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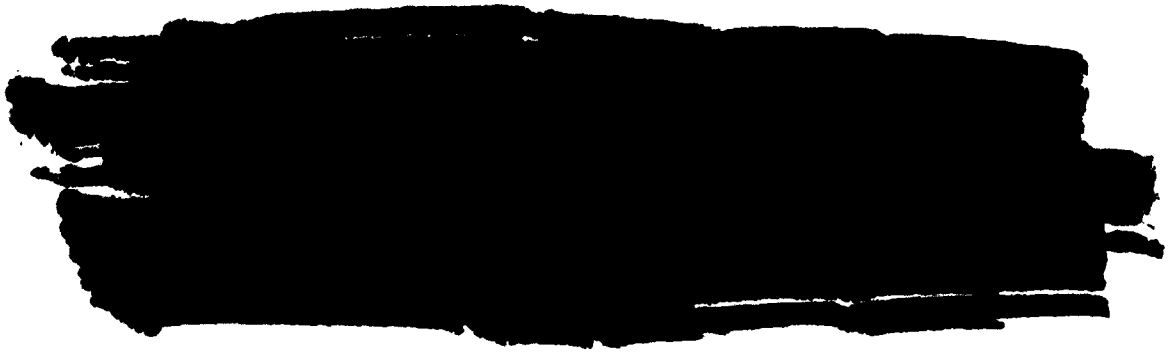

AEROBIC FERMENTATION APPARATUS DESIGN FACTORS

[Following is a translation of an article by Raffaele Falini in the Italian-language periodical, Chimica e l'Industria (Chemistry and Industry), 41, 1959, pp 304-307.]

Summary

The author examines the process of transferring oxygen from the gaseous to the liquid phase in the light of the theory of absorption with reaction in the aerobic fermentations used to produce microorganisms and their metabolites.

The variables characteristic of the process and which need to be known in designing the apparatus are analyzed on the basis of these considerations.

The method of making design calculations for a standard fermentation apparatus is then described; this method tends to arrive at a type of apparatus having minimum cost of construction and operating at maximum efficiency in achieving the oxygen transfer.

Lastly, an apparatus is described which serves the same purpose but is built differently, that is, on the basis of the principles and methods used for absorption columns for dissolving gases in liquids. This apparatus is compared with the former from the standpoints of cost of the original equipment and efficiency of operation.

Text

The developments which techniques of aerobic fermentation have undergone in recent years following discovery of the antibiotics have brought to the foreground the problems associated with design of the best equipment for this purpose.

The purpose of this paper is to describe some of the hypotheses used in the calculations which have proven to be particularly useful in the designing work.

1. Considerations on the mechanism of the transfer of oxygen

The basic condition to be met is that of ensuring a supply of oxygen to the organisms undergoing fermentation sufficient to meet their requirements so that any shortage of it which might occur would not reduce the efficiency of the process. The oxygen is normally supplied by feeding in air. Calculation of the design of the apparatus can therefore be carried out on the basis of the laws which apply when a specific substance, (oxygen), is available in a gaseous phase (air) and is transferred to a liquid phase, (the culture medium) and then again from this to a solid phase (microorganisms in the culture). The microorganisms, in reality, present a liquid phase separated from

the culture liquid by semi-permeable membranes; however, for the purposes of calculation, the problem can be treated as one of a reaction which takes place on the surface of a dispersed solid phase.

This "solid phase" in most industrial processes picks up the oxygen dissolved in the liquid phase at a rate faster than or equal to the rate at which the oxygen succeeds in passing from the gaseous phase to the liquid phase. The mechanism by which the oxygen is absorbed by the culture medium is therefore similar to that which controls the absorptio of gases into liquids when a reaction takes place in the liquid reaching equilibrium in the immediate vicinity of the gas-liquid interfaces (1). This leads, as a result, to a first approximation of the law which governs this operation in the form of an equation of the type:

$$Q = KS\ (C_g - C_l) \qquad (1)$$

in which:

Q = the quantity of oxygen transferred per unit time through surface S

K = the coefficient which expresses the specific resistance offered by the zone of separation between the gas and the liquid to the transfer, itself; K is therefore expressed in quantity of oxygen per unit of time, of surface area and of change in concentration

S = gas-liquid contact surface

C_g = concentration of oxygen in the gaseous phase

C_l = concentration of oxygen in the liquid boundary layer at the plane of the reaction.

The apparatus to be designed must make possible the above operation in such a way as to make the total cost per unit of oxygen (transferred a minimum. This cost is given by the sum of the following factors;

- cost of the equipment (depreciation quota)
- cost of the electric energy required to create an adequate gas-liquid contact surface
- cost of the electric energy needed for compressing the required air
- cost of maintenance

An examination of equation (1) shows that the quantity of oxygen transferred can be influenced by three factors, K, S, and the difference between C_g and C_l, the concentrations of oxygen in the two phases. To obtain a solution giving a first approximation, we will introduce the simplifying hypothesis that the last of the three factors is a characteristic of the process, based on the following considerations:

a. That the total pressure under which the operation is carried out can be preestablished as a function of the type of container to be used.

b. That the available gas will be air having a known and constant oxygen content.

c. That the concentration of oxygen in the liquid will be based solely on the type of organism to be cultivated.

It follows from the above that the design of the apparatus

consists above all in achieving values of K and S which will reduce the cost of production to a minimum.

The design will therefore follow these steps:

- determination using a suitable method (manometer, polarograph, etc.) of the specific oxygen requirements of the microorganism to be cultivated.

- experimental tests of various apparatus capable of satisfying the above oxygen requirement with direct or indirect measurements of K and S or of KS.

- transfer of the results obtained to a larger scale in such a way as to obtain the same efficiency in the operation of the oxygen transfer in an apparatus in which the total operating and depreciation costs will be held to a minimum.

The first step falls completely outside the scope of this paper, since they concern biochemical investigations such as are carried on in the laboratory. The second step, too, represents more a research problem in a certain sense than a design problem. It is necessary, nevertheless, to distinguish between the two different chief versions which can be used to carry out the process.

a. creation of the exchange surface by means of bubbling the aie through the liquid, with or without means of mechanical agitation.

b. creation of an exchange surface by causing the liquid to flow in a thin film over a mechnical support with exposure of the film surfaces to an air current.

Let us examine the two versions separately.

In the first of the two versions, which is the one most often used nowadays, one has available a means for blowing the air through the liquid and almost always, but not necessarily so, one or more mechanical devices whose specific function is that of bringing about a further subdivision of the air into smaller bubbles and distribution of the smaller bubbles as evenly as possible throughout the liquid.

The experimentation carried out in this case is done using small-scale models, changing the way of blowing the air, the quantity of air, the dynamic characteristics of the agitator and the container's geometric properties. We wish to emphasize here that the experiments carried out in these cases, based on measuring the amount of oxygen transferred give for the most part only an overall value for the K and S factors, without making it possible to separate them individually (3). This fact could render the following calculationcof the design difficult or even impossible, because one must know as in the case of all transfer operations what the surface area to be created is and the process's total coefficient of transmission. Nevertheless, in this particular case, changes in the characteristics of the model such as these do not affect the coefficient of transmission, which is a constant characteristic of the process to be carried out and of the fact that the air-blowing method is being used. The coefficient of transmission can, in fact, be considered as the resultant of three factors, namely:

- coefficient of transmission in relation to the gas boundary layer, K_g

- coefficient of transmission in relation to the interfaces, K_i
- coefficient of transmission in relation to the liquid boundary layer, K_l

In the blowing of gas bubbles, the first of these three factors, K_g, is conditioned by possible turbulence of the gas inside the bubbles. Because of the fact that this turbulence cannot continue once the bubble has formed, at least when using the usual procedures, it becomes clear that this factor becomes a function of the gradient of concentration between the center and the walls of the bubble.

The second coefficient, K_i is conditioned solely by the physical-chemical properties of the culture liquid as is proven by the effect of adding wetting agents to the liquid, itself. It is then admitted as a first approximation that the interfaces do not offer any resistance to the exchange and such being the case there is no reason for speaking of any second factor (4). The presence of the wetting agents used in fermentation seems, nevertheless, to have a powerful effect on the chemical and physical properties of the interfaces (5) and the simplified hypothesis outlined above may then no longer be acceptable. The fact remains, however, that in any case, K_i is one factor in the process which is independent of the model.

The third factor, (for a given speed of reaction) is a function of the relative speed between the bubble and the liquid which surrounds it. K_l therefore can be affected to some extent by the degree of turbulence given the air-liquid mixture. It is, in fact, evident that if the bubble were standing still, a different gradient of concentration would form in the liquid at the boundary in the vicinity of the interfaces, which would oppose any further oxygen transfer through the walls of the bubble; nevertheless, in this paper we have assumed that the speed of absorption of oxygen on the part of the microorganisms is such as to cause the actionto take place right in the vicinity of the gas-liquid interfaces.

The increase in K_l would only take place when the bubble was standing still, provided that at the same time the speed of reaction were less than the speed of diffusion and hence the plane of reaction would be different than that of the interfaces. Normally in this type of operations the absorption of oxygen seems to be at least equal to the speed of the diffusion. It is probably for this reason that factor K_g is held to be predominant in the determination of total K (6).

It further follows that K_l, even if bound up with the characteristics of the model and hence capable of being influenced by the turbulence, can be ignored and can also be considered to be characteristic of the process at least under normal conditions of high relative speed between the bubble and the liquid and a high rate of absorption of oxygen by the organisms.

In conclusion, it can be said that the measurement of the total value of K and S leads, in the case of the blowing method, to correct results given the fact that experiments carried out on models by varying the geometrical and dynamic characteristics affect only S; K, instead, will be constant, at least as a first approximation. This will not be

true, however, for the flow method in which the K_g factor can be very greatly affected by the relative speed between air and liquid. In this case, though S can be known and hence, also K.

2. Hypotheses for calculating bubbling systems.

In the actual design stage -- still referring to type a. -- we can state the conditions which must remain unchanged to have the same product of K and S between the model and the full scale unit, basing on what has been given beforehand.

These conditions are:

- Keep the average bubble diameters and the relative speed between the bubbles and the liquid constant.
- Always have the same number of bubbles per unit volume, dispersed evenly among the liquid.
- Keep the contact time between gas and liquid the same.

Some general laws are also valid as a guide to the designer in these cases: for example, the power dissipated by the agitator per unit volume of liquid should be kept practically constant once the exact amount of air to be used has been established (volume of gas per volume of liquid and per unit of time) and other similar criteria (7). Basing on our experiments, we believe the three conditions outlined above could be held to be trying to design the equipment on a large scale taking the following considerations into account:

1. Keep the turbulence constant. To do so one must first establish the relationship between the diameter of the agitator, the diameter of the tank and the clearance between the end of the agitator and the antivortex. A relationship of this type could be introduced later to modify the peripheral speed of the agitator, to suit changes in tank size. Experimental data in our possession indicates that a relationship of the type $n.R^a$ = constant, where n is the agitator rpm, R is the radius of the agitator and a is a function of the geometrical characteristics outlined above.

2. Establish a relationship between the surface area created per unit of time by the agitator blades and the total volume of the liquid placed in fermentation. This relationship should remain the same in two similar systems (agitator with restricted vortex) and would be the same as requiring that the quantity of liquid exposed per unit of time to the action of the blades used to create the transfer surface be kept constant. This condition would satisfy the second requirement.

3. As far as the equal length of contact time is concerned, it can be said that this requirement does the most to invalidate any direct carry-over of the results obtained on an experimental scale to a larger scale. One must keep in mind duringthe design work that this factor leads to a decrease in the specific horsepower of the agitator, while, on the other hand, it increases the power needed for compression, since it increases the head of liquid (pressure) present. Therefore, the first condition to be imposed is to establish a definite ratio between the length and diameter; this ratio will determine the cost of the container as well as the cost of electric power needed for compression.

since the specific quantity of air to be used has already been established. Since the volume has been determined, the choice of this ratio will determine, in turn, the diameter of the container. This, by way of paragraphs 1 and 2 above will determine the diameter of the agitator and the number of rpm, while by way of paragraph 2 it will determine the total surface area of the blades, to be subdivided into a number of elements suited to the dimensions of the agitator, itself. We believe, in substance, that this could be one way of setting up the calculations correctly. The greater advantage offered by this method consists in having limited the experimentation to a single model from which the necessary specific and absolute turbulence data can be obtained without having to go on later to build other models to make comparisons.

We wish, though, to emphasize once more that in this way we will only be sure of having kept the product of K and S within the same order of magnitude as the experiments had required. On the other hand we are not sure that the specific horsepower required will be the same nor, what is more important, that we will have definitely retained the same process efficiency, since, as we have already said, we will have certainly changed the time of contact. This can be solved to the advantage of the apparatus, in any case on the larger scale, because the time will then be longer and we will definitely have utilized the oxygen supplied to the apparatus in a more effective manner.

3. Creation of the exchange surface by the flow method (liquid film system) compared with the blowing or bubbling method (batch system)

We now wish to mention the second version, b, which we have shown to be useful in carrying out oxygen transfer operations.

This is substantially a case of applying the methods commonly used by industry to absorb gases into liquids to fermentation techniques. This means percolating the liquid containing the microorganisms to be cultivated over solid supports, causing the liquid, itself, to be invested by a current of air. The equipment normally used for this purpose is an absorption column filled with suitable means for aiding the absorption. The liquid culture is pumped to the top of the tower and made to fall down inside the tower while a current of air is sent upwards from below against the stream of liquid, whereby differences in oxygen concentrations are achieved which are approximately constant throughout the entire apparatus. Considerable advantages are offered by this system compared to the conventional system; the basic principles of this new system are the following:

1. The difference in concentrations ($C_g - C_l$) remains practically constant for the duration of the entire operation and remains independent of contact time (which is not the case with the air bubbles inside the liquid in the first version).

2. The exchange surface area which can be created can also be varied over a broad range without changing the amount of power used. In fact, this surface area is given by the type of packing material used (not taking into account wettability factors, flooding conditions, etc), and hence a specific quantity of liquid culture medium which goes down per unit time through a unit cross-section of the column will spread

to cover a surface area inversely proportional to the size of the dispersive elements (packing) inside the column. The only obstacle which, however, is important to what has been stated above, is the fact that the type of packing to be used must be determined on the basis of the culture's microorganism content, from both qualitative and quantitative standpoints, which means that one must have on hand a type of packing which will make possible a ready, constant flow during the entire period of the operation.

3. If it is true as it seems that the factor limiting diffusion is the gaseous boundary layer, dur to the absence of turbulent motion in this layer inside the air bubble, here, instead, we have turbulent motion of the air which invests the liquid surface. As a result there will be a very effective increase in total K, dominated by the first of the three partial K's.

4. Another extremely important aspect is the fact that the power which is needed to compress the required air is really negligible compared to the conventional system. One only need overcome the loss of pressure due to the column's being packed, on the order of an inch or so of H_2O, as against 12 to 15 ft. of pressure found in ordinary fermentation apparatus. The power needed to pump the liquid culture to the top of the column can be estimated to be of about the same order as that needed for an agitator.

5. The design calculations for this apparatus are well defined and there are no indeterminates of the discontinuous type found in boiler calculations. Oneonly need determine the basic characteristics of the material transfer operation by way of experiment for the specific process to be carried out, in order to be able to design apparatus on almost any scale without too much trouble.

6. Continuous processes can be carried on in this apparatus much more satisfactorily than by using the usual, discontinuous batch-type, boiler method. Since a minimum level of concentration of nutrilites must be ensured at all times in the liquid medium, it is theoretically impossible to remove the liquid when it has been fully exhausted. The continuous, liquid-film system does not prevent one at all from thinking that the nutrilites added at the top of the column could be supplied in such amounts that the culture liquid obtained at the bottom of the column may be completely used up.

It was also noted that the coupling of two film-type apparatus in series was particularly well adapted to testing and carrying out research on metabolites. Since the exhaustion of certain nutrilites can be readily observed, as has been said, the first apparatus can be used for growth, while the second, by adding new substances and, if necessary, also with the use of different controls can be made to guide the metabolism of the culture in the desired direction.

Economic comparison between the batch-type apparatus and the type described above was made on a small scale. It showed up the advantages pointed out in paragraphs 1, 2, 3, and, in particular, 4, above. It will be necessary, though, to operate on a scale larger than that of the laboratory to obtain confirmation of this fact.

The facts pointed out in this paper have been confirmed by

experimental data, both in respect to the method for calculating the batch system and that used for the liquid film system. This data will be published in detail in a later paper because the brief time available has not made possible a complete description and a critical discussion. We wish, nonetheless, at this time, to state that as far as design methods are concerned, the relationships which were suggested to exist among the different variables have been recognized as valid on different scales.

In particular, the production of a specific metabolite was rendered possible on a pilot scale after a certain number of experiments in flasks with rotary shaker antivortices; this stemmed from a series of observations on absolute and specific turbulence; the transfer of these results from a five-liter scale to scales of 50 and 500 liters confirmed both the two observations made above and a third one on contact times.

Insofar, then, as the liquid-film system is concerned, an apparatus was built on a small scale (about 2 liters capacity) and was operated continuously to produce yeasts of the Torula type for many hundreds of hours with results which were so satisfactory that they left no doubt as to the advisability of constructing a much larger unit (200 liters capacity), which is now ready to be put in operation (the increase in the size, in particular, should favor the possibility of operating the column using organisms which are more complex morphologically, of the Penicillium type. In these cases, in fact, using apparatus on too small a scale, the dimensions of the diameter of the column and the size of the packing tend to become critical in respect to the organisms themselves.

Istituto Superiore di Sanita (Higher Health Institute) Rome, Italy, May 1958.

Raffaele Falini

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