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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
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United Nations Industrial Development Organization

# FERMENTATION PLANTS AND EQUIPMENT [1]

by

Elmer L. Gaden, Jr.
Professor
Colombia University
New York
United States of America

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United Nations Industrial Development Organization

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SUMMARY

# FERMENTATION PLANTS AND EQUIPMENT 1/

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Elmer L. Gaden, Jr.
Professor
Columbia University
New York
United States of America

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# INTRODUCTION

Fermentation technology appears to be about to undergo its first substantial expansion in many years. The prospects for large-scale production of microbial protein are excellent and the manufacture of enzyme products is already accelerating. We should therefore be able to look forward to the construction of a number of new fermentation plants and to increases in the capacities of many old ones. If these expectations come to pass, engineers responsible for design of the new facilities will face a variety of intriguing problems for which past experience and current practice offer little guidance.

The diversity which we see in the products of fermentation technology tends to conceal the uniformity which prevades the design of equipment and plants for producing these materials. In terms of current facilities there are only two types of fermentation processes. The first comprises biomass production by the propagation of cells in a highly aerated medium under conditions which can only be called "aseptic" - or perhaps simply "clean". Yeast manufacture dominates this class. In contrast a wide variety of cell metabolites are produced in media which require both intense agitation and aeration and the maintenance of much more rigorous conditions which we normally term "pure culture". Antibiotics, citric acid, and many of the enzymes and growth factors are examples.

Neither of these process-types has benefited much from the modern practice of chemical engineering. Yeast production techniques were well established long before the chemical engineer was conceived and born. Aside from some contributions to a better understanding of the mechanism of oxygen supply, he has made little impact here. Deep tank processes for antibiotics, enzymes and organic acids were developed much more recently and engineering has been involved from the start. Even so, the arts of microbial process,

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equipment, and plant design have advanced very little in the last two decades. Except for their larger capacities (thanks mainly to improvements in the mechanical design of agitation equipment) and some details of valving, air filters, etc., fermentors installed in the last year show little that is different from their ancestors of the 1945-50 period. Indeed, the older units are working away beside the newcomers and still provide the bulk of fermentation capacity in many plants. This failure to develop design methods for microbial processes is understandable; the industry simply has not generated the demand. Nevertheless, we face the prospect of being called upon to design a wide variety of new facilities with a set of concepts and methods which are outmoded and inefficient. Two facts are especially significant in this respect.

First, any new facilties for microbial protein and enzyme production will have to measure up to standards of economy which simply did not apply when many of the existing fermentation plants were built. Most capital cost items and many elements of operating cost are extremely sensitive to design decisions and it will be necessary to introduce every possible saving in these areas.

The second factor is the one which underlies this very meeting. If microbial technology is to provide benefits to the economies and societies of developing areas, it must be suited to their needs and technical resources. Many design considerations operating in developed areas are absent or less important while others become much more critical. In the discussion which follows a number of specific illustrations will be cited to support this contention.

## MICROBIAL PROCESSES FROM THE DESIGN STANDPOINT

Before we consider the aspects of microbial processes which are of special significance to the designer of equipment and plants we ought to define what we are talking about. The term microbial processes is used here to denote chemical processes carried out in the presence of metabolically active cells of microorganisms.

This is obviously a practical definition rather than a theoretical one and it omits, for the purposes of this discussion, chemical transformations brought about by cell-free extracts, purified enzymes, etc. The future potential of these techniques is very great indeed but the design problems are both simpler and more akin to conventional chemical reactions. Our "practical" definition also fails to include processes catalyzed by plant and animal tissues, simply because the prospects for their commercial use are still quite remote.

Microbial process types

We can recognize three broad classes of microbial processes in terms of the objectives for which they are carried out. The first of these is the production of cell tissue (biomass) itself. Yeast propagation for food and feed is the classic case - and almost the only one of significance. Now the preparation of a much greater variety of microbial cells for their protein values is at hand. Biomass production seems certain to comprise a substantially greater fraction of the total output of fermentation technology in the years ahead.

Second, and most significant in economic value, is the production of metabolites elaborated by the cells as they grow. Some of these arise from biosynthetic activities; others are end or intermediate products of carbohydrate oxidation. Examples are (1) citric acid, (2) amino acids, (3) growth factors, (4) enzymes, and (5) antibiotics.

The third class of microbial process is more difficult to define. It includes those processes in which the cells are used to bring about a limited and often simple chemical change in the substrate. Microbial transformation of steroids is an excellent example but the production of gluconic acid by the oxidation of glucose is an equally valid one.

It is true that we could consider this type of process to be only a variant of the second (metabolite) category. Still there is a difference. In this case only a limited number of the cell's enzymes are being used - perhaps only one. In a real sense this kind of process approximates a simple enzymatic conversion in which we have neglected to remove the cells.

Physical forms

Of much greater importance to the designer is the physical form of the microbial process with which he must deal. Figure 1 summarizes the range of physical situations which are encountered. Media may be fluid or solid - and here again the distinction is a very practical one. "Fluid" media are those readily moved by conventional pumps, "solid" media are the rest.

Most commercially significant processes today (except for alcoholic beverage manufacture) are aerobic and oxygen must be supplied. This can be done in various ways all of which lead to an impressive and often confusing spectrum of specific apparatus.

Operational modes

Finally microbial processes may be carried out in a variety of operational modes. Batch processes exhibit inherent unsteady-state behavior and do not provide for efficient utilization of available equipment. On the other hand they are well suited to the production of a wide range of products each in limited amounts. Since this pattern is generally typical of current fermentation technology, batch processes predominate.

In theory continuous processing offers economic incentives and operational advantages over batch methods yet it is little used in microbial technology. Feed yeast production is the only significant example. Again, a relatively large product requirement is necessary if the theoretical advantages of continuous processing are to be realised in practice. Microbial technology has seldom provided this in the past but the new microbial protein processes will make continuous operation obligatory.

A point which often seems to be lost in discussions of continuous cultivation is the fact that very few - if any - chemical process operations are truly continuous. Even a large petroleum refinery, often considered to be the epitome of continuous, steady state operation, is not. Parts of it are shut down from time to time and an overall approximation of continuity is only achieved through the judicious use of large volumes of intermediate storage tanks.

It is quite possible that the adoption of continuous methods in fermentation technology would be hastened if its advocates and developers would aim at steady-state operation for periods of 30-60 days at most. Even shorter periods would offer real economic incentives. Deliberate shutdown to permit preventive maintenance and reinoculation would avoid or mitigate many of the technical difficulties, especially contamination and culture degeneration, which are feared

Aseptic operation

A design constraint unique to microbial processes is the requirement for aseptic, or "pure culture" operation. This means that the process system should be free of all microorganisms except the chosen agent which we have deliberately introduced. Since absolute freedom from extraneous organisms is difficult to achieve in plant operation a more practical standard of asepsis is in order. We can say that operation is satisfactory when the population of extraneous organisms is kept so low as not to: (1) interfere with the formation of desired products or their subsequent recovery,

(2) cause significant loss of these products once formed or (3) bring about an unacceptable level of foreign contamination in the final product.

In the case of metabolite-type processes, the first two criteria are the most important for the final product is ordinarily isolated from the broth by complex chemical procedures which effectively eliminate any contaminants. For microbial protein production, however, the third criterion may well be the most important. It is conceivable that a trace of some undesirable contaminant too small to impede successful propagation could still render the product unacceptable for food use.

## PROCESS SYSTEMS

Microbial processes exhibit a common process sequence which is summarized in Figure 2. The first step is substrate preparation (or pretreatment) in order to make the primary carbon source available to the microorganism. Next the primary substrate is combined with other ingredients - nitrogen source, minerals, growth factors - in a balanced medium which is then sterilized. This medium is then inoculated (or seeded) with the desired organism in more or less pure culture and the conversion (or reaction) phase ensues. Next, cells are separated from the spent medium and, finally, products are recovered from either the medium, the cells or both.

Regardless of the type of organism and medium employed or the operational form, this basic process scheme appears in all fermentation processes. Sometimes the first step is unnecessary because the carbon source in the raw material is already biologically available (corn sugar, sucrose in molasses, etc.). Still, in the case of molasses and many other raw materials, some pretreatment may be needed for other reasons; removal of inhibitory cations, colloidal matter, etc., for instance. It may also be possible to eliminate the final step but this is rare. For example, some crude animal feed components are prepared by simple spray-drying the complete broth, organisms included, at the end of the reaction phase.

### The batch process

Most industrial fermentation processes today are carried out in the batch manner. The only substantial exception to this is the manufacture of yeast, especially feed yeast, which is ordinarily a continuous operation. Batch processes are inherently unsteady state, some or all of the process variables change with time. As a result, productivity is not constant and the average output of such a process is always less than the maximum output. A schematic diagram representing the various phases of a typical batch process is given

in Figure 3.

Productivity, the average rate of production of the unit, is reduced in batch fermentation processes because of the lag which occurs after inoculation but also because of the time required for "turnover" (emptying, cleaning, and servicing) of the unit and preparation for the new batch. Good scheduling and a well-organized reduces turnover time but there are inherent difficulties if the plant is making a variety of products utilizing different media and requiring different batch times. It is sometimes impossible not to have fermentors idle for periods longer than needed for turnover. Continuous sterilization also helps, as we shall see, by reducing the batching and sterilization time. It too is limited by the total plant operation, however. If, as is so often the case, many products, each in relatively small volume, are manufactured, continuous sterilization is not practical.

## REACTOR SYSTEMS

The fermentation reactor - or fermentor - has been the subject of most of the attention so far given to the design of microbial process equipment. This is entirely fitting because in this one unit, most of the activities which uniquely characterize fermentation take place - either by intent or accident. Here the microorganisms grow and bring about product formation and it is here that the process is most susceptible to contamination.

Because of the economic dominance of aerobic, deep-tank processes, aeration and agitation of the reaction mixture (organisms plus medium) has been examined in great detail. Heat transfer, on the other hand, has received little attention. It has not ordinarily been a problem in conventional fermentation processes carried out in temperate climates. Microbial protein production from non-carbohydrate substrates releases heat at substantially higher rates, however, and the removal of this heat of reaction imposes a new and significant burden on fermentor design. In tropical or semi-tropical climates it will surely be the most critical factor.

The primary factors which affect the choice of the basic reaction configuration for any fermentation process are these:

(1) Is the process to be batch or continuous?
(2) Is the fermentation "reaction" rapid or slow?
(3) Is the oxygen demand very high, moderate, or low?
(4) Is there a heat removal problem?
(5) What are the physical characteristics of the cell-medium mixture and how do they change as the fermentation proceeds?

Figure 1, summarizing the various physical forms which microbial processes may take is also a useful guide to the reactor systems which have been or could be employed. These are also enumerated

in Figure 1.

Anaerobic processes

Anaerobic processes using fluid media are, of course, rare today. (NOTE: Anaerobic digestion is very important in biological waste treatment but this area is not being covered here.) The traditional anaerobic processes (ethanol, butanol, etc.) rarely used any form of mechanical agitation since the gas bubbles arising from fermentation were sufficient to keep the medium well mixed. Heat removal, more than blending of the reaction mixture, can easily limit the rate of an anaerobic process so mechanical agitation might be required in large-volume fermentors. A useful alternative in such cases would be pumping of the medium through an external heat exchanger.

Aerobic processes

Aerobic processes, as we have noted, dominate fermentation technology today. Within this broad classification, however, oxygen requirements vary markedly as do the other process variables - especially medium properties - which affect the efficiency of oxygen absorption. Consequently a wide spectrum of equipment types for aerobic processes has developed. Some of these have found little commercial application; others are widely used.

Tray fermentations - citric acid is the best known example - are mentioned simply because they exist. It is difficult to conceive of any new situation in which a static pan process would be used commercially. Indeed, the nature of current fermentation process development techniques virtually rule them out. Agitated (shaken flask) cultures are used from the start in practically all laboratory work today.

Drum fermentors

Fermentors consisting of horizontal cylinders rotating on their axes were introduced for a number of processes many years ago. They have

been used with liquid media (gluconic acid) and solid (amylolytic enzymes). The contents, liquid or wet solids, are tumbled over and over through the atmosphere of air (sometimes enriched with oxygen) which passes through the chamber.

These drum units can be very effective aeration devices. Indeed, it was the high oxygen requirement of the A. niger gluconic acid fermentation which caused them to be developed in the first place. Conventional aerators used in yeast production were unsuitable for the viscous mixture which resulted from growth of the mold. Since deep-tank processes had not been well developed at the time, the drum system proved reasonably satisfactory. With the advent of penicillin, however, deep-tank methods were rapidly advanced and soon replaced drum fermentors in most applications. The critical weaknesses of the drum-type unit are:

(1) increasing mechanical problems in rotating the drum as capacity goes up.
(2) poor control of temperature
(3) difficulties in controlling other process variables, pH for example.

Despite these problems, investigators have shown renewed interest in drum-type units in recent years. Once again it is their relatively high aeration efficiency that attracts. Also there is the possibility of carrying out multistage continuous processes within a single vessel wall. In any case, all the recent drum fermentor proposals have avoided the main operational problem - rotation of the drum - by substituting mechanical agitation with multiple blades, discs, etc., mounted on a horizontal shaft (Figure 4). Since it is also possible to achieve the same objectives in a tower-type fermenter, especially where continuous processing is employed, the prospects for commercial development of drum-type units are not good.

## Deep tank fermentors

In terms of total volume in operation, tank-type reactors are certainly the most common. Again because aerobic processes are so important, most of these units employ forced aeration and mechanical agitation. The few continuous processes in operation (mainly feed yeast plants) also employ aerated, agitated tank systems. The only difference between these and standard batch units is that specialized, patented aeration-agitation systems are often employed.

A typical tank fermentor is shown in Figure 5. Agitation is provided by standard flat-bladed turbine agitators (up to three in larger capacity vessels). Air is introduced through a sparger located beneath the lowest turbine and heat transfer surface in the form of internal coils, an external jacket, or both, is provided. Inoculation, sampling, and medium addition ports, exhaust lines and control devices are installed according to the experience and specific requirements of the operation.

Experience has shown us that the critical factors in the selection of a specific design for a tank-type fermentor are:

(1) the oxygen requirement for maximum productivity
(2) physical properties of the cell-medium mixture.

The variety of specific design configurations which can be used for deep-tank processes is summarized in Figure 6.

### Low viscosity processes

Elements which lead to a "low-viscosity" environment are:

(1) an organism which grows individually or in small aggregates (clumps or chains) only
(2) a medium containing only soluble materials with little or no suspended solids
(3) soluble products of low molecular weight.

Yeast propagation on molasses or microbial protein production from hydrocarbons are typical.

In such processes oxygen absorption is the primary concern. Mechanical agitation is therefore introduced only (1) to enhance gas-liquid contact and oxygen absorption or (2) to ensure uniformity of the reactor contents (blending). Since this blending requirement is ordinarily significant only in very large vessels, reactors for low-viscosity processes often have gas-spargers only, without mechanical agitation.

A wide variety of sparger designs have been employed in order to produce fine bubbles of air. In general it is desirable to disperse the air in this way when mechanical agitation is not used. Pipes or discs drilled with a large number of small holes are the simplest and usually the most satisfactory performers. Spargers made up of fritted metals and ceramic materials show a tendency to become clogged by filamentous organisms but are adequate for other types. Their greatest drawback is the relatively high pressure drops which they introduce.

"Sonic" nozzles are designed to operate with a sufficiently high pressure difference so that the air velocity through the nozzle reaches its maximum possible value, the velocity of sound. Such a device not only produces fine bubbles but is also capable of delivering a modest level of mechanical energy (power) to the medium. In practice, however, the power delivered is too little to be significant if mixing is really a problem; mechanical agitation should be used. If mechanical mixing is not necessary then sonic nozzles are a very expensive way of producing fine bubbles.

The airlift fermentor has received considerable interest recently in connection with microbial protein studies. Preliminary studies with laboratory and pilot-scale units (Figure 7) indicate that air-lift units can be much more efficient aerators, in terms of oxygen

absorbed per unit of power expended, than mechanically agitated tanks. This advantage will only be found in low-viscosity media of course, but as this is the case for most microbial protein proposals, the prospects for this type of fermentor are good.

External circulation

External circulation devices have been proposed many times but seldom used. Heat transfer requirements rather than aeration or mixing are usually the basis for their design. An external heat exchanger operating under forced convection is a much more efficient heat transfer device than internal coils or a jacket. The practical limitation on external circulation units has arisen from our inability to develop circulating pumps which can operate for sufficiently long periods without causing contamination. The heat-removal problems encountered in microbial protein production are again drawing attention to this type of system.

High-viscosity processes

The ability of microbiologists to develop microbial strains capable of more and more luxuriant growth, as well as productivity, poses a serious problem for fermentor designers. A number of process situations already exist in which the cell-medium mass reaches extremely high "viscosities." In such cases, conventional turbine agitators are not capable of adequately mixing the fermentor contents and ensuring adequate air dispersion and oxygen absorption.

This problem is extremely complex but there are clearly two elements involved. First we must provide for air dispersion and subsequent dissolution of oxygen from the bubbles; second, we must ensure that the entire fermentor contents are adequately mixed (blended) so that nutrients and air bubbles are evenly distributed throughout. No single agitator design now available appears to meet both these requirements so compromises must be sought.

In turbine-agitated fermentors with low or medium viscosity media, air dispersion is ordinarily accomplished mainly by the impeller. It has been demonstrated that under these conditions sparger design matters little; the immense local shear generated by the impeller determines bubble size distribution. In high-viscosity media, however, sparger design again becomes important because the impeller is no longer as effective a dispersing device. As a result fermentors for such service are again equipped with fine-bubble spargers in place of the simple pipes, etc., which were long considered adequate.

In addition to sparger modifications, special agitators have also been designed for high viscosity media. One design which has proven useful in pilot-scale units is made up of a group of vertical bars (looking very much like an animal cage) mounted on the shaft above the main turbine. These bars ensure thorough mixing throughout the contents of the fermentor. Here again, the same difficulty has been encountered in putting this improvement into plant use. The total production of the material made in this extremely viscous process is too small to justify conversion of plant units which must also be used for other processes.

Reactors for continuous processes

Virtually all the continuous processing carried out so far have used a standard tank-type fermentor adapted for continuous addition of fresh medium and overflow of spent broth. This kind of arrangement limits the process to a single-stage conversion. Multistage systems have been set up by simply connecting several such units in series by means of pumps. Each stage is operated as a separate unit with its own systems for agitation, aeration, and control.

An alternative to this arrangement which has attracted recent attention is the tower (or column) fermentor (Figure 8). This

fermentor consists of a column divided into stages by perforated plates. Medium is fed continuously to the top chamber and the product stream is removed from the bottom. A single, central agitator shaft operates mixing blades in each stage.

This system has important advantages over the conventional multi-stage set-up. The pumps linking the units and separate systems for level control, agitation, and aeration have been eliminated. This not only means a considerable savings in investment but also reduces the possibility of contamination and malfunction.

## ASEPTIC OPERATION

As we have seen, the requirement that process equipment be operated without extraneous biological contamination is unique to microbial technology. A generally high standard of cleanliness certainly exists in the food industry but it is rarely as strict as that maintained in the so-called "pure culture" processes. It may be that fermentation practice is unduly rigorous in many cases. Here again we suffer from the fact that our introduction to modern microbial technology was the production of penicillin, a singularly labile substance. In any case, fermentation technologists have elected to hold the barriers high and bear the extra cost burdens which result.

Practical asepsis

Before outlining the methods employed to maintain "aseptic operation", the fundamental weakness of this concept must be noted. First of all, there is no reliable, quantitative method for measuring the number - or concentration - of contaminants in a process system. Secondly, individual contaminants vary widely in their potential effect. The penicillinase producer was the real enemy of the penicillin process; a potential pathogen or toxin producer is more to be feared in microbial protein production. It may well be time for fermentation technology to adopt more of the practices of the food industry and pay more attention to overall plant sanitation than to the potential contamination of individual pieces of equipment. Then it should be possible to define realistic levels of permissible contamination.

System integrity

The typical fermentation process is susceptible to contamination in many ways but the following elements are the most critical:

(1) the medium

(2) the inoculum (or seed culture) and the inoculation step

(3) the air supply

(4) addition (nutrients, antifoam, etc.) during processing

(5) the fermentor itself

Unfortunately, the lack of precise techniques for detecting contaminant origins, coupled with human prejudice and fads, has led to a number of impressions which are rarely in accord with the facts.

Typical of these is the tendency to blame the air supply system whenever massive contamination occurs. Existing air supply systems have notable weaknesses as we shall see but they also have many inherent safeguards. Indeed it is often difficult to deliberately contaminate a process unit using air alone! Far more likely candidates for blame when contamination occurs are faulty design of the reactor, especially shaft seals and fittings, and transfer techniques - inoculum, additives, etc.

Medium sterilization

Batch sterilization of medium in the fermentor is still the common practice. In this method the medium and reactor are sterilized together and no transfer of sterile medium is necessary. The presence of the medium in the tank may also aid equipment sterilization by dislodging traces of caked solids and improving heat transfer.

Arguments against batch sterilization are that it is time-consuming and often non-uniform. The first is certainly valid because the conventional fermentor (Figure 5) design is notably inefficient in heat transfer. In large volume units several hours of heating up and cooling down accompany a sterilization period of 30-60 minutes. As we have seen, this problem can be reduced by improved design of the heat transfer surfaces in a large fermentor.

The other argument against batch sterilization - non-uniformity - is much less valid. It is certainly true that medium sterilized in large vessels is usually quite different than the same medium sterilized in small batches. It should be for it has been heated a lot more. Techniques for "scaling-up" the batch sterilization process more accurately have been proposed and tested but little plant use seems to have been made of them.

More serious are the deviations in sterile medium properties from one batch to another. Assuming that raw materials are uniform - and this is a poor assumption - batch-to-batch variation is generally the result of inadequate control of the sterilization process. For example, the heat transfer surfaces in one tank may be less efficient than in another - or the steam may be wetter. In either case the total heat input to medium in order to achieve a certain nominal sterilization period will be different and different total heats ordinarily give different sterile media.

Continuous sterilization offers many advantages over batch procedures. It saves time; the tank can be sterilized empty (or with some water) quite rapidly and the addition of sterile medium only takes up the time ordinarily used for batching. Furthermore, the continuous process tends to produce media much more uniform in properties. A complete system for continuous medium sterilization is shown in Figure 9. Note the emphasis on overall heat economy.

Although many continuous sterilizers have been built and operated, they are still not used widely in production. Technical problems do exist; media containing suspended solids (soy bean meal, etc.) cause problems and may require extra heating to guarantee full sterilization. Probably the most important factor in limiting the use of continuous sterilization is, however, not specifically

technical. It is the overall organization of existing batch fermentation plants. The numbers of products involved and the size of fermentors is often such that it is uneconomical, inconvenient, or both, to operate a continuous sterilizer. Continuous sterilizers are best suited to a plant producing relatively large amounts of a few products. Again, microbial protein production and, probably, the newer enzymes are examples.

Air cleaning and sterilization

If a commercial fermentation becomes contaminated and the reason is not immediately obvious, suspicion normally falls on the air supply system. The highly aerobic processes which dominate current technology do require large volumes of air-normally about one volume per minute (at standard conditions) for every volume of liquid medium. All this air must be treated so as to kill or remove all the organisms which might enter the fermentor during the operating period.

Air sterilization system in practical use are of two types: (1) heat sterilization and (2) filtration. Systems employing heat as the only agency for air sterilization are rare today. On the other hand virtually every air supply system enjoys a degree of heat sterilization because of the heat of compression. Indeed this is one of the inherent factors noted above which operate to reduce the possibilities of contamination from the air.

Heat sterilization systems are not favored for several reasons. The easiest and surest method is to burn fuel (gas or liquid) directly in the air stream. This will, however, use up some of the oxygen and produce undesirable products of combustion, some of which will be absorbed in the medium. On the other hand, indirect heating of the air stream - the method normally used - is unreliable. Heat transfer to gases is generally poor and great variations in flow can

exist with the result that organisms, especially spores, may safely pass the sterilizer.

Air filtration (Figure 10) is the most common method for sterilizing air. Fibrous filters, mainly glass wool, are widely used. Their action is probabistic and it is only possible to design for a low probability of penetration. Membrane filters capable of retaining all particles above a certain value have never been satisfactory for industrial use because of their structural weaknesses and inability to be steam-sterilized. This is changing, however, and new polymeric membrane materials are available which are capable of retaining all but virus-type particles and can be sterilized repeatedly with steam.

In view of this possibility it is possible to recommend a wholly new approach to the air supply problem. Experience with the standard type of system shown in Figure 9 indicates that it was most likely to fail in a single instance rather than gradually. All too often the local filter would accumulate water as a result of sterilization. When the air was turned on this water, freshly inoculated with contaminants from the air stream, would be blown into the fermentor. More often the air reaching the local filter would contain suspended moisture which it cannot remove. In short, it is free liquids that we must avoid.

For this reason the air system recommended in Figure 9 places much more emphasis on overall air cleanliness and, consequently, less emphasis on the local filter. If the air reaching the local filter is truly free of suspended moisture and dirt, the local filter will be more lightly loaded and less subject to accident. Furthermore it will now be possible to use a membrane unit here since it will have to deal only with those few contaminants which survive the previous obstacles. This will give the air supply system a level of reliability never possible with fibrous, probability filters.

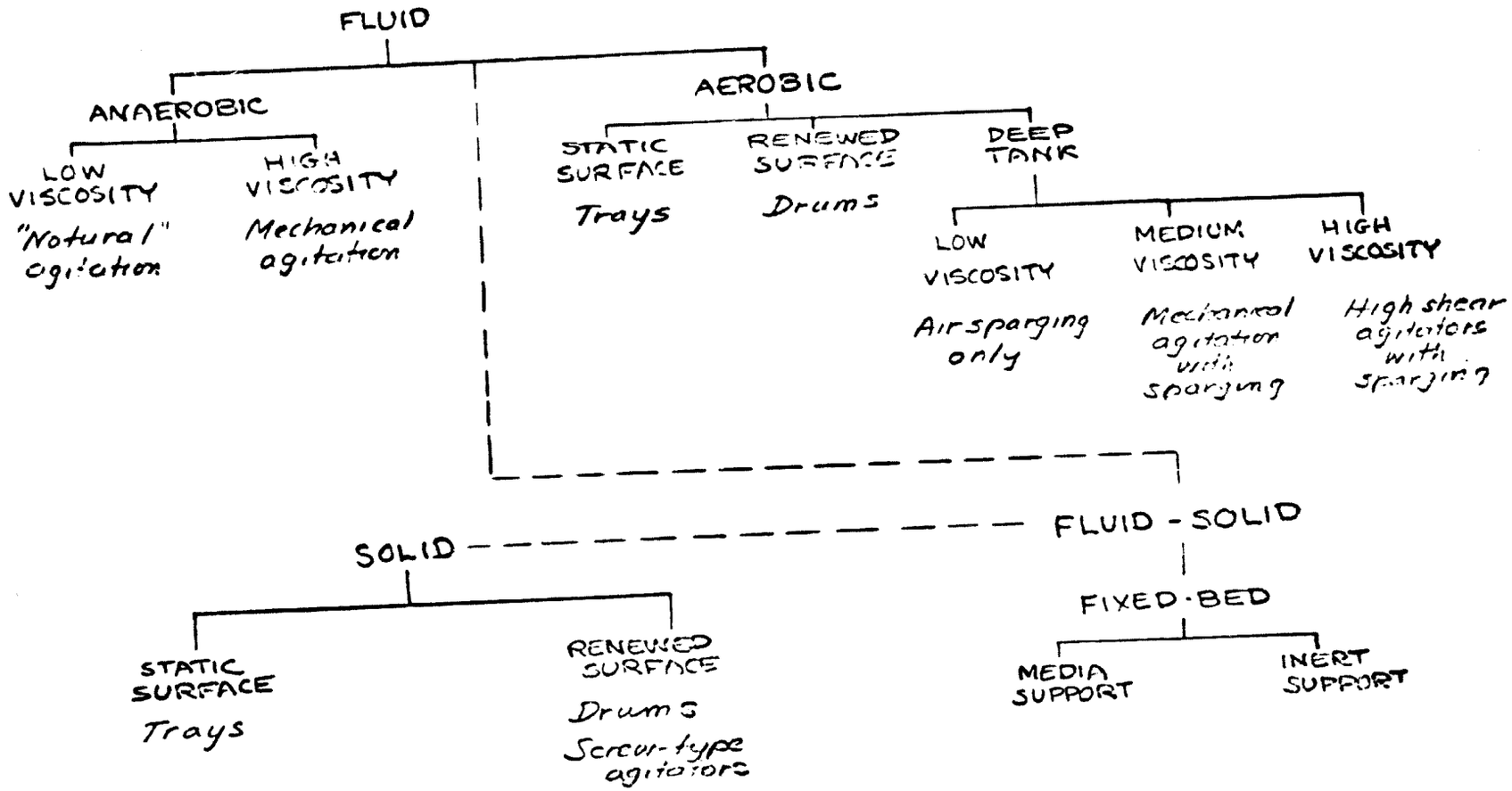



FIGURE 1

MICROBIAL PROCESS SYSTEMS
PHYSICAL FORMS

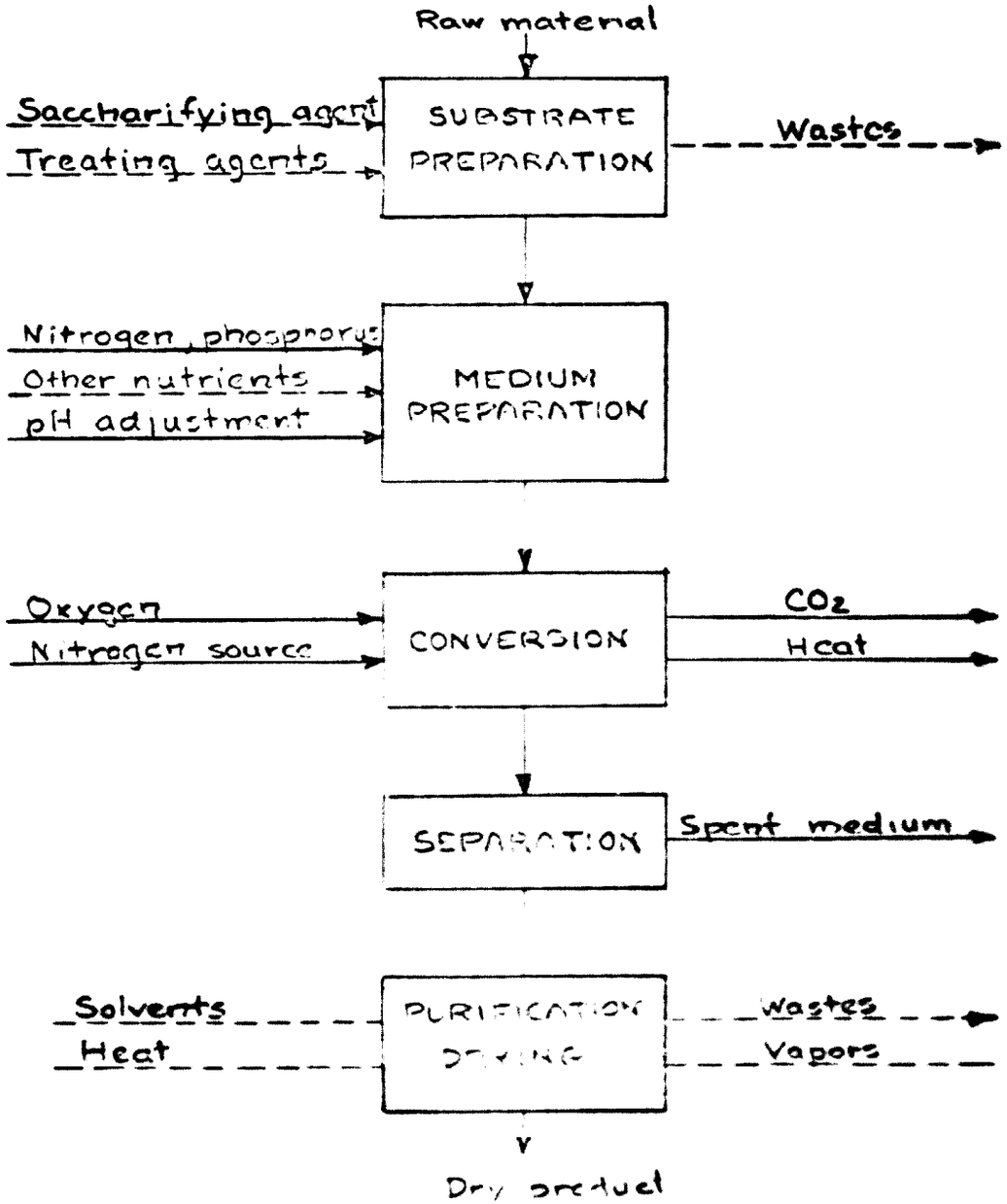

Raw material
Saccharifying agent
Treating agents
SUBSTRATE PREPARATION
Wastes
Nitrogen, phosphorus
Other nutrients
pH adjustment
MEDIUM PREPARATION
Oxygen
Nitrogen source
CONVERSION
$CO_2$
Heat
SEPARATION
Spent medium
Solvents
Heat
PURIFICATION
DRYING
Wastes
Vapors
Dry product

FIGURE 2

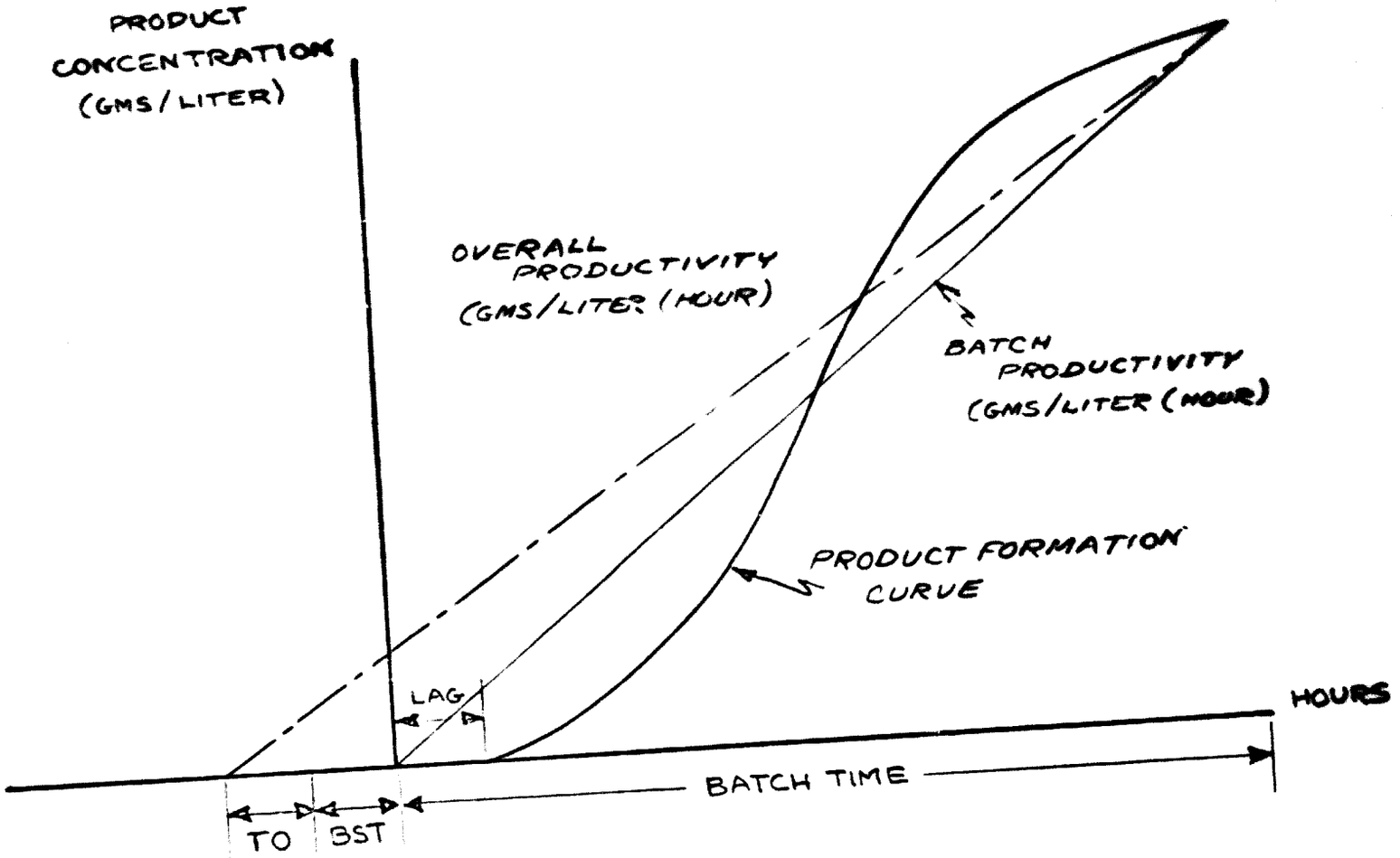
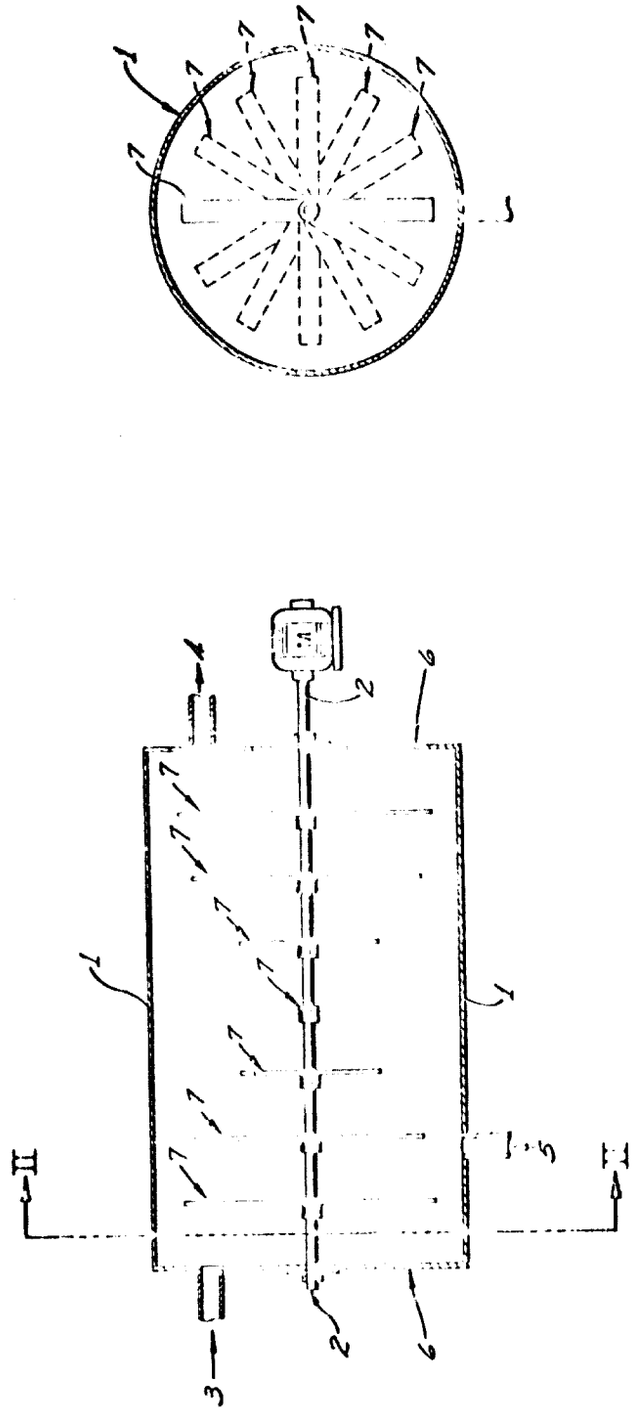



FIGURE 1

TO = "turnover" time - empty, clean, service
BST = "batching and sterilization" time

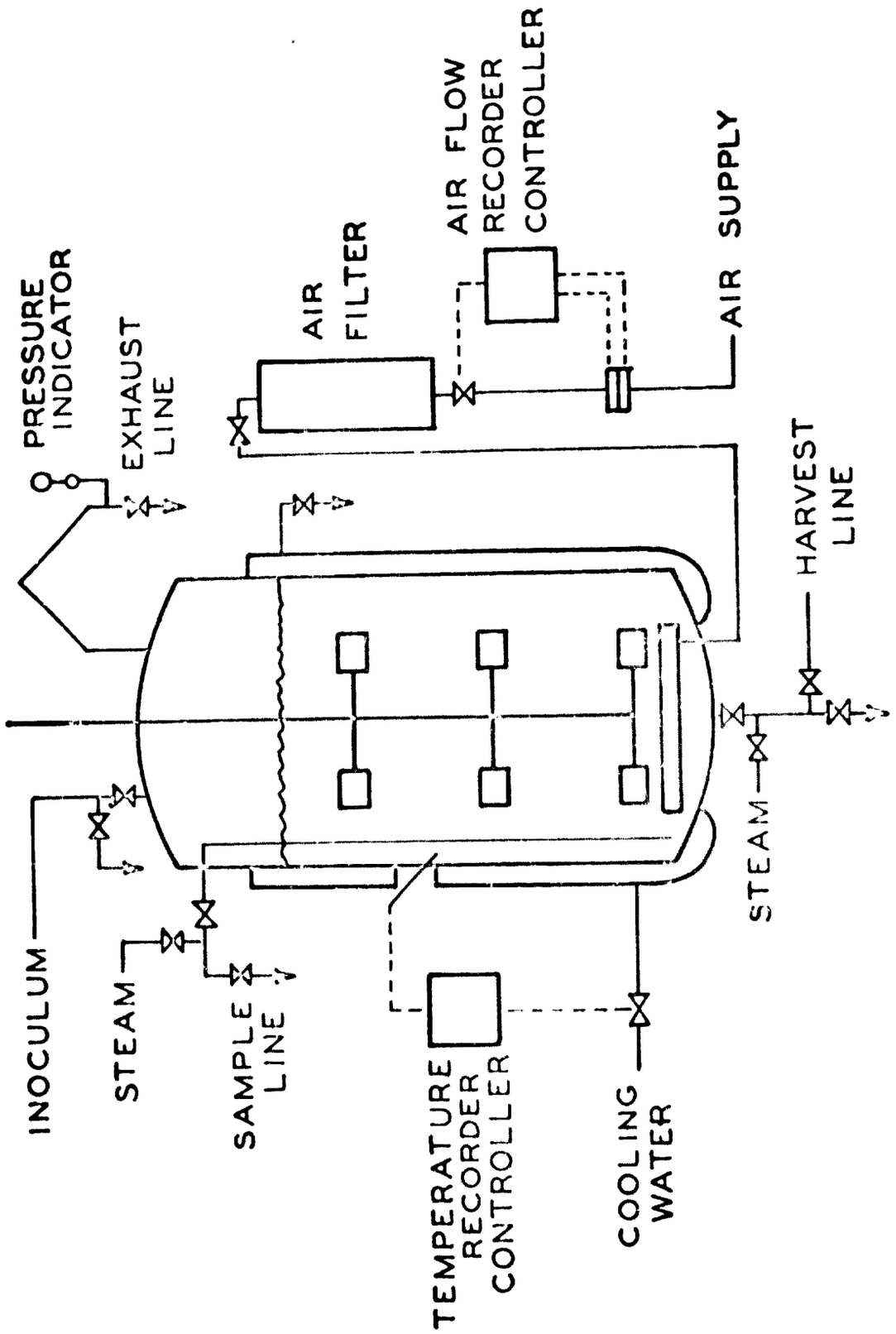
BATCH FERMENTATION PROCESS

FIGURE 4




HORIZONTAL DRUM FERMENTOR WITH MECHANICAL AGITATION

FIGURE 5




**TYPICAL FERMENTATION REACTOR CONFIGURATION**

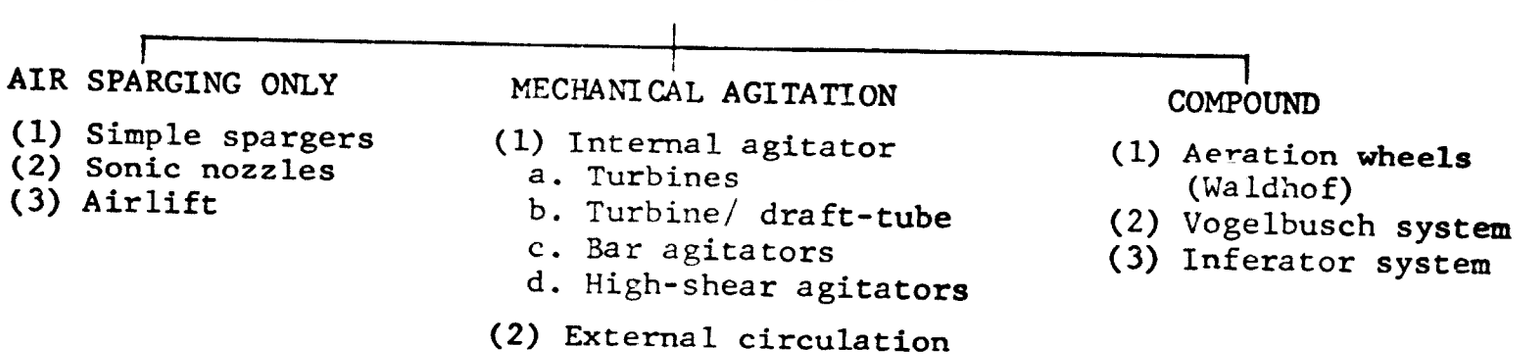
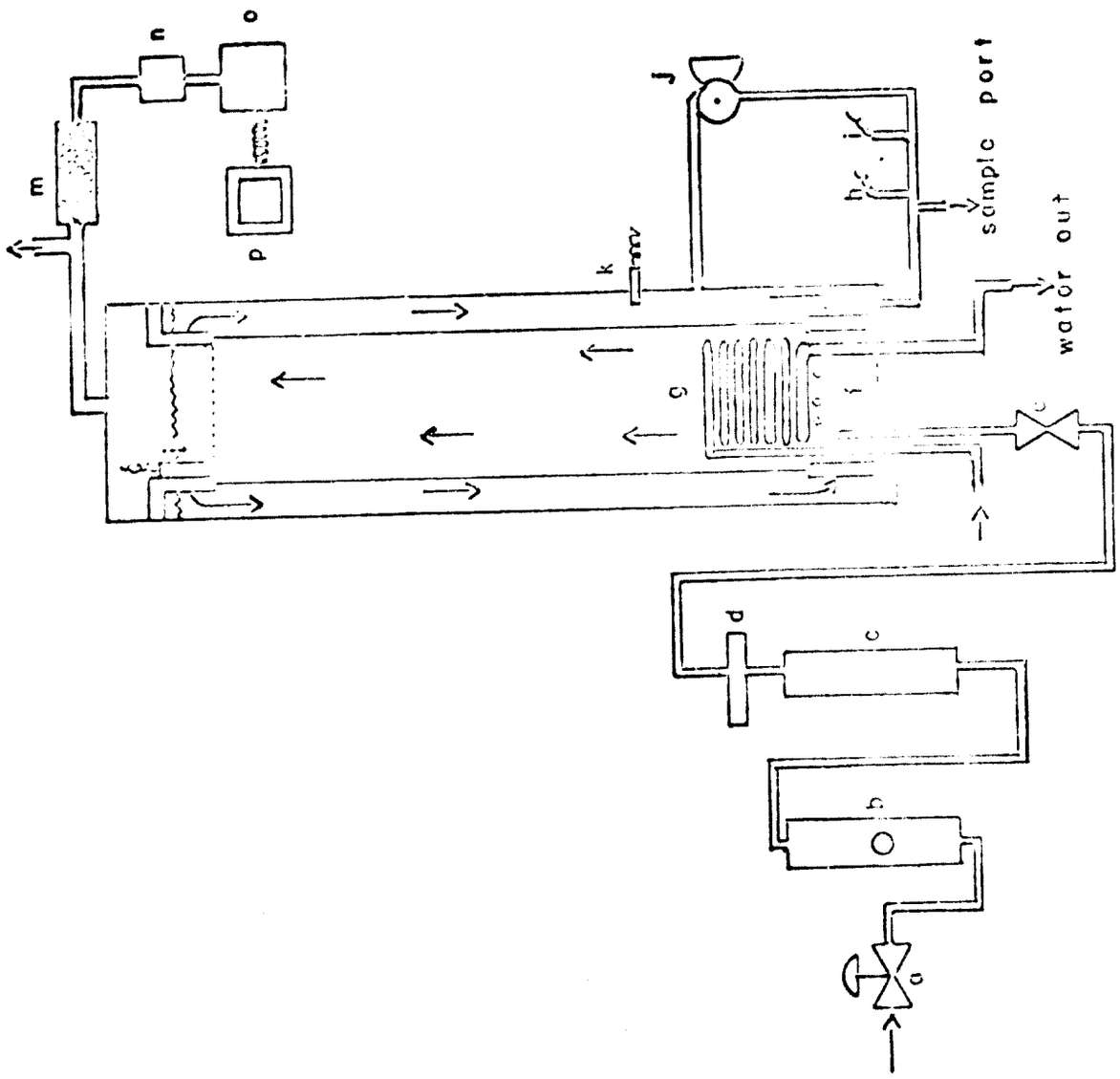



FIGURE 6

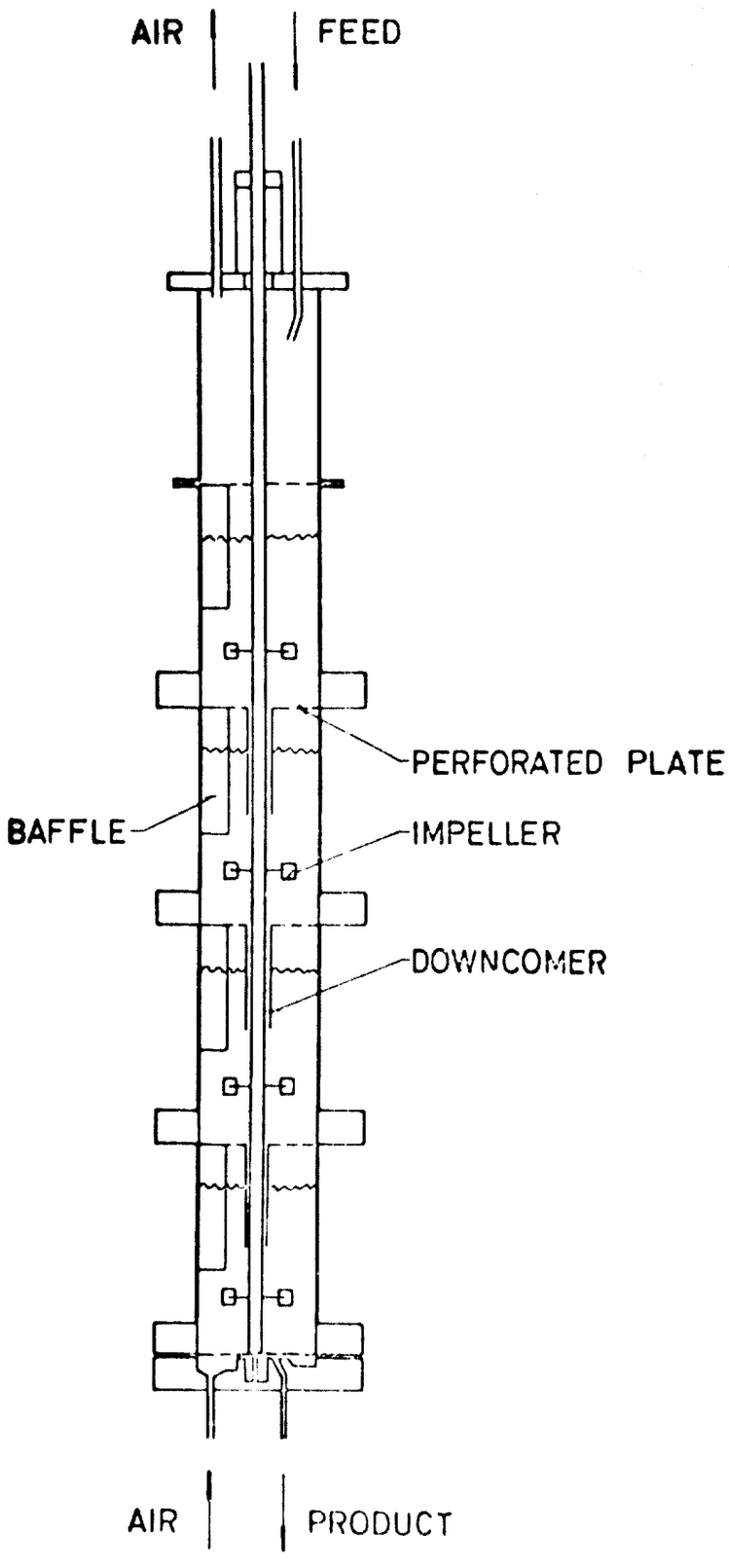
DEEP-TANK FERMENTER TYPES

FIGURE 7



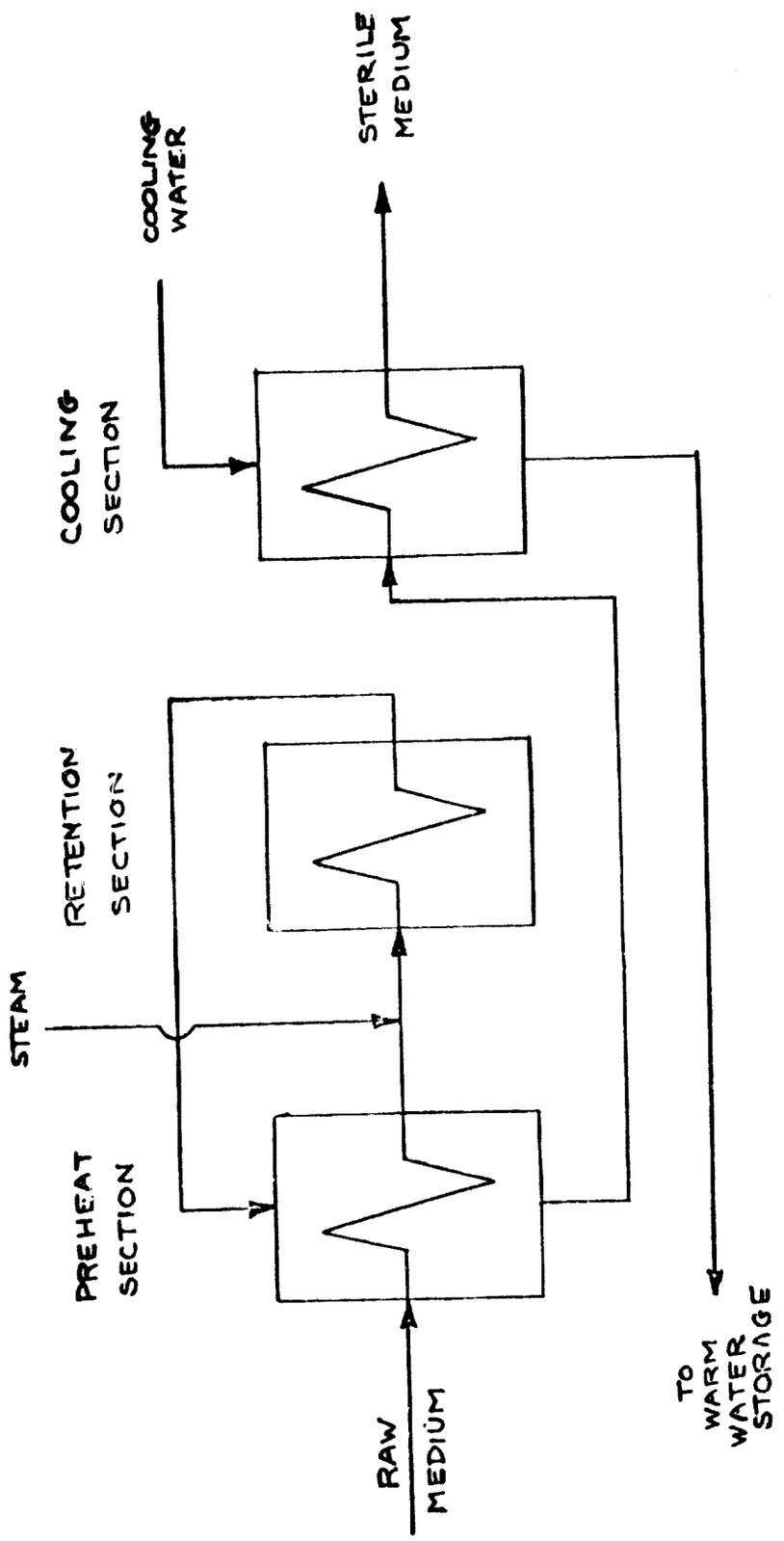

PILOT-SCALE AIRLIFT FERMENTOR

FIGURE 8



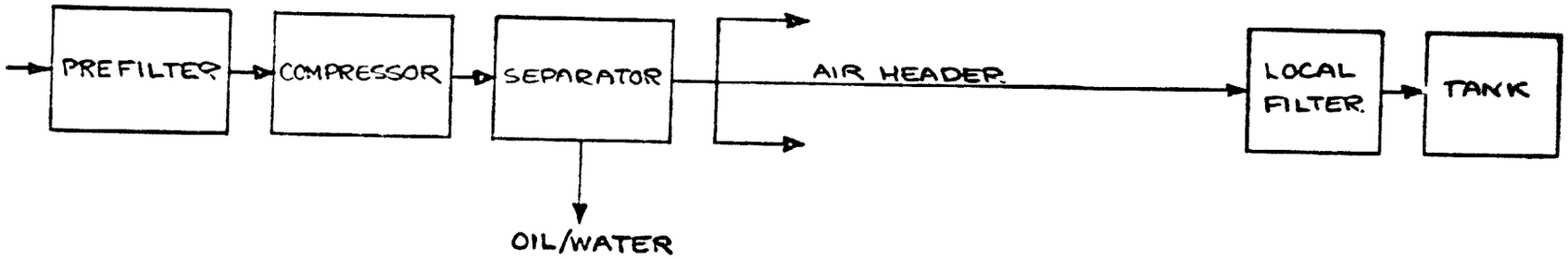

**CONTINUOUS MULTISTAGE TOWER FERMENTOR**

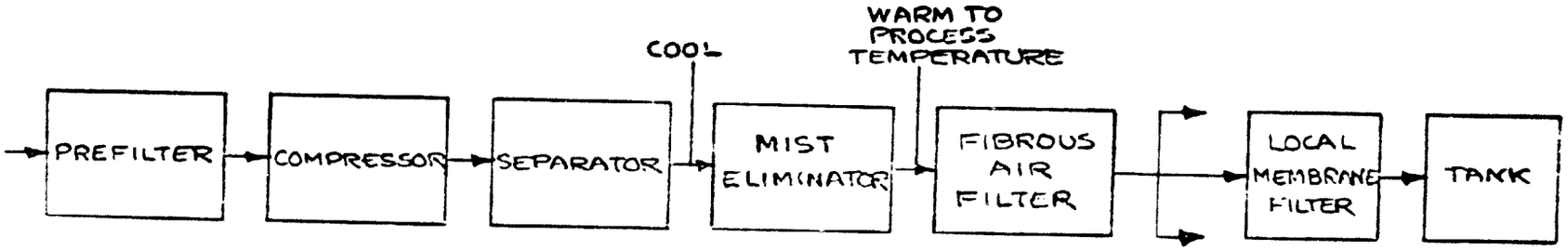
FIGURE 9




CONTINUOUS STERILIZATION SYSTEM
FOR FERMENTATION MEDIA

## STANDARD SYSTEM




## RECOMMENDED SYSTEM

AIR SYSTEMS

FIGURE 10

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