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How are the blood serum proteins distributed inside the PVDF hemodialysis membranes?

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Abstract

The concentration profile of proteins penetrating through a polymer membrane is usually unknown, but it can be characterized using synchrotron radiation tomography. Here, we discuss a paper reporting this using the PVDF membranes with human blood serum proteins.

Keywords: Hemodialysis membranes; Polyvinylidene fluoride-based membranes; Pore size, Blood protein absorption; Synchrotron radiation micro computed tomography

Introduction

Minimization of blood serum proteins interactions with polymer membranes could decrease side effects and lead to drastic improvement of hemodialysis technology. One of Canadian labs is trying to chemically modify commercial membranes, influencing their hydrophobicity and surface charge. To characterize the membranes, they are using Synchrotron Radiation Micro-Computed Tomography. This is a unique method, which should give previously unavailable information regarding distribution of the proteins inside the membrane from one membrane surface to another. It was offered by the biomedical imaging and therapy beamline (BMIT) at the Canadian Light Source (CLS), a national research facility of the University of Saskatchewan.

Used in [1] PVDF membranes as sheet material were supplied by Sterlitech, which sells both hydrophobic and hydrophilic filters and membranes. For membranes, where the company does not see the pores, it gives only molecular weight cutoff, which may be from 30,000Da to 800,000Da. https://www.sterlitech.com/flat-sheet-membranes.html. For filters the pore size may be up to 0.45 micron, but they cannot be used for hemodialysis, which is not mentioned on company's web page as a possible application. Paper [1] describes distribution of human serum proteins inside polyvinylidene fluoride-based membranes, and it also gives references to previous publications from this group. Probably, because of that many experimental details are absent. SEM micrographs in [1] did not have the scale, but magnified scanning electron microscopy (Fig. 4b) shows the pores with the size up to 0.1 micron, i.e. too large for hemodialysis membranes. So, it is not clear why in the title of [1] these filters are called dialysis membranes. According to https://www.sterlitech.com/hydrophilic-pvdf-membranes.html, PVDF filters are hydrophilic. Nevertheless, the authors write that PVDF membranes are hydrophobic and believe that it is a good idea to use modifications with hydrophilic agents.

The paper [1] does not say what were the major properties of the membrane, including membrane thickness. It was modelled as 10 parallel regions, but their thickness also was not given. It is unknown if the membrane was asymmetric (all hemodialysis membranes are), so it is not clear what side was on top, what was on bottom and if the protein distribution depended on filter orientation. Some of the PVDF membranes were modified by zwitterionic fragments, and they "had a surface charge of -2.5 and 0.35, respectively." No units were given. What was really measured was zeta potential ("with a precision of ±0.01mV"). So, were the authors talking about mV, or coulombs, or the surface charge per unit area, stays unknown.

Gold nanoparticles of different shapes were linked to the proteins and produced bright spots on the image, thus providing quantitative information about the amount of protein adsorbed

at each scanned layer, but none of these images were given. In several figures authors give adsorption data (should it not be an absorption inside the membrane?) for three different proteins. Everywhere the units are mass %, which makes it impossible to compare with other papers. Fig. 8 gives information for fibrinogen transported from a solution of single protein and a solution of three proteins together. Comparison was done for initial and modified membranes, and fibrinogen adsorption changed in the range 1x10(-10) % to 3x10(-10) %. In other figures this value is in the few % range. How could the authors measure these small numbers, and why they are at least 10(-10) times less than others, is not clear. According to Sterlitech, PVDF filters have low binding of bovine serum protein, 4μg/cm^2. Finally, the fundamental question is how did the proteins penetrate into the membrane? Solutions were "injected" into membranes, with further analysis of the membranes using in situ the X-ray-based synchrotron imagine technique. What does the word "injected" mean is not clear because for solution to enter the 0.45μm pores one would need some external pressure? For smaller pores the pressure should be only higher. Was the injection pressure high enough, and was transport determined by hydrodynamics? If hydrodynamics is dominant, with time concentration profile should disappear.

Another option was that it was diffusion, determined by the first or the second Fick's laws. In both cases initially the concentration in the membrane at the donor surface should be relatively large and decrease inside towards the acceptor side. For diffusion in a homogeneous membrane the profile should slowly change with time and finally reach the straight line changing in relative coordinates from unit to zero along the membrane thickness. Time was not mentioned in the paper, and whether the process was time-dependent is not clear.

In no case does the experimental data in [1] follow well-known theoretical tendencies. Probably, the membrane was asymmetric, with traditional very thin and selective layer and the rest was a porous mechanical support, which is not interesting for hemodialysis step. Thus, without proper explanation it is possible that unique and expensive Synchrotron Radiation Micro-Computed Tomography does not give important results, not only in this, but also in many previous papers from this group. It seems that the title of this paper should be changed from given in References to "Investigation on Human Serum Protein Depositions Outside Polyvinylidene Fluoride-Based Filters." As previously [2,3], the authors are politely invited to discuss this and other related scientific issues.

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