28 Application of Automatic Control Strategies to SSF Bioreactors

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28.1 Why Do We Need Automatic Control in SSF Bioreactors?

Here, we will discuss what is important to control in SSF bioreactors and how it can be done. The simulations at the end of this chapter show that performance of SSF bioreactors will be better with control schemes; for example, when the temperature in the inlet air is decreased in response to a rise in the average temperature in the bed, or when water is added in response to a drop in the humidity of the off-gases.

As with classical submerged liquid fermentation, in SSF processes there is an optimal set of conditions that will lead to maximal cell growth and metabolite production. As discussed in Sect. 5.1, two of the key process variables are the temperature and water content of the solid bed. In order to maximize the performance of industrial-size SSF bioreactors, these variables must be maintained close to the optimum values for growth and product formation.

In small-size cultures the ratio of the heat transfer capacity of the bioreactor to the metabolic heat generation rate is high; consequently the metabolic heat can be dissipated effectively. Under these conditions, it is straightforward to keep the culture reasonably homogenous. However, this is much more difficult to achieve in industrial or pilot size SSF bioreactors (See Chap. 5). If operated without control, temperature differences between different regions of the solid bed can be as high as 20°C, resulting in disappointingly low productivity, the growth of contaminants, or complete failure of the fermentation run.

Manual control may be useful to regulate the conditions within the solid bed; however, large-scale SSF bioreactors are difficult to operate manually since many variables must be measured and manipulated simultaneously. Under manual control it is not possible to run the bioreactor effectively with just a single operator. In addition, the effects of the many manipulated variables interfere unpredictably with each other throughout the fermentation run. The operators then have a hard job trying to coordinate their respective control actions. Consequently, the bioreactor operation is not reproducible and optimum performance is unattainable.

These difficulties have contributed to the fact that only a minor fraction of the many SSF processes that have been successfully developed at laboratory scale have been scaled up for industrial production.

28.2 How to Control SSF Bioreactors?

As discussed above, no SSF bioreactor can operate efficiently without a good bed temperature control system. The first requirement of a temperature control loop, namely measurement of the temperature, is easy, since Resistance Temperature Detectors (RTDs) or thermocouples can be placed in the bed at desired locations (Sect. 26.3). However, the decision about which operating variable or variables to manipulate in order to try to bring the bed temperature back to the set point value is not so simple. Several control strategies have been designed and tested from laboratory to industrial production scale. These strategies use one or more of the following cooling mechanisms during periods of metabolic high heat production:

- *Conductive cooling*, through cold surfaces like reactor walls or internal plates.
- *Convective cooling*, by forcing cool air through the solid bed.
- *Evaporative cooling*, by forcing partially dry air through the solid bed.

Usually, these mechanisms are enhanced by continuous or periodic bed agitation.

In small size cultures (with beds volumes of the order of 100 cm^3), conduction provides effective cooling due to the large surface-to-volume ratio. Placing the bioreactor (typically a thin column, see Fig. 15.3) inside a thermo-regulated bath ensures good temperature control of the culture. However, in static bioreactors as small as 1 L volume, large temperature differences have been observed inside the solid bed (Saucedo-Castañeda et al. 1990). Therefore, in static pilot-scale or industrial size reactors, metabolic heat must be removed with internal cooling plates, although the design and operation of the reactor becomes complex. Finally, continuous or periodic bed agitation, if not too damaging for the microorganism, may be a convenient alternative to dissipate metabolic heat through the reactor walls. However, Nagel et al. (2001a) showed that this technique becomes insufficient to cool solid beds up to 2 m^3 during the maximum heat production phase, for standard length-to-diameter ratios. Additional advantages of bed agitation are that it reduces temperature gradients, homogenizes the solid bed, and decreases its compactness.

On/Off control (Sect. 27.2.1) performs well with conduction cooling in small bioreactors; however, PID control (Sect. 27.2.2) or Model Based Control (Sect. 27.2.3) are better options for pilot or industrial scale bioreactors.

Effective conductive cooling in large-scale SSF bioreactors may call for excessive agitation, causing a noticeable degradation in process performance due to a low biomass growth rate. Convective cooling can be of great help here, reducing the frequency, intensity, and duration of the mixing events. Of course, bed tem-

perature can be controlled with convection cooling alone, but this is restricted to relatively low bed heights (less than 40 cm height).

Conductive plus convective cooling with agitation cannot remove more than about 50% of the metabolic heat in many types of large-scale SSF bioreactors (see Figs. 22.8 and 23.7). Therefore, the other 50% must be removed by other means. The most effective mechanism for removing metabolic heat in industrial SSF bioreactors is evaporative cooling. Here, the evaporation rate and the consequent cooling rate are determined by the humidity of the partially saturated air that is forced into the solid bed. Therefore, a complete scheme for controlling bed temperature in large-scale SSF bioreactors includes manipulation of inlet air flow rate, temperature, and humidity. The dynamic response of the process and the control configuration can get very complicated when evaporative cooling is used in large-scale SSF bioreactors. Here for example, manipulation of the inlet air temperature affects both controlled variables: bed temperature and bed moisture. Similarly, manipulation of inlet air humidity also affects both controlled variables. This is called *loop interaction*, and it is not usually possible to control this kind of process with PID algorithms alone. In addition, the process can take a long time to respond to changes in the manipulated variables, this is called *time delay* and causes serious difficulties in PID tuning. Moreover, the dynamic response of the system is non-linear, or in other words, the bioreactor does not respond the same at all fermentation times. Hence, PID settings should be changed often since a specific tuning is only effective for a short period. In the face of these various complications, Model Based Control has a better chance of achieving optimum bioreactor performance.

Control of the water content of the bed is also critical to attain good bioreactor performance. For example, an excess of water can cause a reduction of the growth rate due to a low O_2 transfer through the biofilm growing on the surfaces of the solid particles. At the other extreme, a lack of available water can limit growth of the microorganism (in other words, microbial growth is limited by low water activities). If evaporative cooling is used for temperature control, excessive bed drying may occur; however, even if saturated air is fed into the bioreactor some degree of bed drying will occur. Therefore, water content control is usually necessary in large-scale bioreactors. Most large-scale SSF bioreactor types will require periodic addition of fresh water plus agitation to avoid bed over-drying. The amount of water that needs to be added can be established based on humidity measurements of samples removed periodically from the bed. Hence, this control is usually performed manually. The lack of low-cost and reliable on-line sensors for the solids water content makes it difficult to implement an automatic control loop for this variable. If the evaporation rate is high, it is advisable to use a dynamic water balance to get an on-line estimation of the water content, so that the water will be added at the right time (Peña y Lillo et al. 2001).

It may also be beneficial to control the CO_2 or O_2 concentrations in the outlet gas. For example, it has been observed that homogeneous growth in static beds can be attained with a high degree of aeration. Nevertheless, high aeration rates are costly and cause excessive bed drying. Consequently, an optimum aeration rate can be established by regulating either the CO_2 or the O_2 concentration of the

outlet gas. This regulation is rather simple and good results can be obtained by switching between different aeration rates or by using PID control coupled with a modulated valve or variable speed blower.

Finally, if a controlled nutrient or pH level in the solid bed is required, appropriate nutrients or acid/base solutions can be sprayed directly over the solid bed or into the inlet air. Typically this is achieved by on/off control. In the case of pH, there is the question of whether reliable on-line measurements can be achieved using pH probes designed for use in SLF bioreactors (Sect. 26.3). However, since pH changes will typically be slow, it may be possible to remove a sample and homogenize it in distilled water and determine the pH, in order to make a decision about whether to implement a control action or not.

The next section will focus on the most difficult aspect of the control of large-scale SSF bioreactors, namely the simultaneous control of bed temperature and water content. The difficulty arises from the fact that evaporation is one of the most effective heat removal mechanisms, meaning that temperature and water control are intrinsically interlinked. Two case studies are presented. The first summarizes practical experience obtained with two pilot-scale SSF bioreactors. The second presents a model-based investigation of control schemes.

28.3 Case Studies of Control in SSF Bioreactors

28.3.1 Control of the Bioreactors at PUC Chile

Two aseptic packed-bed bioreactors (with nominal capacities for 50 kg and 200 kg of fresh solids) with periodic agitation and forced air were built at Pontificia Universidad Católica (PUC) of Chile to scale up the production of gibberellic acid by the filamentous fungus *Gibberella fujikuroi*. This process is particularly difficult to control since *G. fujikuroi* is sensitive to temperatures above 36ºC and, due to its slow growth, to contamination by other microorganisms. Due to its filamentous nature, its growth increases bed compactness, which creates a reduction in heat and mass transfer rates, but this filamentous nature also means that it is sensitive to mechanical stresses when the solid bed is agitated. In addition, bed overheating can easily occur during the growth period. Air channelling is also a major problem, causing heterogeneous growth and large temperature differences within the solid bed. Finally, the processing time is long, demanding a robust control system. Key points are outlined below. More information is given in Fernández et al. (1996) and Fernández (2001).

The measured process variables used in these bioreactors are shown in Table 28.1 and the manipulated variables in Table 28.2. Figure 28.1 shows schematically how the instrumentation and control devices presented above were put together to define the control loops used in both bioreactors. The control strategy shown in Fig. 28.1 is described in Table 28.3.

Table 28.1. Measured variables in the PUC SSF bioreactors

Variable	Instrument	Measurement
Inlet and outlet air temperature	Type K thermocouples	On-line
Relative humidity of inlet air	Vaisala HMP 122B (absorption of water on a thin polymer film)	On-line
Solid bed temperature	Type K thermocouples (3 in 50-kg reactor and 6 in 200-kg reactor)	On-line
pH of the solid bed	Schott pH-meter	On-line
Solid bed water content	Precisa IR scale	Off-line (1 sample/hour)
Outlet air CO_2 concentration	IR analyzer (Horiba PIR 2000)	On-line
Outlet air O_2 concentration	SMC Transmitter (electrochemical device)	On-line
Inlet air velocity	Dwyer Inst. 640-0 (Hot wire sensor)	On-line

Table 28.2. Manipulated variables in the PUC SSF bioreactors

Variable	Actuator	Type of control
Inlet air temperature	Electric heater (6 kW) Cooler with fins (6.6 kW)	On/off
Air velocity	Inverter drive Hitachi (50 to 500 $m^3\ h^{-1}$)	Continuous
Steam addition	Solenoid valve + boiler	On/off
Bed rotation	Electric motor with variable frequency (3 to 15 rpm)	On/off
Bed mixing	Local screw stirrers plus inverter drive ABB CDS 150 (for 200-kg reactor only)	On/off
Fresh water addition	Millipore peristaltic pump (60 rpm)	On/off
Pressure drop across the bed	Modus Inst. T30 (Deflection diaphragm)	Continuous

Table 28.3. Control strategies applied in both PUC bioreactors

Controlled variables	Manipulated variables	Type of control	Control algorithm
Bed water content	Fresh water addition plus agitation	Manual	Water balance plus operator experience
Bed porosity and homogeneity	Agitation	Semi-automatic	Operator experience
Inlet air temperature	Heater/Cooler	Automatic	on-off
Inlet air relative humidity	Steam addition	Automatic	on-off
Bed temperature	Inlet air temperature and relative humidity	Semi-automatic	PID plus operator experience
Inlet air flowrate	Air blower velocity	Automatic	PID

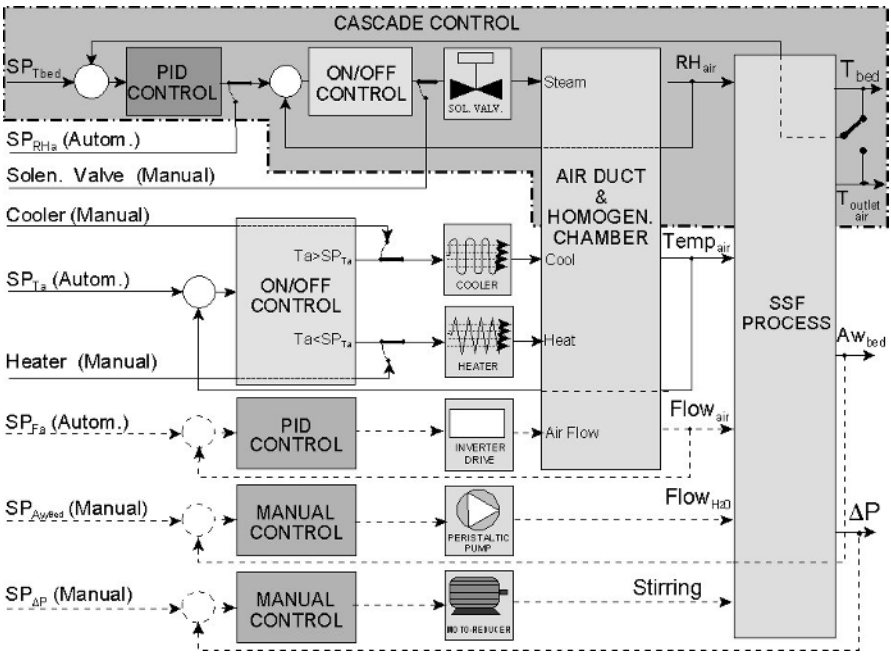

Fig. 28.1. Scheme of the conventional control loops implemented in the PUC bioreactors

A Programmable Logic Controller (PLC) was used for data acquisition and to control the primary actuators. Operator and control calculation interaction were carried out via an IBM-compatible personal computer, linked to the PLC. Project-specific software was developed for the personal computer with a graphic interface to handle the control systems in either automatic or manual mode.

The primary objective of the control system was to regulate the average temperature of the solid bed at a fixed value and to control the bed water content (according to a varying set point). The secondary objectives were to minimize temperature gradients within the bed and also to prevent the bed from becoming overly compact.

Control of the bed temperature was based on evaporative cooling, by manipulating the relative humidity of the inlet air and maintaining its temperature at a low value. During the period of high heat generation, in order to avoid bed overheating, it was necessary to intervene manually to manipulate the inlet air flow rate and temperature and to initiate agitation events. The average bed temperature was fed into a digital PID control algorithm to drive the set point of the inlet air relative humidity. This in turn was controlled with an on/off algorithm with a dead band and hysteresis that commanded a solenoid valve adding steam. The inlet air temperature was further controlled with another on/off algorithm with a dead band and hysteresis that manipulated the heater or cooler, according to process needs.

The water content of the bed was controlled through the periodic addition of fresh water. The reference trajectory of the water content was computed in the

laboratory based on water activity studies. A solid sample was taken each hour from the bioreactor for an off-line measurement of the water content. The amount of water to be added was determined by the operator using an approximate water balance and his experience. The bed was agitated upon each addition of water.

In order to keep the bed as homogeneous as possible and to avoid excessive inter-particle aerial growth, which would reduce porosity, a periodic agitation policy was established. The degree of homogeneity was defined by the temperature gradient inside the bed, while inter-particle aerial growth was estimated from the pressure drop through the bed. This involved a semi-automatic loop that employed heuristic logic. The operator could establish the agitation speed, its duration and, in the case of the 200-kg bioreactor, the path of the agitation (left or right).

The control strategy enabled efficient operation of the pilot SSF bioreactors. When the 50-kg bioreactor was run manually, it required the permanent attention of at least two operators. The automated control system required only one operator, even at the 200-kg scale, who intervened relatively little in the process. The system even allowed bioreactor operation without direct supervision at certain times (Fernández 2001). Figure 28.2 shows the performance of the average bed temperature control loop between hours 10 and 40 of a fermentation run in the 200-kg bioreactor. The control system performed reasonably well, since the average bed temperature deviated no more than 4ºC from the set point, although most of the time the deviations were smaller than 1ºC. However, to achieve this performance, the inlet air temperature had to be changed manually. Moreover, the differences between maximum and minimum temperatures within the solid bed were considerably high (5ºC average difference and 15ºC maximum differences).

On the other hand, water content control did not perform so well, with deviations of more than 25% with respect to the set point. This was due to the several limitations that this control loop presented, such as manual control, the lack of an on-line sensor and the fact that water had to be added while the bioreactor was being agitated such that control actions could only be taken infrequently. In addition, water content measurements were noisy due to bed heterogeneity.

However, it is noteworthy that the control strategy was successfully scaled up from the 50-kg bioreactor to the 200-kg one with only minor adjustments.

The operation of the bed temperature control loop can be simplified if a model predictive control algorithm is used. When this kind of control was applied in the 200-kg bioreactor, within the same time-span shown in Fig. 28.2, better overall performance was achieved. Temperature differences within the bed and high temperature peaks were reduced when compared with standard control (Fig. 28.4). In addition, the loop was fully automatic therefore no manual operation of the inlet air temperature was necessary.

It should be noted that even better performance could be achieved by tuning the algorithm; however this was not done with the PUC bioreactors since it would have required several fermentation runs, each of which is long and expensive. Despite this, it is probably correct to say that, to attain good performance in industrial-scale SSF bioreactors (2 to 3 tons or more), it is necessary to apply model predictive control in the bed temperature control loop.

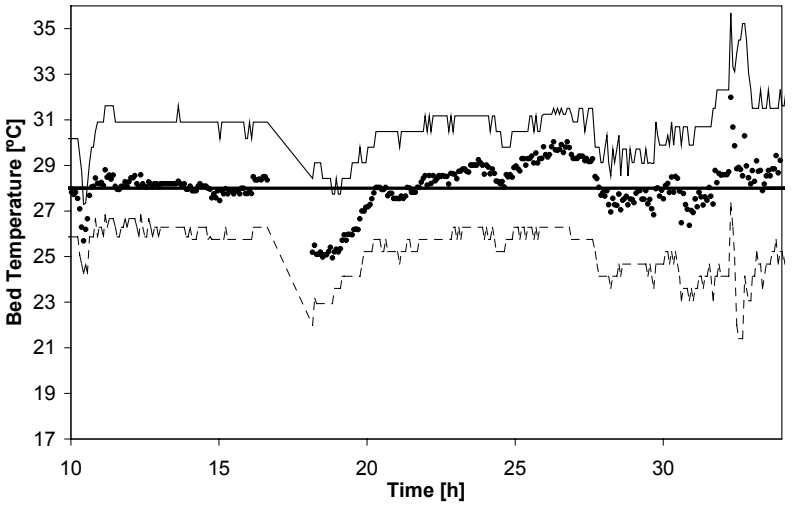

Fig. 28.2. Bed temperature control during a fermentation run with the 200-kg bioreactor. Key: (**━━**) Bed temperature set point; (—) maximum bed temperature; (•), average bed temperature; (- - -) minimum bed temperature

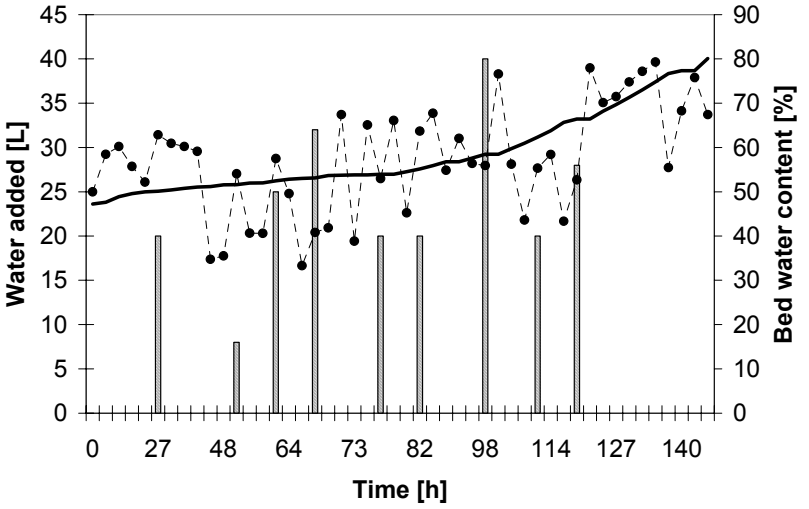

Fig. 28.3. Water content control during a fermentation run with the 200-kg bioreactor. Key: (**━━**) water content set point; (- • -) measured water content of the bed. The vertical bars represent the volume of water added

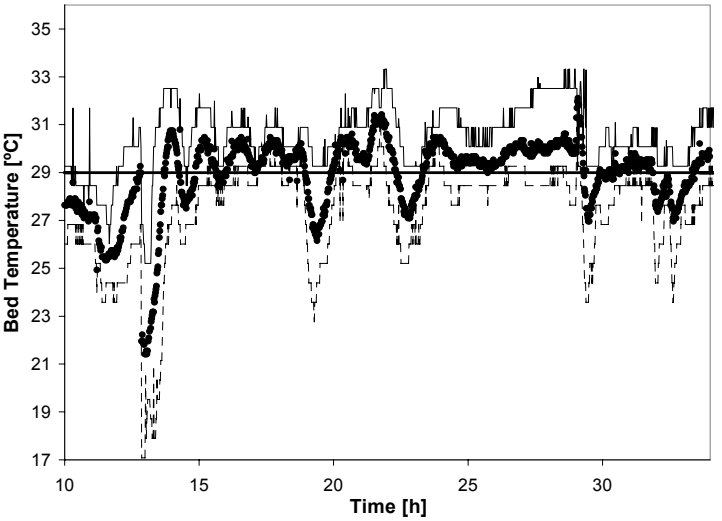

Fig. 28.4. DMC strategy applied to the 200-kg bioreactor. Better temperature control is achieved when two manipulated variables are moved simultaneously, which can be seen by comparing this figure with Fig. 28.2. Key: (**━━**) Bed temperature set point; (—) maximum bed temperature; (•) average bed temperature; (- - -) minimum bed temperature

28.3.2 Model-Based Evaluation of Control Strategies

An intermittently-mixed forcefully-aerated bioreactor, presented in Fig. 25.1, was modeled using the program presented in Chap. 25, the equations of which are shown in Fig. 25.2. Mixing was triggered when the outlet gas water activity fell below a set point. However, unlike the case study in Chap. 25, in which the inlet air conditions were maintained constant during the fermentation, in the present case study a control scheme was implemented to control either or both of the temperature and humidity of the inlet air, based on the average of the temperatures measured at different heights within the bed (Fig. 28.5). The success of the control scheme was evaluated on the basis of the fermentation profile for the average biomass concentration within the bed.

The present case study highlights the main points of interest that were identified in the work of von Meien et al. (2004). Readers interested in a deeper analysis should consult the original paper.

Figure 28.6 shows simulations done with a PID (Proportional-Integral-Derivative) controller, using two different strategies:

- **Humidity control.** In this case the relative humidity of the inlet air is varied by the controller, while the temperature is maintained at 38°C. Figure 28.6(a)) shows that the average temperature in the bed varies significantly from the optimum of 38°C throughout the fermentation.

- **Temperature control.** In this case the temperature of the inlet air is varied by the controller, while the relative humidity is maintained constant. In different simulations the constant relative humidity is maintained at 80% (Fig. 28.6(b)), 90% (Fig. 28.6(c)), and 99% (Fig. 28.6(d)). In this case it is possible to control the average temperature of the bed much better, in other words, the deviations from the optimum temperature are smaller.

The effect of the better temperature control in the case in which the inlet air temperature is manipulated is clear: The growth profiles obtained with "temperature control" (Fig. 28.6(f)) are closer to the optimum than the growth profile obtained with "humidity control" (Fig. 28.6(e)). Note that the relative humidity of the inlet air has no effect on the predicted growth performance in the case of "temperature control". Therefore, it is best to maintain the air saturated since this is easier to achieve in practice than attaining a particular relative humidity set point (see Chap. 29).

Figure 28.7 shows simulations done with a DMC (dynamic matrix control) controller. DMC is a form of Model Predictive Control, which was discussed in Sect. 27.2.3. Again "temperature control" and "humidity control" strategies are compared, with "temperature control" being superior, as it was in the case of PID control (von Meien et al. 2004). Figure 28.7 also shows that DMC control presents an interesting challenge. As discussed in Sect. 27.2.3, model predictive control

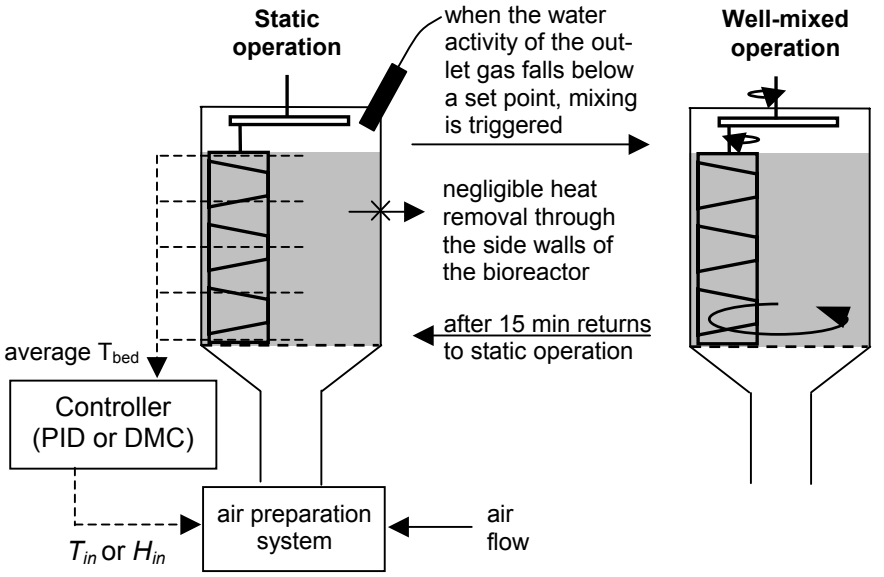

Fig. 28.5. Bioreactor and control scheme for the case study of control of an intermittently-agitated forcefully-aerated bioreactor. The bioreactor simulated is 2.0 m high, with an air flux at the inlet of 0.06 kg dry air s^{-1} m^{-2}. In practice it might be impractical to measure the temperature at many different heights within the bed. In this case a single measurement at a half of the overall bed height will probably be sufficient

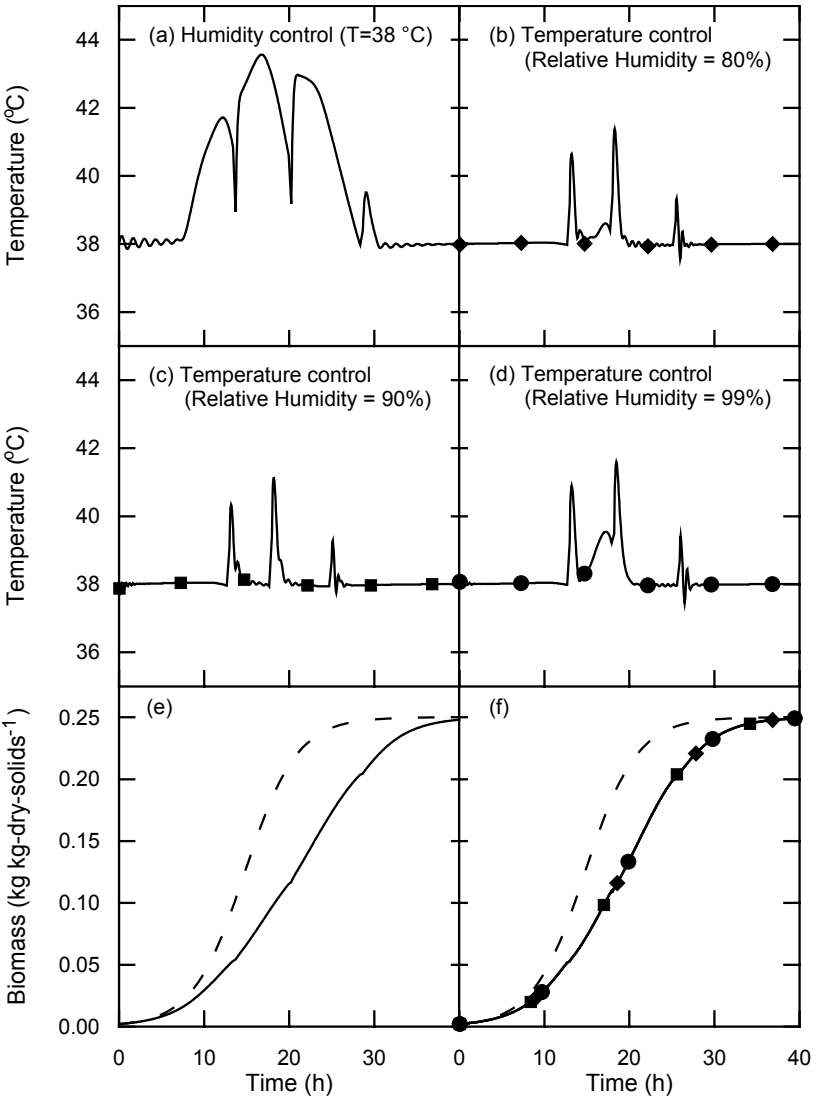

Fig. 28.6. Predictions of performance of an intermittently-agitated, forcefully-aerated bioreactor when PID control is used. **(a)** to **(d)** Predicted average bed temperature (the average of the temperatures measured at various different heights, as shown in Fig. 28.5) for the various control schemes. **(e)** Predicted average biomass profile for the case of humidity control with the inlet air temperature maintained at 38°C (—). **(f)** Predicted average biomass profiles for the case of temperature control with the inlet air humidity maintained at 80% (—♦—), 90% (—■—), and 99% (—●—). In graphs (e) and (f) (- - -) represents the growth curve that would occur if optimum conditions were maintained throughout the entire fermentation. Adapted from von Meien et al. (2004) with kind permission of Elsevier

schemes such as DMC use a linear model to calculate the required future changes in the manipulated variable that will result in optimum set point tracking for a specified performance index. This linear model, normally obtained from the initial dynamic response of the bioreactor, is used by the controller to guide the control actions during the whole fermentation run.

However, for this fermentation, when this is allowed to happen, the controller makes large control actions in the latter stages of the process, which cause large and frequent oscillations in the manipulated variable, that is, in the temperature of the inlet air (Fig. 28.7(a)) and of course these oscillations cause similar oscillations in the temperatures within the substrate bed (Fig. 28.7(c)). Such large oscillating control actions are undesirable, especially if they are not necessary. The problem is that the controller had worked out its control strategy based on the initial part of the process during which growth was accelerating and temperature control was becoming ever more difficult. The controller worked out that it is necessary to apply large "preventative" control actions and when growth decelerates in the latter stages of the process, it still applies such large control actions, even though they are not necessary. This problem can be overcome by instructing the controller to establish a new linear model after each mixing event. Since there are three mixing events, four different linear models are used (i.e., the original one plus a new one after each mixing event). In other words, the controller changes its control strategy during the fermentation and this minimizes the oscillations in the inlet temperature (Fig. 28.7(b)) and therefore also the oscillations in the temperatures measured in the bed (Fig. 28.7(d)).

The necessity for the use of multiple linear models can be explained in a different way. The behaviour of the fermentation process is history dependent, that is, the evolution of the system from a particular point relies on what happens before this point. This can be easily understood when it is recognized that the rate of growth at any instant depends to a significant degree on the amount of biomass that was produced in the fermentation from the time of inoculation up until that instant. Since the underlying behaviour of the system (the rate of growth) varies significantly during the process, then the dynamics of the control system need to be changed.

As shown by comparing Figs. 28.7(e) and 28.7(f), it actually makes no difference to the biomass growth curve whether a single linear model or multiple linear models are used, however, it is obvious that multiple linear models should be used since the same performance is achieved, but without large and frequent control actions.

Note that the predicted growth with DMC control is superior to that predicted for PID control (Figs. 28.7(e) and 28.7(f)).

As a final point, this case study has shown that mathematical models of SSF bioreactors are useful tools in the initial stages of the development of control strategies and in the initial tuning of controllers.

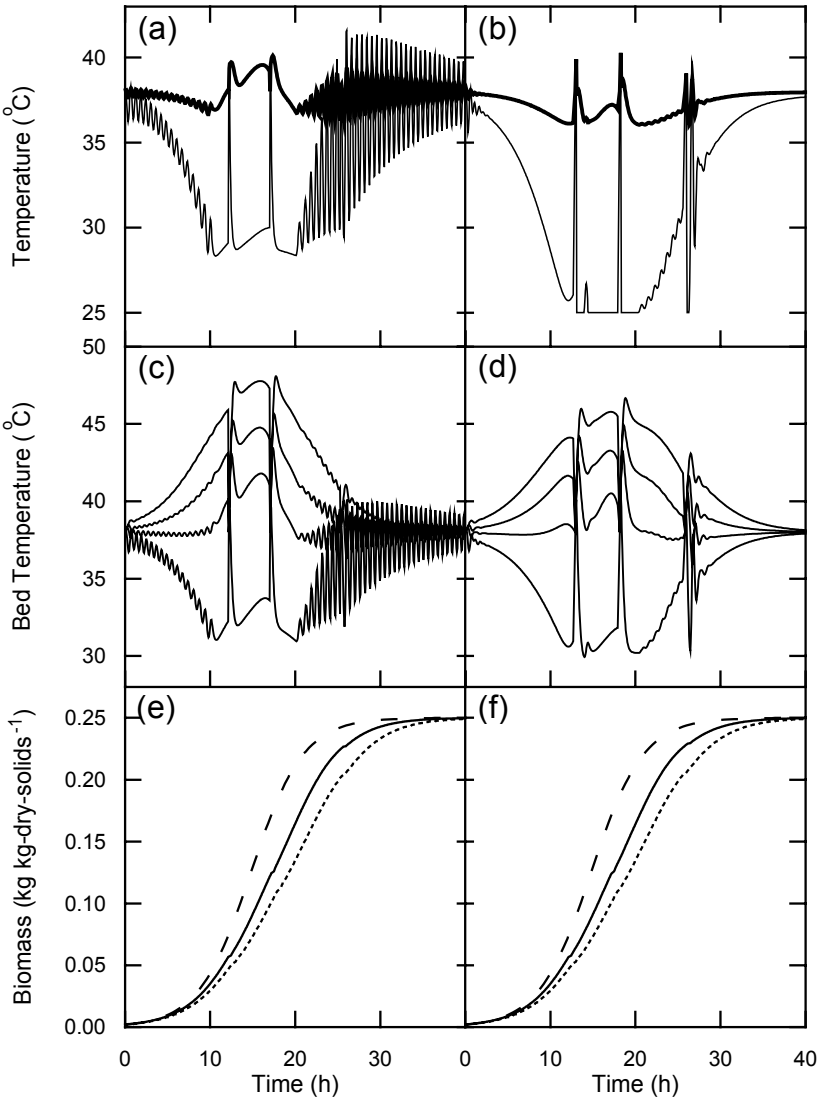

Fig. 28.7. Performance of the bioreactor with DMC control of the inlet air temperature (the relative humidity of the air is fixed at 99%). The results for "a single linear model" and "multiple linear models" are on the left and the right, respectively. **(a)** and **(b)** inlet air temperature (—), which is not allowed to go below 25°C and the average bed temperature (**- - -**), which the controller aims to control at 38°C; **(c)** and **(d)** temperatures at various heights within the bed (from bottom to top the lines are for 0.5, 1.0, 1.5, and 2.0 m); **(e)** and **(f)** biomass profiles, including the predicted average biomass content (—), the growth curve that would occur if optimum conditions were maintained throughout the entire fermentation (- - -) and, for purposes of comparison, growth with PID control of the temperature of the inlet air (·····). Adapted from von Meien et al. (2004) with kind permission of Elsevier

28.4 Future Challenges in the Control of SSF Bioreactors

The control problem is especially challenging in SSF bioreactors. In bioreactors that are not continuously mixed, the problem is not as simple as trying to control the whole of the bed at one set of conditions. Rather, it is a case of accepting the fact that this is not possible and using the control scheme to minimize the average deviations in time and space from the optimal conditions. The challenge is to be able to prevent one part of the bed from reaching deleteriously high temperatures without the control action causing another part of the bed to fall to temperatures that are so low that growth is restricted. Control in distributed systems has received some attention (Christofides 2001), but it is highly mathematical and has not yet proved to be effective in real cases. Further, the distributed nature of the system brings up the question of how many sensors and actuators should be used and where in the bioreactor they should be placed. Such considerations are further complicated by the unpredictable nature of some of the changes that the control scheme might be intended to counteract. For example, it would be desirable for the appearance of channels in the bed to be counteracted by a mixing action. However, it would be difficult to design a measuring device to detect this. The presence of channels might be indicated by local rises in temperature. Such rises would occur in those parts of the bed that do not receive effective aeration due to the preferential flow of the air through the channels. However, if such rises were localized, then they would only be detected if the sensors were in the right place and there is no way of knowing *a priori* where to place the sensors.

Further, SSF bioreactors present an interesting example of what is called "cascade control". For example, it is already an interesting control challenge to provide an air stream of the desired flow rate, temperature, and humidity, especially when the set points for these variables change as the organism proceeds through its growth cycle. For instance, as the metabolic heat generation rate increases early in the process due to the acceleration of growth, the set point of the inlet air temperature would typically be decreased. However, it must be remembered that the final objective of the control action is not the control of the flow rate, temperature, and humidity of the inlet air. Of course this control is important, but the final objective is actually to use the conditions of the inlet air to control the conditions within the bed. However, the intricacies of cascade control are beyond the scope of this book.

Nonlinear model predictive control (NLMPC) may be necessary in SSF systems. This involves the embedding within the control scheme of a set of non-linear differential equations that describe the microbial and heat and mass transfer processes. In this case the optimization problem is in general "non-convex", which means that the solution is hard to find and there is no guarantee that the optimization routine will find it. Furthermore, there are theoretical issues regarding the stability of the control loop in non-convex problems, and these issues have not been completely clarified yet within the area of control theory. In addition, special optimization routines are required. The main problem of NLMPC is that is too sensitive to lack of model accuracy ("model mismatch") and biased model parameters.

The design of a reliable NLMPC system for a SSF bioreactor has as an absolute requirement the development of effective on-line parameter estimation and filtering algorithm, in order to get reliable model parameters and eliminate the process and measurement noise. This also requires the formulation and solution of a nonlinear optimization problem. As a result, the design of reliable NLMPC system is very complicated and it is still a developing science even in non-SSF applications.

Further Reading

More information about the control of the PUC bioreactor

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A theoretical case study of the application of control strategies to a large-scale intermittently-mixed, forcefully-aerated SSF bioreactor

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Cascade control

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