STATISTICAL EVALUATION OF SIEVE CONSTANTS IN ULTRAFILTRATION

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It is generally agreed that the principal process involved in ultrafiltration is one of sieve action, complicated by adsorption and other effects arising from the extremely large ratio of pore length to pore diameter in all ultrafilter membranes (1–5).

The present paper discusses the rôle of sieving when a monodisperse system is forced through a perfectly isoporous filter membrane, under conditions of "normal" filtration (5), when the primary adsorbing capacity of the membrane has been satisfied, and blocking effects are absent. Under such conditions, it has often been implicitly assumed that the disperse phase either passes the filter in undiminished concentration or is completely retained. Thus, when filtration of a disperse system through membranes of different porosities yields filtrates of different concentrations, it appears that there are different sizes of particles in the suspension or solution. On this basis, it has been concluded, for example, that certain lyophobic hydrosols (6) and suspensions of urease (7) and bacteriophage (8) are polydisperse. However, while some of these systems probably do contain particles of varying sizes, the occurrence of a sieving effect (*i.e.*, partial retention of the disperse phase in ultrafiltration) is not a criterion of polydispersion. As a matter of fact, sieving occurs in the ultrafiltration of proteins (9) which are known through the results of ultracentrifugal analysis to be virtually monodisperse (10, 11). The semi-quantitative theoretical treatment outlined below shows that such sieving in the filtration of a monodisperse system may be anticipated on statistical grounds, on the basis of simple steric limitations in the penetration of filter pores.[1]

[1] The interpretation of sieving on a statistical basis has been suggested in a previous paper (5).

Definition of the Sieve Constant

Manegold and Hofmann (12) defined a "sieve constant" (φ) for the process of ultrafiltration, as follows:

$$\frac{c_f}{c_s} = \varphi \tag{1}$$

where c_f is the instantaneous concentration of a small sample of filtrate, and c_s is the simultaneous concentration of the filtering solution. For complete retention of the solute or disperse phase (*i.e.*, for the case of a semi-permeable membrane), $\varphi = 0$; when the solute passes in undiminished concentration, $\varphi = 1$. These authors suggested the possibility that, in certain cases, the sieve constant may be neither 0 nor 1, even when the membrane is isoporous and the solution (or dispersion) monodisperse.

Assuming the sieve constant to be independent of c_f, Manegold and Hofmann (12, 13) calculated various expressions for the concentrations of the total filtrate and of the residue at any point in the course of filtration, depending on the manner in which the filtration was carried out (in a closed system, or in a system where the volume of residue was kept up by continuous or intermittent addition of the suspension medium). Application of these equations to data for the ultrafiltration of colloidal chromium hydroxide (14) indicated that, for membranes of a certain porosity, at least some of the particulate species in the sol filtered with a sieve constant neither 0 nor 1; unless the membranes were heteroporous.

We shall employ the definition of Manegold and Hofmann, and proceed to evaluate the sieve constant in terms of microscopical quantities.

Scales for Expressing Membrane Porosity

The usual method of calibrating an ultrafilter membrane, by the measurement of the rate of flow of water through it and the application of Poiseuille's law to an assumed structure of cylindrical capillaries of circular cross-section, probably gives a figure for the average pore diameter which is, if anything, too small, especially for a membrane of

low porosity; while the size of the largest particles retained by the membrane is smaller still (4, 15, 5).[2] The continuous scale of porosity grading provided by rate of flow calibrations, calculated in terms of average pore diameter (j), is the most convenient for comparative purposes (5). For statistical evaluation of the sieve constant, however, the pore size will be at first expressed in terms of the diameter effective in filtration (j'), defined equal to the radius of the largest particulate species which absolutely fails to pass the filter under given experimental conditions. This diameter j' will be expressed later in terms of the calibrated average pore diameter.

Evaluation of the Sieve Constant in Terms of j'

If a monodisperse system of particle diameter J is filtered through isoporous filters of different porosities, the sieve constant for filters of $j' < J$ will be 0. For filters of $j' > J$, φ will lie between 0 and 1; for $j' \gg J$, $\varphi \cong 1$.

It is assumed that the membrane structure consists of parallel cylindrical capillaries of circular cross-section, a model whose plausibility as a working basis is indicated by studies of water content, diffusion, and conductivity (15, 5); and that, when the membrane is in adsorption equilibrium with the filtering solution, the pore diameter j' effective in the filtration of the disperse phase is also effectively the diameter of the cylinder through which the dispersion medium flows. The difference between j and j' is thus attributed to primary adsorption of the disperse phase or of some other capillary active substance (*cf.* (4)). It is further assumed that the solution above the membrane remains homogeneous throughout filtration, local concentration of the disperse phase immediately above the membrane surface being prevented.

The filtering solution, considered from a hydrodynamic standpoint, follows streamlines which far above the membrane are uniformly distributed over the membrane area, but in the plane of the membrane surface are concentrated opposite the pore openings and distributed

[2] These statements refer to ether-alcohol collodion membranes, and in particular to those of Elford (23, 24, 16).

according to Poiseuille flow; *i.e.*, at the mouth of any pore, the velocity of flow at a distance ρ from the center is given by

$$v(\rho) = v_1\left(1 - \frac{\rho^2}{r'^2}\right) \tag{2}$$

where v_1 is the velocity at the center of the pore, and $r' = \frac{1}{2}j'$. The volume of suspension medium entering the pore in time dt is accordingly

$$dV = dt \int_0^{r'} 2\pi\rho v(\rho)d\rho = \frac{\pi v_1 r'^2}{2} dt \tag{3}$$

A particle of the disperse phase, carried by the flow of suspension medium toward the pore mouth, will have a certain probability of penetrating the latter, depending on how closely it approaches the rim of the opening. For the purposes of this calculation, it is reasonable to take that probability as unity for all particles falling entirely within the opening; that is, those whose centers strike a circle of radius $r' - R$, where $R = \frac{1}{2}J$. The probability of penetration is taken as zero for all those whose centers strike outside such a circle. It is this steric limitation which introduces a statistical sieving. If the velocity of each particle is the hydrodynamical velocity corresponding to the point occupied by its center, Brownian movement being neglected, the number of particles entering the pore in time dt is

$$dn = c_s dt \int_0^{r'-R} 2\pi\rho v(\rho)d\rho = c_s\pi v_1\left[(r' - R)^2 - \frac{(r' - R)^4}{2r'^2}\right] dt \tag{4}$$

so that the concentration of the filtrate is

$$c_f = \frac{dn}{dV} = c_s\left[2\left(\frac{r' - R}{r'}\right)^2 - \left(\frac{r' - R}{r'}\right)^4\right]$$

and, replacing radii by diameters, the sieve constant is

$$\varphi = \frac{c_f}{c_s} = 2\left(\frac{j' - J}{j'}\right)^2 - \left(\frac{j' - J}{j'}\right)^4 \tag{5}$$

Expression of the Sieve Constant in Terms of Experimentally Measured Quantities

The end-point porosity is defined as the average pore diameter of the most highly porous filter which apparently completely retains the disperse phase (4). At the end-point, equation (5) becomes

$$\varphi_e = 2\left(\frac{j'_e - J}{j'_e}\right)^2 - \left(\frac{j'_e - J}{j'_e}\right)^4 \tag{6}$$

where φ_e is the smallest relative concentration of the disperse phase which can be detected by the analytical methods employed, and j'_e is the end-point porosity measured on the filtration-effective scale (only very slightly greater than J). The end-point porosity in terms of the calibrated average pore diameter, j_e, may be substantially greater than J, and the relationship between the two may be determined for a given type of suspension by filtration of suspensions of known particle size (4, 5), to evaluate an experimental correction factor:

$$q = J/j_e \tag{7}$$

The difference between j_e and j'_e, attributed to primary adsorption of the disperse phase (or of a capillary active substance) within the pores, is now assumed to represent a constant difference between the two porosity scales; thus

$$j - j' = j_e - j'_e = j_e - \frac{J}{1 - \sqrt{1 - \sqrt{1 - \varphi_e}}} \qquad \text{(by equation (6)),}$$

and

$$j' = j - j_e + Jf_e \tag{8}$$

where

$$f_e = \frac{1}{1 - \sqrt{1 - \sqrt{1 - \varphi_e}}}.$$

Substituting (8) into (5), we obtain

$$\varphi = 2\left\{\frac{j - j_e + J(f_e - 1)}{j - j_e + Jf_e}\right\}^2 - \left\{\frac{j - j_e + J(f_e - 1)}{j - j_e + Jf_e}\right\}^4 \tag{9}$$

in terms of experimentally measured quantities—the calibrated porosity j, the calibrated end-point porosity j_e, and the particle diameter J.

Factors Ignored in the Above Treatment

It is possible that the above criterion for penetration of a pore is too restricted; a particle may strike the surface of the membrane so that it does not quite fall entirely within the pore opening, and yet may glance off the rim and be carried into the pore by the flow of dispersion medium. Such a particle, however, would probably be delayed by a drag from the membrane surface, so that the resulting enrichment of the filtrate would be minimized. Another factor in the penetration of pore openings which has not been considered is the influence of the electrical charges of membrane and disperse particles. Probably, however, the most serious objection to the calculations outlined above lies in the fact that penetration of a particle into a pore does not assure its emergence at the bottom of the membrane. The ratio of pore length to pore diameter is seldom less than a thousand to one, and, although the tortuosity of pores as pictured by some authors has perhaps been exaggerated (15, 5), it is likely that many particles become lodged in the membrane in the course of filtration. From this standpoint, values of the sieve constant calculated from equation (9) may be too large. The discrepancy, however, should be the least in the range of sieve constants approaching unity. This is found to be the case when equation (9) is compared with experimental data for ultrafiltration of viruses (see below).

Comparison of Equation (9) with Experimental Data

For suitable experimental data with which equation (9) may be compared, reference is made to the work of Elford and collaborators, who have employed graded collodion membranes of a high degree of isoporosity in ultrafiltration studies under standard conditions of normal filtration. Their data give the maximum relative concentration of filtrate, u_{max}, as a function of the membrane porosity j (the "end-point curve" (9) or "filtrability curve" (16)). While u differs somewhat from φ, being the ratio of filtrate concentration to the initial, rather than the instantaneous, concentration of filtering solu-

tion, the curves for u_{max} (experimental) and φ (equation (9)) should be qualitatively comparable. The experimental u_{max} should in general be higher than φ, since the residue becomes concentrated in the course of filtration; this concentrating effect is, however, opposed by the primary adsorption of the membrane.

Comparisons are made for the ultrafiltration of suspensions of horse serum albumin in water at two pH's (9), of hemocyanin (*Helix*) in Hartley's broth (17), and foot-and-mouth disease virus in broth (18). For the proteins, the values of J are taken from Svedberg's data (10), on the basis of spherical particles (ignoring the slight anisodimensionality in the case of serum albumin); the value for foot-and-mouth

TABLE I

Constants Employed for Calculation of Theoretical Curves

	j_e	J	φ_e	f_e
Serum albumin dispersed in water, pH 8.8..	11 mμ	5.4 mμ	0.01	1.08
Serum albumin dispersed in water, pH 4.1..	12 mμ	5.4 mμ	0.01	1.08
Hemocyanin (*Helix*), dispersed in Hartley's broth, pH 7.3.....	55 mμ	24 mμ	0.01	1.08
Foot-and-mouth disease virus, dispersed in Hartley's broth, pH 7.6.....	25 mμ	10 mμ*	10^{-6}	1.00

* Calculated by application of the correction factor $q = 0.41$ (reference (5)).

disease virus is calculated by equation (7) (*cf.* (4, 5)). The constants required for equation (9) are summarized in Table I. The experimental and theoretical curves are compared in Fig. 1.

Serum Albumin.—The theoretical curves for serum albumin, which do not differ much from each other, fall between the experimental curves for pH 8.8 and pH 4.1. This situation might seem attributable to the effect of the charge of the protein (negative in one case and positive in the other), which was not taken into account in the theoretical considerations. However, such an interpretation would mean an enhanced probability of penetration in the case of negatively charged particles; whereas much experimental evidence (19, 20) shows that collodion membranes are *less* readily penetrated by negatively than by positively charged particles. The fact that the experimental

curve for pH 8.8 is high is probably due to the nature of the comparison between u_{max} and φ, as explained above. The experimental curve for pH 4.1 is low, probably owing to the fact that filtration at this pH does not proceed under quite "normal" conditions, some blocking occurring (9). The slight degree of anisodimensionality of the serum albumin molecule probably has little influence on the statistics of pore penetration.

Hemocyanin (Helix).—The agreement between theoretical and experimental curves for hemocyanin, which is practically within

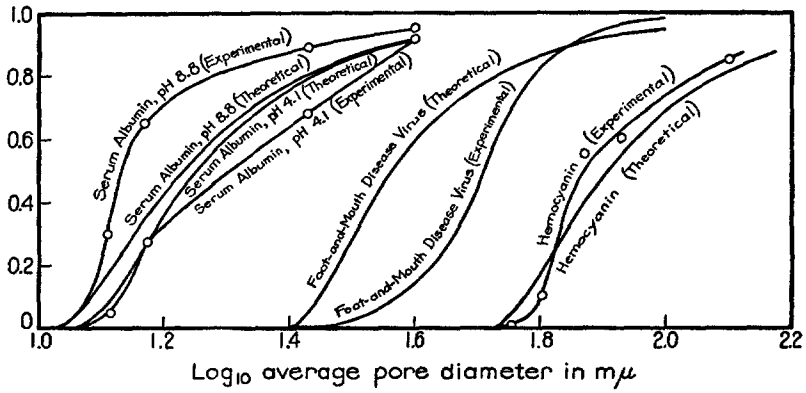

FIG. 1. Comparisons of theoretical and experimental filtrability curves. The sieve constant (theoretical) and maximum relative concentration of filtrate (experimental) are plotted against the logarithm of calibrated average pore diameter in mμ.

experimental error, is probably due to a counterbalancing of the two factors mentioned in the preceding paragraph. The filtration of hemocyanin was, in fact, not quite "normal" (17).

Foot-and-Mouth Disease Virus.—The theoretical curve for foot-and-mouth disease virus rises much faster from the end-point than does the experimental curve. This effect is still more marked for other viruses and bacteriophages, so that it is impossible to reconcile their end-point curves with curves calculated by equation (9). Thus, for membranes of porosity only slightly above the end-point value, the probability for transmission of virus is apparently much lower than that derived from the simple steric considerations of equation (4).

This situation may be ascribed to the difficulty of saturating the primary adsorbing capacity of the membrane in dilute virus suspensions (4, 5). However, the general agreement of the end-point curve for foot-and-mouth disease with the theoretical curve is sufficient to suggest that the shape of the former may be due to statistical sieving alone, without the necessity of postulating the existence of aggregates held back at high porosities, or of a certain degree of heteroporosity in the filters employed.

DISCUSSION

This formulation of statistical sieving supports the viewpoint that the appearance of sieve action is not a criterion for heterodispersion in the system filtered nor heteroporosity in the filters employed. Heterodispersion may be demonstrated by the appearance of sieving over a much wider range of porosities than is the case for a monodisperse system (as was shown by Grabar and Riegert (21) for urease); or by ultrafiltration of fractions separated by centrifugation or previous filtrations (as was shown by Bechhold (22) for a silver sol).

The applicability of equation (9), considering the excessive simplifications employed in its derivation, lends encouragement to the possibility of attacking the problems of osmosis and penetration on a microscopical basis.

SUMMARY

The partial retention of the disperse phase in the ultrafiltration of a monodisperse system through an isoporous filter is interpreted on a statistical basis, and a simple expression for the sieve constant is evaluated in terms of the calibrated membrane porosity and the particle size. Curves calculated from this expression are in reasonable agreement with experimental data for the ultrafiltration of serum albumin, hemocyanin (*Helix*), and foot-and-mouth disease virus.

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