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Calibration of ultrafiltration membranes against size exclusion chromatography columns

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ABSTRACT

Using the extension of the concept of universal calibration parameter, yielding a relation between the hydrodynamic volume of molecules and the elution volume in size exclusion chromatography (SEC), to retention coefficients in ultrafiltration (UF), we propose a direct calibration of UF membranes against chromatography columns. Plotting the retention coefficient by one given UF membrane of a series of probe molecules versus their elution volume in SEC chromatography provides a calibration curve for this membrane. For a wide range of retentions, such calibration can be directly used to predict the retention of any molecule: one only needs to measure its exclusion volume by the SEC column, and read the retention by the calibrated membrane on the calibration curves.

The method has been tested with dextran and PEG for the calibration, and milk proteins as test molecules, for three different membranes. The predicted values of the retention are in rather good agreement with those experimentally measured in a UF cell.

1. Introduction

Despite a widespread use of ultrafiltration (UF) in various industrial sectors and biological or pharmaceutical laboratories, the characterisation of UF membranes has not been standardised yet, and the characteristic parameters most often used, namely the molecular weight cut off (MWCO) and the permeability to water (Lp) provide not more than a vague idea of the selectivity and flux when in operation. This is easily explained by several aspects of membrane filtration. Fouling is one, which depends not only on the membrane material properties and structures, but also on the fluid to be processed and of its interactions with the material, which are many. Another source of unreliability of MWCO values lies in the various ways of measuring it. Operating conditions (concentration, pressure, hydrodynamics, temperature, etc.) modulate the concentration polarization that is a major factor affecting the observed value of the rejection coefficients, from which the MWCO is derived. The variables chosen to represent the selectivity might not be totally appropriate: The molecular weight very well characterises a molecule within a class (e.g. the degree of polymerization), but it does not represent its absolute size when in solution and it is quite well known that whether a membrane has been characterised using dextran, polyethylene glycols (PEG) or proteins, its MWCO will appear different.

This later issue is particularly important whenever an end-user would like to select which membrane (often characterised by its "MWCO") is needed to perform the separation of macromolecules within a mixture. Field or lab tests remain today the safer way to choose the most appropriate membrane from a short list.

In 1995 [1], we proposed to address this question by analogy with the so-called "universal calibration" method proposed by Grubisic et al. [2] for the calibration of size exclusion chromatography (SEC) columns. These authors demonstrate by a series of experiments using a given SEC column, that plotting the elution volume of solutes of a wide range of molecular architectures (e.g. linear "comb" and "star polystyrene, linear metacrylates and various copolymers) versus their "hydrodynamic volume" instead of their molecular weight or their Stoke radius, allowed all the data to fall on the same calibration line. More recently, Hamaliec and Meyer [3] and Jackson et al. [4] have generalized the SEC universal calibration curve for complex polymers. Via a similar approach based on the analogy between SEC chromatography and ultrafiltration operated in conditions where retention only relies on a size exclusion mechanism we showed that for four different membranes (40, 100, 200 kDa and 0.1 μm), made of different materials (sulfonated polysulfone (SPS) and PVDF), plotting the solute retention versus the hydrodynamic volume of the molecules drove to the same type of result: i.e. a single calibration curve, independent of

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Abbreviations: BSA, bovine serum albumin; TDS, total dissolved solutes; SEC, size exclusion chromatography; UF, ultrafiltration.

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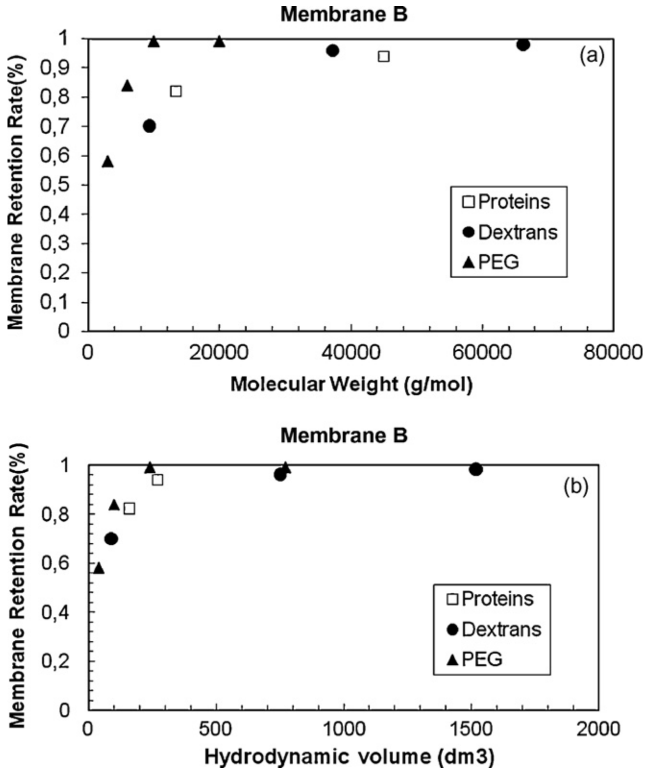

Fig. 1. Comparison of the same retention data obtained for a SPS membrane 100 kDa, when plotted against the molecular weight (a) or the hydrodynamic volume (b) of the tracers molecules. The latter offers a single characteristic which does not depend on the kind of molecule used as a tracer.

the nature of the tracer used. Fig. 1 offers an illustration of the kind of improvement one can obtain when plotting the retention versus the hydrodynamic volume (1b) instead of the molecular weight (1a).

Obtaining a true sieving characteristic curve for UF membranes was certainly a progress in their characterisation, however many aspects of the problem of using these characteristics for the prediction of the membrane performance remained obscure.

As for an example, using such characteristic curves to predict the selectivity that should be obtained for any given molecule is still a problem since the hydrodynamic volume is seldom known *a priori*. Probably for this reason, this approach has not been often used. However size exclusion chromatography appeared as an obvious additional tool which can help complete the membrane users' toolbox, and its use has been further discussed and improved as shown in [5,6]. In 2006, Molek and Zydney [7] have however evidenced differences in the apparent hydrodynamic radii in SEC and ultrafiltration due to the influence of shear stress on the shape of flexible polymer, which does not exist in chromatography.

This is the topic of this paper to discuss on the combination of UF, SEC and various kinds of tracers in order to obtain a fast first approximation of the membrane selectivity for any given macromolecule, prior to any filtration run.

In UF membranes and SEC columns, a simplified model for the selectivity can be obtained by assuming that the selective porous medium is made of ideal capillaries which are straight, cylinders of radius r, and that molecules to be separated can be characterised by a radius a of an equivalent sphere.

In SEC, mass transfer is limited by diffusion of the molecules through the pores of the beads. The volume of elution which is the experimental characteristic of one particular molecule of radius a, depends on the pore volume, V_p, on the exclusion volume, V_o, and on the partition coefficient Φ [8]:

$$V_e = V_o + \Phi V_p \tag{1}$$

The partition coefficient has the form:

$$\Phi_c = \left(1 - \frac{a}{r_c}\right)^2 \tag{2}$$

where a is the solute radius and r_c is the average pore radius of the chromatography beads.

The relative resistance of a membrane on the transfer of a molecule A is characterised by the observed retention coefficient $R_{obs,A}$, defined as a function of the permeate concentration C_p, and the bulk concentration C_b:

$$R_{obs,A} = 1 - \frac{C_p}{C_b} \tag{3}$$

The selectivity of a membrane for a molecule A with regards to a molecule B can be expressed as $S_{A,B} = [1 - R_{obs,A}]/[1 - R_{obs,B}]$.

Because of concentration polarization effects, the concentration of the solution in contact with the high pressure side of the membrane, C_m, is larger than the bulk concentration. The retention calculated between both sides of the membrane R_m (=$1 - C_m/C_b$), and the observed retention are tight together via the Peclet number in the boundary layer adjacent to the membrane [9]:

$$R_{obs} = \frac{1}{1 + ((1 - R_m)/R_m)\exp(Pe_{bl})} \tag{4}$$

where Pe_{bl} is the Peclet number in the boundary layer, defined as:

$$Pe_{bl} = \frac{J\delta}{D} \tag{5}$$

where J is the convective flux density, δ is the thickness of the boundary layer and D is the diffusion coefficient. In particular, one notes that the limit of R_{obs} when Pe_{bl} tends towards zero is R_m.

R_m is known as the membrane retention coefficient, and depends on both diffusion and convection through the pores, which means that R_m is not an intrinsic membrane property, since it may change with operating conditions, as follows:

$$R_m = \frac{1 - \exp(Pe_{pore}) - K_h \Phi_m (1 - \exp(Pe_{pore}))}{1 - \exp(Pe_{pore}) - K_h \Phi_m} \tag{6}$$

Φ_m is the partition coefficient, K_h is an hindrance factor depending on the ratio of the molecule to pore radii and

$$Pe_{pore} = \frac{Jl}{\varepsilon D} \tag{7}$$

l is the pore equivalent length and ε is the membrane porosity.

Here one notes that at high flux, R_m tends towards $(1 - K_h \Phi_m)$, this asymptotic value of R_m, noted R_∞, then characterises the ratio of the molecules apparent size to the pore apparent or equivalent average radius.

This is on such considerations that we have tried to correlate the experimental characteristics of membranes (R) and of columns (V) for a series of molecules.

2. Material and method

As the experimental part of this paper is the same as the one published in our former paper, we provide here a summary of it.

2.1. Membranes

Ultrafiltration Tech-Sep membranes (Novasep, Miribel, France) were made of sulfonated polysulfone, of 100 kDa (Membrane B – permeability after protein adsorption: 3.1×10^{-10} m/Pa/s) and 200 kDa (Membrane C – permeability after protein adsorption: