An organic artificial spiking neuron for in situ neuromorphic sensing and biointerfacing

The effective mimicry of neurons is key to the development of neuromorphic electronics. However, artificial neurons are not typically capable of operating in biological environments, which limits their ability to interface with biological components and to offer realistic neuronal emulation. Organic artificial neurons based on conventional circuit oscillators have been created, but they require many elements for their implementation. Here we report an organic artificial neuron that is based on a compact nonlinear electrochemical element. The artificial neuron can operate in a liquid and is sensitive to the concentration of biological species (such as dopamine or ions) in its surroundings. The system offers in situ operation and spiking behaviour in biologically relevant environments—including typical physiological and pathological concentration ranges (5–150 mM)—and with ion specificity. Small-amplitude (1–150 mV) electrochemical oscillations and noise in the electrolytic medium shape the neuronal dynamics, whereas changes in ionic (≥2% over the physiological baseline) and biomolecular (≥ 0.1 mM dopamine) concentrations modulate the neuronal excitability. We also create biohybrid interfaces in which an artificial neuron functions synergistically and in real time with epithelial cell biological membranes.

Neurons are the fundamental units of the nervous system and are used to transmit and process electrochemical signals. They operate in a liquid electrolyte and communicate with each other via gaps (synapses) between the axon of pre-synaptic neurons and the dendrite of post-synaptic neurons (Fig. 1a). Neuromorphic computing uses hardware-based implementations to mimic the behaviour of synapses and neurons, for efficient brain-inspired computing. The approach could also be used to interface biology with electronics that share similar biocomputational primitives. Synaptic phenomena—the gradual and activity-dependent coupling between neurons—are typically mapped onto memory devices, which can be binary, multistate or analogue. However, to emulate neuronal spiking and oscillatory dynamics, electronic oscillatory circuitry is required.

Neuron-like dynamics can be created with conventional microelectronics using oscillatory circuit topologies to mimic neuronal behaviours. For example, neuromorphic electronic circuits consisting of ring oscillators have been used for the implementation of mechanically flexible, skin-inspired electronics and neuro-inspired mechanoreceptors. Many-element artificial neurons based on solid-state silicon or organic devices have also been reported. However, although these approaches can mimic specific aspects of neuronal behaviour, the integration of a large numbers of transistors and passive electronic

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components results in bulky biomimetic circuits that are not suitable for direct, in situ biointerfacing.

Volatile and nonlinear devices based on memristors or spin torque oscillators can be used to increase the integration density and emulating neuronal dynamics\(^{14,15}\). Metal-oxide memristive devices based on metal–insulator transitions exhibit negative differential resistance phenomena and is responsive to ionic and biomolecular species common to biological environments. The OEND consists of two OECTs, namely, \(T_1\) and \(T_2\) that are connected via the \(RC\) element \((R = 10 \, \text{k}\Omega; C = 6 \, \text{nF to 10 \, \mu F})\) and voltage source \(V_m\). Here \(V_{\text{out}}\) and \(I_{\text{out}}\) are the resulting output voltage and current, respectively, of the OEND under the influence of \(V_m\).\(^{16}\)

Spin torque oscillators are magnetic nanodevices compatible with silicon technology\(^{19}\). Their nonlinearity and dynamics have been recently leveraged for spoken language and audible source recognition\(^{14}\). However, there is no viable route for biointerfacing with spin torque oscillators, as their oscillatory dynamics are too fast (around gigahertz frequencies) for interacting in real time with biological processes. Their operation also requires the presence of magnetic fields. Other approaches for spiking or oscillatory devices and circuits—including Mott-transition-based memristive devices\(^{20,21}\), ferroelectrics\(^{22}\), photonics\(^{23}\) and two-dimensional materials\(^{24}\)—have been developed, but all of them encounter similar problems. By omitting various aspects of actual biological wetware, artificial neurons based on electronics are insufficiently capable of emulating/handling the biosignal diversity and thus of operating in situ in biological environments.

Organic electrochemical devices based on organic mixed ionic–electronic conductor (OMIEC), such as PEDOT:PSS, are bio-compatible with silicon technology. Their intrinsic sensitivity of solid-state memristive devices to moisture prevents in situ biointerfacing in biologically relevant host environments\(^{25}\). Although memristive arrays have been used for pre- and post-acquisition biosignal processing, they have not been used for in situ biointerfacing\(^{20,21}\).
Various capacitances $C = 1–10 \mu F$ and $V_m = 1.75 \text{ V}$. The y-axes are the same for all the subpanels. c. Frequency response of a voltage-controlled oscillator ($C = 1 \mu F$). This response shows the firing frequency versus input voltage difference ($V_\text{in}$ versus $\Delta V_m$), where $\Delta V_m = V_\text{in} - V_m$ is the input voltage above the threshold voltage $V_m$ for spiking. d. Continuous OAN firing under fixed $V_\text{in}$. The insets show the stability of the spiking waveform for $0.5$, $3.5 \times 10^4$ and $1.05 \times 10^5$ spiking cycles. All the measurements are performed in an aqueous electrolyte (100 mM NaCl).

**Organic artificial spiking neuron**

The OAN consists of a compact nonlinear building block made of only two organic electrochemical transistors (OECTs), namely, $T_1$ and $T_2$ (Fig. 1b). Both OECTs are p-type transistors: $T_1$ is a depletion-mode transistor, whereas $T_2$ is an enhancement-mode transistor. The mixed ionic–electronic conductor poly(3,4-ethylenedioxythiophene) (PEDOT) doped with polystyrene sulfonate (PSS) and poly(2-(3,3'-bis(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)ethoxy)-2,2'-bithiophen-5-yl) thiophene (p(g2F-T-T)) are used for the $T_1$ and $T_2$ channel, respectively. The electrical characteristics of $T_1$ and $T_2$ are presented in Supplementary Fig. 1. The OECTs operate in aqueous environments and are sensitive to ionic species and polyatomic ions (Fig. 1c). For instance, the channel of $T_1$ consists of the organic mixed ionic–electronic conductor PEDOT:PSS (ref. 22). Both channel and gate of an OECT are in direct contact with the electrolyte. In the case of a p-type OECT, when a positive gate voltage $V_\text{gate}$ is applied, cations drift into the polymeric channel and reduce the hole concentration, and consequently, drain current $I_\text{D}$ is lowered. When a negative $V_\text{gate}$ is applied, cations are removed from and anions drift into the polymeric channel, the hole concentration increases, and this results in a larger $I_\text{D}$. In OECTs, ions can penetrate the bulk of the polymer and the volumetric nanoscale ionic–electronic charge compensation results in a large current modulation. This high gate voltage to drain current modulation yields a high transconductance, which is the hallmark of OECTs. Another key feature of OECTs is the dependence of $I_\text{D}$ on the ion concentration in the electrolyte. More precisely, the fixed charges in the ion-conducting phase of the polymeric channel are electrostatically compensated by the mobile ions provided by the electrolyte. This Donnan equilibrium results in a concentration-dependent voltage drop at the polymer/electrolyte interface, which is, in turn, mirrored by the OECT threshold voltage. As shown in Fig. 1d, ionic or polyatomic cations (anions) interact with PEDOT, a hole conductor, and PSS, an ionic conductor, and decrease (increase) the doping level of PEDOT, resulting in a decrease (increase) in $I_\text{D}$ and the OECT threshold voltage (Fig. 1d). Here $T_1$ and $T_2$ are connected in the cascade-like configuration with feedback resistors $R_1$ and $R_2$, obtaining a two-terminal organic electrochemical nonlinear device (OEND) (Fig. 1b).

The current–voltage $V(I)$ and voltage–current $I(V)$ characteristics of the OEND are displayed in Fig. 2a. The OEND is accessed either in the $V(I)$ or $I(V)$ mode with current for voltage as the independent variable, respectively. An S-shaped negative differential resistance is accessible only in the $V(I)$ mode, by applying current at the single-valued negative differential resistance characteristic. In the $I(V)$ mode, the OEND...
shows multivalued characteristic with unstable points of operation to be directly accessed by applying a voltage. A detailed analysis of the OEND response with experimental and simulation data is shown in Supplementary Figs. 1 and 2. Consecutive $V(t)$ or $I(t)$ scans display highly reproducible responses of the OEND (Supplementary Fig. 3). The time response $\tau_{\text{OEND}}$ of the OEND element for square-wave input pulses is $\tau_{\text{OEND}} \approx 11$ ms (Supplementary Fig. 3).

When the OEND is coupled to an RC element (Fig. 1b) forming an OAN, its response bifurcates, producing voltage or current oscillations (Fig. 2; load-line analysis is shown in Supplementary Fig. 4). These spike-based oscillations represent the ‘action potentials’ of the OAN (Supplementary Fig. 5). Figure 2b displays the current response $I_{\text{out}}$ of the OAN for different values of capacitor $C$. The firing frequency $f_{\text{firing}}$ can be finely tuned between 6 and 40 Hz by changing $C$, a range that is consistent with physiological levels of instantaneous firing rates in biological neurons. The firing frequency range can be further extended by modifying $C$ or by using high-frequency-response OECTs.

In the case of polymer-based capacitors, capacitances in the range of nanofarads to microfarads can be reached with micrometre-scale PEDOT:PSS-based capacitors. The parametric oscillatory response in the $I$–$V$ plane and the instantaneous power dissipation $P_{\text{inst}}$ of the OAN is shown in Supplementary Fig. 6. The instantaneous power dissipation is given by $P_{\text{inst}} = V_{\text{in}}(t) R_{\text{out}}(V_{\text{in}} - V_{\text{out}})$, where $V_{\text{out}}$, $V_{\text{in}}$, and $R_{\text{out}}$ refer to the input voltage, output voltage and output current of the whole OAN, respectively. The calculation includes all the OAN components (for example, transistors, resistors and capacitor). The mean power dissipation $P_{\text{mean}} = 143 \mu W$. As shown in Fig. 2c and Supplementary Fig. 7, the OAN behaves as a voltage-controlled oscillator and $f_{\text{firing}}$ is modulated by increasing $\Delta V_{\text{in}}$ ($\Delta V_{\text{in}} = V_{\text{in}} - V_{\text{out}}$, where $V_{\text{out}}$ is the OAN oscillation threshold) within the oscillation window. For $\Delta V_{\text{in}} = 0–70$ mV, the relative increase in firing frequency $f_{\text{firing}}$ is modulated between 10 and 80% with a voltage-controlled oscillator sensitivity of $\Delta f_{\text{firing}}/\Delta V_{\text{in}} = 260 \mu W$ per volt.

The amplitude and window of the current or voltage oscillations can be precisely designed (Supplementary Fig. 8), for instance, by engineering the threshold voltage of transistors $T_1$ and $T_2$. In this case, the oscillatory window is shifted to a lower voltage level when decreasing the threshold voltage of $T_2$ by doping PEDOT:PSS with the amine-based molecular dopant N-methyl-2,2’-diaminodiethylamine (ref. 28, and $P_{\text{mean}}$ is decreased from 143 to 24 mW. For a capacitor with $C = 6 \mu F$ and by neglecting the static power dissipation, the energy consumption per spike is $E_{\text{spike}} = 57$ nJ. The amplitude profile of the current oscillations can also be engineered by varying $R_1$, $R_2$, and $R_3$ of the OAN (the effect of $R_1$ and $R_2$ on the nonlinear properties of the OEND is shown in Supplementary Fig. 2). It should be noted that doping causes permanent threshold-voltage shifts and dynamic reconfigurability can be induced by introducing synaptic transistors instead of volatile ones. In the case of PEDOT:PSS, the threshold voltage can be tuned on the fly by changing the ion concentration, a phenomenon that is exploited here to obtain an ion-concentration-dependent firing frequency. The OAN displays fully consistent stability when continuously operated at various amplitude and frequency conditions, as the firing response is practically unaffected for $>10^5$ spiking cycles (Fig. 2d). The OAN stability as a function of the number of spikes is also evaluated. The amplitude of $I_{\text{out}}$ reduces by $2.8 \times 10^{-5}$ % per spike. As a result, after $10^6$ spikes, the OAN current amplitude is equal to approximately 71% of the initial amplitude.

The OAN shows the key characteristics observed in the spiking response of biological neurons. The OAN operates in a liquid, a property that is reminiscent of the extracellular environment of biological neurons in the cerebrospinal fluid. The excitability of the OAN, that is, the tendency of a neuron to fire spikes, can be modulated by the presence of electrochemical oscillations transmitted by means of ionic fluxes in the electrolyte medium. Figure 3a shows that the in-liquid electrochemical oscillations shape the firing properties of the OAN, mimicking the characteristic features of biological neurons.

An increase of only a few millivolts at the potential of the electrolytic medium elicits spikes with high temporal precision (Supplementary Fig. 9), and a forced bursting activity is phase locked with the ionic signal in the electrolyte. During the time window of the input signal that is above the OAN threshold voltage $V_{\text{th}}$, the OAN fires and therefore the input phase coordinates firing. Variation in the electrolyte potential as small as 1–2 mV at the very edge of the OAN threshold $V_{\text{th}}$ results in stochastic firing, thus reproducing the behaviour observed in biological neurons. Such small variations in the electrolytic medium potential are in the same range of the biopotentials of the extracellular electrolyte space (micromvols to millivolts). The OAN threshold allows for additional bioplausible behaviours, such as in-liquid all-or-nothing spiking and subthreshold oscillations (Supplementary Figs. 9 and 10, respectively). The spiking properties of the OAN for input voltage pulses is shown in Supplementary Fig. 9.

Due to its finite response time, the OAN displays a stimulus–response delay (Fig. 3b), as well as behaves as a temporal integrator (Fig. 3c). The stimulus–response delay in biological neurons, known as spike latency, can provide a rapid and efficient neural coding scheme beyond simple rate coding, as latency can be a faster differentiator than the mean firing rates. We further investigate this delay and reproduce the spike latency characteristic of biological neurons. Figure 3b shows that the stimulus–firing phase difference $\Delta \phi$ is modulated by the input voltage difference $\Delta V_{\text{in}}$ (time-domain response is shown in Supplementary Fig. 11). Stronger stimulation induces shorter latencies, as observed in biological sensory systems. Due to the finite and relatively slow time constant of biomembranes, biological neurons temporally integrate inputs and display firing under certain interstimulus timing conditions. This integration lowers the timing precision and offers temporal buffering windows for ongoing neuronal inputs, ensuring the consolidation and stability of neuronal sequences. Analogous to biological neurons, the OAN integrates time, buffers input stimuli and fires for short non-overlapping interstimulus intervals (Fig. 3c).

Biological environments are characterized by seemingly random fluctuations at a range of spatiotemporal scales, and therefore, neurons are constantly operating under noisy conditions. This noise couples with neuronal dynamics, influencing neuronal excitability and firing properties. Although counterintuitive, noise can be beneficial for neuronal communication and processing. For instance, noise can enable the transmission of weak subthreshold signals, smooths subthreshold-to-threshold nonlinearities or even enhances the communication efficiency by increasing the signal-to-noise ratio or by altering the neuronal coding schemes. The noise-induced activity of the OAN is presented in Fig. 3d. The OAN is biased with a d.c. input voltage at the subthreshold regime, and white noise of variable amplitude ($V_{\text{pp}} = 5–150$ mV) is injected in the electrolytic medium to emulate extracellular noise/fluctuations. As the amplitude of the noise increases, a gradual transition from tonic ($V_{\text{pp}} = 0–25$ mV) to irregular firing ($V_{\text{pp}} = 50$ mV) is observed. For low noise levels, the frequency of tonic firing remains practically constant, that is, $f_{\text{firing}} \approx 6.5–7.0$ Hz. As the noise level increases, packets of spikes are observed. Recurrence plots of the interspike intervals and spike-to-spike amplitudes (Supplementary Fig. 12) indicate a change in the coding scheme from tonic to noise-induced bursting activity, as well as the resilience of spiking against noise in the electrolytic medium.

**In situ spike-based neuromorphic sensing**

It is estimated that the extracellular electrolytic space occupies a volume fraction of $\sim 15–30\%$ of the brain tissue. This extracellular space is an aqueous electrolyte comprising various ionic species (mostly Na$^+$, K$^+$, Cl$^-$ and Ca$^{2+}$) and represents a reservoir by maintaining homoeostatic balance of the ion concentrations under physiological conditions. In mammalian cells, the range of physiological concentrations for Na$^+$ is $c_{\text{ext}} = 130–150$ mM and $c_{\text{int}} = 10–15$ mM and for K$^+$, $c_{\text{ext}} = 3–12$ mM and $c_{\text{int}} = 150–160$ mM, where $c_{\text{ext}}$ and $c_{\text{int}}$ are the...
extracellular and intracellular concentrations, respectively. Although homeostatically balanced, these ion concentrations can change in different spatiotemporal scales. Minute concentration variations in the proximal extracellular space of a neuron are induced during an activity transition from tonic firing to bursting, with constant firing frequency over a biologically relevant baseline (100 mM NaCl). Changes in ionic concentration gradients between the intracellular and extracellular medium of biological neurons alter their excitability threshold, and firing can be initiated by varying these concentrations.

As an example, Fig. 4c shows that small variations (~2–10%) in NaCl concentration over a biologically relevant baseline (100 mM NaCl) can increase the OAN excitability and induce firing. Both $f_{\text{in}}$ and time delay between the increase in concentration and neuronal excitation $\Delta t_{\text{in}}$ correlate with the ion concentration (Supplementary Fig. 14). Moreover, the behaviour shown in Fig. 4c is in agreement with the excitation profiles for similar extracellular Na’ concentrations of the Hodgkin–Huxley neuron model (Supplementary Fig. 14).

Dopamine is a modulatory neurotransmitter that regulates essential brain functions including cognition, learning, motivation, motor control, mood regulation and addiction. At the cellular level, dopamine can impact neuronal excitability in a multitude of ways (resulting in excitatory or inhibitory and time- and concentration-dependent activity profiles for similar extracellular Na+ concentrations of the Hodgkin–Huxley neuron model).
effects), both via synaptic and non-synaptic activation of dopamine receptors. For example, dopamine has a net excitatory effect on primate pyramidal neurons. As shown in Fig. 4d, the presence of dopamine in the electrolyte increases the excitability of the OAN and initiates tonic firing. Excitation is observed in shorter time delays $\Delta t_{\text{exc}}$ for higher dopamine concentrations, whereas a slight decrease in $f_{\text{exc}}$ is observed (Supplementary Fig. 15). The behaviour shown in Fig. 4d highlights that the initiation of spikes can be biochemically triggered, a property that resembles the biological neuronal signalling phenomena.

It should be noted that the OAN also exhibits biorealistic diversity in signalling, as dopamine-mediated inhibition can be induced by altering the OAN biasing scheme (Supplementary Fig. 15).

The ion channels of biological membranes pass inward and outward ionic currents, a hallmark of neuronal signalling. The dysregulation of these processes is the consequence of a large number of channelopathies that can lead to serious pathological conditions such as cystic fibrosis and myotonia congenita. Another layer of biophysical realism is added to the OAN response by implementing on-chip selectivity and specificity characteristics, akin to biological ion channels. Figure 4e demonstrates that the OAN function directly incorporates aspects of the molecular machinery that are responsible for the selective processing of the biological carriers of information. OANs displaying ion-specific (Na$^+$ or K$^+$) oscillatory activities are realized by incorporating ionophore-based selective membranes at the channel/electrolyte interface of $T_1$ (Fig. 1b). As an example, a K$^+$-selective OAN shows oscillations in the case of the KCl electrolyte, with $f_{\text{exc}}$ increasing with the ion-selected concentration, but does not show oscillations in a control experiment with NaCl electrolyte (Supplementary Fig. 16). The selectivity library can be further extended with membranes that are selective to other biologically relevant ions such as Na$^+$, Ca$^{2+}$ and ammonium (NH$_4^+$) (refs. 63–64).

**Biohybrid neuron**

The OAN is capable of direct biointerfacing in a biologically relevant environment, and a biohybrid neuron is formed by incorporating a biomembrane between the gate and channel of $T_1$ (Fig. 5). The system consists of a biological and artificial compartment. As a relevant biomembrane model system, the prototypical epithelial cell line Caco-2, which is a model of the intestinal epithelial barrier and widely used for in vitro toxicology and drug delivery studies, is incorporated with the OAN. The biomembrane comprises epithelial cells joined with tight junctions, thus forming a natural barrier for ion passage (Fig. 5a). The biohybrid neuron functions in situ and in real time (Fig. 5b). Initially, the OAN is operated in a plain cell culture medium; in the absence of the biomembrane barrier, electrochemical oscillations are sustained at $f_{\text{exc}} \approx 12$ Hz. A barrier functionality is induced with the incorporation of the biomembrane. This biomembrane barrier blocks the gate-to-channel ion passage and suppresses the oscillations of the biohybrid neuron, with $f_{\text{exc}} \approx 0$ Hz. The addition of a chemical agent that attacks the biomembrane's tight junctions here the toxin hydrogen
peroxide—lowers the barrier of ion passage and results in a gradual recovery of oscillations. This demonstration shows that the biomembrane dynamics change the excitability of the OAN in real time, and this is directly reflected on the firing response of the biohybrid neuron. A more detailed schematic of the biohybrid neuron and a description of the biomembrane disruption mechanism are shown in Supplementary Fig. 17. Such biohybrid systems can be used as controllable in vitro models for basic research, such as to understand the underlying mechanisms of neuronal signalling, as well as a platform for studying the barrier integrity of biological tissues under various physiopathological conditions or the influence of external physicochemical cues (toxins, neuromodulators and so on). It should also be mentioned that interfacing the OAN with biological neurons requires that both domains have similar dimensions. Therefore, careful design of the OAN is necessary, as the device dimensions play a critical role in the spiking response of the OAN. The impact of the device dimension on the OAN spiking response with simulations is shown in Supplementary Fig. 18.

Conclusions

We have reported an OAN based on a nonlinear electrochemical element. Inspired by the properties of biological neurons functioning in wet surroundings, the OAN can mimic the biological sensitivity to ionic and biomolecular species in a surrounding aqueous environment. The artificial neuron exhibits nonlinear phenomena that depend on the composition of biophysically relevant host environments. We experimentally validated its operation with various electrolytes, including common aqueous electrolytes, buffered solutions and cell culture media. We also created biohybrid interfaces in which the OAN was modulated by the biological membrane of epithelial cells in situ and in real time. A comparison with the state-of-the-art technology is provided in Supplementary Tables 1 and 2.

Neuronal excitability, dynamics and spiking properties depend on the electrolytic potential and noise, as well as on the local concentrations of specific ionic and biomolecular species. Therefore, just as in biological neurons—where sensing and actuation is merged and happens locally in the same surroundings—sensing (for example, neurotransmitters) and actuation/communication (via spiking, oscillating or other behaviours) are inherently embedded in the device operation, and this can enable tighter closed-loop control of biological substrates. The operation in close physical, functional and temporal proximity with biology can enable the real-time interaction between artificial and biological rhythmicity, for example, the development of new strategies for understanding, restoring and augmenting biorhythmic processes.

In contrast to conventional organic ring oscillators that consist of multiple transistors, only two transistors are required for the OAN. This compactness means that the OAN can potentially be merged into a single device—a challenging venture for many-element implementations. Negative-differential-resistance-based ionoelectronics can lead to much richer dynamics compared with conventional electronics. For practical applications, the integration density and variability of soft matter devices should be further developed and improved. In addition, although the OAN is externally powered in this work, biofuel-powered and self-sustainable oscillators could be developed that emulate certain metabolic pathways of biological neurons. Non-synaptic modes of neuronal communication that are found in biological networks could be introduced with global electrolytes. Furthermore, synaptic capabilities can be introduced at the function of the OAN circuit, by incorporating organic synaptic transistors. Finally, in the case of dopamine detection, latent ‘memory time windows’ can form the basis for on-chip learning phenomena, such as biomolecular reward prediction error coding.

Methods

Fabrication of OENDs and OANs

Standard microscope glass slides (75 mm × 25 mm) were cleaned in a sonicated bath, first in a 1:1 (vol/vol) solvent mixture of acetone and isopropanol. Gold electrodes for source and drain electrodes were photolithographically patterned with positive Microposit S1813 photoresist (DOW) on the cleaned glass slides. A chromium layer was used to improve the adhesion of gold. Each glass slide contains a series of circuit blocks consisting of T1 and T2 OECTs. The channel dimensions of T1 and T2 are W1 × L1 = 50 μm × 20 μm and W2 × L2 = 50 μm × 10 μm, respectively. The OECTs are separately gated with Ag/AgCl electrodes via aqueous electrolytes. Two layers of parylene C (SCS Coatings) were deposited. Soap (Micro-90 soap solution, 1% vol/vol in deionized water) was used for separation between the parylene C layers to enable the peel-off of the upper parylene C layer. The lower parylene C layer insulates the
gold electrodes. A promoter (Silane A-174 (γ-methacryloxypropyl trimethoxysilane), Sigma-Aldrich) was added to the lower parylene C layer to enhance adhesion. In the second photolithography step used the positive photoresist AZ 9260 MicroChemicals (Cipek Spécialités), the channel dimensions of $T_1$ and $T_2$ are defined. Reactive ion etching ($O_2$/CF$_4$ plasma, 160 W for 16 min with $O_2$ flow rate of 50 s.c.c.m. and CHF$_3$ flow rate of 5 s.c.c.m.) was used to define the channels of $T_1$ and $T_2$ throughout the photoresist mask. The channel of $T_1$ is made with the organic mixed ionic–electronic conductor polymer PEDOT-PSS (Clevios PH1000) mixed with 5.0 wt% ethylene glycol, 0.1 wt% dodecyl benzene sulfonic acid and 1.0 wt% (3-glycidoxypropyl)trimethoxysilane. The film was spin coated in two steps at 1,500 rpm and 650 rpm for 1 min and annealed at 120 °C for 1 min between devices. The devices were subsequently baked at 140 °C for 1 hour. For the implementation of $T_2$, the semiconducting polymer $p$(2T-TT) was synthesized according to another work. Here $p$(2T-TT) was dissolved in chloroform (3 mg mL$^{-1}$) inside a N$_2$-filled glovebox and spin coated in ambient conditions at 1,000 rpm for 1 min resulting in a thickness of 40 nm. The devices were baked at 60 °C for 1 min. The sacrificial upper parylene C layer was peeled off to confine the polymer to the inside of the channel regions. Excess soap was rinsed off with deionized water. A schematic of the OAN is shown in Supplementary Fig. 19.

**Electrical characterization of OENDs and OANs**

The current versus voltage characteristics of the individual OECTs and OENDs were obtained using a Keithley 2400 semiconductor parameter analyser. Ag/AgCl were used as the gate electrodes with 100 mM NaCl electrolyte solution, unless otherwise stated. The nonlinear characteristics of the OENDs were obtained by enforcing current when the corresponding voltage was measured or by enforcing voltage when the corresponding current was measured. The OEND was coupled with $AC$ and $VC_m$ elements (external components) to complete the OAN, which exhibits neuronal dynamics when connected to voltage source $V_{in}$ (Fig. 1b). The voltage oscillation was directly recorded at the $V_{in}$ terminal using an Agilent InfiniVision digital oscilloscope. The output current $I_{OAN}$ of the OEND is measured by measuring the voltage $V_{ac}$ across resistor $R_w$ with a differential amplifier (based on an INA122 integrated circuit) and a digital oscilloscope (Supplementary Fig. 20). To characterize the OAN response in the presence of different electrobiocchemical signals, a Tektronix AFG1022 arbitrary function generator was used for the input voltage. The arbitrary function generator and semiconductor parameter analyser were used together to generate an arbitrary noise signal for the noise-induced neuronal characterization, phase-locking measurements and characterization of the various neuromorphic behaviours. The spectrogram of the short-time Fourier transform was performed using OriginPro 2016 with a Hanning-type window.

**Data availability**

The data that support the findings of this study are available from the corresponding authors on reasonable request. Source data are provided with this paper.

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**Author contributions**

T.S., F.T. and P.G. conceived the project, designed the experiments and analysed the data. T.S., K.L., A.P. and P.G. fabricated and characterized the OENDs and OANs. T.S., K.L., A.P. and P.G. investigated the materials and tuned their properties. I.M. designed and provided the semiconducting material(s). K.L., A.P. and V.M. provided the biomembranes. K.L., A.P. and T.S. performed the biological experiments. P.G. and F.T. performed the simulations and modelling. F.T., T.F. and P.G. prepared the manuscript with input from all the authors. P.W.M.B. and P.G. acquired the financial support.

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**Competing interests**

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