254a Hindered Transport in Biological and Biomimetic Materials

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Hindered transport theory provides a framework for understanding the effects of molecular size on the movement of macromolecular solutes through porous or fibrous media. When the solutes must pass through spaces that approach their own dimensions, the rates of diffusion and convection are reduced by a combination of steric and hydrodynamic effects. The fixed structures, be they pore walls or fibers, prevent mobile macromolecules from occupying certain positions and limit their possible paths. Further, the fixed structures increase the drag coefficient for a solute molecule and thereby decrease its mobility. These concepts were used first in the 1950s to explain microvascular permeability data, and hindered transport theory for rigid molecules in straight pores was highly refined by the 1980s. Although the theoretical framework was mature then, the absence of sufficient hydrodynamic results for eccentrically positioned solutes required that "centerline approximations" be invoked in calculating hindrance factors, even for rigid spheres in cylindrical or slit pores. More recent developments have made such approximations unnecessary, as will be reviewed. The geometric complexity of fibrous media, such as hydrogels, has made it much more difficult to develop detailed hydrodynamic models for hindered transport. There has also been a paucity of experimental data in well-characterized systems, especially for gels that contain two or more types of crosslinked polymers. One of many biological examples is the glomerular basement membrane (GBM), which is part of the blood ultrafiltration barrier in renal glomerular capillaries. The GBM is about 90% water by volume and has a polymeric network consisting of collagen IV, laminin, fibronectin, entactin, and heparan sulfate proteoglycan. We have been exploring the hypothesis that the permeability properties of GBM are dictated largely by its having a certain mixture of fine and coarse fibers, and have sought to mimic those properties in synthetic gels by covalently incorporating varying amounts of dextran ("fine fibers") into agarose gels ("coarse fibers"). It was found that linking small amounts of dextran within agarose gels markedly reduced their Darcy permeability (k), consistent with predictions for flow through fiber arrays. Hindered convection was studied by measuring the sieving coefficient (Q) of narrow fractions of Ficoll in agarose and agarose-dextran membranes. As expected, Q decreased with increasing Stokes-Einstein radius of Ficoll or with increasing concentrations of either agarose or dextran. For each molecular size, Q plotted as a function of k fell on a single curve for all gel compositions studied. The dependence of Q on k and Stokes radius was predicted well by a hydrodynamic theory based on flow normal to the axes of equally spaced, parallel fibers. Diffusive and convective hindrance factors in the synthetic gels were quite similar to those in GBM, when compared on the basis of similar solid volume fractions and values of k. Overall, the results suggest that hindrances to solute transport can be predicted fairly well from a knowledge of k, even in synthetic or biological gels of complex composition.