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Perspective

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Organic mixed conductors for bioinspired electronics

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Abstract

Owing to its close resemblance to biological systems and materials, soft matter has been successfully implemented in numerous bioelectronic and biosensing applications, as well as in bioinspired computing and neuromorphic electronics. Particularly, organic mixed ionic–electronic conductors possess favourable characteristics for their efficient use in organic electrochemical transistors, electrochemical memory and artificial synapses and neurons. Owing to their mixed ionic–electronic conduction, leading to high amplification, these materials are ideal for translating chemical signals, such as ions or neurotransmitters, into electrical signals, as well as for accurately controlling stable conductance states to efficiently emulate synaptic weights in artificial neural networks. Because these mixed conductors operate with ionic charges – similar to signalling in biological neuronal networks – they also exhibit ideal properties to emulate biological spiking neurons. In this Perspective, we consider the potential of soft matter, especially based on organic mixed conductors, for bioinspired systems and their possible applications. We discuss the potential that these materials have in applications in which low power, conformability and tunability are key, such as smart and adaptive biosensors, low-power in-sensor and edge computing, intelligent agents and robotics, and event-driven systems and biohybrid spiking circuits at the interface with biology. We present a comprehensive perspective of the potential of biomimetic and bioinspired electronics based on soft matter to integrate artificial intelligence into everyday life.

Sections

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Introduction

The nervous system is indisputably competent when coping with diverse environmental stimuli and converting them into internal neuronal representations, in order to perceive the environment, take actions and control the body efficiently. Driven by the efficiency of biological systems, a sensible approach for the current high demand of integrating physically artificial forms of intelligence into everyday life is representing the functions of the nervous system with biomimetic or neuromorphic materials, electronics and systems[1–6]. Instead of executing neuronal algorithms on classic computing systems[7,8], biological phenomena are mapped directly on such dedicated biomimetic or neuromorphic technologies. The benefits of this bioinspired, in materio or on-chip integration are multiple and straightforward: efficient intelligence can be potentially embodied in any kind of unconventional form factor that is often inaccessible with conventional electronics[9–11]. Artificial neural networks based on analogue memory crossbar arrays, for example, represent a promising approach to emulating simplified functions of biological neural networks[4,6]. Drawing inspiration from neuroscience, spiking neural networks utilize spike timing and spike-rate processing of signals between artificial neurons – adding a 'temporal' component to artificial neural networks – to create efficient intelligent systems that attempt to emulate more precisely the workings of the brain[2,12]. Hardware-based realizations of spiking neural networks necessitate the creation of both artificial neurons and synapses. The former act as the primary computational units within the network, generating, processing and transmitting electrical impulses (or spikes) through synapses. Synapses act as memory units, regulating the strength of the connections between neurons through short-term synaptic plasticity and long-term synaptic plasticity or modulatory effects. In principle, hardware-based artificial networks can be highly energy efficient for local learning, classification and processing. Therefore, they are promising for low-power, stand-alone and edge computing applications.

Artificial networks based on traditional, solid-state neuromorphic systems are known to be efficient in dealing with temporal, biological-like signals. However, the computational power of biological networks also stems from their diverse carriers of information (ions, neurotransmitters, neuromodulators and so on), their stochasticity and crosstalk and/or noise via the wetware. Indeed, brain chemistry can be very diverse with at least several tens of neurotransmitters and hundreds of corresponding receptors[13]. Although there are excellent and robust artificial networks based on solid-state electronics, the abovementioned biorealistic features are missing from traditional neuromorphic technologies. Many other aspects of biological intelligence that are manifestations of the biological machinery are also absent, such as self-healing ability, vulnerability and physical evolvability. Organic materials, alternatively, do possess many of these characteristics and are now being incorporated in neuromorphic technologies. Soft matter and organic compounds are of particular interest because of their close resemblance to the biological machinery. Organic materials such as small molecules, oligomers and polymers can be used to make dielectrics, semiconductors, mixed conductors and electrolytes. Their corresponding devices or systems can potentially be the basis for materializing diverse forms of biological intelligence[14–18]. Although many different materials classes can be used for bioinspired electronics, organic mixed conductors and, in particular, organic mixed ionic–electronic conductors (OMIECs) seem to be a natural choice as they do not only mimic the biological behaviour but also operate with similar underlying electrochemical processes. Their soft mechanical properties render them ideal for interfacing with biological systems.

We have now reached a critical volume of scholarship in organic bioinspired materials and electronics that leverage organic mixed conductors. The artificial counterparts of the basic building blocks of biological neural networks – that is, organic artificial synapses and neurons – are readily available and are highly tuneable and multi-responsive[19–22]. Such elements enable the realization of on-chip, small-scale artificial neural networks with parallelism in training[23]. Organic neuromorphic architectures emulate high-order phenomena of biological neural networks such as homoeostasis[24], functional connectivity and synchrony[25,26], while displaying multi-stable energy states essential for adaptive and intelligent behaviour[19]. Biorealistic organic neuromorphic electronics[21,22], adaptive sensors and systems for local processing and computation are now closer than ever[27,28]. Real-time biohybrid interfaces showcase the synergetic operation of biological and artificial counterparts for multi-functional and bidirectional bio-interfaces[29,30]. The evolvable nature of soft matter is now leveraged for in materio computing[31] and for the natural-like growth (metabolite-driven) of functional materials into living organisms[32]. Finally, organic neuromorphic devices are incorporated in behavioural aspects of intelligent agents with soft, biomimetic (and potentially self-healable) actuators and adaptive circuitry for on-chip learning in robotics[33]. These advancements are encouraging, but the challenges remain great and multidimensional ranging from basic science to technological implementation. The full potential of organic bioinspired electronics for emulating and interfacing biology, and thus for fulfilling the considerable endeavour of "diverse forms of intelligence everywhere", is yet to be unravelled.

In this Perspective, we present an overview of the state of the art and the novel potential domains of biomimetic and bioinspired electronics based on OMIECs. Such bioinspired electronics can enable new intelligent systems that are able to sense, analyse, interpret, perceive and act upon a dynamic and diverse real-world environment. The aim of this work is to provide a unique and broad perspective of the potential of organic bioinspired materials and electronics based on their distinctive properties. We argue that soft electrochemical matter may also provide less conventional but essential manifestations of biological intelligence, far beyond what conventional artificial networks can currently offer. Potential future directions and long-term ramifications, as well as challenges towards real-world applications, are also discussed.

Materials characteristics: organic mixed conductors and beyond

Because of their unique properties, organic materials could facilitate the development of neuromorphic technologies to emulate diverse forms of biological intelligence (Fig. 1). In particular, organics are highly tuneable via synthesis and additives[34]. For example, the volatility (that is, the memory) of a neuromorphic device based on OMIECs can be engineered with molecular additives and dopants[19,35–37]. Host–guest chemistry can induce ion-selective interactions in (semi)conducting polymers, reminiscent of biological ion channels[38–40]. Moreover, conjugated polymers can be synthesized with mixed conductivity that displays unipolar, ambipolar or antiambipolar carrier transport[22,41,42], phenomena that are essential for inducing diverse nonlinear behaviour at the device level to more accurately replicate the brain processing capabilities.

The high tunability of soft matter can enable diverse functions for bioinspired electronics. Materials properties (such as electrical conductance) can be modulated in operando and in analogue fashion, and thus form the basis for device trainability, adaptivity and learning, and for the realization of on-chip neural networks[19,23]. The tunability of soft matter also enables the realization of artificial sensorimotor systems, bio-interfaces or robotics with diverse properties (electrical, optical, mechanical, thermal or biochemical). Multi-responsive, multimodal systems that exploit interdependent and cross-coupled properties (such as optoelectronic, thermoelectric, electrochemical, electromechanical or piezoelectric properties)[43,44] can form sensory associations, conversions or effector–motor actions by handling diverse (input–input or input–output) signalling. Moreover, soft and stretchable films for organic electronics, such as semiconductors or OMIECs, can offer conformable and intimate interfacing with a diversity of substrates and objects (biological tissues, soft robotics or macroscopic structures)[45–47]. Soft matter can also spontaneously self-heal after having been mechanically damaged owing to intermolecular or ionic interactions and to the low activation energies needed for (macro)molecular (re)association[48,49]. Self-healing and regeneration are inherently embedded in biology – being a key differentiator from the rigid and pre-defined technologies of modern electronics – and is an essential property for enabling long-life intelligence and homoeostasis in artificial systems. However, beyond self-healing, soft materials are vulnerable and prone to injuries. The mirroring of an aversive state such as an injury between peer systems – intelligent systems with similar capabilities, developing an injured–observer interaction – via soft electrochemical matter might provide a path for artificial empathy, and thus prevent the sociopathic behaviour of intelligent systems[50]. Empathy is an important aspect and can potentially offer instruction-free behaviour in artificial intelligent systems mostly focused on the preservation of their well-being. Indeed, an aversive state between biological peers, such as the sight of blood or being at the edge of a height, might trigger real biochemical reactions at the observer side, which could be mirrored in artificial systems with soft electrochemical matter.

The bottom–up processes and the complexity of soft matter can enable computation in (bio)matter. Often, the formation of soft matter happens easily owing to the low-energy barriers involved, and can be assisted (catalysed) or spontaneously initiated at room temperature. Under these conditions, soft matter can evolve over space and time under the influence of triggering cues such as physical and chemical stimuli, catalysts or thermal energy[32,51,52]. The evolvability of soft electrochemical matter is a key property to emulate the phenomenon of synaptogenesis. The development of soft matter can even be guided in a bottom–up fashion with metabolically driven growth processes that are compatible with living organisms[32]. This guided growth can potentially lead to the physical fusion of soft electrochemical matter with living organisms. Typically, soft matter is amorphous or polycrystalline and, therefore, exhibits complex and distributed dynamic processes at the microscale or nanoscale (such as variable hopping frequencies and distances or relaxation times, cascade-like phenomena, recurrent interactions and so on). This dynamic complexity is a necessary condition for a material to incorporate computing and processing abilities, allowing the transformation of inputs into a more complex computational space for in materio realization[31,53].

Soft matter can enable unconventional functions and forms for bioinspired devices and circuits. Because the operation of organic devices based on OMIECs involves natural-like processes such as the transport of alkaline and polyatomic ions in water-based electrolytes[54], device and circuit metrics (including characteristic timescales and voltages) can be on par with those of biologically occurring phenomena[15]. This can endow OMIEC-based neuromorphic devices and circuits with energy efficiency and real-time bio-interoperability (for example, bidirectional responsivity to common biological carriers of information such as ions, neurotransmitters and biomarkers)[15,18,21,22,29]. In a direction that is in sharp contrast with the ultra-high integration density and extremely low fault tolerance of contemporary nanoelectronics, organic neuromorphic devices are compatible with large-area integration on flexible or even stretchable subtrates[45,55]. This compatibility is a key form factor for conformally distributing intelligence in uneven macroscopic structures and bodies.

Bioinspired devices and organic building blocks

Organic neuromorphic devices based on OMIECs come in different forms, with the most prominent ones being the organic electrochemical transistors (OECTs) and organic electrochemical resistive access memories (OEC-RAMs) (Fig. 2). Typically, OECT and OEC-RAM have similar architecture; they both are three-terminal devices consisting of a channel between the source (S) and drain (D) electrodes, and an electrolyte (solid, gel or liquid) between the channel and the gate (G) electrode (Fig. 2a). However, OECTs are volatile devices, which means that they do not store information (in the form of ionic charge, Fig. 2b), whereas OEC-RAMs are a form of non-volatile OECTs and display permanent charge storage or memory phenomena (Fig. 2c). Therefore, OEC-RAMs enable for the realization of artificial synapses and their corresponding networks, whereas volatile OECTs are the building blocks for analogue circuits. In the latter case, OECTs are building blocks for electrochemical oscillatory circuits to create organic artificial neurons (Fig. 2d). Table 1 shows representative metrics and desired properties for OEC-RAMs and organic artificial neurons. Considerations for standardization of metrics for OECRAMs and organic artificial neurons are shown in Table 2.

Organic electrochemical transistors

OMIECs are predominantly pi-conjugated polymers (for electronic conduction) that readily solvate and conduct ions. The inherent ionic–electronic coupling in OMIECs facilitates very efficient transduction from ionic to electronic signals and vice versa, which enables the low-voltage operation of OECTs, making them versatile chemical sensors. We describe the underlying electrochemical processes occurring in OMIECs in Box 1, including the doping and dedoping mechanisms and the formation of the volumetric capacitance. Here, we focus on OMIEC developments directly related to their use in OECTs for neuromorphic and biomimetic systems, including the design of tailor-made synthetic materials, the development of new models to describe their unconventional properties, and the exploration of novel deposition techniques. Each of these developments aim to exploit the biomimetic functionalities of OMIEC-based devices on a different level of abstraction when compared to biology, underlining the necessity of synergistic progress to build complex bioinspired systems.

The prototypical material used in OECTs is poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS)[34]. However, owing to the permanent presence of immobilized sulfonate anions in PEDOT:PSS, it is intrinsically p-type doped, resulting in depletion mode transistors, which alone is unfavourable for most analogue or digital circuits because of the continuous power consumption at the idle state of transistor operation. Indeed, to build power-efficient circuits such as inverters, amplifiers and biomimetic spiking neurons with OECTs, p-type and n-type accumulation mode transistors are required.

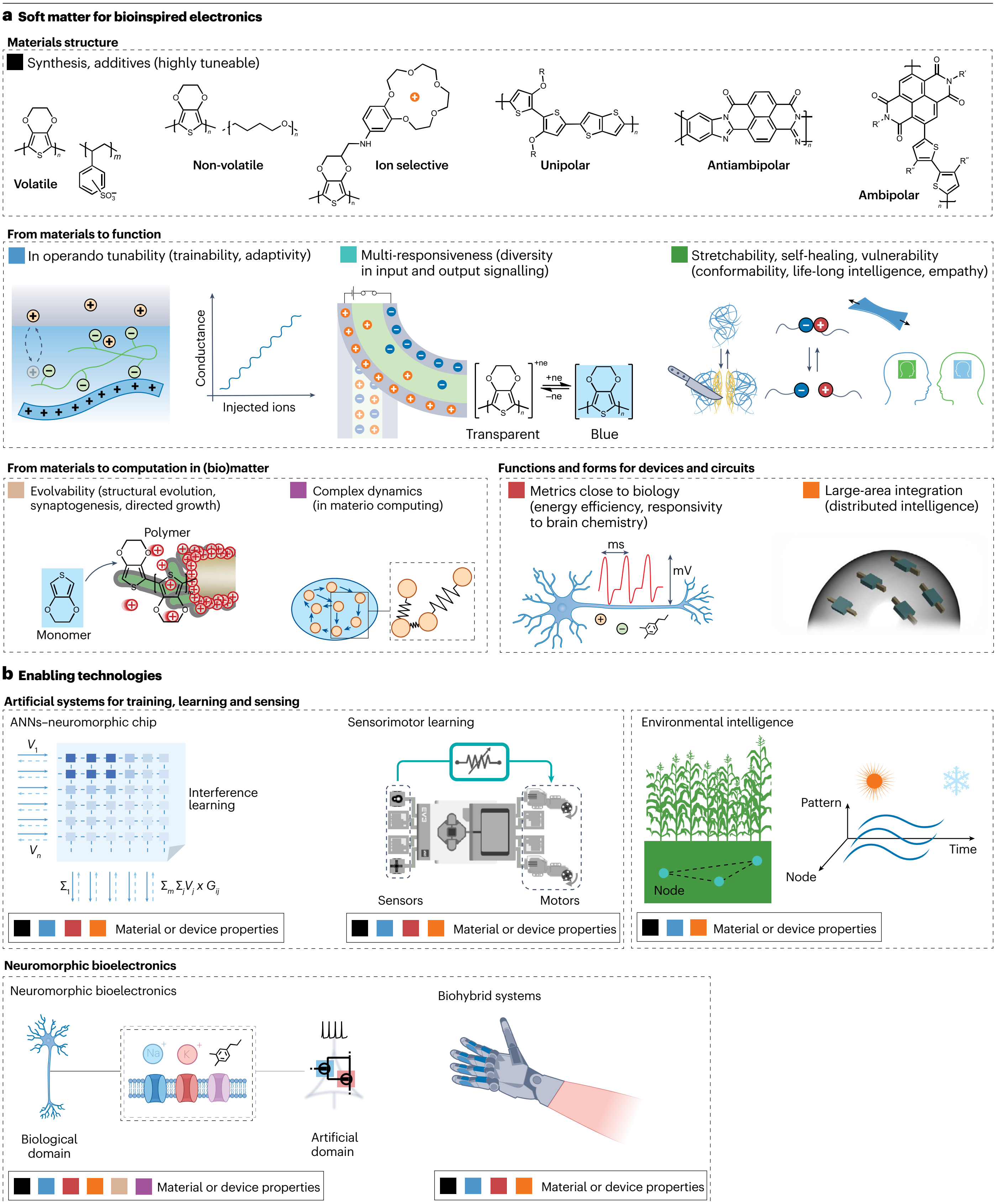
a Soft matter for bioinspired electronics
Materials structure
Synthesis, additives (highly tuneable)
Volatile
Non-volatile
Ion selective
Unipolar
Antiambipolar
Ambipolar
From materials to function
In operando tunability (trainability, adaptivity)
Conductance
Injected ions
Multi-responsiveness (diversity in input and output signalling)
Transparent
Blue
+ne
−ne
Stretchability, self-healing, vulnerability (conformability, life-long intelligence, empathy)
From materials to computation in (bio)matter
Evolvability (structural evolution, synaptogenesis, directed growth)
Polymer
Monomer
Complex dynamics (in materio computing)
Functions and forms for devices and circuits
Metrics close to biology (energy efficiency, responsivity to brain chemistry)
ms
mV
Large-area integration (distributed intelligence)
b Enabling technologies
Artificial systems for training, learning and sensing
ANNs–neuromorphic chip
Interference learning
Sensorimotor learning
Sensors
Motors
Environmental intelligence
Pattern
Time
Node
Material or device properties
Neuromorphic bioelectronics
Neuromorphic bioelectronics
Biological domain
Artificial domain
Biohybrid systems
Na
K
Material or device properties

Fig. 1 | Organic biomimetic and bioinspired materials, electronics and systems. a, Soft electrochemical matter and organic materials have various unconventional properties for fulfilling the venture "diverse forms of intelligence everywhere". Materials structure: the high tunability of the materials structure can enable a wide variety of properties such as volatile or non-volatile device behaviour, ion-selective response and unipolar, ambipolar and antiambipolar carrier transport. From materials to functions: soft matter can enable a range of potential bioinspired functions, for example, in operando tunability, multi-responsiveness and stretchability, self-healing and vulnerability. From materials to computation in (bio)matter: owing to its bottom–up fabrication and complex dynamics, soft matter can be used for computation in (bio)matter. Functions and forms for devices and circuits: soft matter can enable devices and circuits with metrics and qualities close to biology, as well as large-area integration. **b**, Potential key enabling technologies of organic neuromorphic electronics. Artificial systems for training, learning and sensing: organic bioinspired devices, circuits and networks can enable the realization of artificial systems for training, learning and sensing. Neuromorphic bioelectronics: organic bioinspired devices and circuits can potentially greatly enhance the function of bioelectronics with new neuromorphic sensors and biohybrid systems. Materials and device properties are colour-coded (circles) and mapped as requirements on the different enabling technologies. ANNs, artificial neural networks. Part **a** in operando tunability adapted from ref. 34, Springer Nature Limited. Part **a** stretchability, self-healing, vulnerability adapted from ref. 48, Springer Nature Limited. Part **a** multi-responsiveness adapted with permission from ref. 143, Wiley. Part **a** evolvability adapted from ref. 123, CC BY 4.0. Part **b** sensorimotor learning adapted with permission from ref. 33, AAAS. Part **b** neuromorphic bioelectronics adapted from ref. 21, CC BY 4.0.

Complementary circuits that combine p-type and n-type devices (and accumulation or depletion modes of operation) are power-efficient because they dissipate low power when idle (they combine on and off operation for idle conditions). Conjugated polymer electrolytes (CPEs), such as glycolated polythiophenes[56] or glycolated donor–acceptor copolymers[57], have become known as excellent OMIECs for p-type accumulation mode OECTs, allowing the application of known molecular design guidelines derived from the development of semiconducting polymers of organic thin-film transistors. Modifying the length and distribution of the glycolated side chains represents an efficient way to influence the ionic–electronic interaction and the operational stability of the devices[58]. In particular, because CPEs are homogeneous on a molecular level (unlike PEDOT:PSS), they show the highest degree of swelling and the highest product of charge carrier mobility and volumetric capacitance (μC*), which is an important figure of merit for OMIECs[59]. Furthermore, tuning the frontier orbitals or the side chains of the conjugated polymer backbone enables a certain control of the threshold voltage (although there is a compromise with stability and μC*)[56,57]. Alternatively, chemical doping with molecular additives may be used for threshold voltage control[60].

Building stable n-type organic transistors is notoriously more difficult than building p-type devices as n-type materials are more prone to oxidation, a fact that also holds true for OMIECs[61]. The benchmark OMIEC for n-type OECTs is poly(benzobisimidazobenzophenanthroline) (BBL) because of its high μC* product[62]. Important progress has been made to develop pre-doped BBL inks, improving environmental and operational stability and providing additional control over the threshold voltage[62]. However, BBL typically forms nanoparticles, which may lead to variability or poor performance, and is typically dissolved in highly acidic environments, raising issues regarding its biocompatibility and compatibility with other polymers. As a consequence, deposition methods such as screen printing or inkjet printing typically result in inhomogeneities and poor device performance[63], and alternative deposition processes that improve homogeneity have to be adapted and evaluated. Hence, finding alternatives to BBL is desirable, and known molecular design strategies were used to develop stable n-type OMIECs, such as copolymers based on naphthalenediimide (NDI)[42,64], small molecules such as perylene[65], or C60 with glycolated side chains[66]. However, the remaining challenge is to increase the μC* product of these materials to balance the performance of p-type and n-type devices. Indeed, for building complementary building blocks made of p-type and n-type devices, their performance characteristics should be comparable.

Another approach for complementary circuits is using ambipolar OMIECs[27] such as donor–acceptor copolymers with glycolated side chains. These materials are usually composed of polythiophene donor and NDI or diketopyrrolopyrrole acceptor units[67–69], or blends of p-type polymer-based OECTs and small-molecule n-type OMIECs[70]. However, although high-gain inverters have been demonstrated using ambipolar OMIECs, they tend to show unfavourable S-shaped output curves and limited rail-to-rail switching, if p-type and n-type operations are not balanced[70,71].

Effects such as nonlinear electrical characteristics cannot readily be described by established models for OECTs and OMIECs but are rather a manifestation of correlation effects that emerge at high charge carrier densities. For example, the Gauss-like shape obtained in BBL-based OECTs can be assigned to an energy gap emerging owing to Coulomb interactions at high polaron densities[72]. Another interesting observation, promising applications in event-based computation and associative learning, is the appearance of a hysteretic behaviour in the transfer curve of OECTs spanning over several orders of magnitude in time[37,73]. An approach to describe the operation of OECTs within the framework of thermodynamics is deriving the current–voltage curve from Gibbs free energy[74]. This approach was experimentally motivated by time-dependent and temperature-dependent spectroelectrochemical investigations[75,76]. The developed thermodynamic model not only accounts for the entropy of the doping and dedoping processes but also includes enthalpic terms that can be used to describe Coulomb attraction or repulsion between charged species. Therefore, such thermodynamic considerations may provide a more general framework for the description of OECTs capturing interactions on a nanoscopic level. Furthermore, combining such thermodynamic models with in operando characterization will allow researchers to derive more general structure–property relationships[77]. Ultimately, kinetic effects need to be included in the future to describe the transient properties of OECTs entirely.

Electrochemical random-access memories as organic artificial synapses

The realization of artificial neural networks also requires, as building blocks, the development of artificial synapses. Commonly, these systems have been demonstrated with solid-state memristive devices[78,79], a class of two-terminal devices with conductance levels that can be tuned in a non-volatile manner by applying electrical pulses. However, the conductance switching of these materials is inherently stochastic, which substantially reduces control and requires program and

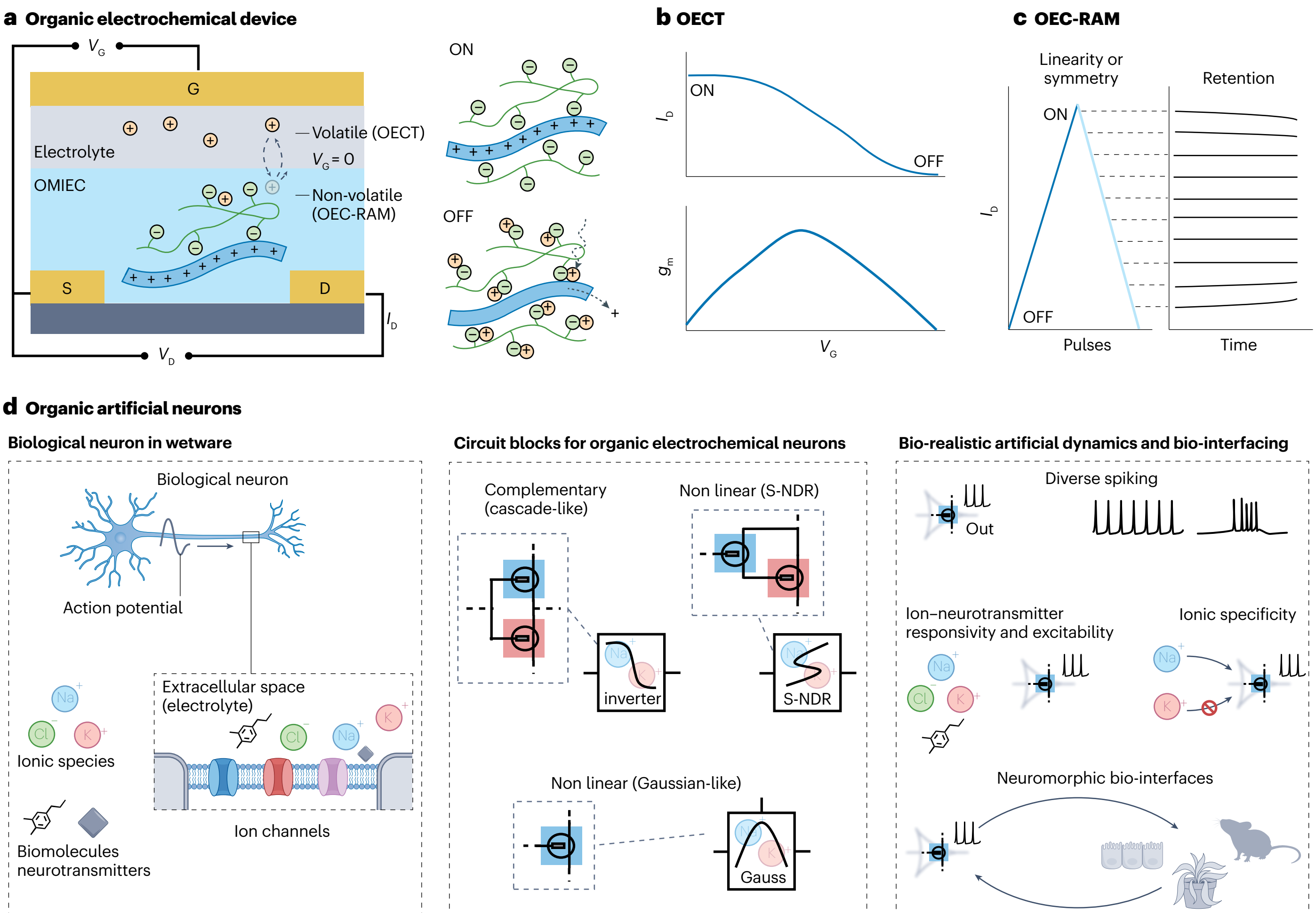

Fig. 2 | Organic neuromorphic devices and building blocks based on organic mixed ionic–electronic conductors. a, Generic schematic of an organic electrochemical device based on organic mixed ionic–electronic conductors (OMIECs). Organic electrochemical neuromorphic devices can be volatile (such as an organic electrochemical transistor (OECT)) or non-volatile (such as an organic electrochemical resistive access memory (OEC-RAM)). **b**, OECT. The presence of ions in OMIECs (from an electrolyte) modulates the hole density of the polymer. At the device level, this ionic–electronic coupling is translated into a change of the drain current versus gate voltage (I_D versus V_G) or a change of the transconductance versus gate voltage (g_m versus V_G) curve. The ion injection (application of V_G) and ion back flow (removal of V_G) are fully reversible and the device is volatile (indicated by the long dashed lines with arrowheads in panel **a**). **c**, OEC-RAM. The output current of the device I_D can be tuned in an analogue fashion under the influence of input voltage pulses V_G. OEC-RAMs are non-volatile and state retention is ensured with an access device (switch, transistor and so on) between the gate and the channel, imposing an open circuit potential or an energy barrier that prevents ion back flow (indicated by the short dashed line with arrowhead in panel **a**). **d**, Organic artificial neurons. Biological neuron in wetware: action potentials are generated and propagate across the axon. Biological neurons are immersed in an aqueous electrolyte, which is a noisy reservoir that contains various carriers for signalling. Ion channels endow neurons with ionic and molecular specificity. Circuit blocks for organic electrochemical neurons: circuit blocks or devices correspond to different nonlinear behaviour (inverter topology: step-like response; cascade-like topology with feedback: S-shaped negative differential resistance (S-NDR); antiambipolar OMIECs: Gauss-like). Colour-coded transistors correspond to different types of OMIECs (p-type and n-type, enhancement mode and depletion mode, and so on). Biorealistic artificial dynamics and bio-interfacing: organic artificial neurons based on mixed conductors display biorealistic dynamics that closely resemble those of biological neurons. Such neurons can be used as event-based components for neuromorphic (bio)sensing, actuation and bio-interfacing. Parts **a** and **b** adapted from ref. 34, Springer Nature Limited. Part **d** adapted from ref. 21, CC BY 4.0.

verification loops or sophisticated closed-loop systems to accurately tune the synaptic weights. Beyond solid-state devices, a wide variety of two-terminal organic memristors has also been demonstrated including molecular memristors based on azo-aromatic moieties[80,81], biomaterial and bio-membrane-based memristors[82–85] and memristors based on filament formation or ion migration[86–89].

At the expense of footprint and scalability when compared with resistive memory, the electrochemical resistive access memory (EC-RAM) has been developed. In principle, these devices are deterministic and, therefore, display more accurate conductance state tuning through a third – a gate – terminal (Fig. 2c). EC-RAMs work similarly to batteries: the electronic and ionic (electrolyte) circuits are decoupled and charges are trapped to achieve the non-volatile tuning of the channel. The most prominent demonstrations of EC-RAM were based on PEDOT:PTHF[35,37], PEDOT:PSS[19] (organic) and on Li-transition metal oxide (inorganic)[90]. OEC-RAMs closely resemble the common organic electrochemical transistor, with a high-capacitance polymer gate replacing the conventionally used gates[19]. An array of OEC-RAMs with inorganic access devices allows for parallel programming[23,91]. Like OECTs, OEC-RAMs are compatible with lithographic and additive manufacturing processes (inkjet, 3D printing)[34,92] and can be potentially integrated in diverse substrates, surfaces and objects as they are flexible, stretchable and can be integrated in small or large scale[93].

The third terminal of OEC-RAMs allows for the reproducible and well-controlled insertion of ions, which ensures greater overall predictability of the conductance[19]. The electrochemical doping process, however, results in undesired side effects. The most important ones include nonlinear or non-symmetric tuning (deviations from ideal behaviour), low stability and retention owing to parasitic side reactions such as oxidation, and relatively low operating speeds as ions are less mobile than electrons and holes. The latter has been overcome by scaling down device dimensions and using fast electrolytes such as ionic liquids[94]. Non-ideal tuning characteristics can also be mitigated by utilizing part of the conduction range – in which the tuning is linear[95] – or by using current pulses[96].

The comparably low state retention resulting from parasitic reactions remains the most important challenge of OEC-RAMs. Because conductance tuning is electrochemically driven, the stable range of conductance is limited by ambient conditions such as the presence of oxygen[97]. This effect is more pronounced for small-scale devices. Another source for limited state retention originates from the fact that OEC-RAMs are essentially non-equilibrium devices, which means that state retention is based on the ionic charge separation between the gate and the channel. In this case, the developed internal electric fields and gradients of ionic charges between gate and channel also contribute to the gradual state loss. In addition, some organic mixed conducting materials such as PEDOT:PSS are blends which can lead to composition variability between different volumes, thus posing a fundamental limit for scaling[98]. State retention is enhanced by the external access device that is necessary to prevent ion back flow. Doping PEDOT with a less (ion) conductive phase can lead to an access device-free configuration[35]. Electrolytes with high ionic resistance such as polydopamine can prolongate state retention with an access device-free configuration (that is, without external access device)[99]. Similarly, a partially crystalline mixed conductor that can trap ions in the crystalline domains of the material was used to prevent ion back flow[100]. However, these approaches reduce the electrochemical operational window and, thus, introduce a trade-off between the on–off ratio and stability.

At the same time, with sufficiently accurate electronics and noise kept to a minimum, it is possible to reduce the conductance range to be within a proper electrochemical range to avoid undesired reactions with oxygen and water[97]. Alternatively, reactions with oxygen can be eliminated with device encapsulation[101], although it requires complex processes such as the deposition of multilayers. An alternative to prevent electronic charges to move in the electronic peripheral circuit is to trap the ions in their meta-stable electrochemical states[102], thus also resulting in the trapping of electronic charges in the channel. Other important metrics for OEC-RAMs are the dynamic range, device-to-device variability, cycling stability and energy consumption. However, comparing certain metrics across different reported results is extremely difficult and can strongly depend on the measurement conditions. As an example, long-term potentiation is sometimes reported as the residual conductance difference, but also, and arguably more useful, as a measure of a stable conductance state modulation almost instantly after an applied pulse. Whereas the former can have use in mimicking short-term plasticity phenomena (for example, in spiking neural networks), the latter is essential for tuning synaptic weights in hardware-based artificial neural networks and in-memory computing. Therefore, a definition of proper device metrology is essential (Table 2). As an example, in the case of reporting analogue programming of OEC-RAMs, real non-volatile reading of a memory state is ensured during a write–read–write cycle when steady state is reached after a write event. Moreover, the type of access device that drives the OEC-RAM should be reported in detail, but also considered in the estimation of switching energy per event. When reporting retention time, it is important to ensure that reading events do not disturb the memory state level. Finally, retention

Table 1 | Metrics for organic neuromorphic devices and circuits

Parameter	Value or characteristic
OEC-RAMs	
Integration size	<1 μm^2 (dense or compact arrays)
Number of states	~100 separable states, or ~6 bit
Conductance tuning	Linear and symmetric
Switching noise	<0.5% of weight range (for 100 states)
Switching energy	<1 pJ per switching event
Writing or reading speed	<1 μs
State retention	1–10^8 s (online learning — inference only)
Endurance (cycles)	~10^9 (online learning)
Temperature stability	<80 °C (for operation), <200 °C (for back-end process)
Organic artificial neurons	
Integration size	<1 μm^2 (dense or compact arrays) <100 μm^2 (single neuron bio-interfacing) >100 μm^2 (neuronal population bio-interfacing)
Spiking frequency	0.5–1,000 Hz
Energy per spike	<nJ
Spike amplitude	~60–100 mV (bio-emulation) ~1–10 V (bio-interfacing)
Main firing modes	Integrate and fire, tonic firing, phasic firing, bursting, stochastic firing, latency, integration, accommodation, resonance, subthreshold oscillations, excitation or inhibition, chaos
Ion concentration for in-liquid biosensing (physiological range)	Na^+: 15–140 mM; K^+: 4–150 mM; Cl^-: 5–120 mM; Ca^{2+}: 10^{-4}–1 mM; Mg^{2+}: 0.5–1 mM; HCO_3^-: 8–27 mM; HPO_4^{2-}: 1–60 mM
Neurotransmitter concentration for in-liquid biosensing (approximate range)	Acetylcholine: 0.1–6 nM; dopamine: 1–10 nM; GABA: 0.1–1 mM; histamine: 1–100 nM; noradrenaline: 1–100 nM; serotonin: 10–100 nM

Representative metrics and desired properties for organic electrochemical resistive access memories (OEC-RAMs) and organic artificial neurons.

time (or memory loss) is usually state dependant because OEC-RAMs are non-equilibrium devices, and reporting a single retention time is incomplete. Therefore, retention time should refer to a specific memory state.

Table 2 | Metrology of organic neuromorphic devices and circuits

Metric and characterization	Considerations for standardization
OEC-RAMs	
Memory	Definition: set clear distinction between short-term and long-term memory
Analogue switching (short-term memory)	Wait for inadequate time between stimulus–read cycle for non-equilibrium conductance state(s)
Short-term memory (dynamics)	Quantification of dynamics: define time constant or distribution of time constants
Analogue switching (long-term memory)	Wait for adequate time between write–read cycle to reach equilibrium conductance state(s)
Long-term memory (linearity in switching)	Quantification of nonlinearity: introduce nonlinearity parameter that expresses deviation from linearity
Long-term memory (asymmetry in switching)	Report quantitively the asymmetry between potentiation and depression with nonlinear parameters
Writing and reading speed	Time width–voltage pulse dilemma: describe time width and voltage pulse amplitude when reporting speed
Switching energy	Consider access device or peripheral circuitry used for switching
State retention	Wait for adequate time between write–read cycle to reach equilibrium of conductance state
State retention (access device)	Describe access device or peripheral circuitry used to probe retention of a memory state
Endurance (cycles)	Report quantitative changes during endurance (linearity, asymmetry, retention)
Temperature stability	Report temperature range for stable operation
Organic artificial neurons	
Integration size	Report circuit footprint
Circuit elements	Report level of integration and the use of off-the-shelf circuit components
Circuit complexity	Report device count (organic and inorganic)
Spiking frequency	Report instantaneous, mean and time-dependent frequency
Energy per spike	Correlate energy per spike to corresponding spiking frequency
Spiking amplitude	Report voltage (for current excitation) and current (for voltage excitation) spiking amplitude
Endurance (cycles)	Report quantitative changes during endurance (spiking frequency and amplitude, action potential profile)
Neuronal firing modes	Definition: set clear distinction between steady-state and transient firing modes
Characterization of neuronal firing	Measurement set-up does not interfere with neuron behaviour
In-liquid biosensing (ions and neurotransmitters)	Record and report history of measurements

Considerations for standardization of metrics for organic electrochemical resistive access memories (OEC-RAMs) and organic artificial neurons.

Organic artificial neurons

Organic artificial neurons can be realized with electrochemical circuits made of volatile OECTs. Various models of hardware-based spiking neurons, including integrate-and-fire model or Hodgkin–Huxley model, have been developed to describe the generation of spikes in biological neurons with varying degrees of accuracy[103]. Despite their differences, these models all simulate how the membrane potential integrates currents from incoming spikes and generates new spikes once a certain threshold is exceeded. In contrast to artificial spiking neurons based on silicon[2], metal oxides[104], 1D and 2D materials[105] or solid-state organic semiconductors[106], the OMIEC implementation of these neurons offers various benefits, such as improved biocompatibility and ion-based and chemical-based operating mechanisms such as those found in biological systems (Fig. 2d). Therefore, such organic artificial neurons can more realistically emulate the behaviour of biological neurons in the wetware (Fig. 2d).

To implement biomimetic spiking neurons with OECTs, the realization of circuit building blocks with nonlinear behaviour is required (Fig. 2d). To obtain nonlinear behaviour for neuromorphic behaviour, p-type and n-type devices with balanced transport properties and steep subthreshold behaviour are required. These properties are ideal for the design of low-voltage inverters[107], which are essential components of biologically plausible neuron models such as the Axon-Hillock neuron[20,21] or Morris–Lecar neuron[108]. For an even more complex relaxation oscillator, that is, the Hodgkin–Huxley neuron, precise adjustment of the threshold voltage is needed to balance the different ion channels and obtain stable oscillations. OECTs show several interesting properties in their electrical characteristics, typically not seen in conventional field-effect transistors, that might lead to very efficient hardware-based implementations of neuromorphic computing. For example, OECTs often show a saturation behaviour in their transfer characteristics[74,109], which might be used to mimic the sigmoidal shape of the activation function of a neuron. For even more interesting nonlinear (non-monotonic) behaviour, a Gauss-shaped transfer curve with negative transconductance has been observed in heavily doped BBL-based OECTs[72], and an S-shaped negative differential resistance has been shown in a cascade connection of OECTs with feedback. Such (non-monotonic) response can potentially emulate more realistic neuronal functions. Indeed, these nonlinear behaviours have been used to mimic the opening and closing of ion channels in a neuron and neuronal excitability, for a biorealistic neuronal implementation[21,22].

The first attempt to develop artificial spiking neurons using OMIECs utilized a leaky integrate-and-fire design, using an Axon-Hillock circuit based on all-printed complementary OECTs[20]. An inverter building block made of a p-type and an n-type OECT is required for this neuron (Fig. 2d). The actual configuration of this artificial neuron requires two sequential stages of inverter blocks with feedback, defining a minimal topology of an electrochemical ring oscillator[20]. These artificial organic electrochemical neurons (OECNs) displayed various neuronal features, such as ion concentration-dependent spiking and spike timing-dependent plasticity, when combined with organic electrochemical synapses. Because of the low-voltage swing, ion-mediated spiking and high compatibility with biological systems, OECNs can interface with the bio-signalling systems of bio-membranes[21], plants[20] and invertebrates[22] to record and/or control their electrophysiology upon input of stimuli. However, as integrate-and-fire model neurons cannot replicate the rich temporal dynamics of biological neurons, they can only simulate a restricted range of neural characteristics such as regular firing.

Box 1

Carrier transport and coupling in mixed organic ionic–electronic conductors

Conduction of electronic and ionic charges does not happen separately in organic mixed ionic–electronic conductors (OMIECs)[144,145]. Indeed, there is an inherent coupling between both species, and the development of a profound understanding of this coupling is essential for the description of organic electrochemical transistors, being the bedrock of bioinspired electronics. In OMIECs, intramolecular transport of electronic charges occurs along the pi-conjugated core of the constituent molecules (such as the delocalized transport along the conjugated backbone of a polymer), and intermolecular transport is governed by the overlap of pi orbitals of neighbouring molecules[146]. In most OMIECs, though, static and dynamic disorders are intrinsic factors, making thermally activated hopping the dominant electronic transport mechanism. Ionic transport in OMIECs is generally more complex than electronic transport (see the figure), and mechanisms are material-specific and whether the OMIEC is in a dry or wet state. For example, as OMIECs swell when in contact with a liquid electrolyte, solvated ions (surrounded by their hydration shell) can drift or diffuse through the OMIEC, and the diffusion constant in the material might be as high as that in the pure liquid phase ($D = 10^{-5}\,cm^2\,s^{-1}$)[147]. In the dry state, though, either ions are fully immobilized or they only move through the OMIEC via hopping transport ($D = 10^{-10}\,cm^2\,s^{-1}$, transport either mediated by defects or ion-coordinated entities[148,149]). However, other ion transport mechanisms are also possible, for example, the Grotthuss mechanism for protons. As ions move through the OMIEC, they may influence the density of electronic charges on the pi-conjugated polymer via faradaic and non-faradaic processes (see the figure). In fact, OMIECs are often considered to be either ideally faradaic or non-faradaic (which simplifies the description). In reality, both processes occur side by side. In the case of an ideal non-faradaic process, the excess ions in the OMIEC are neutralized by electronic charges (polarons) on the conjugated backbone in order to satisfy charge neutrality. Hence, the excess ion and the stabilized polaron form an electrochemical double layer. This process is also referred to as stabilization of the electronic charge via the excess ion or electrochemical doping. As this process happens throughout the entire thickness of the OMIEC layer, the electrochemical capacitance, which is a measure of the strength of the ionic–electronic coupling, is a quantity that scales with the volume of the film. Hence, it is denoted as volumetric capacitance C* in the literature. In order to define a figure of merit for the OECT operation accounting for the electronic transport and the strength of the ionic–electronic coupling, the product μC* of the electronic mobility and volumetric capacitance has been widely accepted[59]. The advantage of the μC* product is that it does not require independent measurement of mobility and volumetric capacitance. It can be readily determined from the transconductance ($g_m = dI_D/dV_G$) by measuring the transfer curve (drain current I_D over gate–source voltage V_G)[34].

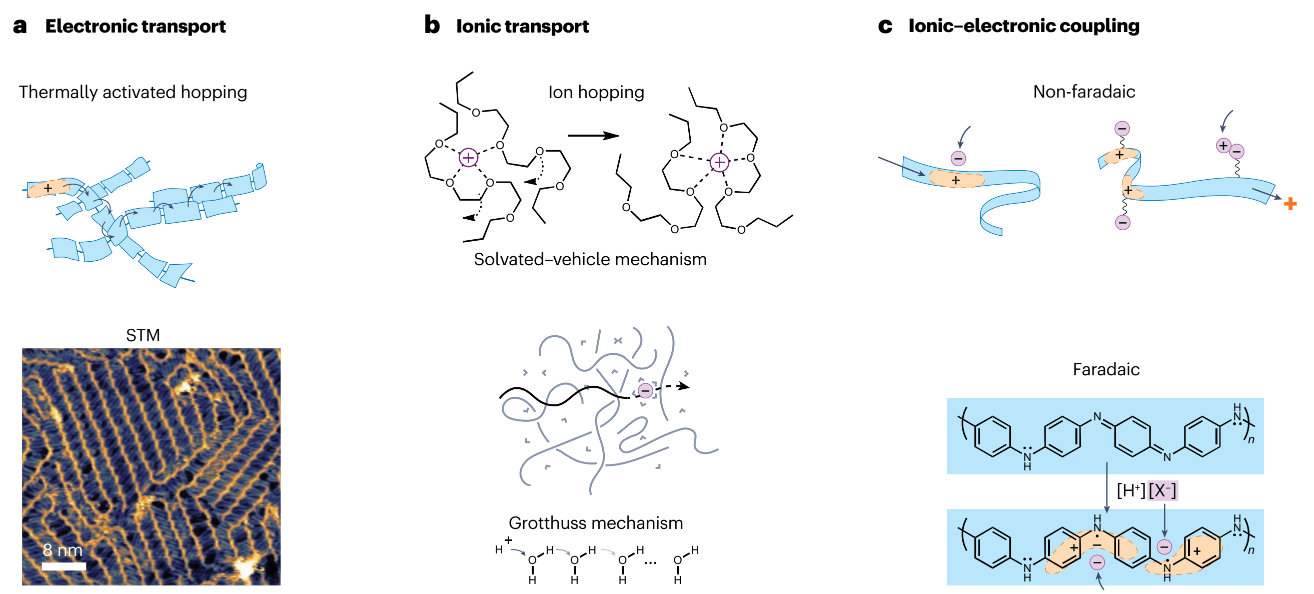

Figure adapted from ref. 144, Springer Nature Limited. STM image reprinted from ref. 146, CC BY 4.0.

Another method for producing biorealistic spiking neurons involves leveraging the nonlinear properties of two p-type thiophene-based OECTs – a depletion mode and an enhancement mode transistor – connected in a cascade-like configuration with feedback resistors[21]. This generic configuration produces a two-terminal organic electrochemical nonlinear block with S-shaped negative differential resistance response (Fig. 2d). When the nonlinear element is coupled at its negative resistance regime to an external load of positive impedance, the whole circuit bifurcates (that is, resonates) and forms an oscillatory circuit, the organic artificial spiking neuron[21]. The artificial neuron is capable of generating action potentials that resemble those of biological neurons with frequencies in the range of 5–70 Hz. The nonlinear behaviour of these devices enables a biorealistic emulation of the excitability and dynamics of neurons in the biological wetware in biophysically relevant ion concentration ranges. Another implementation of artificial spiking neurons with OMIECs involves the development of biorealistic conductance-based organic electrochemical neurons (c-OECNs)[22]. These neurons leverage the highly tuneable, stable and reversible antiambipolar character of BBL-based OECTs (Gauss-like response, Fig. 2d) at high electrochemical doping levels to introduce the complex activation–inactivation dynamics of biological sodium channels in the spiking mechanisms of OECNs. The antiambipolar character of BBL induces a negative differential transconductance OECT response, which is utilized for nonlinear phenomena and circuit resonance (that is, oscillations of the artificial neuron)[22]. These c-OECNs can produce spiking patterns at biologically plausible frequencies of up to 100 Hz, emulate 15 out of 20 neural features and exhibit stochastic spiking.

The spiking behaviour of these biorealistic electrochemical neurons can be modulated by various factors, including ions (concentration and type of ions), amino acids and neurotransmitters, as well as electrochemical noise (Fig. 2d). They can also be synergistically integrated with bio-membranes to form real-time biohybrid interfaces and be used for the in vivo stimulation of biological nerves. This integration makes them suitable as event-based (bio)sensors, allowing the conversion of biochemical signals into a language that living systems can interpret. In this context, the high sensitivity of OECTs to a wide range of (bio-)chemical and physical stimuli could aid in easy signal transduction and sensory fusion at the neurons' level without requiring additional hardware[110–112]. In the long-term, such biorealistic, multi-functional and multi-responsive artificial neurons can form the basis for the emulation, restoration or even the augmentation of biorhythmicity, aiming at intelligent bio-interfaces and neuroprosthetics.

Applications

From devices to integrated networks and architectures

OMIECs and their corresponding devices and networks can lead to novel neuromorphic architectures (Fig. 3).

Artificial neural networks. Historically, a large research focus has been on developing hardware accelerators for in-memory computing. These systems are particularly interesting because they can reduce

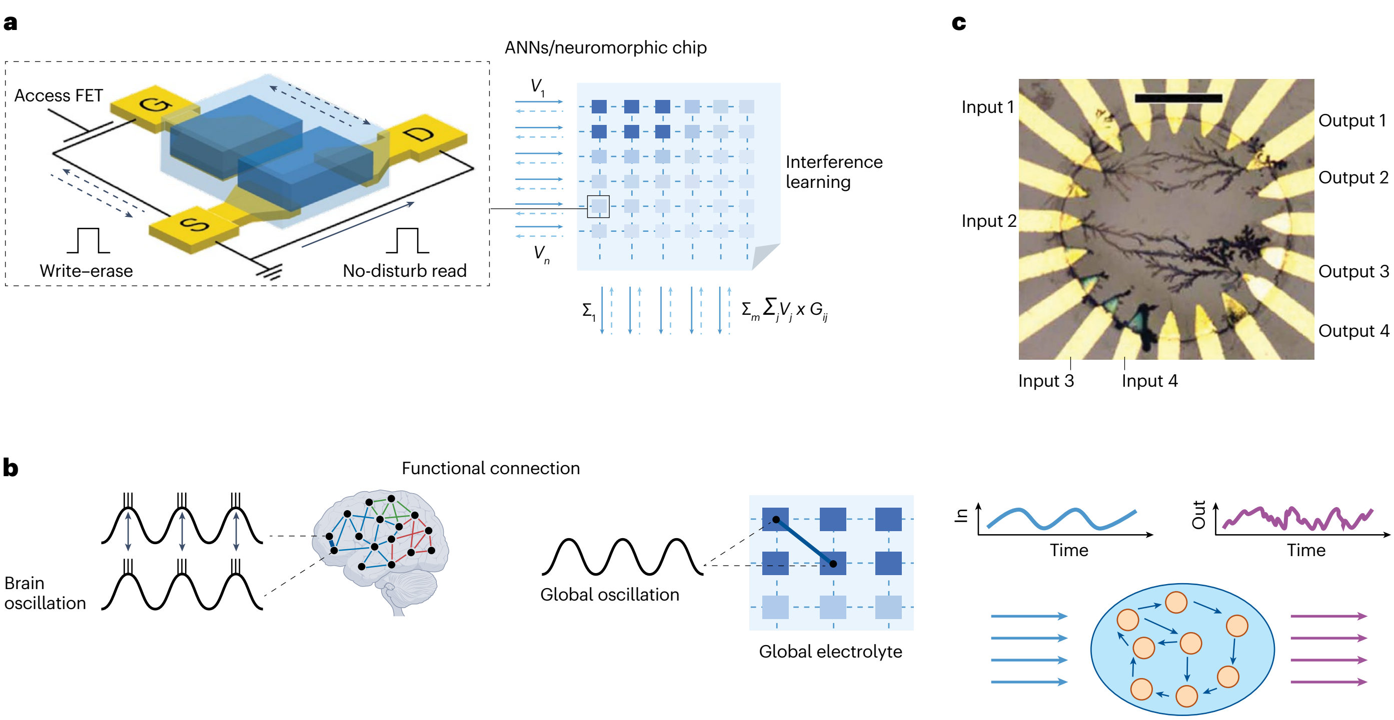

Fig. 3 | From devices to integrated networks and architectures. a, Organic artificial synapse (organic electrochemical resistive access memory (OEC-RAM)) as building block for organic neuromorphic chips. Organic neuromorphic chips can be used for local or distributed learning and inference. **b**, A global electrolyte shared between devices induces a functional type of connectivity between them, in analogy with global oscillations in the brain. **c**, Dendritic-like structures of conducting polymers can be realized with electropolymerization in a monomer-containing solution. These complex structures act as a reservoir and map nonlinear inputs into higher dimensional computational spaces performing in materio computing (for example, classification). ANNs, artificial neural networks; FET, field-effect transistor. Part **a** adapted from ref. 94, AAAS. Part **b** adapted with permission from ref. 31, AAAS. Part **c** adapted from ref. 21, CC BY 4.0.

the most energy-costly step (the multiply–accumulate step, or vector matrix multiplication step) by performing it directly in hardware[4]. There has been an abundance in reported applications of these (or similar) non-volatile devices, ranging from hardware convolutional neural networks[113] to long-term and short-term memory networks[114] and partial differential equation solvers[114], mostly using phase change or resistive memories. Owing to their linearity in programming, the analogue tuning of their conductance levels and their low-voltage operation, organic artificial synapses are promising candidates for the realization of artificial neural networks (Fig. 3a). However, organic neuromorphic electronics can exhibit device-to-device variability when developed in an academic environment, which can be an issue when scaling to larger arrays. Nevertheless, the use of large conductance windows and analogue tuning, combined with relatively forgiving (and fault tolerant) neural network operations and algorithmic co-development,[115] can partially relax the need for low variability and fault tolerance that is usually required in conventional electronics.

Apart from aqueous electrolytes, several solid electrolytes have also been introduced, particularly based on ionic liquids in polymer matrices[94]. Although aqueous electrolytes are relevant for wet bio-interfaces, solid electrolytes are suitable for the development of circuits and arrays in combination with more complex peripheral electronics. One particular challenge is developing a patternable solid electrolyte to allow upscaling of (crossbar) arrays and prevent device-to-device crosstalk and current sneak paths during write–read–inference operations[73]. Although sneak paths in crossbar arrays can be prevented by implementing access devices[23], it is important to note that aggressive integration of OEC-RAM-based circuits beyond proof-of-principle small arrays requires a combined effort of optimized peripheral electronic circuit design and dedicated software tools for device access. To achieve the highest energy gains, parallel updating needs to be implemented, which requires some form of novel combination of block writing as only certain combination of devices can be individually addressed[23].

The most common algorithm in neural networks and deep learning has been the backpropagation algorithm with gradient descent[7]. However, implementing this in hardware (beyond single-layer perceptrons) is far from trivial as it requires storing partial derivatives of the weights in hardware as well, though workarounds and hybrid forms have been reported. Alternative algorithms such as evolutionary strategies to determine hyperparameters or train spiking neural networks could also prove useful for OEC-RAM devices that require low power and are easy to tune[113,116].

Global–local phenomena. The coupling of several OMIEC-based neuromorphic devices via an electrolyte might herald a new era of neuromorphic computing (in liquido computing[52]) in which local mechanisms such as synaptic plasticity or neuronal activity and global regulation (or homoeostasis) are exploited for the implementation of efficient learning rules and biorealistic neuromorphic functionalities[24–26,117] (Fig. 3b). As an example, a shared electrolyte between OMIEC-based neuromorphic devices allows for parallel electrochemical interactions between them through the electrolyte continuum, and thus wire-free device-to-device 'soft' interconnections[25,117]. A global electrochemical oscillation at this shared electrolyte can synchronize an array of devices in a similar way as the brain oscillations synchronize the activity of neural populations[26]. Such global–local coupling phenomena can enable highly diverse neuromorphic architectures in which the topology of the structural network can be modulated flexibly and dynamically depending on transient global activities or even on the state of the coupling medium.

Bottom–up neuromorphic networks. Neuromorphic functionalities using OMIECs may be obtained not only on the single-device level (neuron or synapse) but also possibly on the network scale using bottom–up processes such as electropolymerization starting from a monomer-containing solution (Fig. 3c). For example, an electropolymerization method was developed for PEDOT, allowing the directed growth of fibres with a length of several millimetres and a controlled diameter in a liquid environment[118]. This technique was later modified to grow 'evolvable' OECTs, thereby mimicking the process of synaptogenesis[51,53]. In fact, the time constants of synaptic plasticity in the electropolymerized fibre structures can be tuned by the growth conditions (voltage amplitude and input frequency), enabling learning on the timescale from milliseconds to hours. A chemical polymerization approach was also used for the in vivo growth of CPE fibres acting as a bioelectronic interface[119], and similar in vivo fabrication was used to create soft substrate-free conducting materials within the biological environment via metabolite-driven polymerization[32]. Evolvable networks have even been transferred to the level of complete neural networks. For example, electropolymerization has been used to build organic pattern classifiers[120] or nonlinear random neural networks acting as a physical reservoir for real-time classification of bio-signals[31,121–123].

Overall, combining complexity in materials caused by correlation effects at high charge carrier densities resulting in negative differential transconductance and structural complexity might herald a new era of neuromorphic computing going away from the current paradigm of synapse-centred computation towards dendrocentric learning, by taking into account actual computations taking place at the dendrites of neurons[124].

Learning, sensing and bio-interfacing

Sensorimotor learning and environmental intelligence. Apart from the widely used algorithmic implementation with software-based neural networks, learning can be incorporated on-chip using signals directly from the environment via external sensors. One example includes sensorimotor integration, a form of associative learning in which several external signals are combined and associated (input–input or input–output associations) to adapt to a changing environment and optimize the performance of a system with embodied intelligence (that is, the target behaviour of a mobile robot)[33]. In this particular example, learning occurs locally on an organic neuromorphic circuit in real-time and in a closed-loop fashion, by exposing the circuit directly on environmental signals with iterative interaction[33]. With this sensorimotor integration, a robot in a maze can gradually learn to associate the presence of navigation cues with turning decisions at the maze intercepts and gradually escapes from the maze.

Local and/or distributed learning and sensorimotor control can be enhanced substantially by using low-power and easy-to-tune neuromorphic materials and devices. Delocalizing such properties (that is, distributing spatially on the body of an intelligent system) and using self-healable, flexible, stretchable polymers can potentially lead to more robust systems with lifelong intelligence that are tolerant to mechanical damages[48,125]. Local training and learning can be enriched with multimodalities by introducing locally integrated sensors and

Glossary

Accumulation mode transistor
Type of field-effect transistor that is normally off and requires a positive gate–source voltage to control or enhance its conductivity.

Axon-Hillock neuron
Simplified representation used in computational neuroscience to simulate the behaviour of a neuron, focusing on the integration of incoming signals and the initiation of action potentials at the axon hillock region.

Backpropagation algorithm
Supervised learning technique used in artificial neural networks, which involves iteratively adjusting the internal parameters of a network by propagating error information backward through the network to minimize the difference between predicted and actual outputs.

Depletion mode transistor
A type of field-effect transistor that is normally conducting in the absence of an applied voltage and requires a negative gate–source voltage to control or reduce its conductivity.

Edge computing
Distributed computing paradigm that involves processing data closer to the source of data generation such as in IoT devices or sensors, rather than relying solely on centralized cloud servers, to reduce latency and improve real-time data processing capabilities.

Hodgkin–Huxley model
Comprehensive mathematical model used in neuroscience to describe the complex electrical behaviour of biological neurons, taking into account the dynamics of ion channels and membrane potential, and providing insights into the generation of action potentials.

Integrate-and-fire model
Simplified computational model in neuroscience that accumulates incoming electrical signals (inputs) and generates an action potential (output) when the accumulated signal surpasses a certain threshold, mimicking the basic firing behaviour of biological neurons.

Long-term synaptic plasticity
Persistent changes in the strength and efficacy of synaptic connections between neurons, typically lasting from minutes to indefinitely, and is often associated with processes such as long-term potentiation and depression.

Membrane potential
Voltage difference across the cell membrane of a neuron or other cell, resulting from differences in ion concentrations inside and outside the cell, which has a crucial role in the electrical excitability and communication of a cell.

Morris–Lecar neuron
Mathematical model that describes the behaviour of a simplified biological neuron, particularly in the context of the membrane potential dynamics and ion channel conductance, allowing for the study of neuronal excitability and spiking patterns.

Neural features
Different firing modes of neurons including regular, phasing, stochastic firing and excitability.

Perceptrons
Simplified models of a biological neuron, used in machine learning as a basic unit for binary classification, in which it takes a set of input values, applies weights to them and produces an output based on whether the weighted sum exceeds a certain threshold.

Rail-to-rail switching
The ability of an electronic device or component, such as an operational amplifier, to operate and output signals with minimal distortion or clipping while covering the full range of its power supply voltage.

Reinforcement learning
Machine learning paradigm in which an agent learns to make sequential decisions by interacting with an environment, aiming to maximize a cumulative reward signal through a trial-and-error process.

Sensorimotor integration
A process by which sensory information is received, processed and used to plan and execute motor actions, enabling organisms to perceive and respond to their environment effectively.

Short-term synaptic plasticity
Transient changes in the strength of synaptic connections between neurons that occur over a relatively brief period, typically milliseconds to seconds, and can involve either facilitation or depression of synaptic transmission.

Synaptogenesis
A process by which new synapses are formed between neurons in the developing nervous system, allowing for the establishment of neural circuits and networks.

stimuli-responsive materials acting as novel artificial nociceptors (thermoelectric modules), haptics (pressure sensors) and artificial retina systems (optical or light sensors). In robotics, on-chip biochemical learning schemes with real neurotransmitters could also be interesting to investigate and might open up entirely new dimensions beyond conventional approaches of digital-like reinforcement learning.

The ability of organic (neuromorphic) devices to be distributed in large areas can enable forms of environmental intelligence. For example, low-cost biosensors (which are printable or biodegradable) that monitor plant nutritional levels and extract specific spatiotemporal patterns across the field and within day–night or seasonal cycles could be critical for improving decision-making in precision agriculture[126,127]. Environmental intelligence may also benefit from organic neuromorphic electronics that act as a substrate for large-scale and distributed sensing, processing and pattern recognition[128]. In this way, large objects such as buildings could be regarded as perceiving, acting and adapting structures, with multimodal organic neuromorphic electronics that measure in real-time and extract optical, mechanical or acoustic patterns. Such large-scale intelligence might provide valuable information and real-time control regarding the optimum energy consumption, mechanical integrity or environmental noise.

Biohybrid systems and neuromorphic bioelectronics. Organic neuromorphic devices and their corresponding arrays and circuits have a great potential to operate at the interface with biology and in particular with neuron(-like) cells (Fig. 4). These biohybrid neuromorphic platforms could encode cellular signals and process biological information exploiting electrical and electrochemical transduction processes. In fact, because organic biosensing interfaces have high selectivity and sensitivity, biohybrid synapses have been established with a single neurotransmitter[29]. Electrochemical and collective modulation of multiple neurotransmitters has also been exploited to create biohybrid optoelectronic synapses[30].

Triggered by biological signalling, hybrid platforms can also provide functional actuation and control over synaptic molecules[99], biological membranes[129], cell layers[21], tissue and organ[130] or eventually living organisms[20,131–133]. Ideally, these systems can act as a bridge and establish bidirectional interactions between the living and artificial

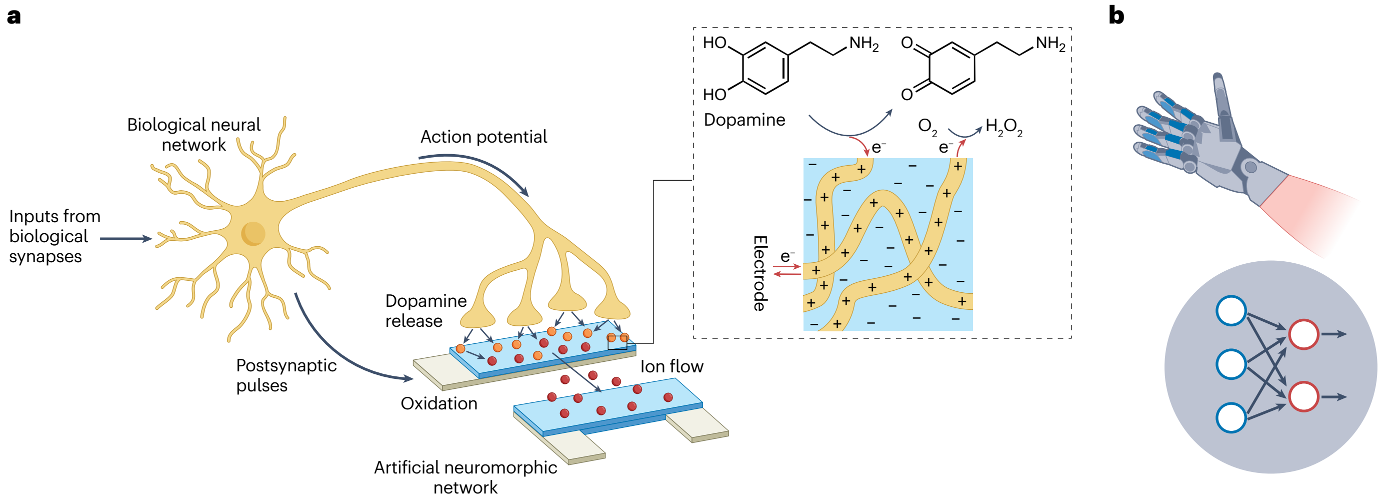

Fig. 4 | Biohybrid devices and systems. a, An organic artificial synapse can process co-current electrical (action potentials) and biochemical signals (neurotransmitters). **b**, Biohybrid artificial nerve systems mimic neural signal transmission – the conversion of biochemical signals (neurotransmitters) into electrical signals by the brain – which are transmitted by the artificial nerve to drive prosthetics. Multimodal (electrical and biochemical) neural networks allow and mediate the conversion, recognition and transmission process. Part **a** adapted from ref. 29, Springer Nature Limited.

world to monitor biological functions and actuate a mean of stimulation if required by means of a closed-loop system[134]. In turn, seamless integration and transparent, soft and conformable interfaces between the artificial neurons and the host biological system will provide mechanical stability over the long term. In order to achieve good interfacing, flexible and stretchable materials represent an excellent choice both for the device support and electroactive materials[135–138]. In this scenario, blending organic semiconductors with tissue-like materials, such as gelatine-based materials, can massively lower the Young's modulus mismatch between the device and the target tissue. Neuromorphic is not only recalling electronic-based operation but should also be seen as a more general concept to recapitulate neuronal-inspired structural and functional factors[18]. In fact, the contact area between the electroactive surface and the cellular environment should be attractive to cells and tissues and recognized as their own matrix. To this end, microstructuring and nanostructuring the electroactive surface with biomimetic designs and tailoring the surface chemistry can trigger tighter engagement (that is, mechanical matching and more efficient signal transduction) of cells or tissue with the devices[47,139]. Furthermore, biohybrid neuromorphic systems might also support in situ multimodal sensing and computing through the combination of optoelectronics, electrochemistry, electrophysiology and iontronics and might provide real-time monitoring and computing of biosignals from the human body[100,140].

However, closed-loop bidirectional communication that resembles the learning and connectivity properties of the human brain is still lacking and requires computing capabilities that are still not fully achieved by organic interfaces. Such capabilities include the post-acquisition treatment of biosignals with operations such as spike sorting and brain wave classification[140]. Here, a visionary design would be the integration of inorganic high-throughput devices and memristors (for information processing and biosignal treatment) with organic neuromorphics (to be the functional ionic–electronic transducing elements at the biological end)[134,141]. A potential application of such design would be to support the operation and maintenance of prosthetics to restore and potentiate, if needed, certain biological functions when key organ functionalities are lost.

Concluding remarks

Since 2015, the field of organic bioinspired electronics with OMIECs has been steadily growing with many important small steps. However, there are still some questions about what the future would look like. By introducing new materials, energy-efficient devices and unconventional functionalities, organic bioinspired electronics hold the synthetic toolkit for transformational changes in bioinspired and neuromorphic technologies. Diverse top–down and bottom–up fabrication and synthetic processes for point-like devices, device arrays or even distributed networks already exist. Owing to the inherent sensing and actuating capabilities and biocompatibility of organic electrochemical materials and devices, energy-efficient and multimodal edge computing and processing locally at the place of interest are only a few steps away. However, materials and device development is mostly laboratory-based and still at a premature stage, and thus requires leaps to reach a high level of technological readiness. Nevertheless, the path towards technological maturity is not completely unknown, as a trajectory has been already shaped by the development and commercialization of organic LEDs and is out there as blueprint. Ad hoc characterization, analysis and modelling techniques, able to identify and describe the various sources of device degradation and variability, are still underdeveloped but necessary. New strategies for materials exploration and synthesis (manual or traditional, semi-automatic, or artificial intelligence-guided or autonomous) could be necessary for overcoming fundamental issues such as material degradation and for improving device metrics (retention time, speed, linearity in artificial synapses, spiking frequency in artificial neurons and so on), as well as for introducing novel functionalities (for example, artificial receptors). Biocompatibility assessment is essential for every additional step (that is, when introducing new OMIECs, dopants or additives). Essential tools for the future development of integrated organic neuromorphic electronics, such as physically based analytical models for accurate computer-aided design circuit simulations, are still missing. Although not trivial for electronics, the biological wetware and its role in neural processing should be considered in circuit modelling and implementation. In a similar direction, hardware–algorithm co-design will most probably be necessary for the development of artificial networks, and to account for the special properties of such a technology (that is, need for access devices, linearity in programming, electrolyte operation and biosensing capabilities).

The community of organic bioinspired electronics still has a lot to learn from the progress of mature technologies such as complementary metal–oxide–semiconductor (CMOS) and solid-state memristors. Indeed, CMOS-based neuromorphic electronics is a mature field that has accumulated decades of technological advancements. Therefore, lessons should be derived from CMOS technology on reliability, low device-to-device variability, upscaling and integration. Moreover, solid-state memristive technologies can be a source of inspiration for organic bioinspired electronics owing to their high level of integration, the advancements in hardware–algorithm co-design and the wide application space that has been demonstrated over the past decade. Co-integration of soft with solid-state technologies should also be considered in order to get the best out of every technology. However, it has to be clear that soft matter is not intending to replace conventional technologies, but rather to augment current capabilities, and for that, technological niches should be clearly identified.

A fundamental challenge, but with great innovation potential, is that biological phenomena are still in many cases not well understood and, therefore, their mapping into organic materials and/or device properties is ambiguous. Biorealism in neuromorphic electronics, for instance, is hard to be tabulated and described by engineering metrics. Therefore, it is still debatable up to which level the computational primitives of biological systems are critical for technological emulation. At least with this approach of biorealistic development, the integration borderline between the neuromorphic and the neural world will gradually fade away. This deeper symbiotic co-operation of biomimetic and neuromorphic technologies with the human activity could unravel new and unpredictable interaction dimensions and will substantially assist humans in various ways in the domains of personal and scientific computing, environmental intelligence, personalized and precision medicine, bioelectronics, point-of-care diagnostics, virtual or mixed reality, and (bio, soft)robotics. In a broader perspective, for instance, such interaction dimensions will open entirely new avenues for the development of strategies for understanding and controlling biology, with many unknown future ramifications. It seems that we are entering a new exploration phase in the domains of biocomputing, neuromodulation, tissue engineering and regeneration, in which novel tools for interacting in a more natural manner with biological systems are necessary. In the future, it is speculated that biohybrid (artificial–neural) systems might work on our side synergistically and accompany us in such a way as animal domestication happened over the past few millennia. These far-reaching perspectives may mark the beginning of ethical considerations[142]. For instance, although a long-term goal of intelligent systems is their autonomous operation, either in in vitro or in vivo scenarios, a solid framework for safe operation is required. The framework for restoring pathological conditions with such novel technologies can be clearly defined. However, the ethical borderline is blurred when it comes to the augmentation of sensorimotor processes or physical capabilities, as such technologies might be more accessible to specific socioeconomic backgrounds. Because such technologies will create new and multimodal data, as well as new ways to control living organisms, an issue that rises is who has access to those (re)sources and how cognitive liberty and privacy are protected. Finally, how intellectual property can be managed in human-made biohybrid systems that perform biocomputing is still an uncharted territory.

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