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What is the molecular weight cut-off of BASi's microdialysis probes? Do you have probes with large cut-offs for sampling small proteins?

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Molecular Weight Cut-Offs (MWCO) of what are fundamentally kidney dialysis-type membranes are rather a nebulous concept when applied to microdialysis. The manufacturers of the membranes give a MWCO value, but they usually don't define how those numbers were derived. Since the manufacturers typically don't reveal how they determined a particular MWCO, most people, BASi included, cannot know for certain how they arrive at a given value.

One might envision their test procedure to be somewhat similar to doing protein purification by dialysis, much as you might have done in an undergraduate biochemistry lab. In such a scenario, one can imagine the manufacturers filling some membrane fibers with markers of various molecular weights. They would then seal the membrane ends and put the filled membranes in a beaker containing several liters of buffer, and then let the buffer and the membranes stir for x hours while dialysis occurs, until everything comes to equilibrium. Naturally, even in this situation, as the MWCO of the analytes increases toward the membrane's cut-off, the amount of those higher MW analytes crossing the membrane declines compared to lower MW compounds, since the larger the analyte, the harder it is to get it through a membrane pore of any given size.

If this is indeed how it is done, that would certainly explain why the MWCOs reported for a given membrane are usually considerably higher than the MWCOs actually seen when doing microdialysis. With microdialysis, since the lumen of the membrane is being continually perfused, the kinetics of microdialysis dictate that you typically would never reach equilibrium with the surrounding solution. As a result, since the larger analytes would not have an opportunity to reach equilibrium, larger analytes are much less likely to cross the membrane, at least not in anything approaching detectable levels. This is probably why, even though a membrane manufacturer may rate a particular membrane at some MWCO, often the effective MWCO one can actually expect to see under the kinetics of microdialysis is perhaps 20-30% of the rated MWCO. For example, the membranes used in BASi probes are rated at 30K Daltons (BR, IBR, LM, DL, SM, and UF probes) to 38K Daltons (MBR probes). However, in practice, when used for microdialysis we would not expect to see recovery of analytes higher than perhaps 6-7K Da.

We have had a report that insulin will cross the membrane, but in its monomeric form insulin is ~6K Da. The same pattern is true of most kidney dialyzer membranes. For ex-ample, with microdialysis probe membranes which are rated at 20K Da, effectively speaking, under microdialysis conditions the largest molecular weight compounds which typically cross (though in low quantities) are in the 5-6K Dalton addition to these basic kinetics issues which, as I envision it are due at least in part to the static versus actively perfused use of the membrane, effective MWCO numbers are further complicated by differing perfusion flow rates, different lengths of membranes on different probe types, globular versus linear analytes and different membrane manufacturers apparently using different approaches to rate their membranes for sampling larger compounds by microdialysis, the solution is not simply to make probes with bigger membrane pores so larger analytes can be dialyzed through them. This is because when larger pores are used, the pore size quickly becomes large enough that water can cross the membrane; so rather than doing MD, one starts to pump very finely filtered water from the probe into the tissue. This is decidedly undesirable.

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