Convective Transport of Macromolecules in Gels

by

Scott Travis Johnston

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Abstract

In porous or fibrous materials where the pore diameter or interfiber spacing is comparable to the dimensions of a protein or other macromolecule, the rates of diffusion or convection of the macromolecule tend to be lower than in bulk solution. This phenomenon, termed "hindered transport," is explained in large part by a combination of steric and hydrodynamic interactions between the permeating molecule and the medium. The primary goal of this thesis was to examine the hindered convection of macromolecules in fibrous gels. This was done by measuring the sieving coefficient (Θ, the ratio of filtrate to retentate concentration) of globular proteins and Ficoll, a crosslinked copolymer of sucrose and epichlorohydrin (Stokes-Einstein radius, $r_s = 2.5 – 7.0$ nm), in agarose membranes as a function of protein size and gel concentration. The proteins used were lactalbumin ($r_s = 2.1$ nm), ovalbumin ($r_s = 3.0$ nm), bovine serum albumin (BSA)($r_s = 3.6$ nm), and bovine immunoglobulin G (IgG)($r_s = 5.2$ nm). The volume fraction of agarose (ϕ) was varied from 0.04 to 0.08. Agarose membranes were prepared on polyester mesh supports and studied in a stirred ultrafiltration cell, and the Carcy permeabilities of the gels were determined in addition to Θ. The values of Θ decreased with increasing r_s or ϕ, as expected. From the measurements of Θ and estimates of the protein diffusivity and equilibrium partition coefficient, the convective hinderance factor (K_c) was calculated for each protein-gel combination. This is the ratio of the average solute velocity (in the absence of diffusion) to the superficial fluid velocity. For the smallest value of ϕ (0.04), it was found that K_c exceeded unity for all macromolecules studies. At this gel concentration, K_c increased with increasing solute size up to approximately 1.5 for the largest Ficoll. For larger values of ϕ, it was found that K_c decreased with increasing solute size. In those gels, K_c exceeded unity for smaller solutes, whereas $K_c < 1$ at larger values of r_s. At an intermediate ϕ (0.06), K_c for the largest Ficoll remained close to unity (0.94). For the most concentrated gels ($\phi = 0.08$), K_c for this Ficoll decreased to approximately 0.5. The observed experimental behavior for K_c was qualitatively, but not quantitatively, consistent with predictions from hindered transport theories for media consisting of parallel fibers or straight pores. Given evidence from previous partitioning and diffusion data that an agarose gel is better represented as a randomly oriented array of fibers, the quantitative discrepancies between the data and models are not entirely surprising. Thus the present results suggest that there is a need to extend theories of hindered convection to random arrays of fibers.

In order to correctly interpret the experimental results, the measured sieving coefficients were corrected for the effect of concentration polarization. A model was developed using laminar boundary layer theory to quantify concentration polarization in ultrafiltration systems in which the membrane forms the base of a stirred cylindrical container. The flow was approximated as a rigid-body rotation above a stationary surface (Bödewadt flow), with a filtration velocity that depended on the osmotic pressure of the retained solute, and therefore varied with radial position on the surface. Because the analysis was limited to moderate solute concentrations and filtrate velocities, physical properties were assumed to be constant. Attention was restricted to large Reynolds and Schmidt numbers, so it was permissible to neglect radial diffusion and to use an analytical approximation for the velocity field. The axisymmeteric convective-diffusion problem was solved using a finite difference method. One set of simulations focused on the osmotic reduction in filtration rate caused by a completely retained solute. The boundary layer results were compared with predictions based on a commonly used stagnant film model, and it was found that the latter consistently underestimated the reduction infiltration rate, although the discrepancies were no more than 21%. A comparison was also made with a "hybrid" model in which stagnant film theory was assumed to be valid locally and local mass transfer coefficients were calculated by the laminar boundary layer model. The hybrid model also underestimated the reduction in the filtration rate; however discrepancies were no more than 15%. A second set of simulations concerned the effects of polarization on apparent sieving coefficients for permeable solutes. (The apparent sieving coefficient is the filtrate concentration dividied by that in the bulk retentate, whereas the true sieving coefficient for the membrane is the filtrate concentration divided by that at the membrane surface.) A comparison of the boundary layer and stagnant film results showed that the latter consistently underestimated the effects of polarization on sieving. The magnitude of the discrepancy in the predicted ratio of true to observed sieving coefficient increased with increasing dimensionless filtration rate and with decreasing sieving coefficient, and was as much as 78% for the conditions considered. Thus the stagnant film approach was found to be much less satisfactory for correcting sieving coefficients than for predicting mean filtrate velocities. It was found that the hybrid model performed considerably better than the stagnant film model in estimating the effect of polarization on sieving, especially at very small values of Θ. For the hybrid model, the maximum deviation from the boundary layer results was only 15%. The predictive capability of the boundary layer model was tested using filtration data with BSA in two ultrafiltration cells. The agreement was found to be excellent, provided that an appropriate value was selected for the angular velocity of the bulk fluid.

Thesis Supervisor: William M. Deen
Title: Carbon P. Dubbs Professor of Chemical Engineering, MIT.