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Bio-inspired anti-fouling strategies for membrane-based separations

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Membrane-based filtration processes are attractive for industrial separation processes, because of energy-savings and cost-effectiveness. However, membrane fouling continues to be a major drawback. To overcome fouling and increase the efficacy of membrane separation processes, disruptive solutions can be found in nature. Nature-inspired chemical engineering (NICE) seeks to understand the fundamental mechanisms behind desired properties in natural systems and then applies these in practical applications where similar challenges need to be overcome, whilst considering all length scales. In this review, examples are provided where the systematic design methodology used in NICE is applied to decrease fouling and its effects on membrane-based filtration. Expanding the application of this framework will facilitate the identification and utilisation of common traits among highly efficient natural systems to propose innovative engineering solutions for water treatment. Beyond membrane separations, the NICE approach has already seen success in other areas, including electrocatalysts for H_2 fuel cells, CO_2 reduction, medical applications, and fluidized beds. We recommend increased modelling efforts to complement experimental work and to deepen the understanding of the mechanisms behind biological, non-fouling membranes, as well as other biological mechanisms relevant to water management, anti-fouling, and antimicrobial strategies. Additionally, we encourage making a clear distinction between biomimicry, bio-inspiration, and bio-integration, with guidelines and standardized nomenclature.

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Introduction

According to the United Nations (UN) World Water Development Report from 2021, over 26% of the global population is already affected by a shortage of fresh water.[1] It is expected that by 2050 the world's population will reach approximately 9.8 billion,[2] and, considering that global living standards continue to improve, the demand for clean water will be, roughly, the water resources of three planet Earths by then.[3] As a result, we need to address the availability and quality of water. Due to the lack of surveillance of what is discharged into the environment, it is estimated that 80% of all industrial and municipal wastewater is released into nature untreated.[1] Alternative sources of fresh water can be considered, such as *via* desalination, however, reusing water is vital for its conservation, and has major benefits, like the recovery of contaminants, which adds value to water treatment.[1]

Membrane-based filtration processes are being increasingly used in industrial environments, due to their energy-saving, cost-effective, and space-efficient characteristics. They can also be implemented in modular designs, which allows flexibility and fast scalability. All these benefits allow for contaminant-tailored solutions and facilities.[4–7] Performance is primarily influenced by concentration polarization, membrane fouling, selectivity, and the flux passing through the membrane (capacity and/or permeability), and it can be assessed based on the membrane's ability to prevent, regulate, or enhance permeation. Permeation is dictated by the membrane's properties and the driving force (gradient in transmembrane pressure (TMP), temperature, chemical potential, and/or electrical potential), the type and concentration of particles to filter, and the fluid dynamics.[7–9] Membrane modules should not only support the membrane but also deliver efficient fluid management, which is essential in membrane processing.[8,10] The hydrodynamic conditions in a membrane module affect membrane performance, because they influence concentration polarization and fouling on the membrane surface.[10]

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Challenges in membrane processes include their stability, the trade-off between permeability and selectivity, and the extensive and expensive cleaning and regeneration processes caused by membrane fouling.[9,11,12] The latter occurs when solutes or particles are irreversibly deposited onto, or adsorbed to, the membrane surface and/or pores by chemical and physical interactions or by mechanical action, and can only be removed by cleaning and regeneration, or by the substitution of the membrane. The species causing membrane fouling are called foulants and the fouling associated with them can be divided into four different groups: particulate or colloidal, organic, biofouling, and scaling. Many factors can influence the complex interaction between foulants and the membrane, such as the size of the particles or solutes, membrane structure (surface roughness, porosity), electrostatic repulsion, pH, hydrophobicity, and ionic strength.[13,14] Fouling is a very important factor that limits performance and increases the costs of pressure-driven membrane processes.[13–15] Therefore, it is essential to minimize membrane fouling and maximize membrane usage time by implementing anti-fouling strategies.

To reduce fouling, the first step is to determine the fouling type and to identify suitable control strategies that can be implemented. Anti-fouling strategies can be divided into different categories, specifically: (1) feed pre-treatment; (2) membrane selection; (3) module design and operation mode; and (4) physical and chemical cleaning.[16] The aggregation and sedimentation or the flocculation of particulate matter are examples of feed pre-treatment. This anti-fouling strategy requires supplementary operation units which consume space and energy, and they are normally achieved by the addition of hazardous chemicals.[6,16–18] Membrane selection and adaptation has been the most used and studied fouling control strategy. When selecting a membrane, some important features to consider are non-fouling materials, suitable surface or pore charge, porosity, pore size, tortuosity, surface roughness, thickness, chemical, thermal, and biological stability, durability, and cost.[13,16] Creating fouling-resistant membrane surfaces has been studied and validated for different foulants, but many suffer from significant flux decline, they normally only work for a limited range of foulants (*e.g.* bovine serum albumin, humic acid, silica, *Escherichia coli* bacteria), and they are not very effective against spreadable and proliferative biological foulants.[6,19] Membrane cleaning, through both physical and chemical processes, is widely used in industry.[6,18] However, physical cleaning only removes a small fraction of the foulants and can damage the thin active layer of the membrane, and chemical cleaning, despite being very good at removing difficult foulants, is membrane and foulant dependent and can be quite harsh on the membrane, leading to degradation of the membrane's materials.[6,16] Also, in many applications, particularly involving high fouling potential, such as sewage treatment, cleaning may be required after only a few hours of operation. For instance, when using ceramic membranes, Kramer *et al.* demonstrated that under a constant pressure of 8 bar, cleaning times of 3 min, 5 min and 1 h were required after 1 h, 24 h and 22 h of filtration using hydraulic backwash, forward flush and chemical cleaning, respectively.[20] Consequently, new approaches to tackle membrane fouling, while maintaining high permeability and selectivity, are necessary to address the clean water availability challenge.

To further improve the efficacy of industrial membrane filtrations, disruptive solutions can be inferred from nature. Natural filtration processes, such as the cell membrane's water transport, the filter-feeding system of certain animals and the kidney's blood filtration, are examples of highly effective filtration techniques. Likewise, membrane-base filtration can also be improved based on inspirations taken from other non-filtration related biological features, especially related to water management, such as the hydrophobicity of some natural surfaces. Rather than imitating nature out of context, an effective nature-inspired solution (NIS) methodology is based on understanding the underlying mechanisms of natural systems across various length scales, then adopting and adapting these mechanisms to designs for practical applications where similar challenges need to be overcome, such as in water treatment.[21–23] Nature-inspired chemical engineering (NICE) applies this NIS methodology in the context of chemical engineering. NICE takes advantage of nature's aeons of evolution to tackle scalability, efficiency and resilience, and it applies these learnings to challenging engineering processes. Many underpinning mechanisms found in nature can be grouped according to recurring fundamental scientific principles that cause desirable properties. This leads to universal themes, including the following four particularly important ones to chemical engineering as well: hierarchical transport networks (T1); force balancing (T2); dynamic self-organization (T3); and ecosystems, control and modularity (T4).[21–23] Consequently, the systematic design approach followed by NICE bridges nature with the engineered application. This approach follows four steps: nature-inspired concept, design, experimental realization, and application. In the first step, the nature-inspired concept is identified, *i.e.*, the critical mechanism universally found in nature that can solve a specific challenge, like scalability or resilience, is identified. In the second, nature-inspired design stage, the concept is translated into a design devised to solve or improve a critical engineering issue of the intended application that mirrors the challenge in nature. This design is then experimentally realized or prototyped. For the implementation of such nature-inspired design, the application's technological requirements, but also other considerations like economics and environmental concerns, are essential, and iterations are normally carried out, supported by experiments and computations, to satisfy the final application.[21–23] The success of the NICE approach has already been demonstrated in various fields, including research on electrocatalysts for CO_2 reduction,[24,25] medical applications[26] and fluidized beds.[27]

The aim of this review is to show how this systematic nature-inspired solution methodology can benefit tackling fouling in membrane-based filtration techniques, by using examples found in literature and presenting opportunities for impactful applications of this procedure to a persistent issue that hampers membrane separation technology.

Nature-inspired membrane design

NICE and the NIS methodology have already been applied to combat fouling for membrane-based water filtration, while also improving other characteristics of membrane filtration.

Aquaporins are proteins found in cell membranes that are responsible for the transport regulation of water, ions and other solutes through the membrane of many organisms, including animals, plants, bacteria, and fungi. The efficiency of their hydrophobic channel with minimal water binding sites, in controlling the flux of water molecules in and out of the cell, make them one of the most important membrane proteins. Additionally, cell membranes contain hydrophilic polymer brushes on the external surface, which protect the cell through the formation of a hydration layer and due to steric hindrance effects.[28,29]

Inspired by these two natural features of cells, Liu *et al.* adopted the dual concepts underpinning the effectiveness for water transport in aquaporins and anti-fouling through hydrophilic polymers into a cell-membrane-inspired design consisting of chitosan-functionalized graphene nanomesh (GNM) pores. As in the cell, the hydrophobic graphene nanomesh pores allow for fast water transport due to the decreased mass transfer length and low friction between the water molecules and the GNM, while the chitosan functionalization improves the hydrophilicity by providing hydroxyl and amino groups, leading to the formation of a hydration layer on the membrane surface.[30]

The graphene nanomesh was synthesized *via* vacuum filtration of a mixture of graphene oxide (GO) nanoplatelets, zinc nitrate and water, with subsequent burning of GO uncovered by Zn salts, leading to pores, and reduction of GO covered by Zn salts. After this, the GNM was modified with chitosan by dissolving the chitosan in water, then adding the GNM, and stirring.[30]

Fig. 1 shows that these membranes have a very high water permeability and exceptional anti-fouling properties for different types of oil-in-water emulsions, while preserving a very high recovery rate of more than 96.7%. Cyclic experiments using a surfactant-stabilized sunflower oil-in-water emulsion were also performed to understand the long-term separation performance of these membranes, and they show great prospects, maintaining the water recovery rate above 95.2% after three cycles.[30]

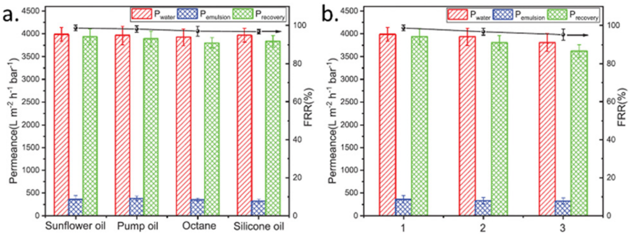

Fig. 1 (a) Permeance of nature-inspired, chitosan-functionalized graphene nanomesh membranes in water-emulsion-water three-stage filtration experiments using different surfactant-stabilized oil-in-water mixtures, (b) cyclic separation experiments with sunflower oil-in-water emulsion. Reproduced from ref. 30 under the Creative Commons Attribution 4.0 licence.

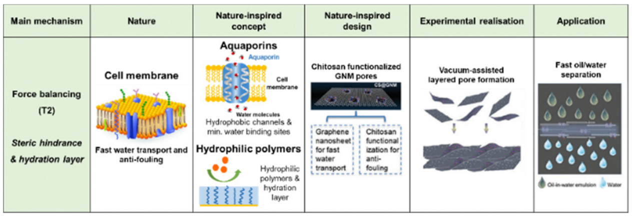

Fig. 2 Systematic nature-inspired solution methodology to design highly water-permeable, stable, and selective oil/water separation ultrafiltration membranes. The figures under "Nature-inspired design", "Experimental realization" and "Application" are reproduced from ref. 30 under the Creative Commons licence. The figure under "Nature", is reproduced from ref. 31 under the terms of the CC-BY-NC-ND license.

Consequently, this highly hydrophilic and super-oleophobic cell-inspired membrane showed outstanding anti-fouling characteristics when separating oil-in-water emulsions, even when stabilized by surfactants, with very high-water permeability. Fig. 2 summarizes the NICE approach to design such highly water-permeable, selective, and stable oil/water ultrafiltration membranes, using a NIS diagram.[30]

Li *et al.* created a cell-inspired microfiltration membrane with increased bio-adsorption resistance. Inspired by a cell membrane's hydrophilic polymer brushes on its external surface, a polyethersulfone (PES) membrane was modified with dopamine as biocompatible glue, and chitosan to create an antifouling screen consisting of a hydrophilic, charged layer that causes hydration and steric hindrance to foulants. The bio-adsorption resistance tests using *E. coli*, demonstrated that the modified membrane adsorbed up to 2.3 orders of magnitude less bio-organisms, however no antimicrobial properties were detected. Also, no substantial quantities of organic components were detected on the membrane surface. The systematic methodology used to design such bio-adsorption resistant nature-inspired membranes is presented in Fig. 3.[32]

The kidney is another example of a highly efficient filtration mechanism found in nature. The membrane situated in the blood vessel walls of the glomerulus have an overall negative charge, which, through electrostatic repulsion, keeps the negatively charged plasma proteins from being filtered out.[33–36] In addition, the glomerulus lumen contains a negatively charged hydrophilic brush structure, called glycocalyx, which retains the plasma proteins and creates a hydration layer, which aids in the prevention of fouling.[37–39] This is true despite

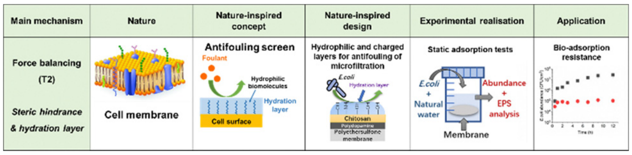

Fig. 3 Systematic methodology for the design of bio-adsorption resistant nature-inspired membranes. Reproduced from ref. 32 with permission from Elsevier, Copyright 2021.

the presence of windows in the membrane that are wider than many foulants. Thus, charge and hydrophilicity of the kidney are believed to be the underlying, primary reasons why this organ can filter about 140 L of urine per day from blood with minimal fouling.[34]

Inspired by these remarkable characteristics of the kidney, Mohamed *et al.* studied the effect of the charge and hydrophilicity of modified polyester membranes. Using polypropylene glycol (PPG) and polyethylene glycol (PEG) with one or two amino end groups, which allowed them to tune the charge and hydrophilicity, they showed how antifouling characteristics can be improved. From this, it was concluded that charge has a higher impact on the anti-fouling properties of the membranes, but that this effect is amplified by hydrophilicity. The inspiration from kidneys for anti-fouling properties can be summarized by the NIS diagram shown in Fig. 4.[40]

From the previous examples, it is noticeable that using the nature-inspired solutions framework is not only effective in improving anti-fouling characteristics of membrane-based filtration processes, but it is also beneficial by being rigorous, and by connecting the natural context with the final application in its technical context, aided by a systematic, stepwise process from concept to realization. The subdivision into specific phases further offers the opportunity for iteration, *i.e.*, in each step, the process context can be considered, and the transition from concept through design to implementation can be reconsidered where necessary. Computationally assisted experimentation is key to understand if more iterations are required, validating or updating the theory, and new manufacturing and synthesis techniques can be deployed to realise practical and economical solutions, beyond the proofs-of-concepts shown in the above examples.[21]

Apart from these applications of the NIS framework developed at the UCL Centre for Nature-Inspired Engineering, where it originated, there is significant potential for it to be used more generally, to accelerate effective innovation. As will be illustrated through the following examples, having such a methodological framework also helps to summarize and find commonalities in bio-inspired research found in the literature, which can trigger new insights for improved designs.

Even natural systems or characteristics that are not directly related to water filtration can provide some clues to improve membrane-filtration systems, through lateral thinking. For example, many migratory birds, such as pelicans, ibises and geese, fly in a V-shaped arrangement, since this is more energy efficient. When flying using this configuration, birds can save energy by using the aerodynamic wake created by the wings of the preceding bird. In addition, these birds also have sensory mechanisms to capture when the wing-beats of a flock should be in phase or anti-phase spatially, leading to energetic benefits.[42–45]

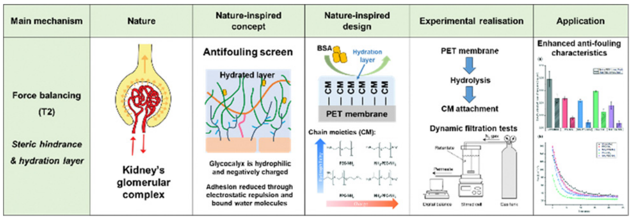

Fig. 4 Systematic methodology for the design of enhanced anti-fouling membranes inspired by the kidney's glomerular complex. The figures under "Nature-inspired design" and "Application" are reproduced from ref. 40 under the Creative Commons Attribution 3.0 Unported licence. Other images are reproduced from ref. 41 under the terms of the CC-BY-NC-ND license.

Luo *et al.*[46] improved the permeability of membranes, without building up the concentration polarization and fouling by getting inspiration from the energy efficiency of bird flocks' V-shaped flying formation. To do so, they proposed a membrane module containing a V-shaped feed spacer that enables increased mass transfer and decreased friction. Through hierarchical optimization using 3D multi-physics simulations, and changing variables related to the module, flow and system design they achieved a 338% increase in the water flux and estimated 18% energy savings when compared to commercially used desalination plants, with minimal fouling. These improvements are due to the hydrodynamics of the new membrane module. Fig. 5 shows the velocity and streamline distributions in three of the optimized spacers studied (a)–(c) and the conventional spacer (d).[46] As seen in Fig. 5, the vortex flow in the transverse section provided by the V-shaped spacer allows an increase in the mass transfer coefficient, while decreasing fouling. This vortex flow is not achieved with the conventional spacer. The improvements are a result of dynamic self-organization of vortices (NICE theme T3). Fig. 6 summarizes this example, by projecting it on the NIS methodology, thus

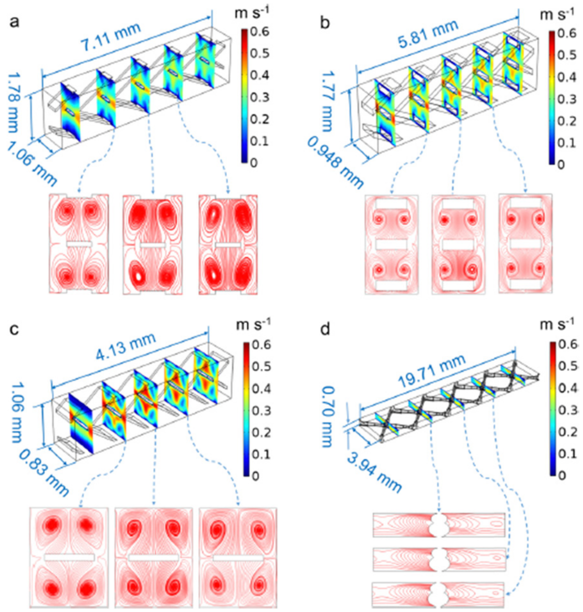

Fig. 5 Velocity and streamline distributions in three of the optimized spacers studied (a)–(c) and the conventional spacer (d). This figure is reproduced from ref. 46 under the Creative Commons Attribution 4.0 International licence.

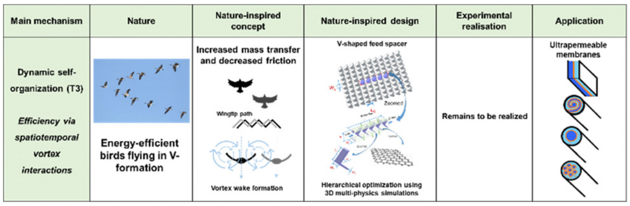

Fig. 6 Systematic methodology for the design of ultrapermeable nature-inspired membrane modules based on dynamic self-organization of vortices. The figure under "Nature-inspired design" is reproduced from ref. 46 under the Creative Commons Attribution 4.0 International licence. The figure under "Application" is reproduced from ref. 47 with permission from Elsevier, Copyright 2018. The figure under "Nature", is reproduced from ref. 48 under the terms of the CC-BY-NC-ND license.

illustrating the steps that could lead to a more efficient, ultrapermeable membrane module.[45,46]

Spider silk is a natural material that is particularly efficient in collecting water from air moisture. This water collection and management is possible due to the wet state structure of the spider silk fibres, which is characterized by periodic spindle-knots separated by joints, made of highly random and relatively aligned nanofibrils, respectively. These provide a surface energy gradient and a Laplace pressure drop, which, only combined, allow for continuous condensation and collection of water.[49,50]

Inspired by the impressive collection and movement of water along spider silk, Zhang *et al.* fabricated membranes for the continuous purification of wastewater with increased anti-oil-fouling. The membranes were manufactured by a Plateau-Rayleigh instability-induced assembly, followed by *in situ* polymerization. The prepared membrane presents a hierarchical roughness and hydrophilic matrix, which provide a combination of superhydrophylic and underwater superoleophobic properties, making this membrane suitable for the separation of both insoluble and soluble pollutants from water. The combination of superwetability, high porosity, and good pore interconnectivity allow the membranes to have a high permeation flux (5403 L m^{-2} h^{-1}), while still achieving outstanding anti-fouling characteristics (total organic carbon content <5 mg L^{-1}). Moreover, the obtained Laplace pressure difference and positive potential allow the possibility of filter cake removal during the filtration.[51] Fig. 7 illustrates how this example can be recast within a NIS diagram, to bring out systematic steps in the design of nature-inspired membranes for continuous purification of wastewater.[50–54]

The lotus leaf (*Nelumbo nucifera*) is known for its so-called "self-cleaning" mechanism or "lotus effect". Due to the combination of surface roughness, reduced particle adhesion, and water repellence, water droplets run along the surface of these leaves, dragging with them external impurities that are unable to adhere to the rough surface of the leaves. The complex surface of these leaves is composed of the papillae, a three-dimensional microstructure of epidermal cells, and a superimposed layer of hydrophobic epicuticular wax crystals. The voids of the microstructure trap air between the water and the leaf surface, and the water is suspended on the tip of the epidermal cells in a Cassie–Baxter state, causing a very high drop contact angle.[55–58]

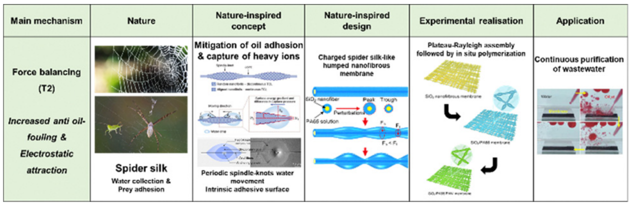

Fig. 7 Design of spider silk-inspired membrane materials for continuous purification of wastewater. Some figures under "Nature-inspired concept" are reproduced from ref. 54 under the Creative Commons Attribution-NonCommercial 3.0 Unported licence, while the rest is adapted from ref. 50 with permission from American Chemical Society, Copyright 2021. The figures under "Nature-inspired design", "Experimental realisation" and "Application" are reproduced from ref. 51, with permission from Nanotechnology, Copyright 2021. Other images are reproduced from ref. 52 and 53 under the terms of the CC-BY-NC-ND license.

Some filter feeding fish are highly efficient in trapping food particles by using a microscopic crossflow based non-clogging filtration mechanism. This filtration mechanism allows them to retain even particles that are smaller than the size of their gill arches and rakers (their comb-like filter apparatus), however the exact mechanism behind this phenomenal skill is not fully understood. Nevertheless, hydrodynamics seems to be a key factor affecting the exceptional anti-fouling performance of these species, with some studies suggesting that 95% of the particles ingested do not contact the gills or any other oral surfaces.[59–65]

Inspired by the hydrophobicity of the lotus leaves and the anti-fouling characteristics of the filter-feeding species, Jiang *et al.* proposed a membrane distillation desalination approach capable of enhancing mass transfer (enhanced permeation flux) while reducing fouling by modifying a commercial polypropylene membrane. Modifying the membrane with bioinspired hybrid hydrophobic micro/nanostructures enhances the interfacial nanoscale turbulent flow, hindering fouling (according to the hydrodynamics and classic nucleation theory). The nanoscale structures provide the membrane with a heterogeneous nucleation barrier (Cassie–Baxter state), successfully decreasing nucleation. Moreover, the support microstructure can increase the efficacy of the evaporation at the surface, followed by improved permeation through the membrane.[66] Fig. 8 summarizes this design of nature-inspired membranes for distillation desalination through a NIS diagram that captures the key steps from nature to application.[63,66–69]

Besides these examples, there are other ones in the literature where NICE with a NIS framework can be applied to enhance anti-fouling properties of membrane-based separations.[70–78] Nevertheless, some literature confounds narrow biomimicry (or biomimetics) with mechanistically founded bio-inspiration, or uses biomimicry to include the latter. However, as the name indicates biomimicry (mimesis) is the act of imitating or copying a biological characteristic, while nature/bio-inspired is about gathering ideas by observing natural/biological characteristics. Whereas biomimicry often focuses on superficial analogies, by reproducing geometries or features in biology, though often not understanding the underlying mechanisms behind these

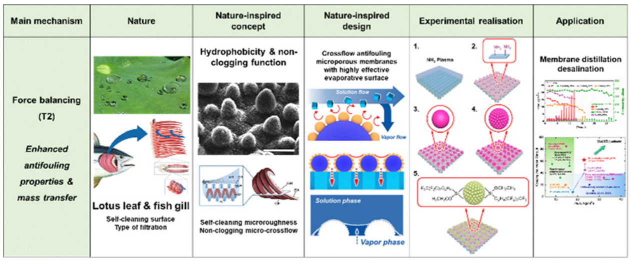

Fig. 8 Design of lotus leaf and fish gill-inspired membrane surfaces for membrane distillation desalination. Some figures under "Nature-inspired concept" are adapted from ref. 67 with permission from The Royal Society, Copyright 2016, while the rest is reproduced from ref. 63 under the Creative Commons CC BY licence. The figures under "Nature-inspired design", "Experimental realisation" and "Application" are adapted from ref. 66 with permission from the American Chemical Society, Copyright 2020. Other images are reproduced from ref. 68 and 69 under the terms of the CC-BY-NC-ND license.

characteristics and disregarding the different context of the application, nature-inspiration looks at finding the universal underpinning mechanism behind the desirable characteristic, that can be applied in different contexts if adapted properly. Due to the complexity of nature, in bio-inspiration it is also necessary to grasp different scales (in length and time) and how these can affect the desirable feature, always considering the scientific link between cause and effect.[21]

There is still a third category that can cause misconceptions. Bio-integration consist of using natural elements in engineered solutions. To do this, the desired biological element/feature is collected from nature and transplanted into engineered solutions to be applied in industrial settings.

For example, when considering aquaporins as having highly desirable features for rapid water transport, the research method can significantly alter the results achieved. Path 1 – Aquaporin mimicry: Huang *et al.*[79] describe an aquaporin mimetic membrane for desalination. Their studies focus on mimicking the surface chemistry and morphology of aquaporins without recognizing why or if the surface chemistry and morphology are important. Path 2 – Bio-inspiration: Liu *et al.*[30] leverage the characteristic mechanism behind aquaporin's water transport efficiency and translate it into engineering solutions for high permeation in membrane filtration processes. Path 3 – Bio-integration: Vogel *et al.*[80] describe how the Danish company Aquaporin A/S[81] integrates aquaporins in their membranes by collecting them from cells and posterior encapsulation of these biological aquaporins into thin film composites.

These three approaches (biomimicry, bio-inspiration, and bio-integration) could all result in improvements in membrane-based filtration processes; however, they are fundamentally different. Bio-integration will work best when the engineering and natural environments are similar: it directly uses nature's evolved structures, but embeds them in a form or shape that is better suited for the intended technical application. Bio-inspiration leverages scientific mechanisms borrowed from nature, and may not use biological components, but artificial, chemical and physical ones. It builds on deeper, mechanistic understanding, rather than what meets the eye. Because biomimicry is more direct in copying nature, it may miss the impact that different environments, scales (in space and time), or engineering and societal context have on the envisioned application. Thus, we advocate for clearer terminology to avoid confusion and misunderstandings. The nature-inspired solution methodology, presented in this paper, provides a systematic framework for bio-inspired research and development.

Creating new opportunities through nature-inspired chemical engineering

As we have seen through the previous examples, inspiration from nature offers tremendous potential to solve fouling issues in membrane-based separations. The demand for bio-inspired solutions to membrane separations has been steadily increasing over the past decade in response to challenges related to water treatment, but also sustainable development more generally.[82–84] The elimination of fouling is not an easy task, and nature has had millions of years to evolve solutions. The aforementioned examples are representative for the literature but offer only a sample of Nature's vast arsenal of solutions that could be the foundation for bio-inspiration. There are many other natural features/species that we can explore. With numerous highly efficient natural filtration systems, such as filter-feeding species (*e.g.* fish, birds, and crabs) and mangroves, and other organisms highly efficient in water management, inspiration can be found everywhere.

Apart from discovering new natural features and species to draw inspiration from, it is important to consider different scales. Most bio-inspiration research focuses on the small scales (nano & micro scales), yet nature encompasses all length scales. All length scales are important, and it is essential to think about the problem as a whole – clean water availability – and not simply as a material problem such as decreasing membrane fouling. Therefore, examining the natural features already studied through a different "magnification lens" can provide enhanced insights into how and why these features are so efficient, and offer ideas for reducing fouling. The combination of the different scales should increase the probability of successfully eliminating or decreasing fouling to a great degree, for example, by combining innovation in membrane materials with pioneering membrane modules. This implies the application of NICE beyond the force-balancing theme (T2) applied to materials design, and venture into applications of hierarchical transport networks (T1), dynamic self-organization (T3), and a nature-inspired systems engineering approach (T4).

Analyzing nature's mechanism before applying them in engineered settings requires fundamental understanding of the biological, physical and chemical underlying processes, insight that can be provided through interdisciplinary collaborations, for example, of engineers, chemists and materials scientists with researchers in physics, biology, and the life sciences.

Scaling up is another hurdle to overcome. Most of the current bio-inspired research has not been applied in industrial settings. The feasibility of scaling up new findings needs to be analyzed and improved. This can be done through the development of computational models that can also assist researchers to address issues associated with the transfer of essential features from the biological system to the bio-inspired design and from the lab scale to the industrial scale. However, compared to the substantial breadth of experimental studies regarding anti-fouling membranes, current modelling work is not yet comprehensive enough to guide bio-inspired designs. Molecular simulations mostly focus on local binding sites, permeability, sometimes on selectivity, and much less on fouling. Multiscale simulations are essential, as well as linking experimental and computational work. To realise systematic bio-inspired designs of anti-fouling membranes in the future, we advocate that more efforts focus on modelling to gain fundamental understanding of mechanisms in nature and guide the adoption of bio-inspired design to engineering applications, following the NICE approach, like efforts in nature-inspired catalysis and reaction engineering.[85]

Recent innovations in manufacturing technology, as additive manufacturing becomes more advanced and practical, can also provide the opportunity to developing new membranes and membrane-modules capable of tackle fouling, as well as validate computational simulations through experimentation.

It is also necessary to standardize terminology to distinguish different types of research methods based on natural characteristics, and to correct the misconception between biomimicry, bio-inspiration and bio-integration.

Conclusions and outlook

The application of membranes in water treatment and other separation processes is often limited by fouling, and inspiration from nature is a valuable approach to addressing this issue.

Using NICE with its systematic design methodology to decrease fouling and its effects on membrane-based filtration has been useful in the examples provided by this review. Applying this framework more extensively, and across other NICE themes (including multiple scales and systems-based approaches), will make it easier to find common characteristics between highly efficient natural system characteristics that can inspire new engineering solutions for water treatment. It is important to understand the relevant mechanisms that give rise to the desired properties and adapt them to be applicable to the context of a technological separation problem. The NICE approach discussed here is a rigorous methodological process that allows for the development of systematic bio-inspired design.

Apart from the examples given in this review, the NICE approach has already achieved success in many other areas, *e.g.*, in catalysis and reaction engineering, and biomedical engineering. Herein, we discussed the principles with some examples that make this methodology a pathway to create bio-inspired anti-fouling membrane-based separations. We advocate for more modelling work to complement experiments and better understand the underpinning mechanisms of biological, non-fouling membranes, as well as other biological examples beyond membranes, related to water management, anti-fouling, and antimicrobial activity. A distinction between biomimicry, bio-inspiration, and bio-integration is encouraged, as standardization and guidelines are needed.

Author contributions

Adriana Filipe Bernardes: writing – original draft, review & editing. Zheyi Meng: conceptualization; writing – review & editing. Luiza Cintra Campos: writing – review & editing; supervision. Marc-Olivier Coppens: conceptualization; writing – review & editing; supervision.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

Conflicts of interest

The authors have no conflicts of interest to declare.

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