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Artificial Water Channel - Progress, Innovations and Prospects

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Abstract: The design of artificial water channels is aiming to mimic natural proteins that effectively mediate the selective transport of water across the bilayer and artificial polymeric membranes. Currently, impressive progresses on synthetic backbones, including self-assembled channels, helical unimolecular and other functional organic molecules have been made to provide artificial alternatives, furthermore applying in real systems for promising product development. In this review, several synthetic channels exploited during last few years were summarized according to their backbone architectures for water transport and ion transport respectively, showing their potentials as natural transporter analogs and their importance of artificial water channels for industrial environmental or medical applications.

Keywords: Artificial water channels, self-assembly, I-quartet channels, pillararenes, aquafoldamers, water desalination.

Introduction

Nature creates protein channels that enable to effectively transport molecular and ionic species with high selectivity through the cell membrane.¹⁻⁴ As a benchmark for water transport, natural aquaporins (AQPs) are enable to effectively facilitate water flow among intracellular and extracellular and selectively transport water against other ionic or molecular solutes. The channel selectivity is believed to correlate with aromatic/arginine (ar/R) region, as well as Asn-Pro-Ala motifs in the narrowest center of pore, where it plays an important role in solutes transport process as a selective filter.^{5,6} It has been showed that the transmembrane selectivity it is attributed to not only to specific charge interactions or water dipole inversion along the protein channel,⁷ but also to the continuous lifetime and collective hydrogen bonding of single waterwires within its dimensionally adapted selectivity filter with a size of 2.8 Å, which is slightly bigger than a water molecule (2.5 Å).⁸ The transport performances as high permeability per channel and perfect water vs. ion selectivity made increasingly promising to use aquaporins as selective components into reverse osmosis membranes for water purification or desalination. The multiple steps for the large-scale proteins production and purification have been experimentally solved, however still brings a series of challenges on recovery rate, protein activity and reasonable per surface area permeability, as it is well known that the liposome embedded AQPs density on membranes surfaces is not well balanced when compared with smaller synthetic counterparts.⁹ Another main limitation of AQPs is their low resistance to high pressure and high salinity used for sea water desalination. However, their structure of the AQP can provide many useful information. Nature should provide answers on how to construct artificial biomimetic channels for an efficient desalination. Inspired by these natural fine crafts, the discovery of artificial water channels^{10,11} have attracted the researchers' attention for a broad range of application including water desalination and medical disease treatment. By tailoring the channel molecular components, it is possible to acquire the desired alternatives for mimicking or even surmounting performances of natural transporters.

Importantly when AWCs are designed to mimic AQPs, they should not only possess AQP-like permeability but also exhibit AQP-like selectivity or salt rejection. Most of the AWC channels described in literature present both important water and ionic salt fluxes, so they cannot be called as AWCs. Because they are not selective over NaCl or KCl such channels are useless for desalination membrane development. The permeability and selectivity should be measured in the presence of competitive osmolyte, such as KCl and NaCl.^{12,47}

We have pioneered this field: the very first biomimetic the self-assembled I-quartet water channel has been discovered by our group in 2011,¹⁰ shortly followed by hydrazide appended pillar[5]arene unimolecular channel proposed by Hou et al.¹¹ Then the term of "*Artificial Water Channels*-AWCs" has been coined in independently by Barboiu¹² and Hou¹¹ groups. After, the field was continuously growing.¹³⁻¹⁶ A prestigious Faraday Discussion Meeting on AWCs was held in Glasgow in 2018 and it was chaired by Professor Barboiu, emphasizing the importance of the newborn field with enormous perspectives in environmental, energy and medical sciences. A dedicated book and an impressive number of papers have been published.¹³ The main actors in the field discussed and summarized the development situation and research direction of this new born field and Professor Gong presented a meeting paper on "Artificial water channels: inspiration, progress, and challenges.¹⁶

For instance, as one of the exceptional mimics of aquaporins, single channel carbon nanotubes have a hydrophobic hollow seamless tubular structure which present relative low friction of water molecules and high salt rejection, this provides a possibility to facilitate water flowing through inner channels.¹⁷⁻¹⁹ Increasing the water-water specific interactions results in the formation of clusters, that increase the transport selectivity of transient dynamic water superstructures. Within this context, the concept of engineering such inner pore-water interactions is clearly important, as it is considerably expanding the number of choices for the innovative design of the future biomimetic membranes embedding AWCs for specific applications. Improvement of the design of artificial channels, it is worth noting that minor changes of structure along the channel at the angstrom scale can result in selective improvements of transporting performances.¹⁵

Nowadays, most of synthetic artificial water channels are hybrid consisting of polar and nonpolar regions, reminiscent of the inherent nature of channel proteins, assisting solutes to pass through the hydrophilic and then hydrophobic cell membrane regions. With regard to the polar region, the hydrogen bonding among channel-channel or channel-water/ion or water-water is regarded as a vital factor for discussing channels' selectivity and permeability, which involves the stabilization of channel scaffolds and translocation of water/ion molecules in the channel interior as reported in the literature.^{15,20,21} So, an important question that came out is: *can the synthetic artificial water channel alternatives keep the unique permeability-selectivity balance for applications*? Despite impressive developments during the last decade there is still an important limitation related to permeability-selectivity trade off and there is a need in Artificial Water Channels innovation.

In this minireview, we aim to highlight the recent advances of artificial water channels and present their performance toward water transport through single channels and multichannel polymeric membranes as well as their selectivity toward the rejection of protons or ion transport. Instead of listing all the channels comprehensively, this minireview is trying to outline the latest relevant examples based on self-assembled channels, unimolecular channels, committing to arouse more potential options for environmental applications¹² and biological trials⁴⁷.

Adaptive self-assembled artificial water channels

The cumulative understanding of the structure and functional behaviors of the aquaporin channels has provided the foundation for exploring synthetic artificial water channels, and developing suitable membranes for selective single channel water transport^{22,23} and desalination applications.²³⁻²⁵ During the last few years, the hydrogen-bonded amphiphilic molecules have provided interesting and multiple possibilities to design performant artificial water channels^{25–27}. In our group, we proposed alkylureido-imidazole compounds,^{10,22,23} that form I-quartet selfassembled supramolecular pores, filled with single water wires having a diameter of 2.6 Å, which is exceedingly close to that of AQPs (Figure 1a,d). With the tubular I-quartets, waterassisted formation of the superstructure is obtained through imidazole-imidazole CH---N and imidazole-water N---H-O, and NH---O-H H bonding interactions between four imidazole and two water molecules. The I-quartets are alternatively oriented in lamellar phases and orthogonally stabilized via successive unidirectional urea ribbons. The appended alkyl chains are positioned in the interdigitated and or face-to-face conformations, wrapped around I-quartets. The variation of their size, from butyl to octadecyl C4-C18 tails induce a progressive and stronger stabilization of the I-quartet single-channels within the bilaver membranes.²³

The net permeabilities show a continual increase when the tail of Cx became longer and they are not only related to a higher solubility of former monomers in bilayer membranes (Figure 1b). The single-channel water permeabilities, P_s constantly increase for higher alkyl tails, reaching values of 10⁷ waters/channels/s for the longer ones, one order of magnitude lower than AQPs. A sharper increase of P_s for the longer **C8-C18** tails compared with the shorter **C4-C8** tails (**Figure 1c**) generating I-quartets with higher stability, reminiscent with the synergetic hydrophobic stabilization of percolated conducting channels via stronger self-assembly.



Figure 1 (a) Structure of alkyl-ureido-imidazoles used for I-quartet self-assembly *via* H-bonding. *Adapted with permission from Reference* [10] *Copyright* © 2011, *Wiley-VCH*. (b) Net and (c) single channel water permeabilities of I-quartets through lipid bilayer membranes as a function of the lipophilicity (log P) of the former C4-C18 components. *Adapted with permission from Reference* [23] *Copyright* © 2021, *ACS publications*. (d) Top and lateral view crystal packing of I-quartets confining oriented water-wires within 2x12 channel system. (e) Permeation events distribution in the plane of the membrane (left panel) and water conductance per channel (right panel)) for a system of 2x12 channels. (f) Averaged water conductance accounted for in central channels with respect of (f) the mean pore radius and (g) the mean number of hydrogen bonds of

water molecules. Adapted with permission from Reference [26] Copyright © 2021, AIP publishing.

In order to study the up-scaling effect from single channel permeability toward of the membraneembedded I-quartet crystalline-patches, a series of crystalline aggregates have been generated *via* MD simulations. For a 2x12ch system (**Figure 1d**), the water transport presents an alternation of neighboring conducting channels with non-conducting ones (**Figure 1e**). The correlations among permeation events and average pore radius (**Figure 1e**) or hydrogen-bond connectivity inside the pores (**Figure 1f**) showed that low permeation events are occurring through narrow channels with water molecules mainly organized in a single file wire. In these structures, as well as in nonconducting channels, each water forms on average 3.46 hydrogen bonds, a connectivity similar to a water molecule in bulk solution. The medium permeation regimes occur when the pore radius exceeds ~ 1.34 Å, while the high conductance regime is associated to larger pore radius of ~ 1.45 Å, resulting in single channel permeability on the order of $3 \times 10^7 H_2O/s/channel$.

The large fluctuations are accompanied by the local breaking of the single-file water wires, enabling water molecules to make exclusive contact with the channel walls at the expense of the contact with the other water molecules within the channel. It leads to an increased number of waters in the channel, with a decreasing H-bonding connectivity. Furthermore, the transition from "medium" to "high" state of permeation arises when some channels stop conducting on the dispense of the other ones becoming highly permeable. This adaptive behavior of such dynamic aggregates suggests a strong coupling between the transport activity of two adjacent channels: the larger one that allows for high permeability constrains the next neighboring one to a lower transport activity.

Hydroxyl, is one of the simplest organic moieties that might form both donor and acceptor hydrogen bonds and, in the meantime, has a natural affinity with water molecules. We then concentrated our studies toward hydroxy heads that may self-assembled in so called **OH** channels, presenting tetrameric motifs with a pore size of around 2.7 Å.²⁷ **OH** channels of ureido- derivatives (**Figure 2a,b**), which upon grafting with different hydroxy moieties using ethanol, propanediol and trimethanol gave excellent AQP-level single-channel permeability of 2.33×10^8 H₂O/s. In contrast to I-quartet, the extremely low proton permeability makes **OH** channels stand out, achieving selective water transport through donor-acceptor H-bonding interactions.



Figure 2. (a) Structure and self-assembly of octyl-ureido-polyols forming OH channels. (c) Molecular dynamics simulation of OH channels (left) a crystal patch arrangement (center) sponge-like structure and (right) cylinder-like membrane-spanning channel. Adapted with permission from Reference [27] Copyright © 2021, ACS publications. (f) Simulation of water chains formed within the different porous organic cages (POCs) nanoaggregates embedded within the lipid bilayer membranes. Adapted with permission from Reference [30] Copyright © 2020, Springer Verlag

The OH channels are very adaptive systems. We may equate that they may form impermeable crystalline patches (**Figure 2c**) or medium permeable sponge like channels architectures (**Figure 2d**) or high permeable cylindric pore (**Figure 2e**) constructs are stabilized in the bilayer membrane. The dynamic H-bonding leads to the specific channel superstructures in a membrane function of the concentration of the monomers. It generates variable adaptive transporting pathways through the transient water clusters stabilized *via* H-bonding to hydroxyls.

Similar trend were observed for I-quartet sponge channels,²⁸ **PAH[4]** channels²⁹ or porous organic cages (POCs)³⁰ predicting orders of magnitude higher permeabilities in such sponge like channels structures. Zhao et al. reported zero-dimensional porous organic cages (**POCs**), showing fast and selective water transporting with a single permeability value of 10^9 H₂O/s. POCs channels with variable pore window size, structural rigidity alternating hydrophobic/ hydrophilic regions are perfect candidates to form water H-bonded networks determining high water permeation and low ion diffusion (**Figure 2f**).³⁰ POCs systems can be easily processed into composite membranes for specific desalination applications.³⁰



Figure 3 (a) Molecular structures and X-ray crystal structures of the amino-triazole (T) amphiphiles and their protonated anion binding counterparts. (b) Chemical structures of amino-imidazole (**Imu**) amphiphiles. *Adapted with permission from References* [31, 32] *Copyright* © 2019, 2020, Wiley-VCH.

The insertion of ions with confined water clusters confined within OH channels, impede and interrupt the continuous H-bonding, relying with very low ion permeation events. The use of more electronegative protonated amino-trizole(T) amphiphiles led to the construction of in selective self-assembled anion channels.

They form columnar superstructures by means of multivalent anion-water recognition of triazole quartets instead of only water molecules (**Figure 3a**). Two anions are necessary to generate channel superstructures through synergistic hydrogen bonding/ion pairing within this design.³¹ While a series of self-assembled amino-imidazole (**Imu**) amphiphilies channels displayed Cl-water transporting ability via synergetic translocation events (**Figure 3b**). A synergetic regulation by pH and voltage was fully investigated, and verifying the inner water molecule-Cl binding configurations within channels, corresponding to the Cl⁻/H⁺ symport via [H₂O Cl⁻] wires in acidic condition and a Cl⁻/OH antiport via [OH⁻ H₂O Cl⁻] wires in basic condition.³²

Unimolecular and self-assembled pillararene water channels.

Pillar[n]arenes aromatic macrocycles have been discovered by Ogoshi in 2008.33-35 Other macrocyclic backbones have been extensively used during the 80' as central relays in the construction of specific unimolecular channels.^{36,37} In their pioneering work of Hou et al. first used pillararenes as central relays and such rim-functionalized pillararenes form water-filled channels with encapsulated water wires used for the proton transport (Figure 4a).^{38,39} Then the field continuously developed and several review has been published during the last decade.^{21,40,41} Importantly in 2012, Hou and co-workers made an important step forward, by reporting the first pillar[5]arene-based unimolecular artificial transmembrane water channel.¹¹ The introduction of hydrazide chains on both sides rims of pillar[5]arenes, results in the formation of tubular superstructures with a length close to the thickness of lipid bilayer having the potential to translocate water across membrane. The crystal structure shows a tubular cavity with four entrapped non-interacting water molecules; consequently, the proton is blocked due to the absence of un-continuous water wires (Figure 4b). Shortly after, Hou et al optimized the rimfunctionalized pillar[5]arene superstructures in order to significantly improve the water translocation and membrane insertion properties of peptide-appended pillar[5]arene (PAP) with D-Phe-L-Phe-D-Phe-COOH chains (Figure 4c).^{42,43} It was found that their water permeability is 3.5×10^8 water/channel/s, while the ionic rejection requires further improvement, as they cannot block the influx of salts and other small solutes. Importantly, these peptide-appended pillar[5]arene (PAP) can also self-assembly into two-dimensional arrays in cm² scaled membranes, that need further engineering for the application of PAP artificial water channels in water purification at industrial scale.⁴⁴ In order to reduce the channel-aperture and make more selective the pillar arene backbone as transporting cavity, peptide-appended hybrid[4]arenes

(PAH[4]s) channels were developed by attaching eight D-L-D phenylalanine tripeptides (triPhe) chains to pillar[4]arene backbone, displaying AQP-level single channel water permeability with a value of $>10^9$ H₂O/s/channel through bilayer membranes.⁴⁵ Our group together with Ogoshi group studied the water transport performance of a class of self-assembled channels, *per*-alkyl-carboxylate-pillar[5]arenes dimers, which present a narrow constriction pore for transporting $\sim 10^7$ H₂O/s/channel.⁴⁶

A tremendous scientific advancement of pillar arene artificial water channels is related to their possible successful application in medical applications by replacing the natural AQPs. Hou et al. studied the potential of pillar[5]arene based artificial aquaporin (**Figure 4d, left**) in restoring wound healing of cells containing impaired AQPs. The obvious wound edge migration was observed after treating cells with channel **1** (**Figure 4d, right**), and compared to blank sample it demonstrated the bilayer-incorporation ability and water permeability of the channel can rival those of AQPs.⁴⁷



Figure 4 (a) X-ray single crystal structure of tubular pillararenes confining water wires. Adapted with permission from Reference [39] Copyright © 2011, Wiley-VCH. (b) Side view of PAH channel and its crystal structure. (c) Chemical structure and MD simulation of PAP self-assembling nanopores. (d) Chemical structures of artificial AQP and the wound edge migration experiments. (e) Chemical structure of channel **1a-c** and its voltage-driven K⁺ flowing with introverted conformations **S1-S2**. Adapted with permission from References [11, 42, 44, 47, 52, 53] Copyright © 2012, 2013, 2018, 2020, 2021, ACS publications, Springer Nature Limited and Wiley VCH.

Pillararene tubular transmembrane channels with terminal positive amino groups displays a strong ability to insert into lipid bilayers. Their high affinity for lipid bilayers led to highly efficient mammalian cell membrane insertion and an effective activity against HepG2 cancer cells.⁴⁸ On the same line Hou's group have reported a unimolecular peptide channel for potassium transport, consisting of NH_3^+ and CO_2^- ends as a nano-diode to maintain a β -helical conformation.⁴⁹ The authors found that the insertion orientation of negative C-end made a great difference to channel conditions, showing an outward-preferred manner. The ion rectifying behavior toward K⁺ transport was investigated at the macroscopic level, this is reminiscent of natural ion channels conducting ions directionally.⁵⁰ Recently, they synthesized a class of rigid peptide-appended bis-resorcin-arenes, achieving a reversible ligand-gating behavior through molecular recognition.⁵¹ It is of remarkable interest of that the binding and releasing of host bis-resorcin-arenes to guest peptide chains can control the off and on of transmembrane channels.

Apart from that, they built a voltage-sensitive zwitterionic channel based on pillar[5]arene backbone (**Figure 4e, left**) to mimic the natural alamethicin channel, displaying a directional alignment in the lipid bilayers as well as the rectifying behavior for potassium transport.⁵² Furthermore, they found that containing introverted groups onto pillar[5]arenes backbone (**Figure 4e, right**) enables the obtained unimolecular channel to present the longest channel opening duration time. Differently to highly membrane oriented natural channel for which the opening duration time is quite short with no effect on their transport efficiency, the correct orientation of the artificial channels through the bilayer membrane is determinant and is highly correlated with the longer opening durations times. This recent work by Hou et al. indicates the greater importance of channel opening duration than ion transport rate for the assessment of transport activity.⁵³

Foldamers and aromatic polyamide macrocycles as highly performant water channels

It is believed that a narrow spatial cavity is indeed necessary for water permeation, which can be defined through bottom-to-up self-assembly of synthetic circular⁵⁴⁻⁵⁶ or open folded^{57,58} molecules. When it comes to polymers, more intuitive tubular structure can be obtained through one-pot polymerization, for example aromatic amide foldamers containing a helically folded backbone driven by intramolecular hydrogen bonds and π - π stacking forces.⁵⁶⁻⁵⁸ Within this context Gong et al. have discovered a self-assembled tubular using m-oligophenylethynyl (**OPE**) macrocycles grafted six secondary amide side chains.⁵⁹ Beyond this, further study on tailored macrocyclic penta-amides suggests the remarkable high-affinity ion binding could attribute to both matched sizes and strong hydrogen-bonding inside the shape-persistent macrocycles **c5** (**Figure 5a**).⁶⁰



Figure 5 (*a*) 5-amino-N-acylanthranilic based Macrocycle **c5** and the crystal structure of **c5c**. *Adapted with permission from Reference* [60] *Copyright* © 2022, *Creative Commons.* (b) Chemical structure of hybrid macrocycle for self-assembling nanopore. (*c*) The illustration of

water-induced self-assembly of amphiphilic discotic molecules. *Adapted with permission from References* [61, 62] *Copyright* © *2021 ACS publications.* Additionally, there is a shape-persistent macrocycle (**Figure 5b**) with hydrophobic-hydrophilic lumen displaying columnar stacking. It is intented to emphasize the effect of alkali metal ions on obstructing water transport, and offering a possible path for controllable water transport.⁶¹ Wang's group have designed a sort of amphiphilic discotic molecules (**Figure 5c**), as it came into contact with water, the self-assembled channels were orientated gradually.⁶² Interestingly, they found dehydrated **ADM** has no water transport performance which indicated that water as orientation-directional guest molecule is necessary for governing the well-aligned channel growth.

Foldamers identified as potential mimics of natural proteins, have been proposed as exceptional candidates for water/ion/proton transport through bilayer membranes.¹⁶ The pyridine/oxadiazole-foldamers, first reported by Dong and Liu are based on polymers with a rigid aromatic backbones that adopts a helical conformation containing inner pores of a defined size.⁶³ Polymer chains with a narrow molecular weight distribution and a length that allows the helices to span the lipid bilayer were separated by fractionation and found to serve as effective transmembrane channels. ⁶⁴ Pyridine/oxadiazole-based foldamers with a pore aperture of 2.7-3.8 Å showed an extremely high K⁺/Na⁺ selectivity of 20-30 in **Figure 6a**, ^{65,66} while the phenanthroline-oxadiazole units with a pore aperture 2.3 Å with and extremely high transport activity (EC₅₀ = 0.017 mol % relative to lipid) and a Na⁺/K⁺ selectivity of 1.9 (**Figure 6b**).⁶⁷ Similar aromatic foldamer- pyridine/ oxadiazole-based channels reported later-on by Zeng et al. present exceptionally high K⁺/Na⁺ selectivity of 16.3 under voltage shock.⁶⁸

Zeng's group has formulated a several classes of amide foldamers as water channels-pyridinebased helical channels which contain 'sticky ends' as shown in **Figure 6c**,^{69,70} driven by the electrostatically complementary functional groups at two helical ends. Thanks to POCl₃ as the polymerization agent,⁷¹ they have obtained a one-pot polymeric foldamer having a sizable diameter 2.8 Å and the length of 2.8 nm, as well as highly selective single-channel permeability of 1.6×10^9 H₂O/s. On the basis of this strategy, they increased one repeating unit and varied the sticky ends (pentamer **1** and **2** in **Figure 6d**) to accommodate water molecules through interior H-bond, obtaining enhanced water permeability without ion transporting.⁷⁰ Furthermore, inner side-chains were varied to ethyl, the obtained channel **4-LA** displayed extremely high single-channel permeability (2.7×10^{10} H₂O/channel/s) with a high level of proton rejection.⁷²



Figure 6 (a) Chemical and crystal structures of foldamers **1-3**. Adapted with permission from *Reference* [66] *Copyright* © 2021 from ACS publications. (b) Chemical structures of **HP1** and

HP2, and the corresponding simulation structures. Adapted with permission from Reference [67] Copyright © 2021 from Chinese Chemical Society. (c) Schematic 'sticky ends' molecular strategy. (d) Chemical structure and crystal structures of the helically folded pentamer **1** and **2**. Adapted with permission from References [70] Copyright © 2020 from ACS publications. Zeng's group constructed poly-hydrazide-helical nanotubes, containing a hollow cavity of around 6.5 Å and a height of 3.6 nm.⁷³ The highly selectivity toward anions rather than cations attracted much attention for possible medical treatment, especially for iodide deficiency disorders.

A quinoline-derived proton channels was revealed by Liu's group, presenting an exceptional high rate of proton flow 10^7 proton/s/channel through a 1 Å pore.⁷⁴ This work highlights the importance of the length of 16mer (2.5 nm), as well as the consecutive NH-chains inside the cavity in transporting protons compared to sufficiently long 8mer-C6-8mer.

AWC-membranes for application considerations

The numerous tailored artificial water channels (**AWC**) bring theoretical possibilities for desalination and water purification due to their high permeability.⁷⁵ However, more factors need to be practically taken into account when going from a single channel permeability to the real m² surface multichannel permeability membrane: for instance the cost and synthesis steps of **AWC** preparation, the effective incorporation of **AWC** into polymeric membranes with optimal densities, tackling the permeability-selectivity barrier of membrane and so on.

Only several AWCs show the prospects of being applied to membranes for desalination processing in during past few years. Tang's group have developed an ultrathin 2D metal-organic framework interlayer lab-scaled membrane (**Figure 7a**) for water purification, a permeable MOF nanosheet layer endowed the tripled water permeability ($4.82 \pm 0.55 \text{ Lm}^{-2} \text{ h}^{-1} \text{ bar}^{-1}$) and reasonable NaCl rejection (> 97%).⁷⁶

Peptide-appended pillar[5]arene has been incorporated into poly(butadiene)-b-poly(ethylene oxide) di-block copolymers using rehydration method (**Figure 7b**), and cm scaled membranes showed an improved permeability value of 65 L m⁻² h⁻¹ bar⁻¹ compared to a reference unfunctionalized one with a permeability of 45 L m⁻² h⁻¹ bar⁻¹.⁴⁴



Figure 7 (a) Schematic illustration of the effects of incorporating MOF nanosheets on IP process and PA structure: (top) TFC membrane; (down) TFC-MOF membrane. *Adapted with permission from References* [76] Copyright © 2020 ACS publications. (b) Depositing procedure of 2D sheets using a layer-by-layer technique of PAP channels on porous substrates. (c) Synthetic procedure for the hybrid **PA/AWC** membrane preparation. *Adapted with permission from References* [25 and 44] Copyright © 2018, 2021 Springer Nature Limited.

Qu et al.⁷⁷ have demonstrated that combining bioinspired amide H-bonding and the dynamic polymerization of poly(disulfide)s can provide a robust and adaptive strategy to combine

reversible covalent and non-covalent bonds in a unique material with an excellent cation conductivity. We previously described a similar strategy using urea H-bonding synthons and silica bonds to self-organize libraries of molecular precursors to fabricate proton exchange membranes (PEMs) containing directional proton-channel superstructures of high ionic group content in a scaffolding hydrophobic hybrid material.⁷⁸

In our group, we firstly introduce alkyl-ureido-ethyl-imidazoles into polyamide membranes for m-scales membranes for the application of desalination including seawater SWRO or brackish BWRO water RO applications.²³⁻²⁵ This hybrid membrane was produced by using polyamide as main host matrix, and incorporating HC6 compound via interfacial polymerization, resulting in a high water permeability (2.8 L m⁻² h⁻¹ bar⁻¹) and NaCl rejection ratio (99.51%) or boron rejection ration (91.4%) under SWRO desalination conditions at 65 bars and 35000 ppm NaCl.²⁴ Subsequently, HC6 was applied to further study due to its optimal solubility compared to other imidazole-quartet during the formation of defect-free membranes (Figure 7c). The role of combination ratio of HC6/m-phenylenediamine in the performance of PA-AWC membranes was stressed for optimizing varied inner morphologies and properties.²⁵ These examples provide potential opportunities for overcoming the permeability-selectivity trade-off, developing nextgeneration high-performance membranes for environmental applications. Recent advances in our group¹⁴ and by Zhao et al.³⁰ have made possible the large-scale fabrication of high density multichannel AWCs-polyamide hybrid materials, for the production of stable and highly performant biomimetic membranes that overcome current industrial RO-membrane performances for desalination.

Conclusion

The latest examples shown in this minireview illustrate the prospects with regard to artificial water channels towards specific functionality. Varied channels are discussed according to the tailored architectures along with discovered transporting goals. Exceptionally as for water transport, potential AWCs are expected to apply in real biomimetic membranes for developing industrial separation systems. During this process, it needs to be noticed that selectivity-permeability trade-off, efficiency-cost trade-off, optimal membrane materials and parameters are expected to be balanced.

The main point for channels-discovering is to create the narrow cavity or binding site, with the participation of water, proton or ions for forming an optimal inner arrangement. Indeed, attention to the structural variants is the prerequisite of all channel design because slight changes to the grafted tails/heads would fine-tune the transport mechanism. The door to design more functional alternatives has been opened toward effective and selective water/ion/proton channels, in the near future their potentials in environmental for water purification and biological applications for solving important medical diseases are worth to be exploited.

Conflict of Interest

There is no conflict of interest to report.

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