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Application of Membrane Bioreator

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膜 生物反応器의 応用

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Introduction

Immobilized enzymes and immobilized whole cells have been the topics of increased interest in the field of biochemical engineering since 1970s. Immobilized systems have been used in packed-bed reactors [1,2], fludized-bed reactors [3,4], or continuous stirred tank reactors.[2,5] However, these immobilized systems have inherent problems such as internal and external diffusional resistances[6-9] although these systems are currently practiced in some commercial processes. [10,11]

Thanks to the advances in membrane technology in recent years[12,15], application of membrane bioreactors is now being exercised in industry for manufacture of optically active amino acids (see NEWSWATCH 3, 7, 1983). Using a novel membrane system it is possible to separate enzyme (and microbial cell) solution from substrate. The aim of this paper is to introduce a membrane bioreactor for various biochemical reactions.

Cross flow filtration

Conventional filtration processes operate with the slurry flow "dead end" into the membrane. If the driving pressure is constant, the filtration rate decreases with time and clogging does eventually occur. However, many of the difficulties associated with conventional filtration can be eliminated if the slurry flow is tangential to rather than directly into the membrane. The alternative mode of operation is termed "cross flow filtration"[12]

In filtration processes, the filtration rate (or permeate flux) is determined primarily by the extent of polarization of the filtration barrier. Polarization refers to the accumulation of the retained species near the membrane. The polarization of the filter occurs because particles are transported to the surface by the solute and are retained while the solute passes through. A gradient in the retained species is established in the direction perpendicular to the membrane. This phenomenon is called concentration polarization. This term should only be used for the dissolved solute case commonly encountered in ultrafiltration. On the other hand, particle polarization is a more appropriate description for the cross flow filtration case where the retained species are particles.

The polarization leads to the formation of a laminar gel layer and a decline in flux is often observed. As illustrated in Fig. 1, the competing transport mechanisms affecting the retained species adjacent to the membrane may be taken to explain the dependence of flux. In simple terms, a retained species mass balance is[13]:

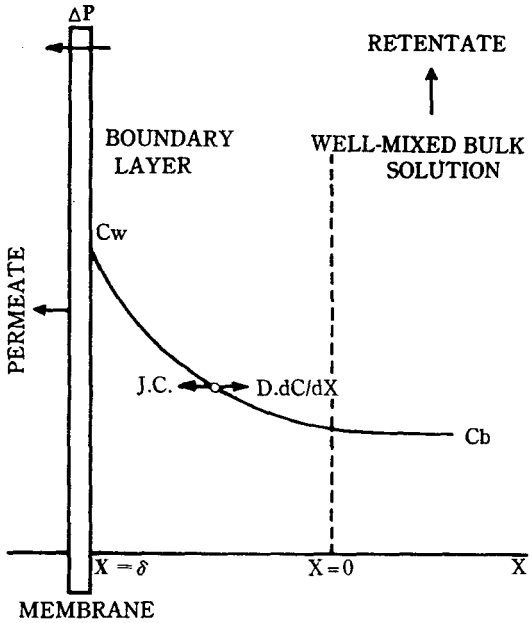

Fig. 1 : Concentration polarization model.

$$\left[\begin{matrix}\text{convective flux to}\\ \text{membrane barrier}\end{matrix}\right] - \left[\begin{matrix}\text{backtransport}\\ \text{from barrier}\end{matrix}\right] = \text{accumulation} \quad (1)$$

At steady-state there is no accumulation and the convective flux is balanced by the back transport term:

$$Jc - D\frac{dc}{dx} = 0,\ C(o) = Cb \text{ and } C(8) = Cw \quad (2)$$

Therefore, the operating flux is given by:

$$J = kln\ (Cw/Cb),\ \text{Where } k = D/\delta \quad (3)$$

Since C_w is constant for a given solute species, this condition represents a limiting value of flux, i.e. is independent of transmembrane pressure drop.[13]

For the case when the gel condition is reached, permeate flux can be expressed[14]:

$$J = \frac{\Delta p}{Rm + Rg} \quad (4)$$

Typically R_g is greater than 10 R_m and therefore equation (4) and be approximated by:

$$J = \Delta P/Rg \quad (5)$$

Equation (5) indicates membrane flux obtained is proportional to ΔP. However, at a critical value of solute concentration flux will decline. Any increase in ΔP causes the gellayer to thicken giving no further increase in flux.

Design of membrane bioreactor

A cross flow filtration system to be used as a membrane bioreactor is illustrated in Fig. 2. A constant volume of the bioreactor can be achieved by recycling some of the permeate back to the bioreactor. From a process control viewpoint, the system is amenable to feedback control to maintain a constant residence time even though the membrane characteristics may change during extended operation.

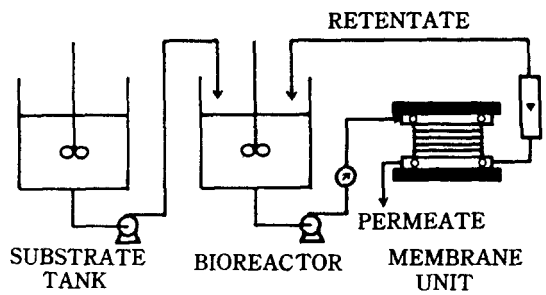

Fig. 2 : Design of membrane bioreactor system.

Assuming negligible diffusion resistance across the membrane, a general kinetic model describing the performance of the bioreactor is as follows:

$$\tau \cdot \frac{ds}{dt} = (S_o - S) - \tau.\gamma \quad (6)$$

When the reaction rate is expressed as a Michaelis-Menten or Monod relationship, at steady-state equation (6) leads to:

$$(S_o - S) = \tau \cdot \frac{\mu E}{V} \cdot \frac{S}{K_{1n} + S} \quad (7)$$

In fact, enzyme or microbial cell activity would decay with time and is function of environmental condition.

Retention of microbial cell

In fermentation processes fermentor productivity may be improved by the employment of elevated microbial cell concentrations. As microbial cell (bacteria or yeast) sizes are in the range 0.3 - 5 microns, effective retention of microbial cell can be achieved by the use of a suitable microporous membrane, and various types of membranes (cellulose acetate, polyamide, polyvinyl chloride, etc.) are commercially available.

Membrane filtration has been extensively used to achieve cell recycle and/or retention.[16-20] In Table 1 examples of membrane filtration systems to produce high density cultures are summarized. The cell recycle and/or retention system can produce a cell free permeate and high fermentor productivities

Table 1. Examples of membrane filtration system

Membrane	Pore size	Strain	Reference
Millipore	3.0 μ	*S. cerevisiae*	16
HFA-300	-	*Methylomonas*	17
Millipore	0.02-0.45 μ	*Z. mobilis*	18,19
Millipore	0.45-5.0 μ	*P. pentosaceus*	20

have been obtained.[16,18,19] The problem with membrane filtration lies in the possibility of decline in permeate flux with time due to membrane clogging. In Fig. 3 a typical permeate flux versus time curve for a bacterial suspension in the range 7-8 g/l is shown.[21] As shown in Fig. 3, the permeate flux was very high at started by equation (3). For a longer times of days or weekss, the flux will gradually decline. However, the problem associated with the long-term flux decline can be overcome by membrane cleaning.

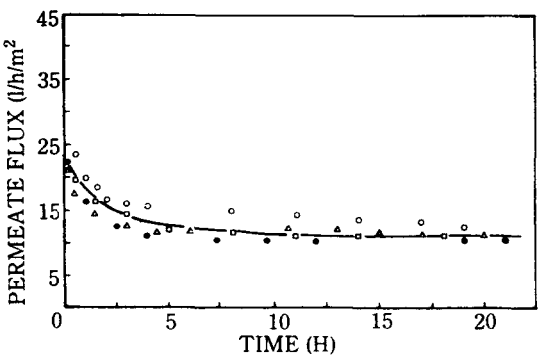

Fig. 3 : Studies on decline in permeate flux with time.

Retention of enzyme

There have been a number of reports on the use of ultrafiltration membrane systems for retention of various enzymes: e.g. invertase,[22] cellulase,[23] and cellobiase.[24] For the continuous hydrolysis of starch by α-amylase, Butterworth *et al.*[25] have demonstrated the feasibility of using an ultrafiltration membrane reactor. The enzymes were retained and reused and no loss of α-amylase activity was found after 30 h at steady-state. Similar studies on the performance of a membrane bioreactor with starch have been reported[26-28] although the feed concentration of substrate starch was too low for producing hydrolysed starch for subsequent fermentation.

By selecting a proper molecular weight membrane cut-off it would be possible to retain enzyme. In order to demonstrate enzyme retention glucoamylase retention by Millipore ultrafiltration membranes is shown in Fig. 4.[21] As shown in Fig. 4, the enzyme activity in the permeate was found to be zero, indicating 100% enzyme retention. However the long-term decay in enzyme activity was evident[24,25,28] which is one of the problems for the commercial application of this technology. Recently Deeslie and Cheryan reported a CSTR-hollow fiber system for continuous hydrolysis of proteins.[29,30] Long-term stability of the system was affected by many factors such as enzyme leakage, thermal degradation, and membrane poisoning.

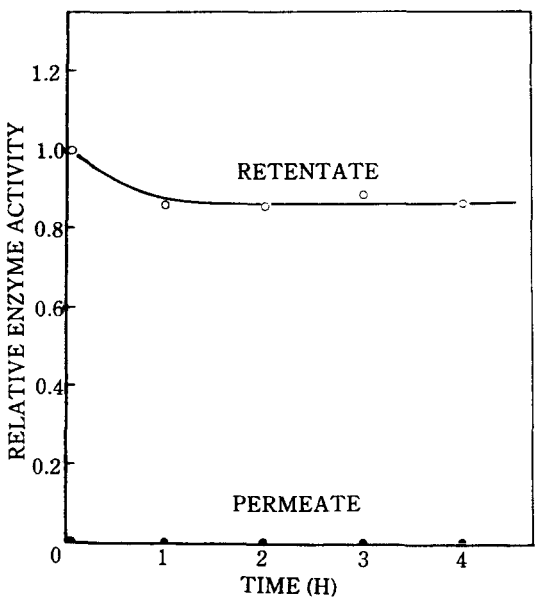

Fig. 4 : Enzyme retention by Millipore membrane.

Application of membrane bioreactor

The recent developments in membrane technology allow the use of membrane filtration to achieve effective bacterial cell and/or enzyme recycle. Membrane bioreactor applications in biochemical engineering have been extensively studied. Table 2 summarizes some of the available informa-

Table 2. Examples of membrane enzyme reactor systems.

Substrate	Enzyme	Reference
starch	α-amylase	25,37
sucrose	invertase	22
starch	ß-amylase	26,28
galactose	α-galactosidase	31
maltose	glucoamylase	32
starch	glucoamylase	27
cellulose	cellulase	23
cellobiose	cellobiase	24
histidine	histidine-ammonia-lyase	33
dextrin	glucoamylase	34
fumaric acid	fumarase	35
fumaric acid	aspartase	36

tion on the application of membrane bioreactors. Membrane bioreactor systems have been used in enzyme kinetic studies[22,24,28,35] and high productivity fermentation processes.[16,18,19,34]

The advantages of a properly designed membrane recycle bioreactor system over immobilized system can be summarized as:

1) better control of pH and temperature which is essential in most biochemical reactions.
2) better performance for enzyme reactions with substrate inhibition.
3) improved effectiveness factor by decreasing diffusional resistances.
4) better application as a trickle-bed (gas, liquid, and solid) reactor.
5) finally, recovering enzymes more economically from the product-containing mixture.

As well as enzyme kinetic studies with the use of membrane bioreactors, specific applications such as concentration/purification of enzymes,[15] activated sludge wastewater treatment,[14] and the breaking of an oil-water emulsion[13] have been demonstrated. In addition, membrane separation for desalting molasses is being tested in industry.

Nomenclature

C : concentration of particulate S_0 14. 24.
C_w : gel-layer concentration at membrane wall
C_b : bulk concentration of particulate
D : particulate diffusivity
vE : activity of enzyme or microbial cell
J : permeate flux
K_m : constant
k : mass transfer coefficient
ΔP : trans-membrane pressure drop
R_m : resistance of membrane
R_g : resistance of gel-layer
r : reaction rate
S : substrate concentration
S_o : feed substrate concentration
t : time
V : volume
δ : boundary layer thickness
τ : residence time

References

1. Weetall, H.H., Havewala, N.B.: *Biotechnol. Bioeng. Symp.* **3**,241 (1972).
2. O'Neill, S.P., Dunnill, P., Lilly, M.D: *Biotechnol. Bioeng.* **13**,337 (1971).
3. Allen, B.R., Coughlin, R.W., Charles, M.: *Ann. N.Y. Acad. Sci.* **326**, 105 (1979).
4. Allen, B.R., Charles, M., Coughlin, R.W.: *Biotechnol. Bioeng.* **21**, 689 (1979).
5. Lin, S.H.: *J. Appl. Chem. Biotechnol.* 28, 677 (1978).
6. Lee, Y.Y., Tsao, G.T.: *J. Food Sci.* **39**, 667 (1974).
7. Marsh, D.R., Lee, Y.Y., Tsao, G.T.: *Biotechnol. Bioeng.* **15**, 483 (1973).
8. Lee, G.K., Lesch, R.A., Reilly, P.J.: *Biotechnol. Bioeng.* **23**, 487 (1981).
9. Swanson, S.J., Emerry, A., Lim, H.C.: *A. I. Ch. E.* **24**, 30 (1978).
10. Nishida, Y., Sato, T., Tosa, T., Chibata, I.: *Enzyme Microb. Technol.* **1**, 95 (1979).
11. Chibata, I., Tosa, T.: *TIBS*, **5**, 88 (1980).
12. Henry, J.D.: Recent Developments in Separation Science, Vol. 2, pp. 205, (Ed. N.N.Li), CRC Press (1972).
13. Fell, C.J.D., Fane, A,G., Lefebvre, M.S.: CSIRO Filtration and Separation Symposium, Australia, (1979).

14. Gebbie, P., Fane, A.G., Fell, C.J.D.: *Water,* **3,** 17 (1976).
15. Lefebvre, M.S., Fell, C.J.D., Fane, A.G., Waters, A.G.: In: Ultrafiltration membranes and Applications, pp. 79, (Ed. A.R. Cooper), Plenum Press, (1980).
16. Margaritis, A., Wilke, C.R.: *Biotechnol. Bioeng.* **20,** 727 (1979).
17. Goto, S., Kuwajima, T., Okamoto, R., Inui, T.: *J. Ferment. Technol* **51,** 47 (1979).
18. Lee, J.H., Woodard, J.C., Pagan, R.J., Rogers, P.L.: *Biotechnol. Lett.* **3,** 177 (1981).
19. Rogers, P.L., Lee, K.J., Tribe, D.E.: *Process Biochem.* **15,** 7 (1980).
20. Dostalek, M., Haggstrom, M.: *Biotechnol. Bioeng.* **24,** 2077 (1982).
21. Lee, J.H.: Ph.D. thesis, University of NSW (1982).
22. Bowski, L., Shah, P.M., Ryu, D.Y., Vieth, W.R.: *Biotechnol. Bioeng. Symp.* **3,** 229 (1972).
23. Ghose, T.K., Kostick, J.A.: *Biotechnol. Bioeng.* **12,** 921 (1970).
24. Hong, J., Tsao, G.T., Wankat, P.C.: *Biotechnol. Bioeng.* **23,** 1501 (1981).
25. Butterworth, T.A., Wang, D.I.C., Sinskey, A.J.: *Biotechnol. Bioeng.* **12,** 615 (1970)
26. Closset, P., Cobb, J.T., Shah, Y.T.: *Biotechnol. Bioeng.* **16,** 345 (1974).
27. Madgavkar, A.M., Shah, Y.T., Cobb, J.T.: *Biotechnol. Bioeng.* **19,** 1719 (1977).
28. Azhar, A., Hamdy, M.K.: *Biotechnol. Bioeng.* **23,** 1501 (1981).
29. Deeslie, W.D., Cheryan, M.: *J. Food Sci.* **46,** 1035 (1981).
30. Deeslie, W.D., Cheryan, M.: *Biotechnol. Bioeng.* **24,** 69 (1982).
31. Smiley, K.L., Hensley, D.E., Gasdorf, H.J.: *Appl. Environ. Microbiol.* **31,** 615 (1976).
32. Swanson, S.J., Emery, A., Lim, H.C.: *Biotechnol. Bioeng.* **19,** 1715 (1973).
33. Kan, J.K., Shuler, M.L.: *A. I. Ch. E. Symp.* **14,** 31 (1978).
34. Lee, J.H., Pagan, R.J., Rogers, P.L.: *Biotechnol. Bioeng.* **25,** 659 (1983).
35. Wandrey, C: *Ann. N.Y. Acad. Sci.* **326,** 87 (1979).
36. Jandel, A.S., Hustedt, H., Wandrey, C.: *Eur. J. Appl. Microbiol. Biotechnol.* **15,** 59 (1983).