Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

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To cite this Article Mullon, Claudy , Radovich, John M. and Behnam, Bahman(1985) 'A Semiempirical Model for Electroultrafiltration-Diafiltration', Separation Science and Technology, 20: 1, 63 — 72
To link to this Article: DOI: 10.1080/01496398508060675
URL: http://dx.doi.org/10.1080/01496398508060675

SEPARATION SCIENCE AND TECHNOLOGY, **20**(1), pp. 63-72, 1985

A Semiempirical Model for Electroultrafiltration-Diafiltration

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Abstract

An exponential relationship between protein concentration and time is used to predict the solution flux when concentrating bovine serum albumin solutions with electroultrafiltration. The time constant can also be predicted from a plot of flux versus the logarithm of the bulk concentration. The limitations of this prediction are also discussed. The average flux during electrodiafiltration is used to predict the exponential relationship between salt concentration and time when using electrodiafiltration to remove NaCl from bovine serum albumin solutions. The processing time saved by using an electric field is easily calculated from these equations.

The combination of a transverse electric field with pressure-driven membrane ultrafiltration to improve flux and separation has been applied to the processing of plasma proteins (*1*, *2*) and electrodeposition paints (*3*, *4*). A mathematical model based on the film theory (*5*) for concentration polarization and a phenomenological law relating flux to the driving force and resistances (*6*) has been successful in relating the solution flux to the applied electric field strength for those applications at steady state and constant feed concentration. Recent use of electroultrafiltration to concen-

 0149-6395/85/2001-0063$3.50/0

trate proteins and to diafiltrate protein solutions has shown higher fluxes and more rapid processing times (*7*). Prediction of the time-dependent fluxes or concentration is possible using the model developed below.

CONCENTRATION OF PROTEINS

Consider a cross-flow, recirculating, batch ultrafiltration system for concentrating protein solutions. Assuming that the protein is totally rejected by the membrane, the solution flux at any time, J, according to the simplified film theory of ultrafiltration is given by

$$J = k \ln \frac{C_w}{C} \tag{1}$$

where k is a mass transfer coefficient, C_w is the concentration at the wall (membrane), and C is the protein concentration in the bulk solution at any time. When combining a transverse electric field with ultrafiltration, the flux is given by

$$J = k \ln \frac{C_w}{C} + Eu \tag{2}$$

where E is the electric field strength and u is the electrophoretic mobility of the protein (*1*). Equation (2) was derived assuming that the electroosmotic contribution to flux was negligible. This assumption is valid for the Amicon Diaflo XM series membranes used in our experiments (*8*).

The flux cannot be predicted by Eq. (2) without knowing how the concentration varies with time. Examination of the concentration versus time plots for bovine serm albumin (BSA) (see Fig. 1 of Ref. 7) suggest the following functionality:

$$C = C_0 e^{Yt} \tag{3}$$

where Y is a reciprocal time constant and C_0 is the initial bulk concentration. Y can be found from a plot of $\ln (C_w/C_0)$ versus t. Substituting this expression for C into Eq. (2) gives

$$J = k \left(\ln \frac{C_w}{C_0} - Yt \right) + Eu \tag{4}$$

A plot of J vs t should yield a straight line with a slope equal to $-kY$ and a y-intercept of $k \ln (C_w/C_0) + Eu$, assuming that E and C_w are constant.

Analysis of the data for concentrating bovine serum albumin (BSA) presented in Figs. 1 and 2 (C/C_0 vs t) in Ref. 7 gives the following equations for C, where t is in minutes:

$$C_0 = 1 \text{ wt\% BSA}, E = 0 \text{ V/cm}: C = C_0 e^{(.00069t)}$$
$$C_0 = 1 \text{ wt\% BSA}, E = 4 \text{ V/cm}: C = C_0 e^{(.00152t)}$$
$$C_0 = 1 \text{ wt\% BSA}, E = 10 \text{ V/cm}: C = C_0 e^{(.00269t)}$$
$$C_0 = 2 \text{ wt\% BSA}, E = 4 \text{ V/cm}: C = C_0 e^{(.00116t)}$$

The values of the reciprocal time constant were determined by a modified linear regression method in which the lines were forced through the point $\ln C/C_0 = 0, t = 0$. Correlation coefficients were greater than 0.97 in each case (a correlation coefficient of 1.0 would indicate a perfect fit).

PREDICTION OF RECYCLING EUF ALBUMIN CONCENTRATION FROM RECYCLING UF CONCENTRATION PROFILE

For concentration of a protein solution with recycle, the mass balance on the retentate solution for an impermeable membrane is

$$VC = V_0 C_0 = \text{constant} \tag{5}$$

where V_0 = initial volume of process solution
V = volume of solution at time t
C_0 = initial concentration of albumin
C = concentration of albumin at time t

The volume V can also be written as

$$V = V_0 - \int_0^t J A_m \, dt \tag{6}$$

where A_m is the membrane surface area.

Combining Eqs. (3), (5), and (6) leads to

$$\frac{C_0}{C} = e^{-Yt} = 1 - \frac{A_m}{V_0} \int_0^t J \, dt \tag{7}$$

A plot of J vs ln C from ultrafiltration data and Eq. (1) should yield a straight line. Instantaneous values of J and C/C_0 for V_0 = 500 mL were used (from Figs. 1 and 2 of Ref. 7). Figure 1 yields

$$k = 0.00837 \text{ cm/min}, k \text{ is constant, slope of the plot}$$

$$k \ln C_w = -0.0186 \quad \text{or} \quad C_w = 11 \text{ wt\% BSA}$$

Thus,

$$J = -0.0186 - 0.00837 \ln C \tag{8}$$

Combining Eqs. (3), (7), and (8) and solving by iteration for the reciprocal time constant, Y, gives,

$$Y = 0.7 \times 10^{-3} \text{ min}^{-1}$$

or

$$C = C_0 e^{0.7 \times 10^{-3} t}$$

This is quite close to $Y = 0.69 \times 10^{-3}$ min^{-1} obtained from the concentration versus time data.

In Fig. 1, k and C_w are constant over some concentration ratio range. Assuming these conditions hold for EUF at low voltage gradients, and low C/C_0 ratios, combining Eqs. (3), (4), and (7) leads to

$$e^{-Yt} = 1 - \frac{A_m}{V_0}(k \ln C_w/C_0 + Eu) + \frac{A_m k}{V_0} Yt^2/2 \tag{9}$$

Equation (9) can also be solved for Y for the 1.0 wt% BSA solution:

At t = 1000 min:

E = 4 V/cm, 1 wt% BSA, $Y = 1.47 \times 10^{-3}$ min^{-1}

At t = 500 min:

E = 10 V/cm, $Y = 2.2 \times 10^{-3}$ min^{-1}

An electrophoretic mobility for BSA at pH = 7.4 in phosphate buffer of ionic strength 0.05 M of 4.5×10^{-5} cm^2/V · s (*12*) was used in this calculation. A value of about 4.0×10^{-5} cm^2/V · s was determined from the experiments (*8*). The reciprocal time constants using this electrophoretic mobility become 1.37×10^{-3} and 1.94×10^{-3} min^{-1} at 4 and 10 V/cm,

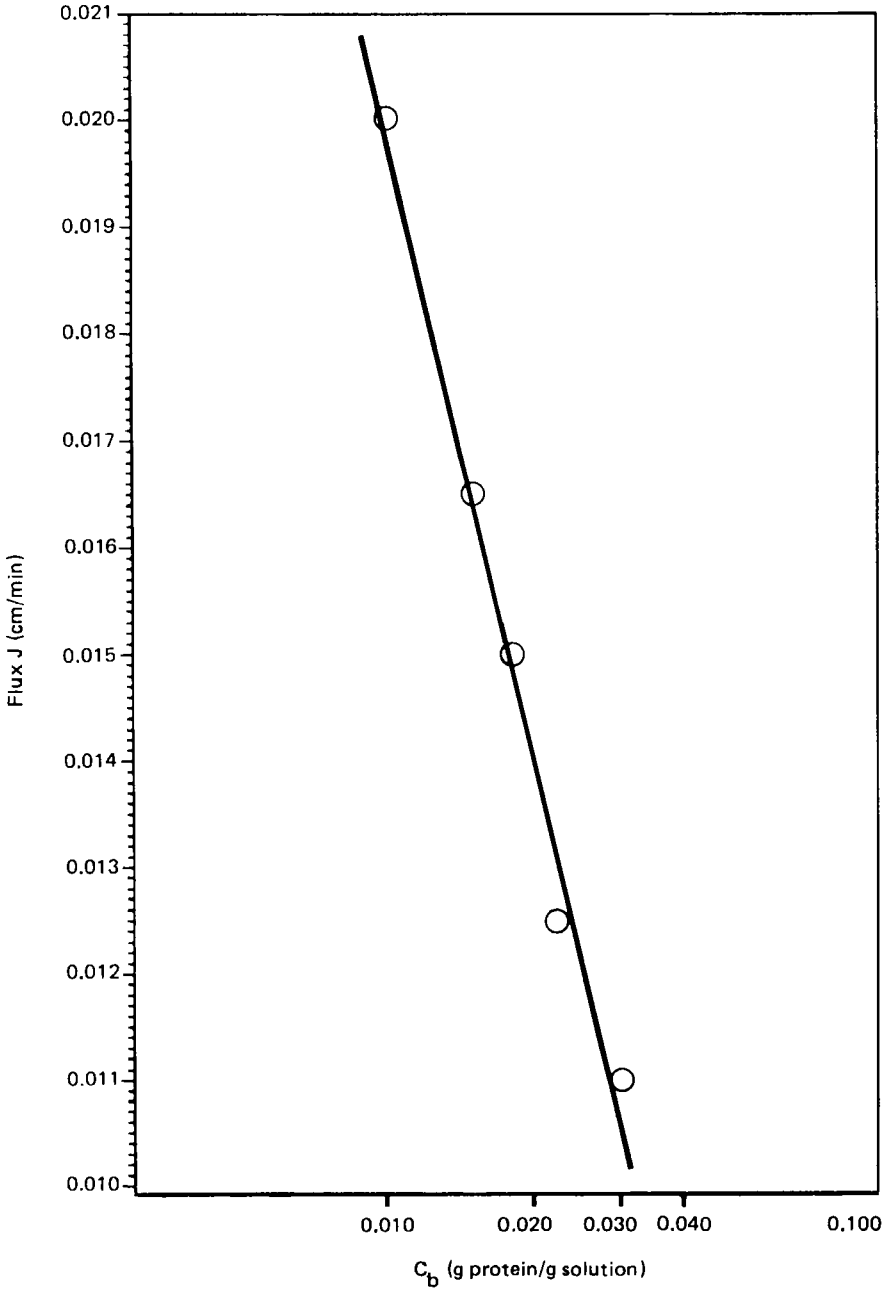

FIG. 1. Semilog plot of flux versus bulk protein concentration for concentrating albumin solutions.

respectively. These values are below the observed values. Equation (9) shows that if C_w increases, the predicted time constant increases.

A plot of J vs t from Eq. (4) for $E = 10$ V/cm and $E = 4$ V/cm (see Fig. 2) gave the following equations from a linear regression analysis:

$E = 10$ V/cm:

$J = -4.16 \times 10^{-5}t + 4.57 \times 10^{-2}$, correlation coefficient = .871

$E = 4$ V/cm:

$J = -5.43 \times 10^{-5}t + 4.17 \times 10^{-2}$, correlation coefficient = .999

The value of k calculated from the slope of J vs t for $E = 10$ V/cm is 1.55×10^{-2} cm/min; for the $E = 4$ V/cm curve, $k = 3.57 \times 10^{-2}$ cm/min. These values should be the same if C_w was constant since the hydrodynamic conditions for each experiment were the same. It was not possible to calculate the value of k using the circulation rate and channel dimensions in an appropriate mass transfer correlation because the flow pattern in the cell was not straight (*8*). The assumption of a constant wall concentration during the protein concentration process is probably not valid. Trettin and Doshi (*10, 11*) indicated that the wall concentration may be constant if the system is operated in the osmotic-pressure limited region. Their analysis was for an unstirred batch cell and a cross-flow, thin channel system at steady state. Our system is a combination of batch and cross flow. Since the concentration of the feed solution is changing with time, the concentration polarization phenomena also changes the wall concentration. The wall concentration probably has the same functionality as the bulk concentration, $C_w = C_{w0}e^{\Upsilon' t}$, because the plots of J vs t are straight lines. The slopes, however, are equal to $k(\Upsilon' - \Upsilon)$. The reciprocal time constant Υ' for the wall concentration would also depend on E. The dependence of C_w on time might be determined from steady-state measurements of flux at a given E for a range of bulk concentrations from the initial value to the final bulk concentration.

For an exponential dependence of C_w on time, Eq. (4) becomes

$$J = k(\ln C_{w0}/C_0 + (\Upsilon' - \Upsilon)t) + Eu \tag{10}$$

Thus, for $E = 10$ V/cm, $t = 500$ min, to get the experimental reciprocal time constant of 2.69×10^{-3} min^{-1}, Υ' is equal to 1.47×10^{-3} min^{-1} for an electrophoretic mobility of 4.5×10^{-5} cm^2/V · s, but 0.87 if u is 4.0×10^{-5} cm^2/V · s. Therefore, the bulk concentration probably increases more rapidly than the wall concentration.

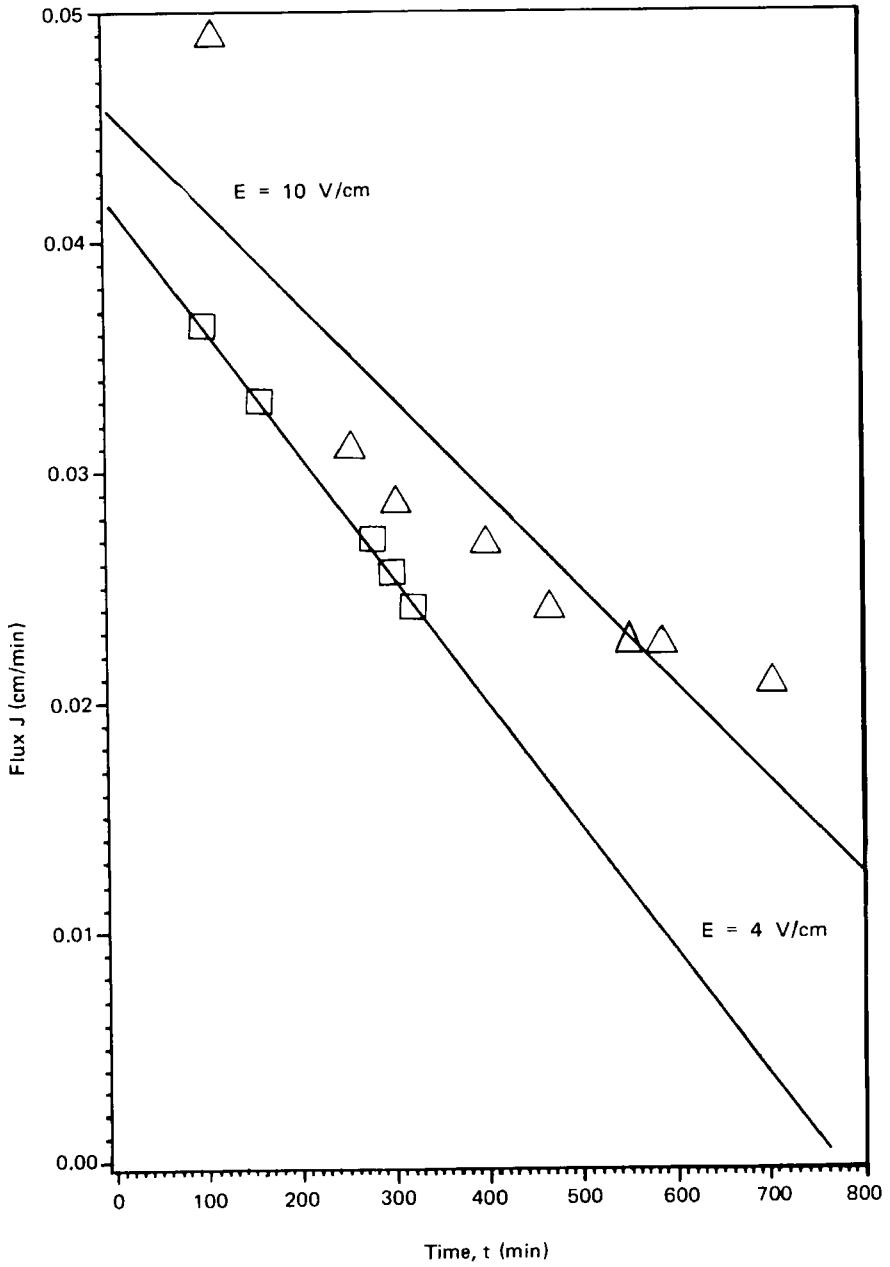

FIG. 2. Flux as a function of time when concentrating albumin solutions using electro-ultrafiltration.

TIME SAVED BY USING EUF INSTEAD OF UF OR BY INCREASING THE ELECTRIC FIELD

Making use of Eq. (3), one can show that for identical concentration ratios

$$Y_1 t_1 = Y_2 t_2$$

where t_1 and t_2 are the time needed to reach a C/C_0 ratio and Y_1 and Y_2 are the time constants. The time saved, Δt, is

$$\Delta t = t_1 - t_2 = t_1(1 - Y_1/Y_2) \tag{11}$$

For instance, from Fig. 1 of Ref. 7, 1000 min are needed to reach $C/C_0 = 2$ for normal ultrafiltration. Using electroultrafiltration, with E at 4 V/cm and $Y_2 = 1.52 \times 10^{-3}$ min^{-1}, Δt is 540 min; with E at 10 V/cm and $Y_2 = 2.69 \times 10^{-3}$ min^{-1}, Δt is 740 min.

DIAFILTRATION

The analysis of the change in salt concentration during diafiltration with an electric field can be done in an analogous manner. Mass and volumetric balances for diafiltration of a completely permeable solute (rejection = 0) which is being "washed out" gives the following equation for the solute concentration:

$$\frac{C_0}{C_f} = \exp \frac{V_w}{V_0} \tag{12}$$

where C_f is the final solute concentration, V_0 is the initial process volume, and V_w is the volume of solution added during diafiltration. V_w is also equal to the volume of solution that permeates the membrane which is equal to the instantaneous flux times the membrane area (A_m):

$$V_w = \int_0^t J(t) A_m \, dt = A_m \int_0^t J(t) \, dt \tag{13}$$

Inspection of the data in Fig. 4 of Ref. 7 and the above analysis leads to the following relationship:

$$C_f/C_0 = e^{-\beta t} \tag{7}$$

where β is a reciprocal time constant. A plot of ln (C_f/C_0) versus t will give β as the slope. For electrodiafiltration to remove NaCl from BSA solutions, this relationship is (t in minutes)

$$C_f/C_0 = e^{-0.0055t}$$

For diafiltration, it is

$$C_f/C_0 = e^{-0.00417t}$$

Using the data in Fig. 5 of Ref. 7, a time-averaged flux can be obtained by

$$\bar{J} = \int_0^t \frac{J(t)\,dt}{t} \tag{14}$$

Substitution of $\bar{J}$ into Eq. (13) and then into Eq. (12) gives

$$C_f/C_0 = e^{-\bar{J}A_m t/V_0} \tag{15}$$

Comparison of the $\bar{J}/V$ factor for diafiltration and electrodiafiltration gave the following results:

	β	$\bar{J}/V_0$	% Difference
Diafiltration	4.17×10^{-3} min^{-1}	3.4×10^{-3} min^{-1}	16.8
Electrodiafiltration	5.5×10^{-3} min^{-1}	5.68×10^{-3} min^{-1}	3.3

For diafiltration, the steady-state flux equation (Eq. 1) can be used to find the time constant β as

$$\beta = JA_m/V_0 \tag{15}$$

For electrodiafiltration using Eq. (4) for the flux and assuming k and C_w are identical to their diafiltration values, the reciprocal time constant can be predicted as

$$\beta' = \beta + \frac{EuA_m}{V_0} \tag{16}$$

Due to the high ionic strength of the buffer in the experimental conditions of

Fig. 5 of Ref. 7, the electrophoretic mobility was certainly very low in spite of the changes in pH from 6.25 to 8.1. An effective electrophoretic mobility of 10^{-5} cm^2/V · s would predict fairly well the electrodiafiltration reciprocal time constant from the diafiltration reciprocal time constant. However, to get better predictions, experiments at constant E should be done and the dependence of C_w on E should be known.

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Received by editor February 9, 1984
Revised April 30, 1984