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# Intrinsic limitations of nanofiltration membranes to achieve precise selectivity in water-based separations

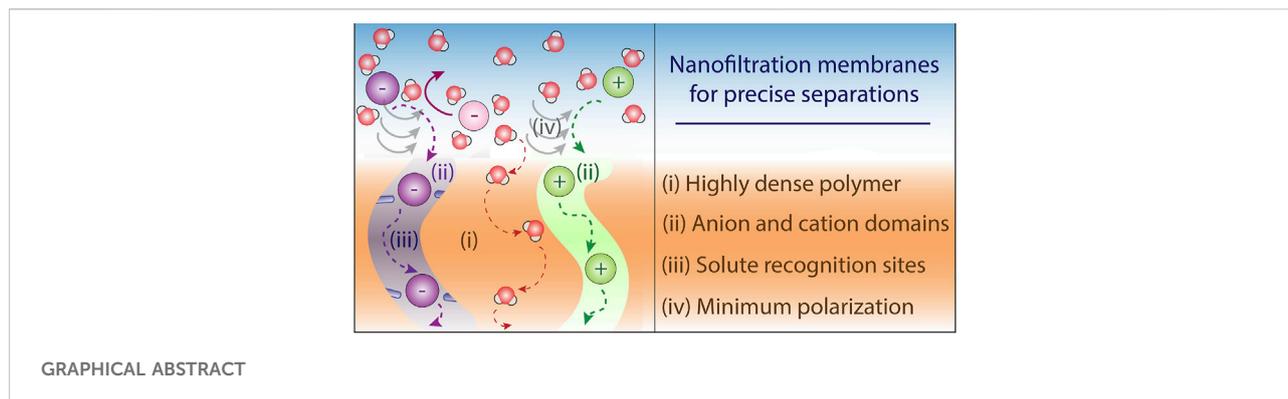
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Over the last decades, nanofiltration (NF) membranes have been used to selectively remove certain solutes from water with recent interest targeting more challenging separations that require precise selectivity between solutes. In this perspective article, we aim to challenge (but not disprove) the prevalent notion that NF membranes are suitable for precise separations. We first provide and analyze selectivity data from the literature of three important separations including monovalent-divalent ion selectivity, separations involving organic molecules, and the more ambitious separations of ions with the same charge. We then introduce the terms rejection-based selectivity and transport-based selectivity to distinguish between the commonly “rough” separations pursued in NF (e.g., water softening) and the more visionary separations required for precise selectivity (e.g., transport of lithium through specific recognition sites), respectively. Using these terms, we discuss two major intrinsic limitations to achieve precise selectivity in NF systems; namely, the need for a solute-specific membrane that can transport simultaneously additional species (i.e., water and the complementary salt ion) and the detrimental effect of concentration polarization. We conclude with guidelines and principles to overcome these limitations.

## KEYWORDS

ion selectivity, ion transport, water permeability, solute rejection, concentration polarization, reverse osmosis, polyamide membranes



## 1 Introduction

Since their first introduction in the late 1980s, nanofiltration (NF) membranes, a “looser” version of reverse osmosis (RO) membranes, have been proposed for applications involving the selective removal of specific solutes from water, such as water softening, sulfate removal, and concentration of organics in certain industries (Hilal et al., 2004; Van der Bruggen et al., 2008; Mohammad et al., 2015; Oatley-Radcliffe et al., 2017). More recently, increasing demands for fit-for-purpose water treatment and recovery of valuable elements from water have accelerated the race for the design of highly selective nanofiltration membranes for more challenging separations such as lithium and nutrient recovery and selective removal of contaminants from different waters (Epsztein et al., 2020; Duchanois et al., 2021; Zhao et al., 2021a; Zuo et al., 2021). While a certain (and important) progress has been reported, it is imperative to analyze the existing literature on solute-solute selectivity in NF, highlight current challenges and limitations, and introduce principles and pathways to overcome these limitations.

In this perspective, we aim to challenge (but not dismiss) the prevalent conception that nanofiltration membranes can achieve precise separations between solutes. We first review and analyze the general trends of achievable selectivities in NF for three main classes of important separations; namely, separation between ions of different charge, separations involving organics, and the highly challenging separation between ions of the same charge. We then discuss key challenges to achieve high solute-solute selectivity and introduce new guidelines to overcome these challenges. Our main takeaway message is that intrinsic limitations in the operation of current NF systems may require the design of a membrane with unique and different properties from those pursued so far.

## 2 Achievable solute-solute selectivity in nanofiltration membranes

To demonstrate the general picture of the achievable selectivity between different solutes (i.e., solute-solute

selectivity) in NF, we extracted data from 43 references for three major classes of separations including separation of ions with different charge (Figure 1A), separations involving organics (Figure 1B), and the more challenging separation of ions with the same charge (Figures 1C,D). While selectivity in membrane processes can be expressed in different ways, the observed selectivity between two solutes, A and B, in NF is most commonly expressed using

$$\text{Selectivity } (A, B) = \frac{1 - R_A}{1 - R_B} \quad (1)$$

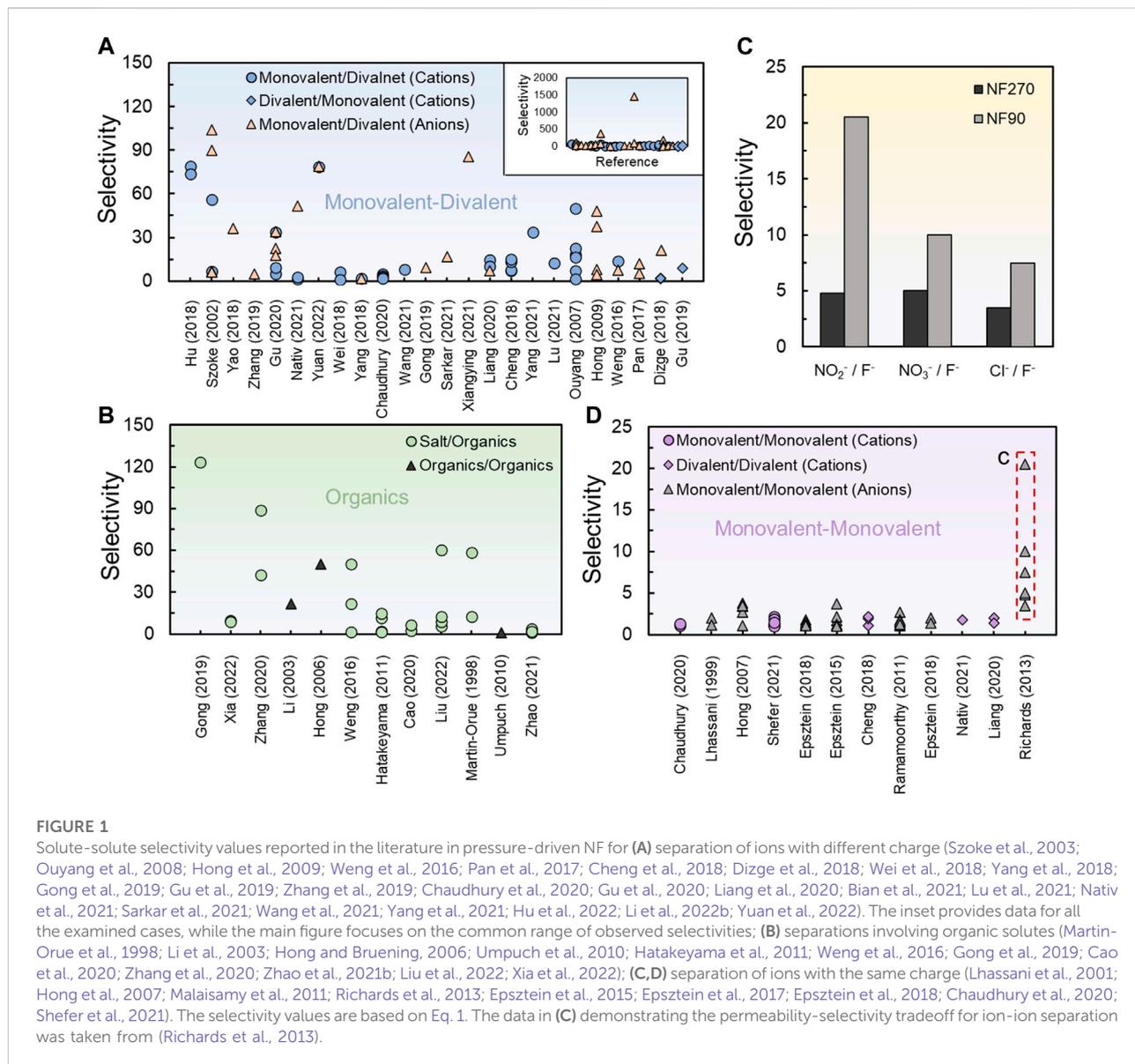
where  $R_i$  is the observed rejection of solute  $i$ , which is defined as

$$R = 1 - \frac{C_p}{C_f} \quad (2)$$

where  $C_p$  and  $C_f$  are the concentrations of solute  $i$  in the permeate and feed solution, respectively. The real selectivity, which accounts for the increased concentration of accumulated solutes on the membrane surface, can be calculated from real rejections (instead of observed rejections) using the evaluated (Song and Elimelech, 1995) or measured (Sutzkover et al., 2000) solute concentrations on the membrane surface,  $C_m$ , instead of  $C_f$  in Eq. 2.

The data in Figure 1 were achieved in pressure-driven NF experiments performed under different conditions (e.g., different concentration, pressure, pH, membrane type, single vs. mixed salt solutions, etc.) and therefore cannot be compared with each other; however, they are representative of the literature and hopefully catch the big picture of achievable selectivities in NF. In addition, many of the studies reviewed here did not account for concentration polarization; that is, the reported selectivity is based on observed rejection only, which hinders the understanding of the real membrane capabilities. We will discuss the underestimation of concentration polarization and its crucial role to obtain high solute-solute selectivity in NF in Section 3.

We note that the expression used in Eq. 1 to quantify the selectivity does not provide the complete picture regarding the



quality of the separation from a practical point of view. More specifically, while this expression reflects the ratio of transmembrane passage between two solutes, it does not provide any information on the separation capabilities of the individual solute; that is, important evaluators of the separation of the individual solute such as rejection, permeability, or concentration in the permeate cannot be deduced from this term. For example, if the rejection of solute A is 99% and the rejection of solute B is 99.999%, the selectivity according to Eq. 1 is relatively high (1,000), but the actual separation is very poor, as both solutes will accumulate in the retentate stream with extremely little gain of pure solute A in the permeate stream. Nevertheless, the expression in Eq. 1 provides information on the ratio between the passage of two solutes, which is important to understand the ability of the membrane to distinguish between

two solutes form a more fundamental perspective. We also note that the measurement of the selectivity becomes highly sensitive when rejections increase above 99% (e.g., a difference between 99% and 99.9% will lead to an order of magnitude difference in the selectivity), hindering the exact calculation of the selectivity.

## 2.1 Separation of ions with different charge

Separation between ions of different valence is perhaps the most popular solute-solute separation pursued by NF due to the relatively large size and/or charge difference of the ions to be separated (Figure 1A). Specifically, separation of divalent ions such as calcium, magnesium, and sulfate from the dominant

monovalent ions in water systems (i.e., sodium and chloride) has been targeted in many studies and applications (Lu et al., 2022). More recently, lithium recovery from salt-lake brines, which contain high magnesium concentration, has been studied extensively (Sun et al., 2015; Li et al., 2019; Li Q. et al., 2022; Lyu et al., 2022). Efforts, therefore, mostly focus on maximizing the synergistic effect of size- and charge-based rejection by adjusting the membrane charge to be the same as the charge of the divalent ion (e.g., imparting a positive charge to the typically negative surface of polyamide membranes to enhance the removal of divalent cations) (Cheng et al., 2018). As will be discussed in later sections, this approach of increasing the rejection of the unwanted solute (i.e., rejection-based selectivity) may play an important role in the upper selectivity limit obtained for monovalent-divalent ion separation in NF.

Generally, most selectivity values for monovalent-divalent ion separation range from 0 to 100 (Figure 1A) with a few studies reporting higher values up to 2000 (Figure 1A, inset). This range of achievable selectivity can be very often satisfactory from a practical view, as the rejection of divalent ions can occasionally reach high values above 95%. For example, a sodium rejection of 10% and magnesium rejection of 95% results in a selectivity of 18, which in many cases can satisfy the softening requirements. While the reported monovalent-divalent ion selectivity demonstrates the potential of NF membranes to separate divalent ions from monovalent ions for various applications, a precise separation of these ions is still not within reach (e.g., high permeation of sodium with ultralow permeation of magnesium). For comparison, the ultra-selective potassium channel transports only one sodium ion per each 10,000 potassium ions traversing the channel, representing a selectivity value of 10,000 with high throughput of potassium (Doyle et al., 1998; Gouaux and MacKinnon, 2005). To put things in context, even if a membrane rejects 99.9% of one ion and 1% of the other ion, the selectivity will be 990. We will discuss the intrinsic limitations to reach ultrahigh selectivities in NF in Section 3.

## 2.2 Separations involving organic solutes

Due to their dense but relatively open structure that allows the permeation of certain solutes, NF membranes have been also widely applied for the selective removal of specific organic solutes over inorganic ions or other organic molecules. This type of selectivity, which mostly relies on size and charge differences between solutes, is needed in various environmental and industrial applications such as water and wastewater purification, recovery of pharmaceuticals and biomolecules, and concentration of products in the food industry (Mohammad et al., 2015). Our collected data from the literature of NF applied for separation of organics aims to provide the general picture of achievable selectivity in this area (Figure 1B).

Overall, good separation can be obtained with selectivity values similar to those achieved for monovalent-divalent ion separation. Such selectivity values are achievable for the selective separation of organic solutes from different organics or inorganic ions due to the relatively large size differences between different organic molecules and the larger size of organics compared to most inorganic ions, respectively. In addition, the pH dependency of the charge of many organic molecules (e.g., amino acids) opens opportunities to enhance size-based separations or induce the separation between similarly sized organics. However, as discussed for monovalent-divalent separation in Section 3.1, achieving ultrahigh selectivity values (i.e., four orders of magnitude and higher) for the separation of organics has not been reported. As we will discuss elaborately in Section 3, a partial reason for the limited selectivity achieved is the fact that the separation is pursued by tailoring the membrane to enhance the rejection of the unwanted solute (i.e., rejection-based selectivity) instead of designing a membrane that permits the transport of a specific solute (i.e., transport-based selectivity).

## 2.3 Separation of ions with the same charge

With the increased demand for resource recovery, fit-for-purpose water treatment, and other related applications, the separation between ions of the same charge, especially monovalent ions, has become a main research avenue in recent years (Epsztein et al., 2020; Zhao et al., 2021a; Shefer et al., 2022a; Shefer et al., 2022b; Pavluchkov et al., 2022). Since similarly charged ions often possess a similar hydrated size (Nightingale, 1959), separation mechanisms beyond simple size and charge exclusion are required to leverage the selectivity. Such mechanisms must involve more gentle, non-electrostatic interactions as demonstrated by many ion-selective biological channels (Gouaux and MacKinnon, 2005; Faucher et al., 2019; Epsztein et al., 2020). To establish these interactions in membrane separation, fabrication approaches with atomic precision are required. Unfortunately, current methods to fabricate polymeric NF membranes cannot reach such precision scales, where even the roughness of the membrane surface exceeds tens of nanometers (Freger, 2003). Nevertheless, due to the non-steric and non-electrostatic selectivity mechanisms that exist naturally under any condition, even state-of-the-art and other custom-made polymeric NF membranes exhibit a certain selectivity between ions of the same charge (Figures 1C,D).

As expected, the selectivity values obtained for the separation of similarly sized and charged ions (Figure 1D) are lower than those obtained for monovalent-divalent ion separation (Figure 1A) and fractionation of organics (Figure 1B), with most values ranging from 0 to 5. Since the current technology to improve the selectivity between ions of the same charge in polymeric NF membranes is limited, most of the data in

Figure 1D represents experiments on commercial NF membranes and only a few studies that attempted to leverage the separation by fabricating NF membranes using the layer-by-layer assembly of polyelectrolytes. We note that over the last decade there has been a progress in the fabrication of channels and membranes that incorporate specific binding groups to enhance or hinder the transport of specific ions, which resulted in increased ion-ion selectivity (Sheng et al., 2014; Warnock et al., 2021; DuChanois et al., 2022). However, most of these studies did not test the selectivity in a pressure-driven NF and did not provide the obtained selectivity (or related parameters to measure this selectivity) as defined in this perspective; therefore, data from these studies were not included in Figure 1D. Increasing the selectivity between ions of the same charge for practical separations may be possible with further progress and technological developments in membrane fabrication, but will be still bounded by some intrinsic limitations governing the separation in NF systems as discussed in Section 3.

Interestingly, our analysis finds the selectivity between monovalent ions to be higher for denser NF membranes (Figure 1C) (Richards et al., 2013), most likely due to the same permeability-selectivity tradeoff that governs water-salt separation (Park et al., 2017); that is, a less permeable membrane reduces more the permeability of the larger species, increasing the selectivity between the two species. This finding is, to some extent, counterintuitive to the common notion that NF membranes can achieve higher solute-solute selectivity than RO membranes. However, from a practical view, the lower selectivity of NF is commonly compensated by the higher throughput of permeate that is rich with a desired solute compared to the almost solute-free (and therefore useless) permeate in RO.

### 3 Key challenges and solutions towards improved solute-solute selectivity

We showed in the previous section that most achievable solute-solute selectivity values reported in the literature of NF can reach the lower range of two orders of magnitude (100–150) with only a few exceptional cases that demonstrate selectivity value of three orders of magnitude (>1,000). These relatively low selectivity values compared to the four orders of magnitude selectivity observed for ion-selective biological channels mostly stem from the low specificity of polymeric NF membranes towards a certain solute. To better discuss the lack of specificity in current NF membranes, we introduce the terms rejection-based selectivity and transport-based selectivity, which represent two main approaches to achieve high selectivity. In most attempts reported in the literature to improve the selectivity of NF membranes, the rejection-based selectivity approach was used; that is, the rejection of the unwanted solute (e.g., magnesium in water softening) is increased with minimal or no increase in the

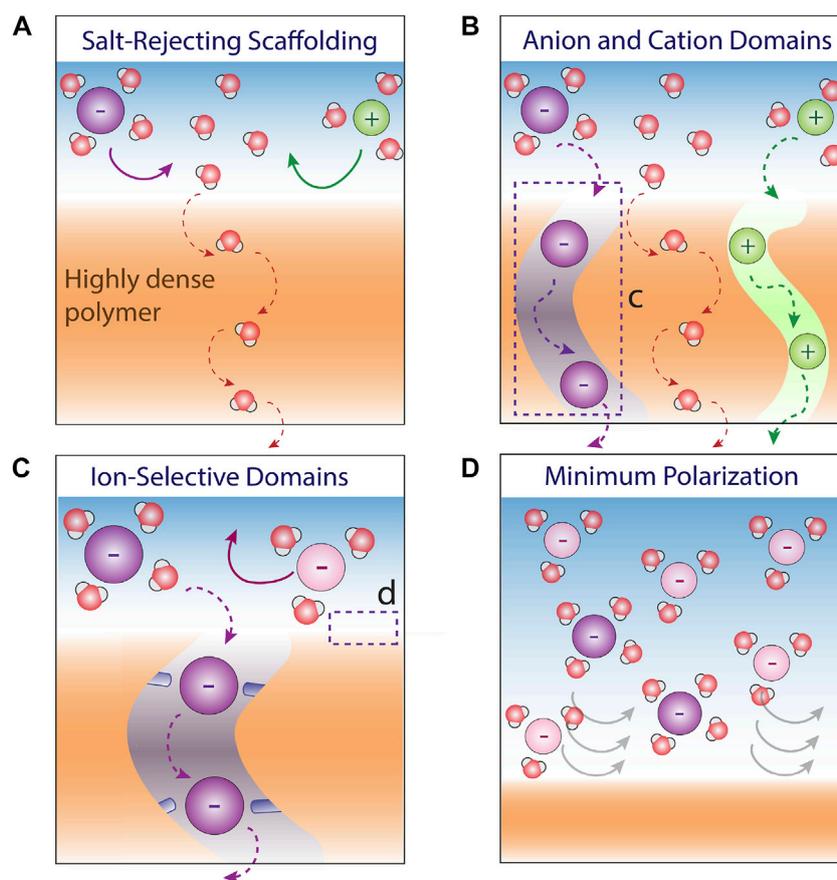
rejection of the wanted solute (e.g., sodium in water softening) (Cheng et al., 2018). This approach suffers from two main drawbacks. First, rejection is based on repulsive forces between the membrane and permeating solutes and therefore it is more challenging to be tuned to act on a specific solute. For example, when magnesium removal is pursued by applying higher positive membrane charge, the rejection of other multivalent cations will also increase, so that the recovery of pure magnesium cannot be achieved. Second, we assert that a higher rejection of solute A can be achieved if efforts will be directed to tune the membrane to specifically transport solute B (i.e., transport-based selectivity, see below) instead of tuning the rejection of solute A.

Using transport-based selectivity, which is manifested in some prominent cases of ion-selective biological channels (Gouaux and MacKinnon, 2005), ultrahigh selectivity values can be achieved through high specificity of the membrane towards the desired solute to be transported. Applying this approach, a permeate containing exclusively the desired solute can be obtained with close to zero passage of unwanted solutes, overcoming the above-mentioned problems associated with rejection-based selectivity. Principles to achieve such specificity, which are based on decreasing the energy barrier for the target solute *via* compensatory interactions (i.e., interactions that thermodynamically stabilize the permeating solute within the pore), were discussed in detail elsewhere (Epsztein et al., 2020). While we believe that it is imperative to apply transport-based selectivity in NF membranes to reach ultrahigh selectivity values, two main limitations intrinsic to NF systems impose a significant challenge for the utilization of such approach.

#### 3.1 A solute-specific membrane that transports simultaneously other species

As opposed to ion-exchange membranes or biological ion channels, which ideally permit the exclusive transport of anions or cations without water, NF membranes inherently must transport simultaneously multiple species including anions, cations, and (mostly) water. This mixture of species entering the membrane hinders a membrane design for transport-based selectivity that permits the transport of a specific solute *via* compensatory interactions. That is, how can a membrane be highly specific to lithium, for example, if it must also transport chloride and water? To overcome this inherent limitation, we propose a few principles for the design of an ideal ultra-selective NF membrane (Figure 2).

First, to have a membrane that is selective to the transport of a specific solute (and water), it will be essential to start with a scaffolding exhibiting ultrahigh salt rejection to ensure that only water and no solute can pass through (Figure 2A). Such scaffolding can be, in fact, a highly dense reverse osmosis membrane with ultrahigh water-salt selectivity (Barboiu, 2012). Next, to reduce the problem of separation into separation of ions



**FIGURE 2**

Guidelines and principles for the design of an ideal ultra-selective NF membrane. **(A)** To avoid permeation of unwanted solutes, the membrane backbone should be highly impermeable to salts; **(B)** To separate the treatment of anions and cations, anion and cation domains should be designed alternately; **(C)** Within each domain, precise selectivity can be applied using principles from ion-selective biological channels; and **(D)** Concentration polarization should be minimized to decrease the driving force of the less permeable species.

with the same charge (e.g., separating lithium from sodium without the interference of chloride), alternating anion and cation domains (i.e., channels that transport exclusively anions or cations) must be designed within the scaffolding (Figure 2B). Such a charge-patterned mosaic membrane with alternating anion and cation domains was recently proposed for a different purpose using inkjet printing (Gao et al., 2016). These domains can be then decorated with selective recognition sites based on previously reported principles that provide the compensatory interactions for the target ion to discriminate between ions of the same charge (Figure 2C).

### 3.2 Counteracting driving force due to concentration polarization

According to the solution-diffusion model (Wijmans and Baker, 1995), the actual chemical potential gradient that moves solutes

from one side of the membrane to the other is the concentration gradient across the membrane. This feature means that the selectivity between two solutes is interfered by the increasing driving force (i.e., concentration gradient) applied on the less permeable species along the filtration module. Such interference becomes even more prominent due to concentration polarization, which is manifested more severely in NF membranes with relatively high flux and especially in the case of highly rejected and heavy solutes with low diffusivity in solution due to their higher tendency to accumulate on the membrane surface (Déon et al., 2013). In the context of transport-based selectivity discussed here that can ideally prevent the passage of unwanted solutes, an unregulated increase in the surface concentration of the rejected solutes can substantially hamper the achievement of ultrahigh selectivity, which requires ultrahigh rejection (>99.9%) of these solutes. It is very likely, for example, that one of the factors that limit the selective rejection of divalent cations over sodium cation in softening processes is the high concentration polarization of the relatively heavy and less mobile

divalent cations. Therefore, the premise for achieving ultrahigh selectivity for any kind of separation in pressure-driven NF is that the flow conditions are optimized to minimize concentration polarization effects (Figure 2D).

## 4 Outlook for precise separations in nanofiltration

Nanofiltration membranes, by their very nature, are designed to transport solvents (e.g., water) rather than solutes. That is, the major species to be transported through the membrane is the solvent. This property of NF membranes imposes a prominent challenge to make these membranes highly selective to a specific solute using the selectivity principles learned from nature (e.g., incorporating intrapore binding sites that stabilize the target solute in the membrane). This challenge becomes even higher in the specific case of ions, where the transport of a target ion must be accompanied by the complementary salt ion to maintain electroneutrality. On top of this inherent limitation, pressure-driven NF systems are characterized by concentration polarization that counteracts solute-solute selectivity by providing additional driving force to the rejected species. Our ongoing investigation shows how polarization effects can not only decrease the selectivity between solutes, but even reverse it. Depending on the specific needs, future membrane design should account for these limitations in different levels. For non-precise separations resulting from rejection-based selectivity (i.e., higher rejection of divalent ions compared to monovalent ions), minimizing concentration polarization should be addressed at high priority. For more advanced and precise separations that make use of transport-based selectivity (i.e., selective transport of a specific solute through recognition sites in the membrane), a more holistic approach should be taken to achieve ultrahigh selectivities that exceed by at least one order of magnitude the existing selectivity data. This approach requires the fabrication of a new class of NF membranes comprising multiple pathways for each type of species in the solution.

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## Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

## Author contributions

RE—Conceptualization, Formal analysis, Resources, Funding acquisition, Writing—Review and Editing, Visualization.

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## Conflict of interest

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