

## Author Manuscript

**Title:** Membrane Filtration with Liquids: A Global Approach with Prior Successes, New Developments and Unresolved Challenges

**Authors:** Georges Belfort, PhD

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record.

**To be cited as:** 10.1002/anie.201809548

**Link to VoR:** <https://doi.org/10.1002/anie.201809548>

REVISED (October 2018) - Manuscript number: 201809548

ANGEWANDTE MINIREVIEW

MEMBRANES

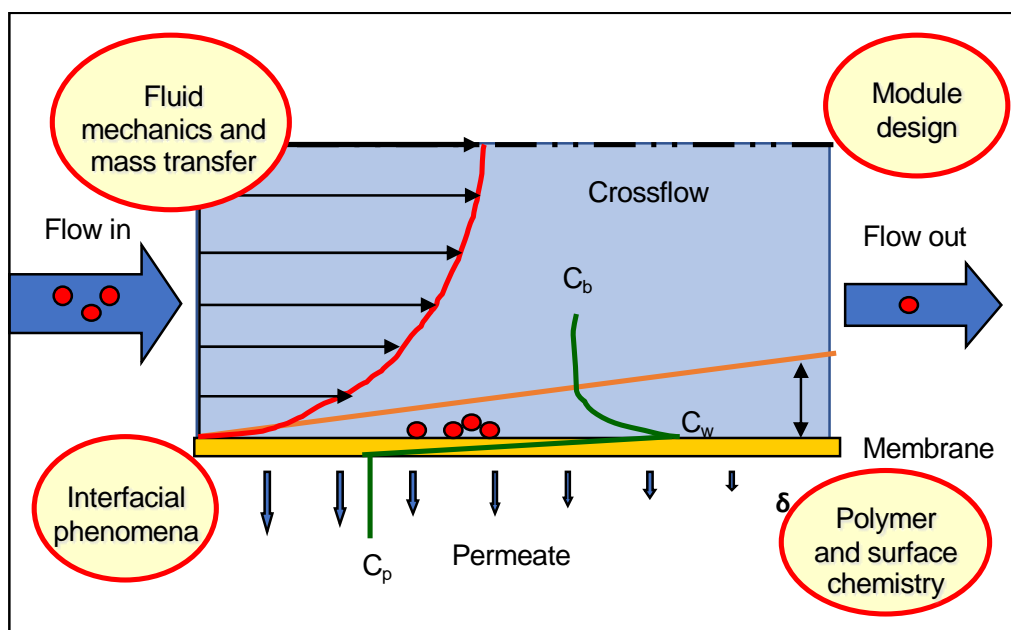
**“Membrane Filtration with Liquids: A Global Approach with Prior Successes, New Developments and Unresolved Challenges”**

Georges Belfort\*

Howard P. Isermann Department of Chemical and Biological Engineering and Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute, Troy, NY 12180-3590, USA

**Key words: Membrane science and technology, materials, mass transfer, fouling diagnostics, liquid applications.**

**\*Corresponding author**



**A RICH COMPLEX FIELD: INTEGRATING MATERIALS CHEMISTRY AND ENGINEERING FOR SUCCESSFUL MEMBRANE FILTRATION WITH LIQUIDS**

After 70 years, modern pressure-driven polymer membrane processes with liquids are mature and accepted in many industries due to their good performance, ease of scale-up, low energy consumption, modular compact construction, and low operating costs compared with thermal systems. Successful isothermal operation of synthetic membranes with liquids requires consideration of three critical aspects or “legs” in order of relevance: selectivity, capacity (i.e. permeation flow rate per unit area) and transport of mass and momentum comprising concentration polarization (CP) and fouling (F). Major challenges remain with respect to increasing selectivity and controlling mass transport in, to and away from membranes. Thus, prediction and control of membrane morphology and a deep understanding of the mechanism of dissolved and suspended solute transport near and in the membrane (i.e. diffusional and convective mass transport) is essential. Here, we focus on materials development to address the relatively poor selectivity of liquid membrane filtration with polymers and discuss the critical aspects of transport limitations. *Machine learning could help optimize membrane structure design and transport conditions for improved membrane filtration performance.*

## GLOBAL APPROACH

Synthetic polymer membranes are widely used to separate molecules in many industries, such as water purification, bioprocessing, healthcare, food, gas, and environmental, because of their low energy consumption (i.e. no phase change and energy recovery for high pressure-applications) and operating costs compared with thermal systems, modular compact construction (relatively small footprint), and ease of scale-up to large transfer areas<sup>[1]</sup>. Although gas applications are growing, the vast majority of applications (i.e. in dollars expended) involve liquid membrane filtration (\$0.353 and 3.0 billion in 2016, respectively)<sup>[2]</sup>. Given this success and the maturity of membrane filtration processes since the development of the modern asymmetric membrane by Loeb and Sourirajan in the 1960s<sup>[3]</sup>, it is noteworthy that the polymer science for preparing synthetic membranes and the underlying mathematical formalism for predicting performance of liquid membrane filtration are so primitive. We cannot design synthetic polymer membranes with desirable pore size distributions and specified morphology (i.e. enable “structure-by-design”)<sup>\*†</sup> and have no predictive theory for design and operation of

---

\* *Structure-by design* is defined as the ability to specify *a priori* membrane formation parameters in order to obtain a desired membrane morphology and pore size distribution.

† Personal Communication with Dr. Martin Smith, Pall Corp. “If you look at ‘membrane based’ plant workflows - eg. Bioprocess of therapeutic protein, food and beverage production, pulp and paper, ethylene, olefin/paraffin & other refinery processes, microchip wet etching..... and so on to name a few), the general opinion we have at Pall is that practitioners go through a dedicated process of scale up (small scale lab to full ‘production floor’) as an act of production readiness proof. This is done in almost all membrane based workflow processes we see, regardless of industry. Why? Simply as you state - practitioners have to develop a prediction of workflow efficiencies, of which membrane fouling, at the variety of unit operation steps we see membranes involved, is a key contributor to energy and target product losses. Our experience tells us that for highly fouling feedstocks such as in the applications I give above - eg. Protein in bioprocess, glucans in beer production, asphaltene in refinery we see minimal use of membrane theory reliance but rather the drive through scale up and empirical experience.”

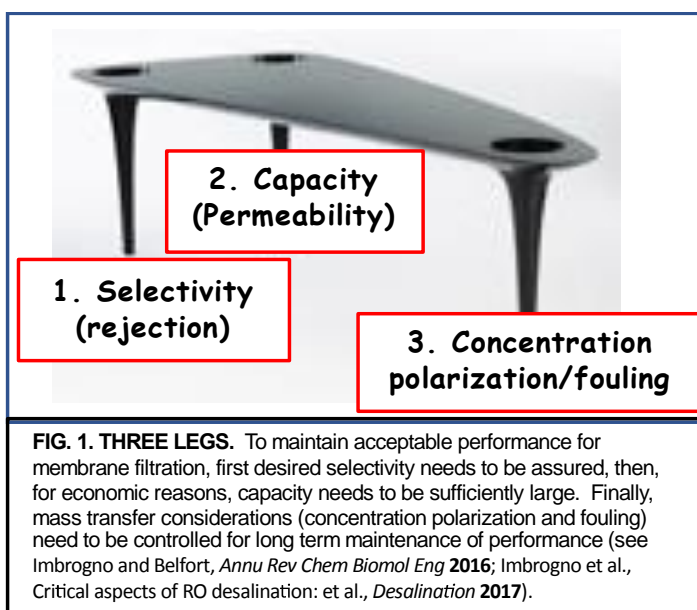
membrane filtration plants when using realistic liquid feeds containing solute mixtures that negatively affect performance<sup>‡</sup>. However, modern pressure-driven polymer membrane processes with liquids rests on a combination of fundamental science and technology that includes polymer and colloid science with fluid mechanics and mass transport.

**Three legs:** Successful isothermal operation of synthetic membranes requires consideration of three critical aspects or “legs” in order of relevance: selectivity, capacity (i.e. permeation flux per unit driving force, called permeability in liquid filtration) and transport of mass and momentum (coupling of mass transfer and fluid mechanics) comprising concentration polarization (CP) and fouling (F) (**Fig. 1**). Omitting one of

these “legs” in evaluating the performance capability or in comparing a membrane filtration process with other separation methods gives incorrect and misleading results<sup>[4]</sup>. Another and more-subtle requirement when comparing the filtration performance of different membranes during liquid filtration is the need to compare the performance for the same volume permeated or on an energy consumption basis<sup>[5]</sup>. Several exciting new reports on gas separations with membranes, have

recently focused on selectivity and in some cases on capacity<sup>[6]</sup>. However, mass transport (CP, F) and scale-up limitations are mentioned but not considered in detail. The three legs are intimately connected and all three should be considered equally for a successful liquid separation. Below, we consider why CP is mostly negligible for gas separation systems. However, membrane fouling does occur with gas systems and, in those cases, should not be ignored.

**Underlying predictive theory:** All common separation molecular processes like distillation, extraction and chromatography have theoretical foundations that allow design (e.g. define the number of stages) and operation<sup>[7]</sup>. Due to fouling (F) and concentration polarization (CP) which



<sup>‡</sup> Personal communication with Dr Caleb V. Funk, Dow Chemical Company. “Every water is different, and every membrane is different, so experience is key. Models that exist today (like Dow’s WAVE program) use extensive amounts of empirical data gathered under a wide range of conditions in combination with theory, but without the data, you have nothing – and that’s just the pre-treated water. Foulants make the problem worse, and you can’t predict how even a pre-treatment system will work from month to month, because water conditions change over time.”

are both difficult to predict, theories associated with pressure-driven membrane filtration are mostly good for “clean” feed solutions prepared in the laboratory and cannot predict performance in the field. Thus, heuristic approaches such as prior experience with laboratory and pilot testing with industrial feeds are critical for membrane selection, plant scale-up and for defining best operating conditions.

**Upper-bound:** Transferring the concept of “upper-bound relations in polymer membranes” (i.e. plotting selectivity versus capacity without consideration of the three legs, i.e. CP and F) from gas to liquid membrane systems is fraught with problems<sup>[8]</sup>. Since these plots for gases and polymer membranes are mostly based on pure compound measurements<sup>[9]</sup> and that pure compound predictions can be different from those obtained with mixtures, especially in those cases where plasticization occurs (i.e. with CO<sub>2</sub>)<sup>[10]</sup>, how valid are these upper-bound relations for such systems? Questions comparing filtration performance for liquid feeds using “upper bound” plots of selectivity versus permeability include the following: Were all the data obtained under the exact same mass and momentum transport conditions (i.e. same CP and F) and were the data taken for the same volume permeated or on an energy consumption basis<sup>[8]</sup>? Thus, more “upper bound” data for mixed feeds especially for gasses like CO<sub>2</sub> where plasticization occurs is needed. For liquids, plotting selectivity for ultrafiltration of a large proteins (like BSA, MW 66.5 kDa) versus a very small molecule (i.e. water, MW 18 Da) versus hydraulic permeability is misleading at best and does not aptly describe the selectivity of the membrane, all it measures is BSA sieving with hydraulic permeability<sup>[11]</sup>. Upper bound plots for water and salt separation is more rational as long as the measurements were conducted under the same mass transfer conditions<sup>[12]</sup>.

Here, we present prior successes, recent developments in materials and mass transfer aspects liquid synthetic membrane filtration and suggest where more work needs to be done.

## MATERIALS ASPECTS

**Prior successes:** For the past ~50 years, one order-of-magnitude in solute size difference has been used as a-rule-of-thumb to ensure desirable membrane selectivity for liquid separations by synthetic membranes. The purported reasons for this poor selectivity is their wide pore size distribution (often log-normal)<sup>[13]</sup> and, as we have learned from studies with gases and polymers, polymer and pore flexibility<sup>[14]</sup>. Polymers with large free-volume also exhibit densification, i.e. loss of free volume, also called ageing and results in loss of performance<sup>[9c, 15]</sup>. Another reason is related to dimensions and has to do with the ratio of a spherical particle,  $a$ , to the cylindrical pore radius,  $r$ , in the Ferry Eq.<sup>[16]</sup>, where

$$R = 1 - [1 - (a/r)^2]^2 \quad (1)$$

and  $R$  is the particle rejection. This simplified analysis is limited to the role of exclusion (partitioning) and effects of convection, drag, electrostatics are ignored. Assuming the size of a

globular protein is proportional to  $a^{1/3}$ , another protein with a molecular weight twice that of first protein is only 1.25 larger, making discrimination through pores challenging<sup>[17]</sup>!

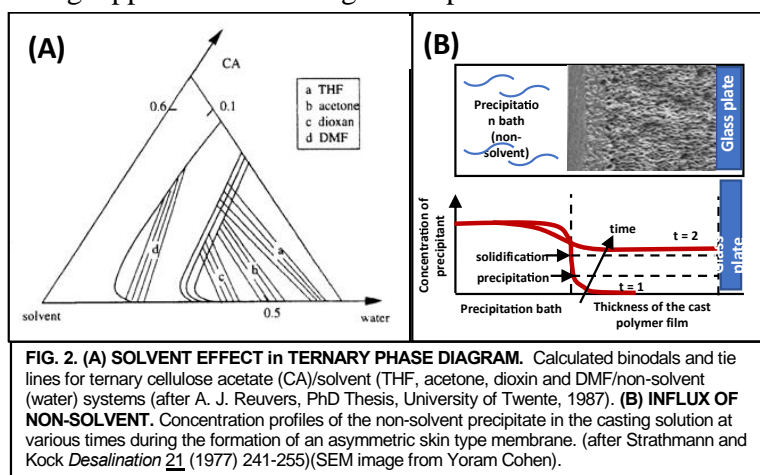
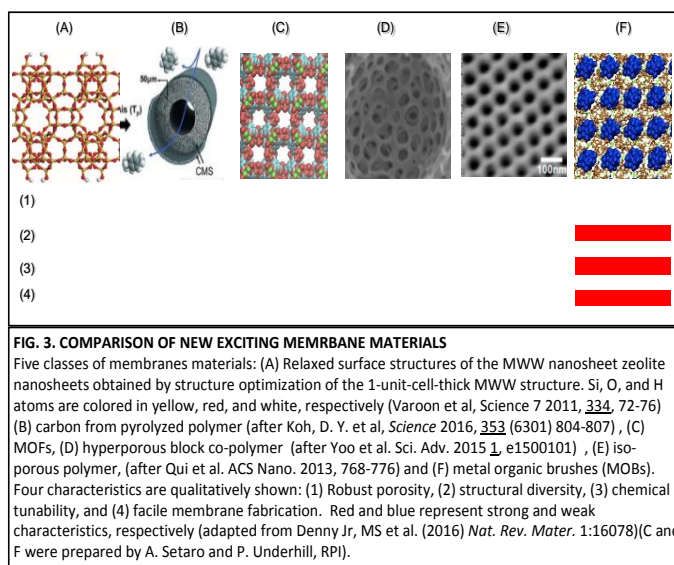
Membrane structure predictions: Iso-porous membranes synthesized from block co-polymers with relatively uniform pore sizes and with very narrow pore size distributions provide an

undesirable exception for structure-by-design since if one pore fouls (plugs and reduces liquid permeation rates) then there is the likelihood that many or all pores will foul<sup>[18]</sup>. Thus, a “desirable pore size distribution” depends on the composition of the feed, its fouling potential and the desired selectivity, permeability and transport conditions (“3 legs”). Clearly too wide or too narrow pore size distribution are mostly undesired and presently a desirable pore size distribution is *a priori* not possible to synthesize. Selection of particular

solvents (say tetrahydrofuran, THF, versus dimethylformamide, DMF) can move the binodal (line separating one from two phase regions) and slope of the tie-lines on a ternary-phase diagram of polymer, solvent and non-solvent from dense to open pore structures [e.g. from a pervaporation (PV) membrane with THF/water to an ultrafiltration (UF) membrane with DMF/water] but cannot define a particular pore size distribution (**Fig. 2A**)<sup>[19]</sup>. Controlling membrane porosity gradient (negative and positive) in the flow direction via activity of the non-solvent (e.g. water versus water vapor) is another approach to compensate for the inability to prepare a desired pore size distribution (**Fig. 2B**)<sup>[20]</sup>.

**New Developments:** Several new exciting approaches are being developed to address the

limitations of wide pore size distributions and unwanted polymer or pore flexibility. These include cross-linked polymer membranes with<sup>[21]</sup>/without<sup>[22]</sup> post pyrolyzation into carbon membranes, formation of homogenous zeolites (aluminosilicate)<sup>[23]</sup> or metal organic framework (MOF) membranes, formation of composite mixed matrix membranes comprising zeolites<sup>[24]</sup>, MOFs<sup>[25]</sup> or polymers of intrinsic microporosity (PIMS)



within polymer<sup>[26]</sup>, and block co-polymer isoporous membranes<sup>[27]</sup>. Each have their advantages and disadvantages as summarized in **Fig. 3**<sup>[28]</sup> and reviewed below.

Briefly, carbon membranes exhibit exquisite selectivity for gas and liquids systems but are expensive and may suffer from brittleness<sup>[29]</sup>. Pyrolyzed carbon membranes are difficult to scale and sensitive to organic poisons and water hold up<sup>[30]</sup>. They were first developed by Koresh and Soffer in 1973<sup>[31]</sup> and have recently exhibited significantly improved selectivity and were scaled as hollow fibers<sup>[21]</sup>. Zeolites have limited application due to their narrow pore size range (0.5-2.5 nm)<sup>[23]</sup> and brittleness, while Tsapatsis' group have made progress in demonstrated the synthesizing and highly crystalline nanosheets of zeolite frameworks<sup>[32]</sup>. While isoporous membranes have low surface porosity and extremely narrow pore size distribution that can catastrophically foul (see above)<sup>[33]</sup>, they can exhibit excellent selectivity and permeability *sans* fouling. PIMs are known to age and lose their structure (free volume) with time<sup>[9c, 34]</sup>. On the other hand, MOFs have a much broader pore size range than zeolites and are without walls so flow can occur in 3 directions (critical during fouling)<sup>[28]</sup>. Recently, covalent organic frameworks (COFs) were grafted onto porous alumina tubes and exhibited high fluxes with good dye rejections<sup>[35]</sup>. The pore size distribution of individual MOFs and COFs, however, is relatively narrow so that these materials can exhibit precise selectivities but are also susceptible to fouling and possibly ageing. MOFs were recently reported by Park et al. as new materials with the potential to transcend the upper bound<sup>[8]</sup>. Based on the early work of Sleyter and Sara<sup>[36]</sup> with S-layers, membranes synthesized from proteins have also recently been reported<sup>[37]</sup>. Whereas each aforementioned method may address one or several limitations of polymer membranes, they will likely increase the cost of production and scale-up.

We have recently proposed new materials based on cross-linked brush polymers with/without additives such as MOFs that could be scalable, cost-effective and exhibit excellent selectivity, permeation and mass transfer (i.e “3 legs”)<sup>[38]</sup>. By controlling the density, branch length and height (using Activators Regenerated by Electron Transfer (ARGET) Atom Transfer Radical Polymerization (ATRP)) of the brushes, in addition to their cross-linking intensity and type of MOFs, stiff well-defined pore size distribution membranes are expected<sup>[39]</sup>. Thus, elucidating the fundamental principles underlying a *structure-by-design* synthetic hybrid *Metal-Organic Brush* (MOB) polymer membranes combining tunable polymer brush layers with complexed metals is needed. These hybrid MOB layers represent a new class of synthetic membrane liquid separators that should exhibit stability and selectivity during Organic Solvent Nanofiltration (OSN) (**Fig. 3F**).

**Unresolved challenges:** For porous membranes, several challenges need to be addressed: For commercial membranes, one cannot design a desirable molecular structure into the polymer-separating layer. As mentioned above, neither very narrow nor very wide pore size distributions are desirable. Thus, for different separations, optimal selectivity will depend *a priori* on design of a porous structure with a desired intermediate pore size distribution. Unfortunately, it is not possible, using standard phase inversion (PI) and interfacial polymerizations (IP) methods of

membrane formation, to relate location on a phase diagram with resultant pore structure or control surface morphology – at best, we can forecast tighter or more open pore structure without molecular details (**Fig. 2A**)! It is of fundamental importance to be able to design a permeable polymer membrane with a desirable pore size distribution for optimal performance. Iso-porous membranes with pores that pass straight through a membrane without transverse flow and low porosity are also undesired in industrial applications since connected pores with transverse flow are able to withstand fouling more efficiently<sup>[40]</sup>. As mentioned above, three component phase diagrams (polymer, solvent and non-solvent) are used for producing phase inversion skinned membranes with different mean porosities such as “tight” reverse osmosis (RO) membrane for desalination or “open” UF membranes for protein fractionation (**Fig. 2A**). However, only mean pore sizes can be estimated and synthesized. Molecular details of a pore size distribution cannot be predicted *a priori*. Unfortunately, our fundamental knowledge of thermodynamics and kinetics of pore formation in polymers is wanting!

A second challenge involves solute-solute and solute-membrane surface interactions, that directly effects selectivity and permeation flux of dissolved and suspended (real) mixtures. The trajectory of a different solutes toward (concentration polarization) and through a porous membrane structure with transverse connected pores is extremely complicated and will depend on solute-solute (aggregation) and solute-membrane surface (internal fouling) interactions, concentration of solutes, fluid mechanics and positive displacement or centrifugal pump among other parameters. A related challenge involves distinguishing molecules of similar size. If these solutes have significantly different pI or surface charge/potential values then, as is well known, surface charge, pH and ionic strength can be used to fractionate molecules of similar size<sup>[41]</sup>.

A third challenge involves the use of machine learning models trained on polymer membrane formation parameters like concentration of polymer, solvent and non-solvent and their measured resultant pore size distributions and filtration results to infer optimal formations parameters without requiring an understanding of the underlying physical or chemical mechanisms<sup>[42]</sup>.

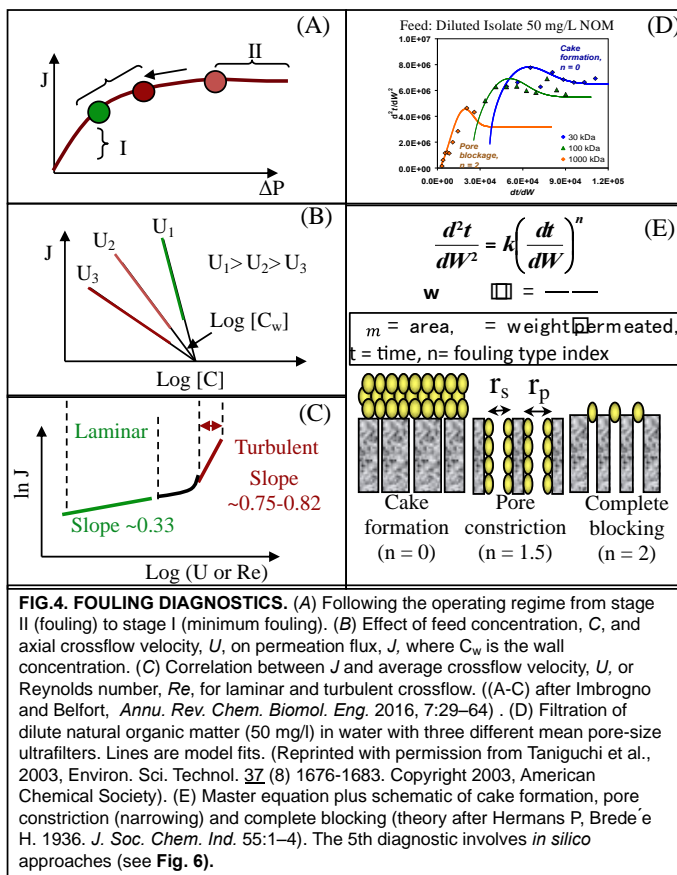
## MASS TRANSFER ASPECTS

**Prior successes:** Mass transfer limitations: To maintain desirable selectivity for a particular separation and an economically acceptable permeation flux with time or accumulated permeate volume, one must also consider and minimize mass transfer limitations, i.e., the Achilles’ heel of liquid membrane separation processes<sup>[4]</sup>. CP and F are two related but separate phenomena that occur to different extents depending on the composition of the liquid feed and the synthetic membrane processes being considered. CP is the result of selective transport of some species over other species through the membrane. Retained species accumulate in the feed solution adjacent to the membrane and may induce a reverse osmotic driving force, the extent to which depends on the solute type (i.e. large, medium, and small effects with salt, proteins and colloids, respectively)<sup>[43]</sup>. Fouling, resulting from the interaction of solutes such as proteins with each other or with the membrane, affects performance such as selectivity or permeation rates and is

the main reason why there is no predictive theory for design and operation of membrane filtration plants when using realistic liquid feeds.

Since mass fluxes toward a membrane and solute back-diffusion for gases is typically an order of magnitude lower and 10,000 times faster, respectively, than for solutes in liquids during pressure-driven membrane separations, CP is substantially lower for gases<sup>[29, 44]</sup>. Hence, CP is often neglected for gas systems and always considered for liquid membrane filtration. Fouling however cannot be dismissed for some gas filtration applications. Gas, reverse osmosis (RO) and PV membranes operate by the solution-diffusion mechanism (i.e. solutes or gases dissolve

into the polymer membrane and then diffuse down a chemical potential gradient)<sup>[29]</sup> and lack easily measurable pores. These are dense membranes, characterized by very low Peclet numbers (ratio of convection to diffusion through the membrane) and by cavities or pores of angstrom dimensions. Porous membranes, such as nanofiltration (NF), UF and microfiltration (MF) membranes have measurable pore sizes of 1-2 nm, 2-100 nm and >100 nm<sup>[29]</sup>, respectively, are characterized by very high Peclet numbers (i.e. ratio of convection to diffusion).



rates, laminar or turbulent regime, and maximum wall solute concentration and type of fouling (Fig. 4) (see Imbrogno and Belfort for additional details)<sup>[4]</sup>. Depositing solutes onto membranes through mostly convection causes cake formation, pore constriction (narrowing) and, complete pore blockage, all part of fouling. Diagnosing which fouling effect dominates was first reported >50 years ago for dead-ended filtration (no crossflow)<sup>[45]</sup> and more recently for crossflow with two and three mechanisms at constant trans-membrane pressure or flux<sup>[5, 46]</sup>. The universal equation and schematics of each fouling type are presented in Fig. 4D<sup>[5, 47]</sup> fitted to filtration data in Fig. 4E illustrating which type of fouling occurred via the n-values.

To address the lack of a predictive theory for porous (i. e. non-solution-diffusion transport) membrane filtration performance, we summarize below briefly what has been reported for predicting CP and F.

**Theoretical prediction of CP:** CP or the build-up of dissolved solutes is shown schematically for crossflow (left) and dead-ended (right) in **Fig. 5A**. Two earlier studies have confirmed the presence of a buildup of salt<sup>[48]</sup> and bovine serum albumin<sup>[49]</sup> with time for dead-ended or normal batch filtration (**Fig. 5A**).

The salt studies compared optically measured interference patterns with predictions from ray-tracing (**Fig. 5B**) and also confirmed that the RO CA membrane behaved according to the solution-diffusion model (**Fig. 5C**, Y-intercept should be close to 1 for the solution-diffusion model to hold)<sup>[43, 48b, 48c]</sup>. They also solved the mass transfer equations, and provided a simple expression (called the dead-ended predictive model) to estimate the concentration of solute at the membrane surface for normal or dead-ended feed flow,  $C_w$ , i.e.

$$\frac{C_w}{C_{bulk}} = \frac{1}{1-R} + 1 \quad (2)$$

where  $C_{bulk}$  is the feed concentration, and  $R$  is the salt/solute rejection ( $<1$ ). Measuring  $R$  values at long times allows an estimate of the salt concentration at the wall,  $C_w$ . The classic gel polarization model, obtained from a balance of mass flux to and through the membrane versus back diffusion (**Fig. 5A, right**), is used to describe CP and expressed as follows for  $R=1$ <sup>[50]</sup>:

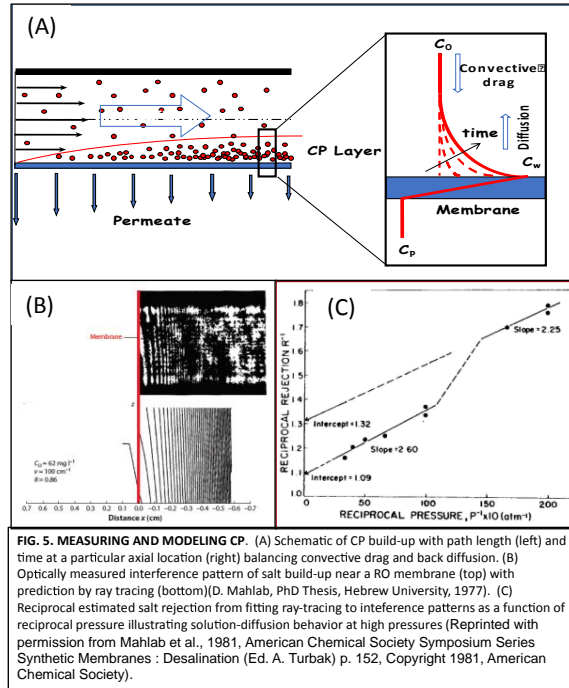
$$v_w = k \ln (C_w/C_b) \quad (3)$$

where  $v_w$  is the permeation flux (cm/s),  $k$  is the mass transfer coefficient (cm/s) and  $C_w$  and  $C_b$  are the wall and bulk concentrations (mol/L), respectively. When the solute adheres to the membrane and does not diffuse back into the bulk, the following expression based on a solid flux model is useful<sup>[51]</sup>:

$$\ln v_w/v_{w,0} = -bC_b \quad (4)$$

where  $v_w$  and  $v_{w,0}$  are the permeation fluxes with and without solute, and  $b$  is a fouling constant. Both models were tested with the same data<sup>[51]</sup>.

**Theoretical prediction of Fouling:** Besides the diagnosis of different mechanisms of fouling describe above (**Fig. 4D & E**), empirical expressions to describe fouling bring little understanding of the fouling mechanisms or their temporal dynamics, i.e.



**FIG. 5. MEASURING AND MODELING CP.** (A) Schematic of CP build-up with path length (left) and time at a particular axial location (right) balancing convective drag and back diffusion. (B) Optically measured interference pattern of salt build-up near a RO membrane (top) with prediction by ray tracing (bottom) (D. Mahlab, PhD Thesis, Hebrew University, 1977). (C) Reciprocal estimated salt rejection from fitting ray-tracing to interference patterns as a function of reciprocal pressure illustrating solution-diffusion behavior at high pressures (Reprinted with permission from Mahlab et al., 1981, American Chemical Society Symposium Series Synthetic Membranes: Desalination (Ed. A. Turbak) p. 152, Copyright 1981, American Chemical Society).

$$v_w = \Delta P / (\mu(R_m + R_f)) \quad (5)$$

where  $\mu$  is the solvent kinematic viscosity,  $\Delta P$  is the transmembrane pressure (kPa), and  $R_m$  and  $R_f$  are the resistance of the membrane and fouling ( $m^{-1}$ ), respectively. Also, *in silico* approaches have previously exhibited encouraging predictions (not fits) to experimental liquid separations (Fig. 6)<sup>[52]</sup>.

**New developments: Mitigation of fouling:** This topic has been covered extensively<sup>[4, 53]</sup> and will not be discussed in detail here except to point out that as early as 1972, the concept of a threshold crossflow velocity, i.e. above which flux-decline (measure of fouling) was substantially reduced, for particle-containing Tennessee River water and primary sewage effluent<sup>[54]</sup>. Much later, Field and Howell published on the critical flux<sup>[55]</sup>. Zydney and Colton and Belfort et al. (see review in Belfort et al., 1994)<sup>[56]</sup> focusing on the behavior of particles in laminar flow fields, used shear induced diffusion and inertial lift, respectively, to explain unexpected high filtration fluxes (called the flux paradox)<sup>[57]</sup>. Preventing or assisting particle (e.g. cells or protein aggregates) or dissolved solute (ions, proteins etc.) intrusion into porous membranes will need in-depth measurements of both intermolecular forces between particles and between particles and internal pore surfaces together with fluid-particle transport modeling within the pores to solve the complete convective-diffusion equations with adsorption. These studies could have direct influence on understanding particle and solute selectivity. New module designs that optimize performance rather than maximize membrane packing density are urgently needed.

**Do we need high-flux membranes?** Several publications have recently described so-called “break-throughs” by demonstrating the potential for very high permeability (permeation flux/transmembrane pressure) mainly based on water flows through hydrophobic channels such as carbon nanotubes<sup>[58]</sup>, and holes in graphene sheets<sup>[59]</sup> and between graphene oxide flakes<sup>[60]</sup>. As emphasized above, permeability, selectivity and mass transfer are connected and highly dependent on each other. Thus, very high permeation fluxes will likely reduce selectivity and increase fouling due to convective drag toward the membrane of the retained species. To address the increased fouling, increased mass transport of foulant away from the membrane surface will be required and increased axial feed flow (and hence increased energy consumption) is often

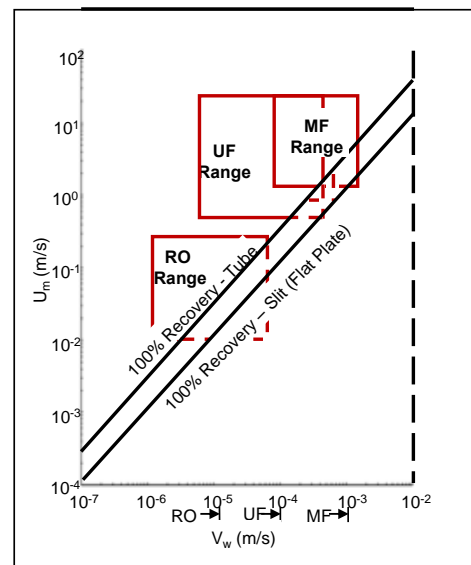


FIG. 7. LIMITATION ON PERMEATION FLUX. Maximum entrance crossflow velocity,  $U_m$ , versus permeation velocity for various pressure-driven membrane processes obtained

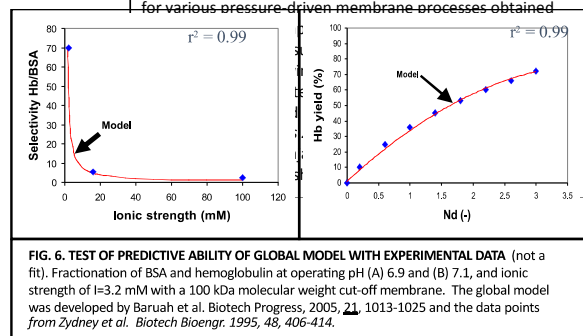


FIG. 6. TEST OF PREDICTIVE ABILITY OF GLOBAL MODEL WITH EXPERIMENTAL DATA (not a fit). Fractionation of BSA and hemoglobin at operating pH (A) 6.9 and (B) 7.1, and ionic strength of  $I=3.2$  mM with a 100 kDa molecular weight cut-off membrane. The global model was developed by Baruah et al. Biotech Progress, 2005, 21, 1013-1025 and the data points from Zydney et al. Biotech Bioengr. 1995, 48, 406-414.

used to do this. One way to see this effect is shown in Fig.7<sup>[61]</sup>, where the axial flow rates used by commercial membrane manufacturers increases with average fluxes for RO, UF and MF. Rearranging Eq. (3), one immediately realizes that the concentration modulus,  $M = C_w/C_b = \exp(v_w/k)$ , is a strong function of the ratio of the permeation flux to the mass transfer coefficient,  $v_w/k$ , which we call a “reduced flux”. The challenge is to increase  $k$  commensurate with an increase in  $v_w$ , while keeping  $M$  constant.  $k$  varies with the axial laminar crossflow velocity,  $U_m$ , as follows:  $k \propto (U_m)^{1/3}$ <sup>[62]</sup>. Since the feed for RO of seawater desalination is heavily pretreated, CP is more of a concern than fouling for ultra-high flux RO membranes. A 5-fold increase in membrane permeability is predicted to reduce energy consumption by only 3.7%<sup>[63]</sup>. The increase in  $k$  (or  $U_m$ ) will not be trivial and will require improvements in device design and membrane engineering and “it is likely that limitations in fluid mechanics and mass transfer will define the upper bounds of membrane performance”<sup>[64]</sup>. Of course, the human body uses high area “hollow fibers” with low permeation flux (kidney, lung) and pulsation (heart) to minimize mass transfer limitations. Industry prefers fast intensive membrane separation processes rather than slow high surface area-low flux approaches. Finally, without selectivity, we have no separation. So, we need to balance all three legs for a given desirable selectivity.

**Unresolved challenges:** Theoretical prediction of membrane performance: RO is a pressure-driven membrane process that separates water from salt solutions and has its foundation in Reid and Breton’s selection of cellulose acetate membranes<sup>[65]</sup>, and Loeb-Sourirajan’s development of semi-permeable anisotropic membranes<sup>[66]</sup>. Today, after nearly 60 years, it is a mature technical process, broadly used in the water industry for producing potable water, especially in arid regions such as Israel and the Gulf. It seems ironic that, in spite of the success of RO, there is no agreed molecular mechanism for selectively allowing water to pass in preference to salt. Although the solution-diffusion model is thought to operate for dense non-porous RO membranes, it provides little molecular understanding of how the salt and water separate. Briefly, several proposed explanations for this preferred selectivity include the following (for additional details see Imbrogno and Belfort<sup>[4]</sup>):

(a) *Hydrogen bond and bucket brigade*<sup>[65, 67]</sup>. Water hydrogen bonds to the hydroxyl groups in cellulose acetate (CA) membranes but ions do not, so “solvent molecules can pass through by successive transfer from one adsorption site to the next: since the association of the solvent molecules with the adsorbing surface need not be completely broken during this process, it requires relatively little energy, compared to that required for a solute molecule, to invade the mass of adsorbed solvent”.

(b) *Dielectric exclusion model*<sup>[68]</sup>. For finely porous membranes, the ions reside in the imbibed water of the RO membrane and are repelled when in close vicinity to materials with low dielectric constants like synthetic membranes ( $\epsilon_r < 5$ ). Thus, water ( $\epsilon_r \sim 80$ ) is preferred in the pores.

(c) *Ice-like water exclusion of ions*<sup>[69]</sup>: Water is preferentially sorbed into capillary pores and forms ice-like structures that exclude ions. With regard to mobility, the water is more like liquid than like ice, but has a definite degree of ordering quite different from that of bulk water<sup>[70]</sup>.

(d) *Fragmented Cluster (FC) model*<sup>[70b, 71]</sup>: Two bound layers of water, one inner layer more

“motionally restricted” than the second outer layer, near the pore surface and “bulk-like” water in the pore annulus are proposed. The inner bound water layer is strongly hydrogen bonded to the membrane pore wall and is thought to exclude ions<sup>[72]</sup>, while the outer layer partially excludes ions. In the presence of bulk water outside these two layers, ions easily hydrate and enter the pore. For complete ion exclusion, the pores need to be  $\leq 6 \text{ \AA}$  in diameters (i.e. lined with a  $\sim 3 \text{ \AA}$  annulus) and exclude both the second layer and the bulk water so that ions cannot enter the pore or hydrate easier to hydrate in the bulk than the first layer). Both experiments with fixed pores of porous glass desalination membranes and fits to the Resing NMR model support the fragmented cluster model<sup>[73]</sup>.

Nature’s water channel, aquaporin, has been used to prepare pseudo-synthetic membranes for desalination of brackish water<sup>[74]</sup>. Synthetic mimics of aquaporin channels with self-assembled imidazole molecules have formed oriented chiral water wires<sup>[75]</sup>. Much work is needed to produce mimics of aquaporin channels with required salt selectivity, sufficient permeation fluxes (volume flow rate per unit area) and optimal transport (i.e. “3 legs”).

In summary, besides the need to develop an accepted molecular theory for RO selectivity and minimize membrane fouling, disposal of the concentrated brine is a major challenge, especially for RO inland plants far from the ocean. In addition, solvent resistant membranes to fractionate organics with the aim of replacing high energy consuming phase-change distillation and evaporation processes with lower energy processes such as membranes, adsorption and extraction are needed<sup>[76]</sup>. These processes have great applied relevance, while the lack of *Structure-by design* should be of great fundamental interest.

## CONCLUSIONS

Although membrane filtration of liquids is a fast-growing mature industry with many benefits to mankind such as desalted drinking water, purified foods (beer, cheese, soft drinks, juices) and biologics (proteins, cells and ribonucleic acids), chemicals, petroleum products, and waste streams, there are tremendous opportunities for improvements. Major challenges remain with respect to increasing selectivity and permeation flux and controlling mass transport in, to and away from membranes. To do this, prediction and control of membrane morphology (polymer stiffness, pore size, pore size distribution and porosity) is essential together with a deep understanding on the mechanism of solute transport (i.e. mass transport and fluid mechanics) above and in membranes. New predictive models are also needed to describe performance including CP and fouling that account for all “three legs”.

Specifically, for polymer membranes, there is a need to design desirable pore size distributions and morphology of membranes (i.e. enable “structure-by-design”), reduce polymer motion and aging (loss of free volume), predict performance *a priori* with realistic liquid feeds containing foulants. Predicting particle or solute intrusion into porous membranes will need in-depth measurements of both intermolecular forces together with fluid-particle transport within the pores. Increased permeation fluxes will require larger mass transfer coefficients with

increased axial flow rates and more energy. Preferably, increasing the selectivity of pressure driven membranes through material design (thin, higher porosity, lower tortuosity, stiff, stable, good transverse flow), will have the biggest impact. To optimize performance, new module designs are also urgently needed.

Finally, the requirements for a commercially viable successful membrane include the following: high selectivity (first critical requirement), large permeation fluxes (reduced footprint with low capital costs), transport control (reduce F and CP), scalability (advantage of scale, economics), processability (polymers are relatively inexpensive compared with inorganic materials), flexibility (not fracture or crack from pump vibrations), stability with time (not loose initial performance excluding CP and F) and both perpendicular and lateral flow (allows full internal pore structure to be used when fouled). This is a tall order for the discovery of new membranes that may take many years to commercialize. It took RO membranes, that were first developed in the 1960s, 30-40 years to be accepted commercially.

However, data science (computer, mathematics and separation sciences) with reference to data processing, statistical analysis and artificial intelligence/machine learning could provide the methodology needed to select optimal conditions to design desired membrane structures and enable structure-by-design. It could also help determine optimal mass transfer and fluid mechanics conditions to minimize membrane fouling and concentration polarization. All this could be possible without requiring an understanding of the underlying physical or chemical mechanisms (personal communications, Roger Rousseau).

#### **ACKNOWLEDGEMENTS:**

I dedicate this article to the late academic and entrepreneur chemical engineer, Professor Alan S. Michaels, who made enormous contributions to membrane science and technology, who recognized earlier than most that transport limitations are critical for a successful membrane process, and who supported my career in more ways than one. I acknowledge and thank my ex- and present-PhD students and post-docs for their insight and creative contributions to our many published papers on synthetic membranes and associated transport phenomena. Research funding during the past 40 years from industry and government (Office of Basic Energy Sciences, US Department of Energy, DOE Grant # - DE-FG02-09ER16005, and the Division of Chemical, Bioengineering, Environmental and Transport Systems, Engineering Directorate, National Science Foundation NSF - Grant #1546589) are acknowledged and thanked. Comments and suggestions by Pierre Aimar, Tony Fane, Jack Keating, Chip Kilduff, Mirco Sorci and Andrew Zydney are much appreciated. Also, Ingo Pinnau and Lloyd Robeson responded to questions regarding the “upper bound”. The views expressed here, however, are my own.

#### **REFERENCES**

- [1] D. S. Sholl, R. P. Lively, *Nature* **2016**, 532, 435-437.

- [2] BCCResearch, BCC Research, **November 2016**.
- [3] S. Loeb, S. Sourirajan, in *Saline Water Conversion II, Vol. 38* (Ed.: R. F. Gould), American Chemical Society, Washington DC, **1963**, pp. 117-132.
- [4] J. Imbrogno, G. Belfort, *Annu Rev Chem Biomol Eng* **2016**.
- [5] J. Imbrogno, J. J. Keating IV, J. E. Kilduff, G. Belfort, *Desalination* **2017**, *401*, 68-87.
- [6] aH. Li, Z. Song, X. Zhang, Y. Huang, S. Li, Y. Mao, H. J. Ploehn, Y. Bao, M. Yu, *Science* **2013**, *342*, 95-98; bM. Y. Jeon, D. Kim, P. Kumar, P. S. Lee, N. Rangnekar, P. Bai, M. Shete, B. Elyassi, H. S. Lee, K. Narasimharao, S. N. Basahel, S. Al-Thabaiti, W. Xu, H. J. Cho, E. O. Fetisov, R. Thyagarajan, R. F. DeJaco, W. Fan, K. A. Mkhoyan, J. I. Siepmann, M. Tsapatsis, *Nature* **2017**, *543*, 690-694; cP. J. Bereciartua, A. Cantin, A. Corma, J. L. Jorda, M. Palomino, F. Rey, S. Valencia, E. W. Corcoran, Jr., P. Kortunov, P. I. Ravikovitch, A. Burton, C. Yoon, Y. Wang, C. Paur, J. Guzman, A. R. Bishop, G. L. Casty, *Science* **2017**, *358*, 1068-1071; dD. L. Gin, R. D. Noble, *Science* **2011**, *332*, 674-676.
- [7] C. J. King, *Separation Processes*, Second ed., McGraw-Hill Book Co., **1980**.
- [8] H. B. Park, J. Kamcev, L. M. Robeson, M. Elimelech, B. D. Freeman, *Science* **2017**, *356*.
- [9] aM. Galizia, W. S. Chi, Z. P. Smith, R. W. Baker, B. D. Freeman, *Macromolecules* **2017**, *50*, 34; bL. M. Robeson, *J. Membr. Sci.* **2008**, *320*, 11; cR. Swaidan, B. Ghanem, E. Litwiller, I. Pinnau, *Macromolecules* **2015**, *48*, 6553-6561.
- [10] S. Y. Lee, B. S. Minhas, M. D. A. D'onohue, D. M., in *New membrane materials and processes for separations, Vol. 84* (Eds.: K. K. Sirkar, D. R. Lloyd), AIChE, New York, NY, **1988**, p. 93.
- [11] A. Mehta, A. L. Zydney, *J. Membr. Sci.* **2005**, *249*, 245-249.
- [12] H. Zhang, G. M. Geise, *J. Membr. Sci.* **2016**, *520*, 790-800.
- [13] A. L. Zydney, P. Aimar, M. Meireles, J. M. Pimbley, G. Belfort, *J. Membr. Sci.* **1994**, *91*, 293-298.
- [14] W. J. Koros, R. Mahajan, *J. Membr. Sci.* **2001**, *181*, 141-156.
- [15] aM. D. Shelby, G. L. Wilkes, *Polymer* **1998**, *39*, 12; bA. Y. Alentiev, N. A. Belov, S. V. Chirkov, Y. P. Yampolskii, *Journal of Membrane Science* **2018**, *547*, 10.
- [16] J. D. Ferry, *Chem. Rev.* **1936**, *18*, 373-455.
- [17] A. N. Cherkasov, E. A. Polotski, *J. Membr. Sci.* **1996**, *110*, 79-82.
- [18] S. Dami, C. Abetz, B. Fischer, M. Radjabian, P. Georgopoulos, V. Abetz, *Polymer* **2017**, *126*, 9.
- [19] M. Mulder, *Basic principles of membrane technology (Second Edition)*, Kluwer Academic Publishers, Dordrecht, The Netherlands, **1996**.
- [20] aM. Ulbricht, O. Schyuster, W. Ansoerge, M. Ruetering, P. Steiger, *Sep. Purif. Tech.* **2007**, *57*, 10; bH. Strathmann, K. Kock, P. Amar, R. W. Baker, *Desalination* **1975**, *16*.
- [21] D. Y. Koh, B. A. McCool, H. W. Deckman, R. P. Lively, *Science* **2016**, *353*, 804-807.
- [22] P. Marchetti, M. F. Jimenez Solomon, G. Szekely, A. G. Livingston, *Chemical Reviews* **2014**, *114*, 10735-10806.
- [23] N. Rangnekar, N. Mittal, B. Elyassi, J. Caro, M. Tsapatsis, *Chem Soc Rev* **2015**, *44*, 7128-7154.
- [24] aB.-H. Jeong, E. M. V. Hoek, Y. Yan, A. Subramani, X. Huang, G. Hurwitz, A. K. Ghosh, A. Jawor, *J. Membr. Sci.* **2007**, *294*, 1-7; bM. L. Lind, D. Eumine Suk, T. V. Nguyen, E. M. Hoek, *Environ Sci Technol* **2010**, *44*, 8230-8235; cM. L. Lind, A. K. Ghosh, A. Jawor, X. Huang, W. Hou, Y. Yang, E. M. Hoek, *Langmuir* **2009**, *25*, 10139-

- 10145; dW. A. Phillip, R. M. Dorin, J. Werner, E. M. Hoek, U. Wiesner, M. Elimelech, *Nano Lett* **2011**, *11*, 2892-2900; eS. Turgman-Cohen, J. C. Araque, E. M. Hoek, F. A. Escobedo, *Langmuir* **2013**, *29*, 12389-12399.
- [25] J. E. Bachman, Z. P. Smith, T. Li, T. Xu, J. R. Long, *Nat Mater* **2016**, *15*, 845-849.
- [26] aN. B. McKeown, P. M. Budd, *Chemical Society Reviews* **2006**, *35*, 675-683; bN. B. McKeown, P. M. Budd, *Macromolecules* **2010**, *43*, 5163-5176.
- [27] S. P. Nunes, , Sougrat R., Hooghan, **B.**, Anjum, D. H., Behzad, A. R., Zhao, L., Pradeep, N., Pinnau, I., , Vainio, U.,, Peinemann, K-V., *Macromolecules* **2010**, *43*, 7.
- [28] J. M. S. Denny, J. C. Moreton, L. Benz, S. M. Cohen, *Nature Reviews - Materials* **December 2016**, *1*, 1-17.
- [29] R. W. Baker, *Membrane Technology and Applications*, 3 ed., John Wiley & Sons, Ltd, **2012**.
- [30] M. B. Rao, S. Sirkar, *J. Membr. Sci.* **1993**, *243*, 8.
- [31] J. E. Koresh, A. Soffer, *Sep. Sci. and Techn.* **1983**, *18*.
- [32] K. Varoon, X. Zhang, B. Elyassi, D. D. Brewer, M. Gettel, S. Kumar, J. A. Lee, S. Maheshwari, A. Mittal, C. Y. Sung, M. Cococcioni, L. F. Francis, A. V. McCormick, K. A. Mkhoyan, M. Tsapatsis, *Science* **2011**, *334*, 72-75.
- [33] X. Qiu, H. Yu, M. Karunakaran, N. Pradeep, S. P. Nunes, K. V. Peinemann, *ACS Nano* **2013**, *7*, 768-776.
- [34] aC. H. Lau, P. T. Nguyen, M. R. Hill, A. W. Thornton, K. Konstas, C. M. Doherty, R. J. Mulder, L. Bourgeois, A. C. Y. Liu, D. J. Sprouster, J. P. Sullivan, T. J. Bastow, A. J. Hill, D. L. Gin, R. D. Noble, *Angewandte Chemie-International Edition* **2014**, *53*, 5322-5326; bC. L. Staiger, S. J. Pas, A. J. Hill, C. J. Cornelius, *Chemistry of Materials* **2008**, *20*, 2606-2608.
- [35] H. Fan, J. Gu, H. Meng, A. Knebel, J. Caro, *Angew Chem Int Ed Engl* **2018**, *57*, 4083-4087.
- [36] M. Sara, U. Sleytr, *J. Membr. Sci.* **1987**, *33*, 27-49.
- [37] C. Li, L. S. Xu, Y. Zuo, P. Yang, *Biomater. Sci.* **2018**.
- [38] J. J. Keating, J. Imbrogno, G. Belfort, *ACS Appl Mater Interfaces* **2016**, *8*, 28383-28399.
- [39] aJ. J. I. Keating, M. Sorci, I. Kocsis, A. Setaro, M. Barboiu, P. Underhill, G. Belfort, *J. Membr. Sci.* **2017**, *546*, 6; bJ. J. V. Keating, A. Lee, G. Belfort, *Macromolecules* **2017**, *50*, 9.
- [40] C.-C. Ho, A. L. Zydney, *J. Membr. Sci.* **1999**, *155*, 14.
- [41] M. Sorci, M. Gu, C. L. Heldt, E. Grafeld, G. Belfort, *Biotechnol. Bioeng.* **2013**, *110*, 1704-1717.
- [42] K. K. Yang, Z. Wu, C. N. Bedbrook, F. H. Arnold, *Bioinformatics* **2018**, *34*, 2642-2648.
- [43] D. Mahlab, Ben Joseph, N., and Belfort, G. , *Chem. Eng. Commun.* **1980**, *6*, 18.
- [44] W. J. Koros, C. Zhang, *Nat Mater* **2017**, *16*, 289-297.
- [45] aJ. Hermia, *Trans. Inst. Chem Engr.* **1982**, *60*; bP. Hermans, H. Bredée, *J. Soc. Chem. Ind* **1963**, *55*, 1-4.
- [46] C.-C. Ho, A. L. Zydney, *J. Membr. Sci.* **2000**, *232*, 10.
- [47] J. E. Kilduff, S. Mattaraj, J. Sensibaugh, J. P. Pieracci, Y. Yuan, G. Belfort, *Environmental Engineering Science* **2002**, *19*, 477-495.
- [48] aM. David, Y. Nissim Ben, B. Georges, in *Synthetic Membranes*;, Vol. 153, AMERICAN CHEMICAL SOCIETY, **1981**, pp. 147-158; bD. Mahlab, N. Ben Yosef, G. Belfort, in *Synthetic Membranes*, (Ed.: A. F. Turbak), American Chem. Soc. , Washington DC,

- 1981**; cD. Mahlab, N. B. Yosef, G. Belfort, *Chemical Engineering Communications* **1980**, 6, 225-243.
- [49] V. L. Vilker, C. K. Colton, K. A. Smith, D. L. Green, *J. Membr. Sci.* **1984**, 20, 11.
- [50] W. F. Blatt, A. Dravid, A. S. Michaels, L. Nelson, in *Membrane Science and Technology*, (Ed.: J. E. Flinn), Plenum Press, New York, **1970**.
- [51] N. Nagata, K. J. Herouvis, D. M. Dziewulski, G. Belfort, *Biotechnol Bioeng* **1989**, 34, 447-466.
- [52] aG. L. Baruah, A. Venkiteshwaran, G. Belfort, *Biotechnol Prog* **2005**, 21, 1013-1025; bR. H. van Eijndhoven, S. Saksena, A. L. Zydney, *Biotechnol Bioeng* **1995**, 48, 406-414.
- [53] aJ. Imbrogno., J. I. Keating, J. E. Kilduff, G. Belfort, *Desalination* **2016**, in press; bR. W. Baker, *Membrane Technology and Applications, Chapter 9*, 3 ed., John Wiley & Sons, Ltd, **2012**.
- [54] O. A. N., *Membrane Digest (Office of Saline Water, US Depart. of the Interior)* **1972**, 1, 23-57.
- [55] R. W. Field, D. Wu, J. A. Howell, *J. Membr. Sci.* **1995**, 100, 259-272.
- [56] G. Belfort, R. H. Davis, A. L. Zydney, *J. Membr. Sci.* **1994**, 96, 1-58.
- [57] M. C. Porter, *Ind. Eng. Chem. Prod. Res. Dev.* **1972**, 11, 234.
- [58] J. H. Holt, H. G. Park, Y. Wang, M. Stadermann, A. B. Artyukhin, C. P. Grigoropoulos, A. Noy, O. Bakajin, *Science* **2006**, 312, 3.
- [59] aK. Sint, B. Wang, P. Kra, *J. AM. CHEM. SOC.* **2008**, 130, 16448–16449; bJ. B. Stetson, J. Mercurio, A. Rosenwinkel, P. V. Bedworth, *Vol. US 20120048804A1* (Ed.: U. P. Office), Lockheed Martin Corp., USA, **2012**, p. 13.
- [60] R. R. Nair, H. A. Wu, P. N. Jayaram, I. V. Grigorieva, A. K. Geim, *Science* **2012**, 335, (2012). 2.
- [61] G. Belfort, R. J. Weigand, J. T. Mahar, in *ACS Symposium Series 281: Reverse Osmosis and Ultrafiltration* (Eds.: S. Sourirajan, T. Matsuura), American Chemical Society, Washington DC, **1985**, pp. 383-401.
- [62] W. M. Deen, *Analysis of Transport Phenomena*, Oxford University Press, New York and Oxford, **2012**.
- [63] J. R. Werrber, A. Deshmukh, M. Elimelech, *Environ.. Sci. Technol. Lett* **2016**, 3, 9.
- [64] A. G. Fane, R. Wang, M. X. Hu, *Angew Chem Int Ed Engl* **2015**, 54, 3368-3386.
- [65] C. Reid, E. Breton, *Journal of Applied Polymer Science* **1959**, 1, 133-143.
- [66] aS. Loeb, S. Sourirajan, *Adv. in Chem. Series* **1962**, 38, 117-132; bS. Loeb, *ACS Symposium Series* **1981**, 153, 9.
- [67] C. Reid, *Desalination by Reverse Osmosis* **1966**, Ch. 1, 1-14.
- [68] aE. Glueckauf, in *Proc., First International Symposium on Water Desalination, Washington, DC, Vol. 1*, **1965**, p. 143; bG. Scatchard, *The Journal of Physical Chemistry* **1964**, 68, 1056-1061.
- [69] S. Sourirajan, T. Matsuura, *Reverse Osmosis and Synthetic Membranes*, Sourirajan, S. (ed), *National Research Council of Canada, Ottawa* **1977**.
- [70] aE. Almagor, G. Belfort, *Journal of Colloid and Interface Science* **1978**, 66, 146-152; bG. Belfort, N. Sinai, in *Water in Polymers: 178th Meeting of the American Chemical Society, Washington, DC, Vol. 127*, Amer Chemical Society, **1980**, pp. Ch. 19, 323-345.
- [71] G. Belfort, N. Sinai, in *Water in Polymers, ACS Symp. Series*, ACS, Washington, **1980**, pp. 323-346.
- [72] W. A. Luck, in *Topics in Current Chemistry*, Springer, **1976**, pp. 114-180.

- [73] aG. Belfort, *Nature* **1972**, 237, 60-61; bG. Belfort, J. Scherfig, D. O. Seevers, *Journal of Colloid and Interface Science* **1974**, 47, 106-116.
- [74] Y. Zhao, C. Qiu, X. Li, A. Vararattanavech, W. Shen, J. Torres, C. Helix-Nielsen, R. Wang, X. Hu, A. G. Fane, *Journal of Membrane Science* **2012**, 423, 422-428.
- [75] I. Kocsis, M. Sorci, H. Vanselous, S. Murail, S. E. Sanders, E. Licsandru, Y. M. Legrand, A. van der Lee, M. Baaden, P. B. Petersen, G. Belfort, M. Barboiu, *Sci Adv* **2018**, 4, eaao5603.
- [76] O. R. Authored by BCS Inc. Columbia MD. and Oak Ridge National Laboratory, TN, **2005, May 4th**, p. 103.