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Static protein adsorption, ultrafiltration behavior and cleanability of hydrophilized polysulfone membranes

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Abstract

A systematic study on the influence of incrementally increased hydrophilicity of UF membranes made from chemically modified polysulfone on static protein adsorption, protein ultrafiltration performance and cleanability was performed. Hydrophilicity was imparted to the polymeric backbone either by carboxylation or sulfonation. Membranes with 100% retention towards sulfhydryl modified bovine serum albumin (cys-BSA) were made by the phase inversion process from unmodified polysulfone, five carboxylated polysulfones (degrees of carboxylation ranging from 0.26 to 1.74) and two sulfonated polysulfones (degrees of sulfonation of 0.24 and 0.58). 1000 ppm aqueous solutions of cys-BSA at pH values 3, 4.8 and 9 were used in KCl medium at either low or high concentration. Static adsorption, ultrafiltration (UF) flux reduction and protein binding strength were lower at pH 3 than at pH 9 but reached an expected maximum at the protein's isoelectric point at pH 4.8. Hydrophilized polysulfone membranes show less static adsorption and lower UF flux reduction than hydrophobic unmodified membranes. In all experiments we found that the higher the degree of carboxylation or sulfonation, the greater this effect. High ionic strengths reduced these advantages at pH values above or below the IEP but had a positive effect at the IEP.

Keywords: Ultrafiltration; Polysulfone membranes; Hydrophilicity; Protein adsorption; Fouling

1. Introduction

There are many examples of the successful use of membrane separation processes in areas such as sea water desalination, food processing, effluent treatment and process stream separation. Membrane-based processes are becoming increasingly important in biotechnology, pharmaceuticals, petrochemicals and other industries which have impact on the environment. However, economic considerations with respect to membrane lifetime, pre/post-treatment steps and flux decline are the main reasons why UF-, MF- and RO-membrane applications on an industrial scale have lagged behind their expected growth. The cost of a membrane system is highly dependent on the surface area required, which is determined by the membrane's flux. Cleaning and membrane replacement contribute up to 50% of the operating costs or 30% of the total

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costs of a typical UF membrane system [1]. While pure water fluxes with ultra- and microfiltration can be very high, fluxes with actual feed streams such as protein solutions are often significantly lower. Routine operation requires membrane cleaning when the flux reaches an unacceptable, i.e. economically unfavorable level. For this reason research is focused on the optimization of the factors determining flux decline. Three significant groups of factors can be identified: (1) feed stream properties, (2) membrane material and (3) chemical engineering aspects. Each of these groups consists of multiple parameters that interact in a complex and often not fully understood way. They contribute to one or more of the five mechanisms causing flux decline: (a) adsorption, (b) steric hindrance, (c) viscosity effects, (d) pore blocking and plugging and (e) concentration polarization. Flux reduction and fouling are often used interchangeably in membrane science literature, although the term ''fouling'' is clearly defined as a ''process resulting in loss of performance of a membrane due to the deposition of suspended or dissolved substances on its surfaces, at its pore openings, or within its pores'' [2]. Therefore adsorption, pore blocking and pore plugging are fouling mechanisms that can have reversible or irreversible character while steric hindrance, viscosity effects and concentration polarization are inherent to membrane processes and cannot be completely avoided.

The role and influence of the membrane material on flux reduction mechanisms as well as aspects of thermal and chemical resistance of the membrane material during separation and cleaning processes have been the subject of considerable research attention. The adsorptive fouling component of flux decline is known as a significant factor [3–6]. Adsorptive fouling alone can account for permeability losses of up to 90%. This finding is a driving force behind many efforts to develop new materials. A wide array of polymers with film forming properties is available today, and many modification techniques have been developed. Still, more than 99% of membranes used in separation applications nowadays are made from polymers that were originally developed for different applications [7]. Many researchers have followed the idea of increasing the hydrophilicity of a membrane material with the goal of reducing fouling. The principal behind this is that hydrophilic surfaces preferentially adsorb water rather than solutes, leaving the membrane surface unchanged. The efficiency of this approach depends also on the nature of the foulant or feed solute. Brink and Romijn [5] studied numerous polymers and surfactants which were used as preadsorbants on polysulfone membrane surfaces to reduce protein adsorption. Cationic polymers increased the adsorption of bovine serum albumin, while non-ionic and anionic polymers had the opposite effect. The results also depended on the type of protein used, since β-lactoglobulin gave different results than BSA. They concluded that electrostatic interactions between the protein in solution and the membrane surface played an important role beside the hydrophilicity aspect. Nyström [8] used unmodified and polyetherimide coated commercial polysulfone membranes to ultrafilter ovalbumin. The hydrophilicity of the membrane surface and the surface charge of the protein were concluded to be more important than the charge of the membrane surface. Hosch and Staude [9] showed that hydrophilized polyamide membranes were less prone to adsorptive fouling by human serum albumin than their unmodified counterparts.

Polysulfone-based membranes show outstanding oxidative, thermal and hydrolytic stability as well as good mechanical and film-forming properties. While scientific literature often compares membranes made from different polymers, our goal was to systematically investigate the influence of incrementally elevated hydrophilicity of PSU-based membranes on their fouling properties. Practicality (e.g. low-cost, large scale production) and durability (e.g. extended membrane lifetimes) as a final goal are major considerations when considering chemical modification routes. Carboxylation and sulfonation were chosen to produce PSU-derivatives (carboxylated polysulfone: PSU-COOH, sulfonated polysulfone: SPSU, the number denotes the degree of substitution per repeat unit) of varying degrees of substitution as shown in Fig. 1. Different levels of carboxylation can be obtained from a two stage process of lithiation, followed by carboxylation with dry ice [10]. Various degrees of sulfonation can be achieved with a sulfur trioxide–triethyl phosphate complex as a sulfonating agent [11]. In order to eliminate complications arising from pore plugging we attempted to fabricate fully retentive UF membranes for BSA ultrafiltration. BSA was selected

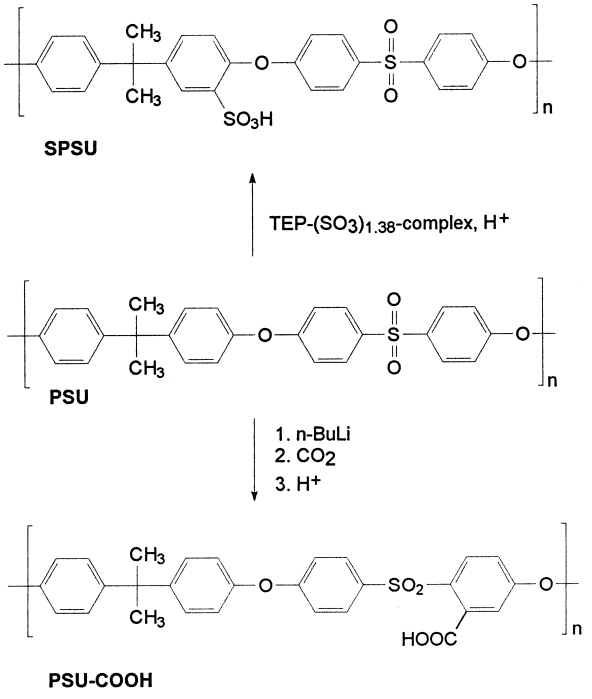

Fig. 1. Carboxylation and sulfonation of polysulfone to hydrophilize the polymer.

as a model protein for our investigations for its comparability with many other studies, for the availability of a rich database on it in literature and for reasons of cost. Kelly and Zydney [12–14] published a series of papers elucidating some of the difficulties of working with BSA. BSA tends to self-associate, forming dimers and larger oligomers. Two mechanisms have been identified: BSA contains 35 cysteine residues, 34 of these are covalently linked forming 17 intramolecular disulfide bonds. The single free cysteine residue can covalently link with another free cysteine from another BSA molecule through intermolecular oxidation by dissolved oxygen catalyzed by trace amounts of copper or iron. This thiol oxidation reaction accounts for the 5–20% dimer content. Trimerization and oligomerization are the results of repeated thiol–disulfide interchange reactions. An ionized thiol group attacks an existing intramolecular disulfide bond in this reaction while the intermolecular disulfide bond of the dimer stays intact. The presence of higher molar mass species was identified using GPC and was highly correlated with the rate and extent of fouling. These association reactions can be largely avoided by using a modified BSA, which has the sulfhydryl group capped or rendered inactive. Therefore we used Bayer's sulfhydryl modified Pentex™ bovine albumin which has all free albumin thiol groups (cysteine residue) blocked to eliminate undesirable interactions. In this study, this protein is referred to as cys-BSA.

Besides membrane thickness and pore radii, pore size distribution and pore density are the other key factors determining the permeability of a UF membrane. If membrane thickness and pore size distribution are similar for a given set of membranes, then pore density becomes important. Hence, instead of comparing absolute permeation figures, it may be preferable to compare reduced numbers. Many researchers have used this concept successfully to assess the impact of membrane material, pH value, ionic strength, etc. [13,15–17].

2. Experimental

2.1. Polymer modification and characterization: carboxylation

Udel™-3500 polysulfone (PSU) was obtained from Amoco Performance Products and used as a starting material in all carboxylations and sulfonations. Carboxylic acid polysulfone derivatives with degrees of substitution (DS) of 0.26, 0.51, 0.86, 1.19 and 1.74 were prepared by a two stage process of lithiation and carboxylation with dry ice as previously described [10]. The chemical structure and the value of DS for modified polymers were determined by ^{1}H-NMR spectroscopy of the methyl ester derivatives.

2.2. Sulfonation: preparation of the $TEP(SO_3)_{1.38}$ complex

Following a procedure [11] that is based on a concept of Noshay and Robeson [18], 100 ml of triethylphosphate (TEP, Merck) were placed in an argon flushed three-neck round-bottomed flask and cooled to 273 K. 50 ml of Oleum (65 wt% SO_3, Merck) were added carefully to the stirred solution for 1 h. The volume ratios selected here yield a

complex with a molar ratio SO_3:TEP=1.38:1, which has a moderate sulfonating capacity. The clear solution was used the same day.

2.3. Sulfonation of polysulfone with $TEP(SO_3)_{1.38}$

A solution of 300 g PSU and 1500 ml 1,2-dichloroethane (1,2-DCE, Merck) was prepared first. The reaction apparatus was a 10 l argon-flushed four neck flat-flanged glass reaction vessel charged with 2000 ml of 1,2-DCE. The PSU/1,2-DCE- and $TEP(SO_3)_{1.38}$-solutions were placed in their respective addition funnels. With vigorous stirring, the two solutions were simultaneously added to the reaction vessel at comparable rates. The amount of sulfonating agent was dependent on the desired degree of sulfonation (DS). Typically the process takes about 30 min. The color of the solution changed to beige and the precipitation of the sulfonated polysulfone (SPSU) in the acidic form was observed. Stirring was continued for another hour. If sulfonated polymer in the acid form is desired, it can be isolated by filtering and washing with 1,2-DCE. However, to prepare the salt form, isopropanol is slowly added to the reaction mixture to dissolve the acid form of the polymer. Isopropanol itself is not a solvent for SPSU, but in the presence of 1,2-DCE this combination of solvents will dissolve SPSU. The volume ratio of the two solvents depends on the DS, i.e. the balance of its hydrophilic/hydrophobic properties. The higher the DS, the more the isopropanol is needed. A clear yellow solution is obtained after approximately 1 h. Then a 10 wt% KOH/methanol solution was added slowly to the reaction solution with vigorous stirring, and the polymer precipitated to yield the desired potassium-salt product. After it had been stirred for about 1 h, the polymer was allowed to settle to the bottom of the vessel overnight. After pH control and possibly adding more base most of the solvent was decanted the next day. The polymer and salt mixture were filtered, washed with 1,2-DCE and dried at 50–60°C under vacuum. The polymer was purified by dissolving it in 2000 ml 2-methyl-*N*-pyrrolidone (NMP) and spraying the solution batchwise through a narrow capillary into a blender filled with isopropanol. Subsequent filtering and washing with isopropanol/water was followed by drying in a vacuum oven at 50°C for 24 h. The degree of sulfonation was determined by ^{1}H-NMR-spectroscopy according to the method of Kopf and described elsewhere [18,19].

Table 1
Composition of the casting solutions used for membrane

Polymer	Polymer (wt%)	NMP (wt%)	LiCl (wt%)
PSU	22	78	
PSU-COOH 0.26	25	75	
PSU-COOH 0.51	22	78	
PSU-COOH 0.86	20	80	
PSU-COOH 1.19	20	80	
PSU-COOH 1.74	20	80	
SPSU 0.24	28	68	4
SPSU 0.58	26	70	4

2.4. Membrane fabrication

The primary goal in the membrane fabrication process was to manufacture membranes that would be fully retentive towards BSA. To achieve this goal we varied either the polymer concentration in the casting solution or added LiCl to it (Table 1). Polymers were dried at 60°C under vacuum for at least 12 h. Casting solutions were made by preparing polymer solutions in NMP.

Ultrafiltration membranes were cast on an automated casting machine that allowed precise control of casting conditions [20]. The solutions were cast onto a nonwoven polyethylene backing using a round bar having a 200 μm gap. The casting speed was 5.08 cm/s. The pregelled membranes were exposed to air (humidity<15%, T=293 K) for 20 s and then gelled into RO water at 276 K. Multiple changes of bath water ensured complete solvent exchange. Membranes were stored in RO water (0.5 wt% NaN_3 to prevent bacterial growth) at 293 K.

2.5. Determination of permeability and cut-off

Membranes were characterized by pure water flux and by successive permeation of dilute solutions containing a single solute of various molar masses. We favor this method over using solutions containing a solute mixture to obtain a molecular weight cut-off curve for the membrane. It has been demonstrated that the use of mixtures tends to underestimate the molecular cut-off and the pore size of the membrane due to

solute–solute interferences that occur during the passage of the mixed solutes through the membrane pores [21,22]. Polyethylene glycols (PEG, Fluka) were chosen as probe solutes since they are water soluble and can be readily obtained commercially with narrow molar mass distributions. This permitted the direct use of these solutes without further processing. In order to minimize solute–solute interactions and concentration polarization, dilute solutions of 200 mg l^{-1} were used in all runs. Membrane permeation experiments with PEG were performed with an automated membrane testing system developed at the National Research Council of Canada [22]. The testing unit is a computer-controlled sampling device which prepares up to five test solutions and successively circulates them through four banks of three, thin channel, crossflow cells. The cells are circular with a impinging feed at the center of the membrane, promoting mixing at the membrane surface beyond that at the mean crossflow velocity of 0.8 m s^{-1} (N_{Re}=800). All permeation experiments were performed at 297±1 K under an operating pressure of 3.58±0.03 bar. A 0.1 μm filter was included in the test loop to eliminate possible contamination particles. The permeation area was 14.5 cm^2. Solute retention R was calculated as follows:

$$R = \left(1 - \frac{c_P}{c_R}\right) \times 100\% \quad (3.1)$$

where c_P and c_R are the concentrations of solute in the permeate and retentate, respectively.

Solute concentrations were determined by total organic carbon using a Shimadzu TOC 5000 analyzer. A series of PEGs of various molar masses and narrow molar mass distributions was used: 1.5, 3, 6, 12 and 35 kDa.

2.6. AFM-measurements

A topographical map of some membrane surfaces was obtained by scanning a silicon tip attached to a cantilever over the membrane surface, while maintaining a constant force between the tip and the sample. The deflection of the tip and cantilever was measured optically by a reflected laser light beam off the back face of the cantilever (NanoScope III, Digital Instruments). The setup was submerged in water to avoid structural changes of the membrane surface as they occur during drying, the scan size was 100×100 μm.

2.7. Fouling experiments

In order to evaluate the influence of various degrees of sulfonation and carboxylation (i.e. hydrophilicity) on fouling behavior, it was necessary to measure the following fluxes (the same coupons were used through steps 1 to 4):

1. J_0, the initial electrolyte solution flux after 10 h of membrane compaction at 3.6 bar and 283 K. All experiments were performed at this temperature due to investigations by Meireles et al. [23] who determined a critical operating temperature below which pump shear-induced albumin denaturation would become negligible. Preliminary experiments revealed that flux reduction due to pressure-induced compaction of the membrane occurred within the first few hours to the most significant extent. These structural changes are partially reversible upon pressure release within a time frame of several hours. For the experiments presented here, they were insignificant because pressureless experimental sections were brief. Moreover, initial electrolyte fluxes were preferred over pure water fluxes as the basis of comparison because of pore size changes due to the pH of the solution [24]. PSU-COOH-membrane pore sizes can be reduced by 10–25% in acidic environments, while basic pH can enlarge them up to 100%. Therefore, when comparing fluxes, it is important to keep the pH and ionic strength constant during all segments of the experiment. J_0 was measured gravimetrically until the flux remained constant.
2. J_a, the electrolyte solution flux of the membrane which has been fouled by static adsorption. A 1000 ppm solution of cys-BSA (pH and ionic strength the same as for J_0) was circulated through the gently stirred cells (500 rpm) at 283 K for 2 h with no transmembrane pressure. It can be safely assumed that static adsorption had ended after this time period as the former investigation by Matthiasson [15] on polysulfone (60 min) and cellulose acetate membranes (10 min) had shown. The cells were rinsed thoroughly three times at the end with protein-free

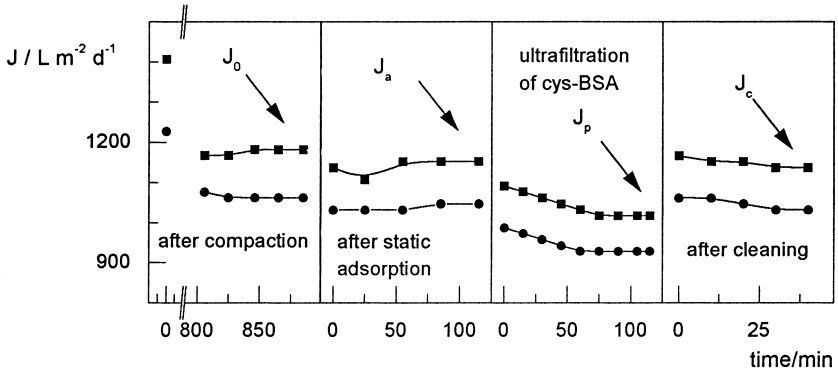

Fig. 2. Typical standard protocol for fouling experiments, two examples.

electrolyte solution. J_a was measured until the flux remained constant.

3. J_p, the ultrafiltration flux after 2 h of ultrafiltering a 1000 ppm solution of cys-BSA through the membrane. Retention was determined successively by sample collection for subsequent TOC analysis.
4. J_c, the restorable electrolyte solution flux after a cleaning procedure. The membrane coupons were removed from the cells, turned over and backflushed with 5 l of electrolyte solution. Upon turning them over once again, J_c was measured until it remained constant.

Fig. 2 shows a typical standard protocol for the fouling experiments. Three pH values (3, 4.8, 9) and two KCl concentrations (0.001 and 0.1 M) were used, yielding a total of six experiments. Two or three coupons of each membrane were tested. These experiments were carried out in an ultrafiltration setup developed at the University of Essen. It consists of four stirred dead-end ultrafiltration cells with Teflon-coated stirring bars close to the membrane surface. The cells are connected to form a closed-loop system. The active membrane area is 9.6 cm^2, the applied transmembrane pressure was always 3.6 bar and was measured at the inlet and the outlet of the cell bank (pressure difference was less than 70 mbar). Electrolyte flow was 510 ml min^{-1}.

3. Results and discussion

3.1. Polymer modification

A wide range of carboxylated and sulfonated polysulfones could be obtained. Degrees of carboxylation were determined to be 0.26, 0.51, 0.86, 1.19 and 1.74. Degrees of sulfonation were 0.24 and 0.58; higher sulfonation DS are obtainable but it is difficult to manufacture mechanically stable phase inversion membranes with ultrafiltration characteristics from those polymers because they are prone to swelling.

3.2. Determination of permeability and cut-off

As shown in Fig. 3 the primary goal of the membrane fabrication process was achieved: all membranes tested had comparable separation properties and could be assumed fully retentive towards BSA. Each cut-off curve in Fig. 3 is derived from curves of at least six coupons per membrane sheet.

The molar masses M of the used PEGs were correlated with their Stokes–Einstein radii r(PEG), determined from intrinsic viscosity measurements [22], where

$$r(\mathrm{PEG}) = 0.0262\,\mathrm{nm}\sqrt{M\frac{\mathrm{mol}}{\mathrm{g}}} - 0.03\,\mathrm{nm}.$$

The correlation being valid for a molar mass range 200–40 000 Da. The obtained values can be found in Fig. 3 (top x-axis).

3.3. AFM-measurements

Analysis of AFM images of the surfaces of the cast membrane films allow estimates of the average surface roughness from the variation about the mean height. Four samples were investigated, their average roughnesses are given as follows: PSU: 43 nm; PSU-COOH

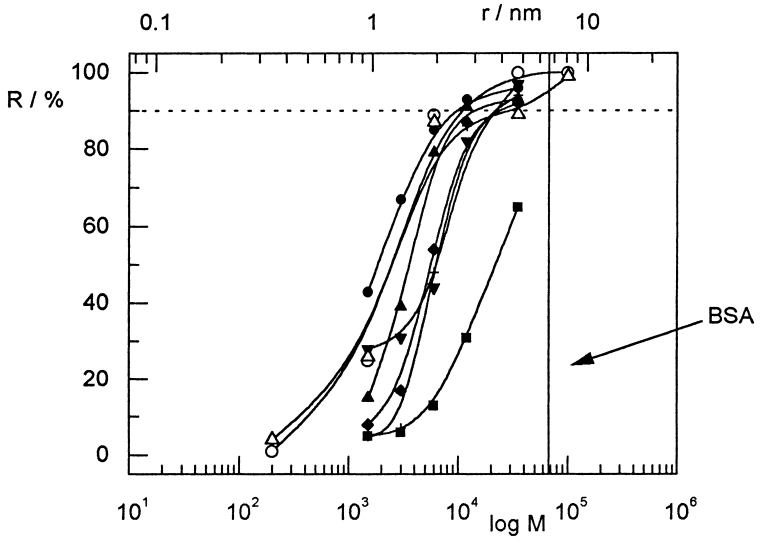

Fig. 3. Averaged retention of the membranes tested with PEGs. (■) PSU, (●) PSU-COOH 0.26, (▲) PSU-COOH 0.51, (▼) PSU-COOH 0.86, (◆) PSU-COOH 1.19, (+) PSU-COOH 1.74; (○) SPSU 0.24, (△) SPSU 0.58. The dotted line marks 90% retention, the *y*-axis parallel marks the molar mass of BSA.

0.86: 57 nm; PSU-COOH 1.74: 84 nm; SPSU 0.58: 229 nm.

The unmodified PSU membrane had the smoothest surface while an increasing degree of carboxylation apparently increased the surface roughness. Sulfonation had an even bigger impact on the surface roughness. However, a clear correlation between average surface roughness and fouling behavior (see below) is not obvious. Although the parent or unmodified membrane was the smoothest, the fouling and cleaning indexes used below as a measure of performance were always worse for the PSU membrane than that for the rougher but more hydrophilic PSU-COOH and SPSU membranes. This situation has been reported before [16] and underlines the importance of surface chemistry as the fouling-determining factor when ultrafiltering a protein solution.

3.4. Fouling experiments

Plots of the J_a/J_0, J_p/J_0 and J_c/J_0 ratios as functions of DS and pH were used to determine the significance of increased hydrophilicity as a result of the chemical modifications. In the following, it is assumed that membranes made from carboxylated and sulfonated polysulfones have increased hydrophilicity. This view is supported by water absorption measurements [10], electrokinetic investigations [28] and contact angle measurements which are to be published later. The TOC analysis of the samples tested throughout the fouling experiments gave 99% or higher retention towards cys-BSA. Fane et al. [25,26] observed a time dependency for BSA retention for partially retentive membranes, which they attributed to initial adsorption processes and which they had to consider in the discussion of their findings. As this was not the case in this study the results of the cut-off curves are confirmed and the assumption is strengthened that the membranes used were fully retentive towards cys-BSA and that pore plugging would be insignificant. These values are not shown in the plots. Figs. 4 and 5 contain the results for the carboxylated membranes, while Figs. 6 and 7 show the findings for the sulfonated membranes. In order to discuss the findings presented in Figs. 4–7, it is necessary to be aware of the surface charge of BSA as a function of pH and ionic strength. This is shown in Table 2.

Results of potentiometric titration have revealed that BSA has about twice the net charge at pH 3 than at pH 9 [27]. Figs. 4 and 6 show that there is insignificant static adsorption at pH 3 and pH 9. J_a/J_0 is between 0.94 and 0.99 with the values being slightly

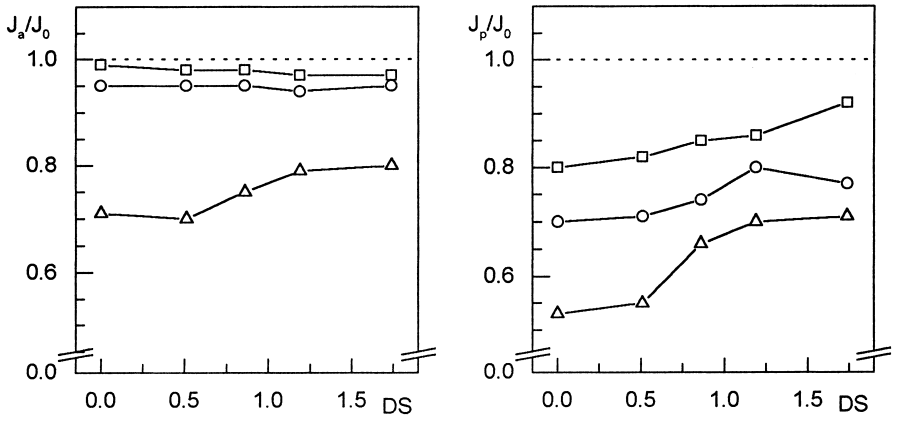

Fig. 4. Averaged characteristic flux ratios of carboxylated polysulfone membranes after static adsorption and ultrafiltration as a function of degree of carboxylation at low ionic strength. 1000 ppm cys-BSA, 0.001 M KCl, 283 K. (□) pH 3, (○) pH 9, (△) pH 4.8.

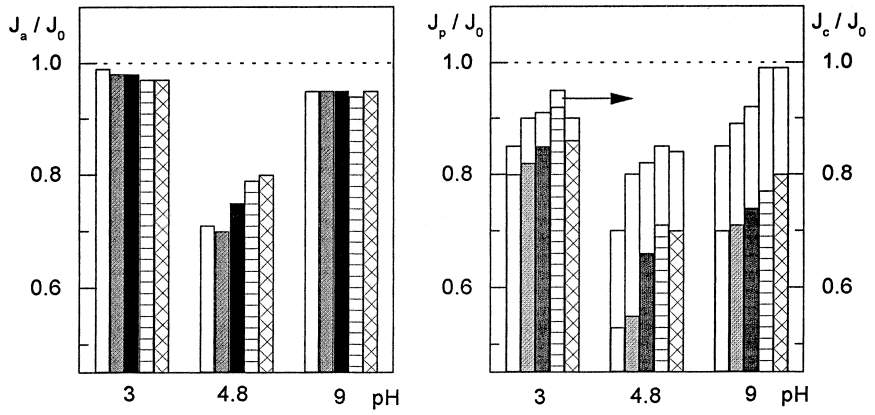

Fig. 5. Data from Fig. 4 as a function of pH. White bars: PSU, grey bars: PSU-COOH 0.51, black bars: PSU-COOH 0.86, horizontally lined bars: PSU-COOH 1.19, and hatched bars: PSU-COOH 1.74 membranes. The white top bars show J_c/J_0.

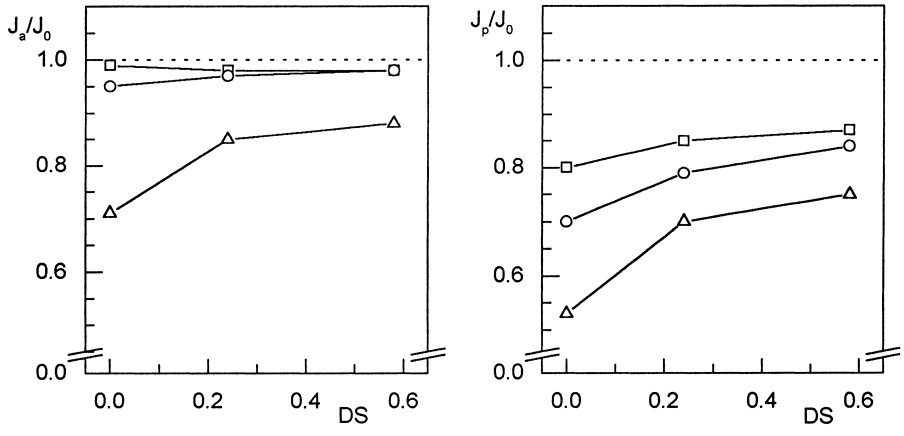

Fig. 6. Averaged characteristic flux ratios of sulfonated polysulfone membranes after static adsorption and ultrafiltration as a function of degree of sulfonation at low ionic strength. 1000 ppm cys-BSA, 0.001 M KCl, 283 K. (□) pH 3, (○) pH 9, (△) pH 4.8.

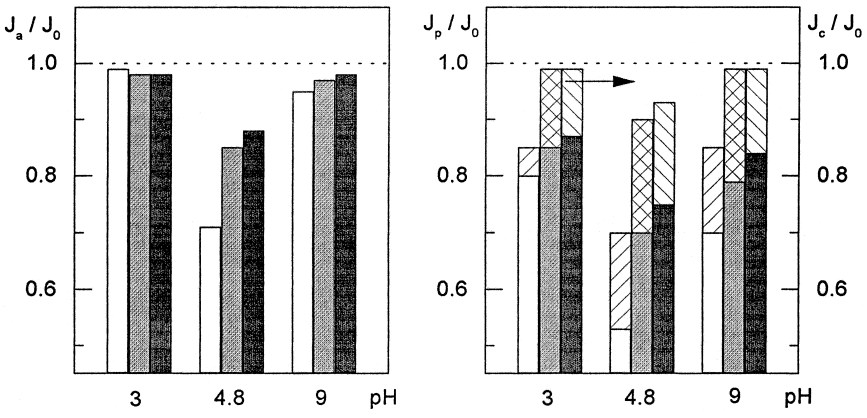

Fig. 7. Data from Fig. 6 as a function of pH. White bars: PSU, grey bars: SPSU 0.24, and black bars: SPSU 0.58 membranes. The hatched top bars show J_c/J_0.

higher at pH 3. From an electrostatic point of view, this is somewhat surprising because the membrane surfaces are clearly charged negatively at pH 9 while they have an almost neutral charge at pH 3 according to tangential flow mode zeta potential measurements [28]. Electrostatic repulsion between BSA and the membrane surface should be less pronounced at pH 3, thus giving lower values of J_a/J_0 compared to pH 9. This is not the case, and this anomaly becomes even more evident for the J_p/J_0 plots. Clearly, there are interactions between the protein molecule and the membrane surface as well as protein–protein interactions. The reduced J_a/J_0 and J_p/J_0 flux values are very much dependent on the structure and compactness of the adsorbed protein layer or layers. It could be assumed that these layers are less densely packed at pH 3 due to stronger intermolecular electrostatic repulsion as the BSA carries a higher charge at this pH. This would help to explain why the reduced J_p/J_0 values are higher at pH 3 than at pH 9. This protein–protein interaction may also offer insight into why static adsorption J_a/J_0 was lower at pH 3 than at pH 9.

One of the most important questions is the influence of increased membrane material hydrophilicity. While J_a/J_0 and J_p/J_0 increased slightly with DS at pH 3 and 9, this became even clearer at the protein's IEP at pH 4.8. At the IEP, BSA contains less water and has a net surface charge of zero. In this state, it is the most compact and is therefore more easily precipitated or adsorbed. At this pH, fouling is most severe for all membranes tested but is less pronounced with membranes of increased hydrophilicity by carboxylation and sulfonation. J_a/J_0 rises from 0.71 for the unmodified PSU membrane to 0.8 for PSU-COOH 1.74 and 0.88 for SPSU 0.58. J_p/J_0 rises from 0.53 for the unmodified PSU membrane to 0.71 for PSU-COOH 1.74 and 0.75 for SPSU 0.58. It should be noted that lower degrees of sulfonation have a greater effect that higher degrees of carboxylation. The reason for this is due to the different chemical nature of these two functional groups and their hydrophilizing capacity.

Table 2
Selected properties of BSA as a function of pH and ionic strength [25]

	Acid pH		IEP		Basic pH	
		Ions[a]		Ions		Ions
Size	Enlarged	↓	Compact	↑	Enlarged	↓
Charge	Net +	↓	Net 0	↑	Net −	↓

[a] Increase of ionic strength.

J_p/J_0 is the most important ratio for practical considerations as it is the ratio value closest to actual industrial applications despite the rather low protein concentration. As these BSA tests were carried out in stirred ultrafiltration cells, it can be expected that the performance could be improved considerably when using more sophisticated equipment, especially those systems that are able to decouple high membrane surface shear rates from high operating pressures. The question remains why the positive influence of increased hydrophilicity continues to be effective during ultrafiltration. Here several layers of proteinaceous deposit are built up and each new layer comes in contact with a protein surface rather than a virgin polymeric membrane surface. This has been observed by Nabe et al. [16] before when working with polysulfone membranes that had been chemically modified and challenged with BSA in an ultrafiltration experiment. Either the chemistry of the surface (intermolecular forces) extends its effect through the surface-associated protein into the solution or the surface in not fully covered and took time to be so. Clearly, the more hydrophilic the surface is, the lower was the flux-decline with protein solutions. The superiority of more hydrophilic membrane materials (cellulose acetate vs. polysulfone) in static adsorption experiments was shown by Matthiasson [15].

Another important aspect for industrial application is the cleanability of the membranes used. Figs. 5 and 7 show the restorable electrolyte solution flux J_c after the cleaning procedure. It becomes clear from the data that the more hydrophilic surfaces seem to bind the protein more loosely. This results in improved cleanability which increases with degree of substitution for both PSU-COOH and SPSU. Initial electrolyte flux is almost completely restorable for SPSU at pH 3 and pH 9 while only membranes made from PSU-COOH 1.19 and PSU-COOH 1.74 exhibit this behavior at pH 9. Interestingly, cleanability seems to be slightly more pronounced at pH 9, although a reason why it is not apparent. The cleanability data is another indication that the SPSU-membranes are somewhat more hydrophilic. Overall it can be concluded that cleanability becomes considerably better for the higher DS materials and that it should be done at basic pH for these materials.

In a separate set of experiments we investigated the impact of increased ionic strength on the different performance indices of the materials used. Figs. 8 and 9 contain the results for the carboxylated species while Figs. 10 and 11 show the findings for the sulfonated polysulfones. The KCl concentration was 0.1 M which is 100 fold higher than in the previous experiments. It can be concluded from the figures that an increase in ionic strength leads to stronger static adsorption and greater flux reduction for pH values on either side of the protein's IEP. In contrast, at the IEP itself salt addition had a positive effect in terms of fouling: static adsorption occurred to a lower extent and flux reduction was not as high as at low KCl concentration. The explanation is fairly simple and has been reported by a number of authors [25,26,29]: salts shield charges

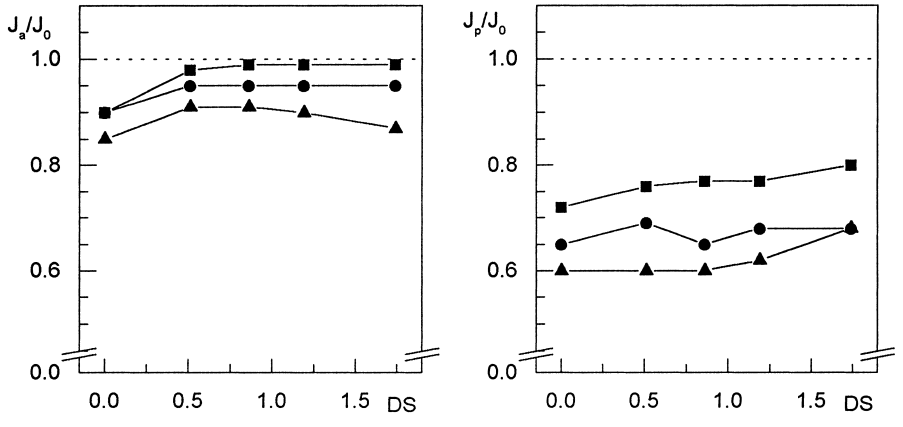

Fig. 8. Averaged characteristic flux ratios of carboxylated polysulfone membranes after static adsorption and ultrafiltration as a function of degree of carboxylation at high ionic strength. 1000 ppm cys-BSA, 0.1 M KCl, 10°C. (■) pH 3, (●) pH 9, (▲) pH 4.8.

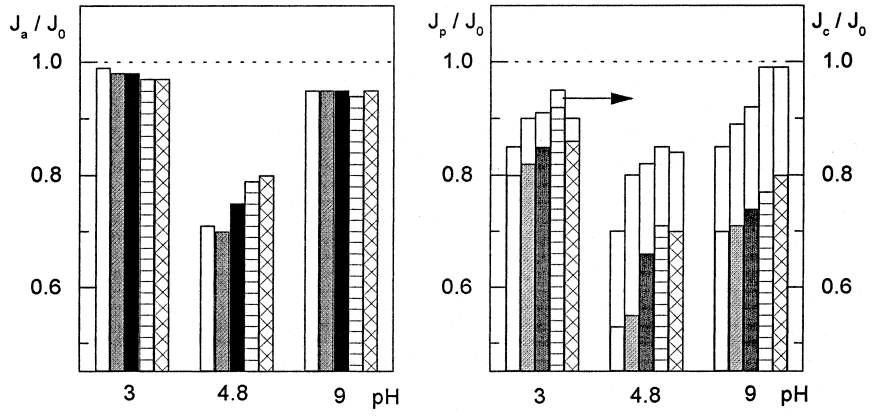

Fig. 9. Data from Fig. 8 as a function of pH. White bars: PSU, grey bars: PSU-COOH 0.51, black bars: PSU-COOH 0.86, horizontally lined bars: PSU-COOH 1.19, and hatched bars: PSU-COOH 1.74 membranes. The white top bars show J_c/J_0.

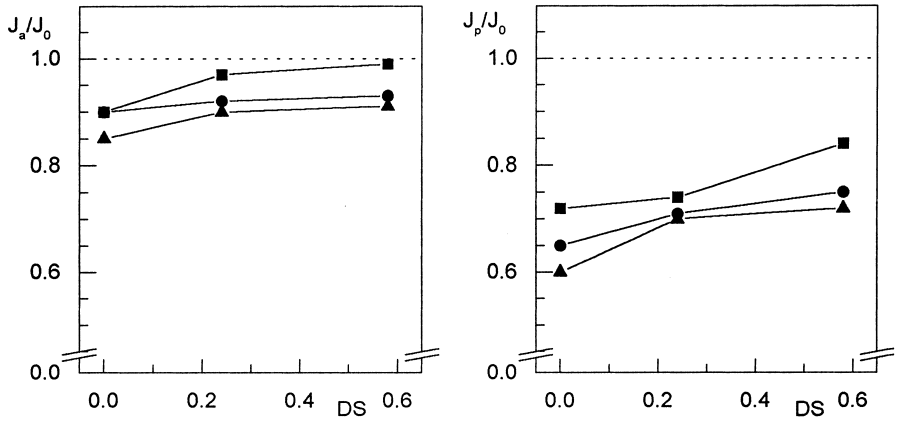

Fig. 10. Averaged characteristic flux ratios of sulfonated polysulfone membranes after static adsorption and ultrafiltration as a function of degree of sulfonation at high ionic strength. 1000 ppm cys-BSA, 0.1 M KCl, 10°C. (■) pH 3, (●) pH 9, (▲) pH 4.8.

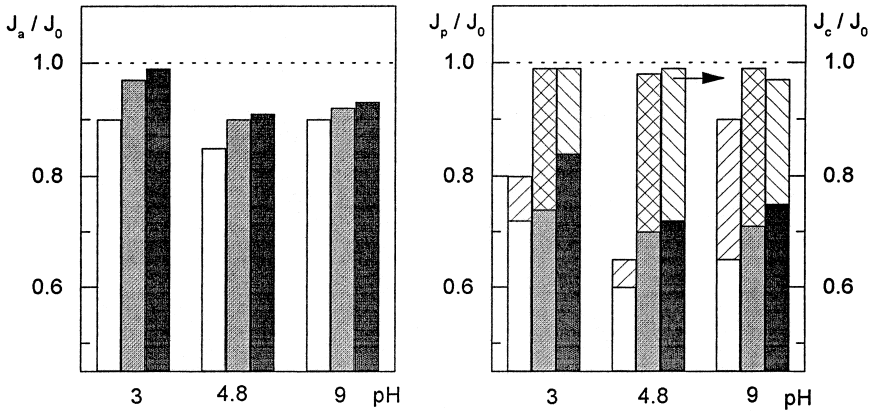

Fig. 11. Data from Fig. 10 as a function of pH. White bars: PSU, grey bars: SPSU 0.24, and black bars: SPSU 0.58 membranes. The hatched top bars show J_c/J_0.

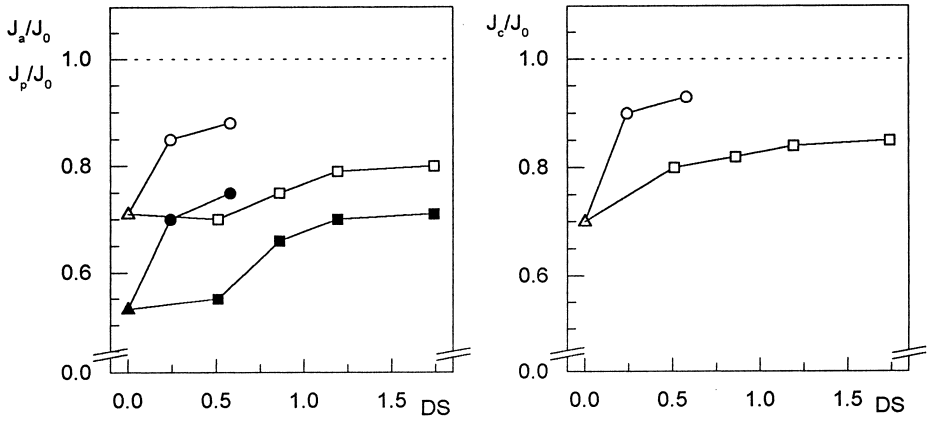

Fig. 12. Averaged characteristic flux ratios after static adsorption (left figure, open symbols), ultrafiltration (left figure, solid symbols) and cleaning (right figure) with a solution of cys-BSA (0.001 M KCl) as a function of degree substitution. (△) PSU-, (○) SPSU- and (□) PSU-COOH-membranes. [cys-BSA]=1000 ppm, pH=4.8, [KCl]=0.001 M.

which means that the contribution of electrostatic repulsion between COOH- and SO_3-groups on the membrane surface and charged functional groups on the protein surface is reduced. At the same time the BSA molecule acquires a lower net charge and contracts, thereby decreasing permeability. At the protein's IEP the effects are reversed: salt addition increases the protein's net charge, its size and overall stability which leads to a less pronounced adsorption affinity. The cleanability behavior was very much similar to the results of low ionic strength.

4. Conclusion

A systematic study was performed to assess the influence of incrementally increased hydrophilicity of membranes made from carboxylated and sulfonated polysulfones of various degrees of substitution. All fabricated membranes had similar molecular weight cut-off curves and were >99% retentive towards cys-BSA. With increasing level of functionality, static BSA adsorption decreased, ultrafiltration flux reduction decreased and cleanability increased. The effects were most pronounced at the isoelectric point of BSA summarized in Fig. 12. This shows that not only electrostatic aspects play a role in protein fouling on UF membranes but also that hydrophilicity is an important factor. Higher ionic strengths reduced these advantages at pH values on either side of the IEP but had a positive effect at the IEP which was explained by electrostatic shielding and charge effects on the BSA molecule.

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