Bioinformation transformation: From ionics to quantum ionics

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In the neural system, a large number of neurons continuously produce and transmit electrophysiological signals, which communicate between neurons and brain regions. Naturally, bioinformation transformation depends on conversion from ionics to electronics, and electronics-based neural recording technologies (Fig. 1) have been extensively developed since the primitive voltage clamp in 1949 [1]. Then patch clamp technology was created by Neher and Sakmann in 1976 [2]. Afterwards, microfabricated silicon Utah-type microelectrode arrays were constructed in 1990 [3]. Recently, field effect transistors [4], nanowire field effect transistors [5], carbon-based electrodes [6], organic electrochemical transistors [7] and mesh electronics [8] have been designed for neural recording with improved performance. However, these electronics-based neural recording technologies according to the Hodgkin theory have made little progress in the field of neural signal research, which hinders the study of the human brain project, such as the failure of Blue Brain Project in Europe. In the traditional Hodgkin theory of neural signal transmission (Fig. 2a), the generation of the action potential is accompanied by disordered entropy-driven ion diffusion along the direction of the axon, which shows slow propagation velocity ($0.2\text{--}120\text{ m s}^{-1}$) [9,10]. Meanwhile, the ion diffusion process in the action potential conduction needs to consume large amounts of energy, which is not applicable to explain the rapid nerve signal transmission with a huge amount of data. In other words, the action potential has nothing to do with the actual instantaneous response of neural signal [11]. Therefore, there is an urgent need to develop a new technology to replace the traditional

electronics-based technology.

Recently, we have found that the ion and molecule transport in ion channels of living systems has similar ordered superfluid process as that of liquid helium [12–14]. This room temperature ionic and molecular superfluid is due to the size confinement of the ion/molecule

Figure 1 Electronics-based neural recording technologies: from ionics to electronics. (a) Voltage clamp; (b) patch clamp; (c) Utah array; (d) field effect transistors; (e) nanowire field effect transistors; (f) carbon-based electrodes; (g) organic electrochemical transistors; (h) mesh electronics. The blue curved arrow indicates time periods, and the image inside the curved arrow represents the Blue Brain Project in Europe, which proves the failure of electronics-based neural recording technologies in the brain science field.

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Figure 2 Biological quantum ionics technology: from ionics to quantum ionics. (a) Schematics of traditional neural signal transmission process based on the action potential theory, which generates through entropy-driven ion diffusion, consumes large amounts of energy and shows low transmission speed. (b) KcsA K⁺ channel from *Streptomyces lividans* allows extremely fast ion transport ($\sim 10^7$ ions/s), ultra-low energy consumption and ultra-low ionic resistance, demonstrating the existence of quantum-confined ion superfluid in K⁺ channel. Reproduced with permission from Ref. [28]. Copyright 2004, Wiley-VCH. (c) Schematics of neural signal transmission process based on enthalpy-driven quantum-confined ion superfluid. (d) Schematic of diffused K⁺ and THz absorption spectra of diffused hydrated K⁺, indicating THz absorption of diffused K⁺ (1 mol L⁻¹) locates at ~ 160 cm⁻¹ with a broad peak. Reproduced with permission from Ref. [21]. Copyright 2009, American Chemical Society. (e) Schematic of quantum-confined K⁺ and THz absorption spectrum of quantum-confined K⁺. The schematic represents quantum-confined ion superfluid is formed in K⁺ channel with a channel size of Debye length (λ_D). The spectrum indicates THz absorption of quantum-confined K⁺ shows two sharp peaks locate at ~ 1580 and ~ 1603 cm⁻¹. Reproduced with permission from Ref. [22]. Copyright 2016, American Association for the Advancement of Science. (f) Schematic of biological quantum ionics technology. Neural signals are studied by THz responses of quantum-confined ions in the biological channels. SNOM (THz) tip represents the tip of THz scanning near-field optical microscope. The source uses high frequency modulating THz light to stimulate the quantum-confined ions at their THz absorption peaks, and the neural signal is collected by a detector and obtained by processing.

channel in the organism. On the basis of biological ion channels, neural signal transmits in an instantaneous response type [11], the brain can process huge amounts of data [15], and the electric eels do not electrocute themselves [16], etc. In particular, K⁺ channel in biological system allows extremely fast ion transport ($\sim 10^7$ ions/s), ultra-low energy consumption and ultra-low ionic resistance [17]. In fact, ion and molecule flows in biological ion channels are regarded as quantum-confined superfluid, which are different from the ion diffusion process in neural networks (Fig. 2b). In this case, quantum states of ions and molecules could be bioinformation carriers with a huge amount of data (Fig. 2c) [11]. As the absorption of quantum states of ions and molecules is in the THz range [18], the THz light could be used as a tool to

realize non-contact bioinformation detection [19]. Coincidentally, Liu [20] also conjectured the quantum states of ions and molecules in the nervous system are key factors for biological information, and the physical field of vertebrate neural signals should be in the THz range. We concretized that quantum states of ions and molecules are in the state of quantum-confined superfluid, and their absorption is in the THz range. Therefore, THz absorption and response could be used as a medium for neural signal detection. We further propose two approaches based on the bioinformation transformation from ionics to quantum ionics. The first one is to study the neural signals in biological systems by THz responses (Fig. 2). THz absorption spectra are employed to detect the signal of quantum-confined ion superfluid in biological ion

channels. According to the Hodgkin theory, ions are in the diffused state, and the THz vibrational signals of diffused K^+ (1 mol L^{-1}) locate at $\sim 160 \text{ cm}^{-1}$ with a broad peak (Fig. 2d) [21]. In comparison, in the biological K^+ channel, THz absorption of quantum-confined K^+ locates at ~ 1580 and $\sim 1603 \text{ cm}^{-1}$ with two sharp peaks, which is obviously different from that of diffused K^+ (Fig. 2e) [22]. Therefore, neural signals could be studied by THz responses of quantum-confined ions in the biological channels (Fig. 2f). THz scanning near-field optical microscope (SNOM) is a good candidate for simultaneous imaging and detection, which could achieve high temporal and spatial resolution [23]. Through the tip of SNOM, high frequency modulating THz light is used as a source to stimulate the quantum-confined ions in the axon at their THz absorption peaks, and the neural signal is collected by a detector and obtained by processing. This non-contact method for bioinformation detection could provide more information about neural signals, which would be superior to the traditional electronics-based

neural recording technologies. However, the neural signal in a biological system is hard to detect because it is difficult to isolate the critical single channel or crystal from the biological environment, which needs new instrument and technology.

Another simple approach is to study the quantum-confined ion superfluid in artificial systems by THz responses, which could offer optimized parameters (e.g., frequency, amplitude, intensity, focus, and stimulation size) for the detection of neural signals in biological systems (Fig. 3). In artificial systems, subnanometer porous materials are used to mimic biological channels to investigate the transport of ions and molecules in biological systems. High frequency modulating THz light is used as a source to stimulate the quantum-confined ions in artificial channels, and the artificial neural signal is collected by a detector and obtained by processing (Fig. 3a). Therefore, subnanometer porous materials, including covalent organic frameworks (COFs) and metal-organic frameworks (MOF), could be used to simulate

Figure 3 Artificial quantum ionics technology. (a) Schematic represents the quantum-confined ion superfluid study by THz responses in artificial systems, which could offer optimized parameters for the detection of neural signals in biological systems. Subnanometer porous materials are used to mimic biological channels, the source is high frequency modulating THz light, and the artificial neural signal is collected by detector and obtained by processing. (b) COFs show high proton conductivity of $2.2 \times 10^{-2} \text{ S cm}^{-1}$ at ambient conditions. Reproduced with permission from Ref. [24]. Copyright 2018, Wiley-VCH. (c) COFs demonstrate both high-water permeation and ion sieving. Reproduced with permission from Ref. [25]. Copyright 2018, American Chemical Society. (d) MOFs with subnanometer pores show ultrafast selective transport of alkali metal ions. Reproduced with permission from Ref. [26]. Copyright 2018, American Association for the Advancement of Science. (e) MOFs with sub-1-nanometer channels demonstrate fast and selective fluoride ion conduction. Reproduced with permission from Ref. [27]. Copyright 2019, Nature Publishing Group.

biological ion channels. The COFs derived from tetrakis (4-sulfophenyl)methane and *p*-phenylenediamine featured high proton conductivity of 2.2 S m^{-1} at 333 K and under high humid conditions, which is comparable to the K^+ conductivity in K^+ channel (Fig. 3b) [24]. The COFs derived from hexamine and tetraone demonstrated both high-water permeation ($\sim 2260 \text{ L m}^{-2} \text{ h}^{-1} \text{ bar}^{-1}$) and a cation size selectivity performance (Fig. 3c) [25]. ZIF-8 MOF porous membrane with an average pore size of $\sim 0.34 \text{ nm}$ showed a high LiCl/RbCl selectivity of ~ 4.6 , and ultrafast ion transport rate of $\sim 10^6$ ions/s (Fig. 3d) [26]. UiO-66 MOF channel with $\sim 0.6 \text{ nm}$ in pore size showed ultrahigh F^- conductivity ($\sim 10 \text{ S m}^{-1}$) and ultrahigh F^-/Cl^- selectivity (~ 240) (Fig. 3e) [27]. All of these subnanometer porous materials would provide artificial ion channel environment to simulate biological ion channel, which could optimize detection technology to promote the investigation of quantum-confined ion superfluid and neural signals in biological systems.

Furthermore, new information technology based on quantum ions as bioinformation carrier would be developed. Something like the emergence of p-n junction transistors has generated integrated circuits and microelectronics, and led to a revolution in electronic technology (Fig. 4a). The emerging research of bionic ion channels and quantum ionics would lead to a revolution in information technology (Fig. 4b). Quantum ion integrated circuits would be superior to electronic integrated circuits, just as the human brain is superior to computers. The remaining challenges are the fabrication of soft-matter-based super ionic conductance materials

and construction of quantum-ion-based logic unit devices.

In summary, bioinformation is based on alternating current signal, and the introduction of quantum ionics concept into the biology field would provide new viewpoint and technology to study bioinformation transformation. It would not only promote the development of neural and brain science, but also generate future information technology.

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Figure 4 Future quantum ionics technology. (a) The first transistor model of p-n junction and highly developed integrated circuit. (b) The first model of quantum ionic diode and the unpredictable future information technology based on quantum ion integrated circuit.

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Author contributions Jiang L proposed the concept of quantum ionics. Antonietti M suggested the absorption of ion in THz range. Zhang X and Jiang L wrote the paper and contributed to the general discussion.

Conflict of interest The authors declare that they have no conflict of interest.

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生物信息转化: 从离子学到量子离子学

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摘要 传统的神经记录技术是基于从离子学到电子学的生物信息转换, 虽被广泛研究, 但其在神经科学和脑科学领域进展很小。最近, 生物离子通道中的离子和分子流动被看作是量子限域超流体, 即离子和分子的量子态可作为生物信息载体, 其吸收光谱在太赫兹范围内, 因此太赫兹光可以作为一个工具来实现生物信号的非接触检测。我们提出两种研究方案: 一种是利用太赫兹响应研究生物体系的神经信号, 另一种是利用太赫兹响应研究人工体系的量子限域离子超流体, 并为生物体系中神经信号的检测提供优化参数。把量子离子学引入生物信息学领域, 将为神经信号研究提供一个新的技术手段, 推动神经科学和脑科学的发展, 并发展量子离子学技术。