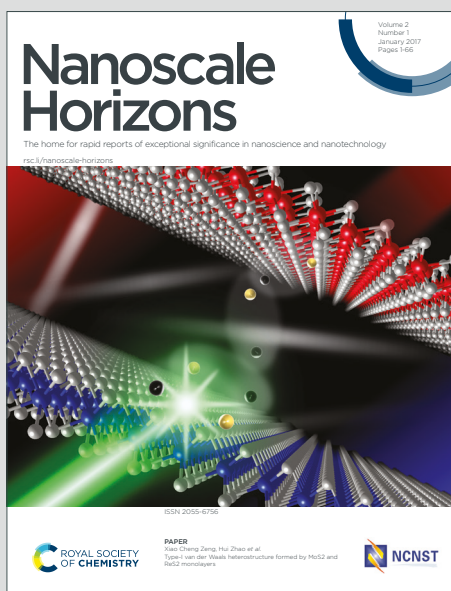


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1 Nanofluidic systems for ionic intelligence

2
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26
27 **Artificial intelligence is rapidly permeating modern technology, but its growth is**
28 **increasingly constrained by the costs of delivering power and removing heat. Neural**
29 **computation offers a striking counterpoint, for it achieves sophisticated information**
30 **processing at exceptionally low energy by exploiting ionic flows and adaptive**
31 **conductance. Inspired by the Hodgkin-Huxley view that function emerges from ion-**
32 **transport dynamics, recent work has begun to implement memory and learning**
33 **directly in fluids, where ions simultaneously carry signals and encode internal device**
34 **state. This Review charts the emerging landscape of fluidic ionic memristors, from**
35 **soft, bioinspired materials to manufacturable solid-state nanofluidic architectures.**
36 **In lipid bilayers, droplet networks, tissues and ionic polymers, electrical activity is**



37 **intrinsically coupled to chemistry and mechanics, enabling plasticity across multiple**
38 **timescales. In rigid nanopores, nanochannels and angstrom-scale slits, the softness**
39 **is transferred from the scaffold to the ionic degrees of freedom, where electric double-**
40 **layer dynamics, concentration polarization and confinement-driven effects produce**
41 **history-dependent transport in robust inorganic frameworks. Hybrid approaches**
42 **integrate gels, brushes, particles, or biomolecules within microfabricated structures**
43 **to combine stability with rich analogue dynamics. We conclude by outlining the key**
44 **requirements for translation from reproducibility to scalable integration towards ionic**
45 **intelligence technologies.**
46



47 1. Introduction

48 Artificial intelligence is becoming an always-present layer of the Internet, yet its
49 rapid expansion is now limited as much by physical constraints as by advances in
50 algorithms. As large language models are trained and deployed at scale, computation is
51 concentrated in dense accelerators and data centers, where increasing heat fluxes, cooling
52 burdens and the life-cycle footprint of electricity now pose major sustainability
53 constraints.¹⁻³ This backdrop has renewed interest in neuromorphic computing,⁴ which
54 pursues brain-like learning and inference through sparse, event-driven signalling rather
55 than the clocked von Neumann architecture. In the Hodgkin-Huxley picture, such
56 computation is performed by voltage- and time-dependent ionic conductance whose
57 internal ionic states store history and govern dynamics, a design principle that inspires
58 ionic intelligence hardware in which ions, rather than electrons, carry signals and encode
59 memory.⁵⁻⁸ Drawing on these biological principles, scientists have sought to create
60 nanofluidic memristors, artificial two-terminal devices in which ion transport under
61 confinement exhibits history-dependent conductance analogous to synapses.⁹⁻¹⁴ Over
62 the past decade, this emerging class of iontronic devices has rapidly emerged as a bridge
63 between living neural networks and semiconductor processors, aiming to emulate brain-

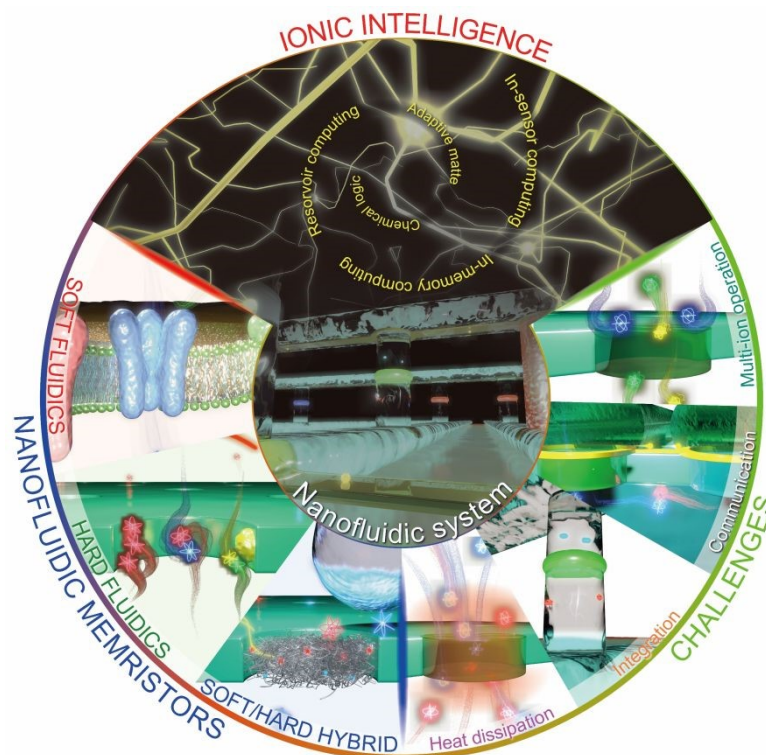


Figure 1. Conceptual diagram summarizing the central theme of this Review: confined ion transport can generate memory and computation when coupled to slowly evolving internal states.

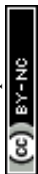


64 like learning and memory with the very same carriers of information used in biology.

65 Early ionic memristors have already captured many canonical synaptic functions
66 while operating at exceptionally low power.¹⁵ Current transients in nanofluidic channels
67 can consume only femtojoules per spike,¹⁶ placing them close to the efficiency of
68 biological synapses.¹⁶⁻¹⁸ Fluidic memristors also share a closer physical analogy with
69 natural synapses than conventional solid-state devices, because they function in water
70 with mobile ions and solvent molecules as active components of transport. This
71 chemically rich environment, together with the multispecies character of ionic carriers,
72 their hydration shells, valence states and reversible binding, enables dynamical behaviors
73 that are inaccessible to purely electronic systems. As a result, ion-driven memristors
74 have begun to reproduce short-term plasticity,¹⁹ long-term plasticity,²⁰ spike-timing-
75 dependent plasticity,²¹ and even higher-order learning-forgetting dynamics,²²
76 highlighting their distinctive potential for neuromorphic engineering.

77 Yet, substantial challenges still separate nanofluidic memristors from their full
78 potential (Fig. 1). Reproducing the ion-selective, multi-ion operation of real neurons
79 and glia remains a central unsolved problem. Devices capable of exploiting several
80 ionic species in parallel, analogous to the distinct signaling roles of Na⁺, K⁺ and Ca²⁺ in
81 biology, have yet to be realized for complex information processing. Scaling fluidic
82 memristors into large iontronic circuits presents a further obstacle, because such systems
83 are intrinsically more difficult to address, interconnect and control than solid-state
84 counterparts. Even so, the field has begun to make important progress, with early
85 demonstrations of logic operations and neural-network computation using small numbers
86 of ionic memristors.²³ As attention shifts towards larger-scale hardware, hybrid
87 architectures that combine rigid nanochannels with soft polymers or hydrogels are
88 emerging as a promising route to unite structural robustness with adaptive ionic
89 functionality.

90 This Review surveys the rapidly expanding landscape of nanofluidic memristors for
91 artificial intelligence, focusing on ion transport rather than electron conduction as the
92 basis of operation. We cover hard fluidic platforms built from solid-state nanochannels
93 and nanopores, soft ionic media including biomembranes, droplets and polymer matrices,
94 and hybrid architectures that combine these approaches (Fig. 2). Throughout, we
95 emphasize how ionic dynamics, ranging from slow counterion accumulation to fast
96 electrowetting at nanoscopic interfaces, generate memristive behaviour. We highlight key
97 mechanisms including electric-double-layer hysteresis, ångström-scale confinement,
98 electrohydrodynamic flow memristors, optically modulated ionic transport and chemical
99 memory in nanopores. We then examine emerging multi-memristor circuits, including



100 ionic logic gates and synaptic networks, to show how such devices can perform
 101 computation. Finally, we discuss the major challenges ahead, including thermal
 102 management and scalable integration. Our aim is to provide a timely and comprehensive
 103 perspective on nanofluidic memristors, and to clarify both the remarkable progress
 104 towards fluid-based artificial synapses and the remaining path to fully ionic intelligent
 105 systems that compute with brain-like efficiency and elegance.

106 To refine this conceptual framework, we move beyond a purely materials-based
 107 soft/hard/hybrid categorization and instead organize the field around four recurring

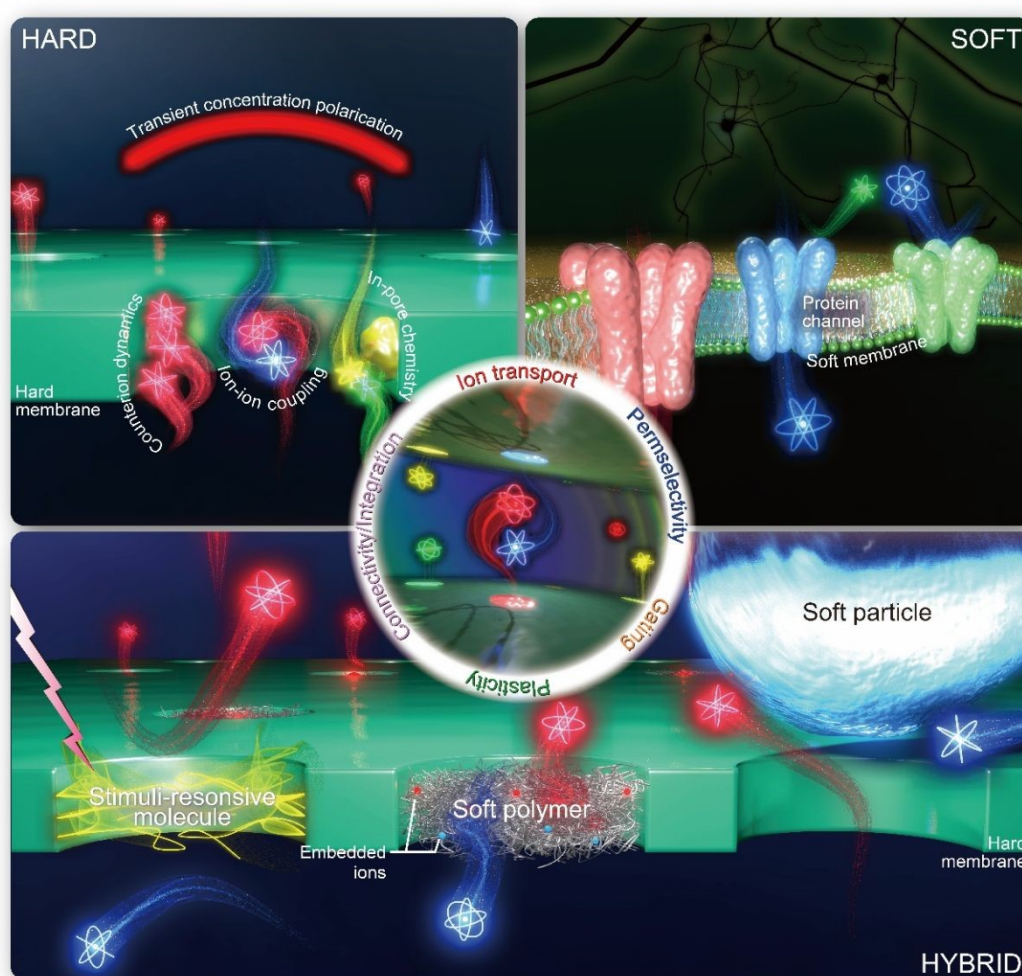


Figure 2. Soft, hard, and hybrid nanofluidic platforms for ionic intelligence. Conceptual map of how ionic memory and computation emerge when ion transport is confined and made state dependent. Hard systems (top left) use rigid membranes and engineered nanochannels, where history dependence arises from slow counter-ion relaxation, ion-ion correlations and in-pore chemistry, often expressed through transient concentration polarization. Soft systems (top right) rely on compliant membranes and biomolecular pores, in which ionic flux is inseparable from conformational and mechanical degrees of freedom. Hybrid systems (bottom) integrate a manufacturable hard scaffold with soft functional elements to enable reconfigurable gating and multiscale plasticity. The central inset highlights shared functional primitives in the form of an ionic circuit in an artificial nanofluidic network.



108 physical mechanisms: electric-double-layer charging and relaxation, concentration
109 polarization and diffusive redistribution, electrochemical reactions coupled to interfacial
110 ion adsorption, and mechano-ionic coupling arising from structural compliance. This
111 mechanism-centered view makes it easier to compare otherwise disparate platforms on
112 common physical grounds and to connect device physics directly to function, including
113 short-term plasticity, long-term retention, spiking and adaptive learning. Soft lipid
114 bilayers and hydrogels, for example, draw primarily on interfacial charging and
115 electrochemical doping, whereas rigid nanochannels intensify diffusion, adsorption and
116 correlation effects under extreme confinement. Hybrid systems are best understood as
117 deliberate combinations of these mechanisms, assembled to balance programmability,
118 robustness and scalability.

119 These platforms are therefore best viewed not as discrete categories, but as a design
120 continuum. In soft fluidics, the state variable resides in reconfigurable matter itself,
121 such as membranes, droplets, polymer networks and living tissues, so memory is
122 inseparable from compliance, chemical binding and slow ionic relaxation. Hard
123 nanofluidic systems retain the same ionic carriers and aqueous transport physics, but
124 confine them within rigid nanopores and nanochannels, shifting plasticity from
125 mechanical deformation to interfacial charge, hydration and reaction landscapes defined
126 by an inorganic scaffold. Hybrid architectures occupy the intermediate regime,
127 preserving the addressability, reproducibility and lithographic precision of hard
128 nanofluidics while reintroducing soft internal degrees of freedom through gels, brushes,
129 biomolecules or confined liquid phases. Conventional solid-state memristors sit
130 adjacent to, rather than within, this fluidic continuum. They likewise encode memory
131 through delayed internal-state evolution, but the relevant variables are typically electronic,
132 lattice-ionic or defect-based configurations rather than a mobile aqueous ionic population.
133 Framed in this way, the comparison highlights both the shared logic of history-dependent
134 transport and the distinct physical substrates that each platform brings to adaptive
135 computing.



136 2. Soft fluidic platform

137 We begin with soft fluidic platforms, where compliance, hydration, and molecular
138 rearrangement are not merely structural attributes but active parts of the memory
139 mechanism.

140 The brain is often described as a soft organ,²⁴ with an elastic modulus of only about
141 100 Pa at 1 Hz.²⁵ This low stiffness is thought to facilitate synapse formation and robust
142 electrical signaling during tissue development.^{26,27} Neuronal membranes are likewise
143 built from ductile lipid bilayers, whose softness allows embedded ion-channel proteins to
144 undergo conformational changes that open or close their pores in response to stimuli such
145 as voltage or neurotransmitters.²⁸ It also permits ion channels to diffuse, reorganize, and
146 be inserted or removed over time, thereby contributing to synaptic plasticity.²⁹ At larger
147 scales, neurons can physically remodel during learning, a process that depends on the
148 mechanical compliance of cellular membranes and scaffolds to reshape existing
149 connections and form new ones for long-term memory storage in neural networks.³⁰

150 The softness of neuronal membranes plays a central part in the energetics and
151 adaptability of neural signaling. Ion channels embedded in lipid bilayers operate
152 between aqueous electrolytes on either side, enabling rapid ion transport through water
153 while minimizing the energetic cost of gating. Individual channels undergo
154 conformational transitions on energy scales comparable to $k_B T$, yet can regulate fluxes
155 exceeding 10^8 ions per second.^{31,32} Synaptic switching therefore consumes only
156 femtojoules per event, giving biological neural systems an energy efficiency far beyond
157 that of conventional electronic circuits.³³ By enabling both efficient biophysical
158 signaling and structural plasticity, the mechanical softness of neural substrates contributes
159 to the extraordinary computational capabilities of the brain.

160 Soft fluidics employs deformable, biomolecular, or entirely fluidic systems to
161 achieve memristive behavior inspired by biology implementing intrinsically soft and wet
162 structures of lipid membranes, ion channels, hydrogels, polymer networks, etc. In soft
163 ionic memristors, the device components can move or reconfigure significantly during
164 operation. They also bring biocompatibility and an ability to host biological entities
165 directly. The interplay between mechanical compliance and ionic transport is a
166 recurring theme, as soft systems can deform in response to ion flows. This deformation
167 can in turn influence conduction, creating a memristive loop. In this section, we explore
168 two major categories, those utilizing biological systems and ionic polymers (Table 1).

169
170



Table 1. Representative soft nanofluidic systems exhibiting memristive ionic dynamics.

System class	Material / fluidic system	Size	Mechanism	Stimulus class	Switching speed	Retention time	Energy consump.
Bio-nanopore ⁴¹	β -barrel nanopore (FraC mutants) in KCl	Protein nanopore with hydrophobic segment of ~1.2 nm	Hydrophobic gating yielding bistable wet/dry (vapour bubble) states	Triangular voltage sweeps (150 mV, 2 s)	~2 Hz	Seconds to tens of seconds	~pJ per synaptic event
Bio-nanopore ⁴⁴	β -barrel nanopores (aerolysin and MspA mutants)	nanopore with nanometre-scale lumen constriction	Field-driven counterion dissociation and local deformation	Pulse trains (110 mV, 5-10 ms)	100-200 Hz	Volatile (state depends on lipid reconfiguration)	N/A
DIB ⁴⁸	Droplet interface bilayer between 100 mM KCl droplets	600 nL per droplet	Voltage-driven electrocompression/electrowetting changing bilayer area/thickness	Pulse trains (0/200 mV, 0.1 s)	~2 Hz	Seconds to tens of seconds	4–8 pJ per spike
DIB ⁴⁹	Droplet interface bilayer between 500 mM KCl droplets	300 nL per droplet	Voltage-driven restructuring of lipid bilayer (area/thickness and headgroup dielectric loss)	Sinusoidal voltage (10-100 mHz; 80-150 mV)	N/A	Volatile (state depends on lipid reconfiguration)	N/A
DIB ⁵⁰	Droplet interface bilayer between 500 mM KCl droplets	200 nL per droplet	Voltage-driven restructuring of lipid bilayer (area/thickness and headgroup dielectric loss)	Pulse trains (150 mV, 1-2 ms)	~100 Hz	~tens of seconds	N/A
DIB ⁵¹	Alamethicin-doped droplet interface bilayer between 500 mM KCl droplets	200 nL per droplet	Channel density/permeability changes via voltage-driven insertion of alamethicin in ion channels	Pulse trains (130 mV, 10-1500 ms)	20-50 Hz	~2 s	pW-nW
DIB ⁵³	Droplet interface bilayer formed by printed networks of aqueous droplets	~500 pL droplets	Platform work	Thermal stimulus for printing (55–60 °C) and mechanical compression tests (mHz–Hz).	N/A	N/A	N/A
Brain organoid ⁵⁸	Human neural organoids interfaced with microelectrode array	N/A	Stimulation-modified neural network activity/connectivity in human neural organoids	Electrical theta-burst stimulation delivered 4x with 13-min interval	Short-term effects milliseconds after stimulation.	Longer-term plasticity assessed from 60–180 min post stimulation and additional assays over hours	N/A
Brain organoid ⁶¹	In vitro cortical neuron cultures on multielectrode array	mm-scale culture on chip	Cultured cortical networks adapting synaptic connectivity and firing patterns	Closed-loop electrical stimulation	Apparent learning/adaptation reported within ~5 minutes in closed-loop task	N/A	N/A
Ionic polymer ⁷¹	Organic electrochemical RAM: p(g2T-TT) channel with ion-gel electrolyte	Channel ~45 μ m \times 15 μ m	Electrochemical doping/de-doping	Pulse trains (1 V, 1 μ s)	~0.05 GHz	~minutes	~80 fJ per write
Ionic polymer ⁷⁵	All-inorganic ionic polymer memristor: Au / APP / ITO on PET	APP layer thickness ~250 nm	Voltage-driven migration/accumulation of mobile ions in ammonium polyphosphate	Pulse trains (0.1-0.4 V, 20 ns-20 μ s)	~0.05 GHz	~10,000 s retention	~nJ per write
Ionic polymer ⁷⁶	Proton-enabled peptide memory: Y7C peptide film coupled to IGZO synaptic transistor	Y7C film thickness ~117 nm, ~200 \times 200 μ m ²	Voltage-driven migration/accumulation of mobile ions in ammonium polyphosphate	Humidity+pulse trains (1 V, 0.1-1 s)	10,000-0.1 Hz	seconds to hundreds of seconds	N/A



2.1 Biological membrane and protein nanopores

Biological membranes, composed of lipid bilayers with embedded proteins (Figures 3a-b), have evolved to perform ionic information processing. Central to this function are ion channels, whose conductance is regulated by voltage, ligand binding and other external stimuli.³⁴ The Hodgkin-Huxley framework can itself be viewed as memristive, in that channel gating variables evolve according to voltage history and thereby produce history-dependent conductance that is essential for action-potential generation.³⁵ Although biological nanopores have been studied extensively as sensors for the detection of small molecules,³⁶⁻⁴⁰ this same principle has also motivated the direct use of biological ion channels as building blocks for artificial synapses.

An instructive example of a bioengineered ion-channel memristor is the hydrophobically gated nanopore based on Fragaceatoxin C (FraC), a pore-forming toxin.⁴¹ Here, a hydrophobic constriction undergoes voltage-driven electrowetting transitions between wet conductive and dry vapor-blocked states, generating strongly history-dependent conductance with large on/off ratios (Figure 3c). When a small number of mutant FraC pores are reconstituted in a lipid bilayer, the device displays analogue switching, stochastic state transitions and synapse-like plasticity under pulsed stimulation. This system illustrates how protein nanopores can serve as genetically encodable, structurally precise building blocks for iontronic memristors (Figure 3d).

A mechanistically distinct route to protein-based neuromorphic elements is offered by beta-barrel nanopores widely studied for sequencing applications,^{42,43} in which lumen charge governs both open-pore rectification and voltage-driven mechanical gating (Figure 3e). A recent mutation-theory-simulation study of aerolysin showed that localized charges in the pore lumen drive ionic accumulation and depletion that set the polarity and magnitude of rectification, whereas gating emerges on slower timescales when strong electric fields dissociate counterions from lumen charges and promote local beta-barrel deformations, yielding a bistable open/closed response and memristive hysteresis. By tuning the spatial distribution of lumen charge with site-specific mutations, the authors engineered an aerolysin mutant with enhanced synaptic plasticity and demonstrated potentiation and depression by voltage pulse sequences, providing a rational design framework for programmable ionic synapses (Figure 3f).⁴⁴

The advantage of genuine cell membranes, or their synthetic analogues, is that they naturally embody many of the features required for computation, including nonlinearity, time dependence and plasticity. For example, incorporating NMDA receptors into a lipid bilayer could in principle reproduce aspects of Hebbian plasticity. Although such systems remain bioengineered and experimentally complex, they illustrate how soft



208 memristors can be directly biomimetic and function in ways that closely resemble natural

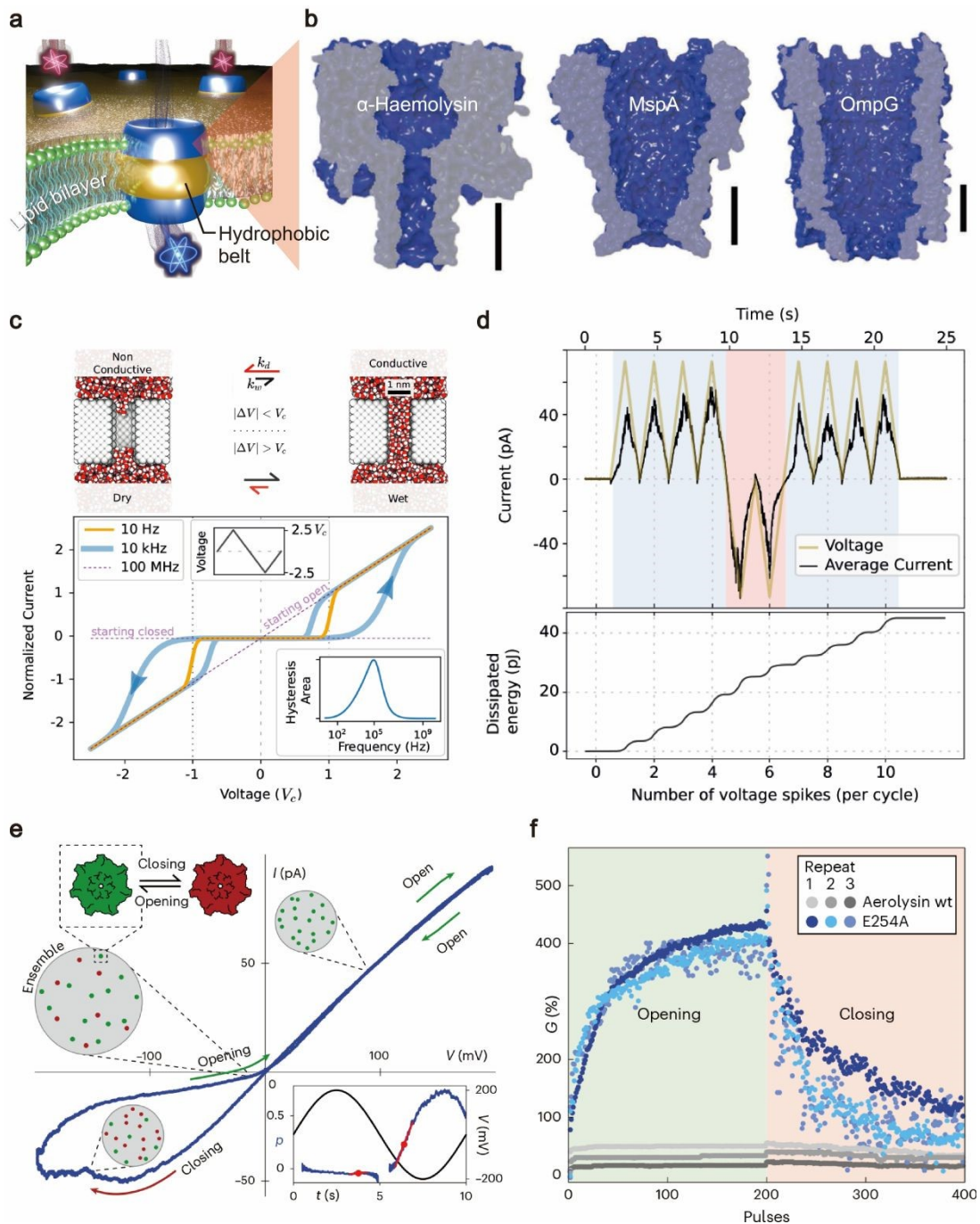


Figure 3. Memristive gating in biological nanopores. **a**, A sketch depicting a simplified model of protein channels inserted in a lipid bilayer. **b**, Structures of α -haemolysin, MspA, and OmpG. Adapted with permission from ref. 42. Copyright 2016 Springer Nature. **c**, Electrowetting mechanism and normalized current-voltage loops showing frequency-dependent hysteresis. **d**, Spike-train operation yielding synapse-like current responses and cumulative energy dissipation. Adapted with permission from ref. 41. Copyright 2023 Creative Commons CC BY. **e**, Ensemble opening/closing produces a pinched hysteresis loop in the I - V characteristics. **f**, Plasticity under repeated voltage pulses for wild-type and charge-mutant aerolysin, illustrating potentiation and depression of conductance. Adapted with permission from ref. 44. Copyright 2025 Creative Commons CC BY.



209 synapses.

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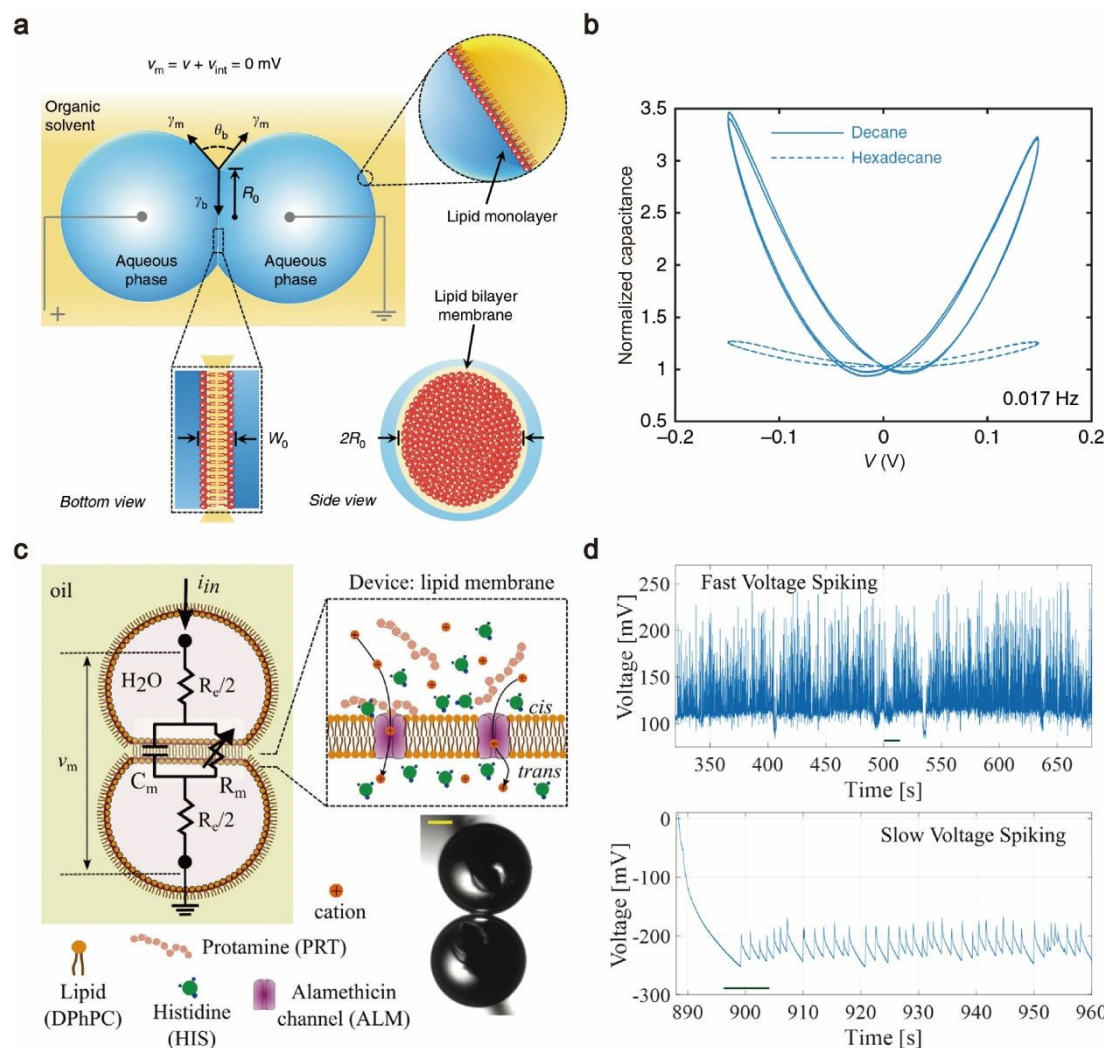
211 **2.2 Droplet interface bilayers**212 Droplet interface bilayers (DIBs) extend the bionanopore concept from a single
213 molecular channel to a mesoscopic, reconfigurable synaptic unit.¹² In these systems,

Figure 4. Droplet-interface bilayers as voltage-responsive memcapacitors and spiking membrane neurons.

a, Droplet-interface bilayer (DIB) platform in which two aqueous droplets in oil self-assemble a lipid bilayer that can host transmembrane channels; schematic (top) and optical micrograph (bottom). **b**, Voltage-driven electrowetting and electrocompression reshape the bilayer geometry, modulating membrane thickness and radius as coupled state variables. The resulting nonlinear pinched capacitance-voltage hysteresis depends on the oil phase, demonstrating memcapacitance. Adapted with permission from ref. 50. Copyright 2019 Creative Commons CC BY. **c**, Equivalent circuit for DIB devices with electrolyte resistance in series with a membrane branch comprising a state-dependent membrane resistance in parallel with membrane capacitance; inset, reconfigurable channel networks and mobile charged modulators coupling ionic transport to membrane state. **d**, Under dc current bias, these internal dynamics can generate neural-like voltage spiking with distinct fast and slow regimes, consistent with a feedback cycle of channel insertion/opening and polyelectrolyte-mediated blocking and charge redistribution across cis/trans reservoirs. Adapted with permission from ref. 51. Copyright 2024 John Wiley and Sons.



214 two electrolyte droplets are brought into contact within oil, where opposing lipid
215 monolayers zip together to form a bilayer patch that is electrically addressable in much
216 the same way as a cell membrane (Fig. 3a).^{46,47} Despite this simple geometry, DIBs can
217 already support a surprisingly rich repertoire of synaptic functions even in the absence of
218 ion channels, including facilitation and depression reminiscent of spike-rate-dependent
219 plasticity, Hebbian learning, and even associative learning in a Pavlovian protocol under
220 voltage-pulse stimulation.⁴⁸

221 The origin of memory in DIBs is mechanistically distinct from protein-pore gating.
222 Here, a voltage sweep couples ionic relaxation to interfacial mechanics (Fig. 4a): residual
223 charge, field-driven ion adsorption within the headgroup region, and the slow recovery
224 of membrane order together bias the conductance reached on the next cycle.⁴⁹ Bilayer
225 capacitance is likewise not a passive quantity, but evolves with voltage history as
226 membrane tension, area and dipole orientation shift. The resulting element therefore
227 behaves as a coupled memristor–memcapacitor rather than as a purely resistive switching
228 device (Fig. 4b).⁵⁰

229 This coupling is what makes DIBs a particularly powerful extension of biological
230 nanopore concepts for neuromorphic devices. Whereas the systems in Section 2.1
231 derive their dynamics primarily from the conformational landscape of a specific protein
232 channel, DIB synapses expose several tunable state variables, including electrolyte
233 composition, droplet size, bilayer lipid chemistry and mechanical boundary conditions.
234 The learning rule can therefore be engineered at the level of interfacial physics. Protein
235 nanopores can nonetheless be incorporated as modular components (Fig. 4c,d).⁵¹⁻⁵⁴
236 Introducing channels such as alamethicin,⁵² MscL,⁵³ or engineered mutants⁵⁴ adds a
237 second layer of memory through channel population dynamics, effectively combining
238 molecular and interfacial plasticity within a single soft element.

239 Equally important, droplets offer a route to scalability that single-bilayer protein
240 devices struggle to match. Droplets can be generated, positioned, and connected in
241 parallel by microfluidics, patterned into networks, or assembled as emulsions into dense
242 soft circuits, turning the bilayer into a repeatable unit cell for wet neural architectures.⁵⁵
243 The remaining hurdles are practical-bilayer fragility and device-to-device variability,
244 motivating polymer-stabilized membranes, partial gelation and chip-based confinement
245 as strategies to make large droplet arrays both reproducible and long-lived.

246

247 **2.3 Living neural networks and organoid intelligence**

248 Brain organoids, three-dimensional neural tissue constructs grown from stem cells,
249 are emerging as soft, living substrates for neuromorphic computing.^{56,57} These mini-



250 brains are physically soft with stiffness on the order of only a few hundred Pascals.⁵⁸
 251 This extreme mechanical softness means organoids are predominantly fluidic systems,
 252 composed of cells and extracellular matrices akin to soft membranes, which enables
 253 efficient ion transport through the aqueous extracellular space and across flexible cell
 254 membranes, much like ionic polymers in artificial devices.
 255 Memristive behavior is intrinsically realized in organoid neural networks via

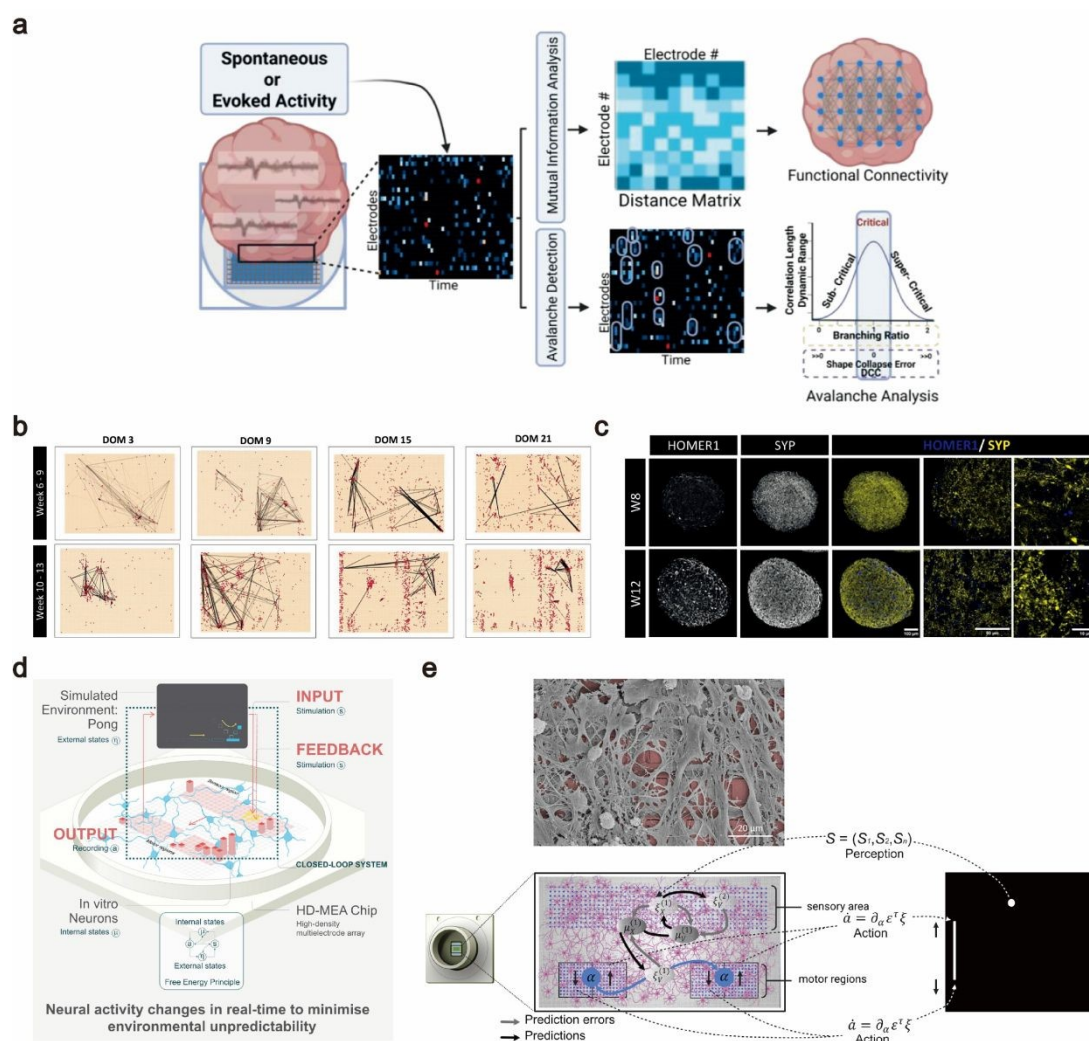


Figure 5. Living neural networks as soft ionic substrates for computation. **a**, High-density microelectrode array interfacing enables simultaneous recording and stimulation of cortical organoids; analysis workflows extract functional connectivity and neuronal criticality from spontaneous and evoked activity. **b**, Example functional-connectivity graphs reconstructed across development, illustrating evolving edge weights and active nodes across the electrode field. **c**, Immunostaining of pre- and postsynaptic markers in cortical organoids indicates progressive synaptogenesis that underpins emergent network dynamics. Adapted with permission from ref. 59. Copyright 2025 Springer Nature. **d**, Closed-loop DishBrain embodiment, in which cultured neurons on a microelectrode array receive sensory stimulation encoding the Pong game state and feedback to drive goal-directed adaptation. **e**, Mapping of sensory and motor channels on the array and a conceptual active-inference loop linking neuronal activity to actions and prediction errors in the virtual environment. Adapted with permission from ref. 62. Copyright 2022 Creative Commons CC BY.



256 synaptic plasticity. In these living networks, each synapse acts like a nanoscale
257 memristor whose strength or conductivity adjusts based on prior activity. Biological
258 synapses achieve this through ionic and molecular mechanisms. For instance, repeated
259 stimulation causes residual Ca^{2+} buildup and receptor modifications that temporarily or
260 permanently change synaptic efficacy. Experiments have confirmed that brain
261 organoids exhibit both short-term and long-term synaptic potentiation and depression in
262 response to stimulation (Figure 5a-c).⁵⁹ In other words, organoids can undergo short-
263 term memory with milliseconds-to-seconds facilitation/depression of a synapse as well
264 as long-term memory allowing persistent strengthening or weakening analogous to
265 learning. Although these plastic changes mirror the memristive behavior engineered in
266 ion-based artificial synapses, they emerge naturally from the underlying biochemistry of
267 the organoids. Notably, recent high-profile work demonstrated that human neural
268 organoids constitute the fundamental building blocks of learning. They form functional
269 synapses with glutamatergic/GABAergic receptors and show activity-dependent gene
270 induction accompanying synaptic potentiation.⁵⁹ Such findings demonstrate that a soft
271 living organoid can perform analog memory storage through ionic synaptic modifications,
272 effectively functioning as a memristive network without any solid-state components.

273 The link to artificial nanofluidic memristors becomes clearer when these biological
274 processes are expressed in physicochemical terms. Residual Ca^{2+} accumulation in
275 synapses resembles the delayed ionic relaxation that sustains electric-double-layer
276 memory, while neurotransmitter binding and release parallel reversible adsorption and
277 desorption processes at functionalized interfaces. These correspondences do not imply
278 strict equivalence, but they do provide a useful design language for translating organoid-
279 like plasticity into engineered iontronic devices.

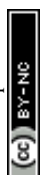
280 By virtue of their intrinsic ionic conduction and synaptic plasticity, brain organoids
281 are emerging as experimental platforms for neuromorphic task execution. Their
282 distributed neuronal circuits support collective information processing reminiscent of
283 biological brains. For example, organoids can generate organized electrical oscillations
284 and synchronized firing patterns analogous to brain waves.⁵⁹ Notably, spontaneous
285 network oscillations in a human cortical organoid have been shown to recapitulate EEG
286 rhythms observed in the preterm infant brain, suggesting the emergence of functional
287 connectivity and critical dynamics favorable for computation. More directly, organoids
288 have been harnessed for computational tasks through learning-based frameworks. In a
289 landmark study, a living brain organoid was incorporated into a reservoir-computing
290 architecture, in which a three-dimensional neural organoid was coupled to a high-density
291 microelectrode array for stimulus encoding and signal readout.⁶⁰ The organoid



292 exhibited rich nonlinear dynamics together with a fading memory of past inputs, enabling
293 time-dependent computation. Remarkably, the system achieved unsupervised learning
294 through network reorganization, allowing it to perform speech recognition and even
295 predict chaotic mathematical equations in real time.⁶⁰ In this setting, the soft organoid
296 functioned as a reconfigurable analogue processor whose internal synaptic weights
297 adjusted autonomously in response to training stimuli.

298 Neuromorphic behavior in biological networks has also been illustrated by
299 demonstrations of goal-directed learning in cultured neuronal assemblies, a line of work
300 often grouped under the emerging concept of organoid intelligence. In 2022, a cultured
301 layer of ~800,000 human cortical cells interfaced with electrodes, frequently described as
302 a two-dimensional organoid or cortical network, was shown to learn to play Pong through
303 feedback-driven training (Figure 5d-e).^{61,62} Over time, the neuronal culture
304 progressively reshaped its firing dynamics in response to the game environment,
305 revealing a rudimentary form of skill acquisition and memory that sustained paddle
306 control. The DishBrain experiment illustrates that living neural networks can acquire
307 adaptive behavior and store memory in a manner analogous to a learning machine.
308 Taken together with three-dimensional organoid studies, these findings offer proof-of-
309 concept that biological soft systems can realize computational functions such as pattern
310 recognition, control, and prediction by leveraging synaptic plasticity.⁵⁹ During learning,
311 the iontronic circuits of these networks are continuously reshaped by the malleable,
312 fluidic tissue itself, exemplifying how mechanical softness and neuromorphic function
313 are intrinsically coupled in organoid computing.

314 Organoids derive their computing capability from a unique combination of material
315 softness and biological architecture, standing in sharp contrast to traditional electronic
316 hardware. They consist of living neurons, supporting glial cells and the extracellular
317 matrix they secrete.⁵⁹ Within an aqueous milieu, neurons self-organize into dense three-
318 dimensional networks interconnected by thousands of synapses. Soft phospholipid
319 bilayer membranes act as the basic ionic capacitive and resistive elements. Owing to
320 their nanometer-scale thickness and mechanical softness, these membranes readily
321 undergo conformational changes in response to ion binding or voltage fluctuations,
322 enabling electrically responsive soft-matter behavior. Protein ion channels and
323 receptors embedded within the membranes respond to mechanical and electrical cues by
324 opening or closing, thus dynamically regulating ion transport. This tunability enables
325 ion transport to display rich nonlinear responses, such as channel inactivation and
326 neurotransmitter depletion, that are essential for computation. Additionally, the
327 nanoscale synaptic cleft forms a soft ionic domain that transiently concentrates



328 neurotransmitters and ions during activity, producing short-lived chemical gradients.
329 Repeated signaling transiently reshapes the chemistry of the synaptic cleft, analogous to
330 the state evolution of an active region, enabling synaptic strength to encode a short-term
331 memory of recent activity.⁶³ At its core, the computational substrate of organoids is a
332 network of soft, ion-conducting components from lipid bilayers and protein ion channels
333 to neurotransmitters. Mechanical softness and flexibility are central to function at every
334 level, with soft membranes and cytoskeletal elements enabling synaptic reorganization
335 during learning, from the creation of new connections to synaptic growth during
336 potentiation. This stands in contrast to rigid silicon chips, where circuit elements are
337 fixed. In organoids, the wiring is fluid. Indeed, studies have observed organoid
338 neurons forming new circuits and strengthening connectivity in response to stimulation,
339 effectively rewiring their microcircuitry as learning progresses. Such plastic
340 reconfiguration is enabled by both the biochemical machinery and the compliant physical
341 matrix in which neurons reside.

342 The advent of brain organoids as computing units carries profound implications for
343 bio-inspired and neuromorphic computing. First, these living systems offer a level of
344 adaptive parallelism and energy efficiency.⁶⁴ Their soft iontronics approach to
345 computation could overcome limitations of traditional rigid electronics by operating in an
346 analog, event-driven fashion with minimal chemical energy. Intrinsic mechanical
347 softness permits conformal biointerface integration, enabling flexible three-dimensional
348 electrode meshes to envelop organoids without damage and opening the door to wetware
349 co-processors that physically integrate with sensing or robotic systems. Moreover,
350 organoid computing systems naturally embody features that hardware engineers struggle
351 to reproduce, such as self-organization and fault-tolerance. Through memristive
352 synapses, these systems achieve on-chip learning and memory without explicit
353 programming, and even when partially damaged, the remaining tissue can reorganize to
354 restore function, echoing recovery mechanisms in the brain. This mortal yet
355 regenerative substrate thus defines a new computational paradigm, in which hardware
356 itself can grow, adapt, decay, and be renewed. Despite their promise, organoids pose
357 major challenges for reliable computing, including biological variability, finite lifespans,
358 and ethical issues inherent to human-derived neural systems. Nonetheless, recent
359 studies have validated the core concept that soft living neural networks can perform
360 meaningful computations. As research progresses, it is conceivable that hybrid
361 approaches integrating organoid-based processors with conventional electronic systems
362 could be explored, potentially harnessing the complementary strengths of biological
363 adaptability and electronic precision.



364 2.4 Ionic polymers and soft iontronics

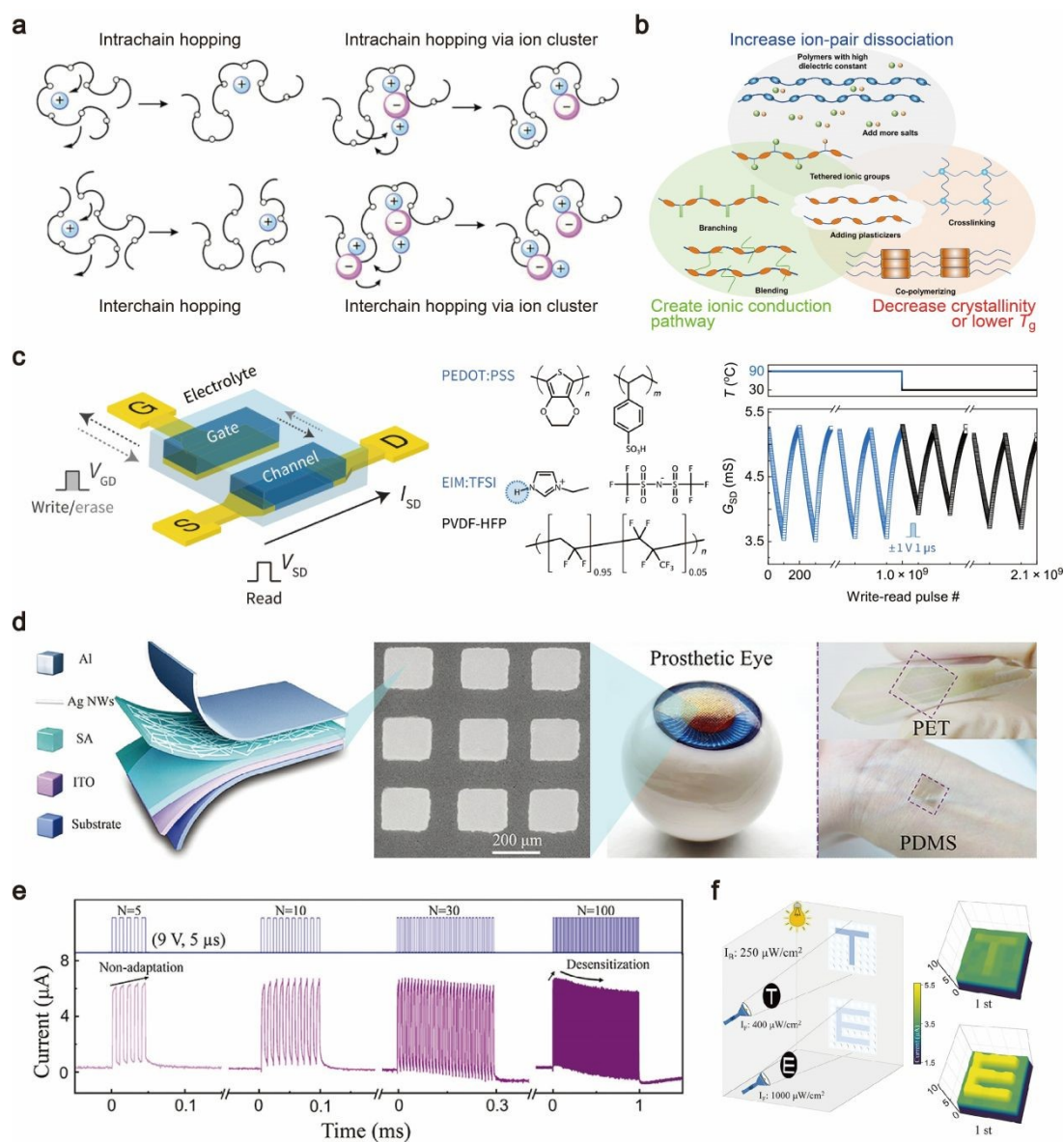


Figure 6. Soft polymer iontronics as a bridge from transport physics to adaptive sensing. **a**, Schematic view of ion motion in polymer electrolytes, highlighting intra-chain and inter-chain hopping that set the intrinsic relaxation times governing ionic conductivity. **b**, Materials-level design levers for raising conductivity. Adapted with permission from ref. 66. Copyright 2023 Creative Commons CC BY. **c**, Solid-state organic electrochemical random-access memory in which an ion-gel gate modulates the doping state of a conjugated-polymer channel, enabling low-voltage analog weight updates and temperature-resilient operation with sub-microsecond programming and $>10^9$ write-read endurance. Adapted with permission from ref. 72. Copyright 2020 The American Association for the Advancement of Science. **d**, Flexible sodium-alginate complementary memristor architecture and array-level integration, illustrating conformable form factors for prosthetic and wearable platforms. **e**, Pulse-train responses in the alginate device that transition from non-adaptation to desensitization as stimulus number increases, implementing a hardware analogue of sensory gain control. **f**, A neuromorphic vision concept in which adaptive preprocessing improves pattern recognition across changing background intensity, linking ionic memory directly to perception-level tasks. Adapted with permission from ref. 73. Copyright 2024 John Wiley and Sons.



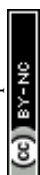
365 Rather than borrowing the molecular machinery of biology, ionic polymers offer a
366 synthetic, processable medium in which memory is written into ion distributions and soft-
367 matter relaxation, enabling devices that are flexible, scalable, and compatible with large-
368 area manufacturing.⁶⁵⁻⁶⁸ They span electrolyte-swollen hydrogels, ionomers such as
369 Nafion, and polyelectrolyte networks built from biopolymers. Their defining feature is
370 that the conductor is not a fixed pore but a dynamic matrix of charged segments binding
371 and releasing counterions, polymer domains swelling or densifying, and nanoscale
372 morphology evolving under bias (Figure 6a-b). These slow internal degrees of freedom
373 provide the state variable for memristive behavior, while the macroscopic form can be
374 cast as films, patterned over centimeters and integrated on soft substrates.^{69,70}

375 The mechanism contrasts with the biological motifs. In protein nanopores,
376 memory is encoded in conformational landscapes of a channel. In droplet bilayers, it
377 emerges from coupled ionic relaxation and interfacial mechanics. In organoids, it is
378 distributed across synapses and gene programs. Polymer synapses, by comparison, store
379 their state in the physics of ion binding, diffusion, and viscoelasticity within a single
380 material layer, trading biological richness for device-level simplicity and
381 manufacturability.⁷¹

382 A common architecture is the ionic gel, in which an electrolyte is immobilized within
383 a polymer scaffold. Because ions move through a crowded network rather than a free
384 solution, relaxation is slowed and conductance lags the applied field.⁷² Fixed charges
385 add a further source of history dependence by transiently trapping counterions and
386 altering local osmotic pressure, while the same redistribution of ions can couple to
387 electromechanical strain so that swelling and conductivity evolve together. The
388 resulting behavior appears as electrical hysteresis, often in the form of a pinched current-
389 voltage loop and, in some materials, a persistent deformation that in turn feeds back on
390 transport (Fig. 6c).⁷²

391 Natural polyelectrolytes provide a clear example of how chemistry and mechanics
392 can become memory.⁷³ In alginate gels, crosslinking is mediated by divalent cations
393 such as Ca^{2+} , so an applied field can drive ion exchange and create spatially
394 heterogeneous crosslink densities (Fig. 6d-f). Because both the ionic profile and the
395 polymer network relax only slowly, regions with distinct mechanical and ionic properties
396 can persist after stimulation, leaving a structural memory that is later read out through
397 changes in ionic conductance. More generally, polysaccharide gels with path-dependent
398 hydration or ionic crosslinking offer a route to purely ionic memory without invoking
399 metallic filaments or electronic charge storage.

400 Denser ionomers provide a complementary pathway in a solid membrane. In



401 Nafion, protons drift through nanometer-scale ionic domains lined with sulfonate groups,
402 and a fraction becomes transiently trapped or stabilized by local hydrogen-bond
403 networks.^{74,75} Slow rearrangement of these ionic clusters makes resistance evolve with
404 voltage history, yielding memristive transport at low bias. Bipolar ion-exchange
405 membranes extend this concept by adding interfacial reaction dynamics: forward bias
406 promotes water dissociation at the junction, whereas recombination proceeds with
407 different kinetics, so the interfacial ionic state carries memory.^{74,75}

408 A major application space in which ionic polymers excel is flexible and wearable
409 electronics. Using gels and polymer electrolytes, researchers have developed iontronic
410 capacitive touch sensors and synaptic transistors for human-machine interfaces, naturally
411 extending to flexible memristive artificial synapses. For example, Zhao *et al.*⁷⁶ reported
412 a flexible all-inorganic ionic polymer-based memristor that exhibited stable synaptic
413 behavior. Although the detailed operating mechanism of this device lies beyond the
414 scope of this discussion, it likely relies on ionically driven internal reconfiguration within
415 an inorganic polymeric matrix to achieve low-voltage, non-volatile resistance modulation.
416 More broadly, such results demonstrate how ionic conduction coupled to slow structural
417 or chemical rearrangements in polymeric systems can support memory effects suitable
418 for neuromorphic functionality.

419 Ionic polymers also allow computation to be coupled to the environment.
420 Humidity-responsive peptide films, for example, gate proton conduction through water
421 uptake, so resistance depends on both electrical history and ambient chemistry.^{77,78} This
422 multifunctionality suggests polymer synapses that sense and learn within the same
423 material, an ability that is difficult to achieve with isolated protein pores or fragile bilayer
424 droplets.

425 In practice, polymer iontronics is defined by a useful compromise. These devices
426 typically operate at low voltage and can retain memory for minutes to hours because ionic
427 and structural relaxation is slow, although switching speeds are often limited by diffusion
428 and viscoelasticity. Their decisive advantage is integration by processing rather than by
429 assembly, in terms of the fact that films can be cast, coated, or printed into dense arrays,
430 positioning ionic polymers as a pragmatic counterpart to the biological systems.

431

432 **3. Solid-state nanofluidic platforms**

433 Having established the role of softness, we next turn to solid-state nanofluidic
434 platforms. Unlike biological synapses or ionic polymer systems, solid-state nanopores
435 and nanochannels are mechanically rigid. Their defining feature is not ductility or
436 deformability, but geometric and chemical stability during operation. At first glance,



437 this rigidity may seem disadvantageous compared with the adaptive softness of neurons

Table 2. Hard nanofluidic systems with memristive ionic dynamics.

System class	Material / fluidic system	Size	Mechanism	Stimulus class	Switching speed	Retention time	Energy consump.
Counterion dynamics ⁸⁶	Track-etched PET double conical nanopores, KCl concentration gradients	Tip diameter ~5–20 nm	Broken symmetry from divalent-ion screening and pH-driven deprotonation	Pulse trains (10 V, 1.0–1.5 s)	~1 Hz	~20 min	NA
Counterion dynamics ⁸⁷	Conical polyimide nanopores, 0.1 M KCl	Tip diameter ~20–50 nm	Voltage-derived transient ion concentration polarization	Pulse trains (2 V, 2–1,000 ms)	1–50 Hz	~40 s	NA
Counterion dynamics ⁹⁴	Tapered microfluidic channel, 10 mM KCl	Channel tip 5 μ m, base 200 μ m, length 150 μ m	Voltage-derived transient ion concentration polarization	Pulse trains (2.5–5 V, 0.75 s)	~1 Hz	~1 s	~1–10 μ J
Space confinement ¹⁰²	Angstrom-scale slit nanochannels (theory)	Slit height ~0.7–1.4 nm	Electric-field-induced ion clustering in Å-scale slits	AC voltage (0.1 V, 100 Hz)	~100 Hz	N/A	N/A
Space confinement ¹⁰³	Active carbon 2D channel, 1 mM CaCl ₂	Channel height ~5 nm	Surface adsorption/desorption-mediated ion transport	Pulse trains (1 V, 10 s)	~0.1 Hz	~hours	N/A
Space confinement ¹⁰⁴	MoS ₂ and hBN 2D nanochannel, KCl, CaCl ₂ , AlCl ₃	Channel height 0.7–2 nm	Transient concentration polarization and ion–ion/surface-charge interactions	Write pulses ~20–60 s	~0.1 Hz	Short (<100 s) and long term (> 3days) memory	N/A
EOF ¹⁰⁵	Immiscible liquid–liquid interface in nanochannels	PDMS nanochannel, 200 nm x 63 nm x 10 μ m	Electroosmosis-derived motion of liquid–liquid interface confined in nanochannels	Pulse trains (4–10 V, 0.5 s)	2 Hz	> 20 min	N/A
Optical ¹⁰⁷	Graphene–MoS ₂ heterojunction nanopore, 1 M KCl	Heterojunction nanopore size ~2–20 nm	Light-induced electron–hole separation in a p–n heterojunction nanopore inducing photovoltage-driven ion pumping	Light pulses (365–1050 nm, 0.2–5 Hz)	Response time 50 ms	N/A	16.3 mW/cm ² per light pulse
Optical ¹⁰⁹	Layered graphene oxide nanochannel	Lamellar graphene oxide nanochannel, spacing ~0.42 nm; length mm-scale	Light illumination driven Na ⁺ migration/ion redistribution in nanochannels	Light pulses (532 nm, 6 mW, 0.2 s)	5 Hz	N/A	~1.2 mJ per light pulse
Optical ¹¹⁰	B ₃ N subnanometer pores, mixed electrolyte (1.0 M KCl + 0.1 M NaCl) (MD simulation)	Subnanometer pores; 16 pores in ~7 nm x 7 nm membrane patch (hBN monolayer)	Light illumination driven Na ⁺ migration/ion redistribution in nanochannels	Pulse trains (0.5 V, 3 ns)	~0.1 GHz	~ μ s	0.1–100 aJ per pulse
In-pore chemistry ¹¹⁷	Conical PET nanopore in PBS+KCl+CoCl ₂	Nanopore tip size 2–7 nm	Voltage-driven nanoprecipitation/dissolution inside a conical nanopore modulating aperture/selectivity	Pulse trains (2 V, 15 s)	Seconds-scale switching	N/A	N/A
In-pore chemistry ¹¹⁸	SiN _x nanopore interfacing MnCl ₂ and PBS	Nanopore size 100–300 nm	Voltage-driven nanoprecipitation/dissolution inside a conical nanopore modulating aperture/selectivity	Pulse trains (0.2–0.8 V, 50 ms)	~20 Hz	>100 s	~0.1 nJ per pulse
EOF ¹¹⁹	SiN _x nanopore membrane decorated with Pd and covered by graphite, 1 M KCl	Nanopore size 100 nm	Voltage-driven mechano-ionic blistering changing atomically thin pore/nanocavity geometry	Pulse trains (1.2 V, 2 s)	>10 Hz	N/A	N/A



438 or ionic polymers. Yet solid-state nanofluidic systems compensate for the absence of
439 mechanical compliance by exploiting field-driven ionic reconfiguration, electrochemical
440 memory, and interfacial phenomena under confinement. Advances in nanofabrication
441 now allow pores to be engineered at dimensions approaching those of biological ion
442 channels, opening transport regimes shaped by ion dehydration, Coulomb blockade and,
443 in some cases, even quantum effects.^{79–82} More importantly, rigidity brings precise
444 fabrication, reproducibility and compatibility with large-scale integration,^{83,84} making
445 solid-state nanofluidics the most realistic route towards mass-produced ionic
446 neuromorphic hardware. Whereas neurons rely on mechanical softness to realize
447 plasticity, solid-state nanofluidic memristors instead harness the electrochemical softness
448 of ionic states. In both cases, memory arises from the delayed relaxation of internal
449 degrees of freedom. In neurons, these include protein conformations and biochemical
450 cascades; in rigid nanopores, they are primarily ionic distributions, hydration states and
451 interfacial configurations. Solid-state nanofluidic memristors can therefore be viewed
452 as rigid scaffolds for wet intelligence: architectures in which ions compute, remember
453 and adapt within mechanically stable confinement.

454 3.1 Counterion dynamics in micro- and nanochannels

455 A central source of memristive behavior in rigid nanochannels is the electric double
456 layer. When a voltage is applied across a permselective nanochannel or nanopore, ions
457 begin to redistribute, creating regions of enriched or depleted ionic concentration (Figure
458 7a).^{85,86} If the voltage is changed before complete equilibration, residual ionic gradients
459 and space-charge distributions from the prior state can persist and modulate subsequent
460 transport, endowing the channel with a memory of its bias history (Figure 7b). Indeed,
461 this mechanism underlies some of the earliest demonstrations of memristive behavior in
462 ionic systems, where slow counterion dynamics in nanopore electric double layers give
463 rise to hysteretic current-voltage responses.⁸⁷ In its simplest form, a fixed-charge
464 conical nanopore rectifies ionic current, and when the bias is swept faster than ionic
465 relaxation, residual depletion and accumulation persist at opposite ends of the pore,
466 producing the pinched I - V hysteresis with inherently frequency dependence, wherein
467 slow voltage sweeps allow ions to equilibrate and eliminate memory, intermediate sweep
468 rates produce strong hysteresis, and extremely fast sweeps yield an almost ohmic
469 response as ionic motion becomes effectively frozen,^{88,89} reflecting the fundamental
470 timescales of ion migration and capacitive charging in nanoscale channels.

471 The same mechanism extends beyond nanometer confinement. Single channels
472 with asymmetric geometry, surface charge or salinity can exhibit ionic rectification^{90,91}



474 and, in some cases, negative differential resistance,^{92,93} because the applied field
475 establishes longitudinal depletion and accumulation regions. Strikingly, memristive

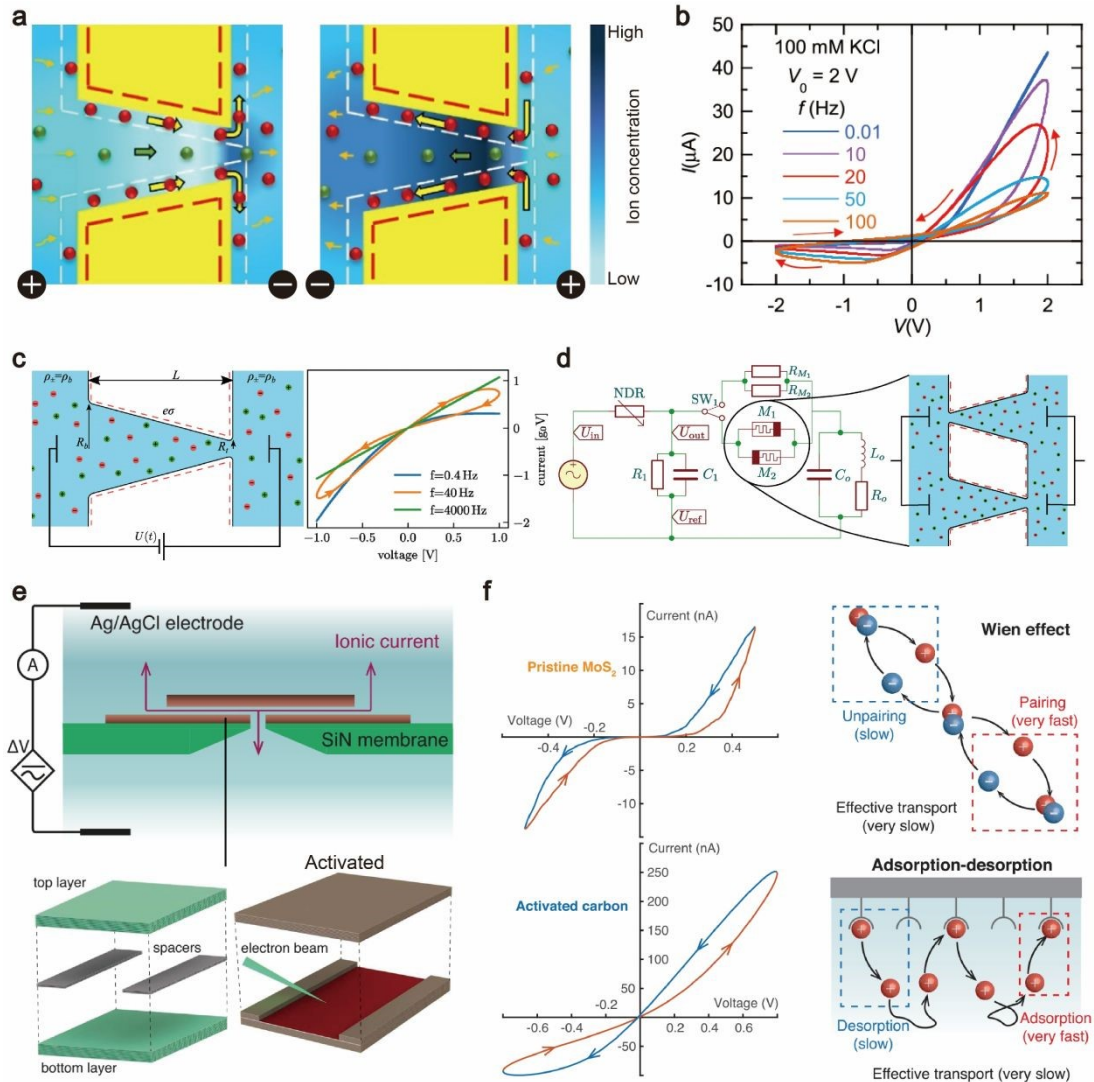


Figure 7. Counterion dynamics- and deep confinement-derived ionic memristors. **a**, Ionic concentration polarization at an asymmetric constriction, where bias-driven enrichment and depletion create a non-equilibrium ionic landscape that relaxes only slowly, imprinting history dependence on the conductance. Adapted with permission from ref. 86. Copyright 2024 American Chemical Society. **b**, Pinched hysteresis loops in the current-voltage characteristics of a multipore conical nanopore membrane under sinusoidal driving, showing the frequency-dependent opening and closing of the memristive window as the drive period approaches the ionic relaxation time. Adapted with permission from ref. 19. Copyright 2023 American Chemical Society. **c**, Minimal conical-pore model highlighting the role of access resistances and permselective enrichment/depletion zones in shaping rectification and hysteresis. **d**, Circuit-level abstraction in which ionic memristors are treated as dynamical elements that can be embedded into neuromorphic signal-processing architectures. Adapted with permission from ref. 94. Copyright 2025 Creative Commons CC BY-NC 3.0. **e**, Two-dimensional nanofluidic channels assembled from layered materials and locally activated to define angstrom-scale transport pathways. **f**, Representative hysteresis in pristine MoS₂ and activated-carbon channels together with proposed microscopic origins of long-lived state variables, including field-enhanced ion-pair dissociation (Wien effect) and adsorption-desorption kinetics under strong confinement. Adapted with permission from ref. 105. Copyright 2023 The American Association for the Advancement of Science.



476 behavior persists even for micrometer-wide channels, where history dependence can be
477 traced to incomplete depletion and delayed re-equilibration of ions within extended
478 space-charge layers upon field reversal.⁹⁴

479 The underlying ion dynamics is set by a diffusion-controlled timescale that can be
480 engineered through geometry. Starting from the coupled Poisson-Nernst-Planck-Stokes
481 equations, the relaxation time is predicted to scale as $\tau \approx L^2/(12D)$ for a channel of length
482 L and ionic diffusivity D (Figure 7c).⁹⁵ The quadratic dependence on L provides a
483 simple design handle: doubling the channel length increases τ by roughly a factor of four,
484 prolonging the lifetime of ionic memory. Channel taper and wall charge further reshape
485 the concentration polarization field⁹⁶⁻¹⁰⁰ and tune the prefactor, offering additional control
486 (Figure 7d). Analytical reductions and finite-element calculations consistently support
487 this diffusive scaling and its sensitivity to geometric and interfacial parameters.⁹⁵

488 This geometric programmability allows to adjust the temporal structure for a target
489 computation. In colloid-filled tapered microchannels that embed a conducting
490 nanochannel network, transient salt concentration polarization yields stable volatile
491 memristors whose retention time can be selected by channel length.¹⁰¹ Exploiting this
492 tunability, individual channels have been used as synaptic elements for reservoir
493 computing, where their nonlinear, history-dependent conductance transforms temporal
494 voltage pulse trains into separable states. In a benchmarking task, time-series encodings
495 of handwritten digits were classified with a simple readout layer, achieving performance
496 comparable to solid-state dynamic memristor reservoirs.¹⁰¹

497 Together, even structurally rigid channels can display memristive ion transport
498 because counterions and co-ions relax on finite timescales after the electric field is
499 changed. In these purely electrostatic devices, memory is encoded in the slow build-up
500 and decay of space charge, producing pinched current. Such systems have provided a
501 clean starting point for ionic memory and have already been assembled into simple
502 networks that execute logic and computing functions. The next step is to move beyond
503 volatile, single-mechanism behavior towards non-volatile switching and multilevel states,
504 while retaining manufacturable, parallel integration. Counterion dynamics in hard
505 nanochannels, therefore, remains a foundational route to nanofluidic memristors as a
506 direct analogue of early electronic memristor concepts, but governed by mobile ions and
507 the physics of the electric double layer.

508 From a design perspective, channel geometry, ion concentration and electric field
509 strength are best treated not as independent parameters but as coupled variables.
510 Shrinking a channel does more than shorten the transport path: it increases the surface-
511 to-volume ratio, strengthens interfacial charging, and amplifies the effects of adsorption



512 and depletion. Increasing electrolyte concentration, meanwhile, reduces the Debye
513 length and can suppress hysteresis, yet under sufficiently strong driving it can also
514 intensify concentration polarization and thereby prolong non-equilibrium ionic states.
515 Device optimization therefore requires the co-design of geometry, electrolyte
516 environment and electrical protocol, because retention, switching amplitude and volatility
517 emerge from their combined action.

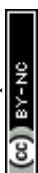
519 **3.2 Ångström confinement and correlated ion states**

520 As nanofluidic channels approach molecular dimensions down to Ångström-scale
521 slits only a few water molecules thick, ion transport can no longer be described as a
522 weakly perturbed continuum.¹⁰² Strong ion-surface interactions, partial dehydration,
523 and enhanced ion-ion correlations create metastable ionic configurations whose
524 rearrangement can be slow. As a result, conductance can depend on stimulus timing and
525 bias history, yielding memory effects even in mechanically rigid, crystalline channels.

526 A first clear route to such memory was articulated through theory and molecular
527 simulations of monolayer electrolytes confined in sub-nanometer slits.^{103,104} In this
528 regime, an applied electric field promotes the formation of correlated ionic clusters, while
529 reversing the field then requires these structures to dissolve and reform, producing
530 hysteretic, history-dependent conduction in an otherwise static channel. In silico,
531 pairing such elements could even yield neuronal-like excitability and spontaneous voltage
532 spiking, illustrating how confinement-enhanced correlations can be promoted from
533 molecular self-assembly to dynamical primitives for computing.¹⁰⁴

534 Building on this conceptual framework, experiments pushed Ångström-scale
535 confinement toward device-level programmability by exploiting the same two-
536 dimensional slit geometry with different wall chemistries (Figure 7e). In pristine MoS₂
537 channels, conductance could be potentiated by one voltage polarity and depressed by the
538 opposite, yielding bipolar memristive updates reminiscent of bidirectional synaptic
539 weight changes.^{104,105} Activated-carbon channels, by contrast, more often showed
540 unipolar and volatile memory, relaxing back toward a baseline after the stimulus is
541 removed. Both the loop polarity and the memory lifetime could be tuned by
542 confinement and electrochemistry, including channel height (sub-10 nm), salt conditions,
543 and pH. A compact scaling argument relates the characteristic memory time to the
544 diffusive transport time multiplied by a Dukhin-number factor that captures the strength
545 of surface adsorption, making geometry a direct knob for programming ionic timescales
546 (Figure 7f).¹⁰⁵

547 Most recently, the same platform has been shown to access the full range of



548 nanofluidic memristor loop styles.¹⁰⁶ By varying electrolyte composition, pH, driving
 549 frequency, channel material and channel height, it was demonstrated that all four
 550 canonical memristor types can emerge in two-dimensional nanochannels, including two
 551 loop styles that had not previously been observed experimentally. A minimal model that
 552 combines ion-ion interactions with surface charge and entrance depletion reproduced
 553 these transitions and clarified how the same device family can be steered between volatile
 554 and non-volatile regimes. In this programmable setting, synapse-inspired dynamics
 555 such as short-term depression with recovery arise as a direct consequence of controlled

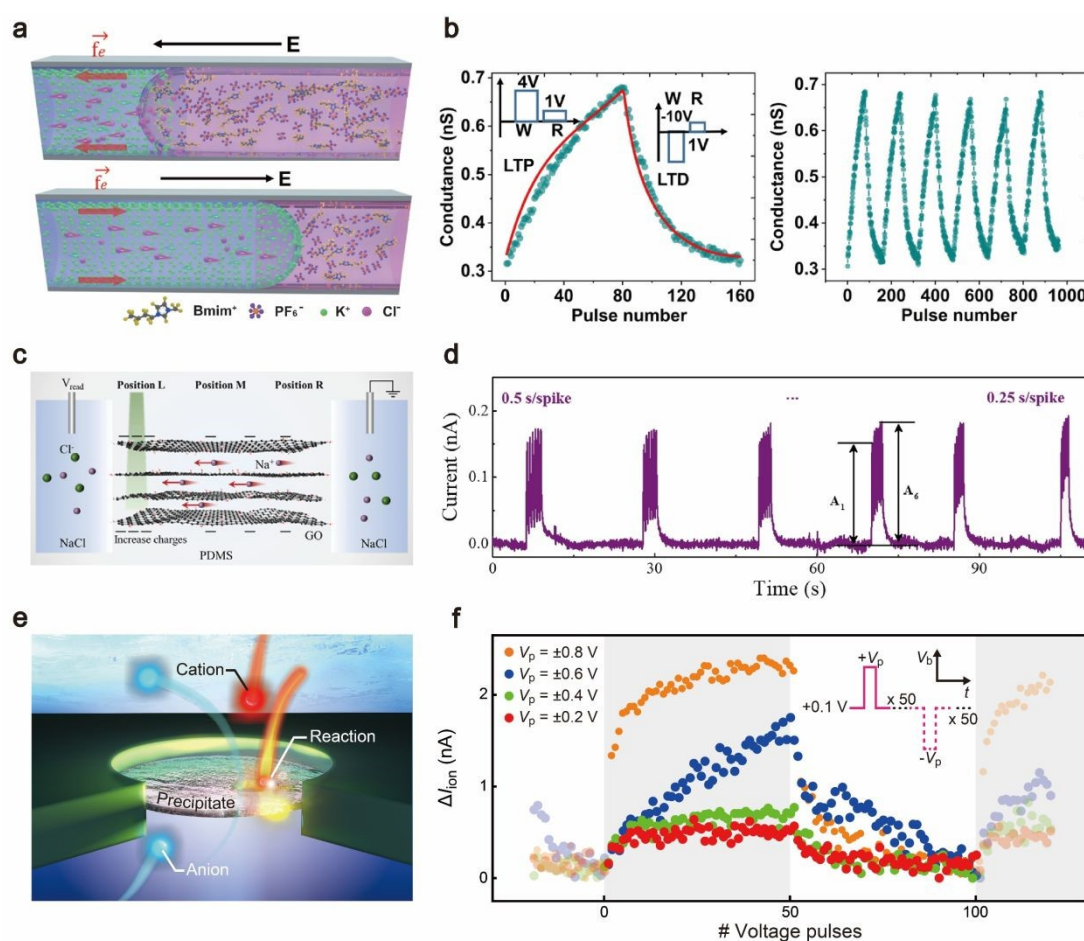


Figure 8. Stimulus modalities for programming hard nanochannels. **a-b**, An interfacial memristor formed by a nanochannel that bridges an aqueous KCl phase and an immiscible room-temperature ionic liquid (BmimPF6), where voltage-driven displacement of the liquid-liquid interface tunes ionic transport and supports analogue conductance updates. Adapted with permission from ref. 107. Copyright 2019 American Chemical Society. **c-d**, Optogenetics-inspired nanofluidic artificial dendrite based on PDMS-coated layered graphene oxide. Localized light illumination generates an internal potential difference that drives Na^+ migration along lamellar nanochannels, producing position-addressable response currents and reconfigurable spiking. Adapted with permission from ref. 111. Copyright 2025 John Wiley and Sons. **e-f**, Chemically gated pores in which transmembrane bias controls in-pore precipitation/dissolution chemistry, enabling pulse-programmable conductance states. Adapted with permission from ref. 120. Copyright 2025 Creative Commons CC-BY-NC-ND.



556 ionic relaxation.¹⁰⁶

557 These advances recast Ångström-scale slits as a chemically programmable substrate
558 for ionic memory, where the internal state is encoded in correlated ion organization and
559 interfacial kinetics rather than in simple double-layer charging. The ability to co-design
560 polarity, volatility, and relaxation time through geometry and electrolyte chemistry
561 provides a direct route from nanoscale physics to neuromorphic function, and suggests
562 that arrays of atomic channels could serve as ultralow-power analogue elements for
563 adaptive information processing.

564

565 **3.3 Electrohydrodynamic memristors in confined channels**

566 Another distinct mechanism for ionic memristors in hard nanofluidic systems
567 involves fluid flow and moving interfaces. In these devices, memory resides not only
568 in the ionic distribution but also in the physical position of a fluid boundary or meniscus
569 that shifts under electrical bias. The operating principle typically relies on
570 electroosmotic flow or electrowetting, whereby an applied voltage drives liquid to
571 advance or recede within a channel, thereby modulating the conductive pathway.
572 Hysteresis emerges when the interface position depends on the history of the applied
573 voltage. For instance, a higher bias may displace the interface further, while upon
574 voltage reduction or reversal, the interface may not immediately return to its initial
575 position because of capillary forces or viscous dissipation. The resulting memristive
576 response is governed by the fraction of the channel occupied by the conductive fluid
577 relative to a nonconductive phase, which acts as the internal state variable.

578 A seminal example is the nanofluidic memristor based on an electrolyte-ionic liquid
579 interface.^{107,108} The device consisted of a nanochannel in PDMS connecting two
580 reservoirs, with one filled with a KCl solution and the other with a hydrophobic ionic
581 liquid immiscible with water (Figure 8a). At equilibrium, the two fluids meet at the
582 center of the channel, forming a well-defined meniscus. Applying a voltage induces
583 competition between electroosmotic flow and interfacial tension, with one polarity
584 advancing the aqueous-ionic liquid interface and the opposite polarity retracting it. The
585 large contrast in ionic conductivity between the ionic liquid and the aqueous phase causes
586 the channel conductance to depend on their relative occupancy. At intermediate states,
587 the channel behaves as a variable resistor composed of a high-conductivity electrolyte
588 segment in series with a low-conductivity ionic liquid segment. The interface motion
589 was hysteretic, with viscous drag and meniscus energy barriers, including contact-angle
590 hysteresis at the walls, preventing immediate relaxation after voltage removal or reversal.
591 Accordingly, voltage sweeps exhibited pinched hysteresis loops, and the device could be



592 programmed into multiple conductance states using voltage pulses of different
593 magnitudes (Figure 8b). The memristor showed excellent endurance and retention, as
594 the negligible vapor pressure of the ionic liquid prevented drying or significant interfacial
595 drift over time. In effect, the system behaves like a nanoscale electrical piston that
596 drives a fluid boundary back and forth, with the piston position serving as the memory
597 state.^{107,108}

598 The hydrodynamic approach is appealing in that it leverages the inherently analog,
599 continuum behavior of fluids. In principle, the meniscus position, and thus the device
600 conductance, can assume a continuous range of values, enabling multilevel memory and
601 gradual weight updates for neuromorphic computing. The approach embodies a trade-
602 off between speed and retention: slow, inertial fluid motion limits switching speeds but
603 enables nonvolatile memory by pinning the interface without power. This nonvolatility
604 arises because, once displaced, the ionic liquid-aqueous interface remains pinned by
605 capillary forces until a sufficiently large reverse bias is applied to overcome the pinning
606 barrier. This is analogous to a mercury droplet in a capillary, which moves under
607 pressure but remains pinned by surface tension until an opposing threshold is exceeded.
608 Although fluid motion and interfacial deformation can dissipate energy, operation is often
609 quasi-static, allowing the energy per switching event to remain low when distributed over
610 time. Hydrodynamic memristors therefore occupy a unique regime in which mechanical
611 and ionic degrees of freedom intersect.

613 3.4 Optical programming and readout

614 Light offers a particularly clean handle for programming nanofluidic memristors.
615 Unlike electrical gating, which requires dedicated wiring and electrodes for each element,
616 optical stimuli can be delivered remotely, patterned in space and multiplexed in time. In
617 optically gated devices, photons act as write pulses that reshape the ionic state though
618 generating photovoltages, redistributing surface charge, or imposing local
619 thermal/chemical gradients, while the resulting ion current provides an immediate read.
620 This sensory-computing coupling echoes optogenetics in biology, although the state
621 variable is not a protein conformation but the evolving distribution of ions and hydration
622 shells within nanometer confinement.

623 Niu et al.¹⁰⁹ demonstrated a minimalist route to optical control by embedding a
624 semiconductor heterojunction into a single nanopore. Upon illumination, the junction
625 generated an additional photovoltage (tens of millivolts under their conditions),
626 effectively turning the nanopore into a self-biased ionic pump. Under steady electrical
627 bias, the ion current increased under light and tracked optical on-off modulation with a



628 response time of about 50 ms, consistent with photocarriers creating an internal field that
629 adds to, or subtracts from, the applied bias and therefore shifts the concentration-
630 polarization state in and around the nanopore.¹⁰⁹

631 Wang and colleagues¹¹⁰ built an optically modulated nanofluidic ionic transistor
632 using a metal-organic framework membrane grown within a porous anodic alumina
633 template. The framework is intrinsically negatively charged, and illumination generates
634 electron-hole pairs that transiently increase the negative surface charge of the MOF
635 crystallites, drawing additional cations into the tortuous pores. This photoinduced ion
636 accumulation produces excitatory post-synaptic current-like transients, paired-pulse
637 facilitation, and a pulse-history-dependent transition from short-term to longer-lived
638 plasticity, as the relaxation time for cation release competes with the optical pulse interval.
639 By using trains and patterns of light spikes to tune synaptic weight, the device reproduced
640 higher-level behaviors such as learning-experience, Pavlovian associative learning, and
641 optical Morse-code encoding/decoding, illustrating how optical addressability can be
642 pushed beyond switching toward information processing within a single ionic element.¹¹⁰

643 An optogenetics-inspired design pushed optical addressability from a single pore to
644 a dendrite-like nanofluidic element by embedding layered graphene oxide (GO)
645 nanochannels in an elastomer (Figure 8c).¹¹¹ Here, light creates an electric potential
646 difference between illuminated and dark regions of the GO, driving directional Na⁺
647 migration and producing pronounced ionic photocurrents. Because the optical input can
648 be applied at different positions and in multiple spots, the device naturally supports
649 distributed integration. It reproduced spatial summation with both sublinear and
650 superlinear regimes, and it expressed temporal plasticity under trains of light spikes,
651 including paired-pulse facilitation as well as spike-duration- and spike-rate-dependent
652 conductance modulation. By combining spatiotemporal optical stimuli with ionic
653 readout, the authors further demonstrated neuromorphic perception and a reflex-like
654 output in a soft robotic actuator, emphasizing that optical control can move nanofluidic
655 memristors beyond two-terminal switching toward computation within a single fluidic
656 element (Figure 8d).¹¹¹

657 Mechanistic insight from atomically thin membranes provides a complementary
658 perspective on how optical write operations might be converted into durable ionic
659 memory. Molecular dynamics simulations of a subnanoporous two-dimensional
660 membrane showed that synaptic-like plasticity can arise from competitive bicationic
661 transport, where strongly adsorbed Na⁺ transiently blocked permeation pathways that
662 otherwise conducted K⁺, and voltage spikes desorbed Na⁺ to potentiate permeability.¹¹¹
663 Because adsorption and desorption introduce distinct time constants, the same structure



664 can, in principle, interpolate between volatile and longer-lived states by tuning ion species,
665 concentration, and stimulus waveform. Notably, the estimated energy cost per
666 conductance update was in the attojoule range, highlighting why optical actuation,
667 capable of delivering localized write pulses without parasitic leakage, may be especially
668 attractive for scaling to large arrays. These studies suggest a general design rule for
669 optical nanofluidic memristors: use light to impose a controllable internal photoelectric
670 bias or a local thermal perturbation¹¹³ that steers ion occupancy in confined junctions, and
671 exploit the ensuing relaxation dynamics to encode computation in the ionic state.

672

673 **3.5 In-pore chemistry and reaction-driven memory**

674 In-pore chemistry offers a direct route to ionic memory, where the internal state is
675 encoded in the local chemical composition and phase within the confined pore volume.
676 Under transmembrane bias, electromigration and concentration polarization bring
677 reactants into contact and drive reversible transformations, most prominently
678 precipitation and dissolution, that open or obstruct the conduction pathway. Because
679 the state evolves through reaction-diffusion kinetics rather than instantaneous
680 electrostatics, the characteristic response time and retention can be tuned over orders of
681 magnitude by pH, reactant concentration, multivalency, temperature, the stimulus
682 waveform, and the confinement geometry. In practice, these levers allow the same
683 physical platform to be pushed towards volatile short-term plasticity or long-lived, quasi-
684 nonvolatile memory.

685 The origins of this concept can be traced to early observations of current instabilities
686 caused by nanoconfined reactions. When two solutions mix within a nanopore, a
687 transient precipitate was shown to repeatedly form and clear, producing oscillatory ionic
688 currents.¹¹³ The resulting nanoprecipitation in a nanopipette tip was demonstrated to be
689 actively created and eliminated by switching the voltage polarity, enabling controlled
690 blockage and recovery.¹¹⁵ The earliest stages of nucleation and crystal growth through
691 transient current blockades were tracked using a nanopipette platform.¹¹⁶ Similar
692 features were also observed from slow Ca²⁺ binding to charged pore walls.¹¹⁷ These
693 studies established that field-driven transport creates a reactive mixing zone whose
694 evolving chemistry becomes the memory variable.

695 Liu et al.¹¹⁸ demonstrated a complementary regime in conical nanopores, where
696 reversible CaHPO₄ nanoprecipitation at the pore tip generates pronounced pinched
697 hysteresis loops. Here, the memristive characteristics are set by precipitation and
698 dissolution kinetics and can be tuned by CaHPO₄ concentration, voltage amplitude, and
699 scan rate. Under pulsed stimulation, the conductance relaxes back once the stimulus is



700 removed, yet remains robustly resettable, resembling short-term plasticity in biological
701 synapses. This chemistry-driven volatility is attractive for temporal filtering and
702 adaptive gain control, where forgetting is a feature rather than a limitation.¹¹⁸

703 Cho et al.¹¹⁸ moved beyond hysteresis in the time-averaged conductance by encoding
704 memory in the frequency of ion-current oscillations. In their conical nanopore, dynamic
705 formation and removal of nanoprecipitates produce stochastic switching between high-
706 and low-conductance states. The oscillation statistics depend on the direction of the
707 voltage scan and on prior stimuli, appearing as a history-dependent open-state probability.
708 Under programmed pulse trains, the device exhibits synaptic-like long-term potentiation
709 and depression, consistent with delayed precipitate formation and clearing, together with
710 slower drift in the effective space charge. A reduced description in which precipitation
711 is limited by the cation arrival rate captures the emergence of oscillations and their bias-
712 history dependence.¹¹⁹

713 A distinct solid-state implementation that spatially separates anionic and cationic
714 reactants across the membrane.¹²⁰⁻¹²² One reservoir contains phosphate-buffered saline,
715 whereas the opposite side supplies mobile cations from chloride salts (Figure 8e). The
716 applied voltage drives these cations into the nanopore, where they encounter phosphate
717 and reversibly form metal-phosphate precipitates that close the pore under one polarity
718 and dissolve under the other. This voltage-gated in-pore chemistry yields extreme
719 rectification and enables memristive switching at sub-nanowatt power (Figure 8f).
720 Because the gate is a reaction product, the dynamic response is, in principle, engineerable:
721 pH controls phosphate speciation and solubility, reactant concentrations set
722 supersaturation and nucleation rates, and the cation identity and temperature tune
723 dissolution kinetics. These parameters offer a practical route to tune the balance
724 between rapid, volatile switching and slowly relaxing states with extended retention.^{45,119}

725 In-pore chemistry memristors expand nanofluidic memory beyond purely
726 electrostatic hysteresis. By co-designing confinement with reaction kinetics, they
727 provide a chemically programmable memory kernel whose volatility, retention and
728 learning dynamics can be tuned using standard chemical control parameters.

729

730 **4. Hybrid architectures: rigid scaffolds with soft ionic states**

731 We now turn to hybrid architectures, in which rigid microfabricated scaffolds are
732 deliberately paired with soft ionic elements. Their appeal is a clear functional split: the
733 hard framework delivers geometric precision and addressability, while the soft phase
734 introduces slow internal state variables, chemical selectivity and analogue adaptability.

735 Soft-hard hybrid nanofluidic systems combine rigid nanostructures, such as solid-



736 state nanopores or nanochannels, with soft ionic components including polymers, gels,
737 biomolecules, and fluids. Such hybrid architectures are designed to balance scalability,
738 reproducibility, and integration offered by hard materials with the adaptive, history-
739 dependent ionic dynamics characteristic of soft matter. From a neuromorphic
740 standpoint, hybrid systems are especially attractive as they reflect the multiscale
741 architecture of biological neural systems, where rigid structural elements coexist with soft,
742 dynamically reconfigurable components. In artificial systems, this division of labor
743 enables a fixed, manufacturable geometry while preserving fluid, reconfigurable degrees
744 of freedom that underpin learning and memory.

745 In hybrid nanofluidic memristors, a solid-state scaffold fixes the transport geometry,
746 providing well-defined channel dimensions, alignment, and connectivity. Such
747 scaffolds can be fabricated using top-down nanofabrication methods compatible with
748 wafer-scale processing, enabling high device uniformity and large-area array integration.
749 Within this rigid framework, soft ionic components like ionic gels and biomolecules
750 introduce internal state variables that evolve in response to electrical, mechanical, or
751 chemical stimulation. Examples include polymer brushes grafted inside nanopores,
752 ionic gels filling nanochannels, or biomolecules tethered to pore walls. These soft
753 components modulate the ionic pathway through swelling, ion binding, conformational
754 changes, or phase transitions while preserving their macroscopic geometries. As a result,
755 device conductance becomes history-dependent not through permanent changes in
756 channel geometry, but rather through memory encoded in the ionic microenvironment.

757 Soft-hard hybrid systems offer a key advantage by decoupling mechanical stability
758 from functional plasticity. In purely soft systems, memory formation is often
759 inseparable from mechanical deformation, which can lead to drift, fatigue, and limited
760 reproducibility over extended operation. By contrast, purely hard systems typically rely
761 on ionic redistribution or chemical transformations to achieve plasticity, which can
762 restrict the diversity and adaptability of functional responses. Hybrid architectures
763 circumvent both limitations. The rigid scaffold absorbs mechanical stress and preserves
764 long-term structural integrity, while the soft component remains free to reorganize
765 internally and encode memory. From a neuromorphic perspective, this feature can be
766 similar to that in biology, where relatively stable axonal and dendritic scaffolds coexist
767 with synapses whose efficacy is continually re-tuned by molecular reorganization. Such
768 decoupling is particularly advantageous for long-term operation and training stability in
769 neuromorphic hardware, as the learning element can undergo repeated adaptation without
770 degrading the underlying device architecture.

771 Hybrid systems also naturally exhibit multiple memory timescales, a defining



772 feature of biological cognition. Rapid ionic redistribution within the liquid phase gives
773 rise to short-term plasticity, whereas slower processes, including ion binding, polymer
774 relaxation, and reversible chemical reactions, govern long-term memory retention.
775 Because these processes occur within a confined geometry defined by the solid scaffold,
776 they can be precisely tuned through design parameters such as pore diameter, pore length,
777 polymer density, grafting length, or electrolyte composition. This tunability potentially
778 enables hybrid devices to emulate a broad spectrum of synaptic behaviors, ranging from
779 volatile, stimulus-dependent responses to stable, non-volatile memory states. In
780 neuromorphic computing, such multiscale plasticity is essential for implementing
781 learning rules that require both transient adaptation and persistent weight updates,
782 analogous to short-term facilitation and long-term potentiation in biological synapses.

783 In this section, we examine several representative classes of soft-hard hybrid
784 nanofluidic systems, including ionic gel-filled nanopores, polymer brush-functionalized
785 nanochannels, and other hybrid combinations. We emphasize how the interplay
786 between mechanical rigidity and softness gives rise to memristive functionality, and how
787 such designs address key challenges such as device stability, reproducibility, and
788 integration density.



789

Table 3. Soft/hard hybrid systems with ionic memory.

System class	Material / fluidic system	Size	Mechanism	Stimulus class	Switching speed	Retention time	Energy consump.
Droplet/ microchannel ⁵⁴	Liquid-liquid interface microdroplet memristor in a microfluidic chip	1.5 mm long droplet	Voltage-driven droplet penetration into a microwell blocking/unblocking ion transport	Spike trains (10 V, 0.1 s); temperature used to modulate phase behavior	0.025–2.5 Hz	~200 s	N/A
Ionic gel/ microchannel ¹²⁴	PDMS microchannels hosting bipolar polyelectrolyte gels, 10 mM KCl	Microchannel ~2 mm x ~500 μ m; P- and N-gel lengths ~1 mm each	Voltage-derived changes in depletion/accumulation zones of bipolar polyelectrolyte gels	Pulse trains (1 V, 4 s)	~0.01 Hz	200–4,000 s	N/A
Polymer blush/ nanopore ¹³⁰	Conical polyimide nanopore with dual-responsive PNIPAAm-co-AAc polymer brushes, 0.1 M KCl	Tip size ~25 nm; base opening ~1.2–1.5 μ m	Stimuli-responsive conformation/charge state modulation of polymer brushes in channel	Environmental pH (3.6–9.4) and temperature; electrical I–V probing (\pm 500 mV)	pH-induced rectification changes typically in minutes	N/A	N/A
Polymer brush/ nanopipette ¹³⁵	Glass nanopipette modified with polyimidazolium brush; 10 mM NaCl	Tip size ~150 nm	Polyelectrolyte-confined ions undergoing strong ion-polymer interactions and slow reorganization	Environmental pH (3.6–9.4) and temperature; electrical I–V probing (\pm 500 mV)	pH-induced rectification changes typically in minutes	~500 ms	~1 pJ per pulse
Ionic liquid/ micropipette ¹³⁶	PimB-modified glass micropipette interfacing $K_3Fe(CN)_6$ and KCl	Tip size ~3 μ m	Adsorption/desorption of ferricyanide switching surface charge and ionic selectivity/EOF in nanochannels	DC voltage 3 V	Oscillatory spiking: period ~4.02 s (~0.31 Hz); frequency tunable up to ~18.7 Hz	Volatile/self-reset	N/A
Liposome/ nanopore ¹⁴¹	SiN_x solid-state nanopore gated by nanoparticles/liposomes	Nanopore size 115 nm, liposome size hundreds nm	Nanoparticle trapping/release inside a nanopore changing effective aperture/resistance	Opening response ~1.2 ms; closing response down to ~0.3 s	N/A	~10 nJ	N/A



790 4.1 Gel-filled nanopores and ionogels

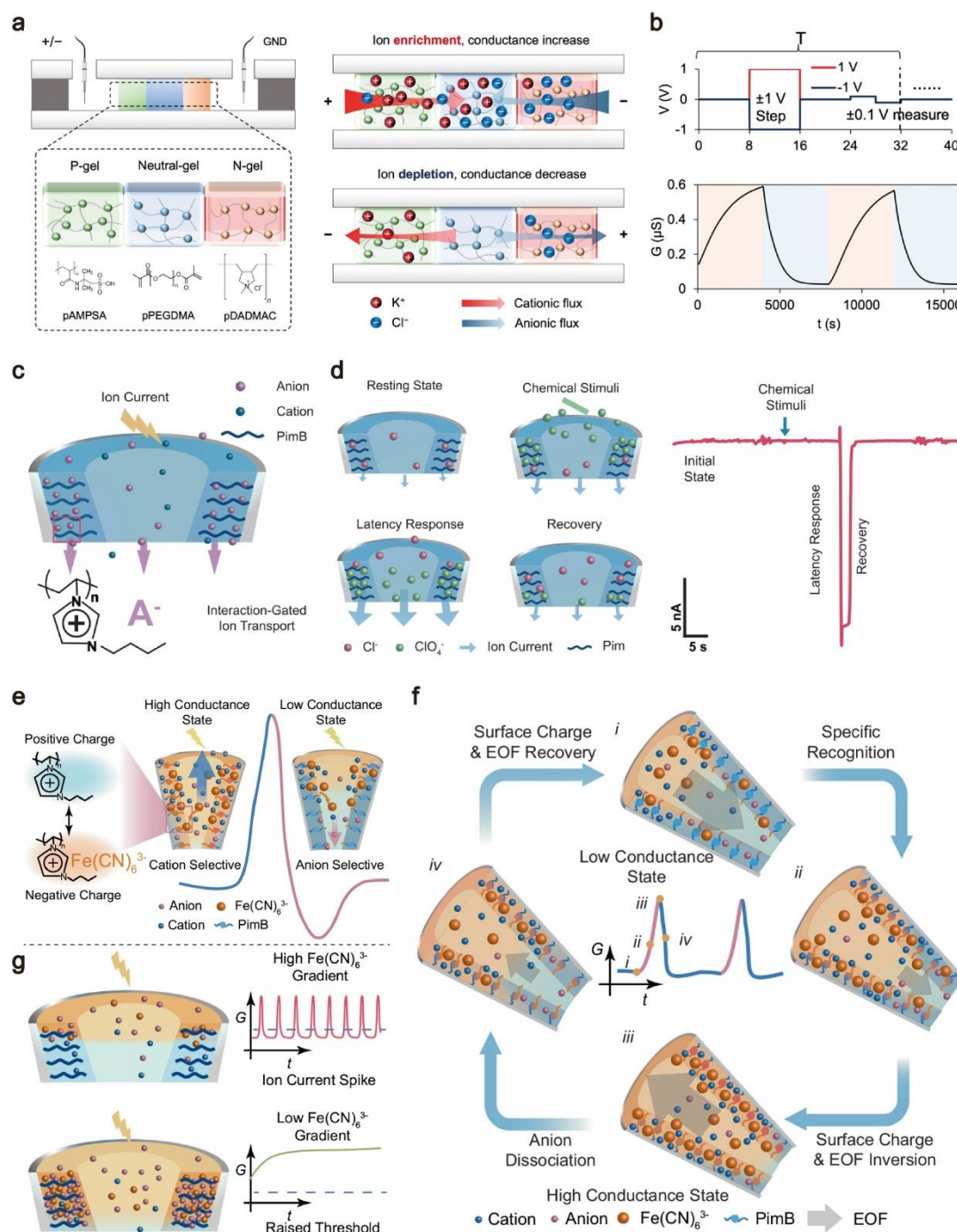


Figure 9. Soft/hard hybrid fluidic systems carrying ionic memory into device-scale functions. **a**, Architecture of an iontronic memristor in which a three-layer bipolar polyelectrolyte-gel stack. **b**, Volatile-to-stable conductance dynamics under step programming and low-amplitude readout. Adapted with permission from ref. 124. Copyright 2024 Creative Commons CC-BY 4.0. **c-d**, A polyelectrolyte-confined fluidic memristor converting molecular/ionic interactions into a history-dependent ionic conductance. Adapted with permission from ref. 135. Copyright 2023 American Association for the Advancement of Science. **e-f**, Mechanistic cycle for autonomous spiking in a nanofluidic oscillating neuron. **g**, Representative ion-current spike trains controlled by chemical gradients, showing repetitive firing and threshold modulation. Adapted with permission from ref. 136. Copyright 2025 Creative Commons CC-BY-NC.



791 One straightforward hybrid strategy involves filling or coating a solid-state nanopore
792 or nanochannel with an ionic gel, such as a crosslinked polyelectrolyte or polymer
793 electrolyte. In this configuration, the solid substrate, typically silicon, glass, or a
794 mechanically robust polymer such as polyethylene terephthalate (PET), defines the
795 channel geometry and ensures mechanical integrity, while the embedded ionic gel
796 provides a continuous, non-volatile ionic medium whose internal dynamics can encode
797 memory. The gels can be patterned at nanometer length scales, for instance, through
798 localized photopolymerization within confined cavities, making them compatible with
799 dense integration. They also mitigate practical issues associated with liquid electrolytes,
800 including evaporation, nanobubble formation, and fluid displacement. In effect, the gel
801 functions as a soft, adaptive core confined within a rigid nanofluidic shell, combining
802 structural stability with dynamic ionic functionality.

803 A representative example is a track-etched PET membrane containing a conical
804 nanopore that is filled with a salt-doped polyacrylamide hydrogel. In this hybrid structure,
805 the conical nanopore provides a rigid, well-defined transport geometry, while the
806 hydrogel introduces a soft, ionically active medium within the pore. Early work
807 demonstrated that ionic current rectification in such conical nanopores is preserved after
808 gel filling and that the gel can actively modulate the ionic response.¹²³ Extending this
809 concept to memristive behavior becomes possible when the gel is made stimulus-
810 responsive. For instance, if the gel contains charged functional groups, a strong electric
811 field can locally deplete counterions and drive electro-osmotic water transport, leading to
812 partial gel contraction. Upon reduction or reversal of the field, the gel does not
813 instantaneously re-swell because of its viscoelastic relaxation, leaving the pore transiently
814 more open or more obstructed than its initial state. This delayed swelling-deswelling
815 cycle introduces a history dependence in the conductance, giving rise to hysteresis in the
816 current-voltage characteristics. In this way, the internal relaxation dynamics in the soft
817 matrix act as the memory variable, while the rigid nanopore confines and stabilizes the
818 overall device geometry.

819 A more sophisticated realization of this concept is embodied in cascade hetero-gated
820 gel systems for ionic modulation (Figure 9a).¹²³ This approach envisions stacking or
821 patterning multiple gels with distinct ionic properties within a single nanofluidic channel.
822 Each gel layer functions as a history-dependent ionic gate, whose conductance evolves
823 according to its own internal dynamics. For example, one layer may slowly accumulate
824 protons and become more conductive under repeated stimulation, whereas another unit
825 may preferentially expel ions or undergo partial deswelling, thereby reducing
826 conductance. Arranged in series, therefore, these layers offer dynamically coupled



827 barriers to ion transport, giving rise to complex hysteresis and rich temporal responses
828 (Figure 9b).¹²⁴ By confining the gels within a rigid channel, the overall geometry
829 remains fixed, so that gel reconfiguration affects ionic pathways rather than deformation.
830 From a neuromorphic perspective, such cascade architectures resemble multilayer
831 synapses, in which distinct molecular processes operating on different time constants
832 jointly regulate signal transmission and plasticity.

833 Ionic compositions can be engineered to tailor the dynamic ion transport
834 characteristics. In this context, polyelectrolyte gels confined within nanopores have
835 been explicitly highlighted as a promising platform for ionic memristors.¹²⁵ Their
836 intrinsic nonlinearity, arising from ion-polymer interactions and swelling dynamics,
837 naturally lends itself to memristive behavior. Furthermore, because the gels can host
838 high concentrations of mobile charge, they enable relatively large ionic currents at low
839 bias, easing impedance matching with electronic circuits compared with highly dilute
840 liquid electrolytes. Experimental support for this concept comes from work¹²⁴
841 demonstrating that filling a micropipette tip with a fixed-charge polyelectrolyte gel
842 produced inverted ionic current rectification and could mimic synaptic neurotransmitter
843 release. Although this system was initially explored as a chemical delivery probe, the
844 underlying mechanism could be extended to memristive operation. In particular, if the
845 gel were engineered to retain ionic composition or charge distribution after stimulation,
846 for example, through multicomponent ion doping or slow relaxation kinetics, the same
847 architecture could encode memory in its transport response.¹²⁶

848 Filling nanofluidic channels with gels also offers clear advantages for scalable
849 integration. Arrays of nanopores can be fabricated on a single chip and subsequently
850 filled in a single step by spin-coating or vacuum infiltration of a pre-gel solution, followed
851 by curing. This approach is substantially simpler than individually addressing each pore
852 with microfluidic plumbing and effectively solidifies the fluidic architecture into a
853 mechanically robust device. The principal trade-off is a reduction in ionic mobility,
854 since diffusion coefficients in gels are typically one to several orders of magnitude lower
855 than in free solution, depending on polymer density and crosslinking.¹²⁷ However, for
856 many neuromorphic computing tasks, where integration, memory retention, and analog
857 weight evolution are more critical, such moderate operating speeds would be
858 acceptable.¹²⁸

859 Ionic gel-filled nanopores represent a compromise between the functional richness
860 of liquid-based systems and the reliability of solid-state devices. They can reproduce
861 key behaviors of purely fluidic architectures, such as threshold ion depletion and
862 interfacial wetting transitions, while offering substantially improved mechanical stability



863 and compatibility with large-scale integration. Challenges remain, including achieving
864 homogeneous gel filling in ultrasmall pores, avoiding bubbles or void formation, and
865 precisely controlling gel chemistry at the nanoscale. Nonetheless, continued advances
866 in nanofabrication, polymer synthesis, and in situ curing strategies are likely to mitigate
867 these limitations.

868

869 **4.2 Polymer-brush nanochannels**

870 A particularly elegant hybrid approach involves incorporating polymer brushes,
871 consisting of densely tethered polymer chains, on channel walls. Instead of filling the
872 entire space, a polymer brush coating on the surface enables dynamic tuning of the
873 effective size, charge, and ionic selectivity.^{129,130} Furthermore, polymer brushes are
874 known to undergo conformational changes depending on the ionic environment, solvent
875 quality, and pH.¹³¹ They can also trap and release counterions in a hysteretic manner,
876 for example when the brush contains multiple charge states or segments with differing
877 ionic affinities.^{132,133}

878 A notable example is the polyelectrolyte brush-confined ionic memristor,^{134,135}
879 consisting of a grafted layer of polyimidazolium chains inside a glass nanopipette (Figure
880 9c). These brushes carry positive charges along their backbone, attracting anions.
881 When a voltage was applied, the brush region could load up with anions, creating a high
882 conductance state. Upon bias reversal, delayed anion release from the brush preserved
883 elevated conductance, resulting in memristive hysteresis. In addition to synaptic
884 functions, the device uniquely enabled chemical-electrical signal transduction, potentially
885 allowing an artificial chemosensitive synapse for converting a chemical input into an
886 electrical memristive signal (Figure 9d-g). This example highlights a broader strength
887 of brush-filled nanochannels through their rich chemical tunability. Polymer brushes
888 can be engineered with functional groups that selectively respond to specific
889 biomolecules or neurotransmitters.¹³⁶ For example, boronic acid-functionalized
890 brushes can reversibly bind glucose, with transient concentration changes modulating
891 conductance and imprinting a temporary chemical memory. Such chemically induced
892 plasticity opens a route to devices that adapt in response to chemical signals or rewards,
893 analogous to neuromodulation in biological neural systems, where neurotransmitters such
894 as dopamine dynamically regulate synaptic strength.^{135,137}

895 Another advantage of polymer brushes is their ability to respond across multiple
896 timescales. At the molecular level, brushes can polarize extremely rapidly under local
897 electric fields, as ions redistribute around individual polymer chains on nanosecond
898 timescales. Concurrently, collective processes such as brush collapse or swelling unfold



899 much more slowly, often over seconds. As a result, a brush-filled nanopore can exhibit
900 both fast, transient changes in ionic current and slower, adaptive drifts in conductance.
901 This intrinsic separation of timescales allows a single device to capture features of both
902 short-term and long-term plasticity, integrating rapid responsiveness with persistent
903 memory within the same physical element.¹³⁷

904 In such hybrid architectures, the inorganic scaffold provides a mechanically robust
905 framework with well-defined geometry, enabling a degree of device-to-device uniformity,
906 while the polymer brush supplies the nonlinear ionic dynamics responsible for memory.
907 Because the brushes are covalently tethered to the surface, they remain spatially confined
908 and do not migrate or leach as free polymers might, leading to improved cycling
909 stability.¹³³

910 Polymer brush-filled nanochannels represent a rational hybrid design that merges
911 the predictability of engineered surfaces with the adaptability of soft matter. They have
912 enabled key advances, including chemical-to-electrical synaptic transduction, linking
913 ionic memristors to chemical neuromodulation. By tuning brush chemistry and
914 architecture such as charge type, grafting density, and chain length, the timescale and
915 analog range of memristive behavior can be precisely controlled, with trade-offs between
916 retention and response speed. At the nanoscale, polymer brushes serve as ionically
917 active layers that endow rigid channels with memory and selectivity, where the solid
918 scaffold provides mechanical stability and electrical interfacing, while the soft brush
919 supplies ionic plasticity and chemical functionality essential for neuromorphic devices.

920

921 **4.3 Stimuli-responsive polymer-filled nanopores**

922 In general, the more manufacturable and dense the scaffold becomes, the harder it is
923 to deliver a stimulus with the spatial precision and speed needed for truly addressable
924 switching. A neat way around this is to move the active degree of freedom into a
925 polymer inside the channel and trigger it remotely. In a recent thermoplasmonic
926 design,¹¹³ poly(N-isopropylacrylamide) brushes on the backside of a solid-state nanopore
927 act as a temperature-responsive gate, swollen below the critical solution temperature to
928 block ion passage, but collapsing when local heating pushes the pore above the transition,
929 reopening the channel (Figure 10a). What makes the approach feel distinctly nano-
930 engineered is how the stimulus is delivered: a gold bullseye resonator concentrates the
931 light illumination onto the nanopore aperture, producing rapid, reproducible temperature
932 excursions and, in turn, robust ionic switching with On/Off ratios up to around 60 over
933 repeated cycles. Beyond proving the principle, the kinetics and addressability start to
934 look device-relevant, where rise/fall times of a few milliseconds were achieved,



935 approaching the kilohertz regime of the conductance switching operation. Because the
936 laser spot can be diffraction-limited to below $1\ \mu\text{m}$, individual pores in an array can be
937 selected and orchestrated into simple current-based logic (Figure 10b), turning a polymer-
938 filled nanochannel from a single switch into an optically programmable ionic circuit
939 element.¹¹³

940

941 4.4 Droplet-on-chip systems

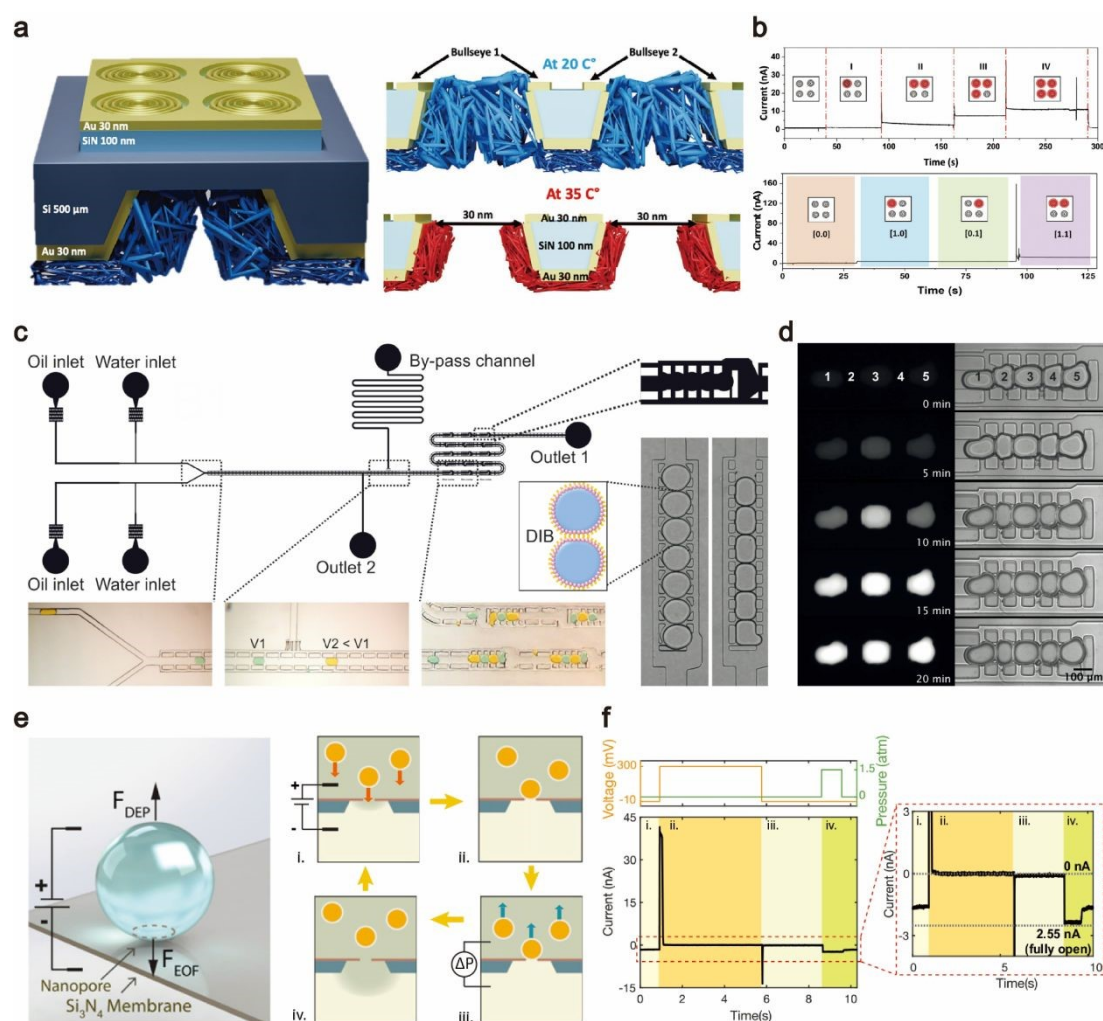


Figure 10. Programmable gating at the soft-hard interface. **a**, Thermoplasmonic optical gating of polymer-functionalized nanopores. A gold bullseye concentrates light illumination to locally heat PNIPAM above its critical solution temperature, selectively switching pores within an array with micrometer-scale addressability. Adapted with permission from ref. 113. Copyright 2025 Creative Commons CCBY-NC-ND 4.0. **b**, A passive microfluidic shift-register architecture positions and stores trains of lipid-stabilized water-in-oil droplets. Adapted with permission from ref. 138. Copyright 2015 Creative Commons CC BY 4.0. Droplet contact self-assembles droplet-interface bilayers, enabling automated arrays for multiplexed assays. **c**, Nanoparticle-blockage-mediated nanopore gating: rigid or soft nanoparticles are driven to a silicon nitride nanopore entrance to reversibly close the conduit in a ball-and-chain-like manner; small voltage or pressure stimuli yield millisecond response and complete closing. Adapted with permission from ref. 141. Copyright 2022 Creative Commons CC BY-NC-ND.



942 Another hybrid strategy integrates droplet interface bilayers into solid microfluidic or
943 electronic frameworks (Figure 10c-d). In this approach, aqueous droplets are positioned
944 in microfabricated wells on a chip, where lipid bilayers form reproducibly between
945 adjacent droplets.¹³⁸ The solid substrate supplies electrodes, fluidic confinement, and
946 addressing infrastructure, while the soft bilayers host the ionic processes responsible for
947 computation.⁵⁵ By arranging multiple droplet pairs into patterned networks, it becomes
948 possible to construct hybrid wet neural circuits that remain physically robust and
949 electrically addressable. Early demonstrations have used techniques such as
950 microdroplet printing to generate arrays of droplet interface bilayers with reasonable
951 reproducibility.¹³⁹ A central challenge remains long-term stability, as bilayers are prone
952 to rupture or drift over time, including partial gelation of droplets or polymer
953 encapsulation have shown promise in mitigating these issues. If such stabilization can
954 be achieved reliably, this architecture could enable large-scale arrays of memristive
955 synapses on a single chip, with each droplet pair functioning as an individual, addressable
956 synaptic element.

957 958 **4.5 Nanoparticle-trapped nanopores**

959 Another hybrid strategy involves embedding nanoparticles or nanoscale inclusions
960 within fluidic channels to introduce field-responsive internal degrees of freedom. For
961 instance, in a conical nanopore, a confined nanoparticle or soft inclusion, such as a protein
962 aggregate or nanoscale droplet, can deform, or reconfigure under an applied bias, thereby
963 modulating ionic transport. It was demonstrated that introducing SiO₂ nanoparticles
964 into a conical nanopore led to elastic deformation-mediated memristive hysteresis, arising
965 from the coupled motion of the particle and the surrounding ionic flow.¹⁴⁰ Although the
966 nanoparticle itself may be mechanically rigid, its mobility within the fluid effectively
967 creates a composite system in which a hard scaffold hosts a dynamically reconfigurable
968 internal phase. This illustrates how embedding responsive nanoscale objects within
969 otherwise rigid nanofluidic channels provides an additional route to memristive behavior,
970 by coupling ionic transport to the history-dependent dynamics of an internal phase.

971 A deformable nanoscale vesicle can function as a plug that couples a nanopore
972 conductance with memory. Yazbeck et al.¹³⁸ demonstrated that liposomes driven into a
973 solid-state pore will irreversibly block ionic flow until a stimulus removes them (Figure
974 10e). Under a modest electric field, a charged liposome is electrophoretically sucked
975 into the pore and elastically deforms to seal it, achieving near-100% current blockade
976 (Figure 10f). Noticeably, the occlusion remains even after the voltage is turned off,
977 enabling a nonvolatile memory effect, because the soft vesicle wedges in place rather than



978 diffusing away. A brief pressure pulse can eject the vesicle, reopening the pore, which
979 then persists until the next voltage stimulus. This nanoparticle-blockage gating is highly
980 repeatable and tunable, effectively emulating a voltage-controlled ionic switch with
981 volatile vs. nonvolatile memory determined by its softness. The key is that the inherent
982 flexibility and surface adhesion give the system a built-in memory of its last blocked or
983 unblocked state.¹⁴¹

984

985 **4.6 Bio-hybrid systems**

986 Perhaps the most fascinating hybrids involve actual biological components
987 integrated with artificial ones. An example is growing living neurons on a solid-state
988 ionic device so that they form a closed-loop hybrid network. The ionic memristor might
989 receive neurotransmitter from the neuron and feedback an ionic current that stimulates
990 the neuron, making a neuron-artificial-synapse hybrid. Early work has interfaced
991 neurons with iontronic devices where the device can release ions like K^+ to trigger neural
992 signals.¹²⁶ As we refine these interfaces, we may effectively bolt an artificial memristor
993 in place of a missing synapse in a neural circuit, a true hard/soft hybrid synapse.

994

995 **4.7 Summary of hybrid strategies**

996 Soft materials, particularly droplet interface bilayers and lipid membranes, offer
997 exquisite biomimicry and dynamic behavior but are often fragile and difficult to scale.
998 Hard materials, such as conical nanopores etched in silicon or polymer substrates, afford
999 integration and reproducibility but can struggle to encode complex ionic histories.¹⁴² To
1000 bridge this divide, researchers are increasingly turning to hybrid systems, combinations
1001 of soft ionic elements embedded within rigid scaffolds, that blend the best of both
1002 approaches. This section illustrates the emerging strategy, highlighting devices where
1003 ionic gels, polymer brushes, or embedded nanoparticles introduce memory functions
1004 within hard geometries. These designs leverage multi-timescale ionic dynamics,
1005 chemical specificity, and tunable conductance, while maintaining the mechanical
1006 integrity and addressability needed for circuit integration. The interplay of materials in
1007 such hybrids enables rich functionality: polymer brushes permit chemical learning, ionic
1008 gels stabilize device geometry while encoding plasticity, and embedded particles offer
1009 new routes to responsiveness.

1010 Overall, these hybrid architectures suggest a design paradigm where complexity is
1011 compositional. Rather than seeking a single material solution, engineers are building
1012 layered systems that mimic biological synapses as mechanically stable, yet chemically
1013 and electrically dynamic. This modular approach is paving the way for scalable



1014 iontronic platforms that retain the nuance of soft matter while embracing the precision of
1015 microfabrication. As the field advances, these hybrids are poised not just to supplement
1016 but to define future nanofluidic computing systems, embodying a pragmatic, multifaceted
1017 strategy for combining softness with scale.

1018

1019 **5. From devices to ionic circuits**

1020 This section makes the system-level progression explicit, moving from single
1021 memristive junctions to coupled logic elements and then to small iontronic networks so
1022 the boundary between device physics and circuit-level function remains clear. Connecting
1023 multiple nanofluidic memristors into circuits is a necessary step beyond single-device
1024 phenomena, because networked ionic memory elements can display collective dynamics
1025 and computational capability that are not accessible in isolated devices.

1026 Beyond digital logic, ion-driven circuits are being explored in which coordinated
1027 ionic dynamics naturally emerge. Conical nanopore memristors integrated into
1028 nonlinear oscillator circuits have been shown to exhibit alternating chaotic and periodic
1029 oscillations reminiscent of neural network dynamics (Figure 11a).¹⁴³ Coupling three
1030 such ionic conductors demonstrated purely ionic XOR and NAND logic gates to a neural
1031 network,^{94,101} and thus the potential to realize a complete set of logic operations using
1032 only memristors and simple electrical components (Figure 11b). Here, ionic currents in
1033 one element entrain or modulate others, with the electrolyte itself serving as the
1034 communication medium. Mutual electrolyte coupling thus allows one memristor to
1035 modulate another state, analogous to synaptic gating in neural networks. Even in
1036 passive structures, similar coupling effects arise, as ordered nanopore arrays exhibit pore-
1037 pore transport interference due to overlapping diffusion layers and shared ion depletion
1038 zones. In other words, ionic transport through one pore can modify local concentration
1039 and electric field profiles sufficiently to gate the conductance of neighboring pores.
1040 Collective effects are enhanced by close proximity or shared reservoirs and can be
1041 exploited for computation.⁹⁰

1042 A landmark demonstration involved an ionic logic gate formed by two memristive
1043 nanopores coupled through a resistor (Figure 11c).²³ Here, each nanopore modulated
1044 the voltage experienced by the other, enabling mutual gating and conditional switching
1045 analogous to electronic logic. The circuit realized a material implication gate, a Boolean
1046 primitive from which all other logic gates can be derived. This result showed
1047 unequivocally that computation can be implemented in ionic circuits using ions in
1048 solution without electronic carriers. Despite operating on second-long timescales, the
1049 demonstration established that basic computing primitives can be realized solely with



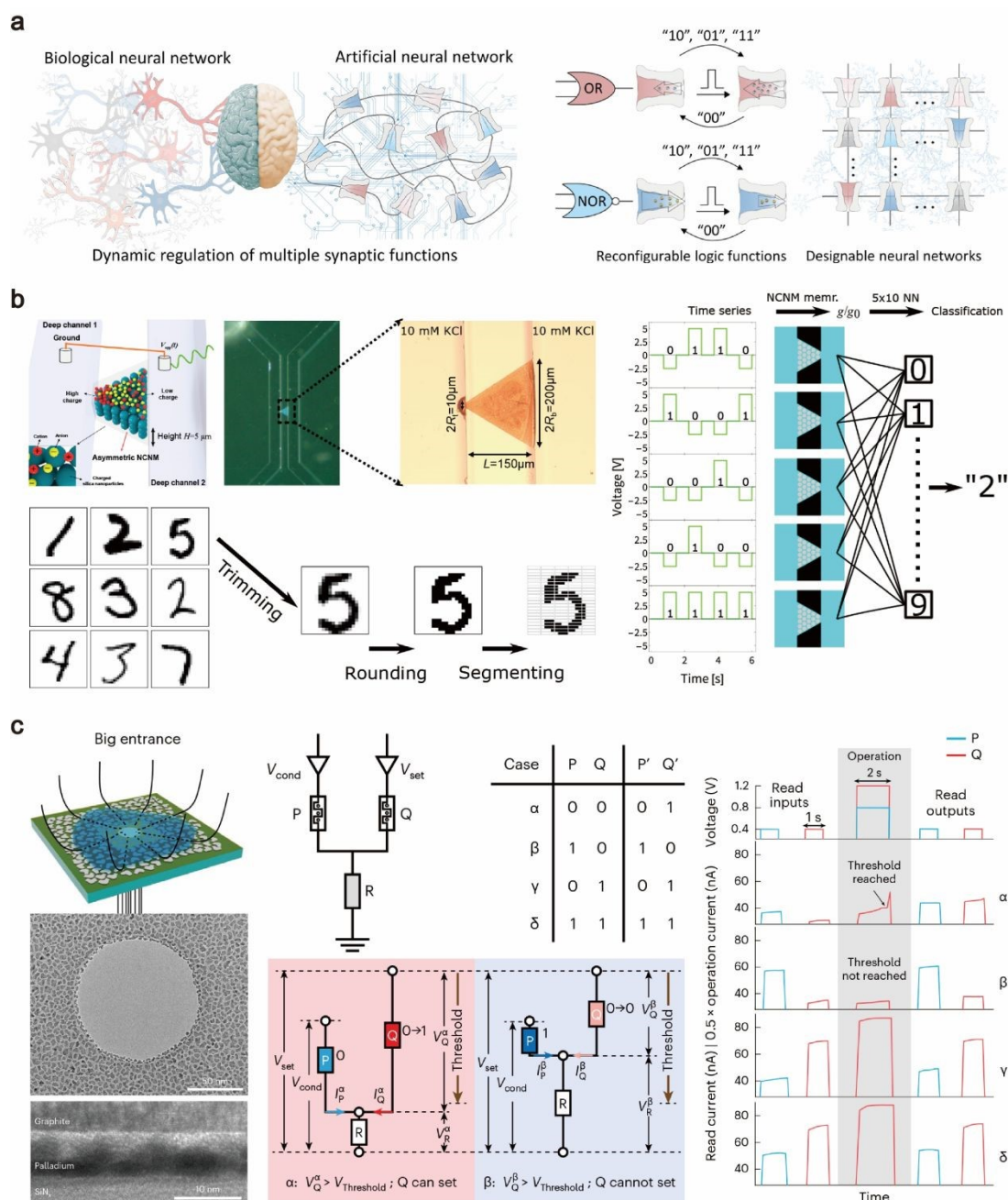


Figure 11. Iontronic circuits and learning architectures. **a**, Single-pore nanofluidic logic memristors leverage ion enrichment/depletion states that coevolve with chemical cues and voltage history to implement reconfigurable synaptic functions and logic, while programmable series/parallel interconnects scale these elements into multi-memristor assemblies and small neural networks. Adapted with permission from ref. 143. Copyright 2024 American Chemical Society. **b**, Tapered microchannels embedding a colloidal nanochannel-network membrane generate volatile yet reproducible conductance dynamics through transient salt concentration polarization, such that handwritten digits encoded as input time series are mapped onto channel responses and classified with a simple readout layer. Adapted with permission from ref. 101. Copyright 2024 Creative Commons CC BY 4.0. **c**, Circuit-scale nanofluidic logic using mechano-ionic memristive switches. Highly asymmetric channels are designed for in-memory processing and can be assembled into logic circuits composed of two interactive devices and an ohmic resistor. Adapted with permission from ref. 23. Copyright 2024 Creative Commons CC BY.

1050 nanofluidic memristors. Importantly, the two memristors in the IMP gate were not



1051 isolated but interacted through the shared circuit, allowing each device to influence the
1052 state of the other.²³ Electrolyte-coupled interactions mark recurrent, state-dependent
1053 dynamics even in simple two-element networks.

1054 Another striking manifestation is in chemical reaction-mediated memristors: in
1055 single nanopores, cyclical precipitation and dissolution of ionic solids can produce self-
1056 oscillating currents.^{119,121} If multiple memristive pores governed by such in-pore
1057 reactions were coupled, their oscillations could synchronize in a manner analogous to
1058 coupled chemical oscillators. Networked nanofluidic memristors can thus exhibit new
1059 dynamical modes, from sustained oscillations to chaotic switching, expanding the
1060 computational repertoire of iontronic circuits.

1061 Theoretical models support the promise of small ionic memristor networks for
1062 neuromorphic function. Brownian dynamics simulations by Noh *et al.*¹¹¹ showed that
1063 just a handful of coupled nanofluidic memristors can reproduce neuron-like spiking
1064 behavior. In their model, quasi-2D slit nanopores with memristive conductance were
1065 connected in a circuit analog of an integrate-and-fire neuron, and the collective ionic
1066 dynamics generated action potential-like voltage spikes.¹¹² There is also work
1067 demonstrated an all-ionic leaky integrate-and-fire oscillator using conical nanopore
1068 memristors and a resistor, which could fire repetitive spikes analogous to neural
1069 oscillations.¹⁴⁴ Notably, these designs achieved neuron functionality with far fewer
1070 components than an equivalent electronic circuit: a direct outcome of the rich physics
1071 within each ionic memristor like electric double-layer rearrangement, ionic adsorption, or
1072 concentration polarization. These theoretical findings suggest that ionic memristor
1073 networks could inherently perform neuromorphic tasks such as pattern generation and
1074 potentially even learning with minimal circuitry.

1075 The prospect of ionic memory circuits also opens intriguing possibilities for bio-
1076 interfacing. Because they use the same carriers as biology, arrays of ionic memristors
1077 might seamlessly interface with living neural tissue. One could imagine an implantable
1078 iontronic chip where each memristor responds to local biochemical signals and drives an
1079 electronic feedback to neurons, effectively communicating in the native ionic language
1080 in the brain.^{145,146} Such hybrid soft-hard systems would blur the boundary between
1081 computing devices and biology, leveraging the biocompatibility and soft mechanics of
1082 fluidic components.

1083 Assessing the potential and limitations of multi-memristor nanofluidic circuits
1084 makes it clear that the field remains at a very early stage. The integration scale today is
1085 on the order of only 2-3 devices working in concert, compared to the billions of transistors
1086 in modern electronic chips, effectively the iontronic analogue of early electronic



1087 computer prototypes from the 1940s. Scaling these systems to large, reliable circuits is
1088 challenging, as ionic devices are orders of magnitude slower than semiconductor switches
1089 and long-distance ionic transport is limited by diffusion and fluidic resistance. The
1090 requirement for specific liquid environments or isolation further complicates large-scale
1091 integration of nanofluidic memristors.

1092 Concerns also remain regarding manufacturability and uniformity, as nanofluidic
1093 elements are likely to show greater device-to-device variability in geometry or surface
1094 chemistry than semiconductor transistors. Nonetheless, a tangible path forward is
1095 emerging: modern micro- and nanofabrication techniques enable the creation of
1096 nanochannel and nanopore arrays with high precision, and recent studies have begun to
1097 exploit these capabilities. For example, some of the memristive nanopore devices were
1098 fabricated in a scalable way on silicon nitride chips, yielding dozens of working devices
1099 that could potentially be addressed in parallel.¹¹⁹ Likewise, two-dimensional
1100 nanochannel memristors have been demonstrated on-chip, showing that multiple fluidic
1101 memories can coexist and even be tuned individually by adjusting their local electrolyte
1102 conditions.¹⁰⁶ As a result, one can envision a future ionic integrated circuit comprising
1103 many memristors arranged in a network, analogous to a crossbar of artificial synapses.
1104 In practice, large-scale iontronic processors are therefore expected to adopt hybrid
1105 architectures, in which electrodes and wiring are used to interconnect and control arrays
1106 of fluidic devices organized into modular units. Signal readout and interfacing present
1107 an additional challenge, as ionic currents must be converted to electronic signals at some
1108 stage. Ultimately, although scaling iontronic circuits to very large-scale integration
1109 (VLSI) complexity is an ambitious goal, the rewards are considerable. Large networks
1110 of ionic memristors would operate in regimes of ultra-low power and inherent parallelism,
1111 potentially achieving brain-like efficiencies. They could be directly merged with
1112 chemical and biological processes, enabling forms of soft computing in environments
1113 where silicon chips falter. In the coming years, it is anticipated that the field will
1114 transition from one-off device physics demonstrations to developing the design principles
1115 and architectures for multi-memristor ionic circuits. By analogy with the evolution of
1116 electronic computing, rudimentary iontronic gates and synapses may become the
1117 foundational building blocks of future ion-based intelligent machines.

1118
1119

1120 **6. Prospects and challenges**

1121 Nanofluidic memristors have proven their ability to emulate synapses and neural
1122 circuits in concept, but transforming these laboratory devices into practical, large-scale



1123 neuromorphic systems comes with significant challenges. In this section, we outline the
1124 key hurdles and prospects for the field, including device integration, scalability and
1125 switching speed. Each of these factors could limit performance or reliability if not
1126 addressed, yet each also offers opportunities for innovation. Whereas many of the
1127 challenges for ionic memristors are shared with those faced by traditional electronics,
1128 there are also issues unique to iontronics, such as water drying and slow ionic mobility.
1129 The prospects, on the other hand, include leveraging the intrinsic advantages of ionic
1130 systems such as super-efficient energy usage and inherent biocompatibility to create
1131 computing platforms that could profoundly impact both technology and bioengineering.

1132 1133 **6.1 Thermal management**

1134 Thermal management is an inevitable issue in integrated circuits.¹⁴⁷ While ionic
1135 memristors operate at extremely low energy per event, often in the femtojoule to picojoule
1136 range, the challenge of thermal management becomes significant when scaling to large
1137 arrays or increasing switching speed. Efforts to accelerate switching by increasing ion
1138 concentrations or bias voltages can introduce ohmic heating.¹⁴⁸⁻¹⁵⁰ Heat accumulation
1139 should be mitigated as it can lead to evaporation, bubble formation, ion mobility drift,
1140 and degradation of soft materials like lipid bilayers or polymer brushes. In this regard,
1141 nanoscale channels offer limited paths for heat dissipation. Solutions include using
1142 thermally conductive substrates, pulsed operation to allow for passive cooling, or
1143 microfluidic circulation of electrolytes. Designs inspired by the brain, i.e., short sparse
1144 spikes and distributed computation, help minimize local heating. The goal can be cold
1145 computing that functions at room temperature without active cooling. The brain
1146 remains a blueprint with minimal energy per event, distributed load, and graceful
1147 operation. Achieving this in engineered iontronics requires both material innovation
1148 and rethinking how we compute.

1149 1150 **6.2 Ionic fatigue**

1151 Like metals under repeated stress, ionic memristors face degradation from cyclic ion
1152 migration and associated chemical or mechanical changes, a phenomenon termed ionic
1153 fatigue. This can manifest as reduced hysteresis, drift in resistance states, or complete
1154 failure due to fouling, delamination, or irreversible reactions. For example, side
1155 reactions, such as unintended water electrolysis, can alter pH and surface charge,
1156 degrading materials like polyelectrolytes or brushes over time. Ion depletion or
1157 irreversible trapping, especially in systems relying on finite ionic species, can exhaust
1158 switching capacity. Mechanical effects like swelling, drying, or interfacial stress can



1159 also fracture gels, rupture membranes, or wear down soft layers.

1160 Mitigating fatigue demands chemically stable architectures, minimizing reactive
1161 species, and confining operation to regimes that avoid extreme ionic or pH excursions.
1162 Some soft materials offer self-healing like hydrogels with dynamic bonds that can restore
1163 structure and conductivity after damage.¹⁵¹ Another strategy is to reserve volatile
1164 switching for frequent activity while limiting non-volatile writes, analogous to dynamic
1165 RAM refresh or memory consolidation in the brain.

1166 Still, more complex architectures, especially those involving redox-active
1167 components or porous frameworks, may face increased susceptibility. As in batteries,
1168 long-term retention may come at the cost of reversibility or responsiveness. Balancing
1169 endurance with plasticity thus remains an open design challenge.

1170 Meanwhile, several devices already exhibit excellent endurance. Zhang et al.¹⁰⁷
1171 report ionic liquid system remaining stable over many cycles, likely due to its non-volatile
1172 medium and reversible interfacial motion.¹⁰⁷ A molecular brush-confined device also
1173 maintained performance through extensive cycling, owing to robust covalent attachment
1174 and non-consumptive ion interactions.¹³⁶ With careful chemistry, mechanical
1175 robustness, and thoughtful operation, future ionic devices could achieve lifetimes rivaling
1176 solid-state transistors while retaining the unique dynamics of soft, ion-driven systems.

1177

1178 **6.3 Mechanical stability**

1179 Mechanical fragility is a key challenge for nanofluidic memristors, especially those
1180 incorporating soft matter such as lipid bilayers, hydrogels, or droplets. These
1181 components are vulnerable to deformation, drying, and rupture under environmental
1182 stress, limiting device durability. Long-term deformation, such as hydrogel creep or
1183 nanopore etching, can shift device baselines, necessitating recalibration. Emulsion-
1184 based systems offer one route to enhanced mechanical stability through droplet
1185 miniaturization and self-stabilization. Equally important is packaging: maintaining
1186 hydration and shielding devices from contamination can dramatically extend operational
1187 lifetimes. Hybrid strategies like polymer-stabilized bilayers, hydrogel encapsulation,
1188 and soft-hard integration offer enhanced mechanical integrity. As fabrication
1189 techniques mature, ionic devices are expected to become as mechanically reliable as
1190 conventional electronic components.

1191

1192 **6.4 Device integration scalability**

1193 Scaling nanofluidic memristors from lab prototypes to large-scale systems remains
1194 a core challenge. Unlike electronics, where lithography processes enable to integrate



1195 billions of transistors, ionic systems require managing liquids, interfaces, and ion
 1196 transport across many channels, thereby posing distinct architectural and fabrication
 1197 hurdles. Device arrays are feasible via microfabrication, since nanopores or

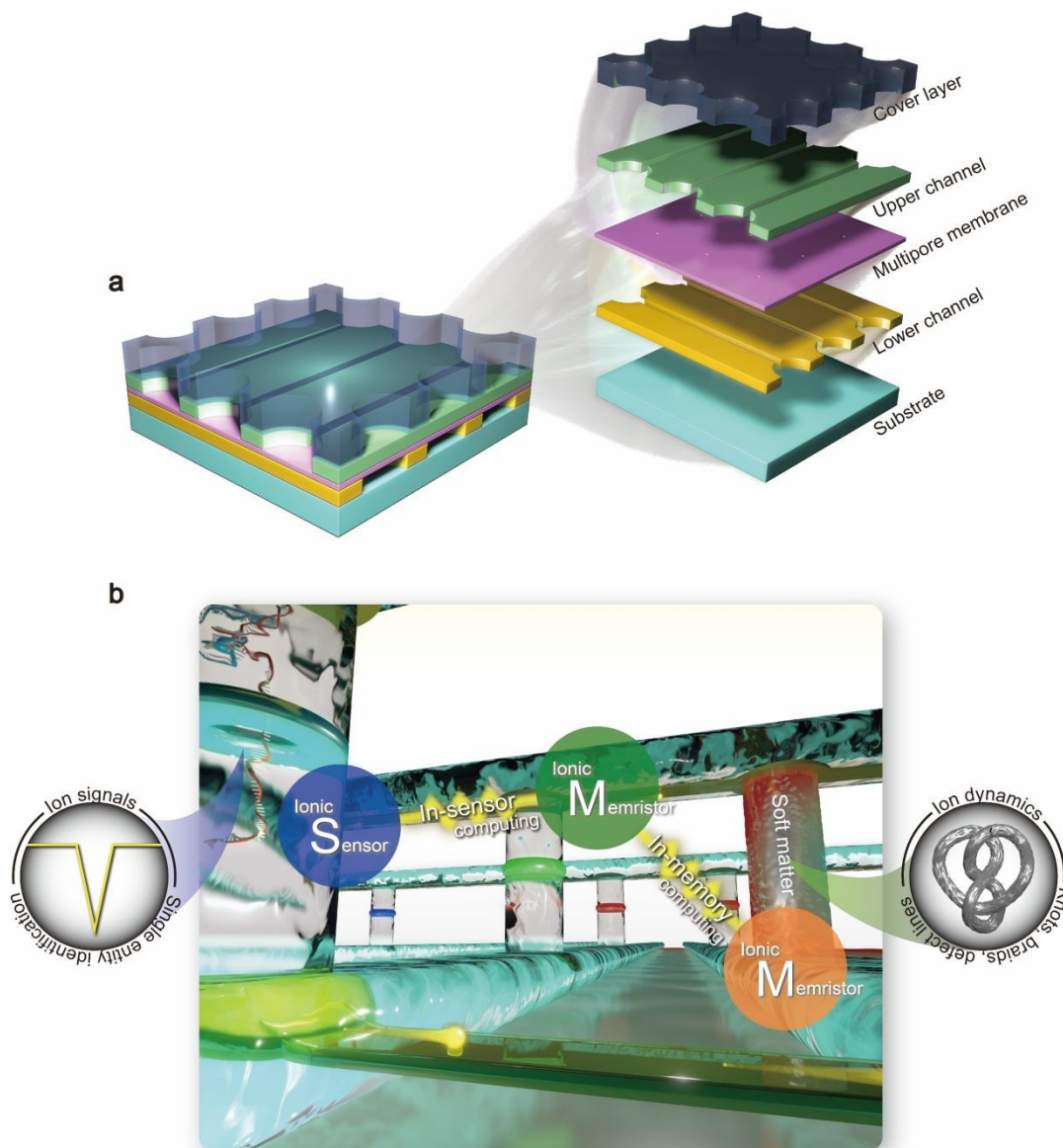


Figure 12. Crossbar nanopore junction system. **a**, Schematic of a crossbar architecture in which row and column fluidic channels are patterned on opposite sides of a multipore membrane, so that each channel intersection defines an individually addressable nanopore junction. Selecting a specific row-column pair localizes the applied bias and ionic flux to the corresponding junction, enabling dense, addressable ionic memristor arrays in a layout analogous to crossbar RRAM. Expanded view of the stacked implementation (cover layer, upper channel layer, multipore membrane, lower channel layer, and substrate) illustrates a manufacturable route to scaling nanopore-junction devices with simplified interconnect routing and on-chip integration. **b**, Conceptual nanopore-junction architecture for in-sensor and in-memory computing. Each addressable junction senses ionic events while nearby adaptive conductance stores local context, enabling in-sensor classification and in-memory computing with analogue ionic weights.



1198 nanochannels can now be defined with sub-100 nm precision. Early demonstrations of
1199 multi-memristor layouts suggest scalable ionic circuits are within reach.¹⁰⁶ Further
1200 refinements can pursue crossbar nanopore junction architectures as an analogue of the
1201 resistive random access memory (RRAM) configurations that could enable dense,
1202 addressable ionic memristor arrays (Figure 12a). Key to this is integrating electrode
1203 networks for local gating, and optimizing designs for functional scalability, where few
1204 devices can perform complex logic.

1205 A complementary route to scalability would be to view integration not only as adding
1206 more devices, but as increasing the function per junction. For example, an addressable
1207 array can operate as a co-integrated sensor/memory fabric, where each junction performs
1208 nanopore sensing¹⁵²⁻¹⁵⁴ while neighboring junctions store and update conductance states
1209 that retain local context. This architecture naturally supports in-sensor computing,
1210 where raw translocation pulses are classified directly at the sensing site, or in-memory
1211 computing, where the adaptive ionic conductance acts as an analog weight so that
1212 computation proceeds where the state is stored rather than shuttling signals across slow
1213 diffusive ionic paths. Ionic polymers would provide a practical materials bridge for this
1214 co-integration, where polymer brushes, gels, and other confined polyelectrolytes add
1215 tunable chemical selectivity and multi-timescale internal state variables that stabilize
1216 memory while remaining compatible with hard nanofabricated nanopores and channels.
1217 Further advances in the state engineering may also be achievable by exploiting soft
1218 matter⁶⁷ in which information is stored not only in ion concentrations but also in
1219 reconfigurable spatial patterns, such as arrays of line defects as well as knotted and
1220 braided filamentary structures, that create a large accessible space of stable configurations
1221 and transitions for robust,^{155,156} low-power physical information processing. In this
1222 view, scalable iontronic systems will likely emerge as modular networks of
1223 sensor/memristor nodes, coupled by short-range ionic dynamics for rich analog
1224 processing and by electronic interconnects for long-range communication (Figure 12b).

1225 At the system level, the most credible near-term architecture is an ion-electron co-
1226 processor. Ionic junctions are well suited to local state evolution, analogue weighting,
1227 and chemically coupled adaptation, whereas electronic amplifiers, multiplexers, and
1228 CMOS circuitry remain superior for addressing, signal conditioning, and long-range
1229 communication. The central engineering task is therefore not to replace electronics
1230 outright, but to build low-leakage interfaces that preserve slow ionic state dynamics while
1231 enabling fast and stable readout. This same logic extends to neural interfaces, where
1232 soft conductive composites and hydrogel-based conductors can reduce mechanical
1233 mismatch with tissue while providing reliable ion-electron transduction.



1234 To approach brain-like computation with many interacting ionic weights, multiple
1235 ionic memristors should be organized as a cross-bar nanopore-junction array in which
1236 orthogonal fluidic or electronically addressed word lines and bit lines intersect at
1237 individually defined nanopore junctions. Each cross-point then functions as a local
1238 ionic synapse, where the applied row/column bias sets the transmembrane field across
1239 that nanopore, the junction conductance stores the synaptic weight, and the summed
1240 current collected along a shared line naturally implements the fan-in operation required
1241 for analogue vector-matrix multiplication. In this architecture, short-range ionic
1242 coupling can support local state adaptation and history-dependent learning, whereas
1243 electronic selectors, amplifiers, or gate electrodes should handle addressing, isolation,
1244 and long-range communication so that write/read operations remain stable despite the
1245 slower relaxation of ions. A practical brain-inspired implementation is therefore not a
1246 purely ionic network, but a hierarchical ion-electron system in which dense crossbar
1247 nanopore junctions provide massively parallel adaptive weighting while surrounding
1248 circuitry orchestrates timing, multiplexing, and error control.

1249

1250

1251 **6.5 Switching speed**

1252 The rate at which ionic memristors change state is constrained by the inherent
1253 slowness of ion transport compared to electrons. While ionic memristors will not rival
1254 the GHz speed of electronic transistors, their efficiency and analog capabilities position
1255 them for applications where millisecond precision and energy-saving characteristics
1256 outweigh clock frequency.

1257 Typical ionic devices switch at rates from hertz to kilohertz, with some reports of
1258 nanopore-based memristors reaching 100 kHz. Such speeds, though modest, are
1259 sufficient for many sensory and learning tasks. Further speed enhancement may be
1260 possible by device miniaturization through shorter channels for smaller droplets to reduce
1261 ion transit times. Pulsed or high-field operation may also transiently accelerate
1262 switching, albeit with trade-offs in energy efficiency and stability. Volatility also shapes
1263 speed. Fast, volatile devices offer quick response but poor retention, while stable, non-
1264 volatile ones tend to switch slowly. Adjusting volatility or pairing ionic elements with
1265 electronic drivers may optimize speed for specific tasks. Parallelism provides a system-
1266 level workaround. Massive arrays of slower devices operating concurrently, similar to
1267 the brain architecture, can deliver high throughput despite modest individual speeds. This
1268 model suits neuromorphic inference at biologically relevant timescales.

1269



Table 4. Benchmark ranges across ionic and electronic memristive platforms.

<i>Platform</i>	<i>Energy per event</i>	<i>Switching time</i>	<i>Retention time</i>	<i>Scalability</i>
Soft fluidics	10 aJ - pJ	ms - s	ms - hours	Low to moderate
Hard fluidics	fJ - pJ	μ s - ms	s - hours	Moderate
Soft/hard hybrid fluidics	10 aJ - pJ	μ s - ms	ms - days	Moderate to high
Electronic memristors (RRAM/CMOS)	pJ - nJ	ns - μ s	days - years	Very high

1270 7. Conclusions

1271 Table 4 shows the emerging landscape of memristive memory into a single cross-
 1272 platform benchmark. By placing soft, solid-state nanofluidic and hybrid ionic systems
 1273 alongside conventional electronic memristors, it makes the governing trade-offs
 1274 transparent across write energy, switching time, retention, on/off ratio and scalability.
 1275 Soft ionic platforms occupy the corner of highest physicochemical richness, lowest
 1276 energy cost and closest compatibility with biological media. Solid-state nanofluidic and
 1277 hybrid architectures, in contrast, sacrifice some of that freedom to gain reproducible
 1278 geometry, addressability and routes to manufacturable integration. Electronic
 1279 memristors remain unrivalled in raw switching speed and industrial maturity,¹⁵⁷⁻¹⁶⁰ yet
 1280 their internal state is typically less entangled with chemistry, hydration and multiscale
 1281 relaxation; features that give ionic platforms distinctive leverage for adaptive, life-
 1282 adjacent computing.

1283 Seen in this way, fluidic and solid-state memristors are better understood as points
 1284 along a continuum than as competing categories. Soft fluidics operate in the most
 1285 biomimetic regime, where memory is inseparable from chemical environment and
 1286 mechanical compliance, although this same coupling can amplify drift and slow dynamics
 1287 as systems scale. Hard nanofluidic devices move closer to the engineering logic of
 1288 semiconductor hardware by fixing geometry and compressing the active volume, while
 1289 preserving the central premise of ionic intelligence: information is stored and processed
 1290 in liquid-phase ionic distributions rather than in electronic carriers within solids. Hybrid
 1291 devices offer the most practical bridge between these regimes, combining wafer-
 1292 compatible scaffolds with fluid-like internal state variables and thereby providing a



1293 credible route towards large-scale ion-electron co-integration. Framed in this way,
1294 benchmarking is not a matter of deciding which platform wins, but of mapping
1295 complementary operating regimes and identifying the design opportunities that arise
1296 when computation is allowed to be both electrical and chemical.

1297 Nanofluidic memristors embody a convergence of chemistry, biology, and electronics,
1298 defining a new class of devices where ions, not electrons, serve as the fundamental
1299 carriers of information. Throughout this review, we have seen how harnessing ion
1300 transport in confined fluids enables rich, synapse-like behaviors, i.e., history-dependent
1301 conductance, short- and long-term plasticity, and the integration of electrical and
1302 chemical signaling within a single device. By operating with ions rather than electrons,
1303 these memristors mimic the signaling mechanisms of biological neural networks, offering
1304 prospects for brain-like energy efficiency and inherent biocompatibility. Proof-of-
1305 concept devices already exhibit a diverse array of functions, from droplet-based synapses
1306 capable of learning and forgetting, to solid-state nanopores executing logic with liquid
1307 blister memories, to polymer brush-lined nanochannels that transduce chemical cues into
1308 electrical responses. These advances point toward an emerging iontronics, where
1309 information is processed through flowing electrolytes, rather than within rigid
1310 semiconductor lattices.

1311 Yet, realizing the full promise of ionic memristors for artificial intelligence
1312 applications will require continued innovation to overcome the challenges. Thermal
1313 management should ensure that these devices, often operating in aqueous environments,
1314 remain cool and stable even as we scale up integration. Materials and designs need to
1315 be refined to prevent ionic fatigue so that devices can learn and re-learn over billions of
1316 cycles without degrading. The delicate soft components of many ionic devices require
1317 reinforcement through hybrid architectures and packaging to guarantee mechanical
1318 stability in real-world operating conditions. Perhaps most critically, methods to
1319 integrate large arrays of ionic memristors, bridging the gap from single demonstrators to
1320 dense networks, will determine whether ionic computing can move from a laboratory to
1321 practical deployment.

1322 A balanced assessment also requires identifying the regimes in which each platform
1323 is likely to thrive, and those in which its limitations become fundamental. Soft devices
1324 are unparalleled in biocompatibility, compliance and chemically rich state dynamics, but
1325 remain susceptible to dehydration, drift and limited clock speed. Solid-state nanofluidic
1326 devices offer tighter control over geometry and stronger prospects for large-scale
1327 fabrication, although their memory can be diminished at high ionic strength when double-
1328 layer contrast is screened. Hybrid architectures widen the design window by combining



1329 robust scaffolds with adaptive ionic materials, but they introduce their own interfacial
1330 challenges, including delamination, solvent loss and packaging complexity. These
1331 boundaries are not weaknesses to be hidden, but design constraints that should inform
1332 platform choice for neural interfaces, soft robotics, sensing and on-chip analogue learning.

1333 In terms of performance, ionic memristors should not be erected to rival the gigahertz
1334 switching of transistors as they do not need to. Their comparative advantage lies in
1335 energy efficiency and rich functionality rather than raw speed. As multiple studies have
1336 highlighted, these fluidic devices can operate at femtojoule or picojoule energy scales per
1337 event, approaching the unmatched efficiency of the human brain. Furthermore, they
1338 inherently support analog storage and computation within the same medium, eliminating
1339 the artificial separation of memory and processing that plagues von Neumann electronic
1340 architectures. For AI tasks like pattern recognition, sensory processing, and adaptive
1341 control, ionic memristor networks are particularly well suited. Indeed, as we build chips
1342 with thousands of ionic synapses operating in parallel, we may find that despite slower
1343 individual devices, the overall system throughput for AI computations is competitive with
1344 or even superior to conventional approaches, all while consuming orders of magnitude
1345 less power.

1346 The road ahead for nanofluidic memristors will likely see increased synergy with
1347 other emerging technologies. We anticipate hybrid platforms where ionic memristor
1348 cores interface with CMOS control circuits, bridging the best of both worlds, the ion-
1349 electron hybrid computers that use electrons for communication and ions for computation.
1350 On the algorithmic front, researchers will explore how to exploit the multivariate nature
1351 of ionic signals to implement novel forms of computation that have no easy electronic
1352 analog.

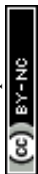
1353 Nanofluidic memristors bring us a significant step closer to the vision of brain-like
1354 artificial intelligence hardware: systems that are not only low-power and highly parallel,
1355 but also adaptive, self-organizing, and intimately linked to the chemical and ionic
1356 processes of life. As these devices mature, we foresee them becoming central
1357 components in next-generation AI as in-memory analog computing units on chips, soft
1358 neuromorphic robots, brain-interface prosthetics, and beyond. Ionic intelligence
1359 remains in its infancy, yet current progress outlines a compelling trajectory toward a new
1360 computing paradigm rooted in ion and fluid physics, with the potential to seamlessly
1361 bridge artificial systems and biological function.

1362 Over the next decade, progress will likely be shaped by four priorities. First, multi-
1363 ion and multi-channel devices should move beyond single-species memory to access the
1364 richer, state-dependent dynamics that support neuron-like behavior. Second, scalable



1365 ion-electron co-integration will be essential, with dense ionic arrays coupled to CMOS
1366 backplanes that provide addressing, low-noise current-to-voltage conversion, and high-
1367 bandwidth readout and control, approach already established in CMOS-integrated
1368 nanopore front ends and in analyses of bandwidth/noise constraints in ionic recordings.¹⁶¹
1369 Third, new materials platforms, including soft conductive composites and chemically
1370 programmable interfaces, should improve stability without sacrificing the chemically
1371 coupled functionality that makes iontronic state variables distinctive. Fourth, the field
1372 needs shared benchmarking standards for endurance, retention, environmental robustness
1373 and energy per update, enabling meaningful comparisons across platforms and
1374 accelerating translation. Progress along these axes will determine whether ionic
1375 intelligence remains an intriguing laboratory concept or matures into a practical hardware
1376 platform, especially as mixed ionic-electronic transducers provide a direct bridge from
1377 ionic state variables to electronic signals suitable for long-range routing and CMOS-
1378 compatible processing.^{162,163} If successful, nanofluidic memristors could become
1379 primary members of the future integrated circuits family, powering a revolution in
1380 computing as profound as the advent of the semiconductor era, but this time driven by the
1381 dance of ions in nanoconfinements.

1382



1384 **Acknowledgments**

1385 A part of this work was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI
1386 Grant Number 25K01639, 24K01511, and Japan Agency for Medical Research and Development (AMED)
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Data Availability Statement:

This Review article does not report new experimental or computational data. Data sharing is not applicable to this work. Any data discussed or re-plotted in figures are available in the cited primary literature.

