Organic electrochemical neurons and synapses with ion mediated spiking

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Future brain-machine interfaces, prosthetics, and intelligent soft robotics will require integrating artificial neuromorphic devices with biological systems. Due to their poor biocompatibility, circuit complexity, low energy efficiency, and operating principles fundamentally different from the ion signal modulation of biology, traditional Silicon-based neuromorphic implementations have limited bio-integration potential. Here, we report the first organic electrochemical neurons (OECNs) with ion-modulated spiking, based on all-printed complementary organic electrochemical transistors. We demonstrate facile bio-integration of OECNs with Venus Flytrap (Dionaea muscipula) to induce lobe closure upon input stimuli. The OECNs can also be integrated with all-printed organic electrochemical synapses (OECSs), exhibiting short-term plasticity with paired-pulse facilitation and long-term plasticity with retention >1000 s, facilitating Hebbian learning. These soft and flexible OECNs operate below 0.6 V and respond to multiple stimuli, defining a new vista for localized artificial neuronal systems possible to integrate with bio-signaling systems of plants, invertebrates, and vertebrates.
Research advancement in brain-machine interfaces, implantable/wearable devices, prosthetics, and intelligent soft robotics calls for close interaction between and integration of technology into nature. Since the fundamental building elements of life differ significantly from those utilized in electronic devices, the ability to link an artificial device with a biological system is crucial to the success of these domains. Neuromorphic systems\(^1\) that borrow design concepts from biological signaling systems promise to bridge this gap. Although several software-based neuromorphic algorithms have been integrated into biomedical systems\(^2\)–\(^4\), hardware-based systems\(^5\) that intimately interface with living tissues, evolve its function based on biological feedback\(^6\)–\(^8\), and utilize event-based sensing\(^9\)–\(^10\), and processing capabilities of the biological systems are ultimately necessary. However, circuits and devices made of silicon (Si)\(^11\)–\(^14\), commonly used in hardware neural networks and neural interfaces, suffer from several drawbacks such as rigidity, poor biocompatibility, the requirement for numerous circuit elements, and operation mechanisms that are fundamentally orthogonal to those of biological systems, making bio-integration difficult.

On the other hand, organic semiconductors are becoming a competitive alternative in this field, as seen by their growing applications in artificial synapses\(^12\)–\(^17\), nerveotronics\(^18\)–\(^19\) and neural interfaces\(^20\)–\(^22\). Their structural kinship with biomolecules makes them ideal for bioelectronic applications\(^23\)–\(^24\). Organic semiconductors are solution-processable, biocompatible, biodegradable, soft, and conformable from a structural standpoint. Furthermore, they can also be easily functionalized to offer specialized excitation, sensing, and actuation capabilities, and they support the transport of both the electronic and ionic signals\(^25\)–\(^26\).

Since biological neurons communicate with each other through a regulated flux and polarization of ion species, organic materials are an obvious choice for creating devices that replicate biological activities due to their ability to couple ionic polarization to the modulation of electronic charge transport.

Despite the success of organic materials in emulating neuro-morphic functions and artificial nerves, there have been limited attempts to fabricate and bio-integrate artificial neurons, which are essential to enable spike-based information encoding that closely mirrors the processing strategies used by biological systems. Recently reported artificial neurons based on organic field-effect transistors (OFETs)\(^27\) are promising in this regard. However, they require high voltage (5V) inputs for operation, which is an obvious critical issue when integrating with biology. In addition, as in the case of Si, their operation mechanism is fundamentally different from the ion-based mechanisms found in biological systems, making bio-integration, sensing, and response feedback difficult.

Organic electrochemical transistors (OECTs), which are modulated by a gate-driven ionic doping/de-doping of the organic bulk channel material\(^25\), resemble the ion-driven processes and dynamics of biological systems. Compared to OFETs, OECTs operate at considerably lower voltages (<1V), have a higher transconductance, maintain excellent threshold voltage stability, demonstrate strong ion concentration-dependent switching properties\(^28\), and are in general highly biocompatible\(^29\). Aside from their use as chemical, physical, and biochemical sensors, they have been implemented as artificial synaptic devices\(^12\)–\(^14\),\(^16\)–\(^17\),\(^19\)–\(^20\) that exhibit both long and short-term plasticity. The robust device architecture and the solubility of the organic materials in benign solvents have also enabled the facile fabrication of large-scale printed OECT-based digital circuits\(^31\)–\(^33\). These properties make OECTs the ideal candidates for developing printed, biocompatible artificial spiking neural circuits with ion-mediated spiking mechanisms closely resembling the signaling characteristics of biological systems.

Here, we report the first organic electrochemical neurons (OECNs), based on all-printed complementary OECTs. The OECNs exhibit several neuronal characteristics, including ionic concentration-dependent spiking, and spike-timing-dependent plasticity (STDP) on integration with printed organic electro-chemical synapses (OECSSs). It responds to a wide range of input currents (0.1–10 µA), resulting in frequency modulation of over 450%. For the first time, we utilize the ionic concentration-dependent switching characteristics of the transistor to modulate the frequency of spiking to a large extent analogous to biological systems and demonstrate its integration with Venus Flytrap (Dionaea muscipula). The electrochemical transistors enable chemical modulation of the spiking behavior, which is impossible in OFET-based or Si-based CMOS neurons. The all-printed OECSSs, which form and evolve in operando by electropolymerizing the monomer precursor of a polymeric mixed ion-electron conductor, exhibits two different modes of operation based on ionic doping and electropolymerization-induced conductivity modulation. This dual-mode of conductance modulation enables short-term plasticity with paired-pulse facilitation and long-term plasticity with retention of over 1000 seconds, facilitating symmetric Hebbian learning upon integration with the OECN. We anticipate that the OECNs’ soft nature, ability to be printed on flexible substrates, ion-modulated spiking and multi-stimuli response will open new avenues for facile integration with biological neural networks and applications in event-based sensors.
increases the voltage \( V \) depolarized near the action potential threshold, voltage-gated Na channels open rapidly, resulting in an increased influx of Na\(^+\), which serves as positive feedback, further depolarizing the membrane and moving the potential close to the Na\(^+\) Nernst potential (+55 mV), resulting in a spike (Fig. 1e).

Analogous to the operation of a nerve cell, a spike is generated in the OECN circuit by integration of the current injected into the input terminal (\( I_{in} \)). As shown in Fig. 1b, c and f, the integration of the current is carried out by the capacitor \( C_{mem} \) which increases the voltage \( V_{mem} \) gradually, and upon reaching a specific threshold value, a nerve pulse is fired at \( V_{out} \). This is enabled by the noninverting amplifier block A and the positive feedback capacitor \( C_f \). The amplifier gain increases rapidly after reaching its transition voltage \( V_T \), which is related to the threshold voltage of P(g42T-T) and BBL OECTs. The capacitor \( C_{mem} \) can be charged linearly until \( V_T \) is reached, but if the current supply is removed before reaching this threshold, the built-up voltage will sink to the ground similar to failed initiations in the biological neuron (Fig. 1e). If \( V_{mem} \) reaches \( V_T \), the amplifier turns on and the \( V_{out} \) increases. A change in the \( V_{out} \) value will result in a change in the input voltage \( V_{mem} \) enabled by the capacitance-voltage divider circuit implemented by \( C_r \) and \( C_{mem} \). A small change in the input will further increase the \( V_{out} \), leading to a feedback sequence and an exponential increase of voltage, resulting in the action potential generation. A similar positive feedback loop is achieved in a biological neuron by voltage-gated Na\(^+\) channels, resulting in further depolarization and opening of even more gated channels causing an exponential increase of cytoplasmic voltage until it is closer to the Nernst

At rest, the extracellular side of a nerve cell has excess positive charge, and the intracellular side has excess negative charge maintained by the insulating property of the lipid cell membrane which acts as a barrier to charges except at the non-gated and voltage-gated ion channels (Na, K, Ca, and Cl). Thus, the cell’s resting potential is negative and is closest to the K\(^+\) Nernst potential (–75 mV) as these are the most permeable species at rest. Any influx of Na\(^+\) is counterbalanced by the efflux of K\(^+\) to maintain the membrane potential constant. As the membrane is depolarized near the action potential threshold, voltage-gated Na\(^+\) channels open rapidly, resulting in an increased influx of Na\(^+\), which serves as positive feedback, further depolarizing the membrane and moving the potential close to the Na\(^+\) Nernst potential (+55 mV), resulting in a spike (Fig. 1e).

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\[ C_{mem} = C_f = 6.8 \mu F, \text{ input current of } 1 \mu A \text{ and } V_{DD} \text{ of } 0.6 V. \]
potential of Na\(^+\). Once the potential reaches this value, Na\(^+\) channels close, and K\(^+\) channels open, leading to an efflux of K\(^+\) and a restoration of the membrane potential to the resting value by the process called repolarization. These processes are repeated in the adjacent regions in the membrane and the action potential is propagated.

The resetting transistor \(T_{\text{reset}}\) works analogously to the voltage-dependent potassium channels in the nerve cell. When \(V_{\text{out}}\) is high enough, \(T_{\text{reset}}\) turns on, and the capacitance \(C_{\text{mem}}\) discharges through the \(T_{\text{reset}}\), resulting in a reduction of \(V_{\text{mem}}\). Once \(V_{\text{mem}}\) reduces to the threshold voltage of the amplifier \(V_T\), the feedback loop is initiated again, resulting in a significant reduction in \(V_{\text{out}}\) for a slight change in \(V_{\text{mem}}\). Thus, \(V_{\text{out}}\) reduces to zero, and the \(T_{\text{reset}}\) turns off, resulting in termination of the nerve pulse, and the cycle is repeated.

The membrane capacitance plays a crucial role in the speed of the conduction of the action potential in a biological neuron\(^36\). A lower membrane capacitance results in faster propagation because it is easier to change the potential of the adjacent region as fewer charges are sufficient to change it (\(ΔQ/C\)) compared to a membrane with higher capacitance. In nerve cells, this reduction in capacitance is facilitated by wrapping an insulating layer called myelin over the axon. Analogous to this, the OECN spike frequency and width can be modulated by altering the \(C_{\text{mem}}\) and \(C_f\) capacitances in the circuit. Figure 2a, b and Supplementary Figure 3 shows the modulation of the frequency and the full width at half maximum (FWHM) of the spikes of the OECN with capacitance for a constant input current of \(1 \mu\text{A}\). A lower capacitance value reduces the charging time to reach the spiking threshold voltage and results in higher frequency spikes. With \(C_{\text{mem}} = C_f = 100 \text{nF}\), the firing frequency approaches 0.1 Hz, which matches the low firing rate of certain single neurons\(^37\). Similarly, the peak width will depend on the discharging time of the capacitors through the resetting transistor \(T_{\text{reset}}\). Hence, the FWHM will be higher for higher capacitance values.

To further investigate the firing frequency dependence on the OECT performance, we built SPICE models for both p-type and n-type OECTs (Supplementary Figure 5). The simulated transient behaviors of both p-/n-type OECTs were matched with measured results (rise time \(t_r \sim 230–390 \text{ ms}\)\(^34\)) by choosing the appropriate value of capacitance \(C_f\), as shown in Supplementary Figure 6 and 7a. The simulated neuron spiking frequency reaches 48 mHz, 75 mHz, and 85 mHz for \(C_{\text{mem}} = C_f = 6.8 \mu\text{F}\), 1 \mu\text{F}, and 100 \mu\text{F}, respectively at an input current of 1 \mu\text{A} (Supplementary Figure 7b–d), showing excellent match with the experimental results (Fig. 2a). Further improving the OECT switching speed, by reducing the channel dimensions, could enable higher firing frequency. For \(t_r = 0.5–1 \text{ ms}\) for both p-/n-type OECTs, typical of short-channel photolithographically-made OECTs\(^38\), the simulated firing frequency reaches 95 Hz for \(C_{\text{mem}} = C_f = 2 \mu\text{F}\) and 1 \mu\text{A} current input (Supplementary Figure 8). Such a relatively high and biologically plausible frequency could mimic most neural

**Fig. 2 Electrical characterization and bio-integration of the organic electrochemical neurons.** a Modulation of frequency and FWHM of spikes with changing \(C_{\text{mem}}\) and \(C_f\) at a constant input current of 1 \mu\text{A}. The 5% deviation in frequency between experimental and simulated values at low capacitances is due to the intrinsic capacitances dominating \(C_{\text{mem}}\) and \(C_f\). b Changes of the spiking patterns at 3 different capacitances (0.1, 1, and 6.8 \mu\text{F}) with \(C_{\text{mem}} = 100 \text{nF}\). c Modulation of spiking frequency and FWHM with various NaCl concentrations. d Frequency modulation of neuron with the input current for two different capacitance configurations. e Spiking patterns at three different input currents (0.1, 1, and 10 \mu\text{A}) with \(C_{\text{mem}} = C_f = 100 \text{nF}\). f Modulation of Venus flytrap using the artificial neuron: the flytrap does not close at a low (2 \mu\text{A}) input current to the neuron but closes when the input current is 10 \mu\text{A}.
firing rates (Supplementary Figure 4)\textsuperscript{39}. Strategies for reaching such high spiking frequency by reducing the device dimensions are discussed in Supplementary Note 1.

A striking feature of this OECN, especially when compared to Si-based or OFET-based spiking neurons, is the ability to control the spiking frequency directly by modulating the ion concentration of the electrolyte. It is observed that the amplifier transition voltage $V_f$ shifts from 0.5 V to 0.2 V as a function of the ion concentration in the electrolyte ($10^{-3}$ to 1 M, Supplementary Figure 9). This shift originates from the threshold voltage dependence of the individual transistors on the ion concentration—the transfer curves of the n-OECTs shift toward lower positive values on increasing the concentration (Supplementary Figure 10), resulting in a shift in $V_f$. A lower transition voltage of the amplifier means that the $V_{mem}$ has to reach a lower value to initiate the exponential rise in $V_{out}$ and the positive feedback in the neuron, thus resulting in a higher spiking frequency. The spiking frequency can be increased by 25% on increasing the electrolyte concentration (Fig. 2c). This is also associated with a concurrent reduction in the FWHM of the spikes. A spiking neuron is generally characterized by its output response for a range of injected currents. The Frequency-Current (F-I) curves of the OECN at two different capacitance configurations are shown in Fig. 2d. Similar to the leaky behavior of the biological neurons that require that the membrane voltage exceeds a given threshold to generate a pulse, the OECN circuit does not fire below a specific current threshold value. In the $C_{mem} = C_f = 100 \text{nF}$ configuration, a current below 100 nA cannot charge the capacitors enough to reach the spiking threshold (Fig. 2e and Supplementary Figure 11). The frequency can be modulated from 46 MHz at 300 nA to 274 MHz at 10 µA as the capacitors can be charged faster at higher currents bringing the $V_{mem}$ closer to the threshold value faster. Further increase in current does not increase the spiking frequency and is limited by the inverter delay time. The $V_{DD}$ of the inverter can also modulate the spiking frequency of the OECN as shown in Supplementary Figure 12.

Low power consumption is crucial for the application of the circuit in SNNs and event-based sensors. The primary source of power dissipation in this circuit is the amplifying block. Hence, the dynamic power consumption of the circuit is the product of $I_{DD,dynamic}$ and $V_{DD}$. Since the inverter can be operated at a low operating voltage of 0.6 V and the maximum value of $I_{DD}$ dynamic is 25 µA, the maximum dynamic power consumption is 15 µW. This value is lower than the dynamic power consumption of 40 µW reported in OFET-based Axon-Hillock circuit. Furthermore, the power consumption of the OECN can be reduced to much lower values by reducing the channel dimensions by lithographic techniques, which will reduce the current flowing through the OECT. A smaller channel will also increase the response time of the OECT and enable a lower FWHM of the spike to reduce energy consumption.

A monolithically integrated version of the neuron is fabricated by replacing the external capacitors with printed ones based on lateral carbon electrodes (Fig. 1c) and 1 M NaCl as the electrolyte. The characteristics of the fully printed neuron are similar to those discussed above, albeit that it spikes at a slightly lower frequency (Supplementary Figure 13). It is observed that the electrolyte concentration of the capacitor does not change the spiking frequency of the neuron (Supplementary Figure 14). Interestingly, the spiking characteristics remain unchanged even in the absence of the capacitors indicating that the internal capacitance of the circuit induced by the OECTs is larger than the carbon electrode-based capacitors and is sufficient to act as $C_{mem}$, eliminating the need for additional capacitors as required in Si-based circuits.

As a demonstration of the bio-integration capability of the OECN, we interfaced this fully printed neuron with a Venus Flytrap (\textit{Dionaea muscipula}). Venus Flytraps (VFTs) have a thigmomonic response and catch insects by closing the lobes when their mechanosensitive hairs are mechanically elicited. Physical stimulation of the hairs triggers the release of Ca\textsuperscript{2+} in the cytosol\textsuperscript{39}. For the trap to close, the cytosolic Ca\textsuperscript{2+} concentration must reach a putative threshold which is typically obtained by stimulating the hair twice within a time interval approximately lower than 30 sec. Trap closure can also be induced by electrical stimulation, including DC stimulation, direct charge injection\textsuperscript{11,32}, AC stimulation, and capacitive induced current flow\textsuperscript{43}, making it ideal for integration with the artificial neuron. We used Ag/AgCl electrodes to feed the output of the OECN to the lobes of the VFT with the ground of OECN connected to the lobe and the $V_{out}$ to the midrib. The detailed experimental setup is described in the Methods section and Supplementary Figure 16. Injection of a high current (10 µA) results in a higher frequency (100 mHz) output of the OECN, resulting in the closure of the VFT (Supplementary Video 1). In contrast, a lower current input (2 µA) causes the OECN to spike at a lower frequency (44 mHz) and does not induce closure (Supplementary Video 2, Fig. 2f). We hypothesize the cytosolic Ca\textsuperscript{2+} threshold is met only when the OECN output frequency is high, while at a lower frequency, the cytosolic Ca\textsuperscript{2+} remains below the threshold required to close the VFT. The possibility of modulating the plant’s electrophysiology using the OECN opens up new avenues for integration of artificial neuromorphic devices and various biological systems. For example, the unique ability of OECTs to sense multiple biological, physical, and chemical signals enables multiple sensory detection, and their possible fusion in the neuron itself allows the development of novel bio-integratable event-based sensors with sensory fusion. In addition, the ion-based operation mechanism enables facile integration and feedback from biological systems. However, the main advantage of OECNs over other modulation techniques will be the capability for supervised or unsupervised learning at the sensor level. For this, the integration of OECNs with organic artificial synapses is inevitable. Here, we utilize printed organic electrochemical synapses (OECs) based on electropolymerization mechanism to enable the same, as discussed in the next sections.

Printed organic electrochemical synapses. The OECs are fabricated on the same printed electrode architecture as described for OECNs. The synaptic channel is formed by electropolymerizing a zwitserionic monomer precursor of a conducting polymer (2-(2,5-bis(2,3-dihydrothieno[3,4-b][1,4]dioxin-5-yl)thiophen-3-yl)ethyl(2-(trimethylammonio)ethyl) phosphate, ETE-PC), similar to our previous reports on evolvable OECTs using the anionic sulfonated form of this monomer, ETE-S\textsuperscript{12,13} (Fig. 3a, b). The zwitserionic nature of the ETE-PC side chain enables better interaction with the PET substrate compared to ETE-S and results in the formation of a conductive channel when ~0.6 V is applied to the gate. The OECT characteristics are reported in Supplementary Figure 17. Figure 3a shows the analogy between a biological synapse and the printed OECs. The voltage applied to the Ag/AgCl gate of the OECT represents the presynaptic input and the current response to a presynaptic input, measured between source and drain, is the postsynaptic output referred to as the Excitatory and the Inhibitory Post Synaptic Current (EPSC and IPSC). Like a biological synapse, the OECs operates in 2 modes—short-term and long-term plasticity modes. The ionic accumulation in the poly-ETE-PC channel during the gate-induced doping/dedoping in the absence of ETE-PC monomer results in a short-term increase/decrease in channel conductance on the timescale of several seconds. This process, caused by the accumulation of ions in the channel is similar to the short-term
The application of gate voltage pulses of electropolymerizing additional ETE-PC in the channel through synaptic spikes (Fig. 3d). PPF is essential for decoding temporal IPSC increasing/decreasing on successive application of pre-PPF/Paired Pulse Depression (PPD) with the peak of the EPSC/over 100 s. The OECS also exhibits Paired Pulse Facilitation 1 s (Fig. 3f). This process is analogous to the signaling characteristics of biological systems (Fig. 3e).

Integration of organic electrochemical neurons and synapses. In biological synapses, the synaptic strength does not change for every presynaptic input, as that would quickly saturate the channel hinders fast reversibility of the process and alternative approaches to induce long-term depression in the system are under investigation (see Supplementary Note 4).

synaptic facilitation (ms to s), which occurs in biological synapses encountering repeated action potentials due to the accumulation of excess Ca\(^{2+}\) and neurotransmitters. Figure 3c depicts the evolution of the EPSC with time on the application of gate pulses with a duration of 1 s. The EPSC can be modulated by tuning gate bias from −0.05 V to −0.2 V, showing an excitatory effect for over 100 s. The OECS also exhibits Paired Pulse Facilitation (PPF)/Paired Pulse Depression (PPD) with the peak of the EPSC/IPSC increasing/decreasing on successive application of presynaptic spikes (Fig. 3d). PPF is essential for decoding temporal information in biological systems. PPF indices of the OECS decay exponentially with the pulse intervals and is similar to the signaling characteristics of biological systems (Fig. 3e).

A long-term increase in conductivity of OECS is achieved by electropolymerizing additional ETE-PC in the channel through the application of gate voltage pulses of −0.6 V for a duration of 1 s (Fig. 3f). This process is analogous to the N-methyl-D-aspartate (NMDA) receptor-mediated insertion of new receptors in the biological synapse, leading to a long-lasting increase in synaptic strength (minutes to hours and more). A total of 150 distinct states are demonstrated in the OECS, with state retention of more than 1000 s (Fig. 3g). This retention is significantly higher than other OECT-based synapses and eliminates the need for external switches to achieve state retention. Long-term depression (LTD) can be initiated in the synapse by over-oxidizing the channel, which is obtained by applying sufficiently high gate voltage pulses of −2 V for durations of 1 s in the absence of ETE-PC. However, LTD is highly nonlinear compared to a more linear LTP in this OECS. The need to remove the monomer solution to over-oxidize the channel hinders fast reversibility of the process and alternative approaches to induce long-term depression in the system are under investigation (see Supplementary Note 4).
pre- and postsynaptic signals coincide and a lower change in strength (conductivity) when the timing of the pulses is mismatched. Figure 4a–c shows the configuration of the pre- and postsynaptic terminals and the characteristic spikes applied to each terminal. Voltage pulses are chosen such that the maximum voltage difference (0.6 V), which is required for electropolymerization, is applied only when both pre- and postsynaptic spikes overlap. The extent of the overlap, which reaches a maximum when the spikes are applied simultaneously, determines the change in channel conductance. The changes in conductance are normalized by the initial channel conductance to present the data in percentage changes in weights. A difference in the timing of the spikes results in a reduced time duration of the spike overlap, and hence lower increase in synaptic strength. This process is analogous to the NMDA receptor-activated insertion of new receptors in synapse leading to LTP; NMDA acts as a biological 'AND' gate and only opens when presynaptic spikes cause glutamate to bind to it, and postsynaptic spike removes the Mg2+ blockade. Since electropolymerization can occur even at millisecond time scales, the STDP behavior can be tuned to match biological time scales by optimizing the pulse duration and amplitude.

To further illustrate the significance of the OECN and OECS, we demonstrate a simple neuro-synaptic system with Hebbian learning using a single synaptic transistor connected to the OECN (Fig. 4d). Instead of excitatory current input to the neuron, a voltage is applied to the synapse, which is converted to current based on its synaptic strength, resulting in modulation of the spiking frequency (Supplementary Figure 20). Since the gate and drain of the synaptic ETE-PC based OECT are kept at a common voltage of 0.5 V, it operates in the fully depleted mode with low conductivity. The presynaptic pulses of magnitude $-0.8$ V and duration of 1 s are applied to the synapse at predefined delays of 0, 5, and 10 s with respect to the time when the value of $V_{mem}$ is maximum. Any delay between the two results in a lower rate of electropolymerization and lower or no change in the spiking of the postsynaptic neuron (Fig. 4e, f). The $V_{mem}$ of the neuron generates the postsynaptic feedback to the synapse. If the presynaptic input arrives in sync with the maximum value of $V_{mem}$, there is a maximum voltage difference across the synapse (0.68 V) for electropolymerization to take place, and the synaptic strength increases significantly. This results in an increase in the firing frequency of the neuron from 22 mHz to 30 mHz, as shown in Fig. 4g, demonstrating the concept of 'neurons which fire together wire together' put forward by Hebb. Si-based systems require complicated circuits with multiple transistors to emulate STDP behavior. Hence, the demonstration of Hebbian learning in this organic electrochemical neuro-synaptic system is an important step and can be extended to build more complicated sensory and processing systems with local learning capabilities.

**Discussion**

We have demonstrated the first OECT-based spiking neuron, here made from an all-printed c-OECT technology, and its
Methods

invertebrates and vertebrates, respectively. OECNs and OECSs, with the signaling systems of plants, and integrate localized artifi
cial synapses exhibit a range of learning behaviors, including long-term and short-
term potentiation and depression and STDP. A neuro-synaptic system with STDP is demonstrated with much fewer elements in comparison to Si-based circuits. The OECT-based circuit can be printed on large scale\(^1\) and with high manufacturing yield\(^8,9\), which greatly simplifies the production protocol, as the driving strengths of p- and n-type transistors can be matched easily by tuning the thickness of the semiconductor layers. The neuron can be fully printed on flexible substrates and operates at a much lower power compared to OFET-based circuits and can thus enable the development of distributed low-cost smart labels for the future Internet of Things (IoT). The spiking frequency of the OECN can be modulated by changing the input current, membrane capacitance, and voltage input to the amplifier. The properties mentioned above and the ability to tune the frequency of spiking via modulation of electrolyte concentration, which is unique to this OECN, offer facile integration with biological systems that work by similar mechanisms and facilitate the development of future implantable devices. We demonstrate this possibility by interfacing the OECN with a Venus Flytrap to induce the closure of its lobes based on the neuron’s firing frequency. Furthermore, we demonstrate the integration of the OECN with an OECS with Hebbian learning capabilities. This, along with the unique ability of the OECTs to sense multiple biological, physical, and chemical signals, enables multiple sen-
sory detection. The possibility to fuse multiple sensing elements in the neuron itself could enable the development of novel bio-
integrable event-based sensors for applications ranging from smart neuromorphic labels for IoT packaging and continuous body health monitoring (i.e., wearable electronics) to brain-
machine interfaces. Our findings open for the possibility to integrate localized artificial neuromysiptic systems, composed of OECNs and OECSs, with the signaling systems of plants, and with the diffusive, peripheral, and central nervous systems of invertebrates and vertebrates, respectively.

**Methods**

**Materials**. The polyethylene terephthalate (PET) substrate Polifoil Bias is purchased from Poliscreen Co. Ag 5000, DuPont Silver Ink is used for printed inter-
connects. Carbon ink 7102 printing paste from DuPont is used for the electrode contacts. Insulating ink (5018, DuPont) is used for electrode isolation. PQ-10, PSSNs, and BBL were purchased from Sigma-Aldrich and used as received. The P(2T-T) and BBL inks are fabricated through a solvent exchange method. The P(2T-T) (30 mg) dissolved in chloroform (15 mL) is added dropwise to iso-
propanol (75 mL) under high-speed stirring for 4 h. The P(2T-T) and BBL nanoparticles are then centrifuged (5000 rpm, 30 min) and washed in IPA six times until neutral. The neutral P(2T-T) and BBL nanos-
particles are re-dispersed in IPA to obtain dispersion inks (about 0.006 mg/mL for P(2T-T) and 0.1 mg/mL for BBL).\(^8\)

**Fabrication of OECTs.** Flatbed sheet-fed screen-printing equipment (DEK Hor-
azon 03X) is used to deposit all materials on top of PET plastic substrates. To form the contacts, a layer of carbon is first deposited on the substrate. This is followed by the Ag 5000 silver ink deposition and the insulating layer of 5018 ink, which is UV-
cured to define the channel and the gate. Ag/AgCl ink is blade coated through a shadow mask and annealed at 120°C for 10 min to form the gate. The P(2T-T) and BBL layers are deposited by spray-casting in air through a shadow mask, using a standard HD-130 air brush (0.3 mm) at an atomization air pressure of 1 bar\(^8\).

**Electrical characterization.** All the OECT characterizations are carried out in a semiconductor parameter analyzer (Keithley 4200 SCS) at a temperature of around 20°C and a relative humidity of around 45%.

**Simulation of OECTs and OECSs.** The SPICE models of p-type and n-type OECTs are developed in B2 SPICE (EMAG Technologies Inc.). Both models are built based on the measured transfer characteristics and transient switching characteristics of printed OECTs. The simulation of OECNs gives the membrane voltage (\(V_{mem}\)) and the output of the Amplifier A (\(V_{out}\)) in the OECN circuits.

**Venus Flytrap measurement setup.** Venus Flytraps (Dionaea muscipula, VFTs) were purchased from Plantagen (Norrköping, Sweden) and kept in greenhouse conditions (day/night temperature of 28/22.5°C, 12 h photoperiod, 60% relative humidity, 400 ppm CO\(_2\)). Ag/AgCl electrodes were prepared by coating two Ag wires (AG1030, World Precision Instruments) with AgCl and insulating them with Teflon heat shrink tubing, leaving the electrode tips open. To electrically stimulate the VFT, the positive stimulation electrode was placed on the midrib and the ground or negative electrode was attached on the lobe, via a conductive gel (SignaGel, Parker Laboratories, Inc., NJ, USA) to ensure stable electrical contact. The positive stimulation electrode was electrically integrated with the output of the OECN and the two ground terminals were connected together to close the circuit. The Action Potential signals at different frequencies were then supplied by the OECN to induce the VFT trap closure.

**Reporting summary.** Further information on research design is available in the Nature Research Reporting Summary linked to this article.

**Data availability**

The authors declare that the main data supporting the findings of this study are available within the paper and its Supplementary Information files. Source data are provided with this paper.

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