$.

$$\ell = \ell_1 = \log_2\left(\frac{575-405}{0.001}\right) \approx 17 \tag{19}$$

Tables 11 and 12 are related to the 2^{6-1} fractional factorial design for case study #3. Tables 13 and 14 present the effect and its statistical significance for, respectively, no factor interaction and with 2-way interaction. As can be extracted from theses tables, only the population size has shown to be a parameter of statistical significance on the objective function of case study #3. Fig.6 brings the Pareto chart of the main effects. No interaction factor is of statistical significance (Table 14).

5.3.4 Case study #4

The calculation for the string length of each variable is made by Eq. (20)-(21), leading to $\ell = 4*24+20 = 116$.

$$\ell_1 = \ell_2 = \ell_3 = \ell_5 = \log_2\left(\frac{1000-1x10^{-3}}{0.0001}\right) \approx 24 \tag{20}$$

$$\ell_4 = \log_2\left(\frac{100-1x10^{-1}}{0.0001}\right) \approx 20 \tag{21}$$

The application of Eq. (12) leads to an overkill, and then, the population size is limited, at first, to 225 individuals. The mutation probabilities are given by Eq. (22).

$$pcreep = pmutate = 1/116 = 8.621x10^{-3} \tag{22}$$

The proposed approach should be a task to be executed in order to provide insight of the significant parameters for the specific case study. Being a prior study, whose motivation is on saving time and computational effort, the approach is not suitable to be applied in long time executions. For large engineering problems, for which case study #4 is a relatively simple example, the execution time is extremely large when a lot of individuals and a large number of generations are stipulated. This can be a challenge, particularly when one looks for real time applications. Apart from that, the evolution rate (that is, the rate upon which the best fitness function in each generation evolves) tends to have a large value in the first generations and then diminishes to near zero (or to zero, in certain cases) for larger generations numbers. For this case study, the time execution, when 225 generations with 225 individuals is used, is about 45 minutes in a PC of 2,4GHz. For a prior analysis, this time is too long in order to execute all runs for the factorial design. In this way, the number of individuals for the level zero was set to 50, whose evolution computation time is about 2 minutes. In this way, Table 15 brings the values for each level of the GA parameters analysed in this case study. Table 16 brings the correspondent 2^{6-1} fractional factorial design. The effects, with no factor interaction and with 2-way interaction, are given in Tables 17 and 18 respectively and the corresponding Pareto chart are presented in Fig. (7) and (8).

The most significant GA parameter for case study #4 is the initial population, as can be extracted from Table 17 and Fig 7. The study of interaction between factors conducted to a great significance of the interaction between the crossover and the creep mutation probabilities as well as of the interaction between the crossover probability and the population size. Apart from that, the population size appears as the least significant effect (Table18 and Fig. 18). The interpretation of these results can be that the crossover probability has an effect that should be considerable, so that its interaction with the creep mutation probability is even larger than the effect of the initial population. The population size has a minor significant effect, but interacting with the crossover probability, they have together a great significant effect. In this way, for case study #4, the

significant GA parameters are the initial population, the crossover probability, the population size and the creep mutation probability.

6. Conclusions

A systematic approach to detect the best set of parameters for GA is proposed, coupling GA to factorial design technique. The evolution of GAs is greatly determined by the values of these parameters and, so, they should be varied in further optimisation works or they should suffer a type of control action. Four case studies were presented in order to demonstrate the application of the approach, which shows that the set of significant parameters is dependent on the case study. However, the proposed approach is useful as a tool to identify the best set of parameters to be considered.

The methodology should be seen as a prior task to be executed in order to give insight of the significant parameters for a problem that is to be optimised using GA. The approach saves time, since gives an statistical orientation of on which GA parameters efforts should be concentrated in the global optimum search. It is worthwhile mentioning that the objective function is part of the problem formulation and obviously it influences on the impact of the GA parameters and this claims to the need of a procedure able to discriminate among the parameters and in order to do an extensive analysis.

The proposed methodology is not restricted to single objective problems and can be normally used in multi-objective optimisation problems.

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Nomenclature

< >: indicates absolute value of the operand, if it is negative, and zero value otherwise.

best_fitness: vector that records the best fitness function in each generation

best_individual: vector that records the best individual in each generation

F(**x**): Fitness function

f(**x**): objective function

f_{max}: Objective function value of the worst feasible solution in the population

GC: generation counter

g_j(**x**): Inequality constraint

idum: GA parameter to determine the initial population of individuals

iniche: GA parameter to determine if niching is used

iunifrm: GA parameter to determine if single or uniform crossover is used

IC: individual counter

K_i: substrate inhibition coefficient (m^3/kg)

K_S: substrate saturation constant (kg/m^3)

ℓ: total chromosome string length

ℓ_i: *i*th variable string length

m: parameter used to describe cellular inhibition

maxgen: Maximum number of generations in the evolution of GA code

microga: GA parameter to determine if migroga option is used

m_p: ethanol production associated with growth (kg/[kg h])

m_X: maintenance coefficient (kg/[kg h])

n: parameter used to describe product inhibition

nc: number of constraints

nchild: GA parameter to determine the number of children per pair of parents

np: number of sample points

npopsiz: GA parameter to determine the number of individuals per generation

p: p-level, probability of error that is involved in accepting an effect as valid

P: concentration of ethanol (kg/m^3)

pcreep: creep mutation probability in the GA code

pcross: crossover probability in the GA code

Pe_i: measured concentration of ethanol at sample time i

Pe_{max}: maximum measured concentration of ethanol

P_i: concentration ethanol at sample time i computed by the model

P_{max}: product concentration when cell growth ceases (kg/m^3)

pmutate: jump mutation probability in the GA code

Q_i: heat rate exchanged in the *i*th heat exchanger

r_p: kinetic rate of ethanol formation (kg/[m^3h])

r_S: kinetic rate of substrate consumption (kg/[m^3h])

r_X: cell kinetic growth rate (kg/[m^3h])

S: concentration of substrate (kg/m^3)

Se_i: measured concentration of substrate at sample time i

Se_{max}: maximum measured concentration of substrate

S_i: concentration of substrate at sample time i computed by the model

t: time

t(freedom degree): t-statistics

T_i: temperature of the *i*th flow in the heat exchanger network (K)

x: vector containing the optimising (adjustable) variables

x_i^{max} : maximum allowed value for *i*th optimising variable

x_i^{min} : minimum allowed value for *i*th optimising variable

X: concentration of cell mass (kg/m^3)

Xe_i: measured concentration of cell mass at sample time i

Xe_{max}: maximum measured concentration of cell mass

X_i: concentration of cell mass at sample time i computed by the model

X_{max}: biomass concentration when cell growth ceases (kg/m^3)

Y_{px}: yield of product based on cell growth (kg/kg)

Y_X: limit cellular yield (kg/kg)

Greek letters

α_i : required precision for *i*th optimising variable

ΔT_i : difference of temperatures in heat exchanger flows (K)

$\varepsilon_i(\mathbf{x})$: error in the output due to the *i*th sample

μ_{max}: maximum specific growth rate (h^{-1})

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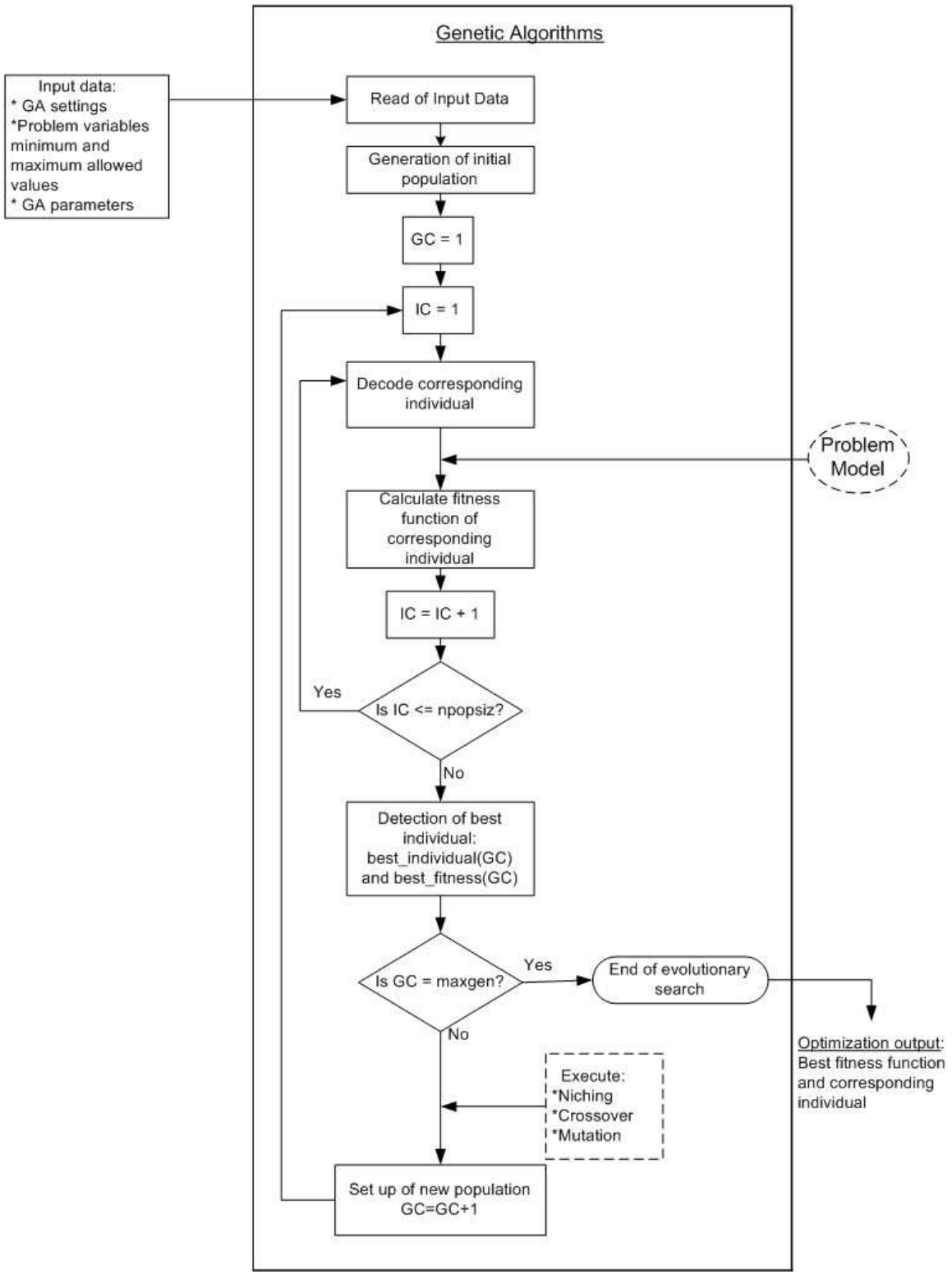

Fig. 1: General working structure of GAs.

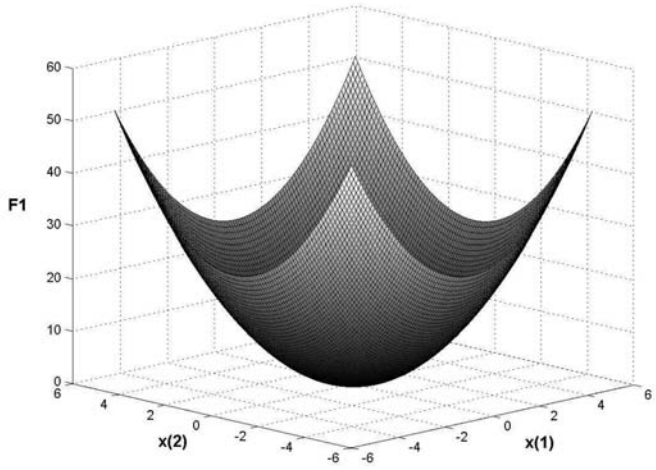

Fig. 2: Profile of f_1

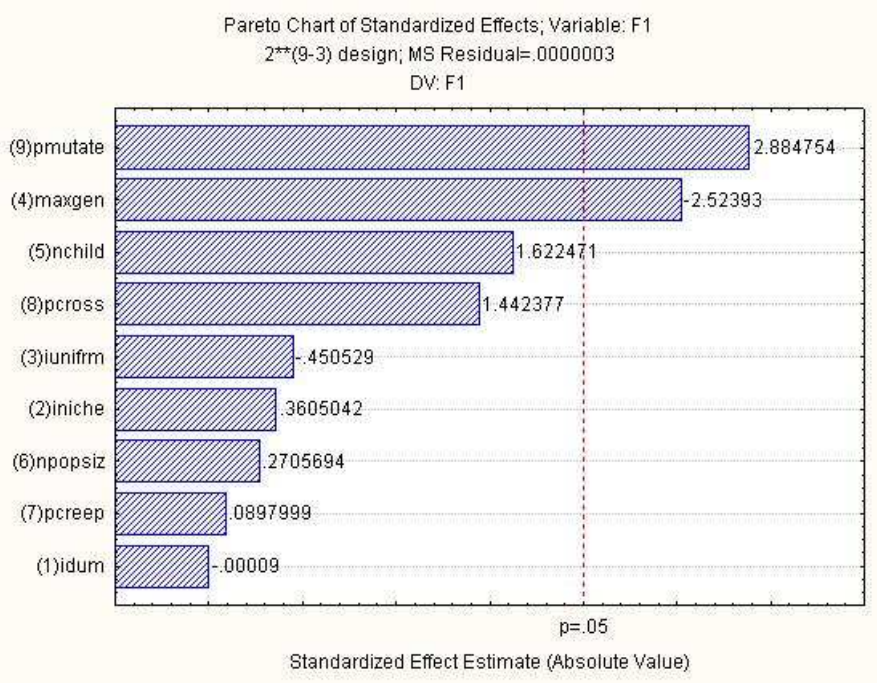

Fig. 3: Pareto chart of variables effects on F_1 of the best individual (at 95% of confidence level), with no factor interactions.

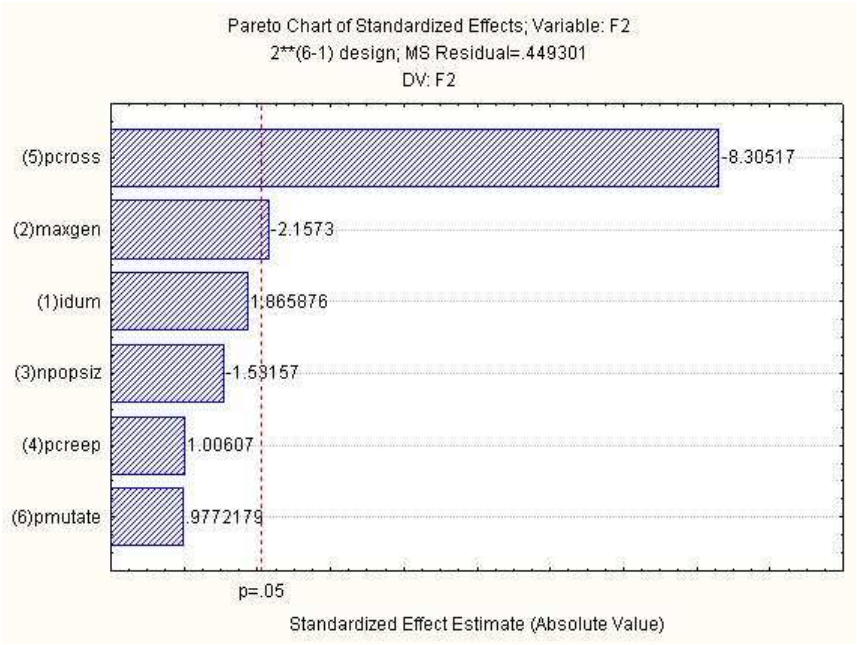

Fig. 4: Pareto chart of variables effects on F_2 of the best individual (at 95% of confidence level), with no factor interactions.

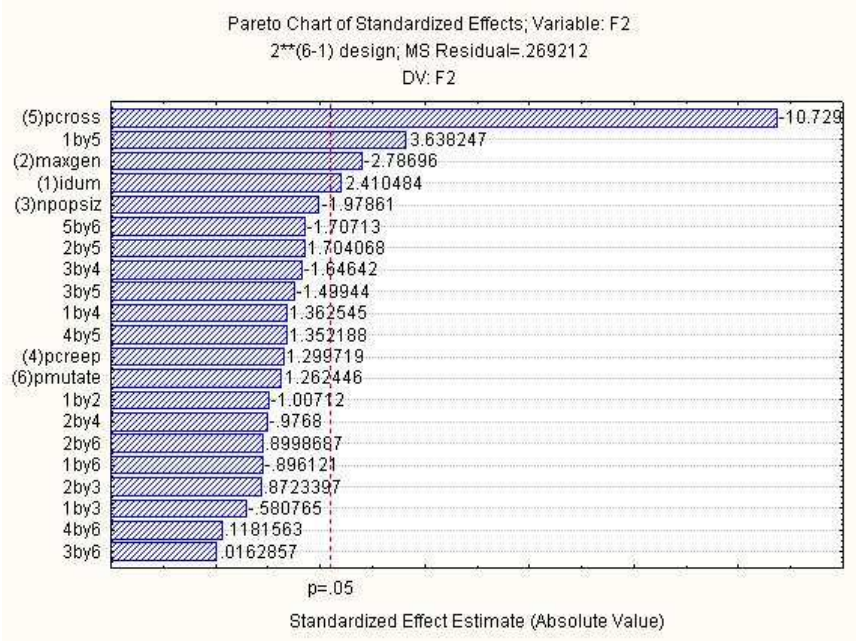

Fig. 5: Pareto chart of variables effects on F_2 of the best individual (at 95% of confidence level), with two factor interactions.

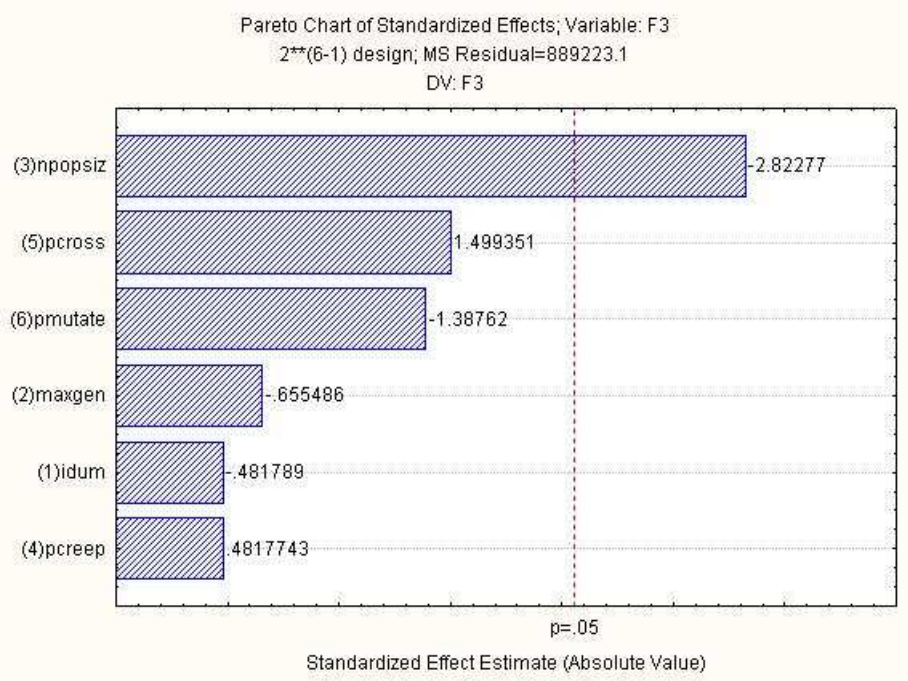

Fig. 6: Pareto chart of variables effects on F_3 of the best individual (at 95% of confidence level), with no factor interactions.

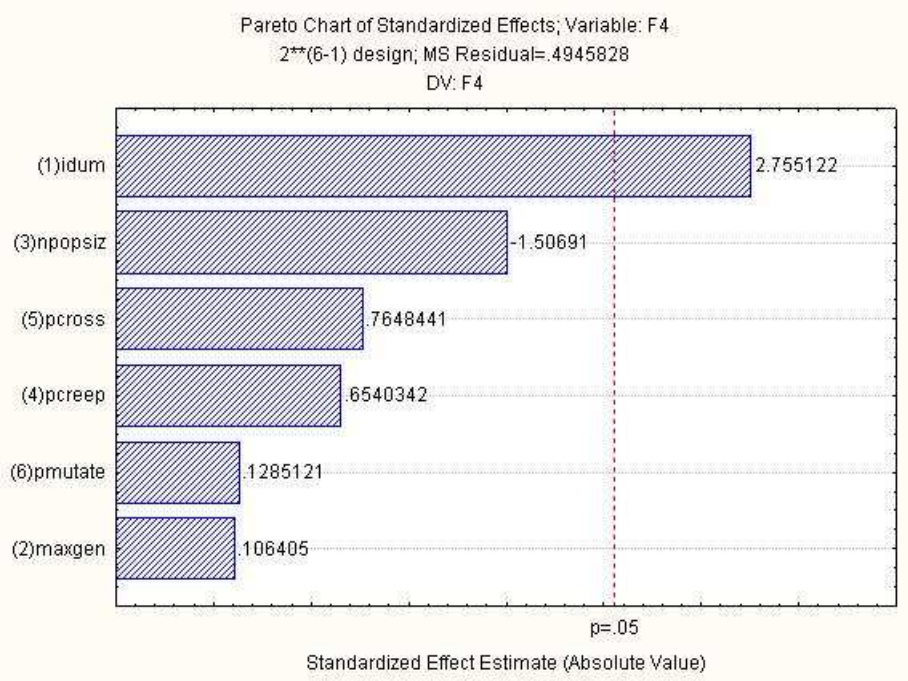

Fig. 7: Pareto chart of variables effects on F_4 of the best individual (at 95% of confidence level), with no factor interactions.

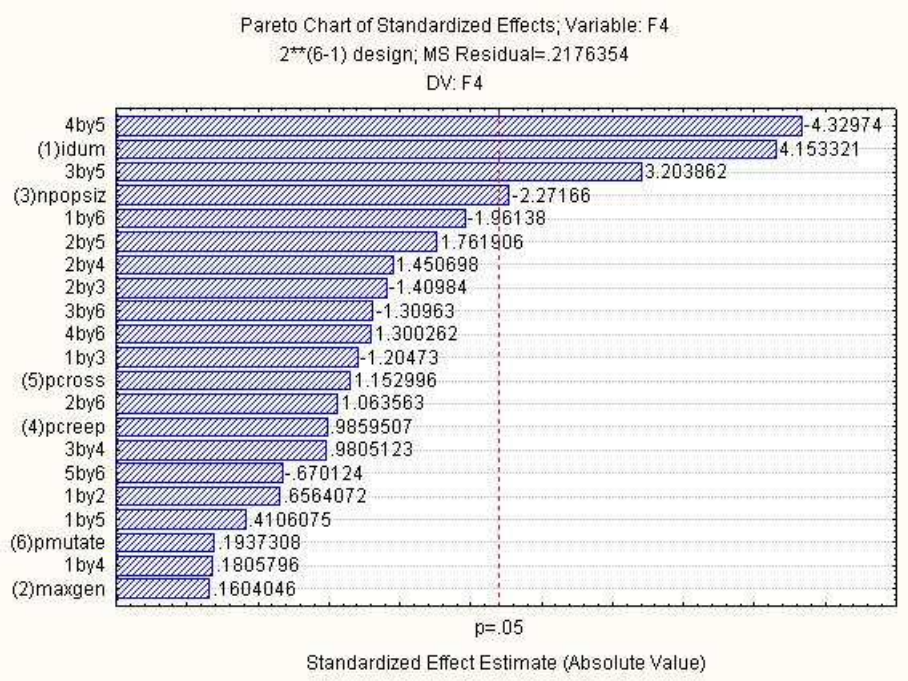

Fig. 8: Pareto chart of variables effects on F_4 of the best individual (at 95% of confidence level), with two factor interactions.

Table 1: Values for the non temperature-dependent kinetic parameters of the batch fermentation form sugarcane molasses using *Saccharomyces cerevisiae*

Batch Fermentation non Temperature-dependent Parameter	Value
K_s	4.1
K_i	4.23×10^{-3}
m	1
n	1.5
m_x	0.2
m_p	0.1

Table 2: Minimum and maximum allowed values, in the GA search, for the temperature-dependent kinetic parameters of the batch fermentation from sugarcane molasses using *Saccharomyces cerevisiae*

Batch Fermentation Temperature-dependent Parameter	Minimum allowed value	Maximum allowed value
μ_{max}	0.001	1000
P_{max}	0.001	1000

X_{max}	0.001	1000
Y_x	0.001	1000
Y_{px}	0.100	100

Table 3: Levels of the parameters used in sensitivity analysis of the GA code applied to case study #1

GA Parameters	(-) level	(+) level
(1) idum[1]	-1200	-800
(2) iniche	0	1
(3) iunifrm	0	1
(4) maxgen	24	36
(5) nchild	1	2
(6) npopsiz	24	36
(7) pcreep	0.04	0.06
(8) pcross	0.64	0.96
(9) pmutate	0.04	0.06

[1] idum assumes negative integer value and is the initial seed for the GA run; each value assigned to idum gives rise to a different initial population

Table 4: Fractional factorial design 2^{9-3} study results for case study #1

Run	idum	iniche	iunifrm	maxgen	nchild	npopsiz	pcreep	pcross	pmutate	F1
CS1-01	-1200	0	0	24	1	24	0.06	0.96	0.06	2.505E-04
CS1-02	-800	0	0	24	1	24	0.04	0.64	0.06	1.453E-03
CS1-03	-1200	1	0	24	1	24	0.04	0.96	0.06	5.010E-05
CS1-04	-800	1	0	24	1	24	0.06	0.64	0.06	1.252E-03
CS1-05	-1200	0	1	24	1	24	0.04	0.64	0.04	5.010E-05
CS1-06	-800	0	1	24	1	24	0.06	0.96	0.04	5.010E-05
CS1-07	-1200	1	1	24	1	24	0.06	0.64	0.04	5.010E-05
CS1-08	-800	1	1	24	1	24	0.04	0.96	0.04	5.010E-05
CS1-09	-1200	0	0	36	1	24	0.04	0.96	0.04	5.010E-05
CS1-10	-800	0	0	36	1	24	0.06	0.64	0.04	5.010E-05
CS1-11	-1200	1	0	36	1	24	0.06	0.96	0.04	2.505E-04
CS1-12	-800	1	0	36	1	24	0.04	0.64	0.04	5.010E-05
CS1-13	-1200	0	1	36	1	24	0.06	0.64	0.06	5.010E-05
CS1-14	-800	0	1	36	1	24	0.04	0.96	0.06	5.010E-05
CS1-15	-1200	1	1	36	1	24	0.04	0.64	0.06	2.505E-04
CS1-16	-800	1	1	36	1	24	0.06	0.96	0.06	5.010E-05
CS1-17	-1200	0	0	24	2	24	0.06	0.64	0.04	5.010E-05
CS1-18	-800	0	0	24	2	24	0.04	0.96	0.04	5.010E-05
CS1-19	-1200	1	0	24	2	24	0.04	0.64	0.04	5.010E-05
CS1-20	-800	1	0	24	2	24	0.06	0.96	0.04	1.252E-03
CS1-21	-1200	0	1	24	2	24	0.04	0.96	0.06	2.054E-03
CS1-22	-800	0	1	24	2	24	0.06	0.64	0.06	1.252E-03
CS1-23	-1200	1	1	24	2	24	0.06	0.96	0.06	2.505E-04
CS1-24	-800	1	1	24	2	24	0.04	0.64	0.06	6.513E-04
CS1-25	-1200	0	0	36	2	24	0.04	0.64	0.06	5.010E-05
CS1-26	-800	0	0	36	2	24	0.06	0.96	0.06	5.010E-05
CS1-27	-1200	1	0	36	2	24	0.06	0.64	0.06	5.010E-05

CS1-28	-800	1	0	36	2	24	0.04	0.96	0.06	5.010E-05
CS1-29	-1200	0	1	36	2	24	0.06	0.96	0.04	2.505E-04
CS1-30	-800	0	1	36	2	24	0.04	0.64	0.04	5.010E-05
CS1-31	-1200	1	1	36	2	24	0.04	0.96	0.04	5.010E-05
CS1-32	-800	1	1	36	2	24	0.06	0.64	0.04	5.010E-05
CS1-33	-1200	0	0	24	1	36	0.06	0.64	0.04	5.010E-05
CS1-34	-800	0	0	24	1	36	0.04	0.96	0.04	6.513E-04
CS1-35	-1200	1	0	24	1	36	0.04	0.64	0.04	5.010E-05
CS1-36	-800	1	0	24	1	36	0.06	0.96	0.04	5.010E-05
CS1-37	-1200	0	1	24	1	36	0.04	0.96	0.06	2.505E-04
CS1-38	-800	0	1	24	1	36	0.06	0.64	0.06	2.505E-04
CS1-39	-1200	1	1	24	1	36	0.06	0.96	0.06	8.517E-04
CS1-40	-800	1	1	24	1	36	0.04	0.64	0.06	5.010E-05
CS1-41	-1200	0	0	36	1	36	0.04	0.64	0.06	4.509E-04
CS1-42	-800	0	0	36	1	36	0.06	0.96	0.06	5.010E-05
CS1-43	-1200	1	0	36	1	36	0.06	0.64	0.06	2.505E-04
CS1-44	-800	1	0	36	1	36	0.04	0.96	0.06	5.010E-05
CS1-45	-1200	0	1	36	1	36	0.06	0.96	0.04	5.010E-05
CS1-46	-800	0	1	36	1	36	0.04	0.64	0.04	5.010E-05
CS1-47	-1200	1	1	36	1	36	0.04	0.96	0.04	5.010E-05
CS1-48	-800	1	1	36	1	36	0.06	0.64	0.04	5.010E-05
CS1-49	-1200	0	0	24	2	36	0.06	0.96	0.06	1.252E-03
CS1-50	-800	0	0	24	2	36	0.04	0.64	0.06	5.010E-05
CS1-51	-1200	1	0	24	2	36	0.04	0.96	0.06	3.256E-03
CS1-52	-800	1	0	24	2	36	0.06	0.64	0.06	2.505E-04
CS1-53	-1200	0	1	24	2	36	0.04	0.64	0.04	2.505E-04
CS1-54	-800	0	1	24	2	36	0.06	0.96	0.04	2.505E-04
CS1-55	-1200	1	1	24	2	36	0.06	0.64	0.04	5.010E-05
CS1-56	-800	1	1	24	2	36	0.04	0.96	0.04	5.010E-05
CS1-57	-1200	0	0	36	2	36	0.04	0.96	0.04	5.010E-05
CS1-58	-800	0	0	36	2	36	0.06	0.64	0.04	2.505E-04
CS1-59	-1200	1	0	36	2	36	0.06	0.96	0.04	5.010E-05
CS1-60	-800	1	0	36	2	36	0.04	0.64	0.04	5.010E-05
CS1-61	-1200	0	1	36	2	36	0.06	0.64	0.06	5.010E-05
CS1-62	-800	0	1	36	2	36	0.04	0.96	0.06	2.505E-04
CS1-63	-1200	1	1	36	2	36	0.04	0.64	0.06	5.010E-05
CS1-64	-800	1	1	36	2	36	0.06	0.96	0.06	2.054E-03

Table 5: Effect estimates on F_1 for the fractional factorial design with no factor interactions (case study #1)

Factor	**Effect**	**Standard error**	**t(54)**	**p**
Mean	*0.000338*	*0.000069*	*4.86804*	*0.000010*
(1) idum	0.000000	0.000139	-0.00009	0.999929
(2) iniche	0.000050	0.000139	0.36050	0.719876
(3) inufrm	-0.000063	0.000139	-0.45053	0.654133
(4) maxgen	*-0.000351*	*0.000139*	*-2.52393*	*0.014579*
(5) nchild	0.000225	0.000139	1.62247	0.110527
(6) npopsiz	0.000038	0.000139	0.27057	0.787754
(7) pcreep	0.000012	0.000139	0.08980	0.928778
(8) pcross	0.000200	0.000139	1.44238	0.154971

(9) pmutate	*0.000401*	*0.000139*	*2.88475*	*0.005617*

Italic values: significant for a 95% confidence level

Table 6: Effect estimates on F_1 for the fractional factorial design with two factor interactions (case study #1)

Factor	Effect	Standard Error	t(21)	p
Mean	0.000338	0.000080	4.21739	0.000386
(1)idum	0.000000	0.000160	-0.00008	0.999939
(2)iniche	0.000050	0.000160	0.31232	0.757878
(3)iunifrm	-0.000063	0.000160	-0.39031	0.700237
(4)maxgen	*-0.000351*	*0.000160*	*-2.18659*	*0.040234*
(5)nchild	0.000225	0.000160	1.40561	0.174462
(6)npopsiz	0.000038	0.000160	0.23441	0.816941
(7)pcreep	0.000012	0.000160	0.07780	0.938726
(8)pcross	0.000200	0.000160	1.24959	0.225198
(9)pmutate	*0.000401*	*0.000160*	*2.49918*	*0.020815*
1 by 2	0.000025	0.000160	0.15606	0.877474
1 by 3	0.000038	0.000160	0.23421	0.817090
1 by 4	0.000075	0.000160	0.46869	0.644117
1 by 5	-0.000075	0.000160	-0.46858	0.644200
1 by 6	-0.000163	0.000160	-1.01499	0.321663
1 by 7	0.000213	0.000160	1.32750	0.198593
1 by 8	-0.000250	0.000160	-1.56191	0.133254
1 by 9	-0.000100	0.000160	-0.62476	0.538861
2 by 3	-0.000088	0.000160	-0.54645	0.590515
2 by 4	0.000050	0.000160	0.31251	0.757732
2 by 5	0.000075	0.000160	0.46877	0.644063
2 by 6	0.000138	0.000160	0.85928	0.399890
2 by 7	0.000113	0.000160	0.70306	0.489740
2 by 8	0.000125	0.000160	0.78101	0.443511
2 by 9	0.000050	0.000160	0.31251	0.757732
3 by 4	0.000163	0.000160	1.01515	0.321590
3 by 5	0.000113	0.000160	0.70306	0.489740
3 by 6	-0.000075	0.000160	-0.46854	0.644227
3 by 7	0.000075	0.000160	0.46877	0.644063
3 by 8	0.000013	0.000160	0.07838	0.938266
3 by 9	0.000038	0.000160	0.23437	0.816970
4 by 5	-0.000125	0.000160	-0.78078	0.443645
4 by 6	0.000113	0.000160	0.70287	0.489859
4 by 7	0.000113	0.000160	0.70326	0.489621
5 by 6	0.000088	0.000160	0.54669	0.590357
5 by 7	0.000013	0.000160	0.07803	0.938542
5 by 8	0.000301	0.000160	1.87431	0.074868
5 by 9	0.000150	0.000160	0.93715	0.359333
6 by 7	0.000000	0.000160	0.00027	0.999785
6 by 8	0.000238	0.000160	1.48380	0.152717
6 by 9	0.000063	0.000160	0.39043	0.700152
7 by 8	-0.000013	0.000160	-0.07799	0.938573

7 by 9	-0.000063	0.000160	-0.39066	0.699982

Italic values: significant for a 95% confidence level

Table 7: Levels of the parameters used in sensitivity analysis of the GA code applied to case study #2

GA Parameters	(-) level	Central	(+) level
(1) idum	-1200	-1000	-800
(2) maxgen	180	225	270
(3) npopsiz	180	225	270
(4) pcreep	0.00500	0.00625	0.00750
(5) pcross	0.64	0.8	0.96
(6) pmutate	0.00500	0.00625	0.00750

Table 8: Fractional factorial design 2^{6-1} study results for case study #2

Run	idum	maxgen	npopsiz	pcreep	pcross	pmutate	F2
CS2-01	-1200	180	180	0.00500	0.64	0.0050	-11.2507
CS2-02	-800	180	180	0.00500	0.64	0.0075	-11.2612
CS2-03	-1200	270	180	0.00500	0.64	0.0075	-11.6875
CS2-04	-800	270	180	0.00500	0.64	0.0050	-12.4535
CS2-05	-1200	180	270	0.00500	0.64	0.0075	-10.3636
CS2-06	-800	180	270	0.00500	0.64	0.0050	-11.3462
CS2-07	-1200	270	270	0.00500	0.64	0.0050	-11.7452
CS2-08	-800	270	270	0.00500	0.64	0.0075	-11.9710
CS2-09	-1200	180	180	0.00750	0.64	0.0075	-10.4403
CS2-10	-800	180	180	0.00750	0.64	0.0050	-11.1042
CS2-11	-1200	270	180	0.00750	0.64	0.0050	-11.7780
CS2-12	-800	270	180	0.00750	0.64	0.0075	-11.7904
CS2-13	-1200	180	270	0.00750	0.64	0.0050	-12.2913
CS2-14	-800	180	270	0.00750	0.64	0.0075	-10.7645
CS2-15	-1200	270	270	0.00750	0.64	0.0075	-11.6599
CS2-16	-800	270	270	0.00750	0.64	0.0050	-12.3273
CS2-17	-1200	180	180	0.00500	0.96	0.0075	-14.3243
CS2-18	-800	180	180	0.00500	0.96	0.0050	-12.5684
CS2-19	-1200	270	180	0.00500	0.96	0.0050	-14.5072
CS2-20	-800	270	180	0.00500	0.96	0.0075	-12.6474
CS2-21	-1200	180	270	0.00500	0.96	0.0050	-14.2432
CS2-22	-800	180	270	0.00500	0.96	0.0075	-14.2581
CS2-23	-1200	270	270	0.00500	0.96	0.0075	-13.5912
CS2-24	-800	270	270	0.00500	0.96	0.0050	-13.6692
CS2-25	-1200	180	180	0.00750	0.96	0.0050	-13.0883
CS2-26	-800	180	180	0.00750	0.96	0.0075	-11.8159
CS2-27	-1200	270	180	0.00750	0.96	0.0075	-13.6570
CS2-28	-800	270	180	0.00750	0.96	0.0050	-12.7025
CS2-29	-1200	180	270	0.00750	0.96	0.0075	-14.4513
CS2-30	-800	180	270	0.00750	0.96	0.0050	-12.3190
CS2-31	-1200	270	270	0.00750	0.96	0.0050	-14.4390
CS2-32	-800	270	270	0.00750	0.96	0.0075	-13.4442
CS2-33	-1000	225	225	0.00625	0.80	0.0063	-12.4769

Table 9: Effect estimates on F_2 for the fractional factorial design with no factor interactions (case study #2)

Factor	Effect	Standard Error	t(26)	p
Mean	-12.4981	0.116684	-107.111	0.000000
(1)idum	0.4422	0.236987	1.866	0.073379
(2)maxgen	*-0.5113*	*0.236987*	*-2.157*	*0.040403*
(3)npopsiz	-0.3630	0.236987	-1.532	0.137706
(4)pcreep	0.2384	0.236987	1.006	0.323654
(5)pcross	*-1.9682*	*0.236987*	*-8.305*	*0.000000*
(6)pmutate	0.2316	0.236987	0.977	0.337467

Italic values: significant for a 95% confidence level

Table 10: Effect estimates on F_2 for the fractional factorial design with two factor interactions (case study #2)

Factor	Effect	Standard Error	t(11)	p
Mean	-12.4981	0.090321	-138.374	0.000000
(1)idum	*0.4422*	*0.183443*	*2.410*	*0.034585*
(2)maxgen	*-0.5113*	*0.183443*	*-2.787*	*0.017682*
(3)npopsiz	-0.3630	0.183443	-1.979	0.073444
(4)pcreep	0.2384	0.183443	1.300	0.220274
(5)pcross	*-1.9682*	*0.183443*	*-10.729*	*0.000000*
(6)pmutate	0.2316	0.183443	1.262	0.232896
1 by 2	-0.1848	0.183443	-1.007	0.335516
1 by 3	-0.1065	0.183443	-0.581	0.573105
1 by 4	0.2500	0.183443	1.363	0.200271
1 by 5	*0.6674*	*0.183443*	*3.638*	*0.003900*
1 by 6	-0.1644	0.183443	-0.896	0.389378
2 by 3	0.1600	0.183443	0.872	0.401663
2 by 4	-0.1792	0.183443	-0.977	0.349661
2 by 5	0.3126	0.183443	1.704	0.116416
2 by 6	0.1651	0.183443	0.900	0.387466
3 by 4	-0.3020	0.183443	-1.646	0.127919
3 by 5	-0.2751	0.183443	-1.499	0.161901
3 by 6	0.0030	0.183443	0.016	0.987298
4 by 5	0.2481	0.183443	1.352	0.203461
4 by 6	0.0217	0.183443	0.118	0.908074
5 by 6	-0.3132	0.183443	-1.707	0.115831

Italic values: significant for a 95% confidence level

Table 11: Levels of the parameters used in sensitivity analysis of the GA code applied to case study #3

GA Parameters	(-) level	Central	(+) level
(1) idum	-1200	-1000	-800
(2) maxgen	16	20	24
(3) npopsiz	16	20	24
(4) pcreep	0.04704	0.05880	0.07056
(5) pcross	0.64	0.8	0.96

(6) pmutate	0.04704	0.05880	0.07056

Table 12: Fractional factorial design 2^{6-1} study results for case study #3

Run	idum	maxgen	npopsiz	pcreep	pcross	pmutate	F3
CS3-01	-1200	16	16	0.04704	0.64	0.04704	36703.240
CS3-02	-800	16	16	0.04704	0.64	0.07056	37224.459
CS3-03	-1200	24	16	0.04704	0.64	0.07056	36182.524
CS3-04	-800	24	16	0.04704	0.64	0.04704	37024.209
CS3-05	-1200	16	24	0.04704	0.64	0.07056	36268.600
CS3-06	-800	16	24	0.04704	0.64	0.04704	36574.062
CS3-07	-1200	24	24	0.04704	0.64	0.04704	36268.600
CS3-08	-800	24	24	0.04704	0.64	0.07056	36574.062
CS3-09	-1200	16	16	0.07056	0.64	0.07056	36607.633
CS3-10	-800	16	16	0.07056	0.64	0.04704	37018.604
CS3-11	-1200	24	16	0.07056	0.64	0.04704	37013.698
CS3-12	-800	24	16	0.07056	0.64	0.07056	37224.459
CS3-13	-1200	16	24	0.07056	0.64	0.04704	36268.600
CS3-14	-800	16	24	0.07056	0.64	0.07056	36574.062
CS3-15	-1200	24	24	0.07056	0.64	0.07056	36172.891
CS3-16	-800	24	24	0.07056	0.64	0.04704	36574.062
CS3-17	-1200	16	16	0.04704	0.96	0.07056	37038.212
CS3-18	-800	16	16	0.04704	0.96	0.04704	37046.606
CS3-19	-1200	24	16	0.04704	0.96	0.04704	39330.948
CS3-20	-800	24	16	0.04704	0.96	0.07056	37049.403
CS3-21	-1200	16	24	0.04704	0.96	0.04704	36356.793
CS3-22	-800	16	24	0.04704	0.96	0.07056	36574.062
CS3-23	-1200	24	24	0.04704	0.96	0.07056	36209.540
CS3-24	-800	24	24	0.04704	0.96	0.04704	36562.493
CS3-25	-1200	16	16	0.07056	0.96	0.04704	41706.395
CS3-26	-800	16	16	0.07056	0.96	0.07056	37224.459
CS3-27	-1200	24	16	0.07056	0.96	0.07056	36812.103
CS3-28	-800	24	16	0.07056	0.96	0.04704	36594.647
CS3-29	-1200	16	24	0.07056	0.96	0.07056	36261.229
CS3-30	-800	16	24	0.07056	0.96	0.04704	36574.062
CS3-31	-1200	24	24	0.07056	0.96	0.04704	36356.793
CS3-32	-800	24	24	0.07056	0.96	0.07056	36574.062
CS3-33	-1000	20	20	0.05880	0.80	0.05880	36185.487

Table 13: Effect estimates on F_3 for the fractional factorial design with no factor interactions (case study #3)

Factor	Effect	Standard Error	t(26)	p
Mean	36870.64	164.1528	224.6116	0.000000
(1)idum	-160.63	333.3960	-0.4818	0.633986
(2)maxgen	-218.54	333.3960	-0.6555	0.517913
(3)npopsiz	*-941.10*	*333.3960*	*-2.8228*	*0.009009*
(4)pcreep	160.62	333.3960	0.4818	0.633997
(5)pcross	499.88	333.3960	1.4994	0.145828
(6)pmutate	-462.63	333.3960	-1.3876	0.177031

Italic values: significant for a 95% confidence level

Table 14: Effect estimates on F_3 for the fractional factorial design with two factor interactions (case study #3)

Factor	Effect	Standard Error	t(11)	p
Mean	36870.64	155.2540	237.4860	0.000000
(1)idum	-160.63	315.3223	-0.5094	0.620532
(2)maxgen	-218.54	315.3223	-0.6931	0.502644
(3)npopsiz	*-941.10*	*315.3223*	*-2.9846*	*0.012418*
(4)pcreep	160.62	315.3223	0.5094	0.620543
(5)pcross	499.88	315.3223	1.5853	0.141207
(6)pmutate	-462.63	315.3223	-1.4672	0.170333
1 by 2	139.41	315.3223	0.4421	0.666960
1 by 3	462.86	315.3223	1.4679	0.170135
1 by 4	-194.49	315.3223	-0.6168	0.549923
1 by 5	-573.40	315.3223	-1.8185	0.096299
1 by 6	593.91	315.3223	1.8835	0.086323
2 by 3	198.67	315.3223	0.6300	0.541535
2 by 4	-395.50	315.3223	-1.2543	0.235736
2 by 5	-192.94	315.3223	-0.6119	0.553048
2 by 6	96.83	315.3223	0.3071	0.764522
3 by 4	-164.68	315.3223	-0.5223	0.611850
3 by 5	-475.62	315.3223	-1.5083	0.159638
3 by 6	421.76	315.3223	1.3375	0.208042
4 by 5	81.34	315.3223	0.2580	0.801202
4 by 6	-119.37	315.3223	-0.3786	0.712222
5 by 6	-385.58	315.3223	-1.2228	0.246953

Italic values: significant for a 95% confidence level

Table 15: Levels of the parameters used in sensitivity analysis of the GA code applied to case study #4

GA Parameters	(-) level	Central	(+) level
(1) idum	-1200	-1000	-800
(2) maxgen	40	50	60
(3) npopsiz	40	50	60
(4) pcreep	0.006897	0.008621	0.010345
(5) pcross	0.64	0.8	0.96
(6) pmutate	0.006897	0.008621	0.010345

Table 16: Fractional factorial design 2^{6-1} study results for case study #4

Run	idum	maxgen	npopsiz	pcreep	pcross	pmutate	F4
CS4-01	-1200	40	40	0.006897	0.64	0.006897	4.008222
CS4-02	-800	40	40	0.006897	0.64	0.010345	4.163750
CS4-03	-1200	60	40	0.006897	0.64	0.010345	3.995767
CS4-04	-800	60	40	0.006897	0.64	0.006897	4.021299
CS4-05	-1200	40	60	0.006897	0.64	0.010345	3.272924
CS4-06	-800	40	60	0.006897	0.64	0.006897	4.049079
CS4-07	-1200	60	60	0.006897	0.64	0.006897	1.864791
CS4-08	-800	60	60	0.006897	0.64	0.010345	2.629927
CS4-09	-1200	40	40	0.010345	0.64	0.010345	3.995312

CS4-10	-800	40	40	0.010345	0.64	0.006897	5.098247
CS4-11	-1200	60	40	0.010345	0.64	0.006897	3.854496
CS4-12	-800	60	40	0.010345	0.64	0.010345	5.988173
CS4-13	-1200	40	60	0.010345	0.64	0.006897	3.998500
CS4-14	-800	40	60	0.010345	0.64	0.010345	3.983345
CS4-15	-1200	60	60	0.010345	0.64	0.010345	4.053518
CS4-16	-800	60	60	0.010345	0.64	0.006897	4.048225
CS4-17	-1200	40	40	0.006897	0.96	0.010345	3.994422
CS4-18	-800	40	40	0.006897	0.96	0.006897	4.814700
CS4-19	-1200	60	40	0.006897	0.96	0.006897	3.981457
CS4-20	-800	60	40	0.006897	0.96	0.010345	4.789001
CS4-21	-1200	40	60	0.006897	0.96	0.006897	4.004197
CS4-22	-800	40	60	0.006897	0.96	0.010345	4.166973
CS4-23	-1200	60	60	0.006897	0.96	0.010345	3.880197
CS4-24	-800	60	60	0.006897	0.96	0.006897	5.609285
CS4-25	-1200	40	40	0.010345	0.96	0.006897	2.615757
CS4-26	-800	40	40	0.010345	0.96	0.010345	4.045827
CS4-27	-1200	60	40	0.010345	0.96	0.010345	3.791794
CS4-28	-800	60	40	0.010345	0.96	0.006897	4.386188
CS4-29	-1200	40	60	0.010345	0.96	0.010345	3.971225
CS4-30	-800	40	60	0.010345	0.96	0.006897	4.152820
CS4-31	-1200	60	60	0.010345	0.96	0.006897	3.784063
CS4-32	-800	60	60	0.010345	0.96	0.010345	4.080427
CS4-33	-1000	50	50	0.008621	0.80	0.008621	4.074593

Table 17: Effect estimates on F_4 for the fractional factorial design with no factor interactions (case study #4)

Factor	Effect	Standard Error	t(26)	p
Mean	*4.035409*	*0.122423*	*32.96287*	*0.000000*
(1)idum	*0.685039*	*0.248642*	*2.75512*	*0.010572*
(2)maxgen	0.026457	0.248642	0.10640	0.916078
(3)npopsiz	-0.374682	0.248642	-1.50691	0.143888
(4)pcreep	0.162620	0.248642	0.65403	0.518833
(5)pcross	0.190172	0.248642	0.76484	0.451251
(6)pmutate	0.031954	0.248642	0.12851	0.898733

Italic values: significant for a 95% confidence level

Table 18: Effect estimates on F_4 for the fractional factorial design with two factor interactions (case study #4)

Factor	Effect	Standard Error	t(11)	p
Mean	*4.035409*	*0.081210*	*49.69124*	*0.000000*
(1)idum	*0.685039*	*0.164938*	*4.15332*	*0.001607*
(2)maxgen	0.026457	0.164938	0.16040	0.875470
(3)npopsiz	*-0.374682*	*0.164938*	*-2.27166*	*0.044179*
(4)pcreep	0.162620	0.164938	0.98595	0.345348
(5)pcross	0.190172	0.164938	1.15300	0.273352
(6)pmutate	0.031954	0.164938	0.19373	0.849918
1 by 2	0.108266	0.164938	0.65641	0.525056

1 by 3	-0.198706	0.164938	-1.20473	0.253587
1 by 4	0.029784	0.164938	0.18058	0.859981
1 by 5	0.067725	0.164938	0.41061	0.689245
1 by 6	-0.323506	0.164938	-1.96138	0.075636
2 by 3	-0.232536	0.164938	-1.40984	0.186230
2 by 4	0.239275	0.164938	1.45070	0.174776
2 by 5	0.290605	0.164938	1.76191	0.105814
2 by 6	0.175422	0.164938	1.06356	0.310318
3 by 4	0.161723	0.164938	0.98051	0.347907
3 by 5	*0.528437*	*0.164938*	*3.20386*	*0.008397*
3 by 6	-0.216007	0.164938	-1.30963	0.217015
4 by 5	*-0.714137*	*0.164938*	*-4.32974*	*0.001195*
4 by 6	0.214462	0.164938	1.30026	0.220095
5 by 6	-0.110529	0.164938	-0.67012	0.516600

Italic values: significant for a 95% confidence level

7.3. Conclusões

A metodologia apresentada é bastante relevante por estabelecer, através de uma técnica simples, um procedimento a ser adotado preliminarmente em estudos de otimização por algoritmo genético para identificação dos parâmetros desse algoritmo que são significativos para o caso de estudo adotado. O procedimento é original e vem preencher uma deficiência da literatura, que não apresenta nenhum desenvolvimento que defina uma metodologia geral de identificação de parâmetros significativos para cada caso de estudo.

Os quatro casos de estudo apresentados para a aplicação da metodologia proposta demonstram que nem todos os parâmetros do algoritmo genético são relevantes em todos os casos e, além do mais, o conjunto de parâmetros significativos é dependente do problema em questão, o que ressalta a necessidade de realmente haver um procedimento que faça essa detecção.

Tendo sido desenvolvida uma metodologia para detecção dos parâmetros do AG significativos, o próximo capítulo apresenta a aplicação desse procedimento geral ao problema de otimização da cristalização do ácido adípico em modo batelada por resfriamento.

Capítulo 8. Procedimento para Seleção de Parâmetros para Otimização Estocástica de Cristalização

8.1. Introdução

O procedimento geral para detecção dos parâmetros mais significativos do algoritmo genético aplicado a problemas de otimização em escala de engenharia é neste capítulo aplicado ao problema de otimização do processo de cristalização em modo batelada operada por resfriamento.

8.2. Desenvolvimento

O desenvolvimento deste capítulo é apresentado a seguir, no artigo intitulado *Factorial design Technique applied to genetic algorithm parameters in a batch cooling crystallization optimisation*, publicado no periódico internacional *Computers and Chemical Engineering* (v. 29, p. 2229 – 2241, 2005).

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Factorial design technique applied to genetic algorithm parameters in a batch cooling crystallization optimisation

Caliane B.B. Costa*, Maria Regina Wolf Maciel, Rubens Maciel Filho

Chemical Engineering School, State University of Campinas (UNICAMP), Cidade Universitária Zeferino Vaz, CP 6066, CEP 13081-970 Campinas-SP, Brazil

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Abstract

An original approach is proposed in this work for the evaluation of genetic algorithm (GA) applied to a batch cooling crystallization optimisation. Since a lot of parameters must be set in a GA in order to perform an optimisation study, factorial design, a well-known technique for the selection of the variables with the most meaningful effects on a response, is applied in an optimisation problem solved through GA. No systematic approach to establish the best set of parameters for GA was found in literature and a relatively easy to use and meaningful approach is proposed. The results show that the parameters with significant (95% confidence) effect are initial population, the population size and the jump and creep mutation probabilities, being the ones in which alterations should be made during a GA study of optimisation, in the search for the optimum.

Keywords: Batch; Crystallization; Dynamic simulation; Factorial design; Genetic algorithm; Optimisation

1. Introduction

Crystallization is a very important unit operation, used in many processes mainly because it leads to the formation of particulate material with high purity. Batch operation offers the flexibility required when there are many simple steps to be executed, with changing recipes. In this way, batch crystallization is the preferred process in pharmaceutical, specialty and fine chemicals industries for obtaining their products. Nowadays, operation requirements involve the trade-off between large throughput and product with specified properties related to size distribution and particle size. Furthermore, the operation employed in the crystallizer during the batch influences all the subsequent processes (downstream processing), since the solids produced constitutes a mass of particulate material, which may exhibit an infinite number of different features, like habit, crystal size distribution (CSD) or solvent hindering (Ma, Tafti, & Braatz, 2002). Optimal operation is then important to obtain the desired product specification, as well as to improve the efficiency of the overall process. In the batch crystallization field, this optimum must be determined in terms of the extent, in each batch instant, of the kinetic phenomena that governs the extraction of solute from solution and its deposition into crystal lattice. The driving force for these phenomena is the supersaturation, which, in batch cooling crystallization, is achieved through the cooling of the solution. Therefore, many optimisation studies in batch cooling crystallization are focused on finding the optimal cooling profile (Costa, da Costa, & Maciel Filho, 2005; Zhang & Rohani, 2003).

The solution of an optimisation problem can be found through, among others, deterministic or stochastic approaches. The former composes the traditional optimisation methods (direct and gradient-based methods) and have the disadvantages of requiring the first and/or second-order derivatives of the objective function and/or constraints or of being not efficient in non-differentiable or discontinuous problems. Furthermore, the deterministic methods are dependent on the chosen initial solution (Deb, 1999). The stochastic methods, such as Genetic Algorithms (GAs), do not possess these drawbacks. Genetic Algorithms (GAs) are part of the so-called evolutionary algorithms and compose a search and optimisation tool with increasing application in scientific problems. They do not need to have any information about the search space, just needing an objective/fitness function that assigns a value to any solu-

* Corresponding author. Tel.: +55 19 3788 3971; fax: +55 19 3788 3965.
E-mail address: caliane@lopca.feq.unicamp.br (C.B.B. Costa).

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Nomenclature

$\langle\,\rangle$ indicates absolute value of the operand, if it is negative, and zero value otherwise
A pre-exponential factor (primary nucleation) ($m^{-3}\,s^{-1}$)
A_1 exponential constant of Type 1 function
A_2 exponential constant of Type 2 function
A_c heat transfer area (m^2)
best_fitness vector that records the best fitness function in each generation
best_individual vector that records the best individual in each generation
B kinetic parameter of the primary nucleation law
c solute molecules concentration in solution, mol m^{-3} of solution
c^* solute molecules concentration in solution at supersaturation, mol m^{-3} of solution
C_i granulometric class of rank i
ΔC_i width of class C_i
C_p slurry specific heat ($J\,kg^{-1}\,K^{-1}$)
C_S solid concentration in the suspension, mol m^{-3} of suspension
C_0 initial concentration of adipic acid, mol m^{-3} of solution
CV coefficient of variation of the crystal size distribution (%)
$f(\mathbf{x})$ objective function
$F(\mathbf{x})$ fitness function
f_{max} objective function value of the worst feasible solution in the population
G growth rate ($m\,s^{-1}$)
GC generation counter
$g_j(\mathbf{x})$ inequality constraint
ΔH_c heat of crystallization ($J\,mol^{-1}$)
(HR) concentration of molecular adipic acid in solution, mol m^{-3} of solution
(HR^*) concentration of molecular adipic acid in solution at saturation, mol m^{-3} of solution
(H^+) concentration of protons in solution, mol m^{-3} of solution
idum GA parameter to determine the initial population if individuals
iniche GA parameter to determine if niching is used
iunifrm GA parameter to determine if single or uniform crossover is used
i' kinetic order of the secondary nucleation law
IC individual counter
j' kinetic order of the integration growth law
K modified acidity constant of adipic acid, mol m^{-3} of solution
k' exponent to the solid concentration in secondary nucleation law
k_a surface shape factor
k_c kinetic constant of the integration law ($m^{3j'-2}\,mol^{1-j'}\,s^{-1}$)
k'_N kinetic constant of the secondary nucleation law ($m^{3(i'+k')-3}\,mol^{-i'-j'}\,s^{-1}$)
k_v volumetric shape factor
L characteristic size of crystals (m)
L_i upper limit of class of number i (m)
m number of constraints
maxgen maximum number of generations in the evolution of GA code
microga GA parameter to determine if migroga option is used
MM molecular weight of the crystal ($kg\,mol^{-1}$)
n number distribution density (population) per unit volume of suspension (m^{-4})
N number of granulometric classes
nchild GA parameter to determine the number of children per pair of parents
$N_i(t)$ number of crystals per unit volume of suspension in granulometric class C_i at time t, m^{-3} of suspension
p p-level, probability of error that is involved in accepting an effect as valid
npopsiz GA parameter to determine the number of individuals per generation
pcreep creep mutation probability in the GA code
pcross crossover probability in the GA code
pmutate jump mutation probability in the GA code
r_N net rate of nucleation ($m^{-3}\,s^{-1}$)
r_{N1} primary rate of nucleation ($m^{-3}\,s^{-1}$)
r_{N2} secondary rate of nucleation ($m^{-3}\,s^{-1}$)
$r(I)$ intrinsic rate of agglomeration of rank $I_{m,n}$ ($m^{-3}\,s^{-1}$)
$R_{A,i}$ net rate of agglomeration in the granulometric class C_i ($m^{-3}\,s^{-1}$)
$R_{B,i}$ net rate of breakage in the granulometric class C_i ($m^{-3}\,s^{-1}$)
t instantaneous time (s)
T crystallizer solution absolute temperature (K)
T_c coolant absolute temperature (K)
t(freedom degree) t-statistics
t_f final time (s)
$t_{intermediate}$ intermediate time, where Type 1 and Type 2 functions have the same value (s)
t_{total} total batch time (s)
U global heat transfer coefficient ($J\,m^{-2}\,s^{-1}\,K^{-1}$)
V solution volume (m^3)
V_{susp} suspension volume (m^3)
V_0 initial volume of the solution in the crystallizer (m^3)
$\mathbf{x}$ vector containing the optimising (adjustable) variables

Greek letters
η_r effectiveness factor

$\nu_{\mathrm{est}\,I,i}$	stoichiometric coefficient of class i in agglomeration of number I
ρ	slurry density (concentration), kg m^{-3} of slurry
ρ_c	crystal density, kg m^{-3} of crystal

tion. Details about the working principle of GAs can be found elsewhere (Deb, 1998, 1999; Fühner & Jung, 2004).

The working principle of the GAs requires setting up a relatively large number of parameters. The history of advance in the evolution of evolutionary algorithms is part provided at random, part by the values of their parameters. Due to this feature, it is recommended, in an optimisation search by GAs, to perform a lot of runs to increase the chance to obtain the global optimum.

The factorial design is a well-known technique based on statistical considerations that brings the most meaningful information about the influences of parameters on a specific problem. The present work proposes the application of factorial design in the Genetic Algorithms parameters to determine which ones affect significantly the optimisation of the cooling profile in a batch crystallization system. The proposed approach needs to be conducted prior to the optimisation trials through GAs, since it removes GA parameters that are not statistically significant for the evolutionary search, saving time and computation burden in evolutionary optimisation studies. The proposed approach makes the GA drive the system to an optimal solution through a systematic procedure. This approach, compared to the trial-and-error setting of GA parameters, leads to less time in the optimum search. The results indicate that the initial population, the population size and the jump and creep mutation probabilities are the parameters with significant relevance in the search for the optimal cooling profile in a batch cooling crystallization system by Genetic Algorithms.

2. Batch cooling crystallization

In a batch cooling crystallization operation, as shown schematically in Fig. 1, the solution is cooled in order to create a supersaturation into the system, which is the driving force for the kinetic mechanisms. The nucleation and growth are the most dominant phenomena. Apart from them, other phenomena, such as agglomeration and breakage, may occur during the process, making it difficult to carry out reliable predictions. Neglecting agglomeration may result in poor representation of reality, especially when the crystallizing substance is classically known as having an agglomerating behaviour (Costa et al., 2005).

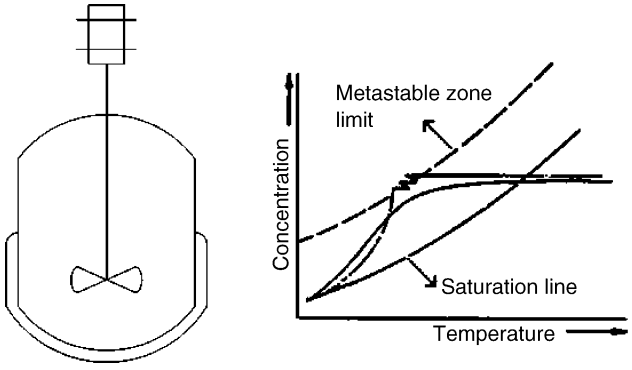

Fig. 1. Schematic drawing of the batch cooling crystallizer and the concentration vs. temperature curve, showing two different cooling profiles.

The modelling of the process involves mass, energy and population balances. This latter is a general approach and constitutes a complex partial differential equation, which accounts how the kinetic phenomena alter the population density both in size and time. A lot of work in literature (Kiparissides, 2004; Puel, Févotte, & Klein, 2003; Rawlings, Miller, & Witkowski, 1993) reviews the many techniques and methods used to solve the population balance equation (PBE). In the present work, the Method of Classes (Costa et al., 2005; Marchal, David, Klein, & Villermaux, 1988; Nallet, Mangin, & Klein, 1998; Puel et al., 2003) is used to solve the PBE in the modelling of an adipic acid crystallization process, the chosen study system. It is worth mentioning that the model of the process is highly nonlinear. The model equations are composed of Eqs. (1)–(3), which represent, respectively, the population, mass and energy balances, coupled with the kinetic equations for the growth, nucleation and aggregation mechanisms, Eqs. (4)–(7):

$$\begin{aligned}
&\frac{dN_1}{dt} + \frac{1}{V_{susp}}\frac{dV_{susp}}{dt}N_1 + \frac{G(L_1)}{2\Delta C_2}N_2 + \frac{G(L_1)}{2\Delta C_1}N_1 \\
&\quad = r_N + R_{A,1} - R_{B,1}, \\
&\frac{dN_i}{dt} + \frac{1}{V_{susp}}\frac{dV_{susp}}{dt}N_i + \frac{G(L_i)}{2\Delta C_{i+1}}N_{i+1} \\
&\quad + \frac{G(L_i) - G(L_{i-1})}{2\Delta C_i}N_i - \frac{G(L_{i-1})}{2\Delta C_{i-1}}N_{i-1} = R_{A,i} - R_{B,i}, \\
&\frac{dN_N}{dt} + \frac{1}{V_{susp}}\frac{dV_{susp}}{dt}N_N + \frac{-G(L_{N-1})}{2\Delta C_N}N_N - \frac{G(L_{N-1})}{2\Delta C_{N-1}}N_{N-1} \\
&\quad = R_{A,N} - R_{B,N}
\end{aligned} \tag{1}$$

$$V_0 C_0 = \frac{(H^+)^2}{K}\left[1 + \frac{K}{(H^+)}\right]V_0 + \frac{V_0}{1 - \frac{MM}{\rho}C_s}C_s \tag{2}$$

$$\rho C_p V \frac{dT}{dt} = -\Delta H_c 3\rho_c k_v V_{susp}\int_0^\infty nL^2 G\,dL - UA_c(T - T_c) \tag{3}$$

$$G = \frac{dL}{dt} = \frac{k_a MM k_c}{3\rho_c k_v}\eta_r (c - c^*)^{j'} \tag{4}$$

$$r_{N1} = A\exp\left[-\frac{B}{\ln^2\left[\frac{(HR)}{(HR)^*}\right]}\right] \tag{5}$$

$$r_{N2} = k'_N[(HR) - (HR)^*]^{i'} C_s^{k'} \tag{6}$$

$$R_{A,i} = \sum_{I=1}^{N(N+1)/2} \nu_{\mathrm{est}\,I,i} r(I) \tag{7}$$

In Eqs. (1) and (7), the subscript i indicates the granulometric class in which the population is being balanced and, so, varies from 1 to N, the total number of granulometric classes.

The mass balance is based on the fact that changes in the solution concentration results in alteration of the mass of crystals per volume unit and on the dissociation constant of the crystallizing substance. Eq. (3), the energy balance, takes into account the heat of crystallization and the heat removed by the cooling device.

The method of classes transforms the population balance partial differential equation into one ordinary differential equation system, Eq. (1), by discretizing the range of variation of the variable L, related to crystal size, and assuming that the number density function is constant at each granulometric class. The discretization is done from the nuclei size to the largest crystals size. All defined sizes determine the existence of N granulometric classes C_i, whose widths are defined by $\Delta C_i = L_i - L_{i-1}$. The obtained differential equations are no longer written with population density functions, but with absolute number of crystals in each class.

The nucleation rate, represented by r_N, includes primary (r_{N1}) and secondary (r_{N2}) nucleation. The former takes place when there are no crystals of the crystallizing substance in suspension, while the latter is more common in industrial practice because seeding is almost always present.

The growth rate expression (Eq. (4)) is based on the film model and the effectiveness factor η_r is found by a proper relation (Costa et al., 2005) to the mass transfer coefficient, k_d. This latter coefficient is found by an expression for Sherwood number. Details can be found in Costa et al. (2005). Each granulometric class has a value for the mass transfer coefficient, which means that the growth rate is size dependent.

Only dual agglomeration is considered and its rate in each granulometric class, $R_{A,i}$, is dependent on an intrinsic rate of agglomeration $r(I)$. Further details about the agglomeration rate expression are given in Costa et al. (2005).

The solubility of adipic acid (c^* as a function of T, the solution temperature) is used in the calculation of supersaturation ($c - c^*$), the driving force for the process of crystallization. The kinetic parameters (A, B, i', j', k', k_c and k'_N) for adipic acid are known and so one has to fix only the initial condition, i.e., the initial seeding (number of seeds added per volume unit for each granulometric class), and the cooling profile (the curve of T_c during all the batch) in order to simulate the crystallization process, i.e., how N_i, the number of crystals per volume unit of suspension in each granulometric class, evolves during batch time.

2.1. The objectives of the optimisation problem

The rate of cooling used during the batch determines the values of supersaturation achieved, which characterize the extent of the kinetic mechanisms. The favouring of nucleation over growth leads to a large crystal size distribution (CSD), with many small crystals, thanks to a great peak of supersaturation at the early stages of the crystallization process. In batch crystallization, a large mean size and a narrow distribution are desired. According to the literature, a cooling profile characterized as having a soft decrease in the beginning and a more pronounced one at the end of the process makes the supersaturation to evolve softly, without peaks, leading to a narrower CSD, due to the favouring of growth (Choong & Smith, 2004; Costa et al., 2005; Mullin, 1993). Due to the importance of the final CSD in the downstream processes and in product applications, the objectives of the optimisation in crystallization problems are normally chosen according to features related to product specifications and market requirements. The most common objective functions in crystallization optimisation problems are maximization of the mean crystal size at the end of the batch, minimization of the standard deviation (σ) of the final CSD or minimization of its coefficient of variation (CV). This latter is a very interesting objective function, since it relates the standard deviation to the mean crystal size. Sometimes, the batch time is also included in the objective function, but this is not considered in this work, since a specified throughput is assumed. Bearing this in mind, the optimisation problem is formulated so as to minimize the CV. The final product CSD depends strongly on the selected optimisation objective function (Zhang & Rohani, 2003) and this, in fact, makes the problem more difficult to be postulated.

The high non-linearity of the crystallization model as well as its dimensionality makes deterministic optimisation methods inefficient and unlikely to be successful, apart from the fact that the derivatives of the system variables are not easily computed (Choong & Smith, 2004). GA is used in the present work in order to determine the optimal cooling profile, with a fixed seeding policy. In addition, a factorial design method is proposed as a tool to improve the performance of the GA method for crystallization processes through a choice of a suitable set of parameters.

2.2. Cooling profile

As mentioned earlier, the cooling profile is part of the operating strategy to obtain the product at desired properties. In practice, it is an usual procedure in industry with two relevant difficulties, to know, to find out the optimal cooling profile batch to batch and how to implement it in real time operations due to design restrictions. This last feature is not considered in this work. In this way, the coolant temperature, T_c, is the considered control variable.

The parameterisation of the control profiles usually takes the form of a sum of a convergent series of linearly independent functions of time. Choong and Smith (2004) propose a new parameterisation framework for the control variable profile, able to produce all types of continuous curves. It consists of two distinct profiles, named Type 1 and Type 2, whose mathematical formulations for the control variable considered in the present work are described by the following equations:

$$\text{Type 1}: \; T_c = T_{cF} - (T_{cF} - T_{c0})\left[1 - \frac{t}{t_{total}}\right]^{A_1} \tag{8}$$

$$\text{Type 2}: \; T_c = T_{c0} - (T_{c0} - T_{cF})\left[\frac{t}{t_{total}}\right]^{A_2} \tag{9}$$

In these equations, T_c is the instantaneous value of coolant temperature at time t, T_{c0} the initial value and T_{cF} is the final value. t_{total} is the total batch time. The whole control variable profile is composed by a combination of Type 1 and Type 2 functions, each one present in a batch period.

This framework is interesting due to the reduction in the dimensionality of the problem, possessing only six adjustable variables, to know: the initial and the final control variable values, two exponential constants, the intermediate time and its corresponding intermediate value of the control variable (there is the constraint for the whole function, composed by Type 1 and Type 2 functions, to be continuous). This proposed framework is chosen in the formulation of the dynamic problem in the present work.

2.3. A constrained problem

The problem to be solved in the crystallization system is the optimisation of the cooling profile, that is, the best values of coolant temperature to be imposed during the batch time are sought through the optimisation algorithm. The cooling of the crystallizer solution causes the appearance of supersaturation, the driving force for the crystallization process to occur. No crystal would appear and/or grow into the system if supersaturation does not take place. In this way, the formulated optimisation problem presents some constraints that must be imposed to the optimisation algorithm. The first constraint deals with the need to have supersaturation. It is necessary in order to dispose of the so-called trivial solutions, in which there is no crystallization at all because of the maintenance of temperature at the initial value (no generation of supersaturation). With no crystal being produced, there is no crystal size distribution and with the objective function being set as the minimization of the CV, it would reach a minimum (zero) value in this condition. It should, therefore, be imposed a constraint of minimum acceptable yield of particles, in order to force the optimizer to search for coolant temperature values that cause the production of a minimum mass of crystals. Furthermore, as mentioned above, the control variable (coolant temperature) must have a continuous profile and the intermediate value of the control variable of both types functions (Eqs. (8) and (9)) must be constrained to have the same value at the intermediate time. Fig. 2 shows in a schematic way two profiles for the control variable. For each profile, Type 1 and Type 2 functions possess the same value for the coolant temperature at the intermediate time (each cooling profile is continuous during the whole batch).

2.4. Optimisation problem statement

The general objective in optimisation problems is to choose a set of variables values subject to the various constraints that will produce the desired optimum response for the chosen objective function. The purpose of the present optimisation problem is the minimization of the coefficient of variation (CV) of the CSD at the end of the crystallization batch and the operating strategy to obtain the product at desired properties is the manipulation of the cooling profile. The cooling profile (i.e., coolant temperature values during batch time) imposed to the crystallizer is determined by a combination of Eqs. (8) and (9). The infinite possible coolant temperature profiles are determined by the initial (T_{c0}) and final (T_{cF}) control variable values, the two exponential constants (A_1 and A_2), the intermediate time ($t_{intermediate}$) where both functions (Type 1 and Type 2) intercept each other and the definition whether the control variable must be represented by Type 1 + Type 2 or Type 2 + Type 1 functions (more details on how the sequence of functions is determined is given in Section 5). The coolant temperature in each instant of the batch time is, therefore, determined by the values assigned to these six variables (T_{c0}, T_{cF}, A_1, A_2, $t_{intermediate}$ and the variable that determines the sequence of functions). These six variables are assigned to a vector, $\mathbf{x}$, containing the optimising (adjustable) variables.

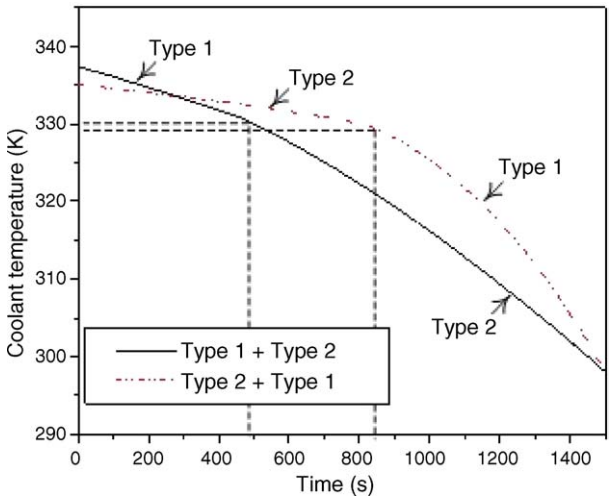

Fig. 2. Two hypothetical cooling profiles, illustrating the feature of continuity of the whole control variable profile.

So, in the sense of an optimisation problem formulation, the CV of the final CSD is the objective function and the optimising variables are joined in $\mathbf{x}$ vector. The constraints that must be imposed to the optimisation problem are the model equations, Eqs. (1)–(7), the minimum acceptable yield of crystals (here translated in mass of particles obtained at the end of the batch), and the need for both functions of Eqs. (8) and (9) to have an interception at the intermediate time, that is, the T_c value calculated by the Type 1 function minus the T_c value calculated by the Type 2 function must equal zero (equality constraint). This equality constraint was handled transforming it in an inequality constraint with the use of a tolerance set to 10^{-4}.

In this way, the formal mathematical description of the formulated optimisation problem is given by Eq. (10):

$$\begin{aligned} &\text{Minimize} && CV_{tf}(\mathbf{x}) \\ &\text{Subject to} && \text{model equations (Eqs. 1–7)} \\ & && \text{mass of crystals } (t_f) \geq 50.0 \\ & && \left| T_{cF} - T_{c0} - (T_{cF} - T_{c0}) \left[1 - \frac{t_{intermediate}}{t_{total}} \right]^{A_1} \right. \\ & && \left. + (T_{c0} - T_{cF}) \left[\frac{t_{intermediate}}{t_{total}} \right]^{A_2} \right| \leq 10^{-4} \end{aligned} \tag{10}$$

The objective function in Eq. (10) presents CV as a function of **x**. The extent of each mechanism in each batch instant will determine how the crystal size distribution (CSD) evolves during the batch. So, at the end of a batch, different CSDs are obtained if different supersaturation profiles were imposed, which, ultimately, can be translated to imposition of different coolant temperature profiles. For each CSD, a CV can be calculated and, so, since **x** determines the coolant temperature profile, CV is an implicit function of **x**.

3. Genetic algorithms

3.1. Framework

Genetic Algorithms have proven to be very adaptable to a great variety of different optimisation tasks (Führer & Jung, 2004). The algorithms work with a population of possible solutions, which suffers evolution during the generations, an analogy borrowed from the Darwin's Evolutionary Theory. Each solution is coded as a collection (chromosome) of binary or real strings; each string representing a variable in the solution. The evolution is achieved by some genetic operators as reproduction, crossover and mutation. The survival of the fittest is achieved by the assignment of a fitness function, usually defined as the objective function for the unconstrained optimisation problem, or a combination of the objective function and a penalty function for constrained optimisation (Deb, 1998, 1999).

The set of solutions (i.e., the population) per iteration (generation) is fixed. In each iteration, pairs of individuals are selected randomly and are recombined into new solutions (crossover operator). A random change on the offspring generation is optionally applied (mutation operator). The newly created solutions are evaluated according to the fitness function (Führer & Jung, 2004).

In a search for the optimum through the use of GA, it is necessary to set the population size, the maximum number of generations allowed during the search, the number of children in the offspring generation per pair of parents and the crossover, jump mutation and creep mutation probabilities. The difference between the two types of mutation is that the jump mutation acts on the chromosome (genotype), while creep mutation acts on the decoded individual (phenotype). Concerning to the crossover operator, it is possible to define single-point, two-point or uniform crossovers. In the first one, just one crossover point is selected and the string from the beginning of the chromosome to the crossover point is copied from the first parent, while the rest is copied from the other parent. In the two-point crossover, two crossover points are selected. The string from the beginning of the chromosome to the first crossover point is copied from the first parent; the part from the first to the second crossover point is copied from the other parent and the rest is copied from the first parent again. Finally, in the uniform crossover, bits are randomly copied from the first or from the second parent.

Genetic Algorithm can also borrow the idea from nature of coexistence of multiple niches in order to deal with multimodal optimisation. A sharing concept (in an analogy to the sharing, in nature, of available resources, such as land and food) may be introduced artificially in GA population. This allows coexistence of multiple optimal solutions (both local and global). More details about the niching in GA may be found in Deb (1999).

Another interesting tool available in the Genetic Algorithms is the micro-GA technique, which uses a very small population (micro-population) that converges towards a single individual representing the best result obtainable with that particular population. Once the convergence is reached, the best individual is preserved and the micro-population is restarted with new individuals. This GA largely depends on the mutation operator, since such a small population cannot take advantage of the discovery of good partial solutions by crossover. This tool works better with unimodal or simple problems (Deb, 1999).

3.2. Constraint handling

Constraint handling in optimisation problems that use GAs is not a simple task. The most usual approach is the use of penalty functions. Nevertheless, its use may require a lot of refinement, in order to determine the most suitable penalty parameters needed to guide the search towards the constrained optimum. Deb (2000) proposed a different constraint handling method, exploiting the feature of the GAs algorithm of pair-wise comparison during the selection of individuals, being the selection done by tournament or not. Penalty parameters are not needed in the proposed method because, in any scenario of comparison between two solutions, they are never compared in terms of both objective function and constraint violation information. The proposed fitness function is formulated in the following manner, where infeasible solutions are compared based only on their constraint violation (for a minimization problem):

$$F(\mathbf{x}) = \begin{cases} f(\mathbf{x}), & \text{if } g_j(\mathbf{x}) \geq 0, \quad \forall j = 1, 2, \ldots, m, \\ f_{\max} + \sum_{j=1}^{m} \langle g_j(\mathbf{x}) \rangle, & \text{otherwise} \end{cases} \tag{11}$$

The parameter $f_{\max}$ is the objective function value of the worst feasible solution in the population. In this way, when two feasible solutions are compared, the one with better objective function value is chosen; when one feasible and one infeasible solutions are compared, the feasible solution is chosen; when two infeasible solutions are compared, the one with smaller constraint violation is chosen (Deb, 2000).

For the present optimisation problem, i.e., minimization of CV_{tf}, the CV at the end of a batch in a cooling crystallization process, Eq. (11) can be translated in the following manner. $F(\mathbf{x})$, the fitness function, is equal to CV_{tf}, the CV at the end of the batch (the objective function, $f(\mathbf{x})$, of the crystallization problem being considered) for feasible individuals, while, for infeasible solutions, it is equal to the worst CV_{tf} among all CV_{tf} of feasible individuals in that generation plus the constraints violation amount.

3.3. The employed code

The GA used was basically the FORTRAN Genetic Algorithm Driver by David Carroll, Version 1.7a (Carroll, 2004),

with some modifications. The code initializes a random sample of individuals with different parameters (problem variables). This initial random sample of individuals is actually dictated by the value assigned to a GA parameter named *idum*: the same initial population is generated every time the code is run with the same value assigned to *idum*. The selection scheme used is tournament selection (Deb, 1999) with a shuffling technique for choosing random pairs for mating. The individuals are coded in binary manner and the routine can apply jump mutation, creep mutation and single-point or uniform crossover. Niching (sharing) and an option for the number of children per pair of parents are added. An option for the use of a micro-GA is also part of the code.

The routine is used coupled with the crystallization model (Eqs. (1)–(7)) in order to optimise the cooling profile parameterised as given by Eqs. (8) and (9). The constraint handling method given by Eq. (11) was implemented to the original Carroll's code in order to perform the needed constrained optimisation of the cooling profile.

Carroll's code has the following variables to be set, in order to run the optimisation:

- *microga*: if set to 1, the micro-GA search is activated. In this work, *microga* is set to 0 (deactivated)
- *npopsiz*: determines the number of individuals in each generation (iteration)
- *pmutate*: jump mutation probability
- *maxgen*: maximum number of generations to be accounted in the evolution
- *idum*: a parameter that determines the initial population of individuals; in the code *idum* is the initial random number seed for the GA run and it must equal a negative integer
- *pcross*: crossover probability
- *pcreep*: creep mutation probability
- *iunifrm*: 0 for single-point crossover; 1 for uniform crossover; in this work uniform crossover is used
- *iniche*: 0 for no niching, 1 for niching. In this work niching is used
- *nchild*: determines if the number of children per pair of parents is 1 or 2. Two children per pair of parents are used in the present work.

More details about these parameters can be found in Carroll (2004).

To accomplish an optimisation with the GA code, it is necessary to study the remaining parameters: *pmutate*, *pcross*, *pcreep*, *npopsiz*, *maxgen* and *idum*. A factorial design was conducted in order to determine which ones of the six parameters have significant effects on the optimisation result, as well as how they interact among themselves. This procedure is proposed in this work, since it allows for a systematic approach to find out the suitable set of parameters for GA method.

4. Factorial design and its application to the problem

The factorial design method is a statistical technique that evaluates at the same time all process (or any focus of study) variables in order to determine which ones really exert significant influence on the final response, which gives a better analysis of the response (Kar, Banerjee, & Bhattacharyya, 2002). All variables are called factors and the different values chosen to study the factors are called levels (Barros Neto, Scarminio, & Bruns, 2001; Box, Hunter, & Hunter, 1978).

In a complete factorial design, all possible combinations of the selected levels for the factors are made, but this procedure may be too time-consuming. On the other hand, the most common factorial designs are the two levels ones, which bring enough information for the purpose of this work. Important trends may be observed with these factorial designs and the effect of each independent variable, on the dependent one are estimated. The values of the resulting first-order effects indicate the more sensitive parameters applied to the case studied and consequently which ones are more important in the seeking procedure. It is worth mentioning that the obtained results depend strongly on the case study to which the methodology is being applied (Rodrigues, Toledo, & Maciel Filho, 2002).

When a relatively large number of factors is evaluated, the total number of combinations may be too large. Furthermore, the high order interactions (third, fourth or superior) are small and may be mixed with the standard deviation of the effects. In this case, it is advisable and convenient to use a fractional factorial. The number of combinations is diminished and the most important effects are determined (Barros Neto et al., 2001).

In the interpretation of the results generated by a complete or fractional factorial design, it is necessary to decide which calculated effects are significantly different from zero. The usual practice is use the concept of statistical significance (generally 95% of confidence).

When analysing the results of a factorial design, two statistic parameters are of relevance. The *t*-statistics of a factor is obtained by the division of its effect by its error. This statistic parameter is dependent on the freedom degree, which is calculated by the subtraction of the number of calculated effects from the total number of experiments/trials available. The higher the *t*-statistics, the higher is the significance of the corresponding factor. On the other hand, the *p*-level, which represents the probability of error that is involved in accepting the effect as valid, is a decreasing index of the reliability of a result. The higher the *p*-level, the less one can believe that the observed relation between factor and effect is reliable. The common practice is to consider 95% of confidence in a result, so that, for an effect to be considered statistically significant, its *p*-level must be less than 0.05.

The two levels evaluated in a factorial design are coded by (+) and (−), representing the upper and lower levels, respectively.

5. Systematic approach in optimisation with GAs—prior detection of significant parameters

The proposal to use factorial design in the selection of the significant GA parameters in the optimisation of coolant temperature profile in order to minimize the coefficient of variation of the CSD at the end of the batch in the batch cooling crystallization is here presented in a systematic way.

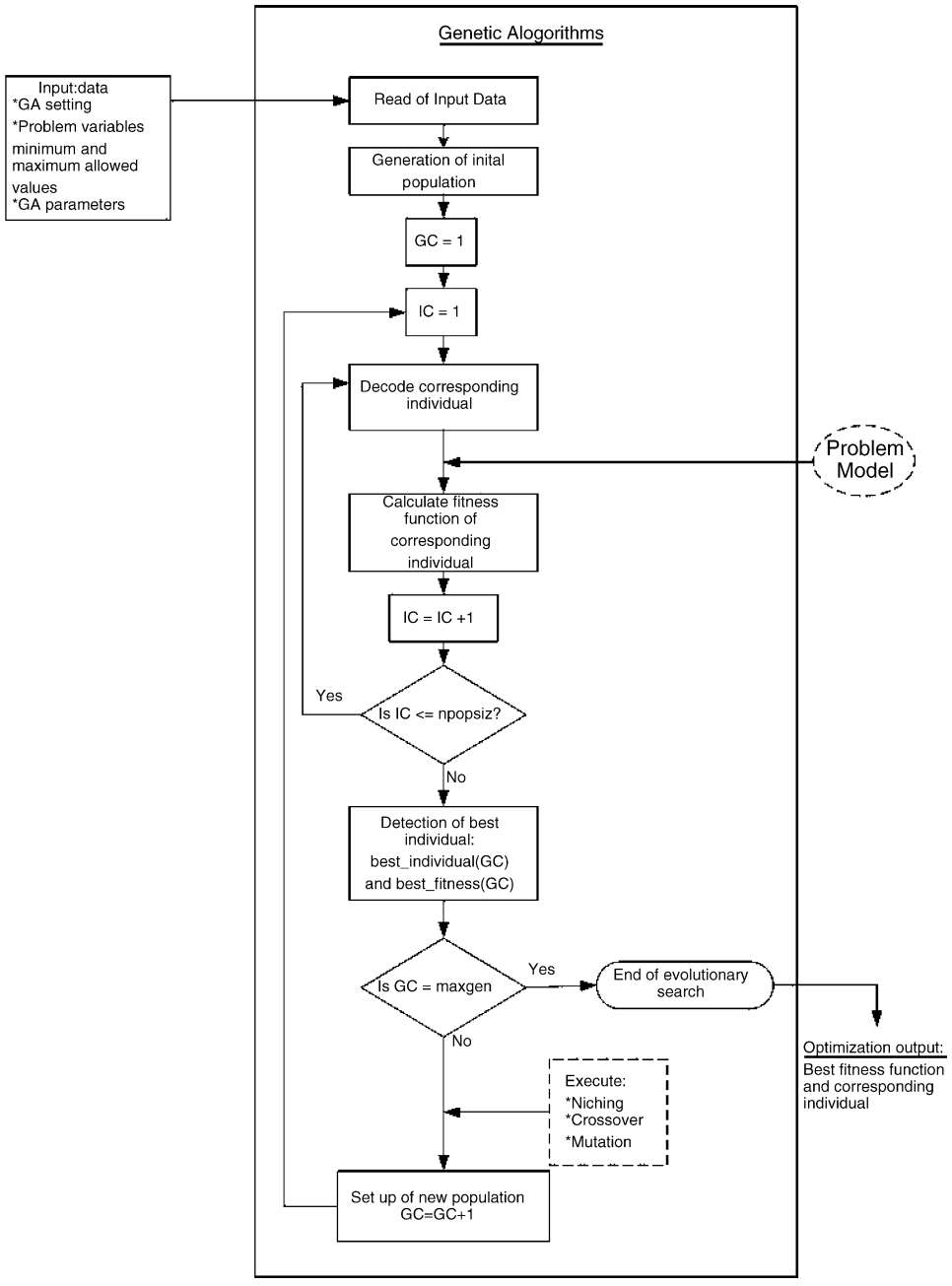

Fig. 3. General working structure of GAs.

A supporting chart, Fig. 3 is presented, which depicts the general working structure of GAs. The input data that must be supplied to GAs is composed by:

- GA settings: the characteristics of micro GA, type of crossover, niching and number of children per pair of parents must be supplied to the GA code. As explained in Section 3.3, these characteristics are determined by the values assigned to *microga*, *iunifrm*, *iniche* and *nchild*, which were respectively 0, 1, 1 and 2 in this particular problem. These values are fixed and are not part of the so-called GA parameters, whose effects on the optimisation response are object of study in the detection of statistical significance.
- Problem variables minimum and maximum allowed variables: the decision on which are these minimum and maximum allowed variables is dependent on the specific problem being considered. In the present work, optimising variables are assigned to **x** vector, which contains the values of T_{c0}, T_{cF}, A_1, A_2, $t_{intermediate}$ and the variable that determines the sequence of Type 1 and Type 2 functions (Eqs. (8) and (9)). In this way, based on the physical problem, T_{c0} and T_{cF} are allowed to vary between 298 and 340 K, the exponentials constants between 10^{-6} and 20, the intermediate time is allowed to vary between 0 and 1500 s, the batch time. The determination of the sequence of Type 1 and Type 2 functions, since the optimisation search should investigate whether it is best

to have Type 1 + Type 2 or Type 2 + Type 1, is delegated to a variable allowed to vary between −1 and +1: negative values determine Type 1 + Type 2, while nonnegative values determine Type 2 + Type 1.

- GA parameters: these parameters must be varied in many GA trials in order to drive so many possible evolutionary paths that the achievement of the specific process global optimum can be more assured. These parameters are, as exposed in Section 3.3, *npopsiz*, *pmutate*, *maxgen*, *idum*, *pcross* and *pcreep*.

The objective function is coupled with constraints violation, as proposed by Deb (2000)—Eq. (11), in order to calculate the fitness function of each individual. The problem model, the batch cooling crystallization, is necessary for the evaluation of both the objective function and constraints violation. GC and IC that figures in Fig. 3 are only counters (respectively generation counter and individual counter) used by the algorithm to make calculations for each individual of each generation. The vectors **best_fitness** and **best_individual** are responsible for recording the best fitness function and the corresponding best individual in each generation.

As can be seen by the structure outlined in Fig. 3, given a set of values of the GA parameters, the GA optimisation code executes the evolutionary search and gives as output the best fitness function, that is, the minimum value found for the objective function (the CV of the CSD at the end of the batch in the crystallization process, for the present work). The outer box of Fig. 3, which encloses all the sequence of steps for Genetic Algorithms, can be seen as a black-box: given an input (GA settings, minimum and maximum allowed values and GA parameters), for a particular problem model, the black-box gives an output. Since the problem is fixed (here, batch cooling crystallization model), the minimum and maximum allowed values are fixed. The GA settings are also fixed. In this way, the only variables able to be varied in the input are the GA parameters. And it is here that it is based on the approach of using factorial design to identify which ones of these GA parameters really exert significant influence on the output. The proposed approach should be seen as a prior and important analysis to be conducted in optimisation trials through GAs in order to discharge GAs parameters that are not statistically significant for the evolutionary search to the specific problem, saving time and computation burden in evolutionary optimisation studies.

A step-by-step description of the proposed approach may be outlined as follows:

1. Define the case study/problem and formulate it mathematically (process model).
2. Define the objective function.
3. Define the constraints of the problem.
4. Define the control variables (optimising variables), i.e., the variables that compose the individuals and that should suffer evolution in order to provide better fitness functions.
5. Stipulate the GA settings and the minimum and maximum allowed values of the control variables.
6. Stipulate the values of the upper and lower levels for the GA parameters to be used in the factorial design study.
7. Build the complete or fractional factorial design spreadsheet, with the many combinations of GA parameters levels that must be supplied to a GA to perform the evolutionary optimisation. For information on how to build fractional factorial designs, the reader is referred to Barros Neto et al. (2001) and Box et al. (1978).
8. Perform the optimisation through GA for each combination of GA parameters in order to obtain the problem response to these GA parameters values.
9. Calculate effects of each GA parameters on the problem response, as well as their errors and statistical significance (p-level). Information on how to calculate the effects, its errors and p-levels, is found in Barros Neto et al. (2001) and Box et al. (1978). Calculate, as well, the effects, errors and p-level for the interactions between factors (GA parameters).
10. The GA parameters that do not show statistical significance on the problem response may be discharged in further optimisation studies because, irrespective of which value is stipulated to these parameters, the problem response will not vary significantly, in statistical sense. The GA parameters that show effects statistically significant should be extensively varied in further optimisation works with this particular problem.

6. Results and discussion

The independent variables considered in this work and their corresponding values for each level are presented in Table 1. A fractional factorial design 2^{6-1} study was conducted, since the following GA parameters are taken into account: jump mutation probability (*pmutate*), crossover probability (*pcross*), creep mutation probability (*pcreep*), population size (*npopsiz*), maximum number of generations allowed (*maxgen*) and the initial sample of individuals (*idum*). Table 2 presents the combinations of GA parameters for the optimisations that were conducted, for the fractional factorial design with a central point. The central point is normally used with repetition for error estimation. However, there is no error in computer simulations (the crystallization model Eqs. (1)–(7) are used) and, therefore, only one point is used. The results of CV of the best individual in the last generation generated by the GA in each case are presented in the final column. An explanation of the crystallization optimisation

Table 1
Levels of the parameters used in sensitivity analysis of the GA code applied to the crystallization problem

GA parameters	(−) Level	Central	(+) Level
(1) *pmutate*	0.0425	0.05	0.0575
(2) *pcross*	0.68	0.8	0.92
(3) *pcreep*	0.034	0.04	0.046
(4) *npopsiz*	43	50	58
(5) *maxgen*	43	50	58
(6) *idum*[a]	−1150	−1000	−850

[a] *idum* assumes negative integer value and is the initial seed for the GA run; each value assigned to *idum* gives rise to a different initial population.

Table 2
Fractional factorial design 2^{6-1} study results

Run name	*pmutate*	*pcross*	*pcreep*	*npopsiz*	*maxgen*	*idum*	Response (CV)
pl01a	−	−	−	−	−	−	103.0
pl02a	−	−	−	−	+	+	127.7
pl03a	−	−	−	+	−	+	129.4
pl04a	−	−	−	+	+	−	99.03
pl05a	−	−	+	−	−	+	112.8
pl06a	−	−	+	−	+	−	105.6
pl07a	−	−	+	+	−	−	110.6
pl08a	−	−	+	+	+	+	120.4
pl09a	−	+	−	−	−	+	104.2
pl10a	−	+	−	−	+	−	118.6
pl11a	−	+	−	+	−	−	99.29
pl12a	−	+	−	+	+	+	131.8
pl13a	−	+	+	−	−	−	102.3
pl14a	−	+	+	−	+	+	110.4
pl15a	−	+	+	+	−	+	131.8
pl16a	−	+	+	+	+	−	125.6
pl17a	+	−	−	−	−	+	125.1
pl18a	+	−	−	−	+	−	97.55
pl19a	+	−	−	+	−	−	98.51
pl20a	+	−	−	+	+	+	115.1
pl21a	+	−	+	−	−	−	100.2
pl22a	+	−	+	−	+	+	104.0
pl23a	+	−	+	+	−	+	116.1
pl24a	+	−	+	+	+	−	100.4
pl25a	+	+	−	−	−	−	100.9
pl26a	+	+	−	−	+	+	113.2
pl27a	+	+	−	+	−	+	128.4
pl28a	+	+	−	+	+	−	99.0
pl29a	+	+	+	−	−	+	108.2
pl30a	+	+	+	−	+	−	102.3
pl31a	+	+	+	+	−	−	108.4
pl32a	+	+	+	+	+	+	122.3
Zero	0	0	0	0	0	0	102.0

problem is given in Appendix A, which brings detailed information on optimisation and model variables for one selected optimal solution, to know, for that of run 'pl32a'.

The software STATISTICA (Statsoft, v. 6.0) was used to analyze the results. Table 3 presents the effect estimates of the GA parameters, calculated with 95% of confidence, with no interaction between the effects. Fig. 4 brings the corresponding Pareto chart, used for identification of the most important factors. The '*t*' statistics that figures in Table 3 is presented with its freedom degree, which is 26, since there were 33 available runs and only 7 effects were calculated (the mean effect plus the effects for each factor). The values for the *t*-statistics are also indicated next to each bar in the Pareto chart.

As can be seen, two parameters, the initial population (expressed by *idum*) and its size (expressed by *npopsiz*) have significant effects on the search for a minimum CV of the final CSD in the batch cooling crystallization system optimisation. The Pareto chart of Fig. 4 shows that the jump mutation probabil-

Table 3
Effect estimates on CV for the fractional factorial design with no factor interactions

Factor	Effect	S.E.	*t*(26)	*p*
Mean	*111.3461*	*1.428299*	*77.95712*	*0.000000*
(1) *pmutate*	−5.8038	2.900876	−2.00069	0.055969
(2) *pcross*	2.5750	2.900876	0.88766	0.382860
(3) *pcreep*	−0.5863	2.900876	−0.20209	0.841416
(4) *npopsiz*	*6.2929*	*2.900681*	*2.16947*	*0.039373*
(5) *maxgen*	0.8992	2.900681	0.30999	0.759037
(6) *idum*	*14.3513*	*2.900876*	*4.94721*	*0.000039*

Italic values denotes significant effect for a 95% confidence level.

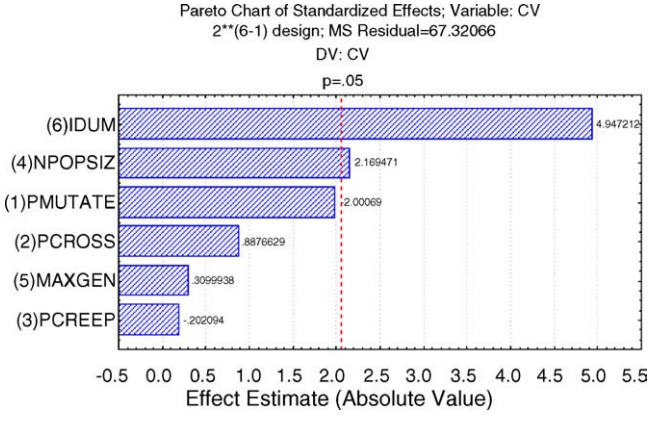

Fig. 4. Pareto chart of variables effects for CV of the best individual (at 95% of confidence level), with no factor interactions.

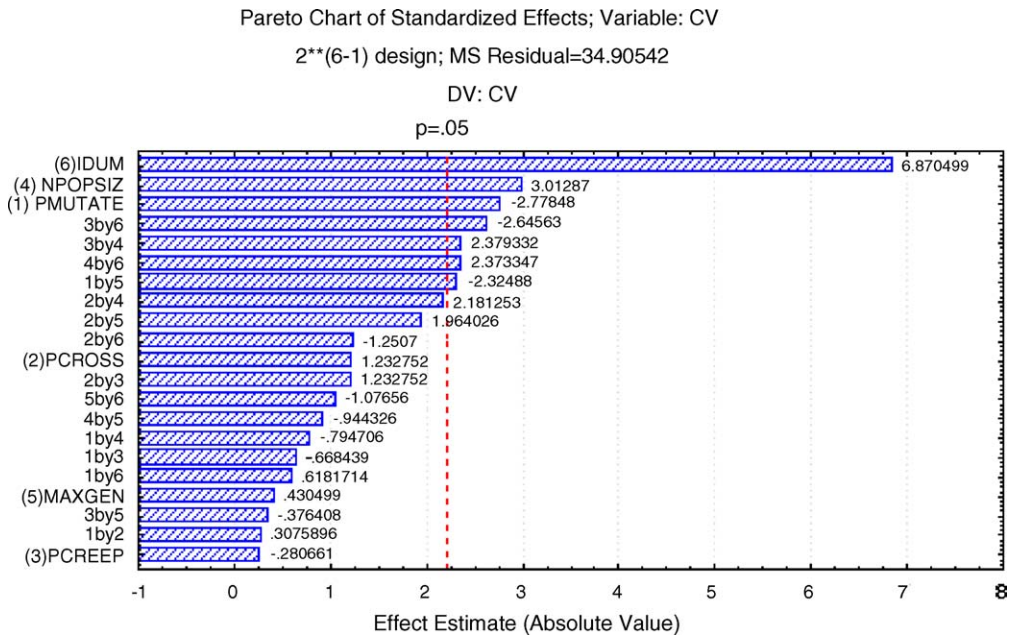

Fig. 5. Pareto chart of variables effects for CV of the best individual (at 95% of confidence level), with two factor interactions.

ity (*pmutate*) has an effect, if considered no interaction between the factors, near the limit of significance. In this way, an analysis with two-way factor interactions was performed. These results are outlined in Table 4 and the correspondent Pareto chart of effects presented in Fig. 5.

Once again, factors (6) and (4) (initial population and its size) have shown a great effect on the CV of the final CSD of the best individual generated by GA at the end of the evolution process. The interactions between the creep mutation probability and the initial population (*pcreep* and *idum*, factors (3) and (6)) and between the creep mutation probability and the population size (*pcreep* and *npopsiz*, factors (3) and (4)) have presented a significant effect. These interaction results carry a great influence from the factors (6) and (4), the most meaningful factors in the GA response in this case study, but also show that the creep mutation probability (factor (3)) is a factor with important influence. As a result from the strong influence of factors (6) and (4), their interaction is also of significant effect on the final response.

Table 4
Effect estimates on CV for the fractional factorial design with two factor interactions

Factor	Effect	S.E.	$t(11)$	p
Mean	*111.3462*	*1.028469*	*108.2640*	*0.000000*
(1) *pmutate*	*−5.8038*	*2.088822*	*−2.7785*	*0.017953*
(2) *pcross*	2.5750	2.088822	1.2328	0.243365
(3) *pcreep*	−0.5863	2.088822	−0.2807	0.784179
(4) *npopsiz*	*6.2929*	*2.088681*	*3.0129*	*0.011805*
(5) *maxgen*	0.8992	2.088681	0.4305	0.675146
(6) *idum*	*14.3513*	*2.088822*	*6.8705*	*0.000027*
1 by 2	0.6425	2.088822	0.3076	0.764140
1 by 3	−1.3963	2.088822	−0.6684	0.517634
1 by 4	−1.6600	2.088822	−0.7947	0.443593
1 by 5	*−4.8563*	*2.088822*	*−2.3249*	*0.040231*
1 by 6	1.2912	2.088822	0.6182	0.549048
2 by 3	2.5750	2.088822	1.2328	0.243365
2 by 4	4.5562	2.088822	2.1813	0.051752
2 by 5	4.1025	2.088822	1.9640	0.075296
2 by 6	−2.6125	2.088822	−1.2507	0.236991
3 by 4	*4.9700*	*2.088822*	*2.3793*	*0.036544*
3 by 5	−0.7862	2.088822	−0.3764	0.713773
3 by 6	*−5.5262*	*2.088822*	*−2.6456*	*0.022763*
4 by 5	−1.9725	2.088821	−0.9443	0.365283
4 by 6	*4.9575*	*2.088822*	*2.3733*	*0.036933*
5 by 6	−2.2487	2.088822	−1.0766	0.304720

Italic values denotes significant effect for a 95% confidence level.

Another GA parameter that should be carefully varied during a GA optimisation study, according to Table 4 and Fig. 5, is the jump mutation probability (*pmutate*, factor (1)), evidenced by the meaningful effect of this factor. The interaction between the jump mutation probability and the maximum number of generations (*pmutate* and *maxgen*, factors (1) and (5)) is presented as of significant importance, but this result is attributed mainly to the strong effect of factor (1) and not to the importance of factor (5) on the final response.

The crossover probability (*pcross*, factor (2)) does not seem to affect significantly the GA optimisation response.

7. Conclusions

An original perspective is proposed to genetic algorithm parameters in the application of this stochastic optimisation technique in batch cooling crystallization systems. Factorial design technique was used in order to select the most meaningful parameters, when optimising the coefficient of variation of the final crystal size distribution. The results guide to the significance (95% confidence level) of the initial population, the population size and the jump and creep mutation probabilities. Future optimisation works should direct focus on alterations in these parameters during GA optimisation.

Acknowledgements

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Appendix A

This appendix brings detailed information on model variables and optimisation results for run 'pl32a' that figures in Table 2.

As can be extracted from Tables 1 and 2, pl32a was run with all GA parameters in the upper level, i.e., the values assigned to *pmutate*, *pcross*, *pcreep*, *npopsiz*, *maxgen* and *idum* were, respectively, 0.0575, 0.92, 0.046, 58, 58 and −850. The 58 individuals defined by *idum*, each one carrying values for all parameters of Eqs. (8) and (9), plus the definition of the right sequence of functions (Type 1 + Type 2 or Type 2 + Type 1) to be followed, evolve for 58 generations, with the rate of GA operators defined by *pmutate*, *pcross* and *pcreep*. Each individual is transferred to the crystallization process model subroutine. Extremely detailed information on the crystallization system variables (like crystallizer dimensions, global heat coefficient, initial solution concentration, solubility data of adipic acid as a function of solution temperature, classes boundaries and so on) can be found in Costa et al. (2005). The seeding policy used consisted of 1.32×10^{12} crystals in the seventh class and 1.62×10^{8} crystals in the 20th class.

The CV that figures in Table 2 for pl32a is the minimum CV calculated from all CSD generated with the crystallization simulations whose input were, for each one of them, the set of parameters of Eqs. (8) and (9) (vector **x**). The minimum CV determines the best individual evolved, that is, the best values for the parameters of Eqs. (8) and (9), as well as the definition of the sequence of functions. The best individual for 'pl32a' is presented in Table A1.

The coolant temperature for the best individual of pl32a is then defined as expressed in Eq. (12), which is determined first by Type 2 function and then by Type 1.

$$T_c = \begin{cases} 337.6164 - (337.6164 - 309.3425)\left[\dfrac{t}{1500}\right]^{1.7613}, & \text{if } t \le 1267.0 \\ 309.3425 - (309.3425 - 337.6164)\left[1 - \dfrac{t}{1500}\right]^{0.7292}, & \text{if } t > 1267.0 \end{cases} \quad (12)$$

Fig. A1 shows the best cooling profile (Eq. (12)), determined by the information presented in Table A1, as well as the profile of the crystallizer medium temperature and of supersaturation during all batch time. Both profiles of crystallizer medium temperature and of supersaturation are generated with the process simulation with the model equations and process parameters, whose details can be found in Costa et al. (2005). An illustration of the obtained CSD for the individual presented in Table A1 is depicted in Fig. A2.

Table A1
Vector **x** for the best individual of 'pl32a'

x component	Value
Sequence of functions	Type 2 + Type 1
T_{c0}	337.6164
T_{cF}	309.3425
$t_{intermediate}$	1267.0000
A_1	0.7292
A_2	1.7613

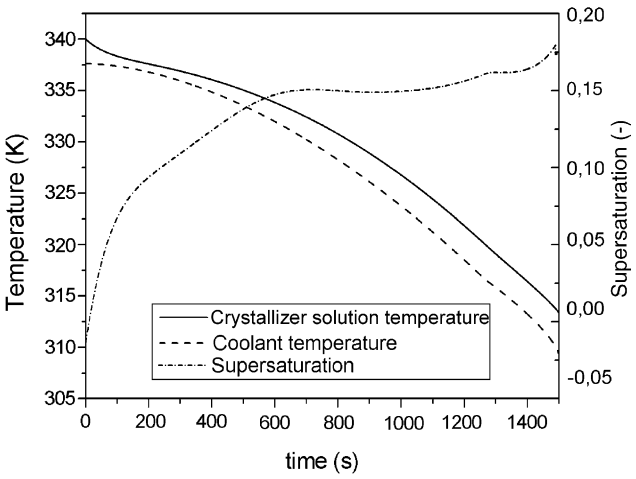

Fig. A1. Profiles of coolant temperature, temperature of solution inside the crystallizer and supersaturation for best individual of run 'pl32a'.

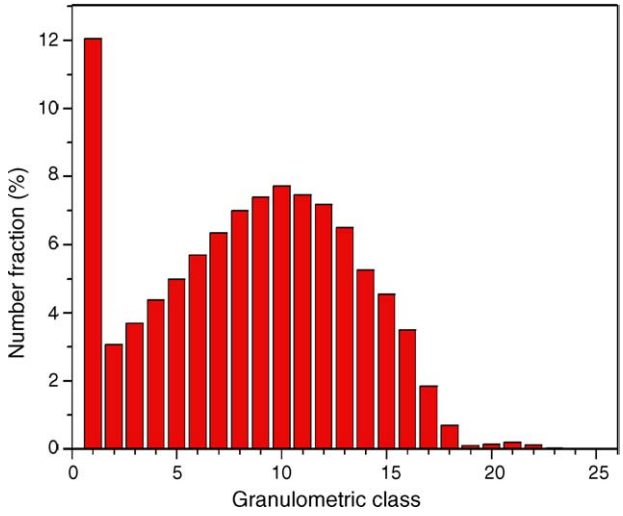

Fig. A2. CSD generated for best individual of run 'pl32a'.

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8.3. Conclusões

Os resultados mostram que os parâmetros mais significativos (95% de confiança) são a população inicial, o tamanho da mesma e as probabilidades de mutação. Estes parâmetros são os que devem ser modificados em estudos de otimização deste processo por Algoritmo Genético, na busca pelo ótimo.

Capítulo 9. Conclusões e Sugestões de Trabalhos Futuros

9.1. Conclusões

É inegável a importância do processo de cristalização para a obtenção de produtos de alto valor agregado na indústria. É também incontestável o excelente nível de trabalhos publicados na literatura na área de cristalização. No entanto, esse processo é marcado por modelagem não trivial e de difícil solução, principalmente quando se consideram mecanismos cinéticos além da nucleação e do crescimento. A consideração de estudos de cristalização no sentido de se tentar investigar a sensibilidade da distribuição de tamanhos de cristal em relação ao perfil de temperatura empregado para resfriamento teve início na década de 70. Porém, até a atualidade, não se tem um completo entendimento do detalhamento dos mecanismos envolvidos e de como representá-los, nem se possui um método numérico padrão estabelecido para solução rápida e confiável das equações que compõem a sua modelagem detalhada. A alta complexidade e não linearidade desse processo impõe ainda uma dificuldade na determinação de políticas operacionais ótimas. Assim, notou-se a necessidade de desenvolvimento de um *software* para avaliação de processos de cristalização e melhoria de processo, através de sua modelagem determinística detalhada e da utilização de métodos determinísticos e estocásticos de otimização.

Dentro desse contexto, este trabalho apresentou inicialmente a modelagem determinística detalhada de processos de cristalização com representação dos mecanismos de nucleação, crescimento e aglomeração. Um levantamento dos métodos numéricos existentes na literatura para solução do balanço de população indica que não há até o presente momento um método estabelecido de resolução do modelo. A seleção do método numérico é ainda sujeita à dependência do caso de estudo em questão e dos mecanismos envolvidos na modelagem. De qualquer forma, qualquer método numérico, por não se tratar da solução real (analítica), traz em si desvantagens inerentes e, portanto, deve-se, na seleção do método a ser utilizado, ponderar entre a

adequação do método ao caso de estudo e suas vantagens (como fácil programação, rapidez e precisão de cálculo) e desvantagens.

A modelagem desenvolvida é acoplada a métodos de otimização de modo a compor um *software* geral para estudos de desenvolvimento de processos orientados a especificações de produto. Os estudos preliminares feitos com o auxílio do modelo do processo apontaram para a real necessidade de se buscar políticas operacionais que levassem à obtenção de produtos com distribuição de tamanhos controlada. A utilização de Programação Quadrática Sucessiva e discretização da variável de controle nos estudos preliminares de otimização indicaram que a abordagem adotada não conduzia a resultados satisfatórios, embora conduzisse a melhorias de qualidade de produto. Estudos subseqüentes de projeto de produto mostraram que, a depender da cinética inerente a cada sistema, certas características de distribuição de tamanhos de cristal são naturalmente favorecidas.

A abordagem não completamente satisfatória por via determinística da otimização do processo levou à utilização da técnica estocástica de otimização por Algoritmo Genético. Essa técnica tem sido aplicada em uma série de processos na área de engenharia e de matemática aplicada, tendo sido relatado na literatura sucesso no tratamento de problemas não-lineares e de alta dimensionalidade. De fato, a sua aplicação no caso de estudo da otimização da política operacional de resfriamento do processo de cristalização do ácido adípico em modo batelada apresentou resultados bastante melhores do que aqueles oriundos da utilização da Programação Quadrática Sucessiva, indicando a sua adequação a estudos de busca por *setpoints* de processo.

Não obstante o sucesso da utilização do Algoritmo Genético em problemas com escala de engenharia, pode ser notada a dificuldade na identificação dos parâmetros para a solução do problema de otimização. De fato, este é um ponto bastante relevante, levando-se em conta que o tempo computacional é uma restrição a ser superada. Não foi encontrado na literatura ou nos *softwares* existentes um procedimento mínimo que pelo menos servisse para auxiliar na tomada de decisão sobre quais parâmetros devem ser usados ou mesmo alterados para um melhor desempenho do método global de otimização.

Nesse sentido, este trabalho desenvolveu um procedimento original e de utilização geral para detecção dos parâmetros do algoritmo que exercem influência significativa na resposta final do problema de otimização. Essa contribuição é relevante por descartar variações em parâmetros sem influência significativa na resposta final. A aplicação do procedimento desenvolvido em diferentes casos de estudo, incluindo-se o processo de cristalização com a definição de sua trajetória ótima de resfriamento, demonstrou que o conjunto de parâmetros significativos é dependente do problema em questão.

9.2. Trabalhos Futuros

O desenvolvimento deste trabalho de doutoramento levantou possibilidades de extensão e/ou investigação mais aprofundada, bem como novas frentes de pesquisa, que são aqui apresentadas como sugestões de trabalhos futuros.

Este trabalho apresentou a parametrização da variável de controle (com os chamados Tipo 1 e Tipo 2 de funções) em oposição à sua discretização, considerada apenas constante por partes. No entanto, trabalhos futuros poderiam investigar mais a fundo a potencialidade da discretização, com a interpolação dos valores discretos encontrados por otimização, ou mesmo a consideração de variável de controle linear por partes.

Outro ponto de possíveis investigações futuras reside na verificação da precisão do número de classes a ser utilizado no Método das Classes, um problema de mínima realização, e na comparação dos coeficientes de variação das distribuições obtidas correspondentes aos sub-ótimos encontrados com aquela decorrente da utilização de resfriamento natural.

Concernente à modelagem do processo, a obtenção e avaliação de modelos simplificados, seja por redução na dimensionalidade, seja pela consideração da real necessidade de levarem-se em conta todos os fenômenos observáveis, são vislumbradas como campo de trabalhos futuros, uma vez que um modelo muito detalhado exige um tempo computacional maior e requer valores de parâmetros muitas vezes difíceis de serem obtidos.

A otimização do processo de cristalização, feita tanto por métodos determinísticos quanto evolucionistas, aponta para a grande dificuldade dos primeiros métodos em lidar com a alta dimensionalidade do problema e, por dependerem da estimativa inicial, levam a ótimos locais, enquanto os métodos evolucionistas se mostraram mais hábeis em encontrar as cercanias do ótimo global, sendo, no entanto, de lenta execução. Isso sugere que se desenvolva e se avalie uma metodologia híbrida de otimização, que una algoritmos de busca locais e métodos estocásticos de otimização, de modo que se obtenha um método que guarde a independência da estimativa inicial (principal vantagem do método estocástico) e a ela alie a rápida solução, típica dos métodos determinísticos. Na concepção da metodologia híbrida, seria interessante a avaliação de outros métodos estocásticos de otimização, como o Recozimento Simulado ou o Enxame de Partículas, uma vez que estes métodos possuem menos parâmetros a serem ajustados e que a literatura aponta resultados bastante satisfatórios com a utilização dos mesmos.

A otimização multiobjetivo não foi o foco de estudo desta tese, mas a sua investigação na otimização da cristalização poderia ser feita futuramente, uma vez que os objetivos costumeiramente tratados em problemas de otimização de cristalização são conflitantes. A investigação segundo a frente ótima de Pareto poderia trazer elucidações acerca de maneiras mais efetivas de se postularem problemas de otimização de cristalização.

A falta de medidas *online* precisas em todas as faixas de operação e o alto investimento necessário para medidas das variações no tempo das variáveis de saída relevantes, como a CSD ou a supersaturação, assim como a alta dimensionalidade e alta não-linearidade (difícil cálculo *online* de políticas operacionais ótimas), têm dificultado a implementação de controladores preditivos em cristalizadores em processos batelada operados por resfriamento em malha fechada. Em trabalhos futuros, técnicas inferenciais de predição de estados (estimador de estados) podem ser desenvolvidas através de modelos determinísticos, de modo a estimar valores das variáveis-chave do processo e de difícil mensuração a partir de valores facilmente mensuráveis na prática, como temperatura e concentração de soluto. O estimador de estados seria bastante útil

em estudos de controle avançado do processo. Seguindo o mesmo conceito de modelos inferenciais, sugere-se também o desenvolvimento de modelos híbridos, acoplando-se os modelos determinísticos com redes neurais.

Dentre as estratégias de controle promissoras para o tipo de problema que impõe a cristalização, destacam-se os controles preditivos multivariáveis e baseados em modelo, uma vez que se pode inserir nas restrições das variáveis de estado as especificações de produto (propriedades da distribuição de tamanhos de cristais). A investigação da melhor estratégia e do tipo de modelo interno (modelos internos lineares – tipo *Dynamic Matrix Control* - ou não lineares – uso de redes neurais artificiais, por exemplo) é um campo de trabalhos futuros.

Por fim, a integração das etapas de otimização e controle poderia ser feita em estrutura de uma ou duas camadas.

O Capítulo 7 ilustrou, no seu quarto caso de estudo, o ajuste de parâmetros para o modelo de fermentação alcoólica. Na abordagem utilizada, a faixa de busca para os parâmetros foi propositalmente bastante larga, de modo a simular as situações em que o pesquisador se depara com uma nova modelagem, nas quais não tem ainda informação de qual a ordem de grandeza dos parâmetros. No entanto, uma faixa de busca larga torna mais difícil e demanda mais tempo para o algoritmo de otimização encontrar o ótimo (valores ótimos para os parâmetros). Assim, seria interessante que trabalhos futuros investigassem que influência a faixa de busca tem na procura pelo ótimo (inclusão da faixa de busca como um dos fatores em estudos de planejamento fatorial).

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