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Review

# Recent advances in solid-state fermentation

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ABSTRACT

Solid-state fermentation (SSF) has built up credibility in recent years in biotech industries due to its potential applications in the production of biologically active secondary metabolites, apart from feed, fuel, food, industrial chemicals and pharmaceutical products and has emerged as an attractive alternative to submerged fermentation. Bioremediation, bioleaching, biopulping, biobeneficiation, etc. are the major applications of SSF in bioprocesses which have set another milestone. Utilization of agro-industrial residues as substrates in SSF processes provides an alternative avenue and value-addition to these otherwise under- or non-utilized residues. Innovation is the key to success and it is imperative to be up-to-date with the changing demands of the industries and meet their needs for better product and services. Better understanding of biochemical engineering aspects, particularly on mathematical modeling and design of bioreactors (fermenters) has made it possible to scale-up SSF processes and some designs have been developed for commercialization, making the technology economically feasible. In future, SSF technology would be well developed at par with SmF if rationalization and standardization continues in current trend. This review describes the state-of-art scenario in totality on SSF although the focus is on the most recent developments of last 5 years or so on SSF processes and products developments.



**Contents**



## 1. Introduction

Solid-state fermentation (SSF) has been defined as the fermentation process which involves solid matrix and is carried out in absence or near absence of free water; however, the substrate must possess enough moisture to support growth and metabolism of the microorganism. The solid matrix could be either the source of nutrients or simply a support impregnated by the proper nutrients that allows the development of the microorganisms. This review focuses on SSF process and product developments mainly from the last 5 years and provides an update to our 2003 review [1]. The potential of SSF lies in bringing the cultivated microorganism in close vicinity of substrate and achieving the highest substrate concentration for the fermentation. SSF resembles the natural habitat of microorganism and is, therefore, preferred choice for microorganisms to grow and produce useful value added products. SmF can be considered as a violation to their natural habitat, especially of fungi. Not even marine microorganism prefer

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swimming in free water, since more than 98% of isolates from marine environment have been obtained from the underwater surfaces of solid substrates, found in marine habitats [2,3]. Fact, that SSF is well adapted to the metabolism of fungi; characteristic of the microorganism employed in this technique is an important feature of this process. At laboratory scale, many of the papers have been published and still publishing over study of effects of various factors on fungal metabolism. SSF reproduces the natural microbiological processes like composting and ensiling. On one hand by utilizing the low cost agricultural residues SSF adds on to economic feasibility of the process and on other hand it solves the problem of its disposal which otherwise cause pollution.

However, all the fermentation processes used in ancient times were based on the principles of solid-state fermentation technology; history indicates that it was lost in oblivion in western countries after 1940 due to emergence of submerged fermentation technology. Perhaps SSF was neglected because development of wonder drug, penicillin took place in submerged fermentation (SmF), which was having enormous importance at that time. Research related to SSF always continued, though in isolated pockets. During 1950–1960, steroid transformation was reported using fungal culture and reports on mycotoxin production employing SSF appeared during 1960–1970, which enabled SSF to attain another milestone and it continued with the reports on production of protein enriched cattle feed by SSF utilizing agro-industrial residues, thus offering a unique process development for value addition of these low cost residues which are also considered as pollutant to some extent. There has been a continuous extension of SSF arena, for the development of bioprocesses, such as bioremediation and biodegradation of hazardous compounds, biological detoxification of agro-industrial residues, biotransformation of crops and crop-residues for nutritional enrichment, biopulping, and production of value-added products, such as biologically active secondary metabolites, including antibiotics, alkaloids, plant growth factors, enzymes, organic acids, biopesticides, including mycopesticides and bioherbicides, biosurfactants, biofuel, aroma compounds, etc. [1]. Thus, though historically known since centuries, SSF gained a fresh attention from researchers and industries all over the world since recent few years, mainly due to few advantages it offers over liquid (submerged) fermentation, particularly in areas of solid waste management, biomass energy conservation and its application to produce high value–low volume products such as biologically active secondary metabolites, etc., apart from the production of food, feed, fuel and traditional bulk chemicals [4,5]. Capability of genetic manipulation of fungal strains has broadened horizon for SSF enabling the technology for the production of recombinant proteins and value added chemicals.

## 2. Important aspects of SSF

There are various important factors that produce immense impact on success of a particular technology hence, needed to be considered for the development of any bioprocesses and so is the SSF. It includes selection of microorganism and substrate, optimum process parameters and also purification of the end product, which has been a challenge for this technology. Fungi and yeast were termed as suitable microorganisms for SSF according to the theoretical concept of water activity, where as bacteria have been considered unsuitable. Still, availability of several research articles [6–8] proves that bacterial cultures can also be well manipulated and managed for SSF process even for scarcely produced tannase enzyme [9]. *Bacillus thuringenesis* production was standardized by SSF on wheat bran to obtain maximum toxin and was found to be cost effective [10].

The establishment of the relationships between the physiology of the microorganisms and the physico-chemical factors is the aim for the development of proper models. These factors include temperature, pH, aeration, water activity and moisture, bed properties, nature of solid substrate employed, etc. Among several critical factors moisture and nature of solid substrate employed are the most important factor affecting SSF processes. Selection of moisture depends on microorganism employed and also the nature of substrate. Fungi needs lower moisture, 40–60% moisture could be sufficient but selection of substrate depends upon several factors mainly related with cost and availability and thus may involve the screening of several agro-industrial residues.

## 3. Challenges and advantages of SSF

Today's environment is rapidly changing, where we can experience constant technological advancement backed by innovation playing major catalyst in this race. SSF appears to possess several biotechnological advantages, though at present mostly on a laboratory scale, such as higher fermentation productivity, higher end-concentration of products, higher product stability, lower catabolic repression, cultivation of micro-organisms specialized for the water-insoluble substrates or mixed cultivation of various fungi, and last but not least, lower demand on sterility due to the low water activity used in SSF [3]. Viniegra-González et al. [11] have attempted to develop a general approach for the comparison of productivity of enzymes employing SSF and SmF and have tried to explain the reason for higher production in SSF. Higher biomass, high enzyme production and lower protein breakdown, contributes to the better production in SSF [11].

Scale up, purification of end products and biomass estimation are the major challenges that led the researchers to thrive hard to find the solutions. Scale up in SSF has been a limiting factor since long but recently with advent of biochemical engineering a number of bioreactors have been designed which could overcome the problems of scale up and to an extent also the on-line monitoring of several parameters, as well as heat and mass transfer.

Separation of biomass is a big challenge in SSF, which is essential for the kinetic studies. However certain indirect methods are there such as, glucosamine estimation, ergosterol estimation, protein (kjeldahl) estimation, DNA estimation, dry weight changes and $CO_2$ evolution, but all of them have their own weaknesses. Recently digital image processing has been developed as a tool for measuring biomass in SSF. The images were acquired by stereomicroscope and a digital camera and processed using KS400 software [12]. In recent times estimation of oxygen intake and carbon dioxide evolution rate are considered to be most accurate for the determination of growth of the microorganism [4,5].

Although, product recovery and purification processes are more expensive employing natural supports, their utilization supposes a reduction in production costs and usually much higher activities are obtained [13]. Hence, an economical evaluation of the overall process should be done in order to determine its feasibility to a specific purpose. This system is especially suitable for the production of high-value products like enzymes. There are particular applications where concentrated end products with high titers are required rather than degree of purity, for example, bioconversion of biomass, requires concentrated crude cellulase, in leather industries crude protease are enough to remove the hairs from the leather.

## 4. Advances in biochemical engineering aspects of solid-state fermentation

There are major challenges that need to be addressed for the successful implementation of SSF technology, such as scale up in

SSF, which is a major bottle neck; providing adequate heat and mass transfer within the substrate bed, to monitor on-line several key processes parameters and also to mix the bed adequately without damaging the microorganisms as well as the substrate particles of bed [14]. Heat generation due to metabolic activities of the microorganisms, which is desirable in composting, is often fatal for biotechnological processes because a large part of the enzymes produced during the fermentation can be heat denatured at the end of the process [15]. High moisture percentage results in low substrate porosity which in turn prevents oxygen penetration, whereas low moisture content may lead to poor accessibility of nutrients resulting in hampered microbial growth [1]. The consequences of these difficulties for bioreactor performance have been well explored [16–18].

Water relations in SSF system is one among the crucial factor, which needs to be critically evaluated. Water activity ($\alpha_w$) of the substrate has determinant influence on microbial activity. Importance of $\alpha_w$ has been widely studied by researchers as, the type of microorganism that can grow in SSF are determined by $\alpha_w$. The $\alpha_w$ of the medium has been attributed as a fundamental parameter for mass transfer of the water and solutes across the microbial cells. The control of this parameter could be used to modify the metabolic production or excretion of a microorganism [19].

### 4.1. Bioreactor design

In spite of strong resurgent of SSF in last few years, design of bioreactor aspect have not been given enough attention from the researchers, yet; there are certain path-breaking developments. Commonly used SSF bioreactors can be divided into four types based on type of aeration or the mixed system employed. These are tray, packed-bed, horizontal drum and fluidized bead having their own advantages and disadvantages, which promoted the necessity to develop novel bioreactors with better design. Although scale-up methods for SmF are well developed [20], ranging from successful rules-of-thumb to semi-fundamental methods, these methods could not be applied directly to SSF bioreactors: due to the differences in the physical structures of the systems, heat removal is a major consideration in the design of SSF bioreactors and has been the limiting factor for commercial viability of SSF since long. Several bioreactor designs have been developed in an attempt to combat this problem, but only a few have been used at large-scale, and information available about their performance is increasing in the form of original research articles as well as review. Durand [21] has given relevant information on various designs of bioreactor for SSF. Review on modeling in SSF has thrown light on various designs which could solve the major problem of heat and mass transfer [17].

**Table 1**
Bioprocesses and products development in solid-state fermentation.

| Microorganism/biocatalyst | Substrate | Product | Type of bioreactor | References |
|---|---|---|---|---|
| *Aspergillus niger* | Buckweed seed | Spores | Packed bed column | [36] |
| *A. niger* | Cassava bagasse | Citric acid | Column fermenter | [47] |
| *Aspergillus oryzae* | Wheat bran + coconut oil cake (3:1) | Neutral metalloprotease | Static flask | [32] |
| *Bacillus amyloliquefaciens* ATCC 23842 | Groundnut oil cake + wheat bran (1:1, w/w) | Alpha amylase | Static flask | [39] |
| *Bacillus subtilis* | Rice bran | Iturin A | Tray | [48] |
| *Bacillus thuringiensis* | Wheat bran and bean cake powder | Bt wet powder | Cylindrical steel container | [10] |
| *Lactobacillus delbrueckii* | Cassava bagasse | Lactic acid | Static flask | [46] |
| *Lactobacillus* sp. | Tamarind seed powder | Tannase | Static flask | [9] |
| *Monascus purpureus* | Jack fruit seed | Pigment | Static flask | [50] |
| *Mortierella alpina* | Rice bran | Polyunsaturated fatty acid | Column reactor | [49] |
| *Penicillium simplicissimum* | Soybean cake | Lipase | Static flask | [45] |
| *Penicillium simplicissimum* | Olive oil cake + sugarcane bagasse (1:1, w/w) | Lipase | Fixed bed reactor | [40] |
| *Rhizopus oryzae* NRRL 1891 | Coconut oil cake + sesame oil cake (1:1, w/w) | Phytase | Static flask | [43] |
| *Streptomyces griseoloalbus* | Soya-bean floor | Alpha galactosidases | Static flask | [38] |
| *Streptomyces clavuligerus* | Wheat rawa with cotton seed cake and sunflower cake | Cephamycin C | Static flask | [51] |
| *Thermoascus auranticus* | Wheat straw | Cellulase | Perforated drum bioreactor | [37] |
| *Trichoderma reesei* | Wheat bran | Cellulase | Static flask | [41] |
| *Trichoderma harzianum* TUBF 927 | Colloidal chitin | Chitobiase | Static flask | [33] |
| *Zygosaccharomyces rouxii* 2547 NRRL-Y | Sesame oil cake | L-Glutaminase | Static flask | [34] |
| Lipase from *Rhizomucor miehei* | – | Hexyl laurate | Packed-bed bioreactor | [52] |
| *Erwinia* sp. | Sucrose + free and calcium alginate immobilized cells | Palatinose | Packed bed reactor | [53] |
| Microbial biofilm developed without prior inoculation | Clay beads + glucose-based synthetic wastewater | Organic acids and hydrogen | Horizontal packed-bed bioreactor | [58] |
| Lipase producing *Rhizopus oryzae* | Cuboidal polyurethane foam biomass support particles | Bio-diesel fuel | Packed-bed reactor | [56] |
| Hydrogen producing sludge | Carbohydrate substrates enriched polyethylene–octane elastomer immobilized anaerobic sludge | Hydrogen and ethanol | Fluidized-bed and packed-bed reactor | [57] |
| *Clostridium tyrobutyricum JM1* | Polyurethane foam enriched with glucose medium | Biological hydrogen | Fixed-bed bioreactor | [59] |

Evaporative cooling has been incorporated for large scale operation of rotating drum bioreactor (RDB). The mass transfer coefficient for evaporation from the bran bed to the head space has been determined by measuring outlet water vapour concentrations for a RDB containing wet wheat bran [22]. Sangsurasak and Mitchell [23] suggested that evaporation can remove as much as 78% of the heat from the bed during the time of peak heat generation, even when bed is aerated with saturated air. This is due to the increase of water vapor pressure at increasing temperature. It results in large moisture losses and drying of the solid. A new generation of small reactors was developed by an INRA-team in France. Such reactors have a working volume of about 1 l, a relative humidity probe, a cooling coil on the air circuit and a heating cover for the vessel. Each reactor is automatically controlled by a computer [24]. A novel bioreactor with two dynamic changes of air (including air pressure pulsation and internal circulation) can increase mass and heat transfers, as well as improve the porosity within the substrate. The reactor can be significant in exploiting numerous socioeconomic advantages of solid-state fermentation [25].

Continuous processes are emerging in SSF like SmF, making it economically viable. There have been reports on development of continuous SSF process for the production of fungal tannase. A laboratory scale prototype reactor, with the specific aim in operating continuously with solid substrates and without inoculation of the feed was built and monitored successfully [26]. Various bioreactor designs and their use for protein production under solid state fermentation (SSF) conditions using various agricultural by-products have been discussed along with their advantages and disadvantages [27]. Various products by different microorganisms employing different agro-industrial residues, using different reactors have been enlisted in Table 1.

### 4.2. Modeling in SSF

The concept of modeling in SSF is the search for mathematical expressions that represent the system under consideration. These expressions have the objective to establish the relationships or functions between two different variables that characterize the system. This is to ascertain the validity of the system, to establish different parameters that characterize a particular process, and to find appropriate mechanisms for development and control of the process [20].

Modeling of bioreactors employed in SSF processes can play a crucial role in the analysis, design and development of bioprocesses based on the phenomena; which encompass a variety of applications ranging from the production of enzymes to the treatment of agro-industrial residues. It can significantly reduce the number of wet experiments, which in turn saves time. Modeling in SSF has been playing major role to solve the problem of mass and heat transfer [22]. A mathematical model has been developed for a packed bed SSF bioreactor employing the N-tanks in series approach, used to analyze production of protease by *A. niger* [28]. Another simple mathematical model has been used by Khanahmadia et al. [14], to quantify performance of continuous solid-state bioreactors having two different solid substrate flow patterns, plug flow and completely mixed flow, where plug flow shown to have superior performance when high product concentration is needed. Hamidi-Esfahani et al. [29], has investigated modeling and optimization of simultaneous influence of temperature and moisture on microbial growth through a quantitative description. A model has been analyzed, for the effect of microbial biomass on the isotherm of the fermenting solids in SSF [30]. Existing models of SSF processes describe coupled substrate conversion and diffusion and the consequent microbial growth neglecting many of the significant phenomena that are known to influence SSF. As a result, available models fail to explain the generation of numerous products that form during any SSF process and the outcome of the process in terms of the characteristics of the final product. Important issues that need to be resolved for improved modeling of SSF have been discussed in a review by Rahardjo et al. [31].

Information regarding modeling in SSF has been limited due to unavailability of suitable method for direct measurement of growth of microorganism due to difficulty to separate microorganism from the substrate and determination of rate of substrate utilization. Among the several approaches to tackle this problem, an important one has been to use a synthetic model substrate. It is well known that the fermentation kinetics is extremely sensitive to the variation in ambient and internal gas compositions. So, the cellular growth of the micro-organisms can be determined by measuring the change in gaseous compositions inside the bioreactor.

The importance of models in SSF, as in any chemical or biochemical process lies in the facts that they allow the establishment of the parameter values that explain a particular process, the basis to evaluate the process, including economically, the way in which a process could be scaled-up, and, the design and control criteria. The developments of models in SSF focused the following main problems: (i) the representation of the microbial activity (kinetic patterns and thermodynamic concerns), (ii) studies of the problems of heat and mass transfer in the solid systems, (iii) the connection between the two above systems and (iv) the selection of the best type of the fermenter.

## 5. Choice of SSF

Japan has been using SSF for commercial production of enzymes. They use SSF for the production of soya sauce, which is also termed as “koji” fermentation. Amylase and protease are mainly produced during growth phase of *Aspergillus oryzae* on roasted cracked soyabeans and wheat, which are then utilized to hydrolyze the substrate completely. Therefore, Japan has a lot of credibility in this field and is a leading supplier of SSF equipment for the soya sauce industry as they continue to be innovative in their designs [32].

## 6. Applications of SSF

In industrial applications solid-state fermentation can be utilized in a controlled way to produce the desired product. Development of bioprocesses, such as bioremediation and biodegradation of hazardous compounds, biological detoxification of agro-industrial residues, bioconversion of biomass, biotransformation of crop-residues for nutritional enrichment, biopulping, and production of value-added products, such as biologically active secondary metabolites, including antibiotics, alkaloids, plant growth factors, enzymes, organic acids, biopesticides, including mycopesticides and bioherbicides, biosurfactants, biofuel, aroma compounds, etc. have witnessed unprecedented growth of SSF. Misinterpreted ‘low-technology’ system; appear to be a promising one for the production of value-added ‘low volume-high cost’ products such as biopharmaceuticals. SSF processes offer potential advantages in bioremediation and biological detoxification of hazardous and toxic compounds [33]. Enzymes such as, phytase, amylase, inulinase, cellulase, protease, alpha-galactosidase, lipase, tannase, laccase, chitinase, L-glutaminase, lipase [34–47] organic acid, such as, lactic acid, citric acid and bio-ethanol, antibiotic such as cephamycin C and other metabolites as polyunsaturated acid, iturin A, pigment, hexyl laureate, palatinose, and also spores, have been successfully produced employing SSF [48–54]. Spores are designated as small

reservoirs of metabolites and can be used as biocatalyst for bioconversion reactions, also as biocontrol agents. Spores production is the only process where SSF dominates over SmF in all aspects such as, better yield, morphology, high stability and various other properties [55].

Biorefineries has added more value to SSF, as biomass is the only foreseeable source of energy to meet needs of the future generation, which adds to the importance of agro-residual waste [56,57]. Cellulase production by SSF using agro-industrial residues for bio-fuel applications is in great demand. Employing packed bed, anaerobic packed bed and fluidized bioreactor, production of hydrogen, organic acids, ethanol and bio-diesel has been successfully materialized using either solid substrate or solid support [58–61]. Table 1 shows various products ranging from enzymes for food industries to pharmaceutical grades, obtained by SSF employing various bioreactors.

Bioremediation is again a very important aspect where SSF has proved its credibility. Various bioreactors have been employed to detoxify hazardous chemicals as well as to decolorize synthetic dyes which are major chemical pollutants of the present environment. Research articles are available which shows potential of SSF for example; to decolorize a synthetic dye (congo red), a continuous decolorization system rice hull-*Schizophyllum* sp. in a packed-bed bioreactor has been successfully employed [62] also the anerobic decolourisation of azo dye Acid Orange (AO7) was studied in a continuous upflow stirred packed-bed reactor (USPBR) filled with biological activated carbon (BAC) [63]. A bench-scale packed-bed bioreactor equipped with a net draft tube riser for liquid circulation and oxygenation (PB-ALR) has been constructed for the aerobic biodegradation of the fungicide and defoliant 2,4,6-trichlorophenol (2,4,6-TCP) [64]. Cells of *Methylibium petroleiphilum* PM1 were immobilized in gel beads to degrade methyl *tert*-butyl ether (MTBE) [65]. Thus there is hardly any bioprocess untouched by SSF.

## 7. Conclusions

The past few years have seen significant developments in SSF technology. Due to the continuous efforts in the areas of biochemical engineering such as modeling aspects and bioreactor design, SSF is on the way to commercialization even for processes which were earlier thought feasible only for SmF. It has been found economically viable for various processes, including pharmaceutical products. Still, continuous efforts are needed in the direction of automation of the process, which could prove it equally efficient to SmF.

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