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Scaling-up and Modelling Applications of Solid-state Fermentation and Demonstration in Microbial Enzyme Production Related to Food Industries

An Overview

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1. Introduction

Solid-state fermentation (SSF) is regarded as one of the most acceptable and convenient technologies for production of microbial enzymes. SSF is understood as the cultivation of microorganisms on solid, moist substrates in the absence of free aqueous phase, at average water activity significantly below 1 (Pandey, 2003). SSF is advantageous over submerged fermentation for the production of enzymes in numerous aspects, especially, fungal enzyme production is preferred in SSF as fungi show higher germination rates, spore formation and hyphae penetration in moist solid substrates (Holker and Lenz, 2005). Keeping in view the market size of the enzymes (£ 2100 million in 2010) and compound annual growth rate (CAGR) of 6 per cent forecast over the next five years, researchers and industrialists are showing tremendous interest in the techno-economic

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feasibility of production of different microbial enzymes (Saxena, 2015). Microbial enzymes are very commonly applied in modern times for the production of different food products. The most important microbial enzymes used in food industries are α-amylase, gluco-amylase, lipase, protease, invertase and pectinase, etc. Several studies in the last decade have developed technologies for overproduction of these enzymes. Researchers have also focused on economical production of the enzymes from cheaper substrates to reduce the cost of the final product (Panda and Ray, 2015). Genetically-engineered strains have been proved to be useful for enhanced production of the enzymes (Panda et al., 2016).

Although several review articles have covered the history and microbiological production of different enzymes related to food processing on the laboratory scale, hardly any article covers the exact scenario in the scaling-up process. The current article covers the developments in modelling, scaling-up equipments and production of commercially important enzymes related to food industries in different types of bioreactors with selected examples.

2. Scale up and Enzymes

The production of bulk chemicals and enzymes has secured an advantage with SSF (Soccol et al., 1994). Several researchers have demonstrated the bulk production of enzymes using SSF. Pectolytic enzymes were produced in large scale by solid-state fermentation using *Aspergillus carbanerius* strain on wheat bran medium. Fermentation for 21 hours with the tray temperature of 30ºC gave maximum production of enzymes. Further, steaming of wheat bran at 15 Pa for 45 min. enhanced the enzyme production (Ghildyal et al., 1981). Roussos et al. (1993) described a novel, large-scale solid-state fermenter designated as *Zymotis*, which aids the upscaling studies at 4–12 kg substrate dry matter (SDM) or 15–55 kg moist solid medium capacity, depending on the initial moisture content of the medium. Sugarcane bagasse and wheat bran [80:20 (w/w)] were used in fermentation for production of cellulase. The fermentation was conducted for 64 hours at 28ºC and the medium was aerated at the rate of 300:l humidified air/h/compartment during the first 12 hours, and further the aeration rate was doubled for rest of the fermentation time. The study was carried out to compare the production of cellulolytic enzymes by *Trichoderma harzianum* in *Zymotis* and a medium-sized laboratory column fermenter. It was observed that the enzyme titres were marginally higher in *Zymotis* at all the substrates when compared with parallel fermentation in the laboratory-scale column fermenter. The improved performance of the *Zymotis* is attributed to better control of cultural parameters in it.

3. Scale-up Approaches and Models

In the natural environment, SSFs occur everywhere—in cultivated grounds, the compost or the ensilage, but the term ‘fermentation’ is not naturally associated with what occurs in these mediums. This term is used with more elaborate processes developed in laboratory and implemented in bioreactors.

The scale-up of a bioprocess is a critical stage which guarantees the economic viability of the bio-product concerned. It consists in increasing the size of the bioreactor in order to reach sufficient productivity, and this, while maintaining as much as possible the outputs obtained at the time of tests in laboratory or on a pilot scale. For most biotechnological products (like enzymes production), a viable process is reached only for volumes of bioreactor of a few hundreds of thousands of liters (Lonsane et al., 1992). Technically, the definition of the scale-up understands several aspects (Trilli, 1986; Glenn and Rogers, 1989; Kossen and Oosterhuis, 1985; Oosterhuis et al., 1985). It would not only be about the increase in the size of the bioreactor, but should take into account the costs, the outputs and the simplicity of the device (Oosterhuis et al., 1985). In the case of microbial fermentation for the production of enzymes, a broad multidisciplinary field is shared (Banks, 1984) and the scale up then becomes an important link for the bioprocess transfer from the laboratory scale to the industrial scale for commercial needs.

The scale up is carried out in several stages (Banks, 1984; Trilli, 1986): from Erlenmeyer flask to the laboratory bioreactor, from laboratory bioreactor to the pilot bioreactor and from pilot bioreactor to the industrial bioreactor. It is impossible to preserve all the parameters identical or proportional to the scaling. Each transfer to a greater scale is complex because various parameters, such as the scale of sterilization, aeration and agitation are modified when one increases volume, the diameter and the height of the bioreactor (Lonsane et al., 1992; Mitchell et al., 2006). Similar physicochemical conditions must be maintained in the environment of each cell in spite of the increase in the volume of culture. With each stage of the scale up, various parameters are analyzed and modified because the physicochemical and enzymatic reactions occurring inside the bioreactor vary according to the volume of the bioreactor used. Moreover, during the scaling, it is essential to take into account the investment costs of equipment (bioreactor, techniques of extraction and purification) and of operation (culture medium and energy); to carry out an automation of equipment if possible; to reduce the production of waste; to obtain products corresponding to desired quality (Mitchell et al., 2006).

The representation of the working system in terms of mathematical expression is what constitutes the modelling in SSF. The application of mathematical modelling techniques to describe the biological and transport phenomena within the system made significant improvements in understanding how to design, operate and scale-up SSF bioreactors. Various features of the conceptually divided microscale and macroscale phenomena that occur within SSF bioreactors are described by equations of the mathematical models of bioreactor (Mitchell et al., 2000). The prediction models for the scale up is taking into account the growth kinetic, rotating-drum, traditional and *Zymotis* packed-bed, intermittently-mixed forcefully-aerated and well-mixed bioreactors. The aspects globally developed are growth kinetic, energy and water balance. Some assumptions are made to handle the models.

3.1 Growth kinetic models

The growth kinetic models are one of the first important models concerning the scale up and especially on modelling and controlling. It can be used to handle the conditions

in the reactor. These conditions take into consideration the parameters involved during biomass growth. Table 1 presents a non-exhaustive number of models used for growth modelling. In a study conducted by Rodriguez-Fernandez et al. (2011), the behavior of

Table 1. Describing equations for microbial kinetics.

Model	Equations	
Arrhenius	$\mu_{\max}(T) = k_g^0 \exp\left(\frac{-E_g}{RT}\right) - k_g \exp\left(\frac{-E_d}{RT}\right)$	[5]
Bovill et al.	$\frac{dX}{dt} = \mu X\left(1-\frac{X}{X_m}\right)\left(\frac{Q}{1+Q}\right)$ (Bovill et al., 2000)	[6]
Esener	$\mu_{\max}(T) = \frac{A\exp\left(-\frac{\Delta H_1}{RT}\right)}{1+k\exp\left(-\frac{\Delta H_2}{RT}\right)}$ (Saucedo-Castaneda et al., 1990)	[7]
Fanaei and Vaziri	$\mu = \left(\frac{\mu_s + (T_{\max} - T_{opt})}{T_{\max} - T_{opt}}\right)\left(\frac{\mu_{opt}(T_{\max} - T)}{\mu_s + (T_{\max} - T)}\right)$ (Fanaei and Vaziri, 2009)	[8]
Okazaki et al.	$X = \frac{X_m}{1+\left[\left(\frac{X_m}{X_0}\right)-1\right]e^{-\mu t}}$ (Okazaki et al., 1980)	[9]
Saucedo-Castaneda	$\mu = \frac{2.964\times10^{11}\exp\left(-\frac{70225}{RT}\right)}{1+1.3\times\exp\left(-\frac{283356}{RT}\right)}$ $X_m = -127.08 + 7.95(T-273) - 0.016(T-273)^2$ $+4.03\times10^{-3}(T-273)^3 + 4.73\times10^{-5}(T-273)^4$ (Saucedo-Castaneda et al., 1990)	[10] [11]
Ratkowsky et al.	$\mu_{\max}(T) = c_0(T-T_{\min})\left[1-\exp(c_1(T-T_{\max}))\right]^2$ (Ratkowsky et al., 1983; Weber et al., 2002)	[12]
Exponential	$\frac{dX}{dt} = \mu X$ (Mitchell et al., 2004; Sosa et al., 2012)	[13]
Linear	$\frac{dX}{dt} = K$ (Mitchell et al., 2004; Sosa et al., 2012)	[14]
Logistic	$\frac{dX}{dt} = \mu X\left(1-\frac{X}{X_m}\right)$ (Mitchell et al., 2004; Sosa et al., 2012)	[15]

Table 1. contd....

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Model	Equations	
Polynomials	$\mu_{max}(T) = -s_0 + s_1T - s_2T^2 + s_3T^3 - s_4T^4 + s_5T^5$ $\mu_{max}(T) = -b_0 + b_1T - b_2T^2$ $X_m(T) = -e_0 + e_1T - e_2T^2 + e_3T^3 - e_4T^4$ (Mitchell et al., 2004; Sosa et al., 2012)	[16] [17] [18]
Two phase	$\frac{dX}{dt} = \mu X,\ t \le t_a$ $\frac{dX}{dt} = \left[\mu L e^{-k(t-t_a)}\right] X,\ t \ge t_a$ (Mitchell et al., 2004; Sosa et al., 2012)	[19] [20]

kinetic parameters in production of pectinase and xylanase by solid-state fermentation was observed. *Aspergillus niger* F3 was applied for production of pectinase and xylanase in a 2 kg bioreactor and citrus peel was used as a substrate. It was revealed that pectinase production was highest at 72 hours whereas the xylanase production increased after 72 hours, which is because of the reduction of pectin in the medium and forcing the microorganism to use xylan as the carbon source. The best air flow intensity noted for the microorganism growth and optimum production of pectinase (265 U/g) and xylanase (65 U/g) was 1 V kg M (volumetric air flow per kilogram of medium). This is because of the sufficient amount of O_2 incorporated into the medium. The following equation (1) was applied to obtain the values for metabolic O_2 balance:

$$\frac{dO_2}{dt} = \frac{1}{Y_{x/o}}\frac{dx}{dt} + mX \quad [1]$$

where *dX/dt* is the biomass production rate; *X*, biomass synthesised during the time interval; *Yx*/*o*, yield based on O_2 consumption for biomass synthesis; dO_2, differential O_2 consumed during the differential time interval; *m*, maintenance coefficient; *dt*, differential time interval.

Along with the growth of microorganisms and consumption of substrates, researchers also studied the modelling of product formation, such as enzymes and bio-ethanol. One of the general modelling used for the formation of products in biological processes is to assume the growth and non-growth-associated components. Therefore, the general equation (2) for a product (*P*) is:

$$\frac{dp}{dt} = Y_{PX}\frac{dX}{dt} + m_P X \quad [2]$$

where Y_{PX} is the stoichiometric coefficient and m_P is the maintenance coefficient.

Mass balances are also used to develop the product formation models. Hashemi et al. (2011) proposed equation (3) to model different phases of bacterial growth curve and the production of α-amylase in the SSF process using wheat bran as substrate and *Bacillus* sp. as inoculum.

$$\frac{dW}{dt} = \frac{dS}{dt} + \frac{dB}{dt} + \frac{dP}{dt} \quad [3]$$

In the study it was assumed that the changes in total dry fermenting medium weight (W) correspond to substrate consumption rate (dS/dt), biomass growth rate (dB/dt) and product formation rate (dP/dt).

Experimental data generated from a series of batch fermentations were applied to validate the proposed models. Prediction of the production of α-amylase during the fermentation process was attempted by using equation (4) which makes a correlation between P (enzyme production) and t (time) based on the variation in the fermented medium weight. According to the equation, α and β coefficients are estimated experimentally to predict the product kinetics derived from $\frac{dW}{dt}$ data:

$$P = (\alpha - \frac{\gamma}{\delta}) \int_0^t B dt + \frac{\beta}{\delta} \int_0^t \frac{dW}{dt} dt \quad [4]$$

3.2 Rotating-drum bioreactors models for scale-up and applications

The rotating-drum bioreactors comprise a horizontally rotating drum, that may or may not have a paddle mixer and rotates slowly for proper mixing of fermentation substrate. For scaling-up purposes, many assumptions need to be made concerning the rotating-drum bioreactors (Fig. 1). The most important ones can be summarized as follows: the bioreactor is cylindrical (with a length L and diameter D) and partially filled; since the solid materials are degraded during fermentation, it will be considered that only the density of the bed is affected; the dry gas remains constant in the headspace; the gas flow rates remain the same between the inlet and the outlet of the bioreactor; the solid particles and gas phase are in equilibrium (moisture and thermal) and the diffusion from the axe is negligible (Mitchell et al., 2002).

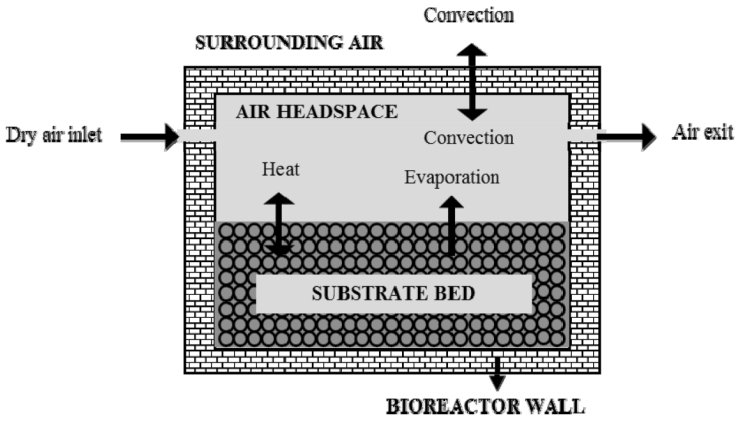

Figure 1. Rotating-drum bioreactor.

The models used for the rotating drum bioreactors scale-up take into consideration mass and heat transfer balances. The mass transfer (for water and air) occurring over the bed and headspace must be considered.

3.2.1 Microbial growth

Initially, at $t = 0$, $X = X_0$, and the microbial growth kinetic which is a logistic equation can be expressed as follows (Mitchell et al., 2002; Wang et al., 2010):

$$\frac{dX}{dt} = \mu X\left(1 - \frac{X}{X_m}\right) \quad [21]$$

where: X, is the biomass concentration, μ, the specific growth rate; X_m, maximal concentration of biomass and X_0, is the initial biomass concentration.

3.2.2 Applications

The theoretical aspects of the rotating-drum bioreactors were applied for different enzymes production. Several successful stories have been reported for upscaling of enzyme production using rotating-drum bioreactors. In the early 19th century manufacture of amylase by *Aspergillus oryzae* on wheat bran, in rotating-drum bioreactors was scaled up to industrial level (Takamine, 1914). It reported the use of fuzzy logic control for amylase and protease enzymes production by *A. oryzae*. That fuzzy logic control system as a scale-up aspect exhibited the highest enzyme activity (Sukumprasertsri et al., 2013). While using the same microorganism, the scale up on a pilot-scale was realized and concerned the oxygen uptake and agitation. Achievement in terms of O_2 utilization was better at 9 rpm than at 2 rpm. This was apparently as a result of the effect of the rotational speed on the performance of the stirring inside the bed (Stuart, 1996). A comparative study was attempted by Alam et al. (2009) for the production of cellulase enzyme in both Erlenmeyer flask (500 mL) and a horizontal rotating-drum bioreactor (50 L) by using empty fruit bunches as substrate. It was observed that the highest cellulase activity on the fourth day of fermentation in the 500 mL flask was 8.2 filter paper activity (FPA)/gram dry solids (gds) of empty fruit bunches, while the same was 10.1 FPA/gds for rotating-drum bioreactor on the second day of fermentation.

3.3 Traditional and Zymotis packed-bed bioreactors models

The scale up purpose for this bioreactor assumes that the traditional packed-bed bioreactor is a cylindrical unit which is aerated with humid air from the bottom (Fig. 2). The humid packed-bed (substrate) is then inoculated and introduced in the unit and that time is considered as zero with no agitation (static bed) (Mitchell et al., 1999; Mitchell et al., 2003). In the *Zymotis* packed-bed bioreactor (Fig. 3) which was modelled by Mitchell and Von-Mein (2000), the heat transfer is realized in two directions (the horizontal direction is normal to air flow direction and the direction

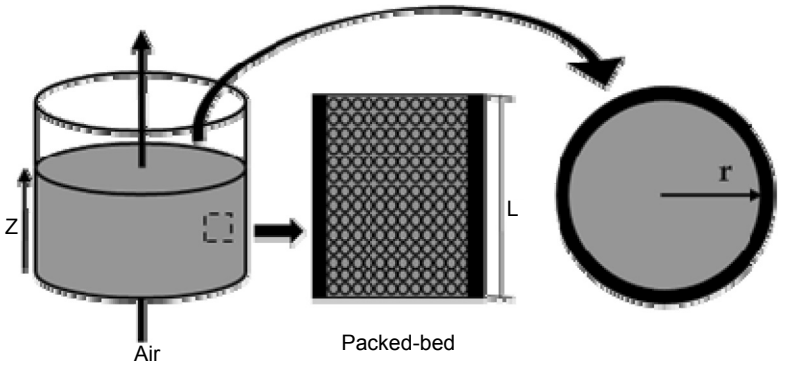

Figure 2. Traditional packed-bed bioreactor.

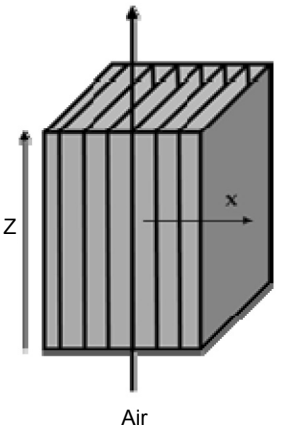

Figure 3. *Zymotis* packed-bed bioreactor.

which is co-linear to air flow exhibiting the removal of evaporative and convective heat). The front-to-back gradients are considered negligible (Mitchell et al., 2003).

3.3.1 Microbial growth

The logistic equation is used to express the kinetic growth of the biomass for both packed-bed and is as follows (Mitchell et al., 1999):

$$\frac{dX}{dt} = \mu X\left(1 - \frac{X}{X_m}\right) \qquad [22]$$

The packed-bed bioreactor presents a limitation on the height of the bed which can reduce significantly the performance. That bed height limit is not constant and varies with the microbe growth rate and superficial air velocity (Mitchell et al., 1999).

3.3.2 Applications

Successful upscaling applications for enzyme production were carried out using packed-bed bioreactor. The production of pectinase was scaled up from 12 g to 30 kg of dry substrate; the best outcome was achieved with a 40-cm high bed having 27 kg of wheat bran and 3 kg of sugarcane bagasse (Pitol et al., 2016). The manufacture of lipase from *Penicillium simplicissimum* was performed also in packed-bed bench-scale bioreactors and the scale up regarding the yield of the enzyme was profitably completed by adjusting the temperature and air circulation rate in the bioreactor, utilizing bagasse and sugarcane molasses (6.25 per cent). The highest lipase activity reached 26.4 U/g at 27°C and a flow rate of 0.8 L/min (Cavalcanti et al., 2005). Also, a model has been established with *N*-tanks in the series approach as a scale up for a packed-bed bioreactor, using solid-state fermentation. The model investigated the production of protease enzyme applying *A. niger* and was confirmed across experimental research accessible in literature (Sahir et al., 2007). Similarly, scale up was realized in a laboratory packed-bed bioreactor to obtain α-amylase from *Bacillus* sp. KR-8104 using SSF by prospecting the control of temperature. Wheat bran (WB) was used as substrate. The coexisting impacts of aeration rate, initial humidity of substrate and temperature incubation on α-amylase manufacture were checked out. The optimum circumstances in which the maximum α-amylase production was attained were 37°C, 72 per cent (w/w) initial substrate humidity and 0.15 L/min aeration. The typical enzyme activity reached under best conditions was 473.8 U/g dry substrate (Derakhti et al., 2012). In another study, α-amylase production by *Bacillus amyloliquefaciens* was executed in 300 mL and 3 L packed-bed bioreactors working volume. The observations pointed out high rates of aeration demand to boost enzyme yield. That yield exhibited a linear relationship with air flow rate. The highest activity of 41.4 U/(mL·h) was attained in 14 hours of fermentation in 300-mL and a similar activity of 40 U/(mL·h) was reached after 12 hours in 3 L (Gangadharan et al., 2011).

3.4 Intermittently-mixed forcefully-aerated bioreactor

The bioreactor is advantageous over the packed-bed bioreactors as it is relatively simple to add water uniformly to the substrate (Mitchell et al., 2006). In this type of bioreactor (Fig. 4), two types of behaviors are to be considered—the static and mixing systems (Durand and Chereau, 1988; Xue et al., 1992; Chamielec et al., 1994; Agosin et al., 1997; Bandelier et al., 1997). The packed-bed system is assumed to be the one observed during the static phase. Other assumptions are: the heat transfer from the wall is negligible so that the heat and mass transfer are in one direction (axial); the solid and air are not in thermal and moisture equilibrium. No degradation of microorganism growth is included in the model (Mitchell et al., 2003; Von-Meien and Mitchell, 2002; Mitchell et al., 2006).

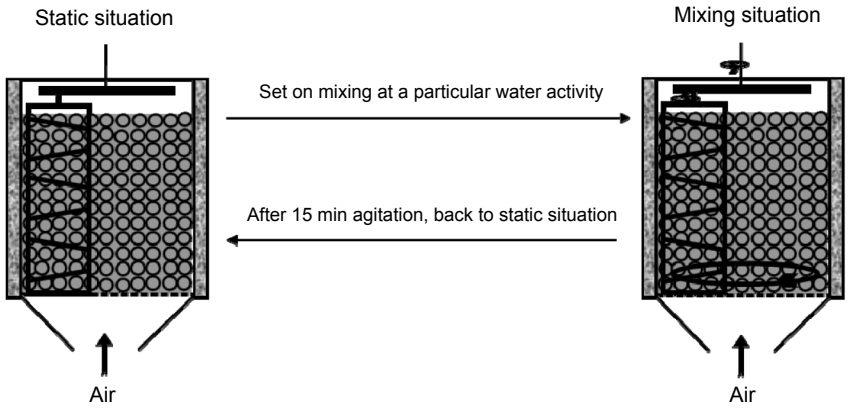

Figure 4. Intermittently-mixed forcefully-aerated bioreactor.

The calculation of changes in the solid and liquid phase takes into consideration the driving forces, when the mass and heat transfer balanced equation is presented. Since the temperature and the water activity affect the microbial growth, the models are used to calculate the water activity of the solid, using its water content and temperature.

3.4.1 Microbial growth

The microbial growth is written as (Mitchell et al., 2003; Von-Meien and Mitchell, 2002; Mitchell et al., 2006):

$$\frac{\partial X}{\partial t} = \mu X\left(1 - \frac{X}{X_m}\right) \qquad [23]$$

The consumption of solid during microbial fermentation can be expressed as follows (Von-Meien and Mitchell, 2002; Mitchell et al., 2006):

$$\frac{\partial M_s}{\partial t} = \left[1 - \frac{1}{Y_s}\right]\frac{\partial\left(XM_s\right)}{\partial t} \qquad [24]$$

3.4.2 Applications

An intermittent spouting with air-bed bioreactor was developed to produce enzymes from rice substrate using *A. oryzae*. The enzyme production was realized in a large scale. The scaling up was to overcome problems like mass transfer, heat transfer and solid handling. High levels of α-amylase, β-amylase and glucoamylase were obtained. It was noticed that an increase of spouting frequency decreased enzyme production (Silva and Yang, 1998). The production of β-mannanase from palm kernel cake was scaled up in a laboratory glass-column bioreactor (consisting of a jacketed vessel with a height of 50 cm, an inner diameter of 16 cm and loaded with 100 g of palm kernel cake) in terms of maximizing the yield. The optimal conditions from the model stated that for the highest level of β-mannanase, the incubation temperature must be 32°C,

initial humidity 59 per cent and aeration 0.5 L/min. This allowed β-mannanase activity of 2231.26 U/g (Abdeshahian et al., 2010).

3.5 Well-mixed bioreactor

In a well-mixed bioreactor, no concentration gradients are observed either in gas or in liquid phase. The assumptions made for the well-mixed bioreactor are: it is cylindrical, with water-jacketed on its sides (Fig. 5); the microbial growth is considered as a logistic equation, with specific growth rate constant affected by the water activity and the temperature of the particles; the gas and air phases are considered as different subsystems (Mitchell and Krieger, 2006).

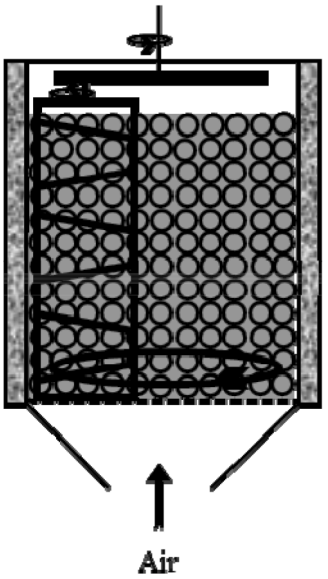

Figure 5. Well-mixed bioreactor.

The microbial growth, solid consumption, water and energy balances are treated here and the equations are written (Mitchell and Krieger, 2006; Von-Meien and Mitchell, 2002; dos-Santos et al., 2004; Marques et al., 2006):

3.5.1 Microbial growth

The logistic equation used for this bioreactor is:

$$\frac{dX}{dt} = \mu X\left(1 - \frac{X}{X_m}\right) \qquad [25]$$

The specific growth rate (fractional) can be influenced by water activity and is obtained by using the following equation:

$$\mu_{aw} = 1.0538 \exp\left(-131.6a_w^3 + 94.996a_w^2 + 214.219a_w - 177.668\right) \quad [26]$$

where: μ_{aw} is fraction of water activity dependence specific growth rate; a_w, water activity.

3.5.2 Applications

Like the other type of bioreactors, the well-mixed bioreactor was used and scaled up for the production of food enzymes. It was a low-cost process developed for apple pomace utilisation in order to obtain pectinolytic enzyme. That enzymes from *A. niger* as well as pectinesterase and polygalacturonase were studied. The scale-up process was from the laboratory tray bioreactor to a 15 L horizontal stirred bioreactor. Process specifications, such as inoculation, mixing, aeration, temperature and humidity on pectolytic enzymes production, were investigated. The highest quantities of 15 $g.kg^{-1}$ of substrate of polygalacturonase, 200 $mg.kg^{-1}$ pectinesterase at activity up to 900 AJDA U ml-1 of enzyme mixture was attained on an average (Berovic and Ostroversnik, 1997). Also, investigations were conducted on the manufacture of protease by slightly halophilic *Bacillus* sp. on agro-industrial waste. The optimal pH (7.0), temperature (30°C) and agitation rate (50 rpm) were found to be the best conditions for protease production during the scale-up fermentation (Prasad et al., 2014). Multiple isolates of *A. niger* were also screened from polluted oil soil samples and isolated for lipase production, using tributyrin medium. The lipase production was successfully scaled up on a 5 L pilot scale stirred fermenter, preserving expansion parameters at pH (7), temperature (28°C), stirring (120 rpm), airflow rate (30 L/hr), O_2 concentration (50 per cent) and pressure (0.05 MPa) (Rai et al., 2014). A model for a well-mixed bioreactor was also executed to investigate the problems that could occur on a large scale. It was suggested that, using high flow rate, up to 85 per cent of the enzyme obtained from the microorganism could be denatured by the end of fermentation, exhibiting the problems of large-scale well-mixed bioreactor (dos-Santos et al., 2004).

4. Limitations

Scale up, product purification and biomass estimation are major challenges that need to be established before SSF can become industrially viable. The reason for scale up is difficult because of transportation limitations within a large reactor. Other major problems encountered are control over different parameters, such as pH, temperature, aeration, oxygen transfer and moisture. Also the used microorganisms are limited as they grow in reduced levels of humidity. Lack of experimental data hampers parameter identification and thus a broader use of mathematical modelling is essential.

5. Conclusion and Future Perspectives

The current article critically discusses the upscaling, modelling, microbiology and biochemical aspects of solid-state fermentation for obtaining enzymes related to the food industry. In addition microbial enzymes are used for treatment in the food industry. Although much work has been done on solid-fermentation bioreactors, the important aspect is to explore the production of enzymes in these industries. Work on different kinetics in bioreactors needs to be investigated. Also, optimization of enzyme production can be one of the primary axes as the ability to obtain high yields within short intervals during fermentation in solid media has been recognized. There is another important research on enzymatic degradation of the substrates. Therefore, optimization of the physical parameters in bioreactors and appropriate kinetics are crucial. The continuous cultivation of microorganisms (using genetically modified strains) and high density culture of cells in order to produce food enzymes needs to be investigated as well as the scale-up bioreactor. More research is needed on physical techniques and computational approaches to allow better model validation and ensure progress in rational bioengineering of SSF.

Nomenclature

A	Area of heat transfer coefficient bioreactor wall	m^2
a_w	Water activity	
$b_0,\ b_1,\ b_2$	Constants	
M_s	Dry mass of substrate bed	kg
m_W	Water production maintenance coefficient	
$S_0, S_1, S_2, S_3, S_4, S_5,$	Constants	
t	Time	s
t_c	Contact time between substrate particles and wall	s
T_a	Air phase temperature	^oC
$T_{\max}$	Maximal temperature for growth	^oC
$T_{\min}$	Minimal temperature for growth	^oC
T_{opt}	Optimal growth temperature	^oC
X	Biomass concentration	$kg\ biomass/kg\ substrate$
X_0	Initial biomass concentration	$kg\ biomass/kg\ substrate$
X_{m}	Maximal concentration of biomass	
Y_{X}	Heat yield metabolic coefficient	$J/kg\ biomass$
μ	Specific growth rate	s^{-1}

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μ_{aw}	Fraction of water activity dependence specific growth rate	s^{-1}
μ_{opt}	Optimal specific growth rate	s^{-1}
μ_T	Fraction of temperature dependence specific growth rate	s^{-1}
ρ_a	Air density	kg/m^3

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