

7 Group II Bioreactors: Forcefully-Aerated Bioreactors Without Mixing

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7.1 Introduction

This chapter addresses the design and operation of SSF bioreactors under conditions where forced aeration is used but the substrate bed is not mixed. Typically these bioreactors are referred to as packed-bed bioreactors. This mode of operation is appropriate for those SSF processes in which it is not desirable to mix the substrate bed at all during the fermentation due to deleterious effects on either microbial growth or the physical structure of the final product.

The characteristics of this mode of operation also apply to the static phases of forcefully-aerated bioreactors that are mixed once every few hours. The operation of such bioreactors will be discussed in Chap. 10; suffice to say for the moment that during the static phase they will act as packed-bed bioreactors, and therefore the principles developed in the present chapter will apply to this static phase.

7.2 Basic Features, Design, and Operating Variables for Packed-Bed Bioreactors

The basic design features of a packed-bed bioreactor have been already presented in Sect. 3.3.1. Figures 7.1 and 7.2 show these features in more detail. Some possible variations in the design include:

- ≠ the column may have a cross section other than circular.
- ≠ the column may lie horizontally, or for that matter, at any angle. This alters the relative directions of the forces due to gravity and air pressure.
- ≠ the column may be aerated from either end. For a vertical column, the air may enter the bed from either the top or the bottom. Aerating from the top avoids the fluidization of particles at high air velocities, but will contribute to bed compaction since the air flow is in the same direction as gravity.

- the column may have a perforated tube inserted along its central axis, allowing an extra air supply in addition to the end-to-end aeration (Fig. 7.1(b)). However, this will only be effective for very small bioreactor diameters.
- the column may be water-jacketed or heat transfer plates may be inserted into the bed. In this chapter, packed-bed bioreactors with internal heat transfer plates will be referred to as “Zymotis packed-beds”, using the name coined by Roussos et al. (1993), while those lacking such plates will be referred to as “traditional packed-beds” (Fig. 7.2).

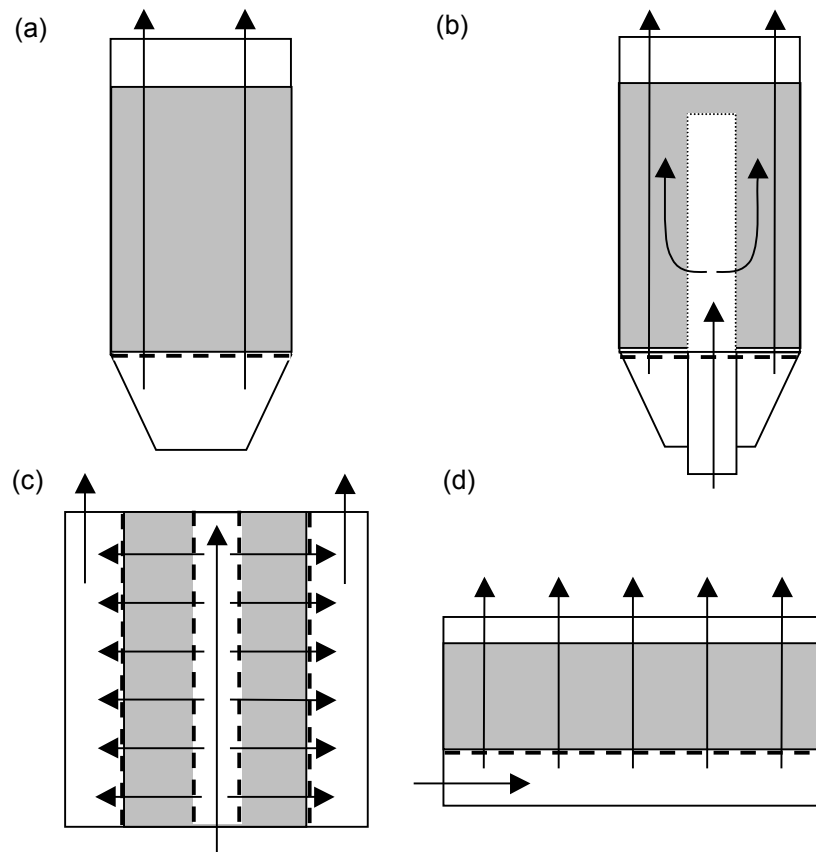


Fig. 7.1. Basic design features of packed-bed bioreactors and possible design variations. **(a)** A simple “traditional” packed-bed design. **(b)** A packed bed with a perforated tube inserted along its central axis: The benefits of this will only be apparent if the bed is relatively thin or, in a wide bed, if many perforated tubes are inserted. This is due to the fact that the forced aeration in the axial direction will tend to force the radial flow to follow the axial direction also. **(c)** Radial flow packed-bed: The advantage of this design is that, compared to a column of the same dimensions, the distance of flow through the bed is decreased. It is similar to the use of a wider “traditional” packed bed with a lower bed height. **(d)** A “short-wide” packed-bed

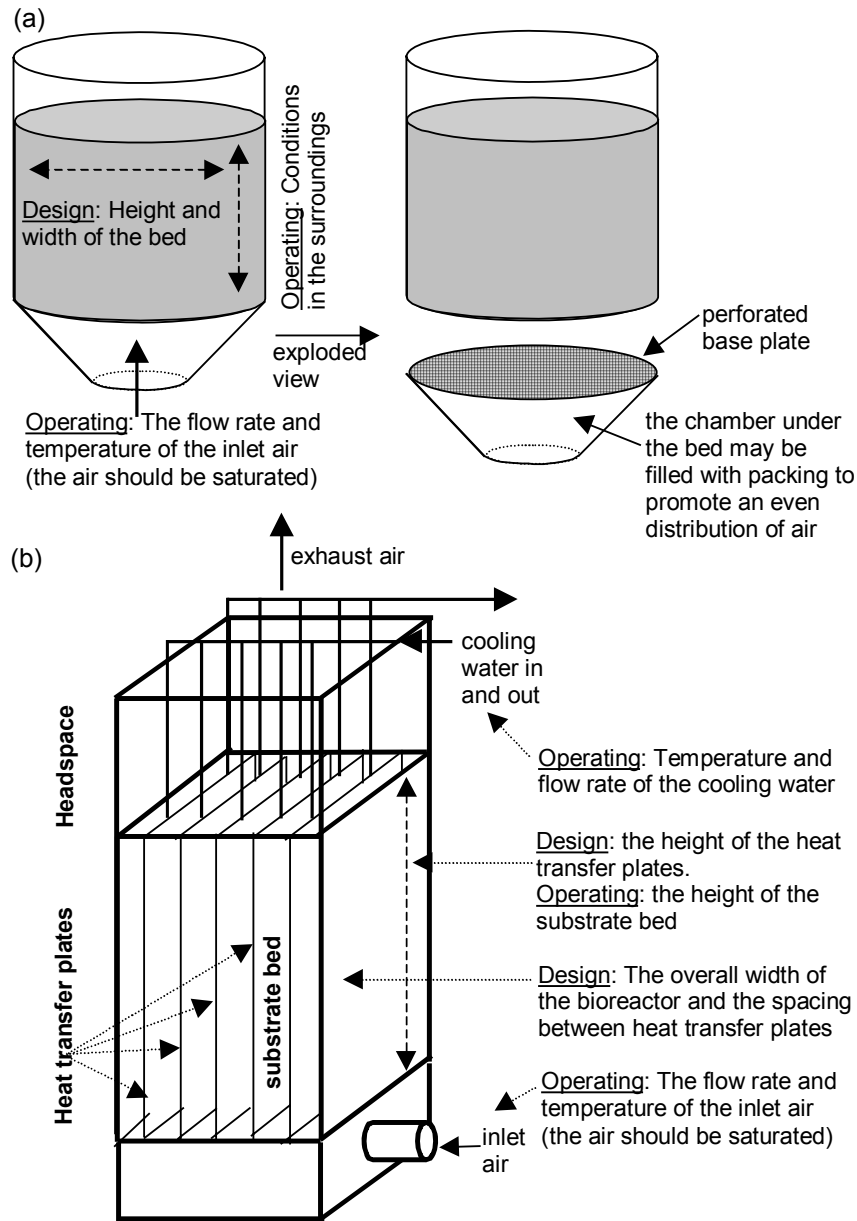


Fig. 7.2. Basic design and operating features of (a) traditional packed beds and (b) the Zymotris packed-bed with internal heat transfer plates of Roussos et al. (1993)

Taking the most common design, namely a vertical column in which the bed is aerated from the bottom and without any internal perforated tubes, the available design variables for a packed-bed are (Fig. 7.2):

- ## the presence or absence of a cooling jacket or internal heat transfer plates;
- ## the height and width of the bioreactor. The height to diameter ratio can vary over quite a wide range;
- ## if internal cooling plates are used, their height and the spacing between them.

The available operating variables are (Fig. 7.2):

- ## the aeration rate;
- ## the temperature of the inlet air;
- ## the temperature of the “surroundings” (which might be cooling water).

In a static bed, the relative humidity of the inlet air is not a useful operating variable. The problem is that it is not practical to add water into an unmixed bed in such a way as to distribute it evenly amongst the substrate particles; therefore evaporative water loss must be minimized. If the air entering the bed were not saturated with water, this unsaturated air would promote evaporation and dry out the bed, eventually decreasing the water activity to values unfavorable for growth and product formation. In order to minimize evaporation, saturated air must be supplied at the air inlet, which removes manipulation of the inlet air humidity as an available operating variable. Note that the use of saturated air does not prevent evaporation from occurring within the bed (see Fig. 4.3), but it does minimize evaporation compared to the use of unsaturated air. As will be discussed in Chap. 10, it is possible to replenish water during the mixing events of intermittently mixed beds, in which case unsaturated air can be used to aerate the bed.

At large scale, water-jacketing of the side walls of the bioreactor is not a good idea for the traditional design, since the water jacket will influence only the outer 20 cm or so of the bed. If cooling surfaces are to be used, then the internal cooling plates used in the Zymotis bioreactor will be more effective, as long as they are reasonably closely spaced. Optimum spacing of the plates will be discussed later. Another option for cooling surfaces is given by the “Prophyta” and “PlaFractor” designs (Fig. 7.3), two bioreactors that use a number of thin beds coupled with cooling plates oriented normal to the air flow (Lüth and Eiben 1999; Suryanarayan and Mazumdar 2000; Suryanarayan 2003). The difference between the two bioreactors is that in the Prophyta design the same air passes through each successive bed while in the PlaFractor design the air is introduced separately into each bed.

Important phenomena that are affected by the values chosen for the design and operating variables are:

- ## the axial and radial temperature gradients in the bed. In packed-beds it is impossible to prevent temperature gradients from arising within the bed, so the aim is generally to minimize the size of any temperature gradients.
- ## the evaporation of water from the bed. Efforts must be made to minimize evaporation in order to prevent the bed or parts of the bed from drying out.

the pressure drop through the bed. This will depend on the bed height and the degree to which the organism fills the inter-particle spaces, with the resulting pressure drop affecting the design of the aeration system and its operating costs, and maybe placing a limit on the bed height that can be used.

In general, O_2 supply to the particle surface will not be considered in the selection of design and operating variables. The aeration rates that are chosen on the basis of heat removal considerations will typically be high enough that sufficient O_2 supply is ensured. However, note that problems such as channeling are possible, in which O_2 transport to large parts of the bed can be limiting (Fig. 7.4). Channeling is discussed in more detail in Sect. 7.3.3.5.

This chapter explains what is known, on the basis of experimental studies, about how these design and operating variables influence bioreactor operation. Later, Chap. 24 will show how mathematical models can be used to explore further the design and operation of packed-beds.

7.3 Experimental Insights into Packed-Bed Operation

This section presents and discusses the knowledge that experimental work has given firstly into the phenomena that occur within packed-bed bioreactors, and secondly into the operability of this type of bioreactor.

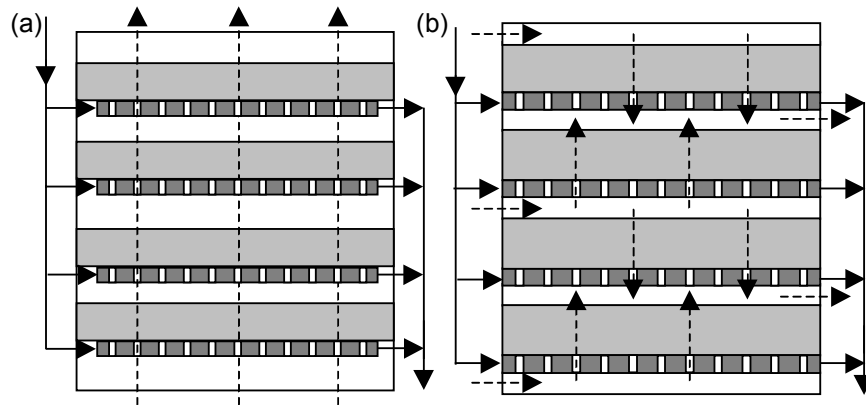


Fig. 7.3. The use of heat transfer surfaces normal to the air flow direction within packed beds **(a)** as used in the Proplyta bioreactor (Lüth and Eiben 1999) and **(b)** as used in the PlaFractor bioreactor (Suryanarayan and Mazumdar 2000; Suryanarayan 2003). In each case the substrate beds are in *light gray* and the heat transfer plates are in *dark gray*. The *white* regions represent empty spaces for air flow. *Solid arrows* represent the flow of cooling water and *dashed arrows* represent the flow of air

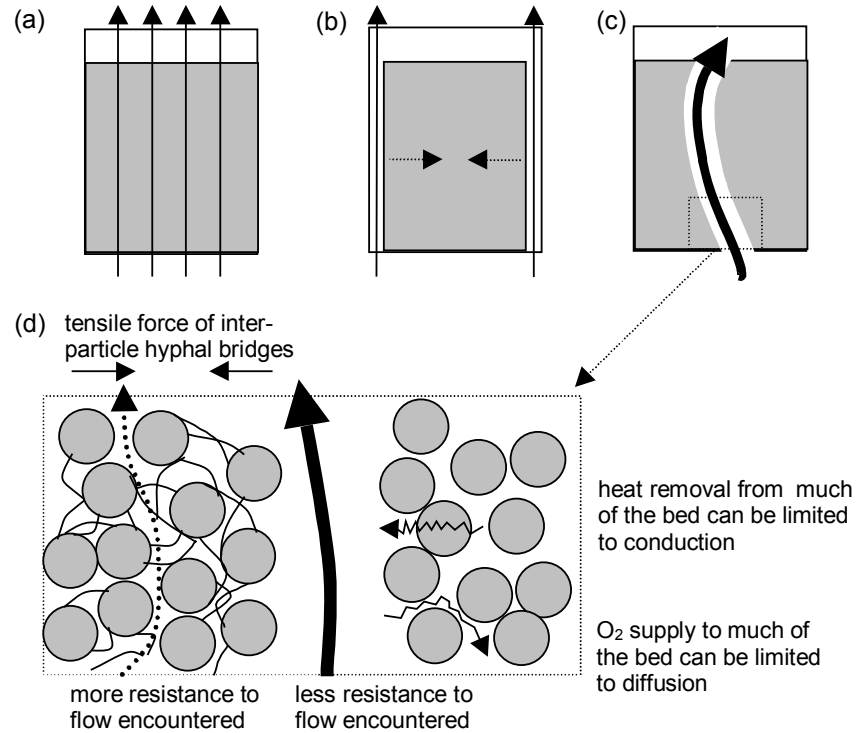


Fig. 7.4. The phenomenon of channeling. **(a)** The desirable situation, with uniform flow across the whole cross section of the bed. **(b)** Preferential flow between the bed and the wall in the case in which the bed pulls away from the wall. **(c)** Preferential flow through a crack in the bed. **(d)** Microscale view of a channel, showing how the preferential flow through the channel arises due to two sources of resistance to flow through the bed of particles, namely the tortuous path through the bed and the fact that the space between the particles is partially filled with biomass. Note that in extreme cases of channeling, there may be no bulk flow through the inter-particle spaces, with mass transfer being limited to diffusion and heat transfer to conduction

7.3.1 Large-Scale Packed-Beds

SSF bioreactors are only rarely operated at large scale as packed-beds throughout the entire cultivation period, although related intermittently stirred designs have been used quite successfully (see Chap. 10). Static packed-bed operation has been used at large scale in the production of *koji*, although details of the operation and performance of the bioreactors involved are not available. Only very brief and general descriptions are available. A simple design (Fig. 7.5) has a capacity for 1000 kg of *koji*, and has no special devices for substrate handling. Also, it is not designed for fully aseptic operation (Sato and Sudo 1999).

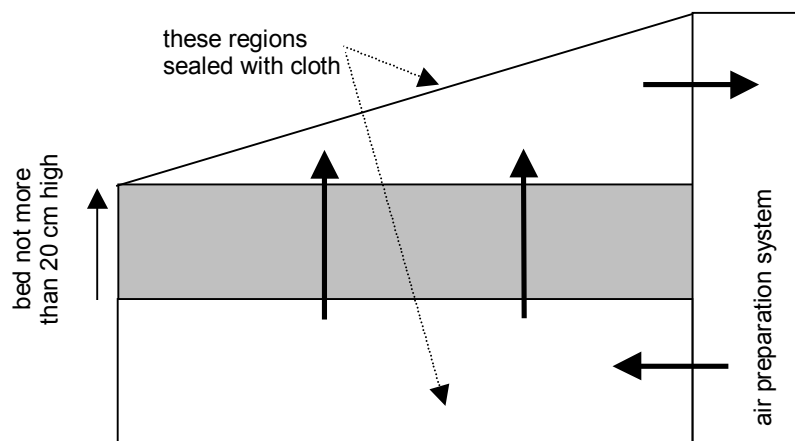


Fig. 7.5. Simple packed-bed of the type used in the *koji* industry for soy sauce production by Churitsu Industry Co. Ltd., Tokyo, Japan. Bioreactors of this type have capacities of up to one ton of substrate. This is a simplified version of a diagram presented by Sato and Sudo (1999)

7.3.2 Pilot-Scale Packed-Beds

Roussos et al. (1993) developed a pilot-scale packed-bed bioreactor with internal heat transfer plates, called the “Zymotis” bioreactor (Fig. 7.2(b)). The outer casing was acrylic, and it was 65 cm high, 50 cm wide, and 40 cm deep from front to back. This gave a total volume of 130 L, with a working capacity of 100 L. The aeration rate was varied from 0.1 to 0.2 L h⁻¹ g-dry-substrate⁻¹.

The stainless steel heat transfer plates were 60 cm high, 38 cm wide (fitting within the 40 cm front to back depth of the outer casing), and 0.46 cm thick. There were 10 of these, and they occupied a volume of 9.44 L of the bioreactor vessel. Each heat exchanger plate contained serially placed tubes through which water was circulated. The bioreactor was designed to be flexible in that the number of heat transfer plates inserted and the spacing between them could be changed as desired. This bioreactor was emptied by raising the whole bioreactor and letting the substrate bed fall out of the bottom, although at large scale this might not be feasible.

Substrate loadings from 4 to 12 kg dry substrate matter (15 to 55 kg substrate on a wet basis) were tested, but detailed performance data was not provided, only the final enzyme levels. Heating of the circulating water was required during the first 10 h of fermentation, after which cooling was necessary. Thermistors placed in different locations were used to control the temperature of the cooling water. Uniformity of growth and absence of temperature gradients was claimed when the gap between plates was no larger than 5 cm, but experimental results showing this were not presented (Roussos et al. 1993). The water content also remained close to the original value, increasing by only 5%.

7.3.3 Laboratory-Scale Packed-Beds

The use of very small and thin packed-bed bioreactors in laboratory-scale studies of growth kinetics will be discussed in Chap. 15. A range of slightly larger bioreactors, typically up to 30 cm high and from 5 to 15 cm diameter, have been used to investigate how macroscale transport phenomena can influence bioreactor performance. The limitation of growth by transport phenomena is possible even at this small scale, as demonstrated in the following subsections.

7.3.3.1 Axial and Radial Temperature Gradients in Static Beds

The gas flow pattern within the bed of a packed-bed bioreactor that does not suffer from channeling problems is probably closest to plug flow with axial dispersion (see Fig. 4.6). However, studies have neither been done to confirm this nor to quantify the degree of axial dispersion. This plug-flow of the gas phase has implications for the operation of packed-beds. Firstly, the inlet end tends towards the inlet air temperature but, due to the lack of mixing and the unidirectional air flow, the temperature of the air increases as it flows along the bed towards the outlet end (Fig. 4.3(b)). One of the major challenges in designing and operating large-scale packed-beds will be to avoid excessive axial temperature gradients.

The increase in the temperature of the air as it flows through the bed increases the water-carrying capacity of the air and therefore evaporation will occur. Note that evaporation will occur even if saturated air is used at the air inlet (Fig. 4.3(c)).

In general, conduction along the axis in the direction of the air flow will be negligible compared to the convective and evaporative heat removal (Gutierrez-Rojas et al. 1996). The contribution of conduction normal to the direction of the air flow will depend on the design of the packed-bed. In traditional packed-beds that have diameters of the order of a few centimeters and in the Zymotis design, it can make a significant contribution, and there can be significant temperature gradients normal to the air flow. In contrast, in large-scale packed-beds, which might typically have diameters of the order of 1 m or more, the amount of energy removed from the bed by transfer through the side walls is likely to be small, even if the bed is water-jacketed. Various studies have been done that show how the appearance of axial and radial temperature gradients depends on the design and operation of the bioreactor. These are described below.

Temperature gradients in thin bioreactors. Saucedo-Castaneda et al. (1990) used a bioreactor of 6 cm diameter, containing a bed 35 cm high. Further, the column was immersed in a constant temperature waterbath at 35°C. They noted a steep temperature gradient in the first 5 cm along the axis of the bed, where the temperature increased by up to 12°C (Fig. 7.6). In contrast, in the upper 30 cm of the bed, the maximum increase in temperature along the axis was approximately 3°C. Note that, at some times and in some regions, the temperature actually decreased with axial distance, which might be related to evaporative cooling. However, Saucedo-Castaneda et al. (1990) did not measure water contents in the bed, so it is not possible to confirm this. The axial temperature in the upper 30 cm of the

column did not remain constant; rather it increased with time over the period of 15 to 26 h. In contrast to the axial temperature gradients, the radial gradients were quite steep: at the time of peak heat production, there was an 11°C difference between the central axis and the bioreactor wall, which represents a distance of only 3 cm. These results suggest that in the case of thin bioreactors a significant amount of heat is removed through the side walls.

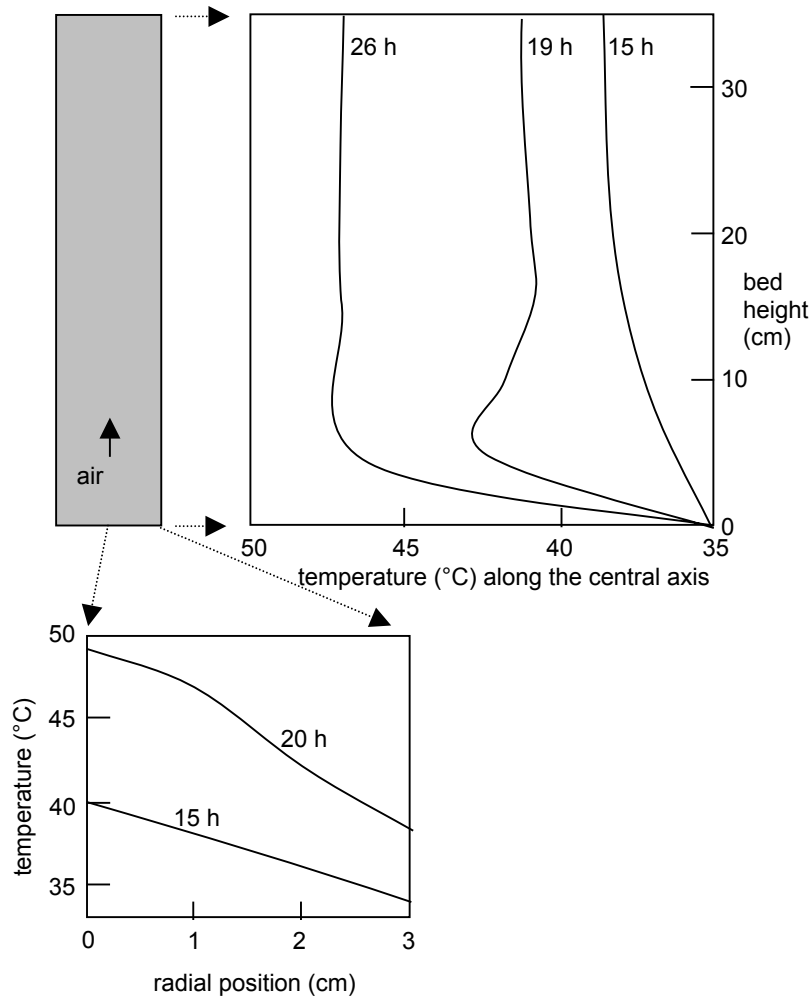


Fig. 7.6. Radial and axial temperature gradients at various times within a thin packed-bed bioreactor when *Aspergillus niger* was cultivated on cassava chips (Saucedo-Castaneda et al. 1990). The radial temperature gradient was determined at approximately mid-height in the bed. The superficial velocity of the air was 1 cm s^{-1} . Adapted from Saucedo-Castaneda et al. (1990) with kind permission from John Wiley & Sons, Inc.

Temperature gradients in wide or insulated bioreactors. The studies of Ghildyal et al. (1994), Gowthaman et al. (1993a, 1993b), and Weber et al. (2002) allow insights into heat transfer in wider bioreactors. The bioreactor of Ghildyal et al. (1994) and Gowthaman et al. (1993a, 1993b) was 15 cm in diameter with a 34.5 cm bed height, while that of Weber et al. (2002) was 20 cm in diameter with a 50 cm bed height. Note that the bioreactor of Weber et al. (2002) was insulated on the sides, in order to mimic the situation at large scale where heat transfer through the walls makes a negligible contribution to heat removal. Note also that different organisms were used in the various studies, with quite different optimal temperatures for growth, so the actual temperatures involved are quite different.

Weber et al. (2002) measured the temperature as a function of time at various axial positions (Fig. 7.7(a)). At all heights, there was a temperature peak, whose maximum value occurred around day 4, with the height of the peak (that is, the maximum temperature reached) increasing with bed height.

Ghildyal et al. (1994) presented results that show the effect of the aeration rate on the axial temperature profile. Three different experiments were done, with air flow rates of 5 L min⁻¹, 15 L min⁻¹, and 25 L min⁻¹. The temperature was monitored at the central axis at mid-height in the bed. The height of the temperature peak increased as the air flow rate was decreased (Fig. 7.7(c)). They interpolated their data points to obtain a three-dimensional graph of the peak temperature obtained as a function of both bed height and air velocity (Fig. 7.7(d)). In general terms, the temperature appears to increase linearly with increase in bed height and also to increase linearly with decrease in the air flow rate, except at the lowest bed height, where the peak temperature first increased only slowly as the air flow rate was decreased, but then shot up steeply at low air flow rates.

7.3.3.2 Oxygen Gradients in Static Beds

The convective flow of air will also lead to axial concentration gradients of O₂ and CO₂, although these are not likely to be important in controlling the performance of the bioreactor. Outlet gas concentrations remain reasonably high, above 18% (v/v), even at low airflow rates (Fig. 7.8) (Gowthaman et al. 1993a,b). Excessive temperatures are always likely to be a greater problem than the supply of O₂ to the particle surface within packed-bed bioreactors.

7.3.3.3 Evaporation and Water Gradients in Packed-Beds

As pointed out in Sect. 7.2, it is impossible to prevent evaporation from occurring in packed-bed operation, even if the air supplied to the bed is saturated. Ghildyal et al. (1994) and Gowthaman et al. (1993a,b) showed that the rate at which bed drying occurred depended on the position within the bioreactor and the air flow rate (Fig. 7.9).

Looking at the effect of air flow rate on the temporal variations in water content at each bed height, the key observations are (Fig. 7.9(a)):

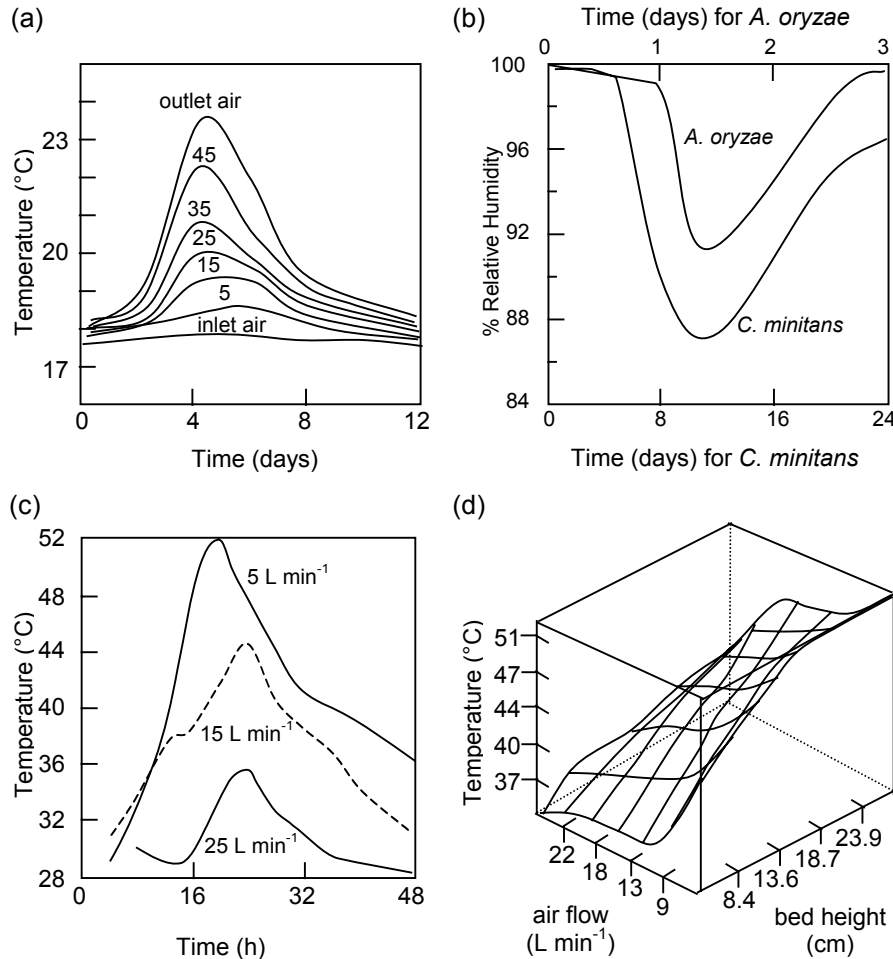


Fig. 7.7. Temporal and spatial temperature gradients in packed-bed bioreactors. **(a)** Temporal temperature profiles at different axial positions in the 50-cm-high packed-bed bioreactor of Weber et al. (2002), for growth of *Coniothyrium minitans* on hemp impregnated with nutrients. The numbers above each curve represent the cm height in the bed at which the temperature was measured. Adapted from Weber et al. (2002) with kind permission from John Wiley & Sons, Inc. **(b)** Off-gas relative humidity for fermentations undertaken with *Coniothyrium minitans* and *Aspergillus oryzae*. Adapted from Weber et al. (2002) with kind permission from John Wiley & Sons, Inc. **(c)** Temporal temperature profiles, at a bed height of 17 cm, in the 35-cm-high packed-bed bioreactor of Ghildyal et al. (1994), during the growth of *Aspergillus niger* on wheat bran. Adapted from Ghildyal et al. (1994) with kind permission of Elsevier. **(d)** Effect of air flow rate and bed height on the maximum temperature experienced during the cultivation. Adapted from Ghildyal et al. (1994), with kind permission of Elsevier

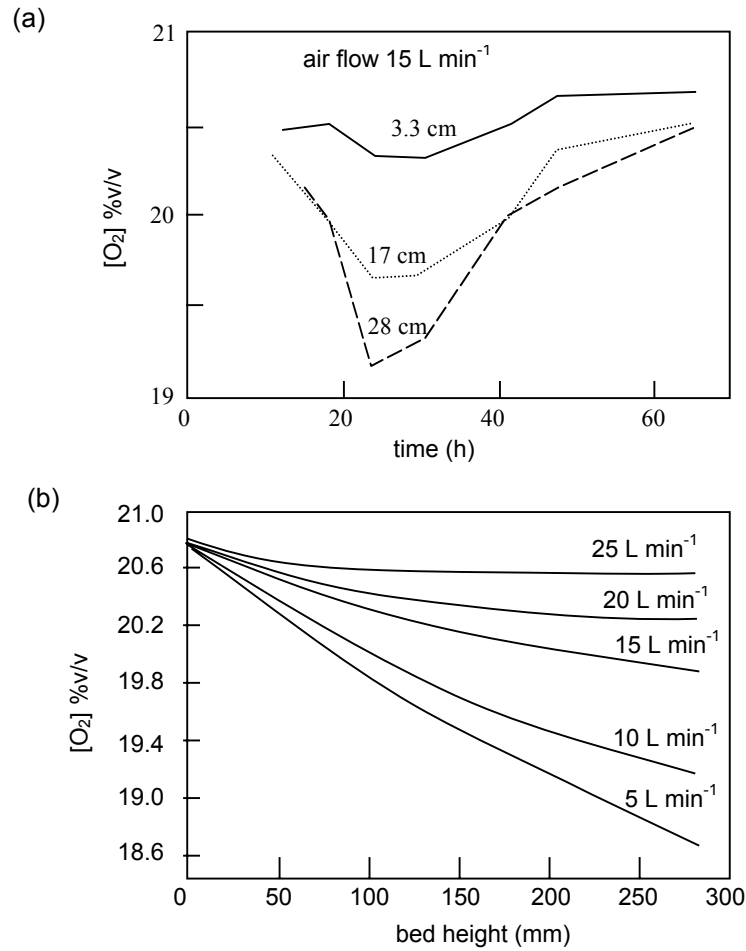


Fig. 7.8. Oxygen profiles during growth of *Aspergillus niger* on wheat bran in a 35-cm-high packed-bed bioreactor (Gowthaman et al. 1993b). **(a)** Temporal O_2 profiles at different axial positions, for an air flow rate of 15 L min^{-1} . **(b)** Axial O_2 profiles, at the time of peak growth rate (24 h), at various different air flow rates. Adapted from Gowthaman et al. (1993b) with kind permission of Elsevier

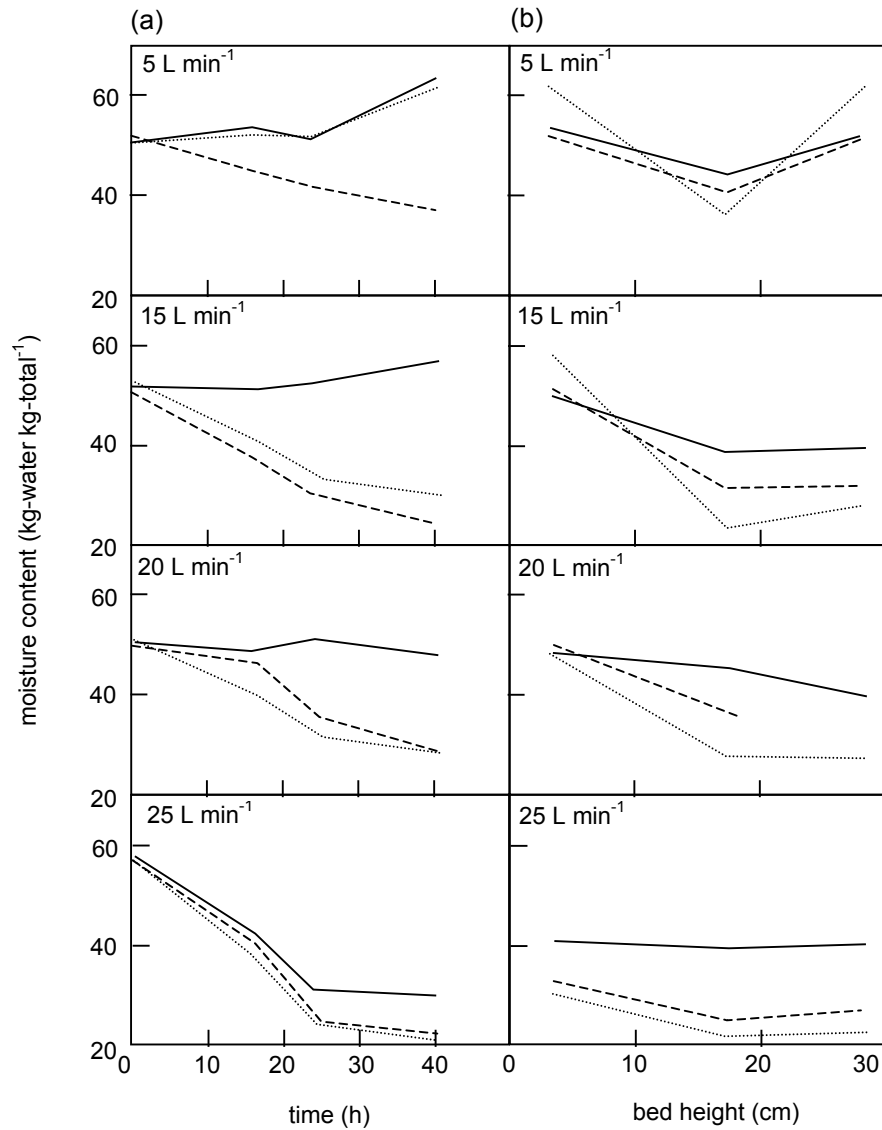


Fig. 7.9. Moisture profiles during growth of *Aspergillus niger* on wheat bran in a 35-cm-high packed-bed bioreactor (Gowthaman et al. 1993b; Ghildyal et al. 1994). **(a)** Temporal moisture profiles at different axial positions, for various different air flow rates. Key: bed heights of (∞) 3.3 cm (---) 17 cm (···) 28 cm. **(b)** Axial moisture profiles, at different times, for various different air flow rates. Key: Times of (∞) 16 h (---) 24 h (···) 40 h. Adapted from a table presented by Gowthaman et al. (1993b) with kind permission from Elsevier

- €# At 3.3 cm height, the water content of the bed increased over time or stayed constant when the air flow rate was 20 L min⁻¹ or below, but decreased at 25 L min⁻¹, although even at 25 L min⁻¹ this lower region did not dry out as quickly as the upper regions of the bed.
- €# The mid height of the bed (17 cm height) tended to dry out at all air flow rates.
- €# The water content of the bed at the upper position (28 cm height) increased during the fermentation for an air flow rate of 5 L min⁻¹ but decreased with time for air flow rates of 15 L min⁻¹ and above.

Inspecting the same results, but looking at the axial temperature gradients as a function of the air flow rate and how the axial temperature gradients varied over time, the key observations are (Fig. 7.9(b)):

- €# at 5 L min⁻¹ the bed was driest at 17 cm, with the 3-cm and 280-cm heights remaining near and even exceeding the original water content of 51% (w/w). This observation holds for 16, 24, and 40 h.
- €# at 15 L min⁻¹ the bed remained wet at 3 cm height, in fact, by 40 h it was significantly wetter than the original value, but became dry at 17-cm and 28-cm heights, with these two upper heights being reasonably close in water content, with values around 25-40 % (w/w)
- €# at 20 L min⁻¹ the pattern was similar to that obtained for 15 L min⁻¹ except that the water content at the 3-cm bed height remained close to the original value throughout.
- €# at 25 L min⁻¹ all regions of the bed dried. By 16 h the water content had fallen to around 40% (w/w) at all bed heights. At 24 and 40 h the 3-cm height still had a water content around 40% w/w, but at both the upper bed heights the water content had fallen to around 22-26% (w/w).

These results suggest that drying patterns can be quite complex. Chapter 25 presents a model that can be used to explore these patterns.

Weber et al. (2002) monitored the off-gas relative humidities during packed-bed fermentations with two different fungi (Fig. 7.7(b)). At the time of the peak heat generation rate, the off-gas relative humidity fell to values around 90%. This could imply that either the transfer of water from the particle to the air is limiting or simply that the bed is drying out. It would be necessary to monitor the water activity of the bed contents in order to distinguish between these two possibilities.

7.3.3.4 Pressure Gradients in Packed-Beds

This phenomenon, introduced in Chap. 7.2.4, is of particular importance in packed-beds due to the combination of static operation with forced aeration. The static operation means that the hyphae that grow into the inter-particle spaces are not disrupted or squashed onto the particle surface, and therefore these hyphae represent an extra impediment to air flow, increasing the pressure drop. The maximum pressure drop expected during the fermentation is an important consideration because it will affect the pressure that the blower or compressor must be capable of supplying.

Excessive pressure drop tends not to be a problem in intermittently agitated packed-beds because the agitation prevents the hyphae from binding the substrate bed into one large mass and it also squashes the hyphae onto the particle surface. In fact, infrequent agitation events might be used in packed-beds with the major purpose of decreasing the pressure drop. Figure 7.10 illustrates this point.

Despite its potential importance at large scale, pressure drop has received most attention in small-scale packed-bed bioreactors, and in these experiments the interest was in using the pressure drop to quantify the growth.

Auria et al. (1993, 1995) used a column of 6.5-cm height and 2-cm internal diameter, and a superficial velocity (calculated as volumetric flowrate divided by the total cross-sectional area of the column) of 0.435 cm s^{-1} . The substrate was an artificial substrate based on an amberlite resin impregnated with nutrients. The maximum pressure drop observed during the fermentation ranged from 0.21 to $0.69 \text{ cm-H}_2\text{O cm-bed}^{-1}$, for various different initial nutrient concentrations. With bagasse as the substrate and a superficial velocity of 0.379 cm s^{-1} the maximum pressure drop obtained in the same column was $2.75 \text{ cm-H}_2\text{O cm-bed}^{-1}$. In this case the pressure drop was already $0.45 \text{ cm-H}_2\text{O cm-bed}^{-1}$ at the beginning of the fermentation. In a larger column of 15-cm height and 4-cm diameter, they obtained a maximum pressure drop of $0.12 \text{ cm-H}_2\text{O cm-bed}^{-1}$ with a wheat bran substrate and a superficial velocity of 0.675 cm s^{-1} . With a much higher superficial velocity of 11.2 cm s^{-1} Gumbira-Sa'id et al. (1993) obtained a pressure drop of $1.38 \text{ cm-H}_2\text{O cm-bed}^{-1}$ with a substrate based on cooked sago-beads.

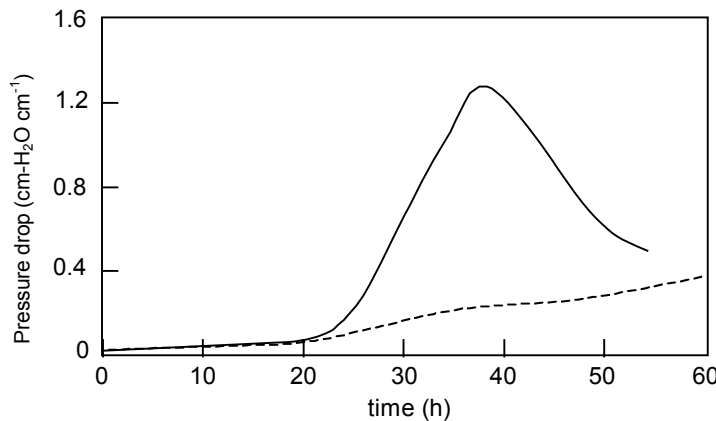


Fig. 7.10. Typical temporal profiles for the pressure gradient in the bed, based on the results of Gumbira-Sa'id et al. (1993) for the growth of *Rhizopus oligosporus* on a substrate based on sago beads. (∞) Evolution of the pressure drop in a fermentation in which the bed was not disturbed by the removal of samples. Note that the decrease in the pressure drop after 40 h is due to the substrate bed shrinking and pulling away from the bioreactor wall; (- -) Evolution of the pressure drop in a fermentation in which the bed was periodically disturbed by the removal of samples. Adapted from Gumbira-Sa'id et al. (1993) with kind permission of Elsevier

As yet there is insufficient information to predict the pressure drops that can be expected during a large-scale fermentation, although the experimental values reported here give some idea of the orders of magnitude that might be expected. The initial pressure drop will depend on the substrate and how it packs together, which in turn will depend on how the substrate is prepared. The maximum pressure drop achieved during the fermentation will depend on how the microorganism grows within the bed, although it is also a function of the superficial velocity.

Note that the pressure drop across the bed can decrease later in the fermentation. This can happen due to the bed pulling away from the walls, leaving a gap through which the air can pass (Gumbira-Sa'id et al. 1993; Weber et al. 2002). As described in the next subsection, this is undesirable because it will lead to heat and mass transfer limitations within the bed.

7.3.3.5 Channeling

Channeling is a potential problem in packed beds and the static phase of operation of intermittently-mixed beds. Channeling in intermittently-mixed beds will be discussed in Chap. 10. Channeling is problematic because air will flow preferentially through the cracks, such that in the regions of the bed where the particles are bound together, there will be no bulk flow, such that O_2 transfer will be limited to diffusion and heat transfer will be limited to conduction (see Fig. 7.4).

One of the major causes of channeling in packed-beds is the shrinkage of particles due to the consumption of the solid material of the particle, combined with the fact that, in many fungal fermentations, the substrate bed is bound together by “inter-particle hyphal bridges”. These two phenomena mean that, as the bed volume reduces, the particles will not simply settle downwards but rather the bed is drawn inwards, pulling away from the walls or cracking in the middle. For fungi that do not produce these hyphal bridges, the substrate particles remain free flowing as the bed shrinks and the bed does not pull away from the wall or develop cracks, but simply reduces in height (Weber et al. 2002).

For fungal fermentations in which the fungus does bind the particles together, shrinkage problems can be minimized by the use of “inert” hemp impregnated with nutrients (Weber et al. 1999). However, there is not necessarily free choice of substrates in SSF processes.

7.3.3.6 Condensation on the Bioreactor Walls in the Headspace

Often the bioreactor wall in the headspace is cooler than the temperature of the gases leaving the bed, which can cause condensation of water on the inner surfaces of the bioreactor walls in the headspace. This can be problematic, since the water can run down and flood the top of the bed, greatly interfering with O_2 transfer in this region.

7.4 Conclusions on Packed-Bed Bioreactors

Packed-bed bioreactors are the natural choice when the microorganism does not tolerate mixing well. The major challenge in developing large-scale packed-bed bioreactors for new applications will be to minimize the axial temperature gradients. There are two main strategies by which this can be done:

- ## to use traditional packed-beds but use a low bed height
- ## to use a Zymotis-type bioreactor, with internal heat transfer plates.

If the organism can tolerate infrequent mixing events, of the order of once every few hours, or even as infrequent as once per day, then the traditional design should be chosen. These mixing events allow the pressure drop to be decreased, and also the addition of water to replenish the water lost in evaporation. This mode of operation is discussed in more depth in Chap. 10. Agitation is not a feasible option in the Zymotis packed-bed due to the presence of the heat transfer plates.

If a traditional packed-bed is chosen, then the bed height will need to be no more than say 20 cm to 1 m, in order to prevent high temperatures at the outlet end of the bed. The other possibility, of using tall water-jacketed columns of 15 cm or less in diameter, is unrealistic, since, to hold large amounts of substrate, the bioreactors will either need to be very tall or a large number of bioreactors will be needed.

If it is not desired to mix the bed at all, due to the sensitivity of either the organism or the substrate to damage by mixing, then the Zymotis design should be strongly considered, on the basis of considerations of the water balance. The contribution of conduction to heat removal will decrease the axial temperature gradient, and this will decrease the evaporation rate, as long as saturated air is used at the air inlet. Further, the greater the sensitivity of the process to high temperatures, the more the Zymotis bioreactor is indicated. For the same bioreactor height, the maximum temperature reached in a Zymotis bioreactor is lower than for the traditional bioreactor. This will be explored in the modeling case study in Chap. 24.

However, the Zymotis bioreactor does have some disadvantages in its operability compared to the traditional bioreactor. Both bioreactors have a potential problem with water condensing from the saturated outlet air onto the exposed bioreactor surfaces above the substrate bed, and this condensate can flood the top of the bed, causing O₂ limitations in this region. This problem will be greater with the Zymotis bioreactor than for traditional packed-beds if the cooling plates extend above the top of the bed.

Additionally, the traditional packed-bed will be easier to load and unload than the Zymotis packed-bed. For example, for the traditional packed-bed it will probably be possible to (1) have a hinged base plate, in which the substrate can be dropped into a screw conveyor or (2) open a side and use a backhoe or (3) insert a pneumatic conveying tube to suck the substrate out. These operations will not be so easy in the Zymotis packed-bed due to the presence of the heat transfer plates.

A more detailed comparison of these two designs will require more work than is currently in the literature. The Zymotis design has not received much experimental attention since the early 1990s. However, as Chap. 24 shows, mathematical models can be used in a preliminary evaluation.

Further Reading

Early studies to elucidate the importance of temperature and gas gradients in packed-bed bioreactors

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Solid-State Fermentation Bioreactors
Fundamentals of Design and Operation
Mitchell, D.A.; Krieger, N.; Berovic, M. (Eds.)
2006, XXXVIII, 448 p., Hardcover
ISBN: 978-3-540-31285-7