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Stimuli-responsive smart gating membranes[†]

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Membranes are playing paramount roles in the sustainable development of myriad fields such as energy, environmental and resource management, and human health. However, the unalterable pore size and surface properties of traditional porous membranes restrict their efficient applications. The performances of traditional membranes will be weakened upon unavoidable membrane fouling, and they cannot be applied to cases where self-regulated permeability and selectivity are required. Inspired by natural cell membranes with stimuli-responsive channels, artificial stimuli-responsive smart gating membranes are developed by chemically/physically incorporating stimuli-responsive materials as functional gates into traditional porous membranes, to provide advanced functions and enhanced performances for breaking the bottlenecks of traditional membrane technologies. Smart gating membranes, integrating the advantages of traditional porous membrane substrates and smart functional gates, can self-regulate their permeability and selectivity via the flexible adjustment of pore sizes and surface properties based on the "open/close" switch of the smart gates in response to environmental stimuli. This tutorial review summarizes the recent developments in stimuli-responsive smart gating membranes, including the design strategies and the fabrication strategies that are based on the introduction of the stimuli-responsive gates after or during membrane formation, and the positively and negatively responsive gating models of versatile stimuli-responsive smart gating membranes, as well as the advanced applications of smart gating membranes for regulating substance concentration in reactors, controlling the release rate of drugs, separating active molecules based on size or affinity, and the self-cleaning of membrane surfaces. With self-regulated membrane performances, smart gating membranes show great power for use in global sustainable development.

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Key learning points

- (1) Combination of traditional porous membranes and smart polymeric gating materials creating stimuli-responsive smart gating membranes.
- (2) Chemical science of strategies for creating smart gates in membranes and stimuli-responsive conformational switches and the mechanism of functional gates at the molecular level.
- (3) Self-adjustment of the pore sizes and/or the surface properties with functional gates for manipulating the permeability and selectivity of membranes.
- (4) Chemical technologies of stimuli-responsive smart gating membranes for wide applications in not only traditional, but also extended or even brand new fields.
- (5) Potential self-cleaning functions of the new-generation membranes based on the stimuli-responsive pore sizes and surface properties.

1. Introduction

Membranes are selective barriers that can separate components with different physical/chemical properties. Usually, mass transfer and separation based on membranes show fantastic features, because of many advantages such as no phase change, no additives and low energy consumption in the membrane processes, as well

as the compacted structure and small space-occupancy of the membrane equipment.¹ Therefore, membrane technologies show great importance for global sustainable development in myriad fields such as the conservation and regeneration of energy,² the reduction of pollutant emissions,³ the highly-effective utilization of resources,⁴ and hemodialysis.⁵ Typically, the performance of membranes is determined by the permeability and selectivity.¹ The permeability is characterized by the trans-membrane flux that evaluates the productivity of membrane processes; while the selectivity is defined by the ability of membrane for the rejection/permeation of specific substances, which implies the efficiency of membrane separation. Both permeability and selectivity depend on the pore size and surface properties of

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the membrane. Generally, increased pore size enables enhanced permeability, and the pore size also decides the membrane selectivity for size-based separation. Meanwhile, the membrane selectivity also depends on the affinity between the pore surface



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and the substances. However, the pore size and surface properties usually remain unalterable for traditional porous membranes due to their unchangeable physical/chemical structures. Thus, their performances will be weakened upon unavoidable membrane fouling, since foulants deposited on the pore surface can reduce the pore size and hinder the interactions between the substances and membranes.⁶ Moreover, such unalterable pore size and surface properties may restrict the wide and efficient applications of traditional membranes in extended fields. For example, membrane-based ethanol fermentation usually requires a constant ethanol concentration in the reactor for efficient continuous fermentation.⁷ Therefore, with increasing ethanol concentration during the fermentation, increased membrane permeability is needed to instantaneously remove the additional ethanol to maintain the concentration. For size-based membrane separation, tunable pore sizes are fantastic for single membranes to achieve adjustable selectivity for the efficient separation of versatile substances with different sizes. However, these requirements remain challenging for traditional membranes,



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although traditional membranes have already played paramount roles in myriad fields. The development of smart membranes with self-regulated permeability and selectivity can create new opportunities for membrane applications.

Inspired by cell membranes with stimuli-responsive channels for self-regulating permeability and selectivity in response to environmental signals,⁸ artificial smart gating membranes have been created by chemically/physically incorporating stimuli-responsive materials into porous membrane substrates as functional gates.^{9–11} In response to environmental stimuli, such as changes in temperature, pH, specific ions/molecules, light, magnetic fields, and redox, their functional gates provide a conformational switch for adjusting the pore sizes and/or the surface properties of the membranes and thus for manipulating the permeability and selectivity. Such gating membranes combine the advantages of porous substrates and smart gates for advanced performances and enhanced applications. For example, for membrane fouling, such as that induced by silt, protein, and bacteria, the permeability of gating membranes can be increased by “opening” the gates to enlarge the pore size for flux enhancement. Meanwhile, the membrane surface properties can also be adjusted by changing the wettability of the gates; thus, the affinity between the fouling components and the membrane surface can be weakened for reducing or even eliminating the foulants.³ The self-regulated permeability also benefits the maintenance of ethanol concentration in reactors for fermentation,¹² the controlled release of active molecules from capsule membranes for drug delivery,¹³ and the simple separation of substances with different sizes using a single membrane for size-based separation.¹⁴ Moreover, stimuli-responsive affinity adjustments can also be applied for controlling the interaction between proteins and the pore surfaces that are grafted with stimuli-responsive polymers such as poly(*N*-isopropylacrylamide) (PNIPAM) for protein separation.¹⁵ Therefore, such gating membranes with self-regulated permeability and selectivity enable enhanced and advanced performances for wide applications in not only the traditional, but also the extended or even brand new fields such as the detection of harmful pollutants for environment protection¹⁶ and the stimuli-responsive controlled release of drugs for biomedical application.¹⁷

In this tutorial review, we highlight the recent developments in stimuli-responsive smart gating membranes, including the fabrication strategies and techniques, responsive properties, gating models, and advanced applications. This is introduced by starting with the design strategies of the gating membranes, and following with the fabrication strategies and techniques. Then, versatile smart gating membranes with positively- or negatively-responsive gating models in response to various stimuli are described. Finally, the applications of smart gating membranes in chemical valves, separation, controlled release, and self-cleaning are discussed.

2. Strategies for creating smart gates in membranes

2.1 Design strategy

The cell membrane provides fantastic inspiration for scientists to develop artificial smart gating membranes. The cell membrane

contains channels with stimuli-responsive “smart gates” that can selectively open or close for specific substances to transfer across, so as to maintain the desired intracellular and extracellular concentrations for ensuring life activities.⁸ Such natural models inspire great efforts in creating artificial membranes with smart gates for achieving advanced performances. Artificial smart gating membranes can be designed and fabricated with various styles (Fig. 1). Typically, the membrane type can be flat (Fig. 1A1),¹⁵ fiber (Fig. 1A2)¹⁸ or capsule (Fig. 1A3),¹⁹ and can be skillfully employed for versatile applications such as stimuli-responsive separation, water treatment, and controlled release.^{15,18,19} The functional gates in membrane pores usually can be linear polymer chains (Fig. 1B),²⁰ crosslinked hydrogel networks (Fig. 1B2),²¹ or microspheres (Fig. 1B3),¹⁸ which enables stimuli-responsive swelling/shrinking switches for adjusting the effective pore size and surface properties. The gate materials can be incorporated into membrane pores in pore-filling form (Fig. 1C1) for robust gating performance,²² or in pore-covering form (Fig. 1C2) for rapid response.²³ Based on the versatility of stimuli-responsive materials, versatile smart gating membranes can be developed through incorporating these materials as functional gates. The fabrication techniques for smart gating membranes can be classified into two categories based on whether the gate materials are introduced after or during the membrane formation.

2.2 Stimuli-responsive gates introduced after membrane formation

The strategies that introduce the gates after membrane formation usually incorporate the gate materials on existing porous membrane substrates using “grafting” techniques, which can be divided into the “grafting-from” and “grafting-to” methods. Both methods allow the fabrication of gating membranes with steady gating structures and highly efficient gating performances.

For the “grafting-from” method, gating membranes are fabricated by first inducing active sites on the pore surface, and then polymerizing functional monomers from the active sites to constitute linear polymers or crosslinked networks in the pores as the smart gates (Fig. 2A).^{21,22} With grafting techniques such as chemical grafting,²⁴ UV-induced grafting,²⁵ and plasma-induced grafting,^{15–17} various functional gates can be incorporated into a wide range of membrane substrates for creating smart gating membranes.

For the “grafting-to” method, gating membranes are fabricated by chemically/physically incorporating pre-formed functional gates, usually in the form of polymer chains or microspheres, onto the pore surfaces with pre-treated active sites (Fig. 2B and C).^{18,20} Comparing with the bonding between the gates and pore surface through physical interactions such as van der Waals’ forces,¹⁸ the bonding based on chemical covalent bonds is more robust for application.²⁰ Moreover, since polymer chains or microspheres with well-controlled length or size can be pre-synthesized using well-established methods, the “grafting-to” method offers improved controllability and flexibility for the gate microstructures.

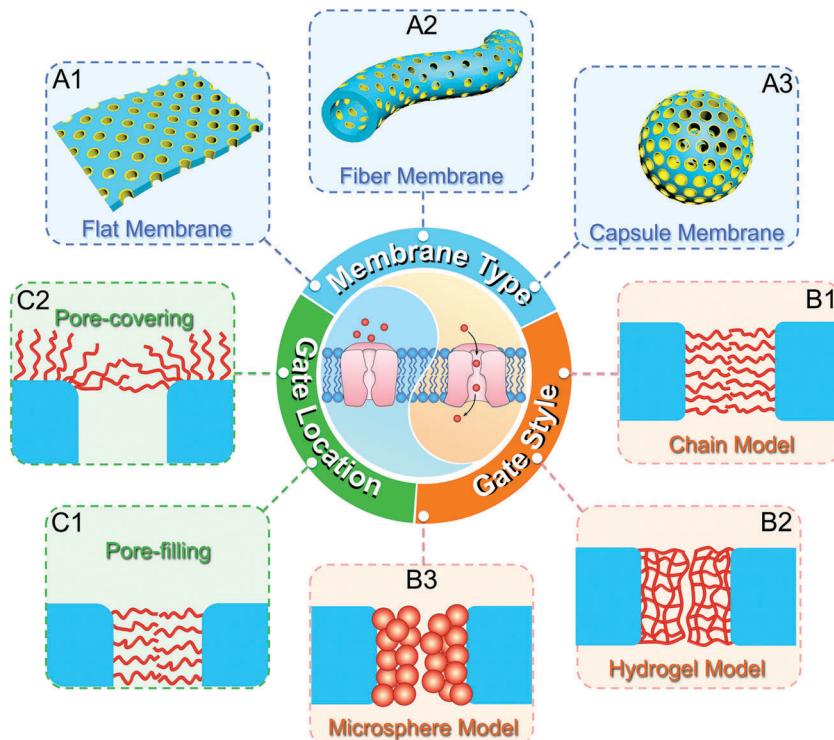


Fig. 1 Smart gating membranes, which are inspired by cell membranes with ion channels (central images), can be designed and fabricated with various styles. The membrane type can be a flat membrane (A1), fiber membrane (A2) or capsule membrane (A3), the gate style can be linear polymer chains (B1), crosslinked hydrogel networks (B2) or microspheres (B3), and the gate location on the membrane pore can be pore-filling (C1) or pore-covering (C2).

2.3 Stimuli-responsive gates introduced during the membrane formation

The strategy that introduces the gates during membrane formation allows the concurrent one-step formation of both membranes and stimuli-responsive gates, showing great potential for easy scale-up. This strategy enables the development of gating membranes by utilizing polymers with stimuli-responsive side chains, or blending these with their pristine forms for membrane formation (Fig. 2D).²⁶ Alternatively, stimuli-responsive block copolymers (Fig. 2E)²⁷ or microspheres (Fig. 2F)²⁸ can also be introduced as functional gates by blending them with the membrane-forming polymers during membrane formation. These approaches that combine the gate incorporation with the membrane formation, provide an efficient and promising strategy for industrial manufacture of smart gating membranes with currently existing equipment.

3. Stimuli-responsive gating

Generally, the development of gating membranes with various gating functions is necessary for meeting the versatility requirements of myriad applications. Typically, the gating can be divided into two models, *i.e.*, positively- or negatively-responsive gating. The positively-responsive gating allows increased membrane permeability when the stimulus appears or increases (Fig. 3A), while the negatively-responsive gating shows reversed

properties (Fig. 4A). The gating functions are achieved through the shrinking/swelling transitions of stimuli-responsive gates, which can open/close the membrane pores for increased/decreased permeability. Also, the hydrophobic/hydrophilic changes associated with the shrinking/swelling transitions of certain gates can adjust the surface properties of the pores. Numerous stimuli, which are important for industrial production or biological activity, can be employed as triggers for achieving responsive gating, due to the versatility of stimuli-responsive materials. The information on the researchers who pioneered the development of each stimuli-responsive smart material as well as gating membranes is summarized in Tables S1 and S2 in the ESI.† For example, temperature and pH are the most common parameters that may vary in biological/chemical reactions, and organs and tissues.²⁹ Ions such as potassium ions (K^+) are essential for biological metabolism,³⁰ while heavy metal ions such as lead ions (Pb^{2+}) are seriously harmful for living organisms.³¹ There are also specific molecules such as glucose, the concentration of which in blood is an important indicator for diabetes and hypoglycemia.³² Light and magnetic fields are usually clean stimuli that can be used for remote control.^{33,34}

3.1 Positively responsive gating

3.1.1 Thermo-responsive gating. Thermo-responsive polymers, such as *N*-substituted polyamides, polyethers, poly(2-oxazoline)s, poly(vinyl caprolactone) and poly(methyl vinyl ether),³⁵ usually present a low critical solution temperature (LCST) that is

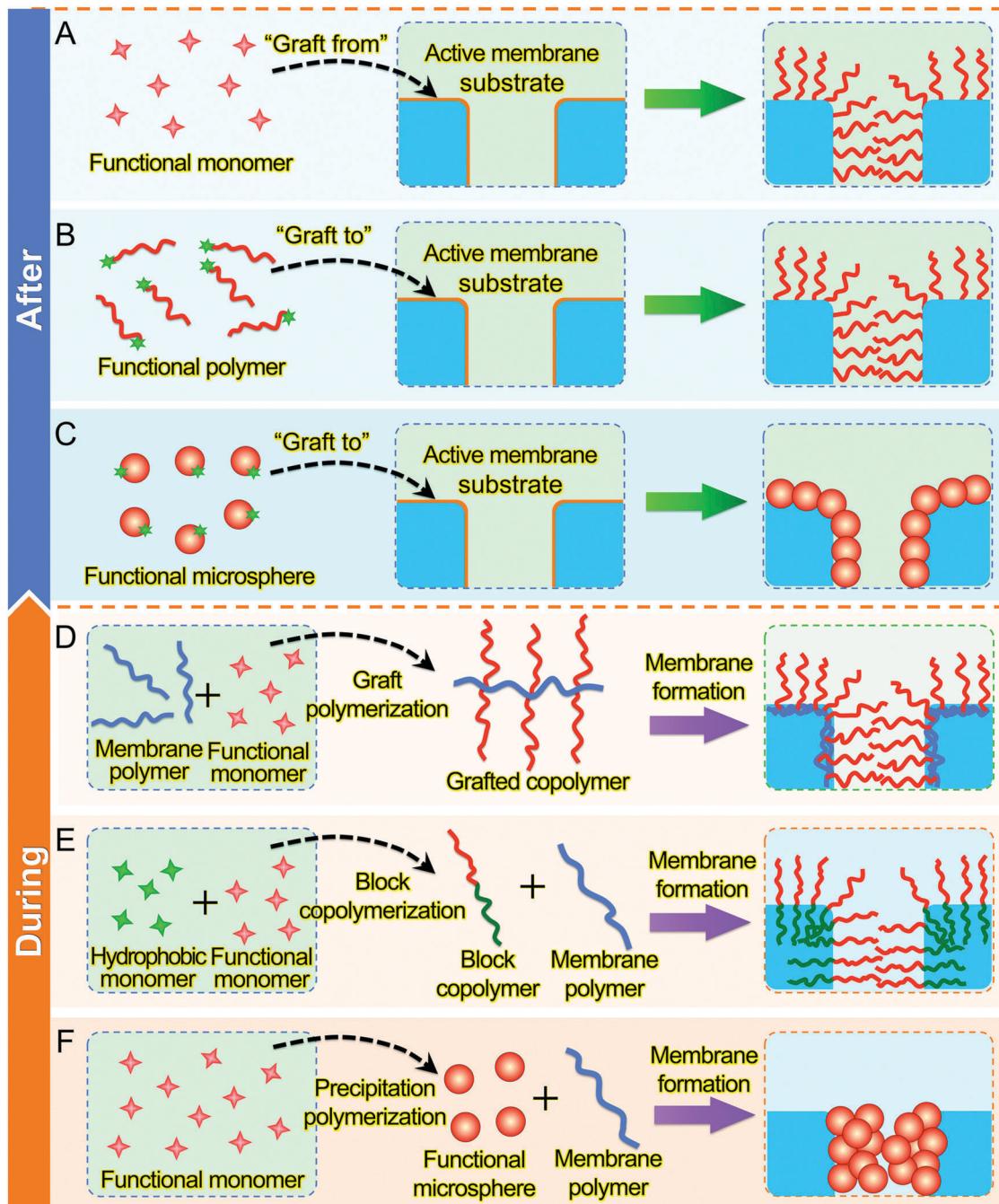


Fig. 2 Strategies for fabricating smart gating membranes by introducing stimuli-responsive domains into membranes after (A–C) or during (D–F) the membrane formation. (A) Gates are fabricated on the membrane substrate by grafting from functional monomers. (B and C) Gates are fabricated by grafting functional polymers (B) or microspheres (C) onto the membrane substrate. (D–F) Gates are fabricated by blending functional grafted (D) or block (E) copolymers, or microspheres (F) with membrane-forming materials during the membrane formation.

critical for the positively responsive gating function. For example, PNIPAM, with a LCST ($\sim 32^\circ\text{C}$) close to human body temperature, is widely used in positively thermo-responsive gates (Fig. 3B).¹⁴ At temperatures below the LCST, PNIPAM chains are swollen and hydrophilic due to the hydrogen bonding between the amide groups and water molecules, thus the membrane pores “close”. With an increase in the temperature above the LCST, the PNIPAM chains become shrunken

and hydrophobic due to hydrogen bonding cleavage, thus the membrane pores “open”. Since the LCST can be tuned by incorporating hydrophilic or hydrophobic groups into the PNIPAM chains, gating membranes with tunable triggering temperatures for gating can be achieved for more flexible applications.³⁶

3.1.2 pH-responsive gating. Typically, polymers containing weak alkaline groups, which can be protonated or deprotonated

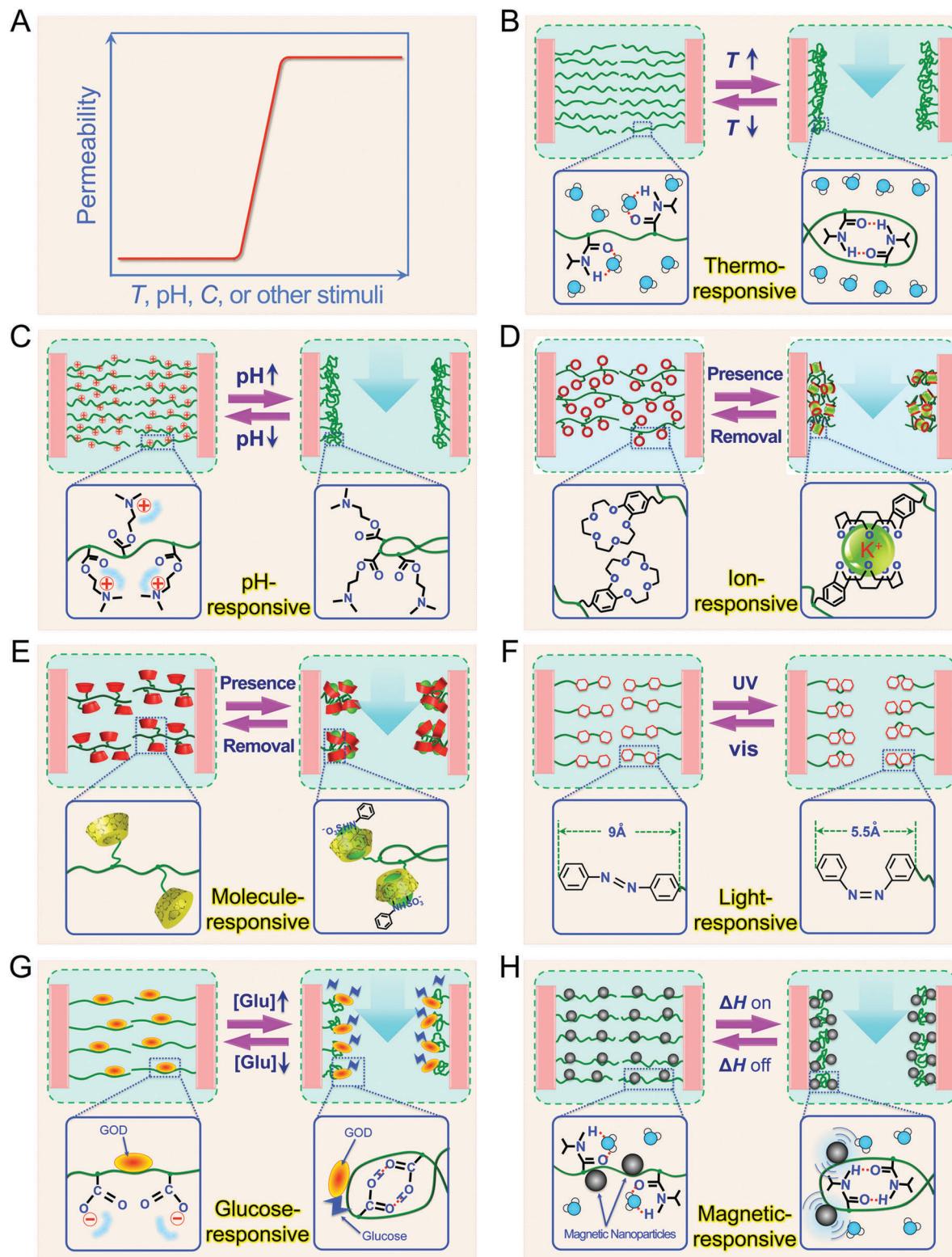


Fig. 3 Smart gating membranes with a positively-responsive gating model. The membrane permeability increases dramatically through opening membrane pores in response to an increase in or the presence of a stimulus (A), such as temperature (B), pH (C), a specific ion (D) or molecule (E), UV light (F), glucose concentration (G), or a magnetic field (H).

for configuration change, can be used as positively pH-responsive gates. For example, poly(*N,N*-dimethylaminoethyl methacrylate)

(PDM) can swell in acidic environments due to the electrostatic repulsion between protonated $-\text{N}(\text{CH}_3)_2$ groups; by contrast,

in basic environments, the PDM can shrink due to the deprotonation of the amine groups (Fig. 3C).²⁶

3.1.3 Ion-responsive gating. Copolymers based on PNIPAM and crown ether are typical examples of ion-responsive gates, which employ the crown ethers as ion receptors and the PNIPAM units as actuators. Typically, for positively K⁺-responsive gates based on PNIPAM and 15-crown-5, once the K⁺ ions appear, the 15-crown-5 moieties capture the ions and form stable 2:1 “sandwich” complexes. Such host-guest complexations break the hydrogen bonding between the crown ether and water molecules, leading to a contraction of the copolymer chains to achieve a “close” to “open” pore switch; as a result, the pore size changes from *ca.* 43 nm to *ca.* 118 nm (Fig. 3D).³⁷

3.1.4 Molecule-responsive gating. Positively molecule-responsive gates are usually designed by integrating the molecular recognition ability of beta-cyclodextrin (β -CD) and the thermo-responsivity of PNIPAM for separating or detecting specific molecules (Fig. 3E).³⁸ These gates can be isothermally opened by recognizing guest molecules with a hydrophobic side group (*e.g.*, 8-anilino-1-naphthalenesulfonic acid ammonium salt (ANS)) at a certain temperature, due to copolymer shrinking induced by the β -CD/ANS complexation.

3.1.5 UV-light-responsive gating. Positively UV-light-responsive gates usually utilize azobenzene-based materials, which can undergo a *trans*-*cis* isomerization transition in response to UV light (Fig. 3F).³⁹ Upon UV irradiation, the azobenzene groups can change their planar configuration into a non-planar one, with a drastic decrease in the distance between the *para* carbon atoms from 9.0 Å to 5.5 Å. Such configuration changes of azobenzene groups effectively control the membrane pore size.

3.1.6 Glucose-responsive gating. Typically, positively glucose-responsive gates can be developed by combining glucose oxidase (GOD) and pH-responsive polymers with weak acid groups such as carboxylic acids groups.¹⁷ For example, when poly(acrylic acid) (PAAc) chains immobilized with GOD are used as gates, the carboxyl groups are dissociated at neutral pH in the absence of glucose; thus the gates “close” due to the PAAc chain extension caused by the electrostatic repulsion between their negatively-charged carboxyl groups. When the glucose concentration increases, the GOD catalyzes glucose into gluconic acid, leading to a lower pH and the protonation of the carboxylate group; thus the gates “open” because of the reduced electrostatic repulsion between the carboxylate groups (Fig. 3G).

3.1.7 Magnetic-responsive gating. Magnetic-responsive properties can be incorporated into the gates by doping magnetic nanoparticles such as iron oxides with thermo-responsive polymers. Usually, superparamagnetic Fe₃O₄ nanoparticles are used to obtain positively magnetic-responsive gates by incorporating them with temperature-responsive PNIPAM polymers because of the advantages of Fe₃O₄ nanoparticles, such as their ease of synthesis and high heating efficiency (Fig. 3H).⁴⁰ Since the nanoparticles can generate heat under an alternating high frequency magnetic field, such gates can be remotely opened or closed through turning “on/off” the magnetic field.

3.2 Negatively responsive gating

3.2.1 Thermo-responsive gating. Polymers with interpenetrating networks (IPNs) composed of poly(acrylamide) (PAAm) and PAAc can be used as negatively thermo-responsive gates (Fig. 4B). The polymeric gates can shrink due to the formation of a PAAm/PAAc complex *via* hydrogen bonds at temperatures below the upper critical solution temperature (UCST) of IPNs, resulting in pore “opening”. While at temperatures above the UCST, the IPNs can swell due to their dissociation through the breakage of hydrogen bonds, leading to pore “closing”. Thus, the membrane pores can switch from an “open” to a “closed” state once the temperature increases above the UCST.²¹

3.2.2 pH-responsive gating. Negatively pH-responsive gates usually possess weak acidic groups that can gain or lose protons in response to pH changes. For example, the polymer chains of negatively pH-responsive PAAc gates can shrink due to the formation of intermolecular hydrogen bonding between their carboxylic groups at low pH (Fig. 4C).²⁷ In basic environments, the PAAc chains can extensively swell due to the electrostatic repulsion between the protonated carboxylic groups.

3.2.3 Ion-responsive gating. As a typical example, negatively ion-responsive gates can be fabricated by incorporating PNIPAM with 18-crown-6 groups.¹⁶ The 18-crown-6 moiety can selectively recognize certain ions such as Pb²⁺ to form a stable 1:1 host-guest complex. When the Pb²⁺ ions appear, the opened pores can close due to the ion-responsive isothermal swelling of the gates, causing a change in pore size from 159 nm to 94 nm (Fig. 4D).

3.2.4 Molecule-responsive gating. Copolymers with cyclodextrin and PNIPAM can also be used as negatively molecule-responsive gates, because they can isothermally change from shrinking to swelling through recognizing guest molecules with a hydrophilic side group or without side groups (*e.g.* 2-naphthalene-sulfonic acid) at a certain temperature.³⁸ Thus, membrane pores can change from an “open” to a “closed” state due to the molecule-responsive volume transition of the gates (Fig. 4E).

3.2.5 UV-light-responsive gating. Negatively UV-light-responsive gates are usually spiropyran-containing polymers.⁴¹ The non-polar form of the spiropyran groups under visible-light is hydrophobic and shrunken in solution. When exposed to UV, the spiropyran groups can be isomerized into the polar merocyanine form with charges, which are hydrophilic and swollen (Fig. 4F). This allows the membrane pores to close when triggered by UV light.

3.2.6 Ion-strength-responsive gating. Zwitterionic polymers such as poly(*N,N'*-dimethyl(methylmethacryloyl ethyl)ammonium propane sulfonate) (PDMAPS) are usually used as negatively ion-strength-responsive gates due to the concurrent presence of positive and negative charges on their structures. Such zwitterionic polymers can exhibit configuration changes depending on the ion strength of ions such as sodium chloride (NaCl).⁴² For example, at a low ion strength of NaCl, the electrostatic attraction between the cations and anions forces the PDMAPS polymers into a coiled conformation (Fig. 4G). While at a high ion strength, the Na⁺ and Cl⁻ ions disrupt these electrostatic interactions through forming ion pairs with the anions and cations of the PDMAPS polymers, resulting in an increase in the net charge

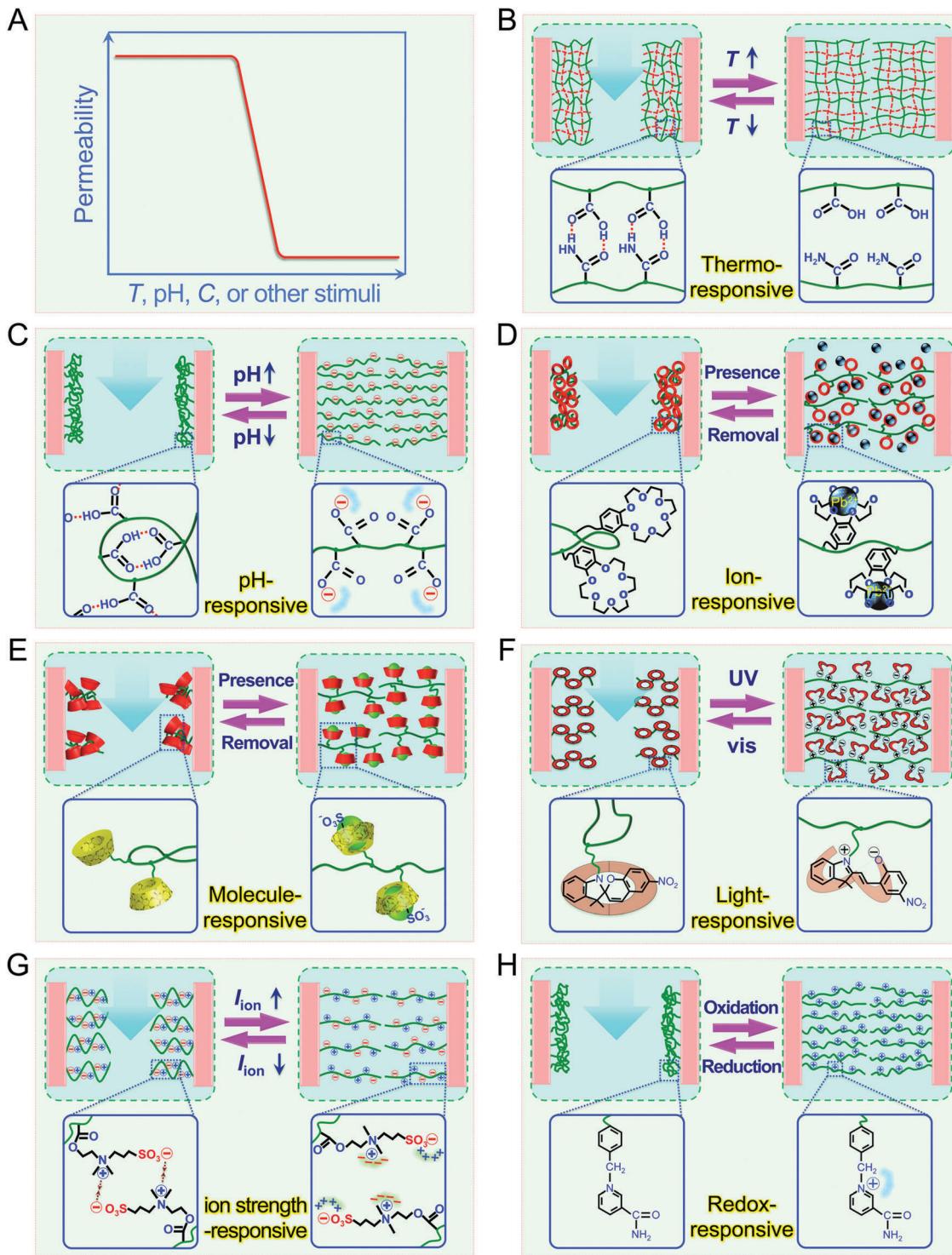


Fig. 4 Smart gating membranes with a negatively-responsive gating model. The membrane permeability decreases dramatically through closing membrane pores in response to an increase in or presence of a stimulus (A), such as temperature (B), pH (C), a specific ion (D) or molecule (E), UV light (F), ion strength (G), or oxidation (H).

and a more stretched conformation of the PDMAPS chains.⁴² So, the “open” and “close” of the membrane pore can be effectively controlled through changing the ion strength.

3.2.7 Redox-responsive gating. Negatively oxidation-responsive gates usually consist of polymers that can be easily oxidized,

such as poly(3-carbamoyl-1-(*p*-vinylbenzyl)pyridinium chloride) (PCVPC) (Fig. 4H). The PCVPC polymers are water-soluble in their oxidized state, but water-insoluble in their reduced state. In the reduced state, the polymers are deionized; thus they shrink and “open” the pores. In contrast, in the oxidized state,

the PCVPC polymers are ionized due to the charges formed *via* oxidation; thus they swell and “close” the pores.⁴³

4. Applications of smart gating membranes

The positively- and negatively-responsive gating functions, in response to various stimuli, enable the precise control of the pore size and surface properties of smart gating membranes, as well as the permeability and selectivity. The versatilities of smart gating membranes and their flexible gating models provide flexible strategies to meet the demands of specific applications for myriad fields.

4.1 Stimuli-responsive permeations

4.1.1 Self-adjustment of hydraulic permeability. With self-regulated hydraulic permeability, which is defined as the convective flow of solvents driven by a pressure difference, smart gating membranes are promising as chemical valves for maintaining concentrations in reactors or sensing specific components in solutions. For example, gating membranes with ethanol-responsive gates¹² provide opportunities for regulating the ethanol concentration (C_E) at a relatively stable level in reactors for more efficient fermentation (Fig. 5A). The gates that swell when C_E is below a certain value (C_{E1}) (Fig. 5B), can shrink when C_E increases above C_{E1} during the fermentation, causing the

increased permeability to remove the excess ethanol for concentration maintenance. Although further increasing C_E above another certain value (C_{E2}) leads to the swelling of the gates, such a high value of C_{E2} is difficult to achieve since the maximum C_E in ethanol fermentation is usually lower than C_{E2} . Both the values of C_{E1} and C_{E2} vary with changing the operation temperature. For example, at 22 °C, 25 °C and 28 °C, the corresponding C_{E1} values are respectively 16.8 vol%, 12.3 vol% and 10.8 vol%, and the corresponding C_{E2} values are 35.0 vol%, 32.0 vol% and 28.3 vol%, respectively (Fig. 5C).¹² Thus, we can infer that the membrane permeability can be flexibly regulated depending on the C_E at a certain temperature for maintaining concentrations for efficient fermentation. Such concentration-dependent self-regulated hydraulic permeability can also be used for sensing special metal ions and/or degrading toxic organics. For example, positively K⁺-responsive gating membranes enable the “open/close” switch of their pores for regulating their permeability in response to K⁺ concentration specifically (Fig. 6A).³⁷ Such membranes can achieve high permeability in 0.1 M K⁺ solution with low permeability in pure water (Fig. 6B). Similarly, negatively Pb²⁺-responsive gating membranes can reduce their permeability in response to trace Pb²⁺ levels of $1.3\text{--}10 \times 10^{-6}$ mol L⁻¹ in solution (Fig. 6C).¹⁶ Both ion-responsive gating membranes can be applied as sensors for specific ion detection in water *via* measuring the flux change. Moreover, the Pb²⁺-responsive gating membranes are promising for Pb²⁺ removal based on the complexation between Pb²⁺ and the crown ether on the gates.¹⁶

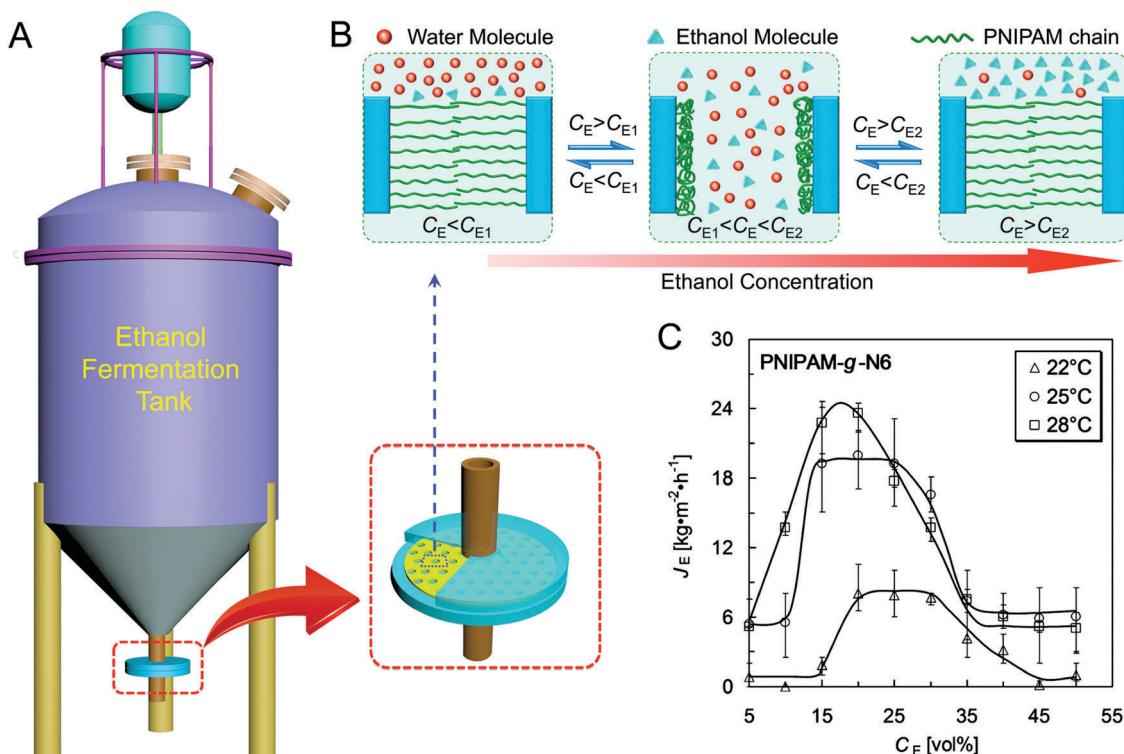


Fig. 5 Smart gating membranes for regulating ethanol concentration in fermentation. (A) Schematic illustration of a fermentation reactor equipped with ethanol-concentration-responsive gating membranes for maintaining the ethanol concentration (C_E) inside. (B) Membranes with PNIPAM gates for ethanol-responsive gating, in which C_{E1} and C_{E2} are the two critical response concentrations of the PNIPAM gates. (C) Isothermal regulation of membrane permeability through varying the C_E value. (B) and (C) are reproduced with permission from ref. 12, Copyright 2012 American Chemical Society.

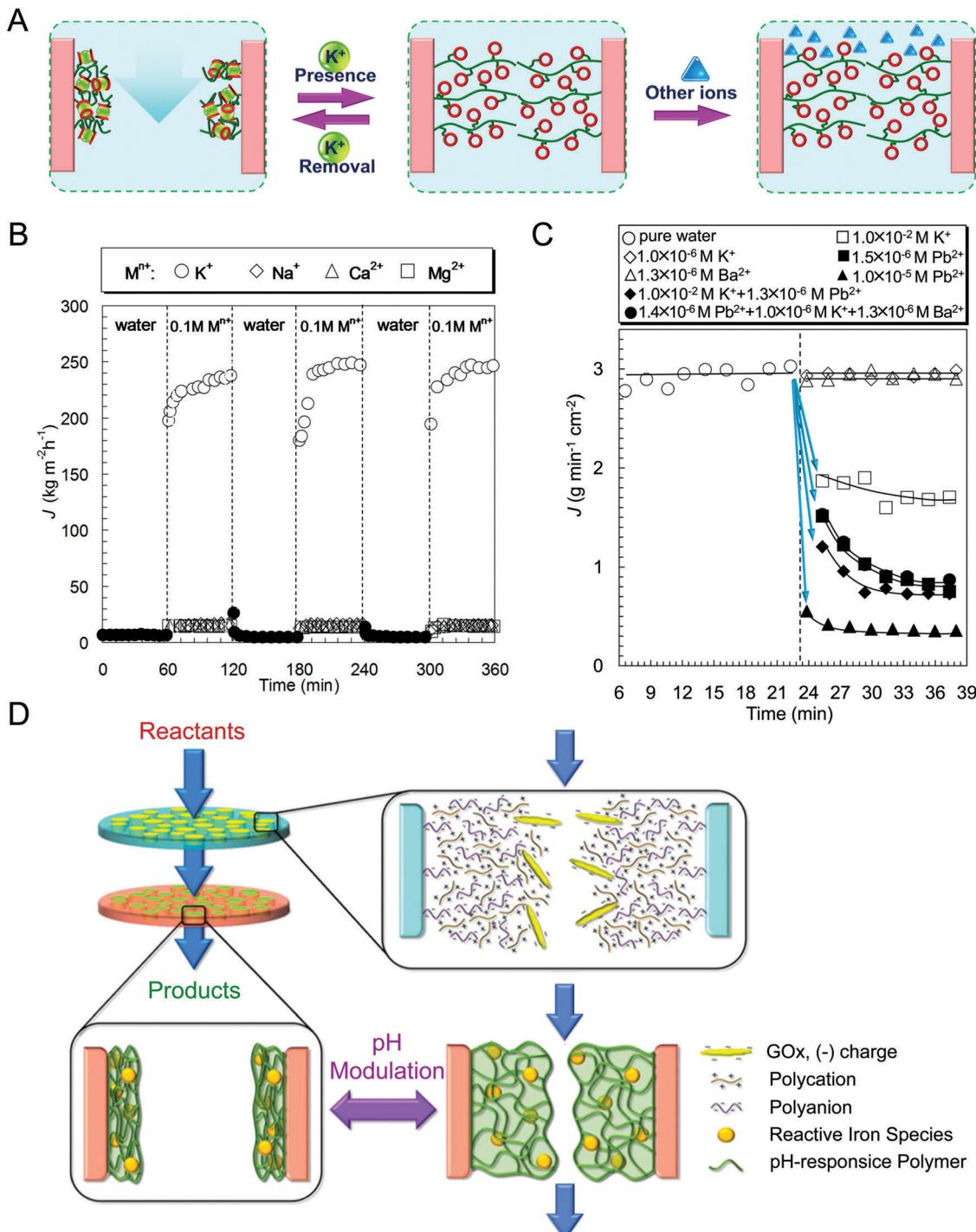


Fig. 6 Smart gating membranes for sensing ions and treating toxicants. (A and B) K^+ -responsive gating membrane (A) and the K^+ -responsive permeability (B). Reproduced with permission from ref. 37, Copyright 2012 Wiley-VCH. (C) Gating membranes with Pb^{2+} -responsive self-regulated permeability. Reprinted with permission from ref. 16, Copyright 2013 The Royal Society of Chemistry. (D) Integrated membrane system for degrading toxic organics for water purification. Reproduced with permission from ref. 44, Copyright 2011 National Academy of Sciences, U.S.A.

Besides, by combining bioactive membranes with pH-responsive gating membranes, water purification systems can be developed for degrading toxic organics (Fig. 6D).⁴⁴ The pores of the top membrane contain polycations and polyanions immobilized with GOD for the catalytic production of hydrogen peroxide from glucose. The bottom membrane contains pH-responsive

PAAc hydrogel gates with doped iron species, which can decompose the hydrogen peroxide into free radical oxidants for degrading toxic organics, such as trichlorophenol, into alkali ions to increase pH for pore closing. Thus, this leads to a reduced flux of toxic organics, and allows a longer time for their efficient degradation.⁴⁴

4.1.2 Self-adjustment of diffusional permeability. Smart gating membranes with self-regulated diffusional permeability, which is defined as molecular diffusion driven by a concentration gradient, are promising for regulating the mass transfer of active molecules across the membrane for controlled release. Particularly, capsule membranes are important for controlled drug release due to their enclosed internals for encapsulation. For example, positively glucose-concentration-responsive gating membranes enable controllable insulin release for diabetes therapy (Fig. 7A).⁴⁵ When the glucose concentration changes

from 0 to 0.2 mol L⁻¹ *in vitro*, the insulin release rate increases 9.4 times, and the diffusion coefficient elevates from 0.79 cm² s⁻¹ to 7.4 cm² s⁻¹ (Fig. 7B).¹⁷ Moreover, such membranes can reversibly increase/decrease their release rate of insulin by repeatedly changing the glucose concentration between 100 and 400 mg dL⁻¹ (Fig. 7C).⁴⁶ The gating membrane can also be incorporated into enclosed systems for improved controlled release (Fig. 7D).⁴⁷ The gating membrane with negatively pH-responsive gates serves as a functional valve for controlling the substance release from such a system, while the positively pH-responsive hydrogel inside the

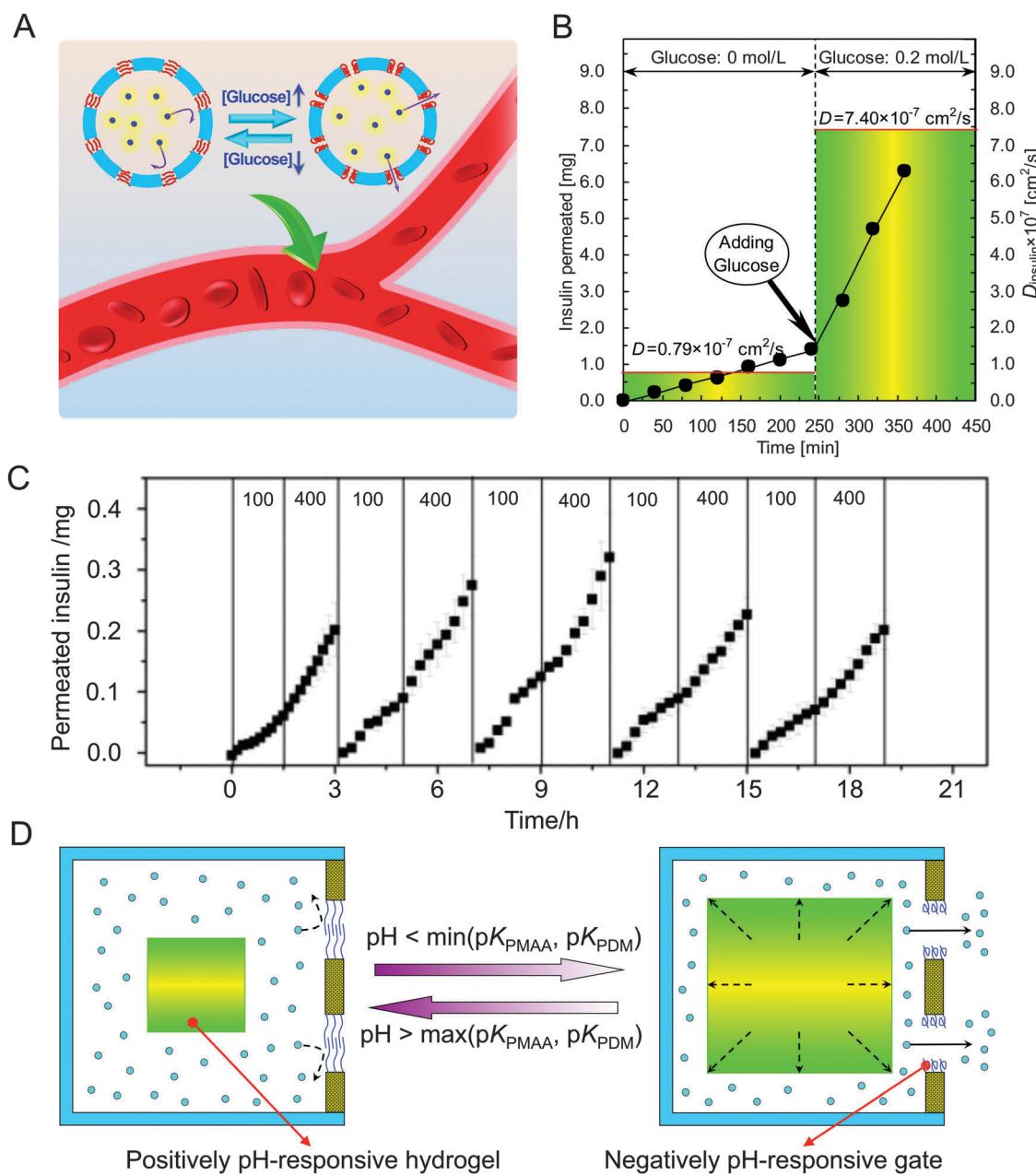


Fig. 7 Smart gating membranes for controlled release. (A) Smart microcapsule membrane with glucose-responsive gates for controlled release. Reproduced with permission from ref. 45, Copyright 2004 Elsevier. (B and C) Glucose-responsive release of insulin from the glucose-responsive gating membrane. Figure B is reprinted with permission from ref. 17, Copyright 2004 Elsevier; figure C is reproduced with permission from ref. 46, Copyright 2010 Wiley-VCH. (D) Pumping systems with gating membranes containing pH-responsive gates for enhanced controlled release. Reproduced with permission from ref. 47, Copyright 2006 Wiley-VCH.

system works as a pump for pumping the substances out. Upon request, the membrane pores open and the hydrogel swells; thus the encapsulated substances can be pumped out through the open pores to achieve an enhanced release rate, beyond the limit of concentration-driven diffusion.

4.2 Stimuli-responsive separations

4.2.1 Size-effect-based sieving. With the stimuli-responsive self-regulation of pore size, gating membranes can be applied for graded sieving separation. Generally, only smaller molecules/particles can permeate across the membrane with closed pores, while both smaller and larger molecules/particles can permeate when the pores open (Fig. 8A). Thus, the separation of substances with different sizes can be achieved by using single

gating membranes, with the pore size regulated by designed stimuli. For example, pH-responsive gating membranes can selectively reject dextran molecules with appropriate molecular weights of 10, 40 and 70 kDa, depending on the environmental pH (Fig. 8B).²⁷ Temperature-responsive gating membranes enable the fast permeation of small molecules such as NaCl (hydrodynamic radius ~ 0.1 nm), showing large diffusional coefficients at both 25 °C and 40 °C (Fig. 8C); while large molecules such as VB12 (hydrodynamic radius ~ 2 nm) can only permeate through the membrane with opened pores at 40 °C.¹⁴ Similarly, Ba²⁺-responsive gating membranes can sieve molecules with different sizes such as dextran molecules with radii of 2–30 nm (Fig. 8D).⁴⁸

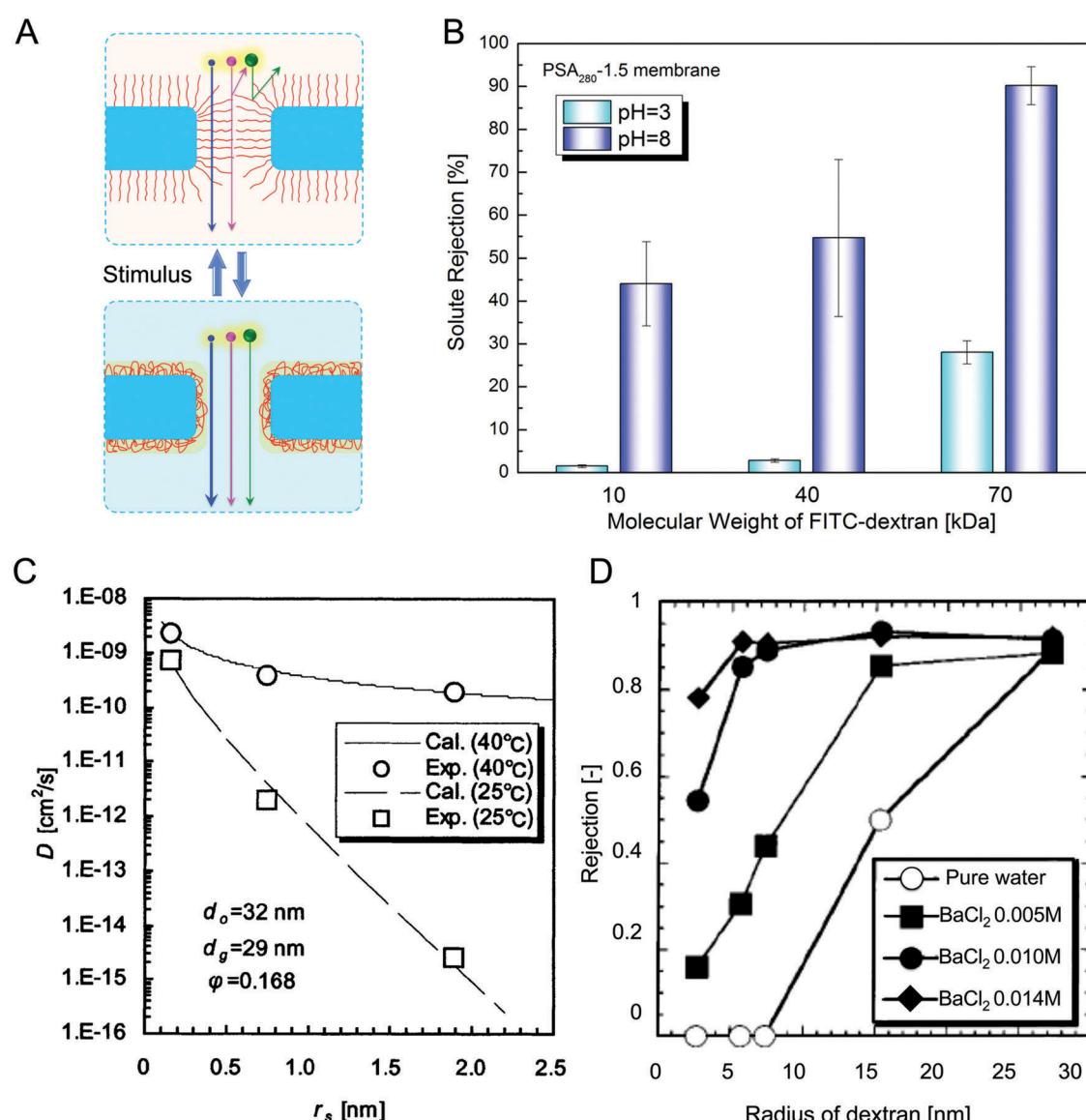


Fig. 8 Smart gating membranes for size-sieving-based separation. (A) Schematic illustration of the stimuli-responsive size-sieving-based separation. (B–D) Graded size-sieving-based separations using pH-responsive (B), thermo-responsive (C), and ion-responsive (D) gating membranes. Figure B is reprinted with permission from ref. 27, Copyright 2014 Elsevier; figure C is reprinted with permission from ref. 14, Copyright 2003 American Institute of Chemical Engineers (AIChE); figure D is reprinted with permission from ref. 48, Copyright 2002 American Chemical Society.

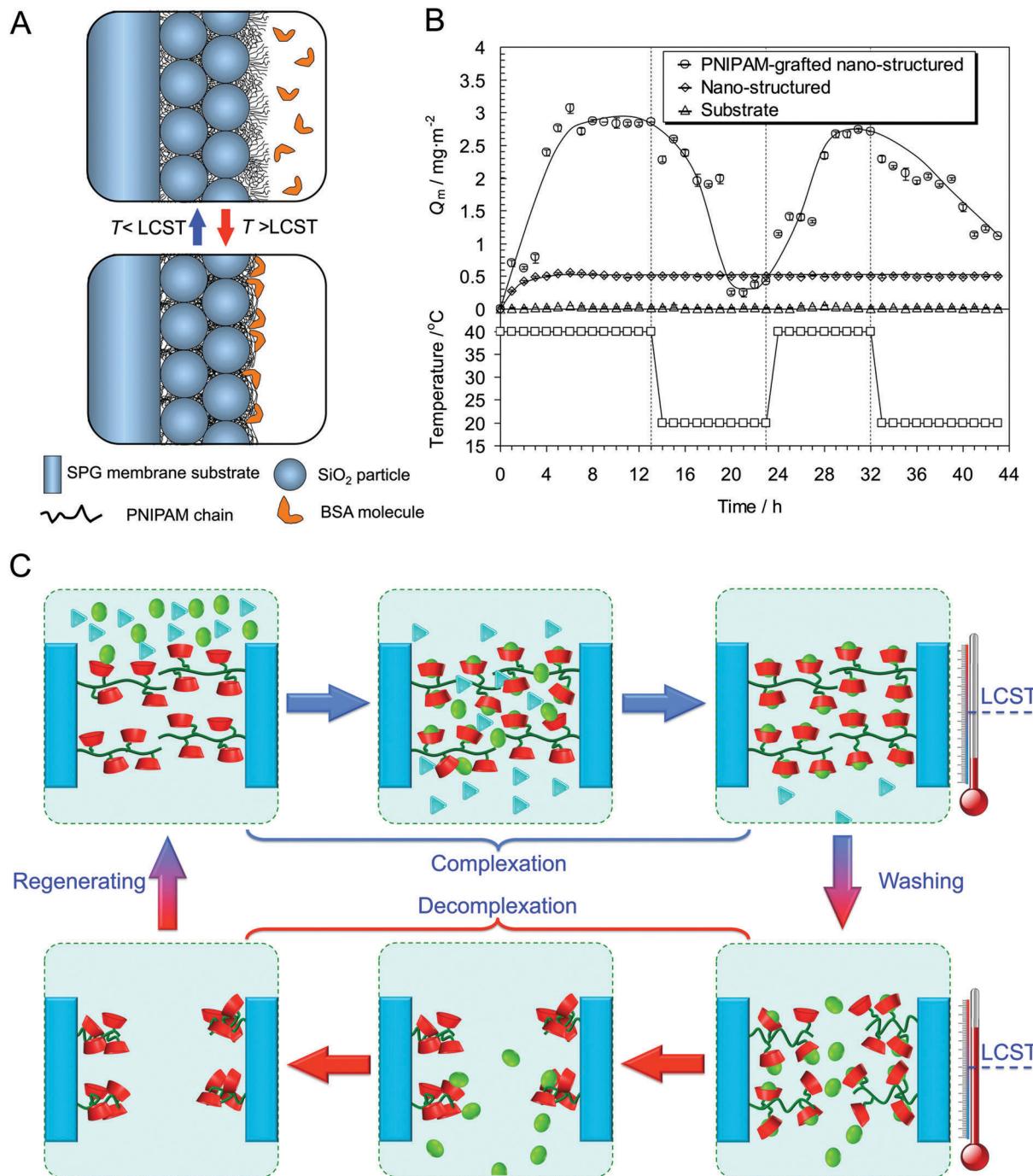


Fig. 9 Smart gating membranes for affinity-based separation. (A and B) Schematic illustration (A) and experimental data (B) showing membranes with PNIPAM-based gates for thermo-induced adsorption/desorption of BSA molecules. Reproduced with permission from ref. 15, Copyright 2010 Elsevier. (C) Membranes containing thermo-responsive PNIPAM chains with appended β -CD moieties as functional gates for chiral resolution. Reproduced with permission from ref. 22, Copyright 2008 Wiley-VCH.

4.2.2 Affinity-based adsorption/desorption. With self-regulated surface properties for controlling the affinity between pore surfaces and substances, smart gating membranes offer ingenious tools for stimuli-responsive separation or purification of substances such as proteins and chiral molecules. For example, gating membranes with gates that allow a thermo-induced switch between the hydrophilic and hydrophobic states can be used for

separating hydrophobic substances such as bovine serum albumin (BSA) based on hydrophobic adsorption (Fig. 9A). The BSA can be adsorbed when the gates are hydrophobic, and desorbed when the gates become hydrophilic. This can be simply controlled by varying the operation temperature (Fig. 9B).¹⁵ As another example, by combining PNIPAM with functional β -CD, which can act as a host molecule or chiral selector, gating membranes for chiral resolution

are achieved (Fig. 9C).²² At temperatures below the LCST of PNIPAM, the PNIPAM/β-CD gates are swollen and hydrophilic. During the solution permeation, one of the enantiomers can be selectively captured by the β-CD groups based on their stronger association. When increasing the temperature above the LCST, the PNIPAM/β-CD gates become shrunken and hydrophobic,

leading to decomplexation of the β-CD and captured enantiomer due to the weakened association constant; thus the enantiomer can be separated. Therefore, smart membranes with functional gates for enantioseparation allow simple membrane regeneration through changing the temperature, and show high efficiency for selective chiral resolution.²²

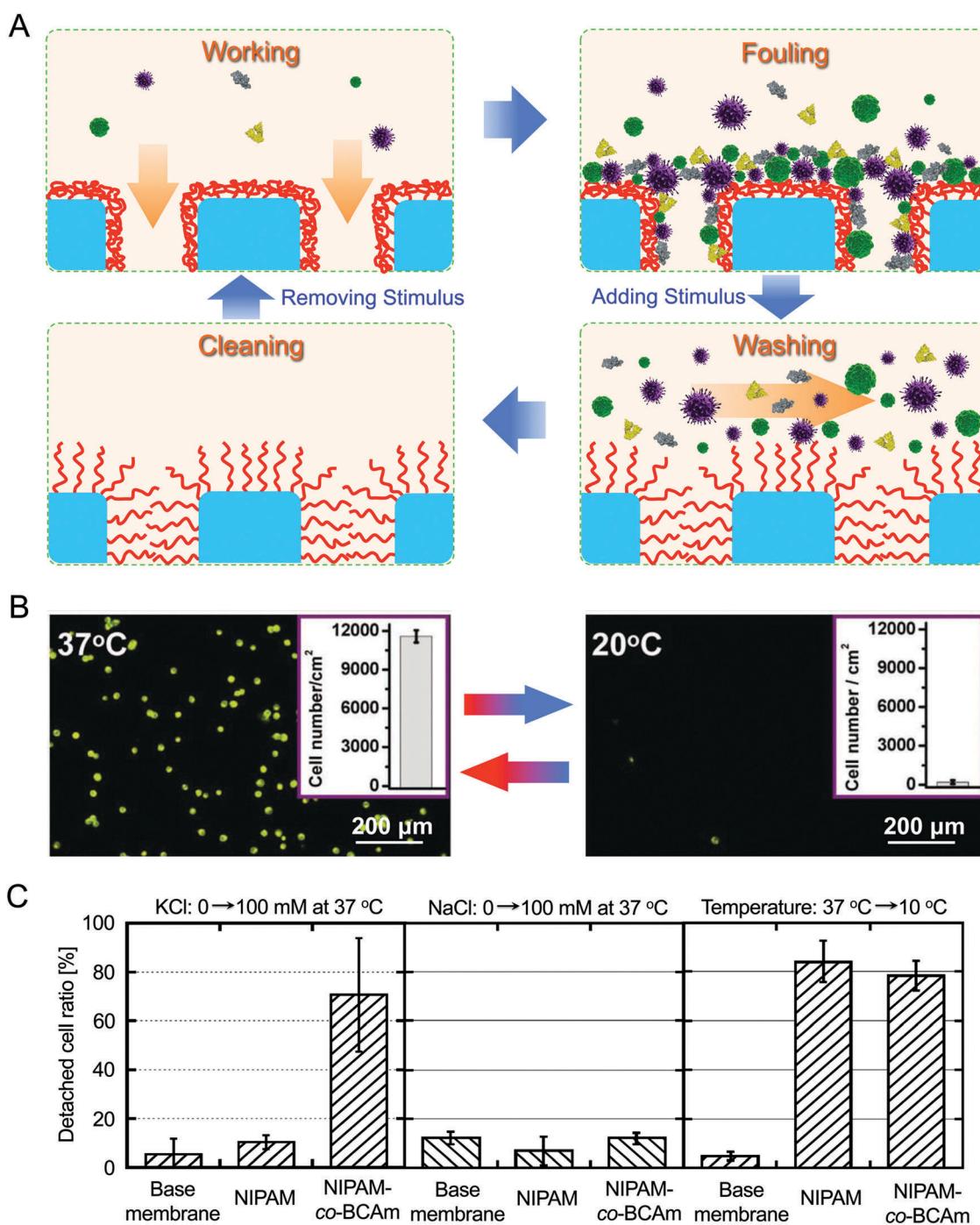


Fig. 10 Smart gating membranes for self-cleaning. (A) Schematic illustration of the self-cleaning principle with smart gating membranes through easily adding/removing a simple environmental stimulus, e.g., temperature decrease for PNIPAM gates. (B) Thermo-induced self-cleaning of cells on smart gating membrane surface. Reproduced with permission from ref. 49, Copyright 2013 Wiley-VCH. (C) Detached cell ratios of the smart gating membrane in response to various signals. Reproduced with permission from ref. 50, Copyright 2005 American Chemical Society.

4.3 Self-cleaning of membranes

Membrane fouling, which usually leads to a weakened membrane performance such as permeability loss, is an unavoidable problem for membrane-involved processes. Generally, polymers used for porous membrane manufacture are usually hydrophobic in nature; as a result, the organic foulants in water are highly susceptible to depositing on the membrane surface due to the hydrophobic interaction between the membrane and foulants.³ Thus, hydrophilic polymers grafted on membrane surfaces can provide steric-osmotic barriers against the fouling adsorption for reduced membrane fouling; however, the grafted polymers also reduce the intrinsic permeability owing to the partial blocking of the membrane pores.³ Smart gating membranes with tunable surface properties create opportunities to achieve self-cleaning functionality for reducing membrane fouling while retaining the permeability. Upon adding a stimulus, the shrunken and hydrophobic gates become swollen and hydrophilic; such transitions weaken the interactions between the foulant and membrane surface for foulant detachment (Fig. 10A). Thus, the foulant could be easily cleaned by water washing. After that, the gates can be recovered to a shrunken state to preserve the permeability (Fig. 10A). Recently, thermo-responsive surfaces have been shown to reversibly capture and release targeted Michigan Cancer Foundation-7 cells with temperatures changing between 37 °C and 20 °C (Fig. 10B).⁴⁹ This offers opportunities for the gating membranes to be used as smart substrates with a self-cleaning function for cell cultures. Moreover, the negatively K⁺-responsive gating membranes can self-clean dead A549 lung carcinoma cells on their surface during the cell culture, due to the swelling of the polymer brush in response to K⁺ ions from the dead cells, or in response to a temperature change from 37 °C to 10 °C for dead cell detachment (Fig. 10C).⁵⁰ Such gating membranes with stimuli-induced self-cleaning functions could be a new-generation of membranes.

5. Summary and outlook

This paper reviews recent progress in stimuli-responsive smart gating membranes, including the design strategies, fabrication approaches, stimuli-responsive properties and gating models, and the emerging applications. Inspired by the intelligent channels across cell membranes, smart gating membranes are fabricated by chemically/physically tailoring the membranes with stimuli-responsive gates after or during membrane formation. The gating membranes allow the self-regulation of the pore size and surface properties, as well as the permeability and selectivity, in response to various stimuli. Such smart features enable not only enhanced performances for wide applications in traditional fields, but also advanced performances for exploiting new applications in extended fields. However, challenges still remain for further applying the smart gating membranes to industrial manufacturing and/or biomedical applications. For example, the mechanisms for mass transfer in the pores of gating membranes are still not clear enough, and the long-term stability of gating membranes in large-scale industrial applications still needs to be tested.

Up to now, the greatest technical challenge for applying gating membranes in large-scale industrial applications is the lack of facile and controllable methods to achieve industrial-scale production of the desired gating membranes. For biomedical purposes, the biocompatibility of gating membranes is also an important and crucial issue that needs to be verified before practical applications. Future efforts should focus on the exploitation of novel materials for fabricating new smart gating membranes, and the investigation of the synergistic effect between the chemical/physical structures and the responsiveness of gates for designing novel gating functions, as well as the mechanisms for mass transfer and separation, the development of facile membrane formation processes for industrial-scale production, and the enhancement of the sensitivity and response rate for process intensification. We believe this research would benefit the development of novel smart gating membranes for industrial production and/or biomedical applications.

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