New Aspects on the Difference in Permeability Between Proteins and Polysaccharides in the Glomerular Filtration Barrier

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Background:
One of the many unresolved questions regarding the permeability of the glomerular filtration barrier (GFB) is the reason behind the marked difference in permeability between albumin and polysaccharide probe molecules such as Ficoll. The difference in sieving coefficients between albumin and a Ficoll molecule of the same molecular size (~36 Å) is ~2-3 orders of magnitude. Although this large difference in permeability has been attributed mainly to charge effects, we have previously shown that this would require a supraphysiological amount of charge on the filtration barrier, being about ~10 times more than the charge on the albumin molecule (~0.02 C/m^2).

Methods:
The classic heteroporous model by Deen, Bridges, Brenner and Myers (Deen et al, AJP Renal Physiology, 1985) was extended by introducing size distributions on the solute molecules, making them flexible in their conformation. Experimental sieving data for Ficoll, both from the rat glomerulus and from precision-made nanopore membranes, were analyzed using the model. The variation in solute size was quantified in terms of the geometric standard deviation (gSD) of the solute size distribution. The (mode) solute radius was assumed to be equal to the SE-radius and the pore size distribution gSD was set to unity.

Results:
For the glomerulus (n=7), a gSD for the Ficoll size-distribution of 1.16 (± 0.01) was obtained, along with a small pore radius of 36.1 Å (± 0.5 Å) and a large pore radius of 152 Å (± 7 Å). For the nanopore membranes (n=16), a gSD of 1.24 (± 0.01) was found.

Conclusions:
In the current study, we show, for the first time, that a variation of only ~15-17% in the size of the molecule is sufficient to explain the difference in permeability between albumin and Ficoll. In addition, we show that the effects of applying a size-distribution on the solute molecule are only evident when the molecular size is close to the size of the selective elements of the barrier. This is well in line with experimental data, both from the GFB and from synthetic membranes.