Distribution Control of Particulate Systems Based on Population Balance Equation Models

Michael A. Henson[1]
Department of Chemical Engineering
University of Massachusetts
Amherst, MA 01003-3110

Abstract

Manufacturing processes in which the desired product takes the form of individual particles are ubiquitous in the chemical, pharmaceutical and agricultural industries. Particulate processes often are modeled using a form of the population balance equation (PBE) which describes the evolution of the particle distribution. In many applications, control of the particle distribution is necessary to achieve the desired product properties. In this paper, a model predictive control strategy based on a discretized representation of a general one-dimensional PBE is proposed for particle distribution control. The controller is formulated to minimize the least squares difference between the predicted and target distributions assuming the availability of particle distribution measurements. The proposed method is applied to the problem of cell mass distribution control in a continuous yeast fermentor.

1 Introduction

A particulate system is characterized by a large number of interacting particles which differ with respect to certain physical and/or chemical properties [13, 15]. The dynamics of these complex systems can be captured with population balance equation (PBE) models which describe the evolution of an appropriate distribution function [13]. The distribution function evolves in a p-dimensional space where p represents the number of internal coordinates used to differentiate the particles. When a single internal coordinate is used to parameterize the particle distribution, the PBE is written as [15]:

$$\frac{\partial W(\xi,t)}{\partial t} + \frac{\partial [k(\xi,t)W(\xi,t)]}{\partial \xi} = h(\xi,t) \qquad (1)$$

where: t is time; ξ is the internal coordinate; $W(\xi,t)$ is the number density of particles; $k(\xi,t)$ is the particle growth rate; and $h(\xi,t)$ represents the net creation of particles. The PBE typically is coupled to integro-differential equations that represent the driving force for particle growth [13]. The internal coordinate can be discretized using well known solution techniques for partial differential equations such as finite differences, finite elements, orthogonal collocation and spectral decomposition [7]. The discretized PBE model consists of a potentially large number of nonlinear ordinary differential equations in time which can be solved using standard numerical integration codes.

Control of the particle distribution often is required to achieve satisfactory process performance. The following examples illustrate some of the control objectives associated with these complex systems:

- *Crystallizers* – Control of the particle size distribution is necessary to ensure pharmaceutical products have the desired physiological effects [16, 20].
- *Emulsion Polymerization Reactors* – Control of the particle size distribution allows the manufacture of coatings, adhesives, pigments and latex paints with the desired physiochemical properties [3, 5].
- *Biochemical Reactors* – Control of the cell mass distribution has the potential to increase the production of key metabolites produced by microbial and mammalian cells [4].

The development of increasingly sophisticated PBE models and the availability of cheap computing power makes particle distribution control a realistic goal. While distribution control strategies have been proposed for selected particulate systems [2, 3, 22], the development of a more general approach is needed.

In this paper, a distribution control strategy based on model predictive control (MPC) is proposed for continuous particulate processes in which the single variable distribution of interest can be measured or reconstructed from on-line measurements. The control problem is formulated as the least-squares minimization of the predicted distribution and a target distribution over a moving time horizon. The discretized PBE model used for controller design is characterized by a large number of state variables (most of which

[1]Phone: 413-545-3481; Fax: 413-545-1647; E-mail: henson@ecs.umass.edu

represent the density of particles at the discretization points) and a small number of manipulated inputs (the feed conditions and possibly the process temperature). Consequently, the available degrees of freedom usually are insufficient to achieve the target distribution in the presence of modeling error. Methods for selecting an appropriate subset of the state variables for inclusion in the least squares objective function are discussed. The proposed methodology is applied to the problem of cell distribution control in continuous yeast fermentors.

2 Particle Distribution Control Strategy

2.1 PBE Model Discretization

Consider a continuous particulate process described by the following coupled set of nonlinear partial and ordinary differential equations:

$$\frac{\partial W(\xi,t)}{\partial t} + \frac{\partial [k(\xi,z)W(\xi,t)]}{\partial \xi} = h[\xi, W(\xi,t), z(t), u(t)]$$
$$\frac{dz(t)}{dt} = g[\xi, W(\xi,t), z(t), u(t)] \qquad (2)$$

The first equation represents the PBE (1) where the the particle growth rate $k(\xi,t)$ is assumed to depend implicitly on time through the differential variables $z(t) \in R^l$ and the dependence of the net creation of particles $h(\xi,t)$ on the particle distribution function $W(\xi,t)$, the differential variables $z(t)$ and the input variables $u(t) \in R^m$ is shown explicitly. The second equation represents the integro-differential equations associated with the driving force for particle growth. The model structure (2) is sufficiently general to represent a wide variety of particulate system models.

The proposed controller design strategy is based on discretization of the PBE model (2) with respect to the internal coordinate ξ. In addition to specialized techniques developed for particular classes of PBE models [14], discretization can be performed using general purpose methods such as finite differences and orthogonal collocation [7]. Integral terms involving $W(\xi,t)$ which are often contained in the functions $h(\cdot)$ and $g(\cdot)$ can be approximated using techniques such as Gaussian quadrature [7]. The discretized model consists of nonlinear ordinary differential equations in time:

$$\frac{dW_j(t)}{dt} = H[W_j(t), z(t), u(t)], \quad j \in [1,n]$$
$$\frac{dz(t)}{dt} = G[W_j(t), z(t), u(t)] \qquad (3)$$

where: $W_j(t)$ is the value of the particle distribution $W(\xi,t)$ at the discretization point ξ_j; and $H(\cdot)$ and $G(\cdot)$ are nonlinear algebraic functions. By defining $x^T = [W_1 \;\; W_2 \;\; \cdots \;\; W_n \;\; z^T] \in R^{n+l}$, the discretized model can be represented in nonlinear state-space form:

$$\begin{aligned} \frac{dx(t)}{dt} &= F[x(t), u(t)] \\ y(t) &= E[x(t)] \end{aligned} \qquad (4)$$

where the output map $E(\cdot)$ is to be determined. Jacobian linearization of this model at a steady-state operating point leads to a linear state-space model:

$$\begin{aligned} \frac{dx(t)}{dt} &= Ax(t) + Bu(t) \\ y(t) &= Cx(t) \end{aligned} \qquad (5)$$

Discretization of the state-space model (4) or (5) with respect to time leads to a set of nonlinear or linear algebraic equations, respectively, which can be posed as equality constraints in the MPC problem.

2.2 MPC Controller Formulation

The MPC controller is designed to drive the particle distribution $W(\xi,t)$ to a (possibly) time varying reference distribution $W_r(\xi,t)$. The reference distribution is assumed to be specified *a priori* based on knowledge of the relationship between the particle distribution and the target process/product properties. For example, certain particle size distributions of latex paints are known to correlate to desirable processing behavior [3]. The reference distribution is discretized in the internal coordinate ξ to yield $W_{r,j}(t)$ where the points $\xi_j, j \in [1,n]$, are identical to those used for model discretization. The MPC formulation also requires that setpoints z_r be specified for the differential variables z. A second assumption is that the particle distribution $W(\xi,t)$ and the differential variables $z(t)$ associated with particle growth are measured or reconstructed from available on-line measurements. Analyzers which provide measurements of the particle size distribution and various differential variables are available for crystallization [1, 16], emulsion polymerization [5] and fermentation [17] processes. This assumption eliminates the need to develop a state estimation strategy such that basic controller design issues can be addressed.

The controlled outputs (y) are selected such that the MPC controller is capable of driving the particle distribution "close" to the reference distribution. The selection of an appropriate set of controlled outputs is nontrivial because the available manipulated inputs (u) do not provide sufficient degrees of freedom to achieve an arbitrary reference distribution. Because offset elimination generally is not possible, a disturbance model is not included in the MPC design. For the moment, the output vector (y) is assumed to be known and the MPC controller is formulated as follows [10, 11]:

$$\min_{U_M(k)} \sum_{j=0}^{P} \{[y(k+j|k) - y_s(k)]^T Q [y(k+j|k) - y_s(k)] + [u(k+j|k) - u_s]^T R [u(k+j|k) - u_s] + \Delta u^T(k+j|k) S \Delta u(k+j|k)\} \qquad (6)$$

where: $y(k+j|k)$ and $u(k+j|k)$ are predicted values of the output and input variables, respectively; y_s

and u_s are target values for the outputs and inputs; $\Delta u(k) = u(k) - u(k-1)$; and P is the prediction horizon. The decision variables are current and future values of the inputs $U_M(k) = [u(k|k) \ \ldots u(k+M-1|k)]$, where M is the control horizon. Only the first calculated input actually is implemented, $u(k) = u(k|k)$, and the problem is resolved at the next time step with new measurements. The input and output variables may be subject to constraints chosen such that the controlled process remains in the desired operating regime [10]. A temporally discretized version of the nonlinear model (4) or the linear model (5) is posed as a set of equality constraints. If the linear model is used, the optimization problem (6) can be solved using standard quadratic programming software [11]. A considerably more complex nonlinear programming problem [10] is obtained when the nonlinear model is used.

2.3 Selection of Controlled Outputs

The MPC design is completed by specifying the manipulated inputs u and the controlled outputs y. The flow rate and/or concentration of components in the continuous feed stream typically are employed as input variables. Such inputs include: feed solute concentration for crystallizers [16]; feed surfactant, initiator and inhibitor concentrations for emulsion polymerization reactors [5]; and dilution rate and feed substrate concentration for fermentors [4]. Other inputs such as process temperature and fines removal flow rate in crystallization processes also may be available.

The MPC problem (6) is formulated to allow tracking of a reference particle distribution. An obvious approach is to choose the particle number density W_j at each discretization point as a controlled output:

$$y^T = \left[\begin{array}{cccc} W_1 & W_2 & \cdots & W_N \end{array} \right] \tag{7}$$

The resulting control problem will be highly non-square with many more outputs than inputs. Given the limited number and non-distributed nature of the inputs, the state-space models (4) and (5) are expected to be unreachable in the sense that an arbitrary reference distribution is not achievable. Furthermore, the regulation of some differential variables z associated with particle growth may be desirable. While the reachability problem associated with particle distribution control has received some attention [9, 18], a general theory is lacking. Therefore, we pursue practical methods for determining a reduced-order output vector such that the reference distribution can be achieved in an approximate sense.

A simple approach to choose a subset of the discretized cell number densities W_j and a subset of the differential variables z as output variables:

$$y = \left[\begin{array}{ccccccc} W_{j_1} & \cdots & W_{j_p} & z_{i_1} & \cdots & z_{i_q} \end{array} \right]^T \tag{8}$$

where the indices $\{i_1, \ldots, i_q\}$ and $\{j_1, \ldots, j_p\}$ denote, respectively, the differential variables employed and the discretization points where the associated particle number densities are used. The reduced-order output vector (8) can yield a MPC problem which is much less non-square than the full-order vector (7). The selection of the differential variables is problem specific. For the fermentation example presented in the next section, inclusion of the substrate concentration is desirable to avoid washout. Given the output vector defined in (8), the MPC controller (6) is formulated to drive the particle distribution "close" to the reference particle distribution at the discretization points $\{\xi_{j_1}, \ldots, \xi_{j_p}\}$. These discretization points are chosen such that satisfaction of the tracking objective implies that the full particle distribution $W(\xi, t)$ is driven sufficiently "close" to the full reference distribution $W_r(\xi, t)$. If the PBE model is solved using orthogonal collocation on finite elements [3, 22], a reasonable approach is to select the controlled outputs as the boundary points of the finite elements. This method is explored in the next section.

A more systematic approach is to use multivariate statistics to derive a reduced-order output vector which captures most of the "energy" present in the full-order state vector x. This approach is motivated by the observation that there are strong collinearities between the discretized cell number densities W_j and (possibly) between the differential variables z_i. This approach should yield a reduced-order output vector whose dimension is more commensurate with the degrees of freedom provided by the available inputs. Moreover, tracking of the reference distribution should not sacrificed because only "unimportant" dynamics are neglected.

Principal component analysis (PCA) [6] can be used to systematically derive the reduced-order output vector for the linear model (5). Application of singular value decomposition to the A matrix yields the mapping:

$$y = Px, \quad P \in R^{s \times (n+l)} \tag{9}$$

which transforms the $(n+l)$-dimensional state vector x into a s-dimensional output vector y. The dimension s is chosen such that at least 95% of the "energy" is preserved. Given measurements of the state variables x, the output vector (9) can be incorporated directly in the MPC problem (6). The mapping (9) also allows the MPC target vector $y_r = Px_r$ is to be computed from the reference distribution W_r and the differential variable setpoints z_r. A similar order reduction strategy can be developed for the nonlinear model (5) using proper orthogonal decomposition [21].

3 Yeast Cell Distribution Control

Saccharomyces cerevisiae (baker's yeast) is an important microorganism in a number of industries including brewing, baking, food manufacturing and genetic engineering. Many investigators have shown that continuous cultures of *Saccharomyces cerevisiae* exhibit sustained oscillations in glucose limited environments under aerobic growth conditions [12, 19]. In most situations, oscillations adversely affect fermentor operability and the control objective is to eliminate limit cycle behavior by stabilizing a chosen steady state. On the other hand, induction of oscillatory dynamics may be desirable to increase the production of metabolites which are produced during a certain phase of the cell cycle [8]. Below we show that both these objectives can be achieved with a MPC controller that provides direct control of the cell number distribution.

3.1 PBE Model

Zhu *et al.* [22] have developed a yeast cell population model which yields qualitative predictions of sustained oscillations. The PBE for the cell mass distribution is coupled to the substrate (glucose) mass balance through a phenomenological model of the budding yeast cell cycle. Cell growth and division are captured with two cell cycle model parameters: the transient mass (m_t^*) where a growing cell begins to form a new bud; and the division mass (m_d^*) where the bud divides from the mother cell producing two newborn cells of different masses. The PBE model is briefly reviewed below to facilitate the subsequent development.

The cell PBE has the general form (2) where the internal coordinate ξ is the cell mass m, the differential variables $z^T = [S \;\; S']$ are discussed below and the net creation of cells is represented as:

$$\begin{aligned} h[\xi, W, z, u] &= \int_0^\infty 2p(m,m')\Gamma(m',S')W(m',t)dm' \\ &\quad -[D+\Gamma(m,S')]W(m,t) \end{aligned} \tag{10}$$

The dilution rate D is a manipulated input. The newborn cell probability function $p(m, m')$ and the division intensity function $\Gamma(m, S')$ depend on the cell cycle parameters (m_t^*, m_d^*), which in turn are increasing functions of the effective substrate concentration S' [22]. The initial cell distribution is denoted $W(m, 0)$ and the boundary condition is $W(0, t) = 0$. The zeroth moment of the cell number density represents the total number of cells per unit volume and is defined as: $m_0(t) = \int_0^\infty W(m,t)dm$.

The substrate mass balance is:

$$\frac{dS}{dt} = D(S_f - S) - \frac{k(m,S')}{Y}m_0 \tag{11}$$

where S is the substrate concentration, Y is the cell mass yield and the feed substrate concentration S_f is a second manipulated input. The cell growth rate $k(m, S')$ is assumed to follow Monod kinetics [22]. The filtered substrate concentration is generated as:

$$\frac{dS'}{dt} = \alpha(S - S') \tag{12}$$

where the parameter α reflects how fast cells respond to environmental changes. Equations (11) and (12) represent the integro-differential equations associated with the driving force for cell growth in the general form (2). A more complete description of the model and parameter values are given elsewhere [22].

3.2 MPC Controller

A nonlinear state-space model of the form (4) is obtained by discretizing the PBE model using orthogonal collocation on finite elements and Gaussian quadrature [7]. Discretization is performed over a finite cell mass domain, $0 \le m \le m_{max}$, such that the number of cells with $m > m_{max}$ is negligible. In the following simulations, we use 12 equally spaced finite elements, each with 8 internal collocation points. A state-space model suitable for linear MPC design is obtained from (4) by Jacobian linearization and temporal discretization with a sampling interval $\Delta t = 0.1$ hr. The linear design model has the form:

$$\begin{aligned} x(k+1) &= Ax(k) + Bu(k) \\ y(k) &= Cx(k) \end{aligned} \tag{13}$$

where: $x \in R^{111}$ is the state vector comprised of the cell number density at each collocation point (W_j) and the substrate and filtered substrate concentrations (S, S'); and $u \in R^2$ is the input vector consisting of D and S_f. The output vector $y \in R^{14}$ includes the cell mass densities at the boundary points of the finite elements as well as the substrate concentration:

$$y = \begin{bmatrix} W_1 & W_{10} & \cdots & W_{100} & W_{109} & S \end{bmatrix}^T \tag{14}$$

The quadratic program resulting from the MPC problem (6) with $M = 5$ and $P = \infty$ [11] is solved using the Optimization Toolbox in Matlab.

3.3 Simulation Results

Figure 1 shows the ability of the MPC controller to stabilize an oscillating cell culture at a desired steady-state operating point. The initial cell number distribution $W(m, 0)$ is obtained from a stable periodic solution, while the discretized cell distribution setpoints represent the desired steady-state solution. The MPC weighting matrices are chosen as:

$$Q = \begin{bmatrix} 0.1\mathrm{I}_{13\times 13} & 0 \\ 0 & 8 \end{bmatrix} \tag{15}$$

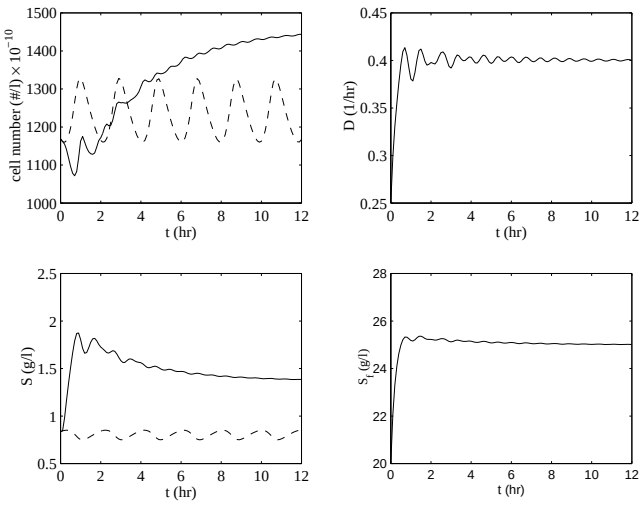

Figure 1: MPC stabilization of a desired steady-state distribution.

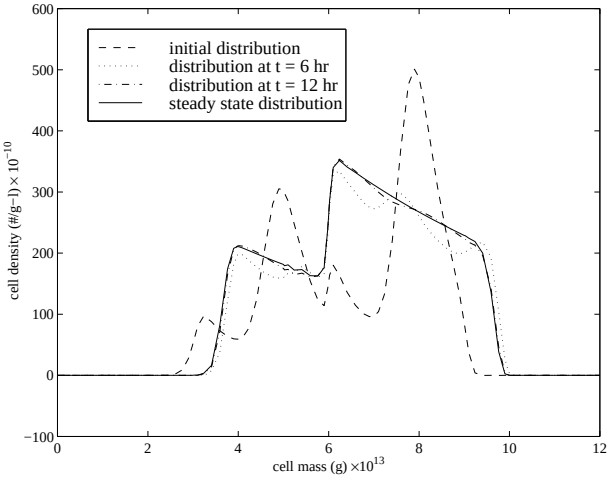

Figure 2: Cell number distribution corresponding to Figure 1.

$$R = \begin{bmatrix} 2\times10^5 & 0 \\ 0 & 500 \end{bmatrix}, \quad S = 4R \tag{16}$$

The zeroth-order moment of the cell number distribution and the substrate concentration are shown as representative output variables. The solid line is the MPC response and the dashed line is the open-loop response. The MPC controller is able to stabilize the reactor under initial conditions that lead to open-loop oscillations. Figure 2 shows the time evolution of the cell number distribution. The initial distribution is synchronized with distinct subpopulations that lead to sustained oscillations. The controller attentuates the oscillations via dispersion of the subpopulations. The distribution approaches the desired steady-state distribution by the end of the 12 hour simulation.

Figure 3 shows the ability of the MPC controller to

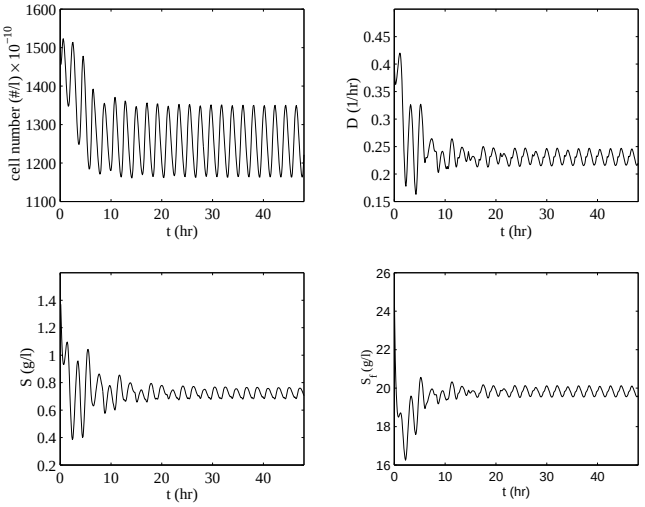

Figure 3: MPC stabilization of a desired oscillatory distribution.

stabilize a desired periodic solution. The initial cell number distribution corresponds to a steady-state solution, while distributions corresponding to the desired periodic solution are defined as a time-varying setpoint trajectory. The weighting matrices are chosen as:

$$Q = \begin{bmatrix} 0.01\mathrm{I}_{13\times13} & 0 \\ 0 & 10 \end{bmatrix} \tag{17}$$

$$R = \begin{bmatrix} 10^5 & 0 \\ 0 & 100 \end{bmatrix}, \quad S = 2R \tag{18}$$

The controller stabilizes the desired periodic solution by generating oscillatory input moves. Although not shown, the oscillations are sustained with same period when the controller is switched off and the system runs under open-loop conditions. The evolution of the cell number distribution is shown in Figure 4. The oscillating dynamics are accompanied by marked synchronization of the cell population. Two distinct subpopulations can be identified after 24 hours of operation.

4 Conclusions

A distribution control strategy for continuous particulate processes described by one-dimensional population balance equation (PBE) models has been developed and evaluated. The single variable distribution of interest is assumed to be measured or reconstructed from on-line measurements. A model predictive control (MPC) problem is formulated to minimize the least-squares difference between the predicted distribution and a target distribution over a moving time horizon. A state-space model suitable for MPC design is obtained by discretizing the PBE model in the internal coordinate chosen to characterize the particle distribution. Two methods for selecting an appropriate subset of the state variables for inclusion in the least squares objective function were discussed. The proposed method

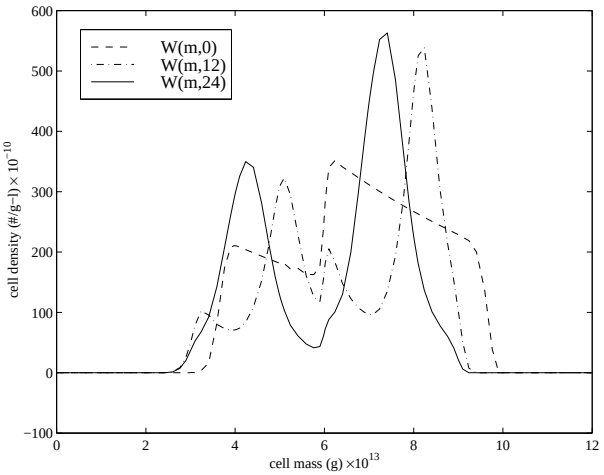

Figure 4: Cell number distribution corresponding to Figure 3.

was applied to the problem of tracking stationary and periodic cell mass distributions in a simulated continuous yeast fermentor. Our future work on the particle distribution control problem will focus on reachability analysis of PBE models, estimation of particle distributions from available on-line measurements and further development of the reduced-order MPC formulation.

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