



Bioinspired Ionic Sensory Systems: The Successor of Electronics

Kai Xiao,* Changjin Wan, Lei Jiang, Xiaodong Chen,* and Markus Antonietti*

All biological systems, including animals and plants, communicate in a language of ions and small molecules, while the modern information infrastructures and technologies rely on a language of electrons. Although electronics and bioelectronics have made great progress in the past several decades, they still face the disadvantage of signal transformation when communicating with biology. To narrow the gap between biological systems and artificial-intelligence systems, bioinspired ion-transport-based sensory systems should be developed as successor of electronics, since they can emulate biological functionality more directly and communicate with biology seamlessly. Herein, the essential principles of (accurate) ion transport are introduced, and the recent progress in the development of three elements of an ionic sensory system is reviewed: ionic sensors, ionic processors, and ionic interfaces. The current challenges and future developments of ion-transport-based sensory systems are also discussed.

1. Introduction

Sensors in modern devices are mainly based on electron transport systems,^[1–3] while biological systems transmit signals via ions or molecules.^[4,5] Despite the impressive achievement in speed and precision of electron-transport-based sensory systems, they still suffer from limitations when interacting with biological systems. For instance, it is difficult to realize a direct human-computer interface (bioelectronic interface) without a

transducer, since both sides speak “different languages.” Specifically, biological systems contain numerous nanoscale ionic elements, which exist in the form of ion channels and ion pumps in cell membranes. They work together to control the ion concentration gradients across cell membranes, enabling information encoding/decoding through action potentials.^[6] This is the biological mode of communication within an organism, and also the way of detecting and interpreting information from the environment.^[5] To narrow the gap between biological systems and artificial systems, various electronic/ionic couplers (ionotronics) have been developed.^[7–9] Ionotronics function by a hybrid circuit of mobile ions and mobile

electrons, which are incorporated to support broad applications including smart human–machine interfaces and energy storage devices. Furthermore, to realize the seamless communication between biological systems and man-made devices, ion-transport-based sensory systems should be developed, as they operate in the same way as nature.^[10,11]

The concept of ionic sensory systems is inspired by ion transport in biological systems, which is the movement of ions across a membrane, passively through ion channels or actively through ion pumps such as symporters and antiporters.^[4] This makes ion transport in cells is more controllable in terms of ion species, direction, speed, etc. Beyond biology, ion transport is integral to the chemiosmotic theory, not only in bulk systems but also at interfaces. Ion transport is also involved in many important scientific issues, e.g., membrane science,^[12,13] energy conversion and storage (for example fuel cells and lithium battery),^[14–16] nanofluidics,^[17,18] water desalination^[19] and ionic sensory systems.^[20,21]

In general, the ion-related modulations are based on two mechanisms: 1) formation of an electric double layer (EDL) (Figure 1A) and 2) electrochemical reactions (Figure 1B). Electrical double layer formation is a typical capacitive process, that involves ion accumulation and depletion at an interface. The charged surface will repel ions with the same charge (co-ions) and attract ions of opposite charge (counter-ions) by the electrostatic force.^[18] The ion redistribution on the charged surface will lead to the formation of a local ion-based field dipole, which can be further used for ion transport or for detecting or interpreting signals from biological systems directly. Electrochemical ion modulation is a faradaic process, in which electrons are transferred between different substances.^[22] Obviously, the key difference between the capacitive and the faradaic model

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is that the latter involves oxidation/reduction processes while the former does not. Many literature studies have discussed the difference between electrochemistry and capacitive charging in organic electronics.^[23–26] Moreover, sensory systems based on electrochemistry in ion–electron-coupled systems, e.g., ion-gated transistors^[27] and ion-gated superconductors,^[28] are intrinsically electron-based systems and have previously been well reviewed.^[7,8,29] Therefore, the central point of this essay is the accurate control of ion transport in man-made devices through a nanoconfined channel or an ionic conductor based on the EDL concept, offering a more efficient and controllable methodology to construct ionic sensory systems that resemble their biological counterparts.^[30] Those ion-transport-based sensory systems can be categorized into three groups—ionic sensors, ionic processors, and ionic interfaces—all of which center on ion transport. In addition, some new concepts of ion-transport-based integrated devices are proposed.

2. Mechanism of Accurate Ion Transport

In biological systems, the success of initiation, processing, and transmission of information is closely related to the accurate ion transport across cell membranes.^[31] The precise ion selectivity (e.g., Na^+/K^+ selectivity),^[32] directionality (e.g., outward K^+ flow and inward Na^+ flow),^[33] and ion transport against concentration gradients (e.g., proton/ion pump) in cells are the molecular basis for all electrical activities. In solid-state systems, these accurate ion transport properties—ion selectivity, rectifications and “pumping” against a concentration gradient—also set the foundation for their broad applications.

Ion selectivity in biology means only specific ion species can be transported by a type of protein pores, while the definition of ion selectivity here is that only one ionic component (either cation or anion) can be transported across an ionic conductor.^[34] Ion selectivity can be realized not only in a solid electrolyte, ionic liquid, or ionic gel, but also in aqueous saline solutions by an ion-selective channel or membrane. Ion selectivity is generated when the dimension of an ionic conductor with surface charge (diameter of nanochannel or polymer network size) matches or is smaller than the Debye screening length (λ).^[35] In this condition, the electrical double layers are overlapping and the channel or ionic conductor is filled with a unipolar solution of counter-ions (Figure 1C). Beyond the dimensions of the ion transport medium, ion selectivity can also be controlled by electrolyte salinity due to the inverse correlation between Debye screening length and ionic strength.^[18]

Ion rectification is a phenomenon with asymmetric ion transport properties based on ion selectivity.^[36] It indicates that ions (or charged molecules) show a diode-like transport characteristic with a preferential direction of ion flow (Figure 1D). Ion rectification can be observed only when the transport medium (nanochannel or ionic polymer) is asymmetric in structure and/or surface charge, as both create an electric field gradient within the ionic conductor.^[36] Ionic diodes and their applications in the fields of sensory systems and controllable release are constructed based on this principle. For example, Simon and co-workers realized neurotransmitter release at synaptic speeds by constructing miniaturized ionic polarization diodes;^[37] Sun et



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al realized ionic signal amplification through an open-junction ionic diode.^[38]

“Ion pumping” is a process of consuming energy to decrease entropy, in which ions are actively transported from low concentration to high concentration (Figure 1E). In biology, ion pumps drive ion transport by using the energy of adenosine triphosphate (ATP), while the energy to drive artificial ion

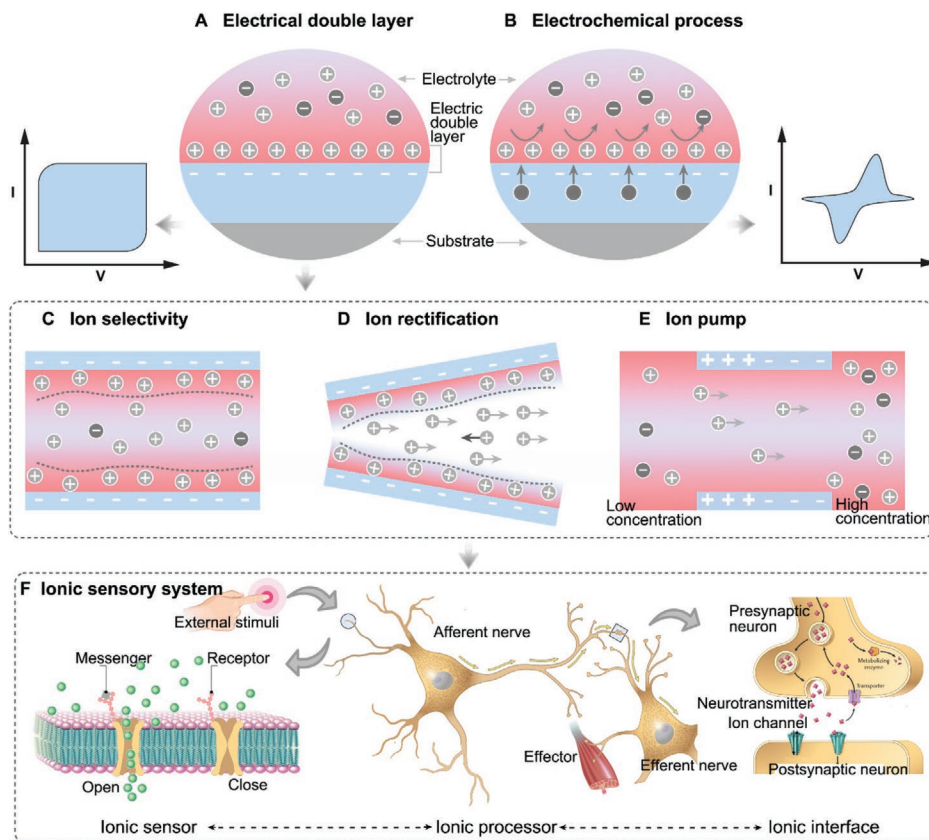


Figure 1. Basic ion-related effects and ion-transport-based sensory systems. A) Schematic diagram of the electrical double layer (EDL) formation and corresponding cyclic voltammogram. B) Schematic diagram of the electrochemical gating mechanism and corresponding cyclic voltammogram. C–E) Ion transport including ion selectivity, ion rectification and ion pump. C) Ion selectivity: the electrical double layers (Stern layer and Diffusion layer) near the surface are overlapping when the diameter of the nanochannel is comparable with the Debye length. This leads to the co-ions being excluded from the channel while the counter-ions can pass through. D) Ion rectification in an asymmetric charged nanochannel: the ions pass through the channel with a preferential direction which is suppressed in another direction when the nanochannel or membrane is asymmetric in structure and/or surface charge. E) The ion pump is an active ion transport from low concentration to high concentration along with energy consumption. F) A typical example of an ionic sensory system, which is based on accurate ion transport and can realize the signal transformation cascade: external stimuli → ionic signal → biological signal.

pumps is diversified, e.g., from light,^[39,40] pH gradients,^[39,41] or electricity.^[42,43] The development of artificial ion pumps is just in its infancy and still far from matching the performance of biological ion pumps, which are not only able to pump one specific ion species, but also to move two types of ions in opposite directions simultaneously ($\text{Na}^+ - \text{K}^+ - \text{ATPase}$).^[4]

Utilizing ion selectivity, ion rectification, and ion pumping, accurate ion-transport-based sensory systems can be realized. Most importantly, signal transmission between external and biological environments is reliably achieved in such a transducing process: external stimuli–ionic signal–biological signal (Figure 1F). The external stimuli such as thermal, pressure, or light signals can be converted to ionic signals by ionic sensors, for example in the form of specific ionic concentration. These signals can then be processed by ionic processors, such as ionic diodes for signal amplification and ionic memristors for signal storage. Finally, the processed signals can be used for communication with biological systems via an ionic interface. At the moment, in some simple cases the signal transformation between external stimuli and biological activity has been realized by “all ionic signals.”^[11] We expect much more

complicated biological activities to be realized by accurate ion (or neurotransmitter) transportation.

3. Emergence of Ion Transport Sensory Paradigms

Although sensory systems based on accurate ion transport are still in their early development, recent progress in nanoionic sensory systems underlines their significant potential. Ion-transport-based sensory systems can be divided into three different components: ionic sensors, ionic processors, and ionic interfaces.

3.1. Ionic Sensors

An ionic sensor is a sensory system based on ion transport, very common both in plants and animals. For example, mammals have high sensing capability to external mechanical stimuli, represented by the senses of touch, balance, hearing, and homeostasis, which all are derived from the phenomenon of ionic mechanotransduction that constitute various physiological

processes.^[44] Inspired by these biological ionic processes, the aim of artificial ionic sensors is to realize similar functions with ultrahigh sensitivity and operational stability, e.g., ionic artificial skin inspired by the mechanotransduction phenomenon.^[45]

Mechanoreceptor sensors in mammals are vital to protection from external injury. Piezoelectric materials can be easily used to build electron-transport-based artificial mechanoreceptor sensors. Subsequently, ionic artificial mechanoreceptor sensors can be achieved by combining piezoelectric films with artificial ion-channel systems (Figure 2A).^[20] Briefly, two different signals, a fast adapting signal generated by the piezoelectric film (electrical signal) and a slow adapting signal by the ion channel (ionic signal), are detected when the sensor is pressed and released. By acquiring integrated

signals generated by the piezoelectric film and ion channel, the resulting device enabled signal distinction and detection including surface roughness, mechanical stress, and various vital signs such as heart rate and ballistocardiogram.

Another function of mammalian skin is to alert to external thermal stimuli, which is one of the self-protection functions in mammals. The detection of external thermal stimuli originates from the temperature-sensitive transient receptor potential channels (or thermo-TRPs) in the thermoreceptor cells of the skin, which can transduce thermal signals to ionic signals, then to action potentials for information transfer. Inspired by this biological thermosensory process, Xie et al.^[46] reported an ionic thermoelectric conversion behavior by an ion selective membrane, by which the external temperature stimuli could be

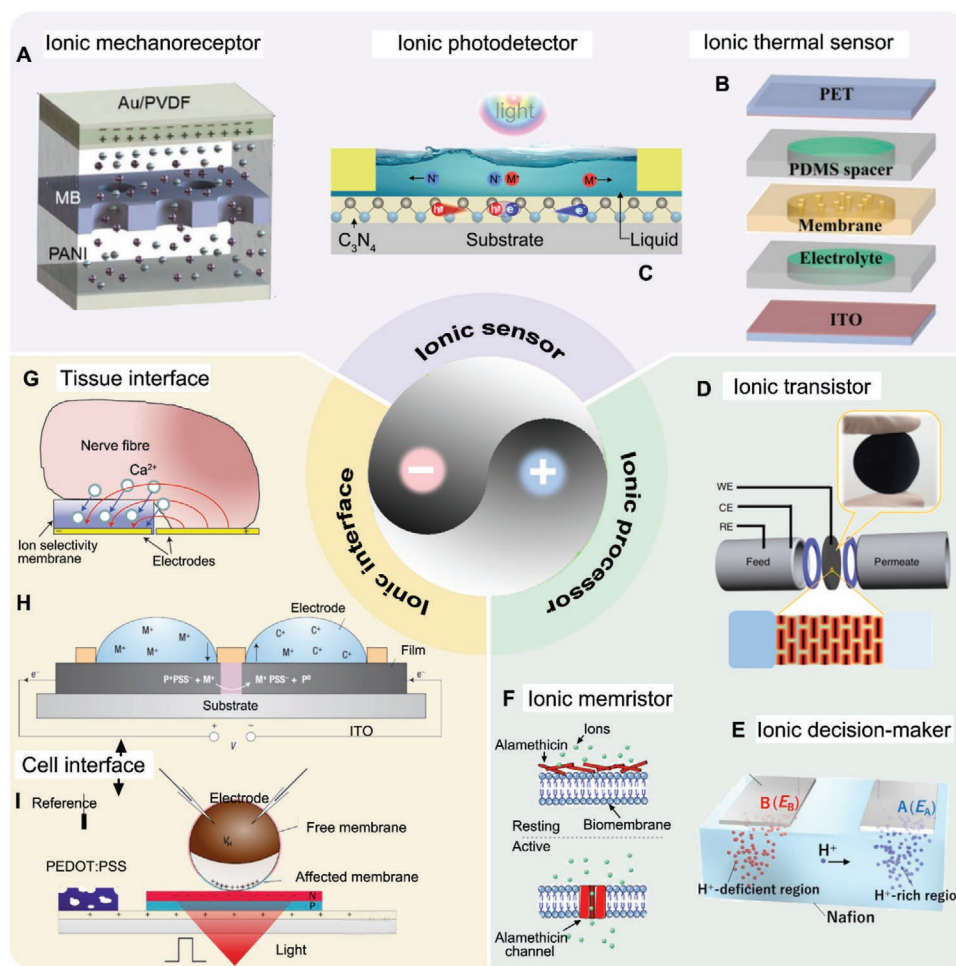


Figure 2. Examples of ionic sensory system. A–C) Ionic sensors: A) ionic mechanoreceptor; B) ionic thermal sensor; C) ionic photodetector. D–F) Ionic processors: D) ionic transistor; E) ionic decision-maker; F) ionic memristor. G–I) Ionic interfaces: G) ionic tissue interface; H, I) ionic cell interface. A) Reproduced with permission.^[20] Copyright 2018, Wiley-VCH. B) Reproduced with permission.^[46] Copyright 2018, Wiley-VCH. C) Reproduced under the terms of the CC-BY Creative Commons Attribution 4.0 International licence (<https://creativecommons.org/licenses/by/4.0/>).^[48] Copyright 2019, The Authors, published by Wiley-VCH. D) Reproduced with permission.^[56] Copyright 2018, Springer Nature. E) Reproduced with permission.^[58] Copyright 2018, The Authors, published by American Association for the Advancement of Science (AAAS). Reprinted/modified from ref. [58]. Copyright 2018, The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. Distributed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC) <http://creativecommons.org/licenses/by-nc/4.0/>. F) Reproduced with permission.^[66] Copyright 2018, American Chemical Society. G) Reproduced with permission.^[71] Copyright 2011, Springer Nature. H) Reproduced with permission.^[10] Copyright 2007, Springer Nature. I) Reproduced with permission.^[11] Copyright 2019, The Authors, published by AAAS. Reprinted/modified from ref. [11]. Copyright 2019, The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. Distributed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC) <http://creativecommons.org/licenses/by-nc/4.0/>.

transduced into ionic signals (Figure 2B). The key aspect of this system was the ion selectivity (anions as the dominant charge carriers) of the nanochannel. The temperature difference at the two ends of the nanochannel will drive anions to move from high to low temperature, resulting in an “ionic current peak.” Moreover, the ionic current signal has an accurate correlation with the temperature gradient, which is similar to the temperature sensitivity of our skin and can also be used as an ionic thermometer.

Artificial visual systems work similarly. In recent years, the development of electron-transport-based semiconductor photodetectors has advanced rapidly, which allows them to mimic visual systems with the advantages of ultrafast, ultrasensitive detection of light.^[47] However, they still suffer drawbacks when used in conjunction with biological systems due to their “different languages.” On top of that, most of these devices rely on an external power supply, which can be highly problematic for various applications, e.g., with implanted structures. Recently, Xiao et al.^[48] reported an ion-transport-based photodetector by polymeric carbon nitride nanotube membrane, which is self-powered and also has the advantages of high selectivity, high sensitivity, and high stability (Figure 2C). In their work, light is first converted into a charge gradient located along the channel caused by the semiconductor property of carbon nitride, which then induces a flux of mobile ions for charge compensation. In this way, an ionic photodetector is constructed. Adapting this mechanism, all the existing semiconductor electron-transport-based photodetectors could be converted into ionic photodetectors. Furthermore, these ionic photodetectors could provide a novel approach to photonic controlled neuronal stimulation.^[10,11,49]

It is worth mentioning that an electrode (ion/electron transducer) is still needed in the existing ionic sensory systems for converting the ionic current to a voltage signal for external monitoring or detection, while biological tissue is expected to react to the local osmotic signals as such. Therefore, the next generation ionic sensory should be able to convert physical forces into biochemical signals directly without the support of electrodes. Furthermore, these ionic sensors should also enable robust bidirectional human–machine communication by constructing “ionic sensor accessories,” e.g., an ionic “gate” to amplify, read out, or modulate optical signals.

3.2. Ionic Processors

Ion-transport-based processes can be applied for signal processing and information storage. Transistors form the backbone of microelectronics and modern industry and are mainly fabricated from inorganic semiconductor materials, e.g., silicon. Some electrolyte-gated field-effect transistors (EGOFETs)^[8,50–52] and organic electrochemical transistors (OECTs)^[53] already work via ion accumulation induced double layer capacitance or ions penetration, but are still primarily based on electron transport. Development of an all-ion-transport-based transistor will provide a unique opportunity for real-time regulation/control of signals from living organisms.

Previous work has shown that both protons^[54] and ions^[55] can be used as charge carriers to fabricate “ionic transistors.” However, ionic transistors are difficult to modulate in most cases because both proton and ion transport in nanoconfinement

is subject to either a local electric field arising from surface charge or an externally applied potential, which on the other hand also provides a unique opportunity. Recently, Cheng et al.^[56] described an electrically modulated “ionic transistor” based on a tunable nanoconfinement in layered graphene-based nanoporous membranes (Figure 2D). Due to the excellent conductivity of graphene, the gate potential can be applied directly to the membrane, which can tune the EDL thickness enclosed between the layers of graphene materials, and then control the ion flux, i.e., ionic current. In this work, a low voltage of 0.5 V can enhance the ion transport rate up to 7 times. Electric field modulated ion transport has potential applications in controlled release of ionic drugs. It is expected that other external stimuli can also be used to tune ion transport with suitable materials, e.g., light for semiconductor materials.^[14]

Decision-making is an indispensable factor for the survival of intelligent beings, making them able to dynamically adapt to changes in their environment. Modern technology nearly exclusively uses conventional computers including central processing units (CPUs), memory, and algorithms (software programs) to emulate biological decision-making systems.^[57] Autonomous, non-centrally controlled systems, e.g., in insects, can however significantly lower the computational demands and simplify robotics. To handle rapidly increasing amount of information, Tsuchiya et al.^[58] developed an ionic decision-maker based on ion motion (Figure 2E), which can overcome the limitations of adaptive decision-making of conventional computers. The ionic decision-maker operates based on electrochemical processes including, accurate ionic transport and redox reactions, and exhibits excellent dynamic adaptabilities to solve multiarmed bandit problems. Again, this system can be used to develop intelligent chips for modern science and technology, while the solid-state ionic principle employed can still bridge the gap to biological systems. In fact, a simple decision-maker is similar to an actuator that is able to react to the stimuli, while “smarter” decision-making must adapt to dynamic changes in environmental conditions. Due to the excellent environmental suitability of biological systems, bioinspired ionic decision-makers which can meet or exceed the accurate ion transport observed in nature, will provide a unique approach to address the problem described above and find applications in intelligent devices.

A memristor is a nonvolatile electrical component that can retain memory without power by regulating the flow of electrical current in a circuit and remembering the amount of charge that has previously flowed through it.^[59,60] Simply put, a memristor is a continuously tunable resistor that emulates biological synapse.^[61] It is believed that the synaptic weight between two neurons can be precisely adjusted by the ionic flow through them, enabling the biological system to learn and function.^[62] Until now, several memristor models including linear ionic drift model (Strukov model), nonlinear ionic drift model, Simmons tunnel barrier model and so on have already been proposed for different applications.^[63] The transport of metal cations or migration of oxygen ions/vacancies in memristors are similar to the accumulation and extrusion of Ca²⁺ in the pre- and postsynaptic compartments of biological synapses, playing a critical role in initiating plastic changes. Inorganic diffusive memristors that closely emulated synaptic Ca²⁺ dynamics^[64] and organic polymer artificial synapses based on ion/electron

integrated transport^[65] are two typical examples developed recently, which yielded memristors more realistic for biology and, consequently, fully memristive neural networks capable of unsupervised learning. Coming even closer to biological synapses, Najem et al.^[66] reported a biomolecular memristor using ionic transport as the switching mechanism (Figure 2F). In their work, alamethicin peptides, acting as the ion transport pathways, were inserted into an insulating lipid bilayer driven by external voltage, in which process current–voltage hysteresis could be observed at potentials above the insertion threshold.

3.3. Ionic Interfaces

The ionic interface is an ion-transport-based connection element that can act as an interfacing device between electronic and biological systems. In biology, cells and tissues use finely regulated ion fluxes for their intra- and intercellular communication. Up to this day, it is still unclear how much information can be read out by an electron-transport-based electrode, although they are the standard technology used to analyze cells and tissues.^[67,68] Therefore, an “ionic interface” should be a more suitable bridge for information acquisition from cells (as ionic information) and manipulation of physiological processes.^[69,70]

Song et al.^[71] described indirect ionic interface to control and manipulate the nervous system by the modulation of ion concentrations. Because of the important roles of ions (including K^+ , Na^+ , and Ca^{2+}) in the propagation of action potentials, the authors changed nerve excitability locally by modulating ion concentration in situ by different ion-selective membranes (ISMs), thereby changing the electrical threshold for stimulation or even blocking nerve conduction (Figure 2G). In the first step, a small ion depletion current (10–100 times smaller than functional electrical stimulation thresholds) was used to deplete the ions temporarily; then an electrical stimulus current was applied while the depletion current was switched off. By comparing the resulting muscle contraction force originating from the stimulation with and without the ion depletion current applied, the author found that the electrical threshold for stimulation was reduced by up to $\approx 40\%$.

Berggren and coworkers^[10] demonstrated that signals in cells can be controlled directly by modulating the transport of Ca^{2+} ions using conjugated polymer devices. In their work, an organic electronic ion pump was used to manipulate the levels of ions in reservoirs, then specific biological responses in neuronal cells attached to the reservoir surfaces were elicited. The authors suggested that the method could be used as a diagnostic tool to investigate biological ion transport (Figure 2H). A similar strategy has also been followed for precise delivery of neurotransmitters to modulate mammalian sensory function.^[72] It is worth mentioning that the organic electronic ion pump used here is still driven by an external electrical field, while energy for biological ion pumps is supplied from various other sources, including sunlight or redox reactions. In considering energy sources, other bioinspired ion transport systems for ionic interfaces could be employed.

Most recently, Głowacki et al.^[11] demonstrated control of electrophysiology in single cells by photoinduced ion transport. Unlike the electrically driven systems, the authors used organic electrolytic photocapacitors in their work, which can be

regarded as light signal to ionic signal transducers to establish the ionic interface between organic semiconductor and single cells. With light irradiation, electric charges were produced by the photoexcitation of the donor-acceptor semiconductor junction, and accumulated at the semiconductor/electrolyte interface, producing oppositely charged electrolytic double layers. When used to modulate the membrane potential of single *X. laevis* oocytes, a rapid photoinduced transient voltage perturbations exceeding 100 mV was recorded. Furthermore, this photo-induced ion transport system can also be used to evoke voltage-gated ion channels, since the ionic signal can effectively depolarize the cell membrane (Figure 2I).

The abovementioned works show that ionic interfaces, as defined above, are a powerful bridging module between external signals (including light signal, electrical signal, and thermal signal) and biological signals. However, future development of ionic interface should not only focus on “speaking” to biological tissue, but also on “reading” of the biological language. Once such bidirectional communication is reached, the real communication between artificial and biological intelligence should not be far away. Beyond that, other additional applications can also benefit from ionic interface, such as the treatment of neural disorders by the integration of ionic devices with implantable platforms.^[43]

4. Challenges and Prospects

Though various ion transport functions have been realized based on different materials, the concepts and layouts of artificial ionic sensory systems are still in the toddler stage compared with electronic sensory systems. For the next steps, more attention should be paid to the following challenges for improved functionality and materials.

In terms of ion transport media, in addition to solid-state nanopores for aqueous solutions, ionic liquids, ionic hydrogels, and ion conductive polymers are also suitable materials for ionic signal conduction. For ionic sensors or ionic processors (Figure 3A,B), there should be no limitation for materials in terms of biocompatibility. Rather, more attention should be paid to explore new materials to realize multiple responsive ionic sensors as, for example, can be found in human skin. For ionic interfaces (Figure 3C), biocompatibility is mandatory. Ionic hydrogels^[73,74] and some polymer materials^[53,75] are the best known options, yet those pose challenges for an accurate ion transport. Therefore, on the basis of existing ionic conductors,^[76] more precise nanostructure by 3D printing technology might be a path to reach this goal. Another challenge is implanting these ionic conductors into living organisms to realize communication with the biological system, to which existing electronic implant systems offer some feasible approaches.^[3] By this way, the electrophysiological study of biological tissues, e.g., brain, heart and muscle, would advance one step further because both electrical and ionic signals could be acquired easily.

Compared with the complicated ion transport functions of protein nanopores, ion transport in a solid-state material is simple.^[30] Take the neural action potential as an example. The Hodgkin–Huxley model suggests that three different protein nanopores, including Na^+/K^+ pump, voltage-gated Na^+ channel and voltage-gated K^+ channel, are involved in the generation

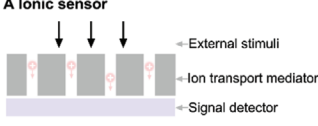
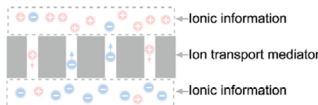
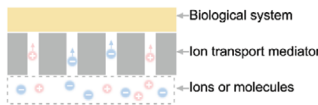
Applications	Materials	Challenges	Perspective
A Ionic sensor 	Solid-state nanopore with surface charge (1D nanopore/nanochannel/nanotube, 2D layered membrane, 3D porous membrane etc); Hydrogel (ion selective hydrogel etc); Organic semiconductor (PEDOT:PSS etc) Ion exchange membranes (IEMs) etc	Sensitivity; Selectivity; Repeatability; Implantation; Multiple responsive	Ionic thermoreceptor; Ionic chemoreceptor; Ionic mechanoreceptor; etc
B Ionic processor 	Solid-state nanopore with surface charge (1D nanopore/nanochannel/nanotube, 2D layered membrane, 3D porous membrane etc); Hydrogel (ion selective hydrogel etc); Organic semiconductor (PEDOT:PSS etc) Ion exchange membranes (IEMs) etc	Ion self-diffusion; Accurate ion transport; Fast ion transport	Ionic synapse; Ionic soma; Ionic dendrite; etc
C Ionic interface 	Hydrogel (ion selective hydrogel etc); Organic semiconductor (PEDOT:PSS etc) Ion exchange membranes (IEMs) etc	Biocompatibility; Implantation; Precise nanostructure; Accurate ion transport; Fast ion transport	Controllable ions/molecules release; Information communication; Human-machine interface; etc

Figure 3. Materials, challenges, and perspectives of: A) ionic sensors, B) ionic processors, and C) ionic interfaces.

and propagation of action potentials.^[77] In the resting state of axons, Na⁺/K⁺ pumps transport K⁺ to the inside of the cell and Na⁺ to the outside of the cell to build an electrochemical gradient of -70 mV, with the inside of the cell at lower potential (resting potential). Voltage-gated Na⁺ channels will be activated in order to transport Na⁺ from outside to inside of the cell when the membrane potential increases up to a threshold (about -55 mV). The voltage-gated Na⁺ channel will be closed and the voltage-gated K⁺ channel will be opened to allow K⁺ transport from inside to outside when the membrane potential is “overshot” (about +30 mV). Taking advantage of the synergistic effect of these different protein channels, the initiation and conduction of nerve impulses can be realized. However,

the existing ion selective membranes or solid-state nanochannels can only realize simple ion selectivity and ion rectification based on different charge properties, which are far from the integrated and complex ion transport in biology. Therefore, efforts are still needed to combine different ion transport functions into one solid-state device. Functionalized devices incorporating biomolecules are one of the easiest way to compensate these weaknesses, but they are still limited.^[78] We expect that integrated and complex ion transport can be easily realized with the development of richly functional ionic polymers as well as nanofabrication techniques.

Another challenge exists in the realization of an accurate and fast ion transport, for instance, specific ion transport,

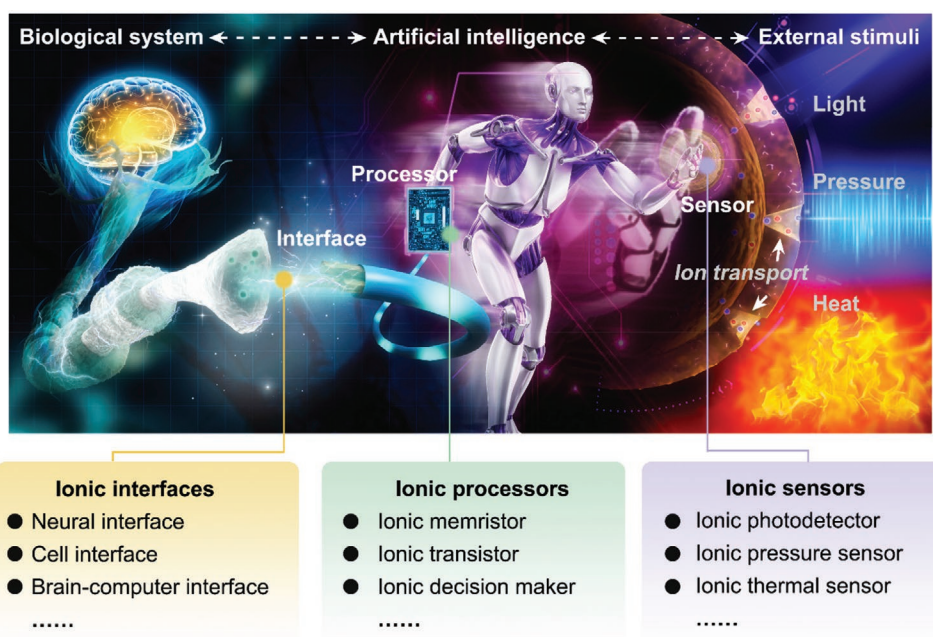


Figure 4. Predictable ionic sensory systems consisting of three parts: ionic sensors, ionic processors, and ionic interfaces. Ions are a potential candidate for realizing the signal transduction as follows: External stimuli → Artificial intelligent data processing → Biological system.

direction, and speed. In biological systems, Na⁺ or K⁺ channels can efficiently discriminate Na⁺ or K⁺ from other alkali cations and even from each other, while maintaining high-throughput ion conduction.^[32] However, current solid-state Na⁺ and K⁺ sensory systems still face issues in realizing similar sensitivity due to the similar physical and chemical properties of Na⁺ and K⁺. A possible solution is to functionalize ionic sensors with specific molecules to improve selectivity,^[79] but there is still a long way to the biological levels of selectivity. Moreover, protein-based selective nanochannels allow ultrafast ion transport (10⁷ ions per channel per second) in living systems, originating from the special structure, size, and surface charge distribution of the biological channels. Although the intrinsic mechanism for this extremely rapid ion transport is still not clearly understood, it is believed that ultrafast ion transport in the biological channel is in a quantum way of ordered ion flow, since the nerve signal transmission resulting from Na⁺/K⁺ ions diffusion across the cell membrane is an almost instantaneous response.^[80,81] Therefore, realizing this quantum-confined ion superfluid (QISF) in solid-state nanochannels will be very important for improving the performance of ionic sensors. Further challenges are: Can we realize specific ion transport in a mixed/complex solutions like cell medium?^[6] Can we realize ultrafast ion transport as in protein pores?^[81,82] Can we “pump” ion transport against deep concentration gradients as in nature?^[6,14,42] Can we amplify weak ionic signals to realize effective signal processing?^[38] All these questions imply exciting possibilities of ionic sensory systems.

The ultimate goal is to construct an integrated ionic sensory system, able to realize seamless signal transduction between external stimuli, responsive artificial machines, and biological systems. Recently Lee et al.^[83] reported an integrated system by realizing the signal transformation: external stimuli/electrical signal/ionic signal/mechanical signal. Kim et al.^[84] described a system involving external stimuli/electrical signal/ionic signal. Nevertheless, there is still a gap between these systems and their biological counterparts, and in most cases, these bio-inspired systems only capture and record signals without subsequent processing them for insightful information. To mimic the real-time processing and manipulation of biological signals and information in living organisms, future ionic sensory systems should contain all essential elements: ionic sensors, ionic central processors, and ionic interfaces (Figure 4). By integrating these components, a “smarter” artificial device with signal transduction and information processing functions will be achieved, operating in ways indistinguishable from living systems.

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Conflict of Interest

The authors declare no conflict of interest.

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artificial intelligence, bioelectronic interfaces, ionotronics, ion transport, ionotronics, nanofluidics

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