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# Nanofluidic membranes: Discover a new avenue in membrane-based processes — A comprehensive review

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ABSTRACT

Nanofluidic membranes, featuring angstrom-to-nanometer transport pathways where interfacial effects dominate, have rapidly evolved into a versatile platform for selective ion transport, energy conversion, sensing, and advanced separations. This review consolidates two decades of progress by (i) summarizing the governing electrokinetic mechanisms in confined nanochannels (e.g., electric double-layer regulation, ion selectivity, and ionic current rectification), (ii) providing a multidimensional classification of nanofluidic membranes based on channel dimensionality, constituent materials, structural origin, and channel-wall properties, and (iii) critically comparing key fabrication strategies alongside modeling and simulation approaches used to rationalize transport and guide design. We further highlight persistent barriers to practical implementation, including scalable manufacturing of well-defined nanochannels, stability and fouling resistance under realistic conditions, and the need for standardized performance metrics and predictive structure–property relationships. By linking mechanism, architecture, and fabrication to performance and limitations, this review offers an integrated framework and actionable perspectives to accelerate the translation of nanofluidic membranes from model systems to robust membrane-based technologies.

## 1. Introduction

Membranes are physical structures that facilitate mass transfer in a specific direction, forming the foundation of separation processes. These processes are driven by gradients in electric potential, concentration, temperature, or pressure. Membrane-based separation has gained widespread attention in areas such as energy production, water and wastewater treatment, and chemical analysis. Key applications in this domain include energy harvesting [1,2], water desalination [3–5], gas separation [6,7], and the synthesis of chemical species [8]. The performance of membrane separation systems depends on achieving an optimal balance between selectivity and permeability while maintaining robustness under operational conditions, including chemical, thermal, and mechanical stresses. Despite significant advancements in membrane science, critical challenges remain to be addressed before these technologies can be economically viable and widely adopted in industrial applications. For instance, overcoming the fouling of membrane, as well as the inherent tradeoff between membrane selectivity and permeability is essential, as is ensuring durability under harsh operating environments [9,10].

Traditional polymeric membranes, although successful in numerous applications, face limitations in ion transport due to their tortuous internal structures, which hinder performance in energy conversion and

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*Abbreviations:* AAO, Anodic aluminum oxide; BN, Boron nitride; BNNT, Boron nitride nanotubes; CNT, Carbon nanotube; CVD, Chemical vapor deposition; COF, Covalent organic framework; DNA, Deoxyribonucleic Acid; EDL, Electrical double layer; EBL, Electron beam lithography; GO, Graphene oxide; IBL, Ion beam lithography; ICR, Ion current rectification; LBL, Layer by layer; MOF, Metal organic framework; MD, Molecular Dynamics; NIL, Nanoimprint lithography; PDMS, Polydimethylsiloxane; PEL, Polyelectrolyte; PMMA, Polymethyl methacrylate; RIE, Reactive-Ion Etching; rGO, Reduced graphene oxide; RFB, Redox flow batteries; RNA, Ribonucleic acid; SMAIS, Surfactant monolayer-assisted interfacial synthesis; UV, Ultraviolet.

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## Nomenclature

*Latin symbols*

| | |
|---|---|
| Bo | Bond number [−] |
| Ca | Capillary number [−] |
| C | Concentration [M] |
| d | Channel Length/ diameter [m] |
| D | Diffusion coefficient [$m^2/s$] |
| $e$ | Elementary charge [C] |
| F | Faraday constant [C/mol] |
| $Fr$ | Froude number [−] |
| g | Gravitational acceleration [$m/s^2$] |
| $G_d$ | Gibbs free energy of ion dehydration [J] |
| G | Conductivity in nanochannel [S/m] |
| h | Nanochannel height [m] |
| $I_c$ | Ionic power [$mol/m^3$] |
| $k_B$ | Boltzmann constant [J/K] |
| k | Debye length-dependent decay constant [1/m] |
| L | Characteristic length [m] |
| $N_A$ | Avogadro's number [−] |
| $n_v$ | Number of oxygen vacancies [−] |
| P | Hydrodynamic pressure [Pa] |
| $Pe$ | Péclet number [−] |
| $q_{edge}$ | Electrical charge at edge of the channel [C] |
| $q_{ion}$ | Electrical charge of the hydrated ion [C] |
| $Re$ | Reynolds number [−] |
| $r_{ion-edge}$ | Distance between hydrated ion and channel edge [m] |
| R | Universal gas constant [J/mol.K] |
| $T_g$ | Glass transition temperature [K] |
| T | Temperature [K] |
| u | Hydrodynamic velocity of the fluid [m/s] |
| V | Fluid velocity [m/s] |
| W | Nanochannel width [m] |
| We | Weber number [−] |
| $z_i$ | Valence of ionic components [−] |

*Greek symbols*

| | |
|---|---|
| $\gamma_{bulk}$ | Conductivity of solution at 20 °C [S/m] |
| $\delta$ | Membrane thickness [m] |
| $\varepsilon$ | Dielectric constant [F/m] |
| $\lambda_D$ | Debye length [m] |
| $\mu$ | Dynamic viscosity of the fluid [Pa.s] |
| $\mu_i$ | Ion mobility of i component [$m^2/V.s$] |
| $\nu_{eo}$ | Electroosmotic velocity [m/s] |
| $\rho$ | Fluid density [$kg/m^3$] |
| $\rho_E$ | Local charge density [$C/m^3$] |
| $\sigma$ | Surface tension [N/m] / Surface charge density [$C/m^2$] |
| $\varphi$ | Electrical potential [V] |
| $\psi/\phi$ | Electrostatic potential [V] |

desalination processes [11,12]. In contrast, the advent of nanofluidic membranes, with dimensions ranging from a few angstroms to several nanometers and exhibiting high surface charge densities, has demonstrated substantial potential [13–15]. These nanofluidic structures significantly enhance osmotic power density and energy conversion efficiency, marking a promising avenue for advancing membrane technologies [16–19].

In recent decades, advancements in nanofabrication techniques with precise nanometer-scale control have spurred rapid and sustained growth in the study and design of nanodevices for a wide range of applications [20,21]. Current innovations include smart nanochannels mimicking ion gating mechanisms, biological systems, sensors, biosensore, filters, ion pumps, molecular and ion sensing platforms, energy conversion devices [22,23], DNA and RNA sequencing technologies [24,25], and seawater purification systems [26,27]. Ions, as fundamental charge carriers, exhibit distinct properties such as size, mass, and mobility, setting them apart from electrons. In nature, ion transport typically occurs through nanochannels, such as those found in cell membranes and tree fibers [28]. Biological ion channels—specialized membrane proteins in living organisms—are integral to essential life processes, offering sophisticated functionalities such as signaling, mass transport, ion manipulation, and the selective separation of ionic species. These channels have become a cornerstone for technological innovations due to their unique attributes, including ionic selectivity [29], ionic current rectification (ICR) [30,31], and responsiveness to specific molecules or physical stimuli [32]. Notably, their dimensional flexibility, mechanical robustness, and chemical adaptability further underscore their potential. Drawing inspiration from the remarkable properties of biological ion channels and embracing the concept of "learning from nature," researchers have developed solid-state nanochannel-based platforms. These platforms have garnered significant attention for their ability to replicate and enhance the capabilities of

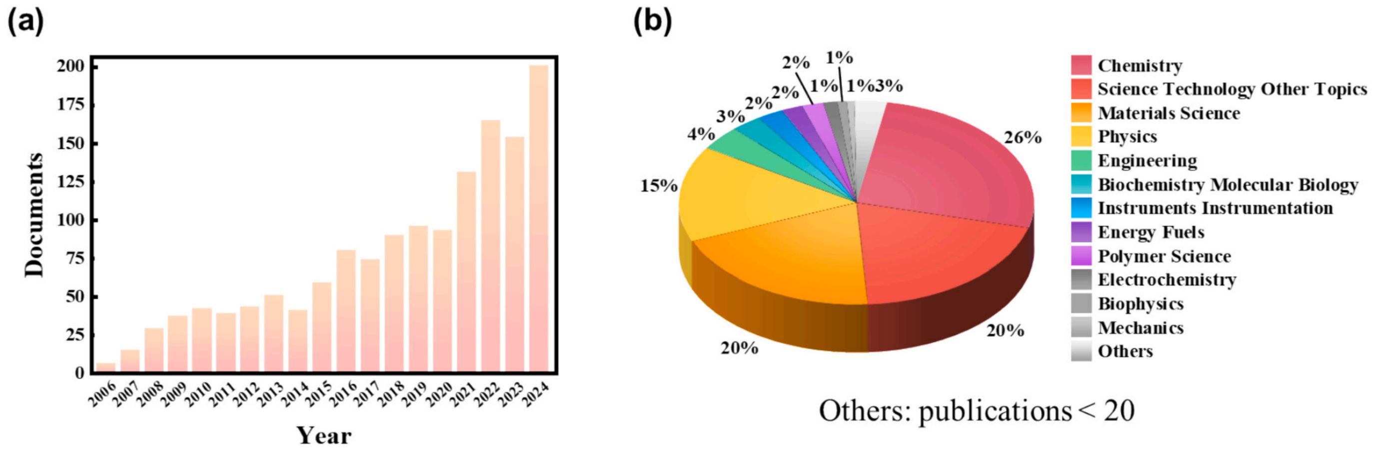


**Fig. 1.** (a) Annual publication trends on nanofluidic membranes, showing growing research activity. (b) Disciplinary distribution of publications (%) underscores the interdisciplinary nature of this field, spanning chemical engineering, biochemistry, energy, and materials science. The data was analyzed from the database of Web of Science.

their biological counterparts [33].

As illustrated in Fig. 1a, the number of publications in this field has increased dramatically in recent years, reflecting the growing interest and focus of the scientific community on nanofluidic membranes. Furthermore, Fig. 1b shows the distribution of these publications across various scientific disciplines, underscoring the broad applications of nanofluidic membranes in areas such as chemical engineering, biochemistry, energy, and materials science. This thematic diversity highlights the critical role of interdisciplinary research in driving innovation and expanding the applications of these advanced membrane technologies.

In the realm of energy conversion, ion-exchange-based systems offer several advantages over electron-exchange systems. These systems are characterized by their safety, reliability, and simplified energy conversion processes, leveraging abundant resources. Furthermore, ion-exchange-based energy harvesting technologies address critical limitations of traditional systems, such as low energy efficiency and poor power density [34]. Ion-exchange membranes have been a focal point of research due to their widespread availability, large surface area, and high ion selectivity. However, these membranes are not without limitations. For instance, their pore dimensions, typically on the scale of several hundred micrometers, are only marginally larger than ionic species, which introduces steric hindrances and high electrical resistance [35]. These factors significantly impede ion transport, leading to reduced ion current flow. Additionally, charge polarization at the membrane-solution interface weakens ion transport efficiency, thereby limiting the energy conversion capability [36]. The small pore sizes of ion-exchange membranes also make them susceptible to fouling caused by either of heavy metals, bio-contaminants, and large organic molecules in practical applications [37].

Nanofluidic membranes, with pore sizes in the range of few to tens of nanometers, offer a promising solution to these challenges [38]. These channels facilitate efficient ion transport while mitigating issues such as charge polarization and contamination. Recent advancements in nanoscale fabrication technologies have broadened the scope of nanofluidic applications across various scientific and technological domains, enabling the development of diverse products. One exciting avenue of research involves the biochemical tuning of artificial nanochannels to create smart systems capable of responding to external stimuli such as pH, temperature, and electric fields [39,40]. This functionality can be achieved through internal or external surface modification techniques, paving the way for highly adaptive and responsive systems [41].

With the rapid expansion of research in nanofluidic membranes and their broad applicability in energy production, purification, and biosensing technologies, the need for a comprehensive and systematic review has become increasingly apparent. While many studies have been conducted, they often focus on specific aspects such as transport mechanisms, industrial applications, or particular types of nanofluidic membranes [20,34,42–47]. This review aims to bridge this gap by providing an extensive analysis of all critical facets of nanofluidic membranes, including their classification, fabrication methods, advanced applications, and the challenges facing their development and implementation.

## 2. Nanofluidic systems

Nanofluidics is a field of research that explores the behavior of fluids, particularly ionic fluids, within nanochannels [48]. It encompasses the study and application of fluid flow and mass transfer in confined spaces at nanometer scales, where intermolecular forces—such as short-range steric and hydration interactions and long-range van der Waals and electrostatic forces—dominate. These forces give rise to unique and often counterintuitive phenomena, including ultrafast liquid flow and anomalous ion transport behaviors [49].

Nanofluidics has emerged as an interdisciplinary field with applications spanning biology, chemistry, physics, and engineering. Over the past two decades, it has attracted significant research attention due to its potential to revolutionize technologies such as energy conversion, biosensing, and molecular separation [50–54]. A pivotal moment in the field occurred in 1998 when McKinnon elucidated the structure of the potassium channel and its molecular mechanisms of ion conductance and selectivity [55]. This groundbreaking work, which earned McKinnon the 2003 Nobel Prize in Chemistry, laid the foundation for biomimetic or nature-inspired nanofluidics—a subfield focused on replicating and adapting the principles of natural ion channels in synthetic systems.

Understanding the transport and structural properties of confined nanofluids necessitates the fabrication of precise porous nanostructures [56–59]. Recent advancements in nanotechnology, biotechnology, and supramolecular chemistry have enabled the development of materials and devices at scales as small as individual molecules. Nanofluidic technologies possess unique functional attributes that distinguish them from their microfluidic counterparts [60]. Key characteristics include the partial overlap of the electric double layer (EDL) within nanochannels [61,62], an increase in fluid viscosity at the nanoscale, and a reduction in the dielectric constant. These properties exhibit significant deviations when transitioning from the micrometer to the nanometer scale, making nanofluidics an indispensable area of research for exploring and exploiting nanoscale phenomena [63].

Over the past four decades, nanoscale science and technology, collectively referred to as nanotechnology, has enabled the manipulation of matter at the atomic level and facilitated the exploration of material properties at the nanoscale. One of the most significant advancements in this field is the discovery and fabrication of nanopores and nanochannels—structural features comprising confined void spaces within solid matrices. These nanostructures enable the selective transport of small molecules at subnanometer scales and have become essential in numerous applications [64]. Structurally, a nanopore is defined as a pore with a diameter of up to 100 nm, where the pore diameter exceeds its depth (length). In contrast, when the depth of a pore is significantly larger than its diameter, the structure is typically referred to as a nanochannel. Nanochannels, often regarded as the most prominent type of nanomaterials, are hollow nanostructures with at least one dimension ranging from 0.1 to 100 nm. Their distinctive geometry and properties make them invaluable across a wide range of fields [65].

Artificial nanopores and nanochannels have demonstrated tremendous potential in applications such as water desalination, ion filtration, hazardous gas separation, and environmental pollutant purification [66–69]. Compared to other nanostructures, nanochannels offer advantages such as a high surface-to-volume ratio, low density, exceptional permeability, and high adsorption capacity [70–74]. Their flexibility in shape and size, robustness, and modifiable surface properties further enhance their suitability for various applications, including biological systems [75,76].

One critical feature of nanochannels is the relationship between their dimensions and the Debye length—the characteristic length scale over which surface charge interactions occur [17,77]. In nanochannels, the Debye length is comparable to the channel dimensions, allowing the surface charge of the channel walls to interact strongly with charged species, such as ions, proteins, or DNA, within the confined fluid. As a result, surface charge effects become a dominant factor in the behavior of these systems [62,63,78]. To enable their diverse functionalities, nanochannel systems are driven by one or more external gradients, including pressure, concentration, temperature, or electric potential. By varying these driving forces, researchers can achieve precise control over ionic transport, unlocking a broad spectrum of functionalities that underpin advances in scientific research and engineering applications [79,80].

Nanofluidic membranes are advanced structures with pore dimensions as small as one nanometer or even below [17,18], designed to enable efficient transport of ions and water molecules [81–83]. Unlike conventional membranes, which are typically fabricated using experimental approaches without molecular-scale precision, nanofluidic membranes leverage precise design principles at the nanoscale. This precision enables the tailoring of structural and surface properties to optimize ion or water molecule permeability, making them highly versatile for various applications [84].

Significant efforts have been dedicated to the design and fabrication of nanofluidic membranes and nanochannels, driven by their unique capabilities. These membranes are increasingly recognized as a superior alternative to traditional ion exchange membranes. Their distinct selectivity mechanism is based on charged nanochannels rather than the functional groups on polymer backbones, as is the case with conventional membranes. This innovation provides highly efficient ion conduction pathways while offering greater control over transport processes [85]. Fig. 2 illustrates a schematic representation of a nanofluidic membrane featuring cylindrical nanopores or nanochannels (e.g., anodic aluminum oxide (AAO) [86,87] or two-dimensional (2D) covalent-organic framework (COF) memrbane [88,89]). As an example, the walls of these nanochannels possess a negative surface charge, in this instance, which plays a critical role in selective ion transport by interacting with the ionic species within the fluid.

## 3. Historical background

Over the past 50 years, fluid flows at the nanometer scale have been studied indirectly across various disciplines. However, nanofluidics only emerged as a distinct scientific field approximately 15 years ago, evolving naturally as a smaller-scale extension of microfluidics. Initially, a significant challenge was to establish nanofluidics as a standalone field by demonstrating the existence of unique nanoscale phenomena absent at the microscale. Until about a decade ago, progress in this area was constrained by technical limitations, such as the inability to fabricate molecular-scale channels artificially [90].

Today, nanofluidics has matured into a well-established scientific field, thanks to advancements in fabrication technologies. Researchers can now construct artificial nanostructures with dimensions as small as a single water molecule (~3 Å) [91]. The journey to this milestone has been marked by key discoveries and innovations [92–95]:

I. In 1939, René Dubos isolated bacterial gramicidin, a natural antibiotic and nanochannel. The nicotinic acetylcholine receptor ion channel was also the first natural ion channel to be isolated.
II. In 1996, α-hemolysin was incorporated into a lipid bilayer, pioneering the practical application of nanochannels for DNA sequencing.
III. That same year, Chou et al. developed nanoimprint lithography, providing a new technique for nanostructure fabrication.
IV. In 1997, Stern et al. fabricated 50 *nm* high nanochannels by etching amorphous silicon layers, demonstrating early advancements in controlled nanochannel synthesis.
V. Goluchenko et al. reported the creation of tunable nanopores in $SiO_2$ and SiN with minimum dimensions of 1.8 *nm* in 2001, further advancing nanofabrication techniques.
VI. The Dekker group at Delft University showcased the patterning of 20 *nm* diameter holes in Si, $SiO_2$, and SiN using electron beam lithography.

Theoretical developments also played a pivotal role. In 2008, Xu et al. [95] proposed a mathematical model for eel electrification based on electrogenic cell models containing nanoscale ion channels and pumps, emphasizing the biomimetic potential of nanofluidic systems. The 2010s saw an increased focus on replicating biological transport functions, often described as one-dimensional nanofluidics due to the constrained, linear flow dynamics characteristic of these systems. Experimentally, smart nanochannels have been developed by combining bioinspired nanostructures with advanced material chemistries. These channels exhibit highly controlled ion transport dynamics, enabling their application in fields such as biochemical sensing, energy conversion, and neuromorphic computing [96]. For example, glass-based nanochannels continue to evolve, with increasing potential for simulating neural functions [97–100]. Fig. 3 illustrates the timeline of key milestones in the development of nanochannels and nanopores, highlighting the rapid advancements in this field over recent decades.

## 4. Electrokinetic principles and transport mechanisms in nanochannels

Due to their nanoscale dimensions and exceptionally high surface-to-volume ratio, nanochannels exhibit unique physical and chemical properties that significantly differ from those of larger systems. At these scales, the interactions between ions and molecules in the fluid and the nanochannel walls become dominant, profoundly influencing system behavior. Key effects include the formation of EDLs, which define the charge distribution near the channel walls, and the Debye length, which determines the extent of electrostatic interactions within the channel. These factors govern the type of ionic current that prevails in the

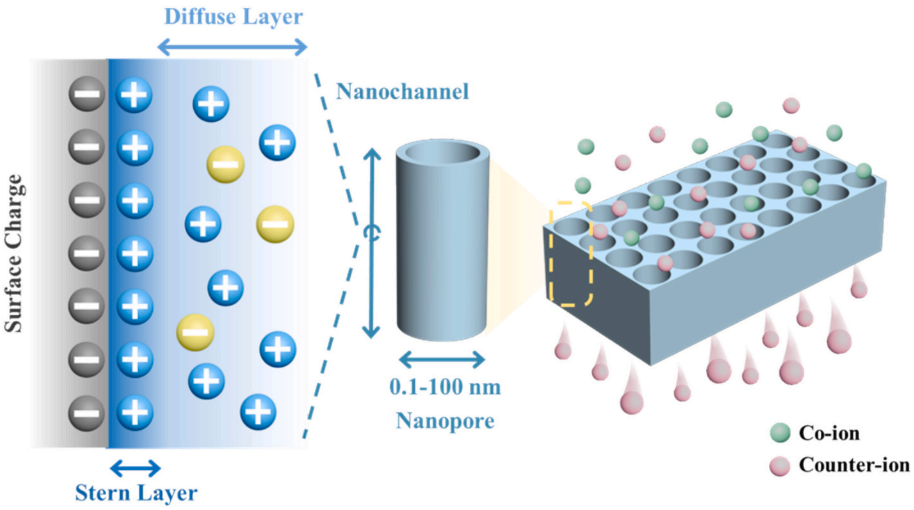


**Fig. 2.** Schematic representation of a nanofluidic membrane featuring cylindrical nanopores/channels with negatively charged surfaces.

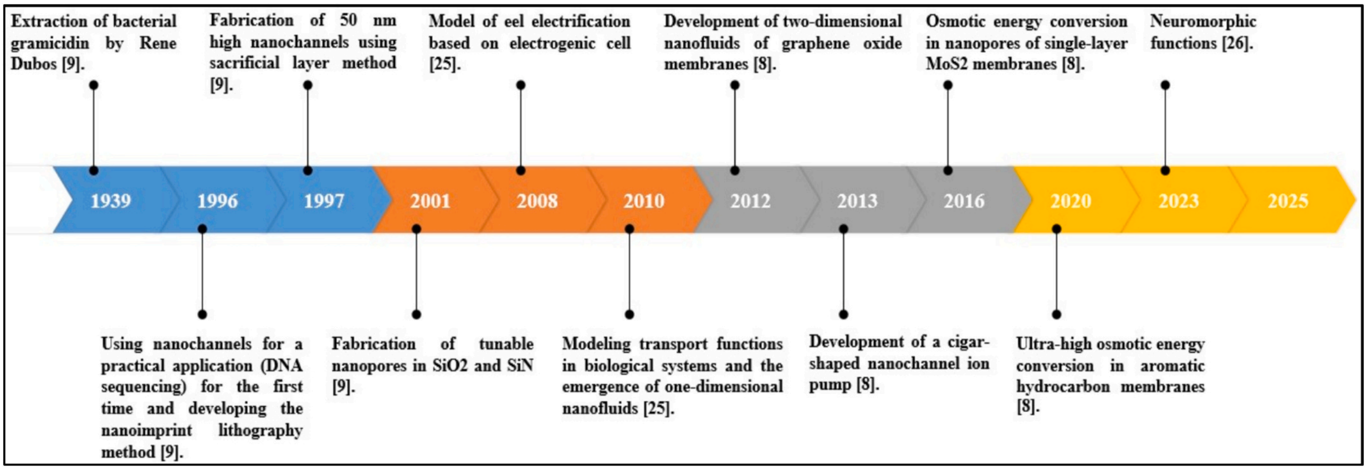


**Fig. 3.** Timeline showcasing the significant milestones in the development and advancement of nanochannels and nanopores, illustrating the progression of fabrication techniques and applications from their initial discovery to their current technological innovations.

nanochannels and give rise to electrokinetic phenomena such as electrophoresis, electroosmosis, and streaming potentials [101]. Understanding these nanoscale effects is crucial for accurately predicting and optimizing transport processes in nanochannels, enabling their effective application in fields such as energy conversion, biosensing, and filtration.

### *4.1. Electric double layer and Debye length*

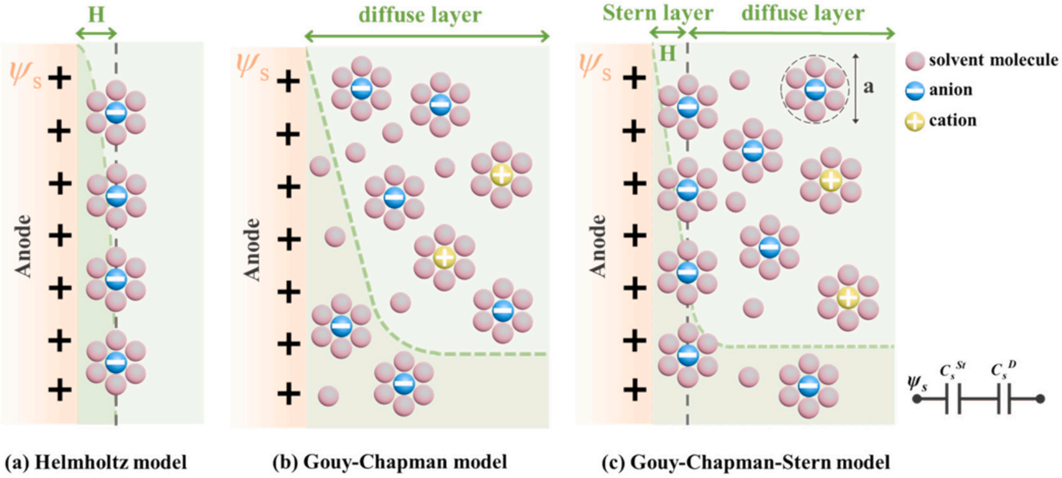
The electric double layer at the solid-solution interface plays a pivotal role in various applications, including electrochemistry, energy conversion, desalination, and separation processes. The EDL refers to the heterogeneous distribution of dissolved ions near a solid surface, arising from the interplay between electrostatic forces and ion mobility. This non-uniform ion distribution forms the structural foundation of the EDL and governs key interfacial phenomena. At an electrode, the EDL is characterized by the enrichment of counterions and the repulsion of co-ions [102]. Fig. 4 illustrates the structural evolution of EDL models adjacent to a positively charged electrode. Helmholtz initially proposed that a compact layer of oppositely charged ions forms at the interface between the electrode and the electrolyte, separated by a fixed, small distance (H), as shown in part (a) of Fig. 4. In the early 20th century, the Helmholtz model was refined by Gouy (1910) and Chapman (1913) to account for the mobility of ions within the electrolyte. They proposed that counterions form a diffuse layer, extending beyond the compact layer and characterized by a thickness significantly larger than H. This region, termed the diffusion layer, is depicted in part (b) of Fig. 4 [103].

In 1924, Stern further advanced the EDL theory by integrating the Helmholtz and Gouy-Chapman models. His model delineates two distinct regions: the Stern layer, a compact region near the electrode where ions are tightly bound, and the diffusion layer, where ions are more loosely distributed. This combined model, shown in part (c) of Fig. 4, provides a more comprehensive understanding of the electric double layer and its structural dynamics [104].

The electrostatic attraction within the diffusion layer is weaker than that in the Stern layer; as a result, ions in the diffusion layer are not fixed but remain mobile, influenced by both electrostatic forces and thermal motion. Unlike the bulk solution, the EDL exhibits a non-zero net charge density due to the imbalance of ions near the interface. The EDL is characterized by a finite thickness, commonly described in terms of the Debye length, which quantifies the extent of charge screening within the electrolyte. The Debye length ($\lambda_D$) can be calculated using Eq. 1 [9]:

$$\lambda_D = \sqrt{\frac{\varepsilon RT}{2F^2 I_c}} \tag{1}$$

where $\varepsilon$, $R$, $T$, $F$, and $I_c$ represent the permittivity of the medium, the



(a) Helmholtz model (b) Gouy-Chapman model (c) Gouy-Chapman-Stern model

**Fig. 4.** Schematic representation of EDL models. (a) The Helmholtz model, illustrating a compact layer of counterions adjacent to the electrode. (b) The Gouy-Chapman model, highlighting the diffuse layer of counterions extending beyond the compact region. (c) The Stern model, combining the Helmholtz and Gouy-Chapman frameworks, delineating both the Stern layer and the diffusion layer [104].

universal gas constant, absolute temperature, Faraday constant, and ionic strength of the solution, respectively. For a given solvent, $I_c$ is determined by the solvent concentration, making the Debye length a fixed parameter under these conditions. When $\lambda_D$ is constant, reducing the channel dimensions becomes advantageous as it enhances the overlap of the diffusion layers within the EDL [105]. High ionic selectivity can be achieved when the channel height $(d)$ or pore diameter $(D)$ approaches or falls below twice the Debye length, i.e., $d \leq 2\lambda_D$ or $D \leq 2\lambda_D$. The Debye length typically ranges from 0.3 to 50 $nm$, depending on the ionic strength of the solution. As the electrolyte concentration increases, the ionic strength also increases, leading to a reduction in $\lambda_D$. This relationship highlights that higher salt concentrations result in thinner EDLs, a critical factor in nanofluidic applications where precise control over ionic transport is essential [106].

### 4.2. *Types of flow and influencing forces*

To determine the flow characteristics within channels, the dimensionless Reynolds number (Re) is employed, representing the ratio of inertial forces to viscous forces. This parameter highlights that flows in micro- and nanofluidic systems are predominantly laminar due to their low *Re* values. In nanofluidics, where channel dimensions are typically less than 1 $\mu$m, intermolecular forces such as electrostatic interactions, van der Waals attractions, hydrogen bonding, and steric repulsion become significant and cannot be neglected. Additionally, since the channel dimensions are often comparable to or smaller than the Debye length, the electric field arising from charged surfaces significantly influences ionic motion within nanochannels. These unique interactions render nanofluidic transport inherently complex, involving a combination of various intermolecular forces [107].

Unlike macroscopic fluid systems, where mixing is predominantly driven by turbulence, mixing at the microscale primarily relies on molecular diffusion, which can be unacceptably slow. In microscale systems, convection is nearly absent, diminishing its role in momentum or mass transport. In contrast, diffusion plays a critical role in determining the performance of such systems. Conversely, macroscopic fluid systems are dominated by convection, with diffusion effects typically negligible [108]. Surface effects, which are often minor in macroscale systems, become critically important in micro- and nano-scale systems due to their high surface-to-volume ratios. Similarly, gravity—an essential factor in macroscopic fluid dynamics—is generally negligible in micro- and nano-fluidic systems, except for considerations like gravitational pressure drops in storage tanks. Surface tension, another force of significant importance in microfluidics, is rarely a factor in macroscopic systems [109]. To better understand the relative importance of various forces in micro- and nano-scale systems, dimensionless numbers representing these forces are summarized in Table 1. This comparative framework helps illustrate the transition in dominant forces as systems scale down from macroscale to nanoscale.

**Table 1**
Summarizing key dimensionless numbers used in the analysis of micro/nanofluidic systems.

| Effective forces | Equation | Number |
|---|---|---|
| $\frac{\text{Gravitational forces}}{\text{Surface Tension}}$ | $Bo = \frac{\rho g L^2}{\sigma}$ | Bond |
| $\frac{\text{Viscous Forces}}{\text{Surface Tension}}$ | $Ca = \frac{\mu V}{\sigma}$ | Capillary |
| $\frac{\text{Reaction Rate}}{\text{Diffusion Transport}}$ | $Da = \frac{KL}{V}$ | Damköhler |
| $\frac{\text{Inertial Forces}}{\text{Gravitational forces}}$ | $Fr = \frac{V^2}{gL}$ | Froude |
| $\frac{\text{Mean Free Path of Molecules}}{\text{Characteristic Length}}$ | $Kn = \frac{\lambda}{L}$ | Knudsen |
| $\frac{\text{Convection Transport}}{\text{Diffusion Transport}}$ | $Pe = \frac{VL}{DL}$ | Péclet |
| $\frac{\text{Inertial Forces}}{\text{Viscous Forces}}$ | $Re = \frac{\rho VL}{\mu}$ | Reynolds |
| $\frac{\text{Viscous Forces}}{\text{Diffusion Transport}}$ | $Ca = \frac{\mu}{\rho D}$ | Schmidt |
| $\frac{\text{Inertial Forces}}{\text{Surface Tension}}$ | $We = \frac{\rho V^2 L}{\sigma}$ | Weber |

### 4.3. *Distinctive behaviors in nanochannels*

At the nanoscale, the high surface-to-volume ratio significantly amplifies fluid-channel interactions, making them a dominant factor in governing fluid transport phenomena. Within these confined dimensions, several unique and intriguing behaviors emerge, including hydrodynamic slip boundary conditions, diffusion-limited reactions, EDL overlap, surface charge-mediated ion transport, and molecular transport. These phenomena have profound implications across various scientific and engineering disciplines, enabling groundbreaking applications in areas such as molecular separation, water desalination, energy conversion, and biosensing [110]. One of the most notable features of nanoscale fluid transport is the hydrodynamic slip boundary condition, which has been a focal point of extensive research in recent decades. Unlike traditional no-slip boundary assumptions, hydrodynamic slip allows fluids to move more freely along the channel walls, reducing drag and enhancing flow efficiency [84,90,111]. Materials such as carbon nanotubes and graphene have demonstrated exceptional slip properties, significantly minimizing frictional resistance and boosting flow velocities [20,112,113].

In addition to hydrodynamic slip, nanochannels exhibit other remarkable phenomena, including ion selectivity, where specific ions are preferentially transported through the channel; diffusion osmosis, which leverages concentration gradients for fluid movement; and ICR, a diode-like behavior enabling directional ion transport [63,114–116]. These effects are intrinsically tied to the interplay of nanoscale dimensions, surface charge densities, and external driving forces, providing a versatile platform for innovation in nanoscale fluidic systems [117].

#### 4.3.1. *Ionic selectivity*

Ion selectivity refers to the capacity of a nanometer-scale channel to preferentially transport certain ions while effectively excluding others [66]. This property arises from the interplay between the channel's charged walls and the ions in solution. When a channel wall carries a surface charge, electrostatic interactions repel co-ions and attract counter-ions. In nanochannels with dimensions comparable to the Debye length, the EDLs from opposing walls overlap, saturating the channel with counterions. This overlap creates a selective environment that facilitates the transport of specific ions while impeding others, resulting in pronounced ion selectivity. The mechanism of ion selectivity enables energy harvesting in nanofluidic systems through two primary processes:

I. Streaming Current Generation (Fig. 5a): When an ionic solution is driven by an external mechanical force, such as pressure, through charged nanofluidic channels, the hydraulic flow mobilizes the counterions within the EDL. This movement generates a streaming current proportional to the velocity of the net charge transport, enabling the conversion of mechanical energy into electrical energy [118–120].
II. Diffusion Current Generation (Fig. 5b): Under a concentration gradient across the nanochannel, a spontaneous separation of cations and anions occurs within the EDL. This separation drives a diffusion current, where ions selectively move along the overlapping nanochannels of the EDL. Remarkably, this process does not require external mechanical forces or applied voltages, relying solely on the inherent concentration gradient for energy conversion. These ion-selective mechanisms form the foundation for advanced energy conversion technologies, leveraging nanoscale phenomena for

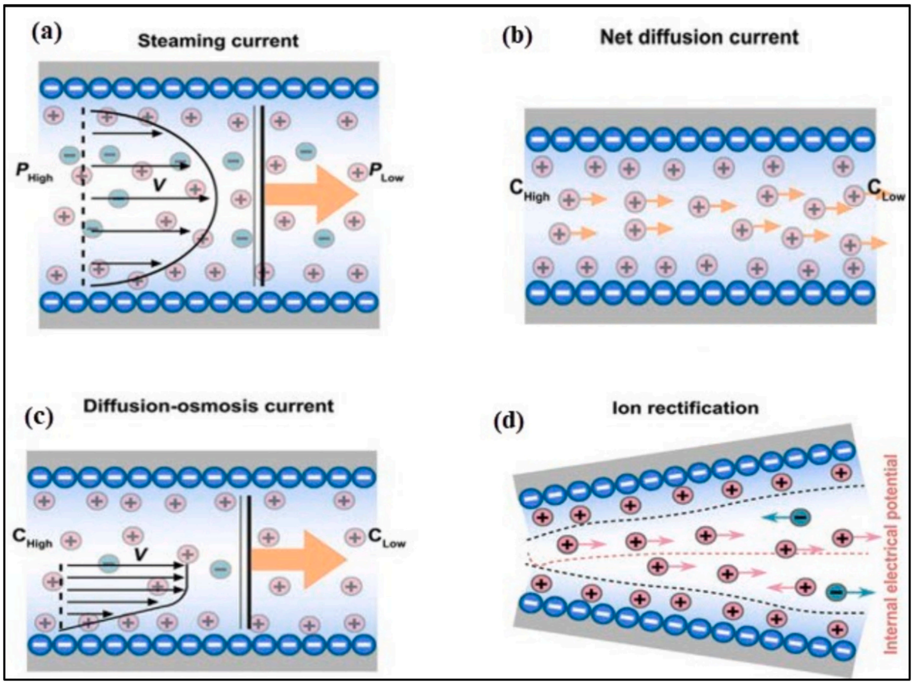


**Fig. 5.** A schematic illustration of specific electrokinetic phenomena in nanochannels, (a) streaming current, (b) net diffusion current, (c) osmotic diffusion, and (d) ionic current rectification [20].

applications in sustainable power generation and energy storage [73,121–123].

### 4.3.2. *Diffusion osmosis transport*

Diffusion osmosis transport (illustrated in slide (c) of Fig. 5), originally introduced by Dergague in the 1940s, represents a hybrid process that combines diffusion and osmosis. This phenomenon occurs due to the establishment of an osmotic pressure gradient across the diffusion layer at the interface, driven by a difference in salt concentration. The gradient causes fluid flow and ion transport, even in the absence of complete ion selectivity. A significant advantage of osmotic permeation is its reduced dependence on stringent ion selectivity for electric current generation. Unlike mechanisms that rely heavily on precise ion filtering, osmotic diffusion allows for the utilization of membranes with larger pores. This flexibility offers two critical benefits [124–126]:

I. Reduced Resistance: Larger pores decrease hydraulic and ionic resistance, facilitating smoother ion transport.
II. Increased Ion Flux: The allowance for larger pore dimensions enhances ion throughput, improving the efficiency of the transport process.

Interestingly, diffusion osmosis transport flow is achievable even in membranes without high ion selectivity due to the interactions between ions and the membrane surface. This interaction-driven transport mechanism broadens the range of applicable materials and designs for osmotic energy harvesting, making it a promising approach for diverse applications in desalination, energy generation, and separation technologies [33,127–132].

### 4.3.3. *Ionic current rectification*

ICR is a prominent electrokinetic phenomenon that governs ion transport in artificial nanochannels. Understanding this behavior is crucial for elucidating the physical mechanisms underlying ionic processes and advancing nanofluidic device technologies. Over the past two decades, ICR has been extensively studied and has emerged as a cornerstone in the design of nanodevices for energy conversion, sensing, and filtration applications [133–138].

ICR refers to the deviation of the current-voltage (I-V) curve from ohmic behavior in nanofluidic systems. This deviation manifests as diode-like behavior, where the ionic current at a votage differs significantly from that at an opposite voltage. The phenomenon is particularly pronounced in asymmetric nanochannels, such as conical or funnel-shaped channels [139,140], where geometric and charge asymmetries induce selective ion transport at different voltage polarities. ICR primarily arises when the characteristic dimensions of the channel, such as its diameter, are smaller than the Debye length, leading to significant interactions between the EDL and the ionic fluid [141].

The rectification effect can be attributed to the asymmetric distribution of ions within the channel in response to different bias polarities. When a potential bias is applied, ions either accumulate or deplete at specific regions of the channel, depending on its polarity (illustrated in slide (d) of Fig. 5). This asymmetry in ion distribution results in nonlinear I-V characteristics. The extent of ICR depends on several factors [142–144]:

I. Channel Geometry: Asymmetric geometries, such as conical or funnel-shaped channels, enhance rectification by creating directional preferences for ion flow.
II. Surface Charge Distribution: A non-uniform surface charge density amplifies rectification, particularly when combined with geometric asymmetry.
III. Environmental Conditions: Ionic strength, pH, and temperature of the solution significantly influence rectification by altering the properties of the EDL and ion mobility.
IV. Electric Potential and Concentration Gradients: The magnitude and direction of the applied bias affect ion accumulation and depletion patterns, directly impacting ICR [145].

Ramirez et al. [146] explored the influence of nanochannel geometry on ionic current rectification and selectivity in rigid nanochannels. Their study demonstrated that morphological variations significantly affect rectification behavior, revealing a fascinating correlation between channel shape and ion transport properties. Similarly, Tseng et al. [147]

examined the impact of taper angles in tapered nanopores and uncovered their role in modulating current rectification and ion selectivity. These findings emphasize the critical interplay between geometric factors and transport behavior, underscoring geometry as a key determinant in the design and optimization of nanofluidic systems [148,149].

## 5. Classification of nanofluidic membranes

Nanofluidic membranes, featuring ultrafast selective transport channels at molecular and ionic scales, serve as essential tools for efficient separation, catalysis, ion distillation, and energy storage and conversion. Their classification provides a structured understanding of this emerging technology and its diverse industrial applications [150]. In this section, nanofluidic membranes are categorized based on several criteria, including channel dimensions, material composition, membrane type, channel wall properties, and channel geometry. This multidimensional classification not only highlights the unique structural and functional characteristics of each category but also identifies their optimal applications across various fields, paving the way for tailored solutions in advanced technologies.

### *5.1. Classification by nanochannel dimensions*

Nanofluidic membranes can be classified into four categories based on the channel dimensions: zero-dimensional, one-dimensional, two-dimensional, and three-dimensional porous membranes. Each category represents a distinct structural configuration, with variations in channel geometry that influence their transport properties and potential applications [40,151]. A schematic illustrating these structural categories is shown in Fig. 6.

### *5.1.1. Zero-dimensional nanofluidic membranes*

Short nanochannels with lengths less than 1 nm and diameters comparable to their longitudinal dimensions are referred to as zero-dimensional (0D) nanopores. These nanopores are integral components of zero-dimensional membranes, which often utilize solid-state nanopores embedded in thin films, such as single-layer graphene [152], $MoS_2$ [153] and hexagonal boron nitride (hBN) [154]. Zero-dimensional membranes have a significant advantage in terms of high conductivity, attributed to their ultra-thin film thickness [155]. This structural configuration allows for the formation of atomically thin pores, making them highly effective for applications in gas, solute, and ion separation. Their atomic-scale dimensions enable precise selectivity and ultrafast transport, critical for advanced separation technologies. Historically, research on zero-dimensional membranes began with solid-state nanopores fabricated in ceramic materials such as silicon nitride (SiN) or silicon carbide (SiC) [156]. These membranes were created by drilling nanopores through the ceramic structure. However, the advent of two-dimensional (2D) materials has significantly expanded the potential of 0D membranes. Materials like graphene, boron nitride, and $MoS_2$ have opened new avenues for the design of atomically thin nanopores, offering superior performance in separation and filtration processes due to their exceptional mechanical strength, chemical stability, and selective transport properties [153].

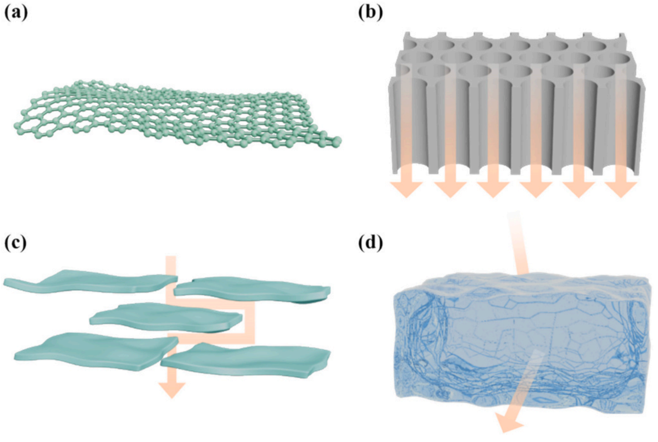


**Fig. 6.** Schematics of (a) zero-dimensional, (b) one-dimensional, (c) two-dimensional, and (d) three-dimensional nanofluidic membranes [33,49].

### *5.1.2. One-dimensional nanofluidic membranes*

A one-dimensional (1D) nanochannel is characterized by two dimensions on the nanometer scale, with a diameter significantly smaller than its length, enabling selective transport along its longitudinal axis. Typical examples include biological ion channels [157], synthetic nanotubes such as carbon nanotubes (CNTs) [158] and boron nitride nanotubes (BNNTs) [27], and ion-track-etched nanopores [159,160]. These channels can adopt various geometrical shapes, including cylindrical, hourglass-shaped, cigar-shaped, bullet-shaped, and conical configurations, each tailored for specific transport characteristics. Cylindrical nanochannels feature a uniform diameter, while hourglass-shaped ones have a constricted midpoint, enhancing selectivity. Cigar-shaped channels taper at both ends for controlled transport, whereas bullet-shaped channels, with a broader inlet and narrower outlet, promote directional transport [161]. Conical nanochannels, widely studied for their asymmetric geometry, exhibit ICR and enable directional ion selectivity. Each of these geometrical configurations offers unique properties and functionalities, as illustrated schematically in Fig. 7, making them versatile for applications in filtration, energy harvesting, biosensing, and separation processes [162]. Because ionic current rectification and selectivity strongly depend on geometrical asymmetry and its coupling with surface charge regulation, we explicitly summarize the most common 1D geometries in Fig. 7 and link them to recent analyses of ICR in asymmetric nanochannels [163,164].

Polymer-based nanofluidic devices with one-dimensional nanochannels hold significant promise for a wide range of applications, including the study of molecular behavior, DNA analysis, and chemical sensing [165]. These devices are particularly valuable for investigating the fundamental principles of ion transport, as they provide simplified nanochannel structures with precise control, facilitating both experimental measurements and theoretical analyses. Despite their potential, the fabrication of 1D nanochannel membranes poses considerable challenges. The process requires complex instrumentation and is often expensive and time-consuming, limiting their scalability and practical implementation in real-world applications. Overcoming these barriers remains a key focus for advancing the use of 1D nanochannels in scientific and industrial domains [166,167].

### *5.1.3. Two-dimensional nanofluidic membranes*

A two-dimensional (2D) nanochannel is characterized by having only one dimension in the nanometer range. Correspondingly, a 2D nanofluidic membrane consists of stacked two-dimensional nanomaterials, which create interconnected 2D channels for ion transport [168–174]. The interlayer gaps between these stacked nanosheets form highly selective nanochannels, typically at nanometer-scale dimensions or smaller. Structurally, 2D materials are defined by their sheet-like morphology, with horizontal dimensions exceeding 100 *nm*, but a thickness of just one or a few atoms. These membranes have gained significant attention due to their dual ion transport capabilities, facilitating both vertical and horizontal ion movement, making them versatile components in nanofluidic devices and on-chip systems (Fig. 8) [175,176]. Recent 2D membrane designs increasingly rely on engineered extrinsic/auxiliary pathways (beyond intrinsic interlayer galleries) to raise permeability while preserving selectivity, enabling stable osmotic-energy operation even under realistic natural waters [177,178].

Two-dimensional nanofluidic membranes are categorized into layered membranes, and ultrathin membranes, based on their thickness

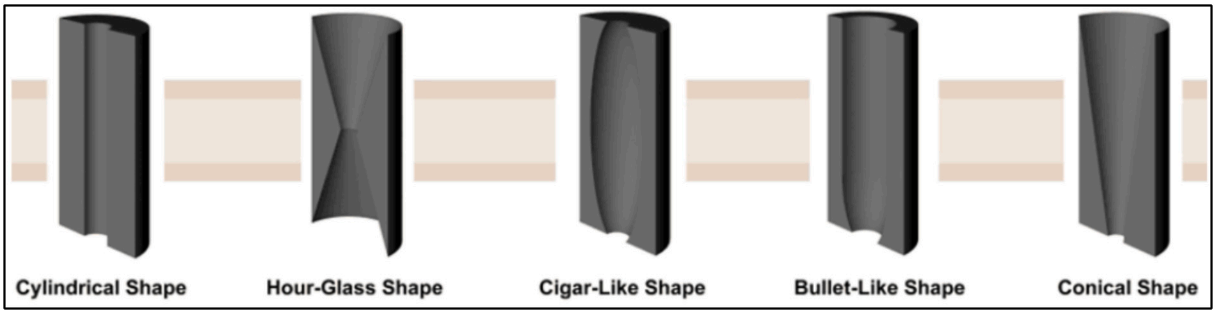


**Fig. 7.** Representative one-dimensional nanochannel geometries used in nanofluidics (e.g., cylindrical, conical, hourglass, bullet/cigarette, funnel-shaped, and other asymmetric profiles). These geometries are central design knobs for tuning electric double-layer overlap, ion selectivity, and ionic current rectification (ICR), and they provide the structural basis for device-level functions such as ionic diodes and nanofluidic transistors [75].

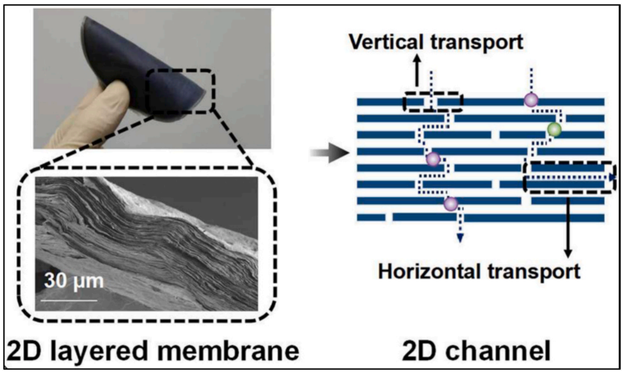


**Fig. 8.** Schematic illustration of ion-transport pathways in two-dimensional (2D) lamellar nanofluidic membranes. The diagram distinguishes (i) in-plane transport along interlayer galleries, (ii) through-plane transport across stacked nanosheets, and (iii) shortcut pathways introduced by edges/defects or engineered extrinsic nanochannels, which can mitigate the classical flux–selectivity trade-off in practical osmotic energy and desalination settings [179].

and structural characteristics [96,180]:

I. Layered Membranes: Constructed from atomically thin 2D nanosheets such as boron nitride, graphene oxide, MXene, $MoS_2$, and clay, these membranes feature nanoscale or smaller interlayer spacings, forming dense nanofluidic channels. Ion transport can occur in both horizontal and vertical directions, offering excellent ion selectivity. The adjustable size and surface chemistry of interlayer channels provide flexibility and enhance functionality [181,182].
II. Ultrathin Membranes: Typically multilayered with thicknesses ranging from a few nanometers to hundreds, ultrathin membranes maintain dense interlayer channels that ensure high ion selectivity. Their reduced thickness minimizes mass transfer resistance, significantly increasing ion flux, making them highly efficient for transport processes [183–185].

High-performance 2D nanofluidic membranes require strong mechanical integrity and environmental stability to resist long-term degradation and structural corrosion. Furthermore, reducing production costs is critical for enabling commercial-scale manufacturing and widespread adoption.

Very recent studies have further demonstrated that two-dimensional materials can exhibit ion transport performance that surpasses conventional nanofluidic systems due to their atomic-scale confinement and intrinsically high surface charge densities. For example, Jiang et al. [186] reported ultrafast and highly selective ion transport through two-dimensional conjugated metal–organic framework–based composite membranes, where angstrom-scale confinement and ordered charge pathways enabled efficient nanofluidic ionic photoelectric conversion. Their results highlight the critical role of atomic-level structural precision and surface charge regulation in accessing non-classical transport regimes. Similarly, Lei et al. [187] demonstrated high-performance solid-state proton gating membranes based on two-dimensional hydrogen-bonded organic framework composites, showing that strong electrostatic interactions coupled with confined hydration structures can yield exceptional proton mobility and selectivity. Collectively, these studies underscore the unique advantages of two-dimensional materials as nanofluidic building blocks and reinforce the central theme of this review: that the synergy between atomic-scale geometry and surface chemistry in 2D materials provides a powerful platform for next-generation nanofluidic membranes with enhanced transport efficiency, selectivity, and functional tunability.

#### 5.1.4. *Three-dimensional nanofluidic membranes*

Three-dimensional (3D) membranes are characterized by their microscale networks with interconnected pores, such as porous-polymer-based [188–190], hydrogel-based [191–194], and metal-organic framework (MOF)-based membranes [82,135,195–197], where ion transport occurs through these interconnected channels and pores. These membranes represent a practical and scalable approach in nanofluidic applications. Due to their flexibility in starting materials and straightforward fabrication processes, 3D porous membranes can be produced on a large scale, making them highly attractive for industrial applications. However, their inherent thickness often leads to increased ion transport resistance, which can significantly reduce permeation flux [169]. Fig. 9 illustrates the classification of nanofluidic membranes based on the dimensionality of their nanochannels, showcasing the structural differences and transport characteristics of zero-dimensional, one-dimensional, two-dimensional, and three-dimensional membranes.

### 5.2. *Classification by constituent materials*

Nanofluidic membranes are primarily fabricated using inorganic or organic materials, with the potential for creating heterogeneous membranes by combining both types. Inorganic membranes and nanotubes, such as those made from ceramics or carbon-based materials, offer exceptional stability and high selectivity, making them suitable for demanding applications [198]. However, these advantages are offset by the challenges associated with their manufacturing processes, which are often complex, and their integration into practical systems, which can be cumbersome. In contrast, organic materials, including polymers, are generally easier to process and integrate but may lack the durability and selectivity of their inorganic counterparts.

#### 5.2.1. *Mineral-based nanofluidic membranes*

The commonly used inorganic materials for nanofluidic membranes primarily belong to four main categories: carbon materials (e.g.,

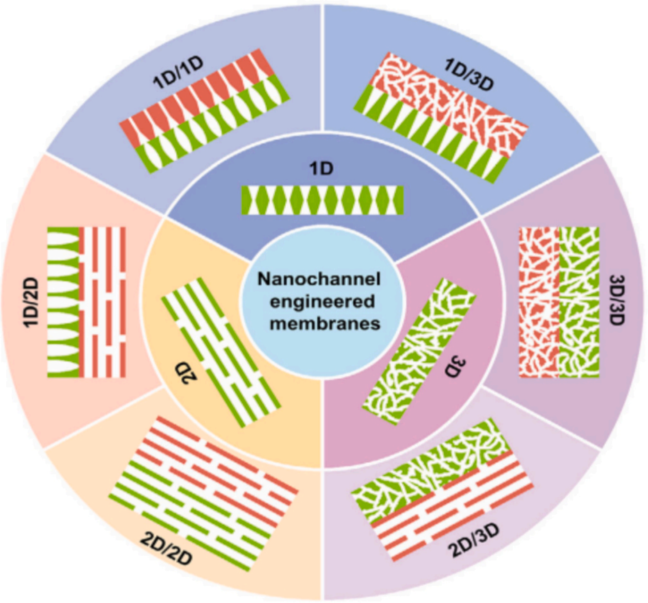


**Fig. 9.** Schematic of nanofluidic membrane by nanochannel dimension [169].

graphene and its derivatives), transition metal dichalcogenides (e.g., $MoS_2$), nitrides (e.g., boron nitride), and transition metal nitrides (e.g., MXene) [44,173,199–203]. Additional materials, such as anodic aluminum oxide (AAO), CNTs, silica ($SiO_2$), and silicon nitride ($Si_3N_4$), are widely employed, particularly in the fabrication of one-dimensional nanochannel membranes [204–207]. Despite their remarkable properties, the high cost and complex production processes of these materials pose challenges for large-scale manufacturing [96]. Below is an overview of some significant inorganic materials:

I. Graphene and Derivatives: Graphene, a renowned two-dimensional carbon nanomaterial, exhibits exceptional properties but lacks functional groups and has poor water solubility, limiting its applications. To address these limitations, graphene derivatives such as graphene oxide (GO) have been developed. GO is produced by oxidizing graphite, introducing epoxy, hydroxyl, and carboxyl groups to the graphite layer. These polar groups enhance GO's hydrophilicity and dispersibility in solvents, although they reduce its electrical conductivity. Partially reduced graphene oxide (rGO), obtained through chemical reduction, offers improved conductivity and retains functional groups that facilitate dispersion. The degree of reduction controls the balance between electrical properties and solubility, with highly reduced rGO approaching pristine graphene properties [208].
II. Boron Nitride (BN): BN is a crystalline material composed of boron and nitrogen atoms, known for its chemical stability in acidic and alkaline environments, making it suitable for harsh conditions. BN nanotubes are particularly promising for ion transport due to the high surface charge on their inner surfaces, which enhances ion selectivity over a wide pH range. BN's high surface charge density and efficient ion transport capabilities make it an attractive option for advanced nanofluidic applications [154].
III. Anodic Aluminum Oxide (AAO): AAO is a highly ordered form of aluminum oxide with uniform, parallel nanopores, fabricated through electrochemical oxidation of aluminum membranes. AAO membranes exhibit excellent chemical resistance and mechanical strength, with pore diameters ranging from a few to several hundred nanometers. These membranes are stable in liquid environments and are often used as a robust base layer for heterogeneous membranes [209].

Each of these materials offers unique properties, making them integral to advancing nanofluidic membrane technology. Fig. 10 illustrates the transformation processes of graphene, graphene oxide, and reduced graphene oxide (rGO). This conversion sequence is emphasized because tuning the degree of oxidation and reduction along the graphene–GO–rGO continuum provides a direct handle on interlayer spacing and surface charge regulation, which are key determinants of ion transport behavior and membrane performance in graphene-based nanofluidic systems [210].

Clay-based nanofluidic membranes constitute an important subclass of mineral-derived systems, as naturally occurring layered clays provide well-defined two-dimensional interlayer nanochannels with high surface charge densities. Among them, montmorillonite has been extensively explored due to its cation-exchange capability and tunable interlayer spacing. For instance, Xiao et al. [211] reported a synthetic bilayer-intercalated montmorillonite membrane in which the clay interlayers act as 2D nanofluidic channels exhibiting dual-responsive ion transport behavior. By exchanging native interlayer cations with quaternary ammonium surfactants and controlling the bilayer phase state, ion transport could be reversibly regulated by external temperature and voltage stimuli. This work exemplifies how natural clay minerals can be transformed into functional nanofluidic membranes with stimuli-responsive transport properties, bridging fundamental nanofluidics and practical membrane design.

### 5.2.2. *Organic-based nanofluidic membranes*

Organic materials for nanofluidic membranes primarily include ultrathin synthetic macromolecular membranes, metal-organic frameworks (MOFs), and covalent organic frameworks (COFs). Additionally, 1D nanochannel-structured organic membranes with various geometric parameters are fabricated from materials such as polyethylene terephthalate, polyimide, polycarbonate, and short cyclodextrin nanotubes. Porous polymer-based membranes, characterized by their high permeability and ease of fabrication, have significant potential [212]. However, challenges such as difficulty in precise surface modification at the angstrom scale, low selectivity, and structural instability limit their widespread application [169]. Below is an overview of prominent organic materials used in nanofluidic membranes:

I. Covalent Organic Frameworks (COFs): COFs feature intrinsic nanopores that can directly serve as nanochannels for molecular or ionic transport [213], distinguishing them from materials like graphene and graphene oxide. A major area of research for 2D COFs is pore engineering, aimed at exploring the structure-property relationships for advanced energy applications [214]. This involves two main processes:

a. Pore Chemical Environment Engineering: Focuses on tailoring the linkages and skeletal units that define the pores. This is achieved by selecting suitable chemical linkages and adjusting the properties of the skeletal units.
b. Topological Pore Engineering: Involves designing the distribution, size, and shape of pores to optimize their performance in specific applications.

II. Metal-Organic Frameworks (MOFs): MOFs are porous crystalline materials with hybrid organic-inorganic structures, consisting of organic linkers and metal nodes [18]. They have well-defined pore structures that act as nanofluidic channels for ion transport. MOFs offer high porosity, versatile pore architectures, and tunable pore sizes, making them attractive for energy storage and conversion applications. However, many MOFs suffer from hydraulic instability, limiting their use in artificial nanofluidic channels. Despite this drawback, their nanoscale pores, large surface area, and customizable structures render 2D MOFs promising candidates for advanced nanofluidic and energy-related technologies [172,215].

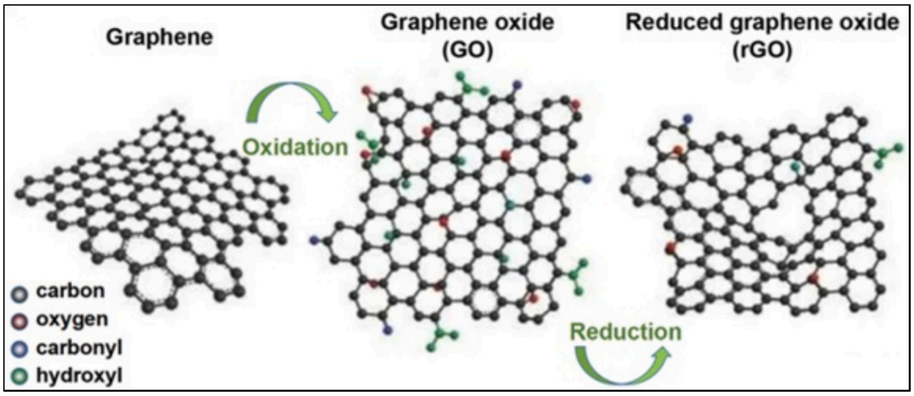


**Fig. 10.** Conversion pathways from graphene to graphene oxide (GO) and reduced graphene oxide (rGO) and their relevance to nanofluidic membrane transport. The progressive introduction and partial removal of oxygen-containing functional groups control interlayer spacing, surface charge density, hydrophilicity, and swelling behavior, which collectively govern ion selectivity, permeability, and stability in graphene-derived nanofluidic membranes [96].

### 5.2.3. *Composite-based nanofluidic membranes*

The heterogeneous construction of materials has emerged as an innovative concept in material design, wherein diverse components are integrated through intermolecular forces to harness their respective strengths while mitigating their weaknesses. This approach often results in enhanced charge transfer kinetics, improved electrical conductivity, and the development of unique physical and chemical properties. Consequently, such heterogeneous structures exhibit superior energy performance. Depending on the combination of materials, these structures can be classified as organic-inorganic, organic-organic, or inorganic-inorganic, each offering tailored functionalities for advanced applications [18,173,216].

## 5.3. *Classification by origin*

As mentioned, nanofluidic membranes are structures with ion-selective nanochannels; these nanochannels can be divided into three main categories based on their origin: biological nanochannels found in living systems, artificial nanochannels designed by humans, and biomimetic nanochannels inspired by natural structures. Each of these categories brings unique properties and advantages, enabling diverse applications across science and engineering [217].

### 5.3.1. *Biological nanochannels*

Normal cells rely on ion channels embedded in their membranes to establish chemical and electrical communication with the extracellular environment. These biological ion channels, which respond dynamically to environmental stimuli by opening and closing, are crucial for regulating ion permeability across the cell membrane [218]. They are essential for many physiological processes, including signal transmission, osmoregulation, and maintaining cellular homeostasis. Structurally, ion channels are complex membrane proteins whose conformational changes, driven by reactive responses to stimuli, regulate ion transport properties. Naturally occurring in living organisms, these channels exemplify nature's precision in facilitating selective and efficient ion transport. A prime example is aquaporins—specialized channels that enable the rapid and efficient transport of water molecules while effectively excluding other solutes. This remarkable selectivity and efficiency make aquaporins integral to biological water management systems in cells [64].

### 5.3.2. *Biomimetic/ artificial nanochannels*

In this review, biomimetic and artificial nanochannels are discussed within a unified framework, as both rely on shared nanofluidic transport principles and differ primarily in their degree of biological inspiration rather than in their fundamental ion transport mechanisms. Artificially constructed nanochannels are designed to replicate the behavior and functionality of biological channels, such as aquaporins, by emulating their chemistry and transport properties. Although synthetic, these channels closely mimic natural systems, making them valuable tools for understanding and enhancing ion transport processes. They serve as fundamental platforms for experimental and theoretical studies aimed at simulating ion transport mechanisms in living organisms [219,220]. Moreover, these artificial nanochannels play a critical role in advancing biomimetic technologies by improving the performance of biological ion channels and fostering the development of smart nanochannel devices. Applications include biosensors, nanofluidic systems, and molecular filtration technologies, highlighting their potential in creating innovative solutions that bridge biological principles and engineering advancements [221].

Synthetic nanochannels are purpose-built for specific applications without attempting to emulate biological channels. Constructed from advanced materials such as carbon nanotubes, graphene, and MOFs, these channels are engineered to deliver targeted functionalities like rapid water transport or precise separation of materials [222,223]. Despite their promising capabilities, synthetic nanochannels face challenges in matching the remarkable selectivity and efficiency of biological channels. Overcoming these limitations requires continued research to enhance their performance and broaden their application potential in fields such as filtration, energy conversion, and environmental remediation [224,225].

## 5.4. *Classification by nanochannel wall type*

Artificial nanochannels are divided into two main categories based on the properties of their internal surfaces: hard-walled and soft-walled nanochannels. Hard-walled nanochannels achieve surface charge by modifying their surfaces with functional groups, enabling specific transport properties. These channels are often constructed from advanced materials such as carbon nanotubes or graphene, which are tailored for particular applications, including fast water transport or selective material separation.

In contrast, soft-walled nanochannels are coated with a polyelectrolyte layer (PEL) that imparts charge to the internal surfaces through acidic or basic functional groups [141]. This coating adds flexibility, allowing for the attachment of biological molecules and enhancing the potential for use in ion-based and molecular sensors.

Surface modification plays a critical role in controlling the transport properties of nanochannels [226]. Techniques like chemical vapor deposition (CVD), physical vapor deposition (PVD), and atomic layer deposition (ALD) are commonly used to improve the performance and controllability of these nanochannels. The polyelectrolyte layer in soft-walled nanochannels significantly influences system behavior in two ways [227,228]. First, the PEL creates resistance to fluid flow, which alters the flow dynamics compared to solid-state nanochannels. Second, the charged groups within the PEL interact with the electrolyte, attracting counterions and affecting the ionic distribution and behavior within the nanochannel [229].

The introduction of a PEL into nanochannels provides the ability to fine-tune the system's properties, optimizing it for specific applications. This tunability is particularly important for achieving precise ion selectivity and transport characteristics. Soft layers are categorized into different types based on their behavior in response to environmental changes (Fig. 11) [230]. In the case of strong soft layers, the charge remains constant regardless of the electrolyte pH, making them ideal for applications where stable ion selectivity is required. Weak soft layers, on the other hand, experience changes in charge depending on the pH, resulting in an increase in counterion release, which enhances ionic flux and electromotive force [145,231]. Diffusive soft layers exhibit a spatial charge distribution, where the charge density varies across the layer, and this distribution can be described by functions like the soft step distribution function, which is particularly compatible with polyelectrolyte soft layers. Through careful modulation of these factors, artificial nanochannels with soft layers offer enhanced capabilities, making them suitable for a wide range of applications in nanofluidics, sensors, and ion transport systems [232]. Weak polyelectrolyte layers provide a practical route to stimuli-responsive transport because pH-driven charge regulation directly reshapes the electrostatic environment and selectivity; recent theory/experiments on weak polyelectrolyte brushes further clarify these mechanisms [233,234].

### 5.5. *Classification by nanochannel geometry*

Nanochannels can also be classified into two types based on their symmetry: symmetric and asymmetric nanochannels. The key difference between these two categories lies in the behavior of the EDLs at the channel surfaces. In symmetric nanochannels, the EDLs overlap uniformly across the entire length of the nanochannel, leading to consistent electrokinetic properties along the channel. This uniformity results in a stable and predictable transport of ions and molecules [236].

In contrast, asymmetric nanochannels exhibit a varying degree of overlap of the electrical double layers along their length. This variation can significantly influence the electrokinetic behavior within the nanochannel, leading to phenomena such as ionic current rectification and ionic selectivity. The asymmetry introduces a ratchet-like mechanism where mass transport is driven by the unequal oscillations of the electrical double layers, allowing for more complex ion transport behavior [237]. This characteristic is particularly useful in applications where controlled ionic movement and selectivity are required.

Examples of symmetric nanochannels include cylindrical channels, where the symmetry is maintained throughout the channel length. Asymmetric nanochannels, on the other hand, include shapes such as bullet, cigarette, hourglass, and conical channels. The structural asymmetry in these channels leads to a more dynamic interaction between ions and the channel walls, resulting in unique transport behaviors that can be exploited for various applications in sensing, separation, and filtration technologies [238].

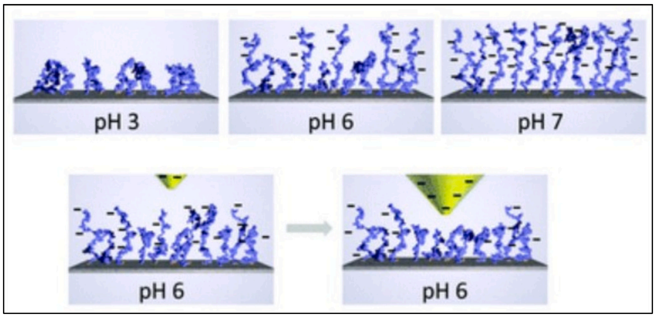


**Fig. 11.** Conceptual response of weak polyelectrolyte layers (soft nanochannel walls) to pH variation and its impact on ion transport. Changes in pH regulate the degree of ionization of weak polyelectrolytes, thereby modifying fixed-charge density, EDL structure, ion partitioning, and ultimately ionic flux/streaming potential and electromotive force in soft nanochannels [235].

## 6. Techniques for fabricating nanofluidic membranes

A significant challenge in advancing nanoporous membrane-based platforms for energy applications lies in achieving reproducible synthesis of the desired nanostructures. The precise control over pore size, shape, distribution, and surface chemistry is crucial for optimizing the performance of these membranes in energy-related processes such as ion transport, separation, and energy conversion. However, such reproducibility remains a technical hurdle due to the complex fabrication techniques required [42].

To address this challenge, researchers have focused considerable effort on developing innovative and controlled fabrication methods. These methods aim to produce nanoporous membranes from a wide range of materials, including inorganic, organic, and hybrid composites, with tailored properties suitable for specific energy applications. Advances in techniques such as template-assisted synthesis, chemical vapor deposition, atomic layer deposition, and electrochemical methods have contributed to the progress in creating membranes with highly defined and reproducible nanostructures [239]. By continuing to refine these fabrication methods, researchers hope to overcome current limitations, enabling large-scale production of high-performance nanoporous membranes. Such advancements will play a critical role in the realization of more efficient and sustainable energy systems.

### 6.1. *Lithography-based fabrication methods*

#### 6.1.1. *Photolithography*

The most straightforward and widely used method for fabricating nanochannels is conventional UV photolithography. This process begins by coating a substrate—commonly silicon, $SiO_2$, glass, or other suitable materials—with a UV-sensitive photopolymer. A glass mask with the desired nanochannel pattern is then placed over the coated substrate, and the assembly is exposed to a UV light source. Depending on the type of photoresist used (positive or negative), the exposed or unexposed regions of the photopolymer are removed through chemical development, transferring the pattern to the photoresist layer [240].

Following this, a wet or dry etching process etches the pattern into the underlying substrate, creating the desired nanochannel structure. Conventional UV photolithography, often used in academic settings, typically produces structures with dimensions ranging from $1-3\ \mu m$. However, by employing advanced photolithography techniques with intense UV or X-ray sources and diamond masks, dimensions smaller than 100 $nm$ can be achieved. Despite these capabilities, the high costs and limited availability of such advanced equipment make them impractical for many applications. As a result, the fabrication of nanochannels using photolithography often focuses on controlling the etching depth to achieve desired dimensions [241]. Nanochannels produced via this method are generally two-dimensional and are sealed by bonding the patterned substrate to a silicon, glass, or polydimethylsiloxane (PDMS) layer. This approach allows for the fabrication of nanochannels with depths as small as 2 $nm$. Fig. 12 illustrates the key steps involved in the photolithographic fabrication process.

#### 6.1.2. *Electron beam lithography*

Electron beam lithography (EBL) is a high-precision technique that uses a focused electron beam to transfer a desired pattern directly onto an electron beam-sensitive material, eliminating the need for a mask. The most commonly used material in EBL is polymethyl methacrylate (PMMA); however, newer materials like hydrogen silsesquioxane (HSQ) are gaining popularity due to their superior resolution. This technique

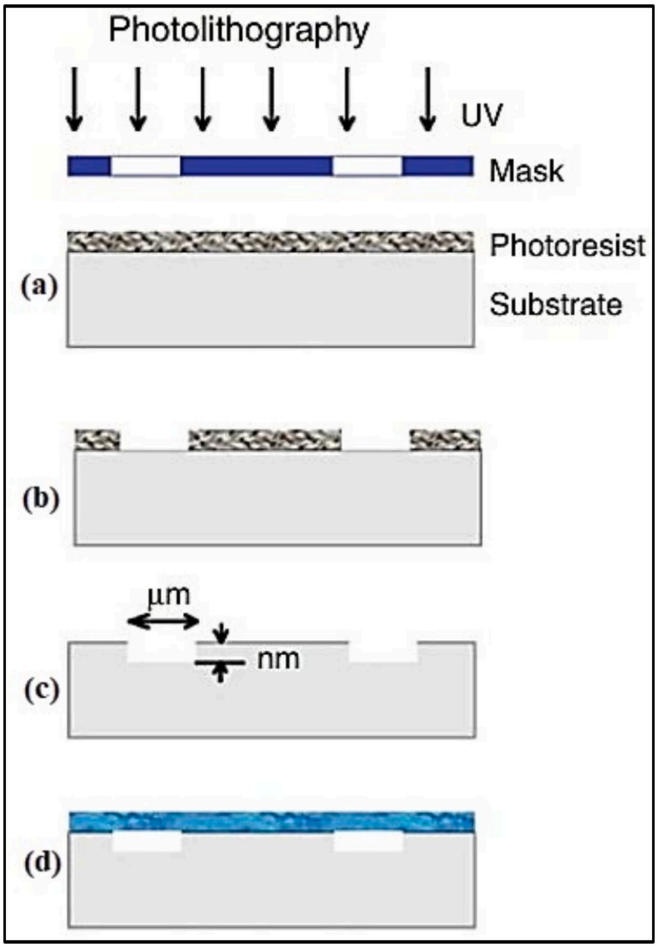


**Fig. 12.** Nanochannel fabrication via photolithography, (a) application of a photosensitive coating on the substrate, exposed to UV light through a patterned mask, (b) Development of the desired pattern in the photosensitive material, (c) Substrate etching to achieve the required nanometer-scale depth, and (d) Bonding of a second layer to enclose the nanochannel structure [242].

allows for the creation of beam diameters smaller than 10 *nm*, enabling the direct patterning of line widths at the nanometer scale [243].

A key advantage of EBL is its exceptional control over the patterning process, making it possible to fabricate nanochannels with varying widths on the nanometer scale. However, the method has notable drawbacks. Since it is a sequential process, EBL is inherently slow and has low throughput, limiting its practicality for large-scale applications. Additionally, the method is costly and requires skilled personnel to operate the equipment effectively. Despite these challenges, the precision of EBL makes it an invaluable tool in applications where exacting control over nanochannel dimensions is critical [244]. Fig. 13 provides an overview of the nanochannel fabrication process using this method.

### 6.1.3. Ion beam lithography

Ion beam lithography (IBL) is another sequential patterning technique that employs a focused beam of ions, such as protons or heavier ions like gallium, to directly etch or deposit patterns onto substrates. Unlike EBL, IBL does not require a photosensitive coating, enabling it to fabricate nanochannels in materials such as silicon and glass directly. This is a significant advantage, simplifying the process and allowing for greater versatility in substrate selection [245].

A notable strength of IBL is its superior resolution compared to EBL, primarily because heavier ions experience less scattering. Using this method, nanochannels as small as 20 *nm* have been successfully created in silicon and glass substrates. Moreover, proton beams have also been utilized for fabricating nanochannels in polymeric materials such as PMMA. Despite these advantages, IBL faces similar limitations to EBL. It is a time-intensive process with low throughput, making it less suitable for large-scale applications. The method also requires highly skilled personnel and expensive equipment. Additionally, the incorporation of heavy metal ions into the substrate during the process is a potential concern, particularly for applications requiring pristine material properties [246]. Fig. 14 illustrates the sequential steps involved in nanochannel fabrication using ion beam lithography.

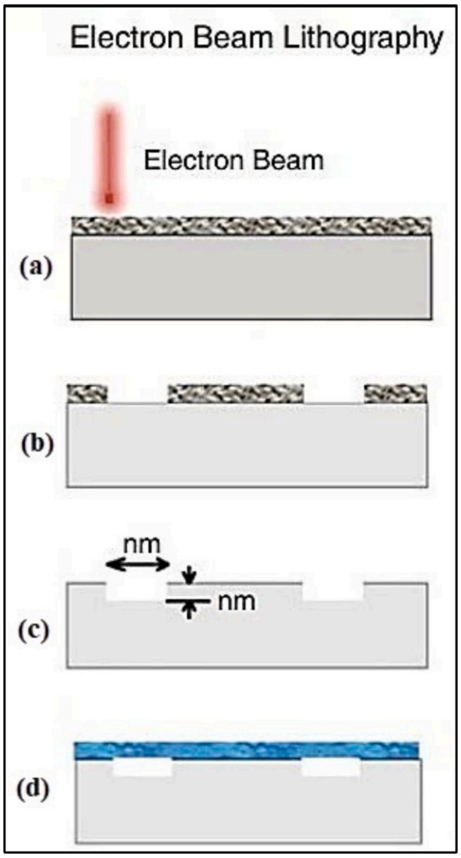


**Fig. 13.** Nanochannel fabrication via EBL, (a) Exposure of the coated substrate to an electron beam, (b) Formation of the desired pattern in the substrate coating, (c) Etching of the substrate to the required nanometer-scale depth, and (d) Bonding of a second layer to seal the nanochannel structure [242].

## 6.2. Chemical and electrochemical fabrication methods

### 6.2.1. Anodic oxidation

Anodic oxidation is a widely used method to create nanochannels, particularly in aluminum oxide ($Al_2O_3$) [247,248]. This electrochemical oxidation process occurs in an acidic environment and results in the formation of ordered nanochannel structures. The method typically involves two stages of anodization. In the first stage, a clean aluminum sheet is anodized in an acidic solution, such as oxalic acid, sulfuric acid, or phosphoric acid, to form an alumina layer on the aluminum surface [249]. In the second stage, the alumina layer is chemically treated with phosphoric-chromic acid to create a recessed pattern on the aluminum substrate. A further anodization process follows, which leads to the formation of highly ordered pores within the alumina layer. The barrier layer of aluminum is then removed either by voltage pulses or chemical treatment, resulting in an anodic alumina membrane with regular, self-organizing pores. This process typically creates honeycomb-shaped nanochannels with pore diameters ranging from 5 to 250 nm and pore densities of up to $10^{11}$ pores per cm$^2$ [86]. The pore arrangement is

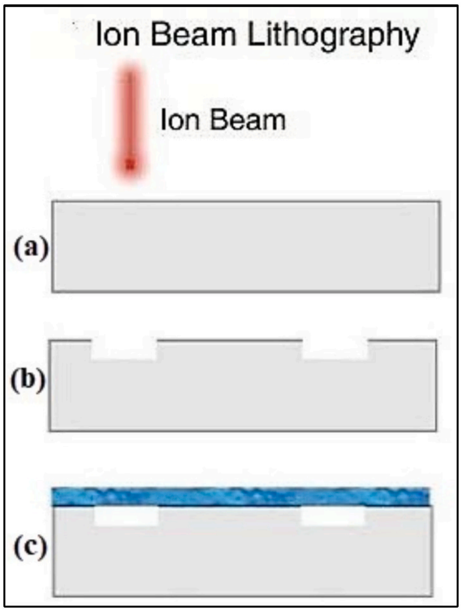


**Fig. 14.** Nanochannel fabrication via IBL, (a) Substrate exposure to an ion beam, (b) Patterning of the desired structure on the substrate, and (c) Sealing the formed nanochannels with an additional layer [242].

hexagonal, meaning that pore density and diameter are closely linked, making it challenging to vary these two parameters independently [250]. Despite this limitation, anodic alumina membranes with regular nanochannels are commercially available in a range of dimensions. In recent years, there has been growing interest in utilizing AAO as nanotemplates for the ordered growth of carbon nanotubes or nanowires, further expanding its applications in nanofluidic systems and other advanced technologies [251].

Anodic oxidation has also been widely employed to fabricate highly ordered $TiO_2$ nanotubular membranes, which provide vertically aligned one-dimensional nanochannels suitable for nanofluidic ion transport. A representative example was reported by Zhang et al. [252], who demonstrated light-regulated ion transport through self-organized $TiO_2$ nanotubular arrays functioning as artificial ion channels. In this system, ultraviolet illumination induces the formation of electrostatic trapping sites within the $TiO_2$ nanotubes, thereby modulating surface charge characteristics and enabling reversible control over ionic conductance. This work exemplifies how anodically fabricated inorganic nanotube arrays can be integrated with external stimuli to realize responsive nanofluidic membranes, further underscoring the versatility of anodic oxidation for nanofluidic membrane fabrication.

### 6.2.2. *Electrochemical exfoliation*

Electrochemical exfoliation is a technique that utilizes electrochemical reactions to separate and prepare materials, particularly for membrane module applications. The basic principle involves initiating an electrochemical reaction on the surface of the material through ion transfer in the electrolyte, which leads to the dissolution, separation, or precipitation of ions on the material's surface, thereby achieving exfoliation. In the case of graphene, electrochemical exfoliation typically uses graphite as the anode and a platinum electrode as the cathode. The exfoliation process occurs in electrolyte systems consisting of various acid, alkali, or salt solutions. During this process, an electric current drives charged ions or molecules into the gap between graphite layers, causing the graphene layers to detach. This procedure is very rapid, usually taking just a few seconds to a few tens of seconds [253].

The electrochemical exfoliation of graphene is considered low-cost, environmentally friendly, and highly efficient. However, graphene products obtained through this method often contain a certain amount of oxygen radicals, which are generated from the decomposition of aqueous free radicals (HO-C and O—C) by water. By adjusting various parameters of the electrochemical exfoliation process, graphene with different oxidation degrees can be produced [254].

In addition to graphene, electrochemical exfoliation has been adapted to produce other 2D materials. For instance, to avoid the risks associated with fluorine-containing reagents used in the production of MXene, Feng et al. developed a fluorine-free electrochemical etching method. They successfully prepared $Ti_3C_2T_x$ using electrochemical exfoliation in a mixed solution of $NH_4Cl$ and TMA-OH. Overall, electrochemical exfoliation is gaining widespread use in preparing 2D materials due to its advantages, such as simple operation, excellent product controllability, small device size, and environmental benefits [255].

## 6.3. *Filtration and sedimentation fabrication methods*

### 6.3.1. *Vacuum-assisted filtration*

Vacuum-assisted filtration is one of the most common methods for preparing 2D membranes [173,256,257]. This process primarily involves using a Buchner funnel, which contains filter paper or a filter membrane, along with a pressure difference that encourages the natural accumulation of materials, leading to the formation of a 2D membrane. One of the main advantages of this method is its simplicity, and the thickness of the resulting membrane can be easily adjusted by varying the concentration of the solution [258].

Vacuum-assisted filtration has emerged as one of the most widely used and versatile fabrication strategies for two-dimensional (2D) nanofluidic membranes. In this approach, exfoliated 2D nanosheets—such as graphene oxide, MXenes, layered metal–organic frameworks, or other lamellar materials—are assembled into stacked architectures under a pressure gradient, forming continuous and highly ordered interlayer nanochannels. The resulting lamellar spacing, channel tortuosity, and membrane thickness can be tuned by controlling nanosheet size, surface chemistry, and filtration conditions. These interlayer galleries act as two-dimensional nanofluidic channels in which ion transport is strongly governed by confinement effects and surface charge interactions, making vacuum-assisted filtration a cornerstone technique for constructing 2D nanofluidic membranes with tailored transport properties.

Shi et al. [259] used vacuum-assisted filtration to prepare a GO membrane with a regular morphology. The graphene oxide membranes produced exhibited surface charge-controlled ion transport properties, thanks to the large number of nanofluidic channels. By modifying the dispersion of the starting materials and further stacking the modified nanosheets during the filtration process, they were able to obtain GO membranes with high surface charge. The highly charged surface of these membranes creates a significant interaction energy barrier, which repels covalent charges and significantly enhances the ion selectivity of the membranes. Beyond pure membranes, the vacuum-assisted filtration method is also effective in preparing hybrid membranes. In this approach, two-dimensional materials are combined with guest materials, such as nanofibers, before filtration is carried out. This process allows for the preparation of membranes with unique properties by incorporating different materials into the 2D matrix, expanding the range of potential applications [260]. For example, 2D materials and guest materials (such as nanofibers) are pre-mixed and then filtration is performed (slide (a) of Fig. 15).

### 6.3.2. *Layer-by-layer deposition*

Layer-by-layer (LBL) deposition is a technique that utilizes the electrostatic interaction between two materials with opposite charges to assemble them onto a charged solid surface through repeated layer-by-layer adsorption. Initially, this method was used for the assembly of polyelectrolytes but has since been extended to the assembly of 2D and 2D/1D materials (slide (b) of Fig. 15) [261]. For instance, Kim et al. employed LBL assembly technology to construct a two-dimensional

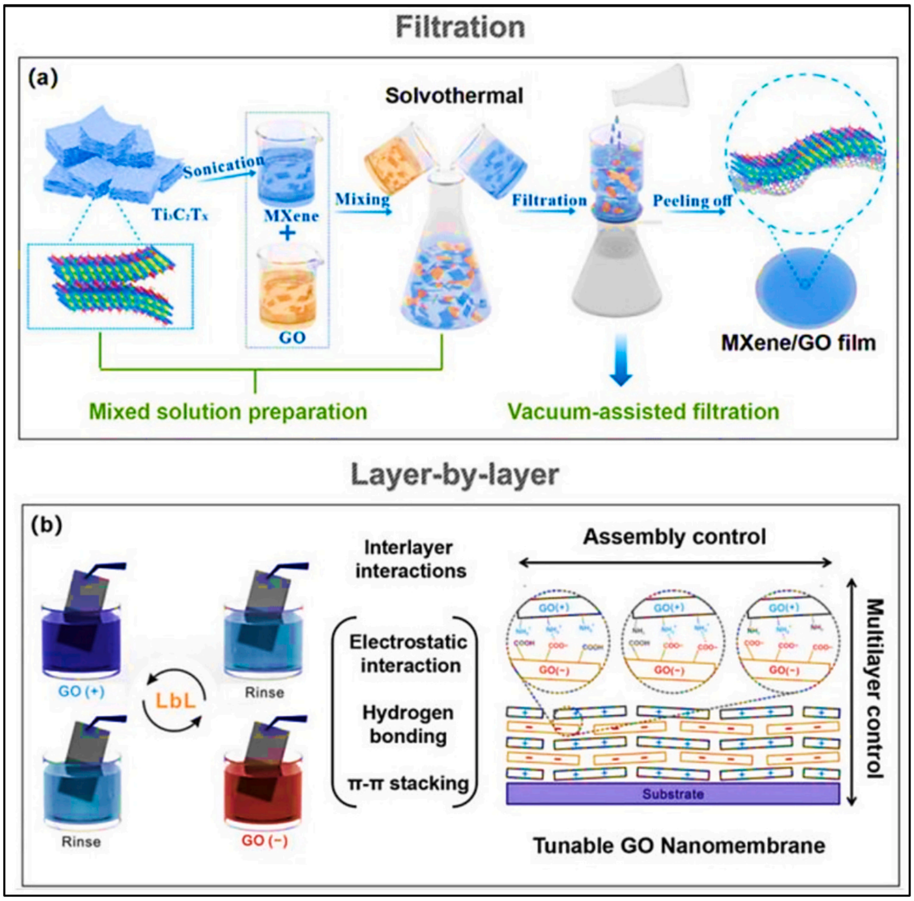


**Fig. 15.** Schematic of fabrication methods, (a) vacuum-assisted filtration, and (b) LbL deposition [96].

multilayer GO membrane [262]. The assembly process was controlled by adjusting the pH conditions, which influenced the thickness, roughness, and charge density of the membrane. By varying the number of alternating layers, the membrane thickness could be tuned from a few nanometers to several millimeters. One of the key advantages of the LBL method is its ability to achieve sub-nanometer precision in membrane fabrication, which is a significant improvement over traditional vacuum filtration methods that typically offer micrometer-level precision. This precision makes LBL deposition a versatile and controlled approach for fabricating membranes with specific properties tailored for various applications [263].

### 6.3.3. *Superspreading*

In 1990, Ananthapadmanabhan et al. [264,265] discovered that adding specific surfactants to a solution significantly enhanced the rate of diffusion and spreading on hydrophobic surfaces, a phenomenon known as fluid superspreading. Building on this concept, Zhao et al. [266] utilized the superspreading method to prepare highly ordered layered GO nanocomposite membranes (Fig.16). The superspreading technique facilitates the rapid assembly of nanosheets into a well-ordered two-dimensional membrane structure, preventing the aggregation of nanomaterials during fabrication [267,268]. By diluting the reaction solution, this method promotes uniform dispersion and enhances the material's properties. This approach is versatile and can be extended to the preparation of other nanomaterials, making it a valuable tool for creating advanced nanocomposite membranes with controlled structures and improved performance.

### 6.3.4. *Chemical vapor deposition*

Chemical vapor deposition (CVD) is a process in which gaseous reactants, such as atoms or molecules, are introduced into a chamber where they are reduced or deposited onto a substrate, typically an oxide surface. Under the influence of external energy, the reactants form a monolayer membrane on the substrate [269]. CVD is a widely used method in material science, particularly for producing thin films and membranes with precise control over thickness. It offers several benefits, including ease of membrane formation, excellent reproducibility, and the ability to scale up for industrial production. CVD has been employed to synthesize a wide variety of membranes, especially those with controllable monoatomic thickness, such as $MoS_2$. Radenovic et al. [270] explored different methods for creating nanopores in $MoS_2$, a material known for its potential in applications such as energy storage, catalysis, and nanoelectronics. The first step involves growing a monolayer of $MoS_2$ through CVD, preferably on a sapphire substrate. Once the monolayer is prepared, nanopores are created using techniques such as electron beam or electrochemical reactions. These methods are crucial for enhancing the material's properties for specific applications, including ion transport and filtration [271].

## 6.4. *Surface synthesis-based fabrication methods*

### 6.4.1. *Liquid-liquid surface synthesis*

In recent years, liquid-liquid interface synthesis has gained significant attention for the preparation of nanomaterials, particularly for creating two-dimensional ultrathin membranes. This method involves the dissolution of one monomer in the organic phase and another in the aqueous phase. The two phases are then brought into contact at the liquid-liquid interface to form ultrathin membranes. The unique feature of this process is that the interface between the immiscible organic and aqueous phases acts as the site for polymerization or other chemical

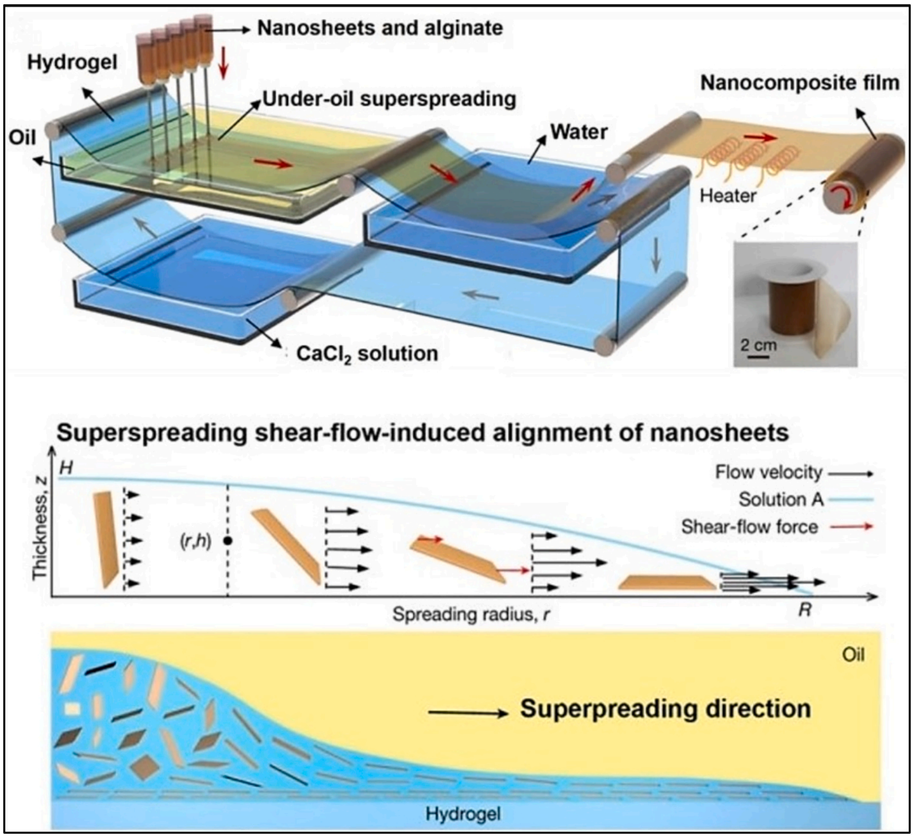


**Fig. 16.** Schematic of superspreading method [96].

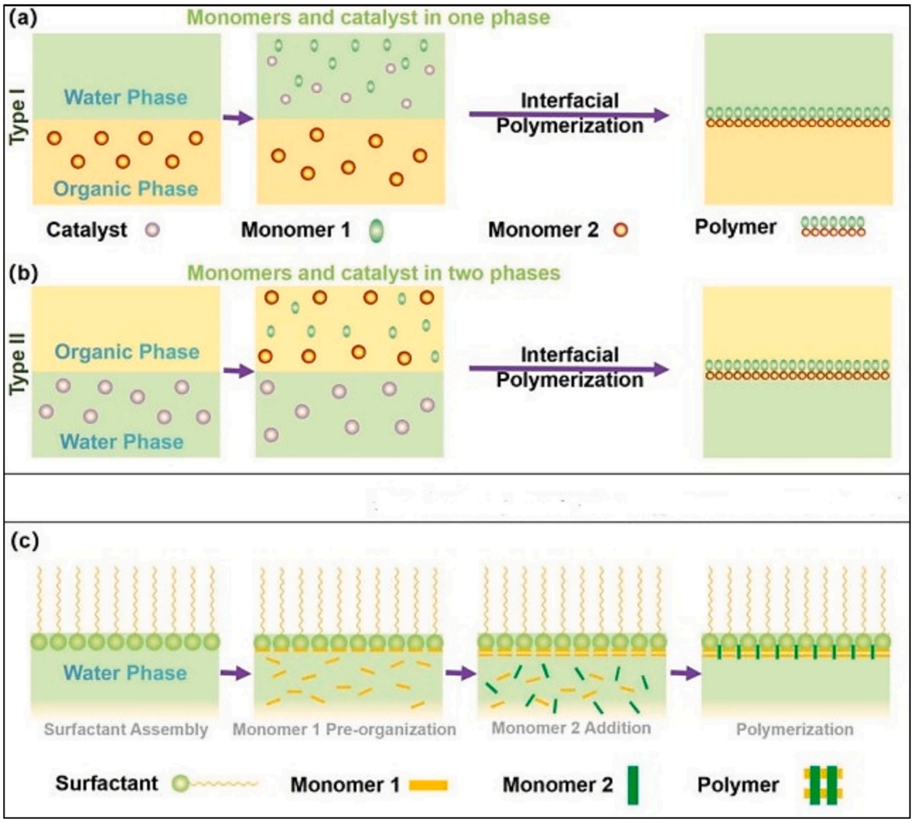


**Fig. 17.** Schematic of interfacial synthesis methods, (a) Liquid-liquid interfacial synthesis with monomer and catalyst in the same phase, (b) Liquid-liquid interfacial synthesis with monomer and catalyst in different phases, and (c) Monolayer interfacial synthesis using surfactant [96].

reactions, enabling the controlled growth of nanomaterials at this boundary [272].

As the method has developed, liquid-liquid interface synthesis can be categorized into two main types: (I) where both the monomer and the catalyst exist in the same phase, and (II) where the monomer and the catalyst are in different phases, as shown in slides (a) and (b) of Fig. 17. In both cases, the catalyst and monomers are separated by the two immiscible solution phases, and polymerization occurs specifically at the interface between them. This controlled reaction environment allows for the precise formation of materials, such as COFs, which can be synthesized into large-area membranes. This method provides a versatile approach to fabricating nanomaterials with well-defined structures and scalable production potential [272].

### 6.4.2. *Surfactant monolayer-assisted interfacial synthesis*

One of the primary challenges in liquid-liquid surface synthesis is the difficulty in controlling the assembly of molecules at the interface. This lack of control can lead to disordered molecular arrangements, resulting in heterogeneous products with poor crystallinity, which ultimately affects the performance of devices made from these materials. However, the surfactant-based single-layer surface synthesis method offers a solution to this problem. By utilizing a surfactant layer at the gas-liquid interface, this approach can confine molecules or precursors to a two-dimensional plane, thus inducing the ordered arrangement of monomers and facilitating controlled polymerization at the interface [273].

Feng's group [273,274] successfully applied this technique, known as the surfactant monolayer-assisted interface synthesis (SMAIS) method, to create multi-layer two-dimensional polymer membranes on a water surface (Fig. 17c). The synthesis was achieved through the reaction of anhydride and amine groups at the water-air interface, with the aid of surfactant monolayers. This method enabled the production of ultrathin 2D membranes, approximately 2 *nm* in thickness, with high crystallinity. Furthermore, crystalline 2D polyamide membranes with a porous structure were also synthesized by polymerizing monomers at the interface between sodium oleyl sulfate and water, under similar conditions. This surfactant-based approach offers a promising route for the controllable polymerization of two-dimensional materials with precise structural and functional properties [272].

## 6.5. *Alternative fabrication methods*

### 6.5.1. *Sacrificial techniques*

In the sacrificial layer method, a sacrificial intermediate layer is used between two substrates that are intended to form nanochannels. The sacrificial layer, typically less than 100 *nm* thick, is deposited on the nanochannel substrate in the desired pattern and thickness. This thickness plays a crucial role in defining the depth of the nanochannel, so it is important to select a sacrificial material that can be deposited uniformly and with high precision at such thin dimensions. Common sacrificial materials include amorphous silicon, polysilicon, and metals like chromium or gold [275].

Once the sacrificial layer is deposited, it is patterned into the desired nanochannel shape using photolithography followed by wet or dry etching. The second layer of the nanochannel structure is then bonded to the substrate that has been patterned with the sacrificial layer. The two substrates are only bonded at the points of direct contact, while the sacrificial layer remains in place. Alternatively, a structural layer may be deposited on top of the sacrificial layer before the bonding process [276]. Afterward, the sacrificial layer is selectively etched away using a suitable wet etchant that removes the sacrificial material while leaving the other layers, including the nanochannel structure, largely unaffected. This method allows for the fabrication of nanochannels with high aspect ratios, and it has been reported that nanochannels can be created with depths as small as 20 *nm*, widths ranging from 0.5 to 200 *μm*, and lengths of up to 4 *mm*. However, the wet etching process required for sacrificial layer removal can be slow, often taking several days to fully etch the sacrificial material due to the reliance on the etchant's penetration into the channels. Additionally, because the selectivity of the etchants is not always perfect, there may be some deviations or inconsistencies in the dimensions of the fabricated nanochannels (Fig. 18).

### 6.5.2. *Nanomolding techniques*

Micro-molding of elastomeric polymeric materials is a cost-effective and efficient method for rapid prototyping in microfluidic device fabrication. PDMS is the most commonly used material for molding fluidic channels due to its ability to replicate molds with up to 99% accuracy. While fabricating nanochannels in elastomeric materials is more challenging, especially due to the tendency of nanoscale materials to deform and collapse, this issue can be leveraged to create nanochannels with the right design [277].

One such method involves the cracking of PDMS to create nanochannels. The process begins by superficially oxidizing a PDMS layer, typically through oxygen plasma treatment. This oxidation hardens the surface, creating a mismatch in the elastic modulus between the surface and the bulk material. When a uniaxial tensile force is applied, cracks form in the surface layer, resulting in triangular-shaped nanochannels. These nanochannels can be sealed by oxygen plasma bonding with another PDMS layer, or with substrates such as glass or silicon. Additionally, this method allows the nanochannel pattern to be transferred to another PDMS layer, effectively replicating the nanochannel structure. Using this technique, nanochannels with a height of 80 *nm* have been successfully fabricated [278].

### 6.5.3. *Nanoimprint lithography*

The nanoimprint lithography (NIL) method developed by Chou et al. [279] involves several key steps for the fabrication of nanochannels. Initially, a nanotemplate or pattern is created, often through electron beam lithography followed by reactive ion etching (RIE) on silicon or glass substrates, or directly using a focused ion beam (FIB). A thermoplastic resist is then coated onto a substrate, such as silicon, and heated above its glass transition temperature (Tg) [280].

Next, the mold, which contains the desired nanochannel pattern, is placed under vacuum on the coated thermoplastic layer. The mold is pressed onto the substrate, and the thermoplastic is allowed to cool and harden. After the mold is released, a short RIE step is performed to remove any remaining thermoplastic and to emboss the nanochannel pattern onto the substrate. The thermoplastic material used can serve as the material for the nanochannels themselves or as a mask for etching the substrate further with RIE. This method has been successfully

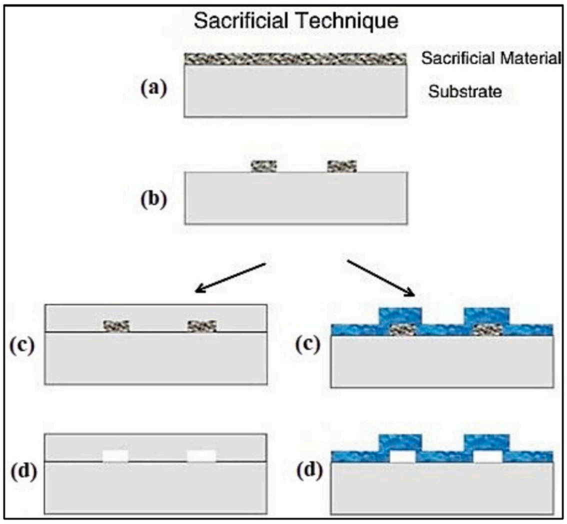


**Fig. 18.** Schematic of manufacturing steps using the sacrificial layer method [242].

employed to create nanochannels with depths as small as 20 *nm* and lengths extending several centimeters, making it highly suitable for nanofluidic applications [281].

### 6.5.4. Dielectric breakdown method

The dielectric breakdown method is a technique used to create nanochannels in membranes by applying a high voltage across them. This method allows for the formation of nanochannels with sub-nanometer precision and offers excellent control over pore diameter. It works by using a multi-level pulse voltage injection to break membranes, such as silicon nitride ($Si_3N_4$). In the process, a high voltage is applied to two electrodes, typically made of silver/silver chloride (Ag/AgCl), which generates a strong electric field within the membrane. This electric field causes the membrane to break at the nanoscale, creating nanochannels with a precise diameter. The method is capable of producing pores with diameters as small as 3 *nm*, making it ideal for applications that require high precision, such as molecular studies [282].

One notable application of this method is the detection of single-stranded and double-stranded DNA, where nanochannels with diameters around 2 *nm* are used to analyze the molecular structure of DNA. Additionally, the dielectric breakdown method has been successfully employed to create nanopores in graphene membranes, showcasing its versatility and potential for creating nanopores in various substrates.

## 7. Modeling approaches and principles

Mass transport in nanochannels is primarily influenced by the charge effects and the size of the nanochannel. In these systems, the EDL plays a crucial role, as its thickness is comparable to the characteristic dimensions of the nanochannel, which leads to unique properties not observed in larger-scale systems, such as micro- or macro-scale channels. As illustrated in Fig. 19, a nanochannel can typically be divided into two distinct regions: the electrostatic interaction region and the free transport region. In nanochannels with relatively larger sizes, both regions can coexist. The electrostatic interaction region is dominated by the effects of the electric double layer, where ion transport is heavily influenced by electrostatic forces. In contrast, the free transport region is characterized by more traditional fluid transport, where the movement of particles or ions is less influenced by these electrostatic effects [283].

The balance between these regions in a nanochannel depends on its size. In smaller channels, the electrostatic interaction becomes more dominant, while in larger channels, the free transport region becomes more pronounced. This unique behavior in nanochannels is crucial for understanding and manipulating fluid flow and particle transport at the nanoscale, especially in applications such as nanofluidics, molecular sieving, and sensing [284].

The mass transfer $(J)$ in nanochannels, under conditions where both electrostatic interactions and free transport occur, can be described by the Nernst-Planck equation, which takes into account the effects of diffusion, migration, and convection. The Nernst-Planck equation in this context is typically written as Eq. 2 [285]:

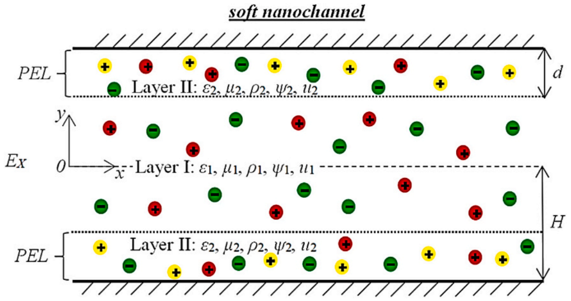


**Fig. 19.** Division of regions in the soft-charged nanochannel [284].

$$J(x) = -D\frac{\partial C(x)}{\partial x} - \frac{zF}{RT}DC\frac{\partial \varphi(x)}{\partial x} + C\nu_{e0}(x) \tag{2}$$

where, $\partial C(x)/\partial x$ represents the concentration gradient, $\partial \varphi(x)/\partial x$ denotes the potential gradient, and $\nu_{e0}$ is the electroosmotic velocity. The parameters $D$, $z$, and $C$ correspond to the diffusion constant, species charge, and concentration, respectively. The three terms on the right-hand side of the equation account for the contributions of diffusion, electrical migration, and mass movement (due to electroosmosis) during the mass transfer process. When an external voltage is applied across the nanochannel, the diffusion term, driven by the concentration gradient, becomes negligible in comparison to the other two terms [285].

The mass flux $(J_M)$ is related to both diffusion and the concentration gradient, while the heat flux $(J_Q)$ is influenced by the thermal conductivity and temperature gradient. Similarly, the electric charge flux $(J_E)$ depends on the conductivity and electric field. These relationships can be generalized as $J = LX$, where $X$ represents the applied force, $J$ is the material's response to this force, and $L$ is a second-order material property tensor. The flux is induced by the applied driving force.

In the context of nanofluidic channels, the three dominant driving forces are the external electric field, the hydraulic pressure difference, and the concentration gradient. Each of these forces drives the flow of ions or molecules through the membrane structure, with the interaction between the forces and the ions governing the movement. Beyond these conventional forces, light can also act as an additional driving source for ion diffusion, inducing a photovoltaic potential difference across the membrane [126].

The transport of hydrated ions through nanochannels is influenced by several factors, including the charge of the channel edge, electrostatic interactions between the channel and the ions, and steric exclusion effects. This transport occurs through a sequence of steps, which typically involve: (I) adsorption of hydrated ions to the channel edge, (II) dehydration of the ions due to the opposite charge of the channel edge, and (III) diffusion of the ions through the channel [286]. Consequently, ion transport is a complex process involving adsorption, dehydration, and diffusion within the channels.

The ionic flux is influenced by a combination of electrostatic interactions, the structural properties of the membrane (such as the channel height), and material characteristics, including the surface charge. A relationship is established to account for these factors, incorporating terms for electrostatic attraction, dehydration energy, membrane structure, and the specific properties of the ions (Eq. 3) [125]:

$$\begin{aligned} J = \sum LX + A\frac{q_{ion}q_{edge}}{r^2_{ion-edge}} + B\left(\exp\left(-\frac{\Delta G_d}{kT}\right) * \frac{q_{edge}}{d}\right) \\ + C\frac{1}{\sigma^n}\left[\frac{1}{\exp\left(\frac{1}{\sigma kT}\right) - 1}\right] + D\left(\frac{1}{\delta}\right)^m d^3 + En_v \end{aligned} \tag{3}$$

In this model, $q_{edge}$ represents the charge of the channel edge that first encounters the hydrated ion, while $q_{ion}$ denotes the charge of the hydrated ion. The term $r_{ion-edge}$ indicates the distance between the hydrated ion and the channel edge. As this distance decreases, the electrostatic attraction between the ion and the channel edge becomes stronger. Once this attraction exceeds a certain threshold, ion dehydration begins. The term $\Delta G_d$ represents the Gibbs free energy associated with ion dehydration. The surface charge density of the membrane is denoted by $\sigma$, and n is an integer that ranges from 2 to 5, depending on the experimental conditions, such as pH, ion concentration, and temperature. Additionally, the ionic flux can be expressed as a function of the membrane's structural properties, such as the height and thickness of the channel. In this equation, d is the channel height, $\delta$ is the membrane thickness, and D is a constant related to the membrane structure. The constant m is also related to the direction of flow; for example, in two-dimensional channels, m = 1 for flows perpendicular to the membrane and $m = -1$ for flows parallel to the membrane. For proton transport, oxygen vacancies play a significant role in enhancing proton conductivity, which is represented as $En_v$, where E is a constant and $n_v$ is the number of oxygen vacancies. Proton conductivity is directly proportional to the number of oxygen vacancies present.

## 8. Practical applications

Nanofluidic membranes have gained widespread application across various fields due to their nanometer-scale dimensions and unique properties. These membranes facilitate fundamental studies of surface phenomena at the nanoscale and enable the realization of advanced functions. Their applications span multiple domains, including biology, energy, electronics, and sensor technologies (Fig. 20), each of which is explored in more detail below.

### 8.1. *Nanofluidic membranes in biology and medicine*

Extensive research has been conducted on the use of nanopores for sequencing biopolymers, with biological nanopores demonstrating sufficient sensitivity to decode DNA sequences (see, Fig. 20). This is achieved by using polymerases to slow the passage of the DNA strand, effectively blocking flow and enabling precise sequence reading. This method has already led to practical, commercially available applications. While nanopore sequencing has been successfully demonstrated for RNA, decoding protein sequences remains a significant challenge due to the complexity of protein structures [24,287].

Nanopores are also capable of distinguishing between individual amino acids, peptides, and proteins, making them valuable tools for studying biomolecular interactions. They can be utilized to measure protein-ligand and protein-protein interactions in real time, providing insights into cellular processes and dynamics. Moreover, protein nanopores show promise as important biomarkers for assessing cell status and disease progression, offering potential applications in diagnostics and personalized medicine [288,289].

### 8.2. *Nanofluidic membranes in energy production and storage*

As shown in Fig. 20, another notable application of nanofluidic structures is energy generation [17,18,216,290,302]. A relatively new approach, known as reverse nanofluidic electrodialysis, utilizes passive ion transport through nanofluidic structures to harvest energy from salinity gradients. This method exploits the difference in Gibbs free energy between two fluids, harnessing the energy created by the variation in water salinity. Several studies have investigated osmotic energy extraction from salinity gradients across nanochannels, where the salinity gradient is converted into usable electrical energy. This conversion is facilitated by the high surface charge of the nanochannels, which imparts selectivity and enhances ion transport. In reverse electrodialysis, asymmetric nanochannel shapes and surface modifications are employed to regulate ion flow across the membrane, optimizing the energy extraction from the salinity gradient [291,292].

Light is also emerging as a promising driving force for remote, noninvasive, and active control of molecular and ionic transport in solid-state nanochannels. Recent advancements in nanofluid photoelectric conversion have attracted significant attention. In nature, solar energy is harvested primarily in two ways: via photosynthesis in green plants, which involves light-induced charge separation, and by archaea such as *Halobacterium halobium*, which utilize photoisomerization [293,294]. Both methods rely on the transfer of protons from low to high concentrations to create an electrochemical potential, which powers various biological processes. Mimicking this process, researchers have focused on developing light-activated artificial ion pumps for active ion transport, particularly protons. Notably, the first light-activated artificial ion pump was constructed using a conical polyethylene terephthalate nanochannel. One advantage of solid-state nanochannel-based ion pumps is the ability to easily connect devices in series or parallel, thereby amplifying their ionic current or voltage output [295,296].

In addition to osmotic and light energy, energy generated by conventional mechanical motions presents a cost-effective and environmentally friendly alternative. Electrokinetic energy conversion can be achieved using two-dimensional nanofluidic membranes with electrically charged surfaces, where electrolyte flows under applied pressure to generate electrical energy in the form of current and voltage. Moreover, the self-induced capillary pressure by capillary action and water evaporation can be used to generate electrokinetic energy through a nanofluidic membrane [303,304]. As society rapidly advances, the demand for sustainable energy sources has become increasingly urgent. Lithium batteries, known for their high energy density, have garnered significant

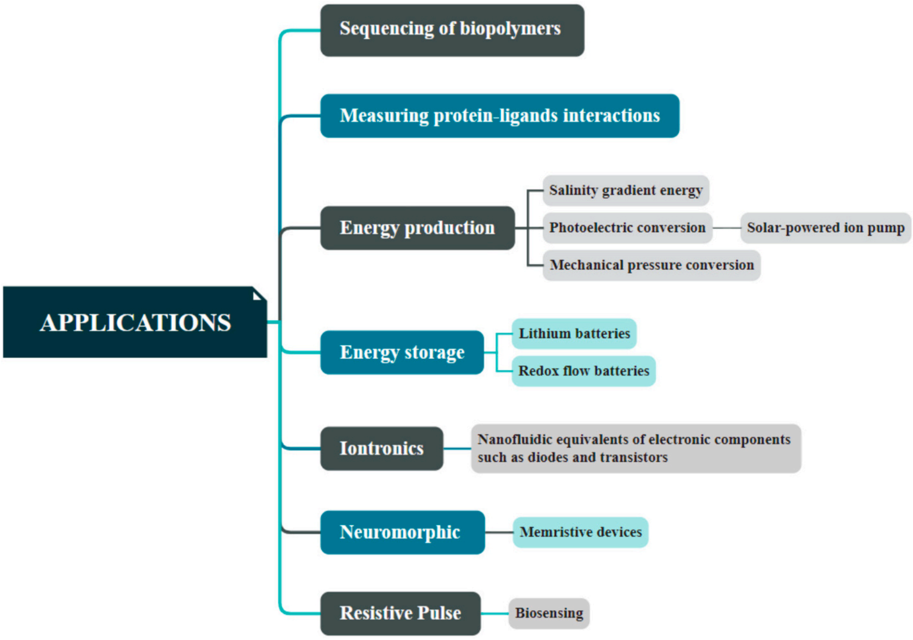


**Fig. 20.** Overview of some applications of nanofluidic membranes [287–301].

attention. Battery electrodes and separators based on two-dimensional layered membranes enable fast, selective ion transport, efficient energy storage, and long-term structural integrity, benefiting from surface engineering modifications [297].

Replacing fossil fuels with renewable yet intermittent energy sources, such as solar and wind, necessitates the development of large-scale, long-term energy storage technologies. Redox flow batteries (RFBs) are promising candidates for large-scale energy storage, offering scalability, high power density, long operational life, low maintenance, and non-flammability in aqueous electrolytes. However, a key challenge in advancing RFB technology lies in the development of low-cost, high-performance separators. The most critical requirements for RFB separators are high ionic conductivity and cost-effectiveness. Two-dimensional nanofluidic membranes offer highly efficient ion-selective transport, making them ideal for separating positive and negative reactants in RFBs, a crucial factor for the advancement of these energy storage systems [298].

Industrial and pilot-scale translation is most advanced for salinity-gradient energy conversion via reverse electrodialysis (RED), where ion-selective membranes are assembled into large-area stacks to harvest electrical power from river/seawater or brine/seawater mixing. Notably, RED has progressed from laboratory stacks to field/pilot demonstrations, including the Afsluitdijk (The Netherlands) blue-energy pilot in which fresh and seawater streams were used to validate operation under realistic conditions. More recent techno-economic and system-level studies have addressed deployment scenarios relevant to existing water infrastructure—e.g., coupling RED to desalination plants by exploiting high-salinity brine streams—highlighting pathway(s) toward improved capacity factors, reduced balance-of-plant costs, and better overall economics. These examples demonstrate that nanofluidic mechanisms discussed in this review (ion selectivity, mitigation/control of concentration polarization, and surface-charge–governed transport) are directly aligned with practical engineering bottlenecks in real systems, including fouling control, long-term stack stability, and performance standardization at scale [305].

### 8.3. *Nanofluidic membranes in electronics*

Nanofluidic devices are also being explored for the design of ionic counterparts to electronic components such as transistors and diodes, as shown in Fig. 20. This emerging field, often referred to as iontronics, holds the potential to create ionic devices with advanced functionalities that could rival their electronic equivalents. By leveraging the inherent asymmetry and surface charge in nanofluidic systems, various types of nanofluidic diodes have been developed. These diodes can be connected in series or used to form fundamental iontronic circuits, demonstrating the potential for ionic current control in device configurations. In addition to nanofluidic diodes, significant progress has been made in constructing nanofluidic transistors, where ionic conductivity is modulated by a third electrode, known as the gate [299].

Another promising development in this field, drawing inspiration from both neuroscience and electronics, is the concept of brain-inspired nanofluids, or neuromorphic nanofluids, which rely on ionic memory effects. Memristive devices, which exhibit memory behavior, can store and process information within a single component. In electronics, memristive devices are integrated into artificial neural networks to perform complex computations such as image processing and pattern recognition. Ionic neuromorphic systems, based on nanofluidic memristors, more closely mimic biological processes than their electronic counterparts, as biological systems use ions to process and transmit information [300]. Notably, in 2023, neuromorphic nanofluids made substantial strides, with low-voltage memory effects being successfully demonstrated using simple ions in activated carbon nanochannels to simulate synaptic behavior, offering a more biologically inspired approach to information processing.

### 8.4. *Nanofluidic membranes in sensing*

As can seen in Fig. 20, another well-documented phenomenon in single-pore nanochannels is the partial or complete blockage of the pore by molecules or particles [306,307]. By monitoring these blockages and performing a thorough statistical analysis of the data, it is possible to estimate the size and number of molecules in solution. This technique, known as resistive pulse sensing, was originally developed for biosensing applications with micropores in the Coulter counter, a method that remains widely used in biochemical assays today [301,308].

### 8.5. *Nanofluidic membranes in water treatment and resource recovery*

Although many nanofluidic membranes remain at the proof-of-concept stage, several technology directions have already demonstrated practical relevance for water treatment through either commercial traction or pilot-scale validation.

(i) Biomimetic water-channel (aquaporin-based) membranes for water and wastewater processing. Biomimetic membranes incorporating aquaporin water channels have advanced beyond fundamental demonstrations toward application-driven testing and early commercialization, motivated by the potential to combine high water permeability with competitive solute rejection. Recent work has evaluated aquaporin-based biomimetic forward osmosis membranes for realistic water matrices (e.g., greywater), explicitly addressing operational parameters and performance stability under practical conditions. In parallel, industrial activity has continued to report membrane-product development, customer-case validation, and pilot-scale progress for aquaporin-based membrane platforms, underscoring the relevance of bioinspired nanochannels to real-world treatment workflows [309].

(ii) Scalable 2D nanochannel membranes (e.g., graphene-oxide laminates) for industrial effluents. Beyond biomimetic channels, stacked 2D laminates provide a manufacturable route to dense nanochannels with tunable interlayer spacing and surface chemistry, which are central design levers in nanofluidic separations. Importantly, pilot-scale/longer-term evaluations have been reported for ultrathin graphene oxide membranes treating real industrial wastewater (e.g., dyehouse effluent), demonstrating practical purification performance and operational stability trends under extended operation. Such examples illustrate how nanochannel-engineering concepts (confined transport, charge effects, and spacing control) can be implemented in scalable membrane formats relevant to industrial water treatment [310].

Collectively, these case studies complement the broader application overview by explicitly linking nanofluidic mechanisms to real deployment constraints—module fabrication, stability/cleaning tolerance, fouling under complex feed waters, and the need for standardized testing—thereby strengthening the practical relevance of nanofluidic membranes to water treatment and energy-related industries.

### 8.6. *Nanofluidic membranes in ion pumping*

Beyond passive ion transport and energy harvesting, nanofluidic membranes have recently enabled active ion pumping, in which ions are driven directionally against concentration gradients by external energy inputs. Such behavior is reminiscent of biological ion pumps and is of particular interest for bio-inspired energy conversion and nonequilibrium transport systems. A representative example was reported by Nie et al. [311], who demonstrated light-powered ion pumping in a cation-selective conducting polymer membrane based on polystyrene sulfonate–doped polypyrrole. In this system, asymmetric visible-light irradiation generates a built-in electric field across an otherwise geometrically symmetric membrane, enabling surface-charge–governed cation transport against a concentration gradient. This work illustrates how nanofluidic membranes combining selective ion transport with photoresponsive electronic properties can function as artificial ion pumps, thereby extending nanofluidic applications from passive separation to active, energy-driven transport.

## 9. Scalability and commercialization

For nanofluidic applications in fields such as purification, desalination, resource recovery, bioelectronics, and energy harvesting, scalability strategies are essential for eventual commercialization. Not all nanofluidic platforms are inherently scalable, and many serve as model systems to explore the fundamental mechanisms of nanofluidic phenomena. These model systems provide critical insights that can inform the development of scalable platforms using more widely available and established materials in the future.

The knowledge gained from nanofluidic studies can be translated to larger-scale platforms, typically at the centimeter scale, that are designed either to directly replicate the architecture of laboratory-scale research units or to incorporate the relevant transfer mechanisms into a scalable framework. The evaluation of these multichannel platforms necessitates additional physical analyses to assess factors such as interchannel interactions, input resistance, and electrode saturation. Once these technical challenges are addressed, it will be possible to manufacture membranes at an industrial scale, taking into account key factors such as production and operational costs, durability, and the environmental impact (e.g., carbon footprint), which must remain competitive with existing technologies.

Notable commercial successes in this area include DNA sequencing technologies and biomimetic membranes inspired by aquaporins. The commercialization of membranes based on artificial water channels is also in progress. Membranes made from two-dimensional materials, such as graphene oxide, hold significant promise for centimeter-scale ion screening, which is crucial for advanced desalination applications. To achieve effective ion exclusion, it is critical to control the spacing between the two-dimensional layers, enabling spatially controlled ion exclusion. This enables tunable ion screening, where membranes with the smallest interlayer spacing (approximately 6 Å) can exclude all ions. However, these compact membranes do not yet exhibit sufficient water permeability for practical applications, and large-scale desalination technologies based on nanomaterials are still in the developmental stages.

Two-dimensional monolayer materials with zero-dimensional pores, such as porous graphene, are also being scaled from proof-of-concept models at the micrometer scale to centimeter-scale devices. High-quality monolayer graphene produced through chemical vapor deposition is now commercially available, with continuous roll-to-roll production capabilities that have reached a capacity of 100,000 $m^2$ per year. Additional successful efforts have been made to scale zero-dimensional and artificial channel membranes to the centimeter scale, including the development of protein nanosheets or artificial water channels embedded in block copolymers and the construction of layer-by-layer membrane structures.

## 10. Challenges in nanofluidic membrane development

In recent years, significant advances have been made in the development of nanofluidic membranes. However, several challenges remain, particularly in the creation of artificial membranes that exhibit excellent biological performance. These membranes must be able to respond dynamically to both external and internal conditions while maintaining their functional state. Additionally, the mechanisms governing water and ion permeability in nanofluidic membranes remain poorly understood. The antifouling performance of these membranes is also not well-defined in terms of power density, water permeability, or ionic conductivity. Efforts to increase ionic flux often involve the use of multiple arrays of nanochannels or nanopores and modifications to surface charge properties. However, these strategies often require complex fabrication processes or chemical modifications, which can be limited by material availability.

Moreover, materials commonly used for fabricating nanochannels and ion-etched nanoporous membranes are typically restricted to silica and organic polymers. For ionic current measurements, patch clamp amplifiers are commonly employed due to their high current accuracy, which is particularly beneficial for measuring very small currents in the sub-picoampere range. However, this high precision comes at the expense of a limited dynamic range, typically up to 100 *nA*. Currently, no widely available, open-source software package exists specifically for nanofluidic data acquisition, which complicates reproducibility, especially when working with small or incomplete datasets. Furthermore, the development of phenomenological models based on sparse data increases the risk of misinterpretation [312].

Another significant limitation in nanofluidic experiments is the complex fabrication process required to produce single- or multi-channel membranes. This typically involves multiple steps, each with a high risk of failure and often necessitates advanced microscopy or clean room techniques. Fabrication methods such as lithography can expose researchers to radiation or chemical hazards and require specialized training. Controlling the geometry and surface functionality of nanofluidic membranes, especially as the dimensions approach the atomic scale, remains challenging. The precise geometry of nanofluidic channels is often poorly defined due to limited fabrication precision, and identification methods generally rely on averaging techniques. Wetting is a common issue in nanofluidics, as nanoscale bubbles can become trapped in the membrane, obstructing fluid pathways and resulting in initially low conductivity. Experimental techniques such as soaking the membranes in water for extended periods or prewetting with ethanol can help to disperse these bubbles and restore fluid flow. These trapped bubbles have also been identified as a source of nonlinear behavior, further complicating experiments [313].

Additionally, many nanofluidic models assume that the membrane does not deform under applied forces. However, several studies have reported reversible deformations during use, either due to applied voltage or water evaporation. While this represents a limitation, it also offers an exciting avenue for further exploration.

These challenges highlight the need for continued research and development to improve the materials and technologies used in nanofluidics. The fabrication of nanofluidic membranes with uniform diameters below 10 *nm* and ultrathin channels (approximately 100 nm in thickness) remains a difficult goal to achieve. Furthermore, the fundamental theory of ion transport needs further development to explain and realize the ability of ultrafast ion transport in biological ion channels at the nano and sub-nano scale [45].

## 11. Summery and outlook

Nanofluidic membrane technology, which leverages nanochannels and nanopores to precisely control the flow of ions and molecules, is one of the most advanced and promising areas in membrane science. This technology holds significant potential for diverse industrial applications due to its unique capabilities in selective separation, enhanced mass transfer efficiency, and reduced energy consumption. In the coming years, the development of nanofluidic membranes is expected to expand into key fields such as water purification, gas separation, and energy storage. With advancements in nanochannel engineering, improvements in ion and molecule selectivity, and increased mechanical stability, it will be possible to design more efficient separation systems with optimized energy consumption.

The application of nanofluidic membranes in energy production, particularly in fuel cells, is expected to play a crucial role in advancing clean and sustainable energy technologies. Over the past two decades, the field of nanofluidics has evolved significantly, from the creation of the first nanopores in silicon nitride to applications in biopolymer sequencing, purification, energy harvesting, and neuromorphic logic circuits. While fundamental understanding is still developing, nanofluidics is entering a more mature phase that emphasizes standards of transparency, reproducibility, and scalability. This transition is crucial for bridging the gap to commercial applications.

The progression of nanofluidics toward practical implementation is being facilitated by several key advancements including reducing barriers to entry in nanofabrication, establishing standardized measurement protocols, developing new model systems for greater control over pore geometries and surface properties, constructing advanced computational approaches for modeling nanofluidic systems, and enhancing standards for representing nanofluidic data.

As these technologies mature, high-performance nanofluidic devices are expected to be produced on scalable platforms, enabling the development of smarter membranes for desalination and osmotic energy harvesting. Complex computational systems, with multiple devices and strategically placed electrodes, will allow for precise tuning of ion transport and the implementation of advanced computational tasks.

Nanofluidic applications are moving closer to real-world relevance, with the potential to revolutionize various industries. While the development of prototypes and large-scale products may be gradual, the insights gained from nanofluidic research are already influencing industrial designs. As the field matures, its impact on membrane performance and real-world applications is expected to grow substantially, driving innovations that could significantly improve energy efficiency, resource management, and environmental sustainability.

## CRediT authorship contribution statement

**Seyed Nezameddin Ashrafizadeh:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Li-Hsien Yeh:** Writing – review & editing, Supervision, Resources, Funding acquisition. **Mahdi Khatibi:** Writing – review & editing, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Parmida Shahhoseini:** Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Ya-Chun Li:** Visualization, Software, Data curation.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Data availability

Data will be made available on request.

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