MODELING OF GLOMERULAR BASEMENT MEMBRANE AS A CHARGED FIBER-MATRIX

Lawrence A. Mark

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James C. Williams, Jr., Ph.D., Chairman

Paul Dubin, Ph.D.

Richard Haak, Ph.D.

Thomas Hurley, Ph.D.

Frederick Kleinhans, Ph.D.

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ABSTRACT

Modeling of Glomerular Basement Membrane as a Charged Fiber-Matrix. Mark, Lawrence A., Ph.D. Medical Biophysics Program, Indiana University School of Medicine, Indianapolis, IN 46202 110 pp. Chief advisor: James C. Williams, Jr., Ph.D.

We set out to determine if the magnitude of fixed anionic charges found in glomerular basement membrane (GBM) is theoretically capable of providing GBM with the degree of restriction necessary to account for the low sieving coefficient observed for negatively charged albumin. Model functions for partitioning of macromolecules into matrix examined were a charged pore model and charged fiber-matrix models based on either the theory of Ogston or Schnitzer. The fiber-matrix models relied on calculations of the free energy of electrostatic interaction for an assemblage of a charged sphere and charged rod. Methods used for calculating this energy were derived from the Derjaguin approximation, a finite element analysis, or an exact formula derived for the interaction between an ion-penetrable rod and sphere. Partition experiments were performed to test the validity of the models using carboxylated Ficoll and polyacrylamide gel containing fixed anionic charges. It was concluded that the charged fiber-matrix models, using either the finite element analysis or ion-penetrable approximation to calculate free energy, could be used to predict the partitioning of a charged macromolecule into a loose gel where solute on average interacts with only one fiber at a time, and that the mathematical models moderately underestimated partitioning in tight gels where fibers are on average separated by less than six Debye lengths. Also, the Derjaguin

approximation consistently overestimated interaction energy in the experimental system tested. The Schnitzer/finite element analysis model was then used to estimate GBM charge from parameters gleaned from the literature. Since GBM is a tight gel, it was expected that the model would predict GBM charge only slightly higher than the true charge. However, this model predicted a GBM charge several orders of magnitude greater than any reported experimentally. We conclude that the model predicts that GBM charge could not significantly contribute to the charge selectivity of GBM.

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