

Some results in the development of polyether sulfone hemodialysis membranes

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Abstract: Development of hemodialysis membranes should be based on knowledge of their physicochemical properties, including surface charge, pore properties, and state of water in a swollen membrane. Here, we analyze the unexpected results of polyether sulfone membrane research conducted in one of the Canadian Universities

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I. Introduction

Hemodialysis is the major treatment for patients with serious kidney problems. Its major purpose is using membranes to remove low-molecular weight toxins from blood and keep larger molecules, especially proteins. This is possible based on rather small pores in the membranes, or even due to mobility of polymer chains forming rather large defects in the hydrophilic membranes swollen in water. It is important to minimize side effects of this process and improve membrane compatibility in contact with blood, minimizing protein coagulation on the membrane surface and possible immune response.

The Membrane Science and Technology Research Center at the University of Saskatchewan conducts research on Advanced Membrane Science and Nanotechnology for Hemodialysis and Biomimetics. We will discuss some of recent publications from this Center.

Results. One of the widely used in Canada hemodialysis membranes is based on polyether sulfone (PES). It appears feasible to enhance its performance by incorporating positively charged groups, such as amino groups. Molecular dynamics simulation demonstrated that after two types of amino-functionalization affinity for fibrinogen decreased and affinity energy was -7.6 and -8.2 [1]. The control value for nonmodified membrane was not given. The units also were not given but we can assume that they are kcal/mol. The calculated difference is not that high. Nevertheless, the authors believe that they proved enhanced antifouling properties and superior hemocompatibility of their new membranes.

Total binding energy with fibrinogen at body temperature was much bigger. It was positive 233,075.42 kcal/mol ([2], Table 2). Simultaneously, hydrogen bonding was characterized by negative 189.33 kcal/mol. The reason for different signs was not discussed. Note that simple elevation of patient blood temperature resulted in nearly 32 kcal/mol higher total interaction energy between fibrinogen and the PES membrane [2].

Some other numbers are also impressive. Computations with fibrinogen “used a docking box centered such that $X = 56.94\text{\AA}$, $Y = 3.209\text{\AA}$, $Z = -54.55\text{\AA}$ aligned directly with the central active site of the fibrinogen protein. Residues containing atoms larger than 7\AA were excluded.” It is known that the largest known atom radius is less than 3\AA . Physically, accuracy like 0.009\AA for Y-coordinate also does not make much sense.

This paper has two other calculated values, and the authors call them water mobilities. We should remind you that A. Einstein introduced the term mobility (U) to describe Brownian motion. Mobility is described by Fokker-Einstein relation $U = D / RT$, and has the meaning of velocity per molar force. The values in [1] are 9.74×10^{-7} and 9.85×10^{-7} (again without units and without a control value). Equation to calculate this value was taken from a paper [3]. The author of this paper calculated mean square displacement, which for the bulk water was equal to $3.4 \times 10^{-9} \text{ m}^2/\text{s}$. It reflects diffusion coefficient and may decrease by 10 times in a membrane. Thus, the authors of a paper [1] calculated the local diffusion coefficient. If the units are the same as in [3], with PES it is ~3000 times more than one should expect for water in a swollen polymer. Paper [7] used the term mobility of hydrates structures. It was calculated using the same equation, but this time the value for PES was 6.96×10^{-6} (Table 6).

Paper [4] from the same lab described superhydrophobic PES membrane with enhanced hemocompatibility and reduced interactions with human serum proteins. However, it is known that synthetic

polymer membranes with extreme hydrophobicity led to membrane fouling due to the adhesion of plasma proteins to the membrane surface. This hydrophobicity could cause platelet adhesion, aggregation, and coagulation [5].

According to [6], when heparin was immobilized covalently and via electrostatic interactions with the positively charged PES surface, both types of immobilizations on the membrane resulted in a decrease of the surface potential from -60 mV (unmodified PES) to -9.16 mV for the covalently attached heparin, and to -13 mV for the electrostatic complex, respectively. The authors called this value "surface charge." Thus, the authors measured the charge in millivolts, with accuracy ± 0.01 mV. Moreover, positively charged (according to the abstract) unmodified PES had negative surface "charge"! Heparin has total negative charge due to sulfate and carboxylic groups. Nevertheless, when it binds to PES, the polymer becomes less negative. For the same PES in [7] the surface "charge" was -6.92 mV.

It is interesting that based on polyarylethersulfone and polyvinylpyrrolidone blend REVACLEAR 400 dialyzer membranes have zeta potential 64 mV [8], i.e., the value is very similar to that of PES (-60 mV) but has an opposite sign.

Another surprise was that the freezing temperature for non-freezable water in PES was $+0.68^{\circ}\text{C}$ [6], though by definition if this water is not freezable it should be less than 0°C !

In paper [7], the authors also claim that the "PES membrane is a microporous structure with pores bigger than 50 nm", though it is an osmotically active membrane permeable only for much smaller molecules and the structure should be called nanoporous. According to Table 12 pore diameter was 1.45 nm. In other papers from the same lab the average pore size of both dry modified and unmodified PES membranes was 10 nm [3]. Similarly, pore size in cellulose-triacetate osmotically active membrane was reported as $0.45\ \mu\text{m}$ [10], but earlier it was near 7.5 nm [11].

Another type of problem with paper [5] is that presented in figures 3a and 3b microscopy images of PES membrane are the same as figures 4b and 4c in [10] for cellulose triacetate membrane. Polymers are different, porosity is different, membrane is different, but illustrations are the same. Pore size in triacetate cellulose membrane was surprisingly large, $0.45\ \mu\text{m}$, and it was possible to see it using optical microscope [10], but one could not see them in SEM micrographs [11, Fig. 1c]. So, in this case the situation is opposite: polymers are the same, membranes are the same, but the images and pore size are very different.

In addition, figures 8-10 in [10] are practically the same as in earlier published [12] with Millipore nitrocellulose membranes impregnated by capric acid. No reference [12] or any comment was given. Note that these figures show stochastic oscillations of transmembrane potential, and according to an elementary probability theory and the Oxford Dictionary this type of process cannot be exactly reproduced in principle.

Summary. It is known that father of reverse osmosis Srinivasa Sourirajan at the beginning of the 1960s settled in Ottawa. His work made the National Research Council in Canada the world's leading center for membrane research. Later he formed the Industrial Membrane Research Institute in the Department of Chemical Engineering at the University of Ottawa. Several times the PI of the Membrane Center at the University of Saskatchewan wrote that she incepted development of new hemodialysis membranes in Canada. Of course, it would be a great achievement, but, first, the fundamental problems raised in this paper should be resolved.

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References.

- [1]. S. Nazari, A. Mollahosseini, A. Abdelrasoul. Computational Analysis of Amine Functionalization in Zwitterionized Polyether Sulfone Dialysis Membranes. *Membranes* 2024, 14, 226-241.
- [2]. A. Mollahosseini and A. Abdelrasoul. Assessment of Fibrinogen Thermal Conductivity and Interaction Energy with Polyarylethersulfone (PAES) Clinical Hemodialysis Membranes at Normal and Elevated Patient Body Temperatures, *Journal of Carbon Research*, 2023, 9, 33.
- [3]. S. Mieda, Analysis of the Interaction between a Protein and Polymer Membranes Using Steered Molecular Dynamics Simulation to Interpret the Fouling Behavior. *Bull. Chem. Soc. Jpn.* 2020, 93, 1443-1448.
- [4]. D. Kalugin, J. Bahig, A. Shoker, H. Doan, S. Kirychuk, A. Abdelrasoul. Superhydrophobic polyether sulfone (PES) dialysis membrane with enhanced hemocompatibility and reduced human serum protein interactions: Ex vivo, in situ synchrotron imaging, experimental, and computational studies. *Separation and Purification Technology* 2024, 335, 126071, 14 pages.
- [5]. Y.-A. Chen, S.-M. Ou, C.-C. Lin, Influence of dialysis membranes on clinical outcomes: From history to innovation. *Membranes* 2022, 12, 152.
- [6]. D. Kalugin, J. Bahig, A. Shoker and A. Abdelrasoul. Heparin-Immobilized Polyethersulfone for Hemocompatibility Enhancement of Dialysis Membrane: In Situ Synchrotron Imaging, Experimental, and Ex Vivo Studies. *Membranes* 2023, 13, 718.
- [7]. A. Mollahosseini, J. Bahig, A. Shoker, A. Abdelrasoul. Uremic metabolite-zwitterionic hemocompatible poly ether sulfone dialysis membranes: Computational and hemocompatibility assessment based on hydration layer stability and ex-vivo investigations. *Surfaces and Interfaces* 2023, 43, 103536, 16 pages.

- [8]. A. Abdelrasoul, H. Westphalen, S. Saadati & A. Shoker. Hemodialysis biocompatibility mathematical models to predict the inflammatory biomarkers released in dialysis patients based on hemodialysis membrane characteristics and clinical practices. *Scientific Reports* 2021, 11, 23080, 16 pages.
- [9]. U. Eduok, S. Saadati, V. Doan, A. Shoker, A. Abdelrasoul. Immobilization of novel synthesized phosphobetaine zwitterions on polyethersulphone (PES) hemodialysis membranes to induce hemocompatibility: Experimental, molecular docking, and *ex-vivo* inflammatory biomarker investigations. *Biomedical Engineering Advances* 2024, 7, 100120, 12 pages.
- [10]. G. S. Rueda Pl'a, M. Maghami, H. Doan, N. Zhu, A. Abdelrasoul. Investigation on the morphology and the permeability of biomimetic cellulose triacetate (CTA) impregnated membranes (IM): *In-situ* synchrotron imaging, experimental and computational studies. *Materials Chemistry and Physics* 2022, 292, 126755, 14 pages.
- [11]. H. Westphalen, S. Saadati, U. Eduok, A. Abdelrasoul, A. Shoker, P. Choi, H. Doan & F. Ein-Mozaffari. Case studies of clinical hemodialysis membranes: influences of membrane morphology and biocompatibility on uremic blood-membrane interactions and inflammatory biomarkers. *Scientific Reports* 2020, 10, 14808.
- [12]. N. Kocherginsky. Biomimetic Membranes with Aqueous Nanochannels. Phase Transitions and Oscillations. *Membranes and Membrane Technologies* 2021, 3, No. 6, pp. 442–447.