Faraday Discussions

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DISCUSSIONS

Iontronic coupling: general discussion

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Serge G. Lemay, Yan Levin, Sophie Marbach, Joan Montes de Oca,
Paul Robin, Zuzanna S. Siwy, Derek Stein, Rene van Roij,
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Alexei A. Kornyshev opened the discussion of the introductory lecture by Yan Levin: Actually, in a very small pore of the size of the ion, any interactions between two ions will be strongly (exponentially) screened, so that when the electrode is polarized, it will be easier to uncouple the ions of opposite sign and to fill the pore with the counterions, creating in the pore the so-called superionic state.[1–4]

[1] S. Kondrat and A. A. Kornyshev, Superionic state in double-layer capacitors with nanoporous electrodes, *J. Phys.: Condens. Matter*, 2011, **23**, 022201; Corrigendum: 2013, **25**, 119501.

[2] A. A. Kornyshev, The simplest model of charge storage in single file metallic nanopores, *Faraday Discuss.*, 2013, **164**, 117–133.

[3] A. A. Lee, S. Kondrat and A. A. Kornyshev, Single-file charge storage in conducting nanopores, *Phys. Rev. Lett.*, 2014, **113**, 048701.

[4] S. Kondrat, G. Feng, F. Bresme, M. Urbakh and A. A. Kornyshev, Theory and simulations of ionic liquids in nanoconfinement, *Chem. Rev.*, 2023, **123**, 6668–6715.

Yan Levin replied: It's true that in metal pores the electric field is screened, with the screening length determined by the separation between the pores. However, even in such pores, we find charge neutrality violation (see ref. 1). The single-file diffusions through a pore are very special. It is not clear to what extent we can use continuum electrostatics for such narrow pores. However, it does provide a lot of simplifications. We have studied similar problems for ionic channels through low dielectric membranes in which the same Green function formalism can be applied. See, for example, ref. 2 and 3.

Metal pores are very interesting to study precisely because of the effective short-range interaction between the ions. When one moves away from extremely narrow pores (single ion type), complications with the standard representation of the Green function appear, *i.e.*, the series representation is not well converged at short separations between ions. We are now working on very efficient methods that will allow us to simulate metal confinement for arbitrary separations between slit surfaces.

1 R. M. Malossi, M. Girotto, A. P. dos Santos and Y. Levin, Simulations of electrolyte between charged metal surfaces, *J. Chem. Phys.*, 2020, **153**, 044121.
2 Y. Levin, Electrostatics of ions inside the nanopores and trans-membrane channels, *Europhys. Lett.*, 2006, **76**, 163.
3 J. R. Bordin, A. Diehl, M. C. Barbosa and Y. Levin, Ion fluxes through nanopores and transmembrane channels, *Phys. Rev. E: Stat., Nonlinear, Soft Matter Phys.*, 2012, **85**, 031914.

(VII:[VII]VII) **Felipe Jiménez-Ángeles** remarked: Thank you for your very nice talk. I have two questions about the breakdown of neutrality discussed for the slit pore. Do you consider any breakdown of neutrality when modelling nanotubes? What would be the conditions to breakdown neutrality in nanotubes and what are the possible implications?

Yan Levin replied: We did not study cylindrical pores. I would expect the same kind of breakdown to occur in this geometry as with the slit pores. However, the extent of breakdown will depend on the length of the pore and also on the medium through which it passes – such as a metal or a low-dielectric membrane. The main difference between the slit pores and the cylindrical pores is that outside the cylindrical pore going through, say, an infinitely thick slab separating two electrolyte reservoirs, the electric field can leak out through the walls of the pore; this will result in a finite electrostatic energy – unless the pore is charge neutral. This is different from what happens with slit pores for which the electric field is screened by the external electrolyte on both sides of the confining surfaces. So an isolated infinite pore passing through an "infinitely" thick slab should remain charge neutral. How the neutrality breaks down for finite pores is a very interesting question!

(I:[I]I) **Aleksandar Donev** said: DFT can help us predict the steady structure of the ions in the radial direction for a cylindrical pore, including steric and polarization effects. Can the result for the density of ions be used to predict the fluid velocity?

The Smoluchowski equation relating fluid velocity to potential comes from the fact that solutions to two Poisson equations with the same RHS but different BCs are the same in 1D up to a constant. So it would also work for slit channels it seems to me, not just cylindrical pores.

Yan Levin answered: DFT allows us to predict both density profiles and the stationary electrostatic potential inside the pore. The stationary potential (and density profiles) are in good agreement with the simulations. If the stationary potential is substituted into the Smoluchowski equation, then we can calculate the full velocity profile inside the pore. For monovalent ions, this is in very good agreement with the flow velocity profile that we get from DPD simulations. However, when we do the same procedure for the divalent ions we see a significant deviation near the pore surface (compare Fig. 7 and 10 of the paper (**https://doi.org/10.1039/d3fd00062a**)) – indicating a breakdown of the hydrodynamics for electroosmotic flows of solutions containing multivalent ions in charged pores.

Sophie Marbach opened the discussion of the paper by Derek Stein: Thank you for a really nice presentation. You wanted to study ions but looked at particles in general; do you think there is a difference when looking at ions?

Derek Stein responded: Particles are a toy model for the counterions inside a nanochannel. Despite the extreme simplicity of this approach, which entirely ignores electrostatics, details about the interactions with the electrodes, and more, it provides a surprisingly good description of the ionic currents we measured in experiments. A full model must account for the important physics we ignored, and perhaps a deeper investigation will reveal when those effects become important.

Sophie Marbach asked: Can you specify whether in the experiments you are measuring ionic currents or particle positions and velocities?

Derek Stein answered: We have measured ionic currents and individual particle trajectories in experiments.

Tim M. Kamsma asked: Do you expect there to be any coupling between viscosity gradients and electric potential gradients? *I.e.*, would any fluxes due to simultaneous gradients simply be the sum of the fluxes when the gradients are imposed separately?

Derek Stein responded: This is an interesting question. I expect there to be a linear regime in which the fluxes from imposed viscosity and electric potential gradients add independently. This would be worth investigating experimentally.

Paul Robin remarked: In the paper (**https://doi.org/10.1039/d3fd00053b**), you considered two types of boundary conditions: reflecting or periodic. But we could consider different conditions, such as absorbing/open boundary conditions.

For example, we could imagine an experiment in a three-way, T-shaped channel using colloids: we constantly input colloids from the central branch, and we let them drift to either the left or right branch. What would it change? Additionally, since there is no "cycling through the electrodes" to provide an excess of particles on one side, there cannot be the same particle accumulation on one side as in the periodic case, I guess. The concentration profile should probably be peaked at the center and asymmetrically distributed (with a heavier tail on the high diffusivity side). Is that correct?

Derek Stein responded: The proposed experiment, where particles are introduced in the center of a channel and absorbed at the right or left ends, has already been treated theoretically by Marchesoni.[1] The drift induced by a viscosity gradient biases the side to which the particles exit. The resulting distribution of particles described in the question is essentially correct. Marchesoni's excellent discussion explains how this situation, which seems to allow Maxwell's demon to transmit information in a preferred direction even in thermal equilibrium, is nevertheless consistent with the second law of thermodynamics.

In the case of open boundaries, where the extremities of the channel communicate with reservoirs with a uniform density of particles, the entire channel achieves the same uniform density of particles with no net flux.

[1] F. Marchesoni, Drift in Diffusion Gradients, *Materials*, 2013, **6**(8), 3598–3609, DOI: **10.3390/ma6083598**.

Lyderic Bocquet commented: The proposed mechanism is subtle, one would like to get to the roots of it in various configurations. I was wondering what happens with immiscible liquids, for example, water and heptanol, and the migration of ethanol across them. How do thermodynamics play a part in the proposed viscosity-gradient driven mechanism, *e.g.*, introducing the partition coefficients of ethanol in the two components, *etc.*?

Derek Stein responded: I don't expect the viscosity gradient to affect the partition of ethanol in this system. The ethanol distribution will simply level the chemical potential across the system. In order for a viscosity gradient to drive transport, one would first need boundaries that act on ethanol in the way that electrodes absorb and release ions. Second, there needs to be a source of free energy, and that is absent in the case of immiscible liquids. The intermixing of liquids like formamide and glycerol, in contrast, can provide a source of free energy to drive transport when different concentrations are maintained at opposite ends of a channel.

Alexei A. Kornyshev said: I have a few questions: (1) How can the experimental variation of $D(x)$ be realised?

(2) What are the characteristic distance scales of this variation?

(3) Do you have independent tools for the measurements of the $D(x)$ profile?

Derek Stein responded: (1) We flow miscible liquids of different viscosity past either end of a nanochannel inside of which the fluids intermix. This creates a gradient in $D(x)$.

(2) The mixing channels were between 100 and 400 micrometers in length, 100 micrometers wide, and typically 50 deep.

(3) We recently completed a series of experiments in which we tracked the motion of individual fluorescent nanoparticles moving within the mixing channel. By analyzing the particle trajectories, using the theoretical approach described by Frishman and Ronceray,[1] we independently measured $D(x)$. The results of that work have been written up and will be submitted for publication.

[1] A. Frishman and P. Ronceray, Learning Force Fields from Stochastic Trajectories, *Phys. Rev. X*, 2020, **10**, 021009, DOI: **10.1103/PhysRevX.10.021009**.

Alexei A. Kornyshev asked: Will the temperature gradient not have a competing effect, as it should also affect the effective diffusion coefficient?

Derek Stein answered: A temperature gradient could indeed induce a competing effect that we wish to avoid. We consequently performed our measurements at a constant temperature.

Felipe Jiménez-Ángeles asked: When you are creating a viscosity gradient, do you have a gradient of permittivity that creates a similar effect? Does it go in the same direction as viscosity?

Derek Stein responded: We endeavored to create a viscosity gradient in a way that does not create a significant chemical potential gradient for the ions (which could derive from permittivity or other properties of the intermixing liquids). We did this by varying the fractions of formamide and glycerol on either side of a mixing channel. Although these liquids have very different viscosities, their solubilities for potassium chloride are similar. The solubility of an ion in a liquid relates directly to its chemical potential in that environment.

Tanja Vidakovic-Koch queried: What do you consider as a driving force for the transport? Do different viscosities cause differences in chemical potentials? How about the influence of the electrical field?

Derek Stein answered: The free energy of mixing provides a source of free energy to drive the transport. If we were to stop flowing fresh liquids past the channel ends, intermixing would eventually homogenize the liquid within the channel, depleting the source of free energy. The chemical potentials of the more viscous and less viscous liquid components (glycerol and formamide, respectively) vary across the system. Ions and particles follow the more viscous component because, according to the Maxwell–Stefan model of diffusion, that component exerts the greater friction force on them. The forces that drive the ions and particles are dissipative, not conservative, so one cannot properly describe their motion as resulting from a chemical potential difference. If a chemical potential difference were applied with an electric field, for example, that would certainly induce drift and/or electroosmotic flow that would add to the viscosity-driven transport.

Zuzanna S. Siwy commented: Your model is shown for particles, while the talk was motivated by a net ion current observed when a viscosity gradient was applied across a pore. How can the model be interpreted when considering the presence of positive and negative ions?

Derek Stein responded: We see particle dynamics as a toy model for the motion of counterions in the electric double layers along the glass surfaces of nanochannels in which we experimentally imposed a viscosity gradient and measured a steady ionic current. Counterions are the relevant particles here because currents from the positive and negative ions in the bulk solution should cancel out.

Tarique Anwar asked: In a system driven by a salinity gradient, the two ends of the reservoir have different osmotic/chemical potentials and this leads to an ionic current from high to low concentration. This can be explained based on the thermodynamics of the system. Similarly, in a system driven by viscosity, what is an analogous physical parameter that is different at the two ends of the reservoir? And does the system go to equilibrium when that physical parameter is the same for the whole system?

Derek Stein replied: We create a viscosity gradient by flowing liquids with different viscosities past opposite ends of a nanochannel within which the liquids intermix. The free energy of mixing provides a source of free energy to drive transport. If we were to stop flowing fresh liquids past the channel ends, intermixing would eventually homogenize the liquid within the channel, depleting the source of free energy.

Accordingly, the chemical potentials of the more viscous and less viscous liquid components are the parameters that vary across the system. Ions move down the chemical potential gradient of the more viscous component because, according to the Maxwell–Stefan model of diffusion, that component exerts the greater friction force on the ions.

Tarique Anwar commented: You mentioned that the system is not in equilibrium and a source term is used as a boundary condition in your simulation. In the presence of this source term, can we say that the flux will always be in the direction of lower viscosity? If so, it would be interesting to provide a thermodynamic explanation, similar to heat transport in a temperature gradient.

Alexander Barnaveli asked: Why would you study charged particles, if electric effects are going to counteract the flow?

Derek Stein responded: Electrostatics are obviously important to the behavior of real ions, so one should include those in a full model of ion transport in viscosity gradients. The simulations of ideal particles we performed are at best a toy model of the counterions in a nanochannel, although that toy model describes the ionic currents we measured surprisingly well. We would like to develop a better understanding of the interplay between viscosity, electrostatics, and osmotic effects in future work.

Tanja Vidaković-Koch said: As far as I know, the Maxwell–Stefan model considers only chemical potential gradients and volume forces (like the electric field) as driving forces for diffusion (also includes migration).

Derek Stein responded: Maxwell–Stefan (MS) theory also accounts for the mole fractions of different chemical species and predicts transport when gradients exist in those mole fractions. In other words, one can get the familiar Fickian diffusion from the Maxwell–Stefan model.

Martin Bazant communicated: I wonder about the possibility of taking the continuum limit of the “isothermal model” and using it to interpret the simulation results. The steady-state problem has an exact solution for the density profile for a given current and a given total concentration, but, although flux can be directed toward lower viscosity, the specific current cannot be determined from the boundary conditions. It is an ill-posed mathematical model, which raises the question: how do the stochastic simulations select a particular current? I suspect it is an artifact of the constrain of non-negative density imposed by simulating discrete particles, as well as the very large gradient in diffusivity (or viscosity) compared to the minimum value at $x = 0$. The transient simulation naturally leads to boundary layers where the concentration goes to zero at one end where depletion occurs, driven by the large diffusivity gradient. This leads to the prediction of a current that scales like $1/L$ as observed in Fig. 10 of your paper (**https://doi.org/10.1039/d3fd00053b**), which a prefactor that can be checked against in the simulations. I think such continuum analysis would help any follow-up work on this phenomenon, especially comparisons with experimental data.

Serge G. Lemay opened the discussion of the paper by Martin Bazant: The parabolas or the electronic degree of freedom are independent of the ionic configuration. Is this realistic? One could expect the reorganization energy to be highly sensitive to the ionic arrangement.

Martin Bazant replied: Indeed, the ionic and solvent degrees of freedom are always coupled in electrochemical reactions to varying degrees. In principle, such effects can be captured by quantum computations of the diabatic free energy surfaces of the reduced and oxidized states, *e.g.* by constrained density functional theory (CDFT). In order to derive a unified analytical theory of the reaction rate, it is necessary (or at least, convenient) to assume a separable free energy landscape, which is a good approximation in the limits of electron-coupled ion transfer (ECIT) and ion-coupled electron transfer (ICET) where one charge-transfer process (ET or IT) dominates and allows for crude approximations of the subdominant process, while maintaining overall accuracy. As described in the paper, strongly coupled ICET in electrocatalysis or electrodeposition leads to Butler–Volmer (BV) kinetics dominated by IT (as seen in experiments) regardless of the detailed model for the relatively small non-separable barrier for adiabatic ET. Conversely, for ECIT in ion intercalation by lithium iron phosphate (LFP), good agreement between theory and experiment is achieved without a detailed model of the non-separable IT barrier, since ET dominates. More generally, we may expect that any process where solvent reorganization involves mostly different atoms from the bond-breaking ion-transfer step could be well described by a separable free energy landscape. This is often the case for ion intercalation in solid electrodes, where the electron transfer process (*e.g.* reduction of a transition metal ion site by a conduction electron) is usually non-adiabatic and well separated from the transferring ion, not only for LFP but also for other Li-ion battery materials (to be described in upcoming publications). However the separable approximation surely breaks down for strongly coupled ion–electron transfer (CIET) processes, such as electrodeposition, where the transferring ion is itself reduced by electron transfer, although the ICET limit would still lead to BV kinetics in that case.

Serge G. Lemay remarked: The choice of energy landscape is motivated here in the context of a specific system. To what extent could one expect this to apply more generally?

Martin Bazant replied: The theoretical framework here is very general and should apply to any electrochemical process that involves bond-breaking chemical changes (with a generalized reaction coordinate related to atomic positions) coupled with electron transfer (with the Marcus reaction coordinate for reorganization of the solvent, or more generally, the local environment of the chemical change). The concept of a two-dimensional diabatic free energy landscape for coupled-ion electron transfer, in which the two surfaces are shifted by the formal overpotential and electron binding energy (relative to the Fermi level), is very general and captures the mechanism of most faradaic reactions at electrode interfaces, including electrodeposition, ion intercalation, electrolysis and electrocatalysis, including the possibility of strong electronic coupling leading to adiabatic blending of these free energy surfaces. The general theory also applies to charge transport by ion–electron polaron diffusion in semiconductors, intercalation compounds, and charged polymers, where each step in the polaron's random walk is a coupled ion–electron transfer reaction between neighboring sites. The same framework can also be extended to a photo-electrochemical process by considering the change in electron energy from photon adsorption, as discussed in the paper (**https://doi.org/10.1039/d3fd00108c**) for X-ray photoelectron emission processes.

Despite the generality of the overall framework, however, the specific formulation presented here, leading to various analytical results, rests on a number of assumptions, which may not always be valid and could be refined in future work, such as the following:

(1) We assume that the entropic contributions to the transition state excess chemical potential do not depend on electron energy or overpotential and thus can be factored out of the Fermi integrals. This makes sense for the configurational entropy for reactions involving countable reaction sites, such as ion intercalation or surface adsorption, where the transition state must exclude (typically one) adsorption site, but might not hold so well for disordered or soft interfaces, where the excluded volume could depend on the overpotential or electron energy.

(2) We also factor out the electron transmission coefficient from the Fermi integrals, which is only valid in the non-adiabatic regime of weak electronic coupling. We further neglect the dependence of the electronic coupling on varying nuclear positions during ion transfer. These approximations will certainly break down for non-adiabatic reactions. However, we argue in Section 9 of the paper, that in the ICET regime of electrocatalysis such details may be negligible compared to the Gurney–Butler effects of ion transfer, which helps explain why the Butler–Volmer equation (in contrast to Marcus theory) has successfully described the kinetics of electrolysis and related reactions for over a century.

(3) Next, we assume that the CIET free energy landscape is separable, with diabatic IT surface functions f_1 and f_2, that depend only upon the IT coordinate x_i, added to Marcus parabolae that depend only upon the ET reorganization coordinate q. This is a tacit assumption in all ET theories and is not upheld in quantum models of CIET reactions, such as those developed by Schmickler[1] for adiabatic reactions at a given overpotential. It could be important to generalize CIET theory for non-separable free energy landscapes, especially for strongly coupled reactions such as electrolysis or electrodeposition. However, the separable assumption should hold in the limiting regimes of ECIT and ICET identified here, which generalize Marcus and Butler–Volmer kinetics, respectively, since one reaction coordinate dominates over the other.

(4) We mainly assume symmetric ET where the Marcus parabolae always intersect, as in most of ET theory. We consider asymmetric ET in the asymmetric Marcus–Hush (AMH) approximation for the ECIT regime, which breaks down at large overpotentials. For the general case, we introduce asymmetry in ET by interpolation in the uniformly valid approximation of CIET kinetics, which may be the best way to introduce asymmetry in the diabatic framework. Of course, the true free energy landscape must have more complicated non-parabolic

dependence on the reorganization coordinate, which can in principle be included, at the expense of analytical complexity and possible difficulties in experimental validation.

(5) For ICET kinetics and the uniformly valid approximation, we make a much more drastic (and analytically convenient) Gurney–Butler approximation of truncated linear profiles for the IT contributions to the free energy landscape, along with Marcus parabolae for the reorganization coordinate. This linear-parabolic approximation is the simplest and most reasonable first approximation of the CIET energy landscape, but more general functions should be considered in future work, again at the expense of analytical convenience. Note that, while it is easy to approximate the energy landscape, it is difficult to perform the resulting Fermi integrations over the electron energies if higher-order polynomials or other nonlinear functions are used for the diabatic surfaces. The beauty of the present approach is that one can perform all of the integrals analytically to obtain simple analytical expressions, which are not much more complicated than Butler–Volmer kinetics.

1 W. Schmickler, *Chem. Phys. Lett.*, 1995, **237**, 152–160.

Tanja Vidaković-Koch remarked: Thank you for the very nice paper. I wonder how many (if any) freely adjustable parameters the kinetic expressions you propose have?

Martin Bazant answered: The theory has only three parameters for the limiting cases and otherwise predicts the dependence of the CIET reaction rate on overpotential, temperature and concentrations. In the ECIT limit of Marcus kinetics, these parameters are the Marcus reorganization energy, the mean ion transfer free energy, and a temperature-independent prefactor related to the electronic coupling. In the ICET limit, there are two ion transfer free energies (for reduction and oxidation), and the same prefactor. In the general case of the uniformly valid approximation of the CIET rate, there are four parameters, two ion transfer energies, the reorganization energy, and the prefactor.

In general, the model also takes the electrode band structure as another input (which need not be fitted), but no additional parameters are required in the typical case of a metal electrode in the wide band approximation.

When fitting experimental data, it may also be important to relate the concentrations of the reduced and oxidized species at the reaction site to the nearby bulk values, related to their activities. For example, we consider Langmuir adsorption isotherms, which are characterized by one fitted surface adsorption energy per species.

Robert A. W. Dryfe said: The comprehensive theory you have developed has been exemplified for the cases of coupled ion and electron transfer, for example the lithium iron phosphate case discussed in Fig. 14 of your paper (**https://doi.org/10.1039/d3fd00108c**), or the case of the hydrogen evolution reaction, as considered by Gurney and Butler. Such cases where electron transfer is coupled to intercalation within a solid, or bond breaking, present challenges for "classical" electron transfer theory, with respect to both potential dependence and any "pre-exponential" (exchange current) term.

Most of the detailed experimental data reported for electron transfer kinetics, however, relates to "simple" electron transfer systems, where molecule X exchanges an electron with an electrode, and kinetic parameters are determined in terms of the Butler–Volmer model, or in some cases, more sophisticated models. In principle, no covalent bond formation, or solid-state transformations, limit these cases. Marcus' original work (*e.g.* see the summary of his Nobel Prize lecture[1]) was motivated by the vast difference in electron transfer rates of superficially "similar" molecules, and the correlation found between the rates of heterogeneous electron transfer of these molecules and their "self-exchange" rates for homogeneous electron transfer. Although the Marcus model can be seen as a limiting case of the more comprehensive treatment you develop here, does your work more satisfactorily predict the "exchange current" (and potential dependence) of, for example, the systems summarised in Fig. 10 of Marcus' *Angew. Chem.* paper[1] from 1993?

1 R. A. Marcus, Electron Transfer Reactions in Chemistry: Theory and Experiment (Nobel Lecture), *Angew. Chem., Int. Ed.*, 1993, **32**, 1111–1121.

Martin Bazant answered: This is an excellent question, which coincidentally has both scientific and historical significance for *Faraday Discussions.*

In his Nobel Prize lecture, Marcus described his 1960 paper on statistical theories of the reorganization energy, which he wrote "in part to stimulate discussion with experimentalists in the field at a Faraday Society meeting on oxidation–reduction reactions".[1] In this paper, he predicted that the rate constant for a cross-reaction of ET between two different chemical species would scale as the geometric mean (square root of the product) of the two self-exchange ET rate constants. For faradaic ET reactions at electrodes, he further predicted that the heterogeneous exchange rate constant (estimated from Tafel plots fitted to the Butler–Volmer equation) would scale as the square root of the homogeneous self-exchange rate constant in solution (measured by isotopic exchange), which was later approximately confirmed by the data shown in Fig. 10 of his 1993 paper [from ref. 2]. The many advances in ET reaction kinetics triggered by Marcus' 1960 paper, paving the way for his Nobel Prize in 1992, could represent the greatest impact of any *Faraday Discussion* of the past century.

Although my paper focuses on bond-breaking electrochemical reactions of coupled ion–electron transfer (CIET), it does contain some mathematical results that could improve on the predictions of Marcus for "simple" ET reactions and extend them for electron-coupled ion transfer (ECIT) reactions, where a fast IT process is limited by slow, coupled ET. The analytical formula for the ECIT exchange current at a metal electrode, eqn (162) in the paper, provides a new nonlinear relationship between the exchange rate $k_{\mathrm{el}} = I_0 A_{\mathrm{s}}/eA\tilde{c}_{\mathrm{O}}$, the reorganization energy, λ_{el}, and equilibrium constant, $K_{\mathrm{el}} = \left(\frac{\tilde{c}_{\mathrm{O}}}{\tilde{c}_{\mathrm{R}}}\right)_{\eta=0}$, for the heterogeneous oxidation reaction at a metal electrode, including integration over the Fermi distribution of electron energies in the wide band approximation. Away from the electrode, where the electron density of states reduces to a delta function for a localized molecular orbital, the ECIT self-exchange rate has a similar (dimensionless) form as classical Marcus theory, $\tilde{k}_{\mathrm{ex}} = \exp\left(-\frac{\lambda_{\mathrm{ex}}}{4k_{\mathrm{B}}T}\right)$, with a reorganization energy, λ_{ex}, that is roughly twice that of the electrode interface.

Marcus first showed in his 1960 *Discuss. Faraday Soc.* paper that $\lambda_{\text{ex}} \approx 2\lambda_{\text{el}}$ is a universal prediction for symmetric, nonadiabatic ET, including contributions from both outer-sphere electrostatics and inner-sphere vibrational modes. Collecting these approximations, we arrive at a new nonlinear relationship,

$$\tilde{k}_{\text{el}} = \frac{1}{2(1+K_{\text{el}})}\operatorname{erfc}\left(\frac{2\ln\left(1/\tilde{k}_{\text{ex}}\right) - \sqrt{1+\sqrt{2\ln\left(1/\tilde{k}_{\text{ex}}\right)} + \ln^2 K_{\text{el}}}}{2\sqrt{2\ln\left(1/\tilde{k}_{\text{ex}}\right)}}\right),$$

where we define dimensionless rate constants for both heterogeneous electrode reactions (el) and homogeneous self-exchange reactions (ex) in the same way,

$$k = \tilde{k}\frac{\Delta_{\text{e}}}{h}\frac{1}{\gamma^{\text{IT}}}\exp\left(-\frac{\alpha(1-\alpha)(\beta_{\text{red}}+\beta_{\text{ox}})}{k_{\text{B}}T}\right),$$

allowing for the possibility of different parameters in each case. For the typical case $\lambda \gg k_{\text{B}}T$ (and thus $\tilde{k}_{\text{ex}} \ll 1$), we arrive at the simple scaling law,

$$\tilde{k}_{\text{el}} = \frac{1}{1+K_{\text{el}}}\sqrt{\frac{\tilde{k}_{\text{ex}}}{2\pi\ln\left(\frac{1}{\tilde{k}_{\text{ex}}}\right)}}.$$

In the limit of low rates, we recover the original scaling of Marcus[1] for symmetric ET, $k_{\text{el}} \propto \sqrt{k_{\text{ex}}}$, provided that all the parameters other than reorganization energy are nearly constant. This includes the classical case of pure ET (without IT), which corresponds to $\gamma^{\text{IT}} = 1$, $\beta_{\text{red}} = \beta_{\text{ox}} = 0$ and similar electronic coupling (chemisorption function), Δ_{e}, for both reactions.

The general result above also includes new cases of ECIT reactions with significant contributions from bond-breaking IT. Important examples would include ion intercalation by ECIT in electrically insulating host solids, such as lithium iron phosphate (LFP), and lithium manganese iron phosphate (LMFP). The paper already discusses the heterogeneous electrode reaction for carbon-coated LFP in detail, which consists of fast IT for intercalation coupled to slow ET from the metallic surface film or contact. The paper also mentions the analogous homogeneous reaction, which corresponds to lithium polaron diffusion in the bulk solid electrode (not the liquid electrolyte). The solid-state polaron diffusion mechanism can be modeled as a random walk of unbiased CIET reactions of the electron–ion pair between neighboring crystal unit cells, where the slow step is electron hopping between iron redox sites ($\text{Fe}^{3+}/\text{Fe}^{2+}$), which is coupled to the fast step of lithium ion hopping to adjacent sites. The polaron diffusivity in the dilute limit is given by $D_0 = k_{\text{ex}}\Delta y/(c_{\text{s}}\Delta x\Delta z)$ where c_{s} is the lithium site concentration, Δy is the lattice spacing along the (010) crystal axis of fast polaron diffusion and $\Delta x\Delta z$ is the cross-sectional area of the unit cell; in concentrated solid solutions, the chemical diffusivity is given by $D = D_0\gamma/\gamma_{\text{TS}}$, where γ is the bulk activity coefficient and γ_{TS} is the transition state activity coefficient for diffusion; since the former excludes one site, and the latter excludes two sites, we obtain the same thermodynamic prefactor related to excluded volume, $\dfrac{\gamma}{\gamma_{\text{TS}}} \sim \dfrac{1/(1-\tilde{c})}{1/(1-\tilde{c})^2} = (1-\tilde{c}) \sim \dfrac{1}{\gamma^{\text{IT}}}$, for both heterogeneous CIET for intercalation and homogeneous CIET for polaron diffusion in a solid solution, where $\tilde{c} = \tilde{c}_R$ (filling fraction of the reduced state of inserted ions).[3] In the ECIT regime, where the reorganization energy dominates activation of the reaction, we could follow the arguments of Marcus predicting $\lambda_{ex} \approx 2\lambda_{el}$ to obtain an analogous scaling law for the exchange current and solid polaron diffusivity in the same intercalation material,

$$I_0 \propto \sqrt{D} \quad \text{(ECIT)},$$

neglecting (possibly large) differences in electronic coupling Δ_e. Such scaling is roughly consistent with the larger activation barrier for polaron diffusion (200–300 meV) compared to that of ion intercalation (120–350 meV) discussed in the paper. This scaling would be interesting to investigate in experiments or quantum calculations, although we expect more complicated behavior to arise, including electrolyte composition effects, perhaps captured by the nonlinear scaling laws above for ECIT.

It would be interesting to further explore the predictions of CIET theory relating heterogeneous and homogeneous reaction rate constants, which need not follow the Marcus scaling. For example, the relation between exchange current and solid polaron diffusivity for ion intercalation may take different forms. The arguments above suggest that these two quantities have essentially the same form using CIET theory (neglecting constants given above):

$$I_0, D \propto \frac{\Delta_e}{\gamma^{IT}} \exp\left(-\frac{\alpha(1-\alpha)(\lambda + \beta_{red} + \beta_{ox})}{k_B T}\right),$$

where the parameters Δ_e, γ^{IT}, λ, β_{red}, and β_{ox} are different for intercalation and diffusion, but may be predicted by microscopic theories or quantum calculations (note that $\alpha = \beta_{red}/(\beta_{red} + \beta_{ox})$ is not an independent parameter). Since $\gamma^{IT} \approx 1/(1 - \tilde{c})$ is roughly the same for both quantities if β_{red} and β_{ox} were related by the same Marcus scaling as reorganization energies, $\beta_{ex} \approx 2\beta_{el}$, then we would predict that the same scaling relation $I_0 \propto \sqrt{D}$ holds for CIET intercalation, in general. However, this is not necessarily the case, as theoretical expressions for β_{red} and β_{ox} based on electrostatics have more complicated forms in CIET theory.[4] Nevertheless, it would be interesting to explore the possibility of such relationships using theory, quantum calculations and experiments in the more typical regime of ICET, which includes most cases of electrodeposition, electrocatalysis, and ion intercalation in metallic electrode materials, where the IT free energies dominate and lead to different scalings for heterogeneous and homogeneous reactions with our quantum-mechanical generalization of Butler–Volmer kinetics. Additional scaling laws could be predicted by the theory and found in nature for different classes of electrochemical reactions.

1 R. A. Marcus, Exchange reactions and electron transfer reactions including isotopic exchange. Theory of oxidation-reduction reactions involving electron transfer. Part 4.—A statistical-mechanical basis for treating contributions from solvent, ligands, and inert salt, *Discuss. Faraday Soc.*, 1960, **29**, 21–31.

2 R. D. Cannon, *Electron Transfer Reactions*, 1980.

3 M. Z. Bazant, Theory of Chemical Kinetics and Charge Transfer based on Nonequilibrium Thermodynamics, *Acc. Chem. Res.*, 2013, **46**, 1144–1160.

4 D. Fraggedakis, M. McEldrew, R. B. Smith, Y. Krishnan, Y. Zhang, P. Bai, W. C. Chueh, Y. Shao-Horn and M. Z. Bazant, Theory of coupled ion-electron transfer kinetics, *Electrochim. Acta*, 2021, **367**, 137432.

Frédéric Kanoufi communicated: The unified model you propose combines IT and ET competitive reactions. This nicely applies to the systems you presented (**https://doi.org/10.1039/d3fd00108c**). It should also apply to liquid/liquid interfaces for which Marcus has also proposed a theory, for electron transfer processes,[1,2] while theory or a model for the ion transfer process has also been documented.[3–5] To what extent can your model be applied or to what extent does it extend those previous works?

It would also comparatively apply to the electrochemical doping of a conducting polymer. In this case, how would it extend the existing models?

1 R. A. Marcus, Theory of electron-transfer rates across liquid-liquid interfaces, *J. Phys. Chem.*, 1990, **94**(10), 4152–4155.
2 R. A. Marcus, Theory of electron-transfer rates across liquid-liquid interfaces. 2. Relationships and application, *J. Phys. Chem.*, 1991, **95**(5), 2010–2013.
3 R. A. Marcus, On the theory of ion transfer rates across the interface of two immiscible liquids, *J. Chem. Phys.*, 2000, **113**, 1618–1629.
4 H. H. Girault and D. J. Schiffrin, Theory of the kinetics of ion transfer across liquid/liquid interfaces, *J. Electroanal. Chem. Interfacial Electrochem.*, 1985, **195**, 213–227.
5 L. Benjamin, Mechanism and Dynamics of Ion Transfer Across a Liquid-Liquid Interface, *Science*, 1993, **261**, 1558–1560.

Martin Bazant communicated in reply: This is an excellent question. CIET theory could certainly be applied to charge transfer at liquid–liquid interfaces, including interfaces between two immiscible electrolyte solutions (ITIES), as well as faradaic reactions at liquid metal electrodes. For ITIES, there is an ongoing debate over the nature of charge-transfer reactions,[1] which are typically categorized as either heterogeneous, involving only electron transfer (ET) between redox species on opposite sides of the interface, or homogeneous, involving ion transfer (IT) back and forth across the interface in series with ET redox reactions occurring in one bulk phase. CIET theory would describe a third possible reaction mechanism where ET is coupled to IT at the interface in a single, coupled heterogeneous reaction.

The cited papers describe various important aspects of ET or IT at liquid–liquid interfaces but fall short of describing a coupled reaction mechanism. Marcus[2] and Girault[3] derived generalizations of the classical Marcus formula of the outer-sphere reorganization energy (in a homogeneous phase) for the case of ET across an interface between two dielectric media without considering any coupled IT processes. Marcus[4] then developed a theory of the IT barrier for a liquid–liquid interface based on the free energy of protrusions (analogous to curvature-dependent chemical potential in the theory of molecular-beam epitaxial growth), motivated by the “water fingers” identified by Benjamin,[5] without considering any coupled ET processes. Such theories naturally lead to Butler–Volmer kinetics of IT for liquid–liquid charge transfer, as shown by Girault and Schiffrin,[6] but cannot predict curved Tafel plots or other effects of coupled ET. Some of these ideas could be integrated into the CIET framework, not only for liquid–liquid interfaces, but more broadly for charge transfer across dielectric interfaces. Fraggedakis *et al.*[7] already derived electrostatic formulae for the free energy of IT across dielectric interfaces, which could be combined with the Marcus–Girault expressions for the analogous outer-sphere reorganization energy[2,3] to describe cases where CIET occurs with both IT and ET crossing the interface. This could describe some cases of electrodeposition or chemical redox processes involving CIET. Such applications of the general theoretical framework would differ from simpler reactions, such as lithium ion intercalation, where only IT crosses the interface, and ET occurs in one phase (the solid insertion electrode). These interfacial CIET reactions could also involve mixed ion–electron conductor (MIEC) materials on one or both sides of the interface, including the case of electrochemically doped polymers. Bulk conduction in MIECs would be also straightforward to describe with CIET theory, similar to polaron transport in intercalation solids.

1 G. C. Gschwend, A. Olaya, P. Peljo and H. H. Girault, Structure and reactivity of the polarised liquid–liquid interface: what we know and what we do not, *Curr. Opin. Electrochem.*, 2020, **19**, 137–143.
2 R. A. Marcus, Theory of electron-transfer rates across liquid–liquid interfaces, *J. Phys. Chem.*, 1990, **94**(10), 4152–4155.
3 H. H. Girault, Solvent reorganization energy for heterogeneous electron-transfer reactions at liquid | liquid interfaces, *J. Electroanal. Chem.*, 1995, **388**(1–2), 93–100.
4 R. A. Marcus, On the theory of ion transfer rates across the interface of two immiscible liquids, *J. Chem. Phys.*, 2000, **113**(4), 1618–1629.
5 I. Benjamin, Mechanism and dynamics of ion transfer across a liquid–liquid interface, *Science*, 1993, **261**(5128), 1558–1560.
6 H. H. J. Girault and D. J. Schiffrin, Theory of the kinetics of ion transfer across liquid/liquid interfaces *J. Electroanal. Chem. Interfacial Electrochem.*, 1985, **195**(2), 213–227.
7 D. Fraggedakis, M. McEldrew, R. B. Smith, Y. Krishnan, Y. Zhang, P. Bai, W. C. Chueh, Y. Shao-Horn and M. Z. Bazant, Theory of coupled ion–electron transfer kinetics, *Electrochim. Acta*, 2021, **367**, 137432.

Frédéric Kanoufi communicated: The beauty of providing a unifying theory with quantum mechanics is the possibility offered to reach prediction from computational chemistry.

If for Marcus theory this requires computing the solvent reorganisation energy term, what type of material characteristic should a theoretical chemist be aiming at to predict a material's Tafel behavior? This is important, as you demonstrated in your manuscript, in batteries and electrocatalysis, but it also has quite some importance in the more complex cases of corrosion where the exchange current evaluation is even more difficult to access experimentally.

Martin Bazant communicated in reply: The presented CIET theory indeed provides a general framework to predict reaction rates from quantum computational chemistry. As mentioned in the paper, the diabatic free energy landscape for non-adiabatic CIET can be predicted using Constrained Density Functional Theory (CDFT), where ionic motion is imposed, while electrons are constrained to lie in the reduced or oxidized state. The adiabatic free energy landscape can be calculated with traditional density functional theory to estimate the chemisorption function or electronic coupling by comparing with CDFT results for the nonadiabatic CIET barrier. In both cases, a challenge is to repeat the calculations for different overpotentials, as discussed in the section on adiabatic CIET, but such complete calculations of the free energy landscape may not always be necessary. The most valuable contribution of the theory is to capture the dependence of the rate on overpotential, temperature and concentrations in terms of a few physically meaningful parameters, Gurney–Butler ion transfer free energies and Marcus reorganization energy, which can be estimated from quantum calculations. In principle, these quantities can be calculated for corrosion reactions and used to predict mixed potentials and corrosion rates of coupled CIET reduction and oxidation reactions.

Sophie Marbach opened the discussion of the paper by Tim M. Kamsma: Thank you for a really nice presentation. Is this setup to create ion spikes the simplest it could be? Is it the “minimal” system?

Tim M. Kamsma answered: Although it is difficult to definitively exclude the possibility of other potentially simpler systems, I do believe that this is the simplest system using these types of channels that exhibits both all-or-none action potentials and spike trains. Perhaps more complicated channels, which feature more non-linearities than “just” current rectification, can facilitate an even simpler circuit with two channels. However, then one could wonder if such more complicated channels would actually make it more “minimal”.

As I understand it now, we need something quasi-instantaneous that forms a double-well potential (*i.e.*, a bistable system); this is what the two fast channels do. Then a slow feature is needed to allow for the spike between these two wells. This fast–slow characteristic actually is quite similar to the Fitz-Hugh–Nagumo model; in the supplementary material of the preceding *Phys. Rev. Lett.* paper[1] on this subject we go a bit more in depth on this. For the slow variable we need at least one “slow” channel, so if one is to make a simpler system, then one would need to create the double-well potential using only one channel, which I do not think is possible, but again, I cannot say so completely definitively.

1 T. M. Kamsma, W. Q. Boon, T. ter Rele, C. Spitoni and R. van Roij, Iontronic Neuromorphic Signaling with Conical Microfluidic Memristors, *Phys. Rev. Lett.*, 2023, **130**(26), 268401.

Martin Bazant remarked: This paper (**https://doi.org/10.1039/d3fd00022b**) nicely demonstrates the principles of resistive switching by bipolar conical channels and their use in constructing aqueous iontronic circuits capable of nonlinear response, resembling neuronal communication. While there has been great progress in understanding the physics of biological ion channels and constructing nanofluidic models, much less is known about the “ion pumps”, which consume energy to drive ions against their chemical potential gradients. In this paper, you achieve the tantalizing result of producing neuron-like spike trains above a critical voltage amplitude, but this is done with some distinctly non-biological elements in the circuit, including a capacitor and (especially) three batteries, playing the role of the ion pumps. What are the prospects of achieving a fully-contained iontronic device that mimics not only nonlinear gating of ion transport, but also the generation and propagation of pulses, by converting stored chemical energy into electrical work without the integration of non-biological microbatteries?

Tim M. Kamsma responded: Although I cannot give any explicit suggestions as of yet, this is certainly one of the interesting directions to look at for further research. We have considered this in the past and briefly looked at the use of ion-exchange membranes to induce different Nernst potentials for different channels. One has to be a bit careful here since these membranes also create their own electric potential drops when a concentration gradient is applied, complicating the internal voltages in the circuit. We initially went for the simplest, most straightforward model with the batteries, to construct a well-understood basis to work from. Now that we have this improved circuit with bipolar (BP) channels, the batteries are of lower potential and in a more suitable range to be generated by a realistic chemical potential. Therefore, this next step of leveraging BP channels also brings the prospect of replacing the batteries with concentration gradients closer. It would then also be fascinating to see if (artificial) ion pumps can be implemented to maintain these concentration gradients and make the system fully self-contained, but I must admit that this is a step I haven't yet given proper thought to. Regarding the capacitor, I believe that this offers some more flexibility. The system is not very sensitive to the capacitance and we chose the capacitance such that it matches with the typical capacitance of a piece of neuronal membrane of the same spatial dimensions as the system (*i.e.*, a few μm^2).

Martin Bazant communicated: (1) The BP conical channel is suggested as a model for the ion channels found in biological cell membranes, including those in neurons, in that it modulates fluxes of ions, depending on the jump in potential and ion concentrations across it. A hallmark of biological ion channels is their selectivity to specific ions, such as potassium, sodium or calcium, which is critical for cell and neuronal functions. What are the selectivity properties of the BP conical channels and how do they compare to those of biological channels? I assume there is some selectivity based on charge, but probably not to specific ions of the same valence, such as K^+ and Na^+. The latter derives from strong interactions with the pore protein walls under molecular confinement, which is difficult to achieve in nanofluidic channels described by continuum models of ion transport.

(2) The present work focuses on models of the "wiring" of the brain, but to truly achieve nanofluidic neuromorphic computing devices, one must also model the interfaces between neurons, the synapses, where information is also stored and propagated. How might one terminate the present neuronal circuit model (even with the batteries) in such a way that mimics synapses with iontronic devices?

Tim M. Kamsma communicated in reply: (1) The channels we consider are in the small Debye-length regime $\lambda_D \ll R(x)$, so transport is dominated by the (neutral) channel bulk and hence the channel is (for all intents and purposes) not selective to ions. This is the reason why we need individual batteries in this configuration, since we cannot give each channel its "individual" Nernst potential as in our biology. If we wish to implement selective channels, then for now we would probably need to rely on ion-exchange membranes that are charge selective. Leveraging chemical regulation by using, *e.g.*, surface groups would be another way to implement different responses to different types of ions (or molecules).

(2) This is a great point and something that we are actively working on. While the biological ion channels that facilitate neuronal signalling can be considered memristors, the synapses also are memristive and various synaptic functionalities can be extracted from the ion channels we consider. How to then couple these systems together is another challenge. One could look at the well-established

Cable theory, which is typically used to extend Hodgkin–Huxley models to simulate full cells and has the benefit of being a "physical" model.

Paul Robin commented: I do not think that there is a solid argument showing that you need three nanofluidic diodes to reproduce the spiking mechanism you showed. The Hodgkin–Huxley model actually uses only 2 memristors, and its mathematical model can be reduced to a 2D dynamical system (corresponding to a single memristor and a single capacitor). Obviously, whether or not it is in practice doable to achieve spiking with less than three nanofluidic channels depends on the details of how they work. However, if you do the mathematical stability analysis of the spiking mechanism, maybe you could get some answer. Did you try that?

I also have some additional side questions:

Is that a Hopf bifurcation?

What is the "frequency curve" of your system, *i.e.*, the spiking frequency as a function of input current?

Is the effect robust against slight parameter changes (*e.g.* slight changes in the battery voltage)?

Tim M. Kamsma answered: This is a great question, which will allow us to nicely see how these (seemingly different) Hodgkin–Huxley (HH) features actually all share direct similarities with the circuit we present. Let's start off with the "full" HH model. Although there are just 2 memristors in the HH model, the "sodium channel memristor" depends on two internal states (typically labelled m and h), and the potassium channel depends on a third internal state (typically labelled n). So, similar to our circuit, the full HH model is actually a 4-dimensional system consisting of the voltage V and the 3 internal state variables, that are each described by an exponential decay-like equation $\mathrm{d}n/\mathrm{d}t = (n_\infty(V) - n)/\tau_n(V)$ (although it is also sometimes presented in a differently written form), with V being described by Kirchhoff's law. So this is actually very similar, both in dimensionality and in form, to our system. There are of course differences, *e.g.* we have constant timescales τ and an additional battery. A reduction to a 2D system is also possible in our case; in fact, we have done precisely this in the supplementary material of the preceding *Phys. Rev. Lett.* paper,[1] where we use that the change in conductance of the fast channels in response to a voltage change can be considered instantaneous. In doing so, we show that our system is very similar to the FitzHugh–Nagumo (FN) model, a well-known model that reproduces HH action potential generation in a simpler 2D system. In summary, our full circuit starts off with the same dimensionality (4D) as, and comparable equation form to, the HH circuit and can also be reduced to a 2D system. We have indeed done some analysis on the spiking behaviour leveraging the simpler 2D system. The two fast channels that are reduced to instantaneous functions result in a cubic term in Kirchhoff's law (*i.e.*, a double-well potential), just like the FN model. I do not see a way to obtain this cubic term with just a single channel or diode. The slow variable in the FN model then corresponds to our slow channel, bringing the total up to (the perhaps minimal) three channels. That being said, this indeed does not definitively exclude the existence of an even simpler circuit exhibiting the same features. The emergence of the spike train in the 2D system then indeed is shown to be a (supercritical) Hopf-bifurcation. The frequency increases as the current becomes stronger, but a spike train typically only occurs for a relatively small current interval. The system is rather sensitive to changes in parameters. The use of BP channels rather than unipolar (UP) channels does allow for some more stability, but even then it remains sensitive to parameter changes.

1 1 T. M. Kamsma, W. Q. Boon, T. ter Rele, C. Spitoni and R. van Roij, Iontronic Neuromorphic Signaling with Conical Microfluidic Memristors, *Phys. Rev. Lett.*, 2023, **130**(26), 268401.

Yan Levin said: I was not very clear on what was adjusted in the model to get the jump between −70 and 50 mV.

Tim M. Kamsma responded: This is facilitated by two things: (1) the stronger conductance tuning of the channels, which allows for (2) batteries of lower electric potential to be used. Basically, the batteries attached to the short fast channels induce a bistable system (if we leave out the third channel), where each short channel drives V_m to E_+ or E_-, respectively. So the battery potentials influence the voltages of these stable states, which eventually dictates the V_m floor and ceiling during spiking. The long slow channel then results in periodic switching between the two and ensures that only the negative V_m state is actually stable.

Since the BP channels exhibit much stronger conductance changes, a much lower voltage range is needed over the channel to achieve the necessary change in channel conductance. Therefore, lower battery potentials are possible and since these battery potentials are what determines the upper and lower range of V_m during spiking, it results in a jump from ∼−70 mV to ∼50 mV.

Amritha Janardanan asked: Can you explain intuitively how the conical configuration and bipolar charge distribution help cause/improve the rectification? Why did you try this bipolar configuration?

Tim M. Kamsma replied: The intuitive and somewhat heuristic explanation would be that some sort of inhomogeneity is needed along the channel, be it geometrical (*i.e.*, the radius), surface charge or something else. By combining both a geometric and surface charge variation along the channel, these effects add up and result in an even stronger current rectification. To make this a bit more explicit, in eqn (7) of the paper (**https://doi.org/10.1039/d3fd00022b**), the second term (the conductive term) effectively forms a source or sink term when a steady-state condition is imposed due to the x dependence of both the electric field and the surface charge. It should be noted that eqn (8) of the paper actually also predicts that these effects can cancel out, resulting in no rectification, despite a geometric and surface charge inhomogeneity. The reason why we specifically focused on a bipolar parameter set is because we were inspired by experiments that used bipolar channels.

Sidahmed Abayzeed said: Thank you for the great presentation. The Hodgkin–Huxley model is used to test the use of bipolar conical channels to model the generation of action potential, treating neurons as iontronic systems. Can your approach be applied to integrate inputs from dendrites to test firing of a neuron?

Tim M. Kamsma responded: This is an interesting suggestion that could warrant some proper explicit calculations. My initial thought would be that the all-or-none law exhibited by our circuit can of course facilitate that the circuit only fires when a sufficiently strong input is received, but the actual conversion of input spikes to a climbing input current I until the postsynaptic system fires is something that would have to be ensured by an additional device or channel.

Joan Montes de Oca asked: Does the bipolar spiking pore operate like a reverse-biased p–n junction in the breakdown regime? Is the charge region at the exit of the pore fully depleted?

Tim M. Kamsma answered: The bipolar channels do not quite act like a reverse-biased p–n junction close to the breakdown regime, although the all-or-none law does suggest some similarities. However, the channels themselves are “normal” iontronic diodes in the steady state and memristors when one considers dynamics. The all-or-none feature resembling this breakdown regime results from the overall circuit architecture, rather than the feature of just a single channel. One can actually show that the two fast channels form a double-well potential, thus a spike only occurs when the voltage can jump from one well to another and thus one might make some interesting comparisons. The salt concentration, which determines the conduction in the channels we consider, can locally be almost completely depleted.

Zuzanna S. Siwy queried: Would your system benefit from a concentration gradient applied across the conically shaped diodes? Harnessing a concentration gradient would make the system more biomimetic and resembling a neuron.

Tim M. Kamsma answered: I am currently not aware of an explicit way to make this specific circuit benefit from concentration gradients. We have briefly looked at ways to replace the batteries with actual concentration gradients, but we thought one would then need selective membranes of some sort and these would introduce their own electric potential differences when a concentration gradient is applied over them, complicating the system. For simplicity, we now stick with “just” the batteries, but revisiting this idea would be interesting for future work, also going beyond just this circuit. The freedom of chemical regulation is one of the unique promises of fluidic iontronic systems so I wholeheartedly agree with the statements that harnessing the features of varying concentrations is of huge interest.

Serge G. Lemay said: While I appreciate the analogy to neurons and Nernst potentials, it seems like the batteries would be nearly impossible to implement in a physical microfluidic circuit as it is not easy to implement different longitudinal DC potentials along coupled channels. Could you comment on this?

Tim M. Kamsma replied: My initial comment would be that the implementation of the batteries is not a goal in and of itself, but rather a means to an end. The “end” being that either fast channel somehow wants to drive the voltage to either a negative or positive state. Indeed, our initial approach just concerns a straight up theoretical implementation of batteries in series with a channel, where we did make sure to model the batteries as actual electric potentials in all parts of the theory, *i.e.* they also affect the voltage dependent channel conductance, unlike in Hodgkin–Huxley theory. However, how to actually implement these is a challenge that I find difficult to address as I have limited experience in the experimental manipulation of such systems. I have the hope that our proposal and our deep theoretical understanding of the functionality of the circuit will offer a platform from which next steps can be made, both in theory and experiment.

Alexei A. Kornyshev opened the discussion of the paper by Gilad Yossifon: How do you see the realm of applications of ionic transistors and logical gates? How can those be integrated into circuits?

Gilad Yossifon replied: While we have realized ionic circuits using only bipolar ionic diodes, more complex ionic circuits can be realized by also combining ionic transistors, either bipolar junction transistors or field-effect transistors, which can extend the level of integration due to amplification of the signal, as well as being used for more sophisticated gating of ions and/or molecules.

Paul Robin asked: Can you explain qualitatively how your device works? Can you walk me through the steps through which your logic gate actually computes an “OR” or an “AND” function?

Gilad Yossifon responded: The logic computation of either the OR or AND logic gate was realized by measuring the open-circuit potential in the microchamber that interfaces all bipolar diodes. The inputs of the logic gates are either 0 or 1 volt and the value of the open-circuit potential is affected by the ionic electrical resistances across the bipolar diodes in both the open and closed states, while the threshold signal differentiating between low (0) and high (1) logic values is 0.5 V. The degradation of the potential signal is due to the parasitic resistances of the bipolar diodes in the open state, as well as leakage current across the diode in the closed state. When connecting several logic gates to realize a more complex circuit, these degraded signals become a limiting factor to the integration level.

Paul Robin queried: Is your implementation of an “OR”/“AND” gate using nanofluidic diodes similar to the usual implementation of these gates in electronics (*i.e.*, replacing nanochannels by actual diodes)?

Gilad Yossifon replied: Our implementation of the ionic OR and AND gate is different from the solid-state version due to the different nature of the charge carriers (ions *versus* electrons) and the electrical response of the components (*e.g.* the ionic bipolar diode is lacking a threshold in the forward bias, and exhibits hysteresis effects due to effects such as ionic concentration-polarization). Specifically, we have used a third bipolar diode in its reverse-bias mode as a resistor to reduce the voltage drop across the diodes in the forward bias.

Yujia Zhang said: Please comment on the potential drawbacks of the ionic diode system, including the low salt concentration, material charge-selectivity, *etc.*

Gilad Yossifon replied: The main drawbacks are the limitation of the number of possible integrated logic gates due to the degradation of the signal and the long transport time of molecules across the diodes. Both of these can be improved but not eliminated when reducing the dimensions of the diodes, which are currently very large ($\sim$2 mm) due to the low resolution of the fabrication process.

Yujia Zhang remarked: Please clarify how to use a transistor to increase the performance of the ionic diode system.

Gilad Yossifon replied: The inclusion of an ionic transistor in the integrated ionic circuit in addition to the ionic bipolar diodes is to amplify the signal as it degrades through a cascade of logic gates due to the parasitic resistances of the diodes in the forward bias and the leakage currents in the reverse bias.

Joan Montes de Oca commented: The logic gates discussed in the paper (**https://doi.org/10.1039/d3fd00061c**) are made of ionic "diodes" with characteristic open or closed states. Would it be possible to use a voltage-gated membrane like the one mentioned in the discussion of the paper by Tim Kamsma *et al.* (**https://doi.org/10.1039/d3fd00022b**) to produce a non-linear response instead?

Gilad Yossifon answered: The bipolar ionic diodes realized in our study were made of polyelectrolyte membranes.

Frédéric Kanoufi remarked: This is a very interesting experimental device, and definitely it will be pertinent miniaturizing it. From its millimetric dimension, I guess that you must completely fill the channel with the polymers, unlike with nanochannels where a partial coating up to electrical double layer overlapping conditions would be enough (as presented in the Sumita Pennathur contribution (**https://doi.org/10.1039/d3fd00074e**)). It might be time-consuming to do such polymerization over mm^2 regions and I wonder to what extent filling only the pore mouth would give a similar efficiency? If not, how far inside the pore should the polymer filling go? Finally, I wonder how long the membrane can be used or if there is not in the long term (with some specific ions, such as Mg or Ca) some clogging requiring recycling processes?

Gilad Yossifon responded: We agree that the bipolar junction region is dominating the response and hence reducing the region where the polyelectrolytes are filled around the junction should give similar results. However, in the rapid prototyping approach that we have used, the resolution of the fabrication cannot enable us to precisely control the region. Using a more precise fabrication approach of the microchannels, *e.g.* photolithography, will surely enable us to reduce the size of the diode and the region of the polyelectrolytes. With regard to long-term operation, we have not yet examined this besides performing several cycles of operation with monovalent electrolytes and observing a robust and repeatable operation.

Derek Stein asked: Have you considered studying multivalent ions and different polyelectrolytes in your devices? This experimental system is very interesting as it may provide opportunities to couple electrostatic forces with conformational changes in polymers in ways that could mimic the nonlinear conductance properties of certain biological ion channels. For instance, multivalent ions passing through a highly charged polymer network could induce condensation. If cooperative binding occurs, it could give strong threshold behavior for the conductance.

Gilad Yossifon answered: Thanks for this suggestion. We have not studied the transport of multivalent ions and we agree that this will add another interesting aspect of transport within our bipolar diodes that is worth investigating.

Rene van Roij said: In your work, specific thresholds are set for the voltage and the fluorescence intensity above and below which the logic output is a digital "1" and a digital "0", respectively. This is perfectly understandable in the context of applications in Boolean logic. However, have you considered analogue rather than digital readouts? This could potentially be relevant for applications in "reservoir computing", because the analog output can represent much more data than a single bit. This may, for instance, be useful to reduce the amount of data that is needed to train a neural network.

Gilad Yossifon answered: Thanks for the suggestion. We have indeed focused on Boolean operations and hence used digital logic gates inspired by previous realizations of solid-state electronics logic circuits. However, since the signals can be also measured continuously, we can also try to realize analog ionic circuits inspired by solid-state analog circuits.

Zuzanna S. Siwy remarked: The *I–V* curves of your diodes showed a linear dependence of the ion current on voltage in the 'on' state. What is the physical mechanism behind this?

Gilad Yossifon responded: The apparent linear response in the forward bias (*i.e.* the ON state) in the voltage range that was used – *i.e.* from −1 to +1 V – is only a rough approximation and, when expanding the voltage range, one can observe beyond this voltage range a non-linear behavior, in particular, the existence of a maximum due to additional competing effects, *e.g.* ionic depletion within the interfacing microchannels.

Sanli Faez asked: Can you please comment on the durability and reproducibility of such iontronic gates? When used in a device, how many times do you expect each gate to be switched on/off before it degrades or loses its function completely?

Gilad Yossifon answered: We have tested their performance for several cycles of operation and obtained a robust and repeatable response. However, we have not tried to examine this further and it is a valid question that we will need to address later on.

conflicts of interest

There are no conflicts to declare. Aleksandar Donev could not be contacted regarding any possible conflicts of interest before going to print.