PNP
What is in a Name?

Version 2

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Abstract and Summary

The name **PNP** was introduced by Eisenberg and Chen because it has important physical meaning beyond being the first letters of **P**oisson-**N**ernst-**P**lanck. **PNP** also means **P**ositive-**N**egative-**P**ositive, the signs of majority current carriers in different regions of a **PNP** bipolar transistor. **PNP** transistors are two diodes in series **PN** + **NP** that rectify by changing the shape of the electric field. Transistors can function as quite different types of nonlinear devices by changing the shape of the electric field. Those realities motivated Eisenberg and Chen to introduce the name **PNP** in 1993.

The pun "**PNP = P**oisson-**N**ernst-**P**lanck **= P**ositive-**N**egative-**P**ositive" has physical content. It suggests that **P**oisson-**N**ernst-**P**lanck systems like open ionic channels cannot be assumed to have constant electric fields. Indeed, the equations of electrodynamics make it more or less impossible that a channel have a constant electric field, if there is permanent charge nearby. The electric field must be studied and computed because its change of shape is unavoidable for charged channels, and the shape of the electric field is likely to be important in the function of biological systems, as it is in semiconductor systems.

PNP is a shortened name for "**P**ositive-**N**egative-**P**ositive" or "**P**oisson-**N**ernst-**P**lanck equation". It was not meant to be just an abbreviation: names are important, beyond their logical meaning, as advertisements show us everyday. The name **PNP** is no exception. The name was chosen to help understand the system it describes.

PNP was a pun introduced by Eisenberg and Chen [1, 2] at a well attended workshop of the 1993 Biophysical Society (USA) annual meeting [3]. Eisenberg and Chen wanted to emphasize the analogy between open ion channels and semiconductor devices. The **P**oisson equation is a version of Maxwell's first equation [4-7] that describes how charge creates electrical forces and thus electrical potential. The **N**ernst-**P**lanck equation [8-27] describes how electrical charges migrate (in the gradient of electric fields) and diffuse (in the gradient of concentration fields).[1] The combination **PNP** is often called the drift diffusion equation in the semiconductor literature [8, 11, 12, 14-17, 20]

PNP meaning "**P**ositive-**N**egative-**P**ositive" describes the spatial distribution of mobile charge produced (mostly) by the spatial distribution of doping in a semiconductor device, a bipolar transistor. Doping is a name for the ionizable impurities (dopants) introduced into pure semiconductors to create the quasi-particles holes **P** and electrons **N**. When dopants ionize, they leave behind a permanent charge (negative or positive) in a fixed spatial distribution, much like the permanent charge of ionized weak acids and bases of ion exchangers or protein side chains. The ionized acid and base side chains of proteins, like glutamates **E** or lysines **K,** are one kind of the permanent charge of proteins. This view of proteins emphasizes the importance of permanent charge because permanent charge usually creates much larger forces than the induced charge of polarization (i.e., dielectric effects) and dielectric boundary charges[28].

Holes and electrons diffuse and migrate according to the **PNP** equations [8, 10, 29]. They are the (pseudo) ions of semiconductors. Note that the 'electrons' [30] of semiconductors are not the electrons [31, 32] discovered by JJ Thomson or the electrons found in atoms [33]. The 'electrons' of semiconductors are quasiparticles defined by properties of the conduction bands of semiconductors [17, 29, 34]. They have rather short lifetimes often measured in microseconds, compared to the infinite lifetimes of ions in water.

[1] Another paper is needed to describe the utility and evident limitations of **PNP**, as well as its antecedents and present uses.

Eisenberg and Chen chose the name **PNP** to emphasize the analogy between doping of semiconductors and the permanent charge of channels, or ion exchange membranes [9, 20, 24, 25, 35-68].

Eisenberg and Chen were thinking of semiconductor devices because transistors and **PNP** equations have a wide range of nonlinear behavior. For example, **PNP** equations can describe an amplifier, limiter, multiplier, exponentiator, or logarithmic converter depending on the range of voltages applied to the transistor through boundary conditions and auxiliary circuits.

Eisenberg and Chen wondered if nonlinear devices, well described by the **PNP** equations in semiconductors, might also exist in biological systems, particularly protein channels and transporters [69]. [70, 71]. Eisenberg and Chen wondered which of the nonlinearities of channels and transporters might come from **PNP** equations like those describing semiconductor devices [72]. These ideas were spelled out in an Abstract [72] presented at the Society of General Physiology Meeting 1992, Woods Hole MA: "Exchange Diffusion, Single Filing, and Gating in Macroscopic Channels of One Conformation" but the name **PNP** was not used there.

Nonlinearities of proteins were particularly interesting because they were thought to be the 'secret of life' by many physicists coming to biology soon after World War 2 [73-77]—at the same time that Shockley invented the transistors [78, 79]. Transistors create the complex nonlinearities of semiconductor devices.

We now know that the nonlinearities of biology exist on many scales [80]. Some of those nonlinearities are emergent properties that exist (i.e., emerge) only on scales much larger than a channel. Many nonlinearities arise on the cellular scale of neurons and dendrites [81, 82]. Some nonlinear properties arise on the molecular scale of proteins. Most models of protein function use rate models (with states connected by arrows and the law of mass action) to describe nonlinear properties. When rate models do not easily describe protein function, the mechanism is often said to be allosteric or to involve conformation changes that are not described by any specific equations.

It should be clearly understood that rate models are not fundamental laws of physics or chemistry. In fact, rate models with fixed rate constants are rarely transferrable, to use the chemists' language. Rate constants must be adjusted as conditions change if the models are to fit experimental data, in most cases. That means, of course, that a rate model with fixed parameters does not describe the underlying free energies of the chemical reaction. In much of physics and engineering, models that do not describe data with one set of parameters or free energies are called 'incorrect' because they cannot predict experiments. In nontransferable models, parameters or free

energies cannot be predicted. If they could be predicted, the models would be transferable!

Most biologists sought other explanations for the nonlinearities of life beyond the properties of channels, let alone open channels. I hasten to add that those biologists seem to be right. Eisenberg and Chen's hope that nonlinear biological devices—e.g., channels or transporters—would emerge as analogs of transistor devices, described by **PNP** equations and auxiliary circuits, has not been fulfilled, as far as I know, probably, I suspect, because the third terminal of transistors—so important to the history of technology and to human life as the source of amplification—has not yet been found (or recognized) in channels or transporters. Transistors connected as two terminal devices provide properties that have not been considered by biologists, as far as I know, so I am not sure we would recognize them even if we were studying them!

Eisenberg and Chen knew of the bipolar transistor **PNP** (along with its fraternal twin **NPN**) because bipolar transistors were the dominant form of solid state device, analog or digital, for much of their lives. Engineers today live quite a different life. Engineers today focus on the unipolar devices of our digital technologies (usually **CMOS** and its cousins) because they allow much higher densities (particularly thermal densities) of devices and are faster than bipolar devices. Bipolar devices have majority and minority charge carriers and are often limited in speed by the kinetics of the minority carriers, which tend to move slowly because they are present in the minority, in small numbers. Knowledge of bipolar transistors has been decreasing in the last two or three decades as they are used less and less.[2]

The bipolar transistor [83] is made of two semiconductor diode rectifiers [84] **PN** and **NP** in series. Crystal rectifiers much like these were used in the early history of radio broadcasting (around 1920) and remained of great interest to hobbyists for many years, including the young Eisenberg and his father. Crystal radios seem to "run on nothing", using only the energy gathered by the antenna system (paraphrase of [85]). They demonstrate in a most practical way that the electric field of radio waves exists and has enough energy to power a (tiny) loudspeaker. Anyone who builds a crystal radio is likely to be entranced forever by the electric field and to be convinced of that power can propagate through empty space [86, 87]. Eisenberg was no exception. (The explanation of how power propagates through empty space is one of the triumphs of electrodynamics. In fact, the equations of electrodynamics predict correctly that energy

[2] It seemed wise to write this paper before the knowledge of bipolar **PNP** transistors and analog circuity disappears altogether.

propagates at the speed of light $c = 1/(\mu_0 \varepsilon_0)^{1/2}$, determined by magnetic μ_0 and electric ε_0 constants that are measured without reference to light or radiation.)

PNP transistors and **PN** diodes are rectifiers that detect asymmetrical signals in radio waves. They make current flow 'the right way', which is the rectified way. "To rectify" is to make something correct, to make something as it should be, in nontechnical English, commonly used in the 1800's. In fact, rectifiers make current flow in one direction as Edison thought it should in the war between Edison's **DC** and Tesla's **AC** systems of electrical power [88]. The resistance of rectifiers depends on the direction of current flow because the shape of the electric fields at the **PN** or **NP** junctions depends on the direction of current flow.

Rectifiers exist in biological membranes and so it was natural to analyze them the way crystal rectifiers of early radios were analyzed. One of the early papers on the crystal rectifier [89] served as the template for the constant field **GHK** theory of Goldman [90] and Hodgkin and Katz [91] of rectification in membranes , according to personal communications to me from Hodgkin, Goldman and Goldman's Ph.D. supervisor, Cole, from the 1960's. It is important to understand that when the theory was published, no one had proposed that the currents being measured flowed through a hole in a protein, itself embedded in a lipid membrane, as far as I know. The theory was used to describe flow through what its authors thought was a lipid membrane. There is little permanent charge inside a lipid membrane. Charge is on the outside of such membranes at the interface between lipid and ionic solution.

The **GHK** theory has been used extensively in electrophysiology to describe the electric field in holes in the proteins that make ionic channels [92-94]. This usage is unfortunate because the theory contains no description of the structure or charge of the channel protein. It is even more unfortunate that it uses a field, a potential profile independent of the charge on the protein. On physical grounds, the potential cannot be independent of charge. On biological and evolutionary grounds the current or selectivity (i.e., reversal potential) cannot be independent of the structure of the channel protein, [92-94]. Indeed, structural and molecular biology shows that current and selectivity depend sensitively on the distribution and structure of permanent charge in a channel protein. Site directed mutagenesis changes that charge distribution and observes the resulting changes in current in innumerable laboratories every day. Structural biologists know this better than I, yet most continue to use the **GHK** theory that denies that reality, because it does not depend on structure at all.

A central aspect of **PNP** physics is rectification. Rectification depends on the shape of the electric field. Rectifiers function by changing the shape of the field and so

the shape of the field needs to be computed [95-99], not assumed. In fact, assuming the shape of the field will prevent understanding of how the device works. If the workers at Bell Labs, led by William Shockley [100-105] had assumed constant fields, they could not have understood how **PN** junctions rectified[79, 106], and it seems unlikely they could have discovered **PNP** [10] and designed the transistors and solid state circuity on which our computer, smart phone, and video technology is based.

This point was emphasized by Eisenberg in a series of reviews [70, 95, 107-111] because he felt the role of the electric field in biological systems (and chemical reactions) could not be understood if the field was assumed constant. Properties of biological systems or chemical reactions [112] that arise from changes in the shape of the field cannot be robustly described in theories that assume a constant field. Constant field theories are not transferable, as (for example) protein permanent charges are changed by site directed mutagenesis. Theories would have to change parameters as they tried to mimic the consequences of a changing permanent charge, or anything else that changed the shape of the electric field.

An important part of **PNP** history was Duan-Pin Chen's (re)-discovery of Gummel's robust and reliable method [113, 114] of integrating the equations.

Most of the work on **PNP** in chemistry before say the 1990's used numerical methods that do not converge, and even worse appear to converge, but do not actually converge to a solution. These issues are now established mathematics, reviewed, explained and cured in [13] where the author is too kind to emphasize the long time necessary before mathematicians and physicists in the Shockley tradition [78, 79, 106]—even with the resources of the Bell Laboratories—learned from an engineer Gummel [113, 114] how to replace a nonconvergent numerical method with one that was strongly convergent indeed.

This issue has undermined the use of the Poisson Nernst Planck equations in chemistry for many decades and it is not clear that many early papers on PNP had solved it [9, 25, 39, 40, 42, 43, 46, 115-119], perhaps even extending to recent times [99, 120-123]. Roughly speaking, if numerical difficulties and procedure are not discussed in an early paper, or indeed in any paper using the **PNP** equations, one must worry that results are not converged to true solutions of the equations. Fortunately for us, Duan-Pin Chen discovered the Gummel iteration independently [124-128], before we knew of computational electronics. Joe Jerome [13], Tom Kerkhoven [129], and Uwe Hollerbach [127, 128] checked DuanPin's implementation carefully and compared his methods to those of [130, 131] and themselves, to be sure it converged as Gummel's did.

Eisenberg and Chen's **PNP** results were presented to the mathematics and physics communities at a series of well attended minisymposia at SIAM (Society of Industrial and Applied Mathematics) annual meetings (2001, 2005, 2006). The 2005 meeting was in New Orleans, just a few weeks before hurricane Katrina destroyed the hotel we had been in and devastated the city. The 2006 meeting in Boston was co-chaired by electrochemist Martin Bazant, who had questioned the presentation in New Orleans, vigorously and appropriately, if my memory serves me right. The subsequent visit and lecture by Eisenberg at MIT, generously arranged by Bazant, may have catalyzed the spread of these ideas to the electrochemical community [9, 115, 116], although of course the Poisson-Nernst-Planck equations had existed long before then, however, usually without permanent charge and with few if any checks that the numerical procedures converged to actual solutions of the equations.

The crucial role of the spatial distribution doping, (permanent charge) and the near identity of **PNP** with the drift diffusion equations of computational electronics is still not given its due, in my opinion, in the community of chemists, electrochemists [132, 133], physical chemists, and biochemists. The spatial distribution of permanent charge provides enormous opportunities for control that might be of great technological use where ions are the main mobile charges. Changes of sign of doping create depletion layers that allow full control of current by a handful of atoms because this is a series system. Particularly note the properties of thyristors (**PNPN**) and power transistors of various types [134, 135].

Useful properties of ion exchangers and other selective macroscopic membranes may be designed if an inverse approach is used. The inverse methods of Burger and collaborators [136-138], allow design of a spatial distribution of permanent charge that will produce a desirable selectivity, as has been shown by actual computation (in the presence of noise and systematic error), not just argument. Indeed, the idea that potential profiles, and rate constants, **must be the computed consequence [95] distribution of permanent charge** on the atomic scale [70, 71] (and of macroscopic boundary conditions describing the structure of the system) is notable by its absence in the chemical, biochemical, biophysical, and (to a lesser extent) electrochemical literature.

Theories and simulations done without computed potential profiles are almost never transferrable. Nontransferable theories need different parameters in different experimental conditions and cannot calculate the different parameters before the experiments are done. Transferrable theories use the same set of parameters in different conditions. Transferrable theories are needed to create stable understanding or robust devices, in my view.

> It should clearly be understood that the shape of an electric field varies as experimental conditions are changed (as they are changed in almost all experiments). Voltage clamp apparatus maintains voltages only at one specific location. To maintain the shape of an electric field, voltage clamp must be applied at many locations (within an ionic channel or membrane) because the only way to maintain a potential, as conditions are changed, is to supply charge from an external device like a voltage clamp amplifier. That charge must come through 'wires' from an external source, because ion channels—like most proteins—are in themselves isolated devices, unable to create charge. These issues are discussed at embarrassing length in the reviews [70, 95, 107-111].

Isolated proteins need to be described as spatial distributions of permanent charge (to a first approximation) just as **PNP** transistors are described as distributions of doping (to a first approximation) and for the same reason. Their materials provide a permanent charge (as a first approximation) that arises from their chemical nature [125]. The second approximation is provided by an term to describe the field dependent induced polarization charge of the dielectric. Further approximations require a fuller description of polarization [4, 87, 139, 140].

The boundary condition describing the potential in isolated proteins like channels is an inhomogeneous Neumann condition defining the (normal) spatial derivative of the potential, that is to say, defining the permanent charge, not the potential itself, to a first approximation (Appendix eq. A25 of [125]). The chemical nature and structure of the amino acids and proteins determine the permanent charge and thus the inhomogeneous Neumann condition on the potential. Adding in the dielectric (i.e., polarization) current does not have a first order effect if permanent charge created by doping (e.g., acid or base side chains of proteins) is present. If permanent charge of that type is not present, the dielectric boundary condition must be used and may be an important determinant of channel properties.

Proteins are almost always isolated from the outside world except at boundaries like baths connected to the outside world by the apparatus of electrochemical cells, i.e., 3M KCl bridges, AgAgCl electrodes, and amplifiers [22, 141]. Proteins have one unchanging spatial distribution of permanent charge as conditions change (neglecting the second order effect of dielectric properties) unless they ionize or deionize. We do not consider those conditions here, although they may exist and contribute to properties of transporters for example, as proposed a long time ago [70]. Proteins cannot be described by a single field of potential as conditions change because the electric field

changes dramatically as conditions change. It is the permanent charge of the protein that does not change as conditions change.

Experiments maintaining a constant field in vacuum (i.e., one spatial distribution of potential) have been done. They are difficult to perform even in a **SQUID** (superconducting quantum interference device) [142].

Acknowledgement

PNP is just a name, no matter what it stands for. The science of the drift and diffusion of charge carriers, computed with a combination of electrodynamics (**P**oisson) and drift-diffusion (i.e., **N**ernst **P**lanck), is very much more than just a name. The community of scholars who have developed that science over more than a century deserve all the credit for what it has brought us, most remarkably, and unforeseen by almost all.

We have an information and audiovisual technology available easily to billions of people that allows human interactions, evolved in a village and tribal setting I suspect, to involve most of the human race in hours or even minutes. That technology is possible only because of the solid state semiconductor devices well described by the **PNP** equations in their various forms with physical or effective parameters.

It is a joy to thank that community of scholars, in general, and Karl Hess and Dave Ferry, in particular for all they and their community have done for me and all of us. It is sad that I could not include more discussion of the wonderful literature of semiconductors. But that would have over-burdened this essay which is, after all, more an historical confectionary, than a comprehensive review.

References

1. Eisenberg, R., and D. Chen. 1993. Poisson-Nernst-Planck *(PNP)* theory of an open ionic channel. Biophysical Journal 64:A22.
2. Chen, D. P., and R. S. Eisenberg. 1993. Poisson-Nernst-Planck (PNP) theory of open ionic channels. Biophys. J. 64:A22. Biophys. J. 64:A22.
3. Eisenberg, R. 1993. From Structure to Permeation in Open Ionic Channels. Biophysical Journal 64:A22.
4. Eisenberg, R. S. 2019. Kirchhoff's Law can be Exact. arXiv preprint available at https://arxiv.org/abs/1905.13574.
5. Lorrain, P., and D. Corson. 1970. ***Electromagnetic fields and waves, Second Edition***. Freeman.
6. Robinson, F. N. H. 1973. ***Macroscopic electromagnetism***. Pergamon.
7. Zangwill, A. 2013. ***Modern Electrodynamics***. Cambridge University Press, New York.
8. Van Roosbroeck, W. 1950. Theory of flow of electrons and holes in germanium and other semiconductors. Bell System Technical Journal 29:560-607.
9. Macdonald, J. R. 1953. Theory of ac Space-Charge Polarization Effects in Photoconductors, Semiconductors, and Electrolytes. Physical Review 92:4-17.
10. Blotekjaer, K. 1970. Transport equations for electrons in two-valley semiconductors. Electron Devices, IEEE Transactions on 17:38-47.
11. Selberherr, S. 1984. ***Analysis and Simulation of Semiconductor Devices***. Springer-Verlag, New York.
12. Markowich, P. A., C. A. Ringhofer, and C. Schmeiser. 1990. ***Semiconductor Equations***. Springer-Verlag, New York.
13. Jerome, J. W. 1995. ***Analysis of Charge Transport. Mathematical Theory and Approximation of Semiconductor Models***. Springer-Verlag, New York.
14. Ferry, D. K. 2000. ***Semiconductor Transport***. Taylor and Francis, New York.
15. Hess, K. 2000. ***Advanced Theory of Semiconductor Devices***. IEEE Press, New York.
16. Lundstrom, M. 2000. ***Fundamentals of Carrier Transport***. Addison-Wesley, NY.

17. Vasileska, D., S. M. Goodnick, and G. Klimeck. 2010. ***Computational Electronics: Semiclassical and Quantum Device Modeling and Simulation***. CRC Press, New York.

18. Bockris, J., and A. Reddy. 1970. ***Modern Electrochemistry***. Plenum Press, New York.

19. Bockris, J. O. M., and A. K. N. Reddy. 1988. ***Modern Electrochemistry. Ionics.*** Plenum, New York.

20. Rubinstein, I. 1990. ***Electro-diffusion of ions***. SIAM, Philadelphia.

21. Barthel, J., H. Krienke, and W. Kunz. 1998. ***Physical Chemistry of Electrolyte Solutions: Modern Aspects***. Springer, New York.

22. Laidler, K. J., J. H. Meiser, and B. C. Sanctuary. 2003. ***Physical Chemistry***. BrooksCole, Belmont CA.

23. Newman, J., and K. E. Thomas-Alyea. 2004. ***Electrochemical Systems***. Wiley-Interscience, New York.

24. Helfferich, F. 1962. ***Ion Exchange (1995 reprint)***. McGraw Hill reprinted by Dover, New York.

25. Buck, R. P. 1984. Kinetics of bulk and interfacial ionic motion: microscopic bases and limits for the nernst—planck equation applied to membrane systems. Journal of Membrane Science 17:1-62.

26. Szyszkiewicz, K., M. Danielewski, J. Fausek, J. Jasielec, W. Kucza, A. Lewenstam, T. Sokalski, and R. Filipek. 2014. Breakthrough in Modeling of Electrodiffusion Processes: Continuation and Extensions of the Classical Work of Richard Buck. ECS Transactions 61:21-30.

27. Fawcett, W. R. 2004. ***Liquids, Solutions, and Interfaces: From Classical Macroscopic Descriptions to Modern Microscopic Details***. Oxford University Press, New York.

28. Nadler, B., U. Hollerbach, and R. S. Eisenberg. 2003. Dielectric boundary force and its crucial role in gramicidin. Phys Rev E Stat Nonlin Soft Matter Phys 68:021905.

29. Lundstrom, M. 2017. ***Fundamentals of Nanotransistors***. World Scientific Publishing Company.

30. Ziman, J. M. 1960. ***Electrons and Phonons. The Theory of Transport Phenomena in Solids***. Oxford University Press, New York.

31. Navarro, J. 2012. ***A History of the Electron: J. J. and G. P. Thomson***. Cambridge University Press.

32. Springford, M. 1997. ***Electron: A Centenary Volume***. Cambridge University Press.

33. Yang, F., and J. H. Hamilton. 2010. ***Modern Atomic and Nuclear Physics: Revised***. World Scientific Publishing Company.

34. Kittel, C. 2004. ***Solid-State Physics, Eighth Edition***. Wiley, New York.

35. Meyer, K. H., and J. F. Sievers. 1936. La perméabilité des membranes I. Théorie de la perméabilité ionique. Helvetica Chimica Acta 19:649-664.

36. Tanaka, Y. 2007. Chapter 4 Theory of Teorell, Meyer and Sievers (TMS Theory). In ***Membrane Science and Technology***. Y. Tanaka, editor. Elsevier. 59-66.

37. Teorell, T. 1935. An attempt to formulate a quantitative theory of membrane permeability. Proceedings of the Society for Experimental Biology 33:282-385.

38. Teorell, T. 1953. Transport processes and electrical phenomena in ionic membrane. Progress in Biophysics and Molecular Biology 3:305-369.

39. de Levie, R., and H. Moreira. 1972. Transport of ions of one kind through thin membranes. Journal of Membrane Biology 9:241-260.

40. De Levie, R., N. G. Seidah, and H. Moreira. 1972. Transport of ions of one kind through thin membranes. II. Nonequilibrium steady-state behavior. The Journal of membrane biology 10:171-192.

41. Simons, R. 1972. The steady and non-steady state properties of bipolar membranes. Biochimica et Biophysica Acta (BBA) - Biomembranes 274:1-14.

42. Coster, H. G. L. 1973. The Double Fixed Charge Membrane. Biophysical Journal 13:133-142.

43. de Levie, R., and N. G. Seidah. 1974. Transport of ions of one kind through thin membranes. 3. Current-voltage curves for membrane-soluble ions. The Journal of membrane biology 16:1-16.

44. Levitt, D. G. 1975. General continuum analysis of transport through pores. II. Nonuniform pores. Biophys J 15:553-563.

45. Levitt, D. G. 1975. General continuum analysis of transport through pores. I. Proof of Onsager's reciprocity postulate for uniform pore. Biophys J 15:533-551.

46. French, R. 1977. Unstirred layer effects on calculations of the potential difference across an ion exchange membrane. Biophysical journal 18:53.

47. Levitt, D. G. 1978. Electrostatic calculations for an ion channel. I. Energy and potential profiles and interactions between ions. Biophys. J. 22:209-219.

48. Levitt, D. G. 1978. Electrostatic calculations for an ion channel. II. Kinetic behavior of the gramicidin A channel. Biophys J 22:221-248.

49. Macdonald, J. R., and D. R. Franceschetti. 1978. Theory of small-signal ac response of solids and liquids with recombining mobile charge. The Journal of chemical physics 68:1614-1637.

50. Cooper, K., E. Jakobsson, and P. Wolynes. 1985. The theory of ion transport through membrane channels. Progress in Biophysics and Molecular Biology 46:51–96.

51. Levitt, D. G. 1985. Strong electrolyte continuum theory solution for equilibrium profiles, diffusion limitation, and conductance in charged ion channels. Biophys. J. 52:575–587.

52. Jou, D., F. Ferrer-Suquet, and C. J. Perez. 1986. On the nonequilibrium chemical potential of open pores in a membrane. The Journal of chemical physics 85:5314-5316.

53. Levitt, D. G. 1986. Interpretation of biological ion channel flux data. Reaction rate versus continuum theory. Ann. Rev. Biophys. Biophys. Chem 15:29–57.

54. Jakobsson, E., and S. W. Chiu. 1987. Stochastic theory of ion movement in channels with single-ion occupancy. Application to sodium permeation of gramicidin channels. Biophys J 52:33-45.

55. Levitt, D. G. 1987. Exact continuum solution for a channel that can be occupied by two ions. Biophys. J. 52: 455–466.

56. Cooper, K. E., P. Y. Gates, and R. S. Eisenberg. 1988. Surmounting barriers in ionic channels. Quarterly Review of Biophysics 21: 331–364.

57. Cooper, K. E., P. Y. Gates, and R. S. Eisenberg. 1988. Diffusion theory and discrete rate constants in ion permeation. J. Membr. Biol. 109:95–105.

58. Jakobsson, E., and S. W. Chiu. 1988. Application of Brownian motion theory to the analysis of membrane channel ionic trajectories calculated by molecular dynamics. Biophys J 54:751-756.

59. Chiu, S. W., and E. Jakobsson. 1989. Stochastic theory of singly occupied ion channels. II. Effects of access resistance and potential gradients extending into the bath. Biophys. J. 55:147–157.

60. Gates, P., K. Cooper, J. Rae, and R. Eisenberg. 1989. Predictions of diffusion models for one-ion membrane channels. Prog Biophys Mol Biol 53:153-196.

61. Levitt, D. G. 1989. Continuum model of voltage-dependent gating. Macroscopic conductance, gating current, and single-channel behavior. Biophys J 55:489-498.

62. Levitt, D. 1991. General Continuum theory for a multiion channel. Application for a multiion channel. Biophysical Journal 59:278-288.

63. Levitt, D. 1991. General Continuum theory for a multiion channel. Biophysical Journal 59:271-277.

64. Chiu, S. W., J. A. Novotny, and E. Jakobsson. 1993. The nature of ion and water barrier crossings in a simulated ion channel. Biophys J 64:98-109.

65. Mauro, A. 1961. Anomalous Impedance, A Phenomenological Property of Time-Variant Resistance: An Analytic Review. Biophysical Journal 1:353-372.

66. Mauro, A. 1962. Space Charge Regions in Fixed Charge Membranes and the Associated Property of Capacitance. Biophysical Journal 2:179-198.

67. Finkelstein, A., and A. Mauro. 1963. Equivalent Circuits as Related to Ionic Systems. Biophysical Journal 3:215-237.

68. Mauro, A. 1966. The electrical conductance of semipermeable membranes. Biophysical Journal 6:371.

69. Eisenberg, R. S. 1990. Channels as enzymes: Oxymoron and Tautology. Journal of Membrane Biology 115:1–12. Available on arXiv as http://arxiv.org/abs/1112.2363.

70. Eisenberg, R. S. 1996. Atomic Biology, Electrostatics and Ionic Channels. In ***New Developments and Theoretical Studies of Proteins***. R. Elber, editor. World Scientific, Philadelphia. 269-357. Published in the Physics ArXiv as arXiv:0807.0715.

71. Eisenberg, B. 2008. Engineering channels: Atomic biology. Proceedings of the National Academy of Sciences 105:6211-6212.

72. Chen, D., and R. Eisenberg. 1992. Exchange diffusion, single filing, and gating in macroscopic channels of one conformation. Journal of General Physiology 100:9a.

73. Schrödinger, E. 1992. ***What Is Life?*** Cambridge University Press, New York.

74. Delbrück, M. 1949. ***A Physicist Looks at Biology***. Connecticut Academy of Arts and Sciences.

75. Luria, S. 1974. What can biologists solve. The New York Review of Books 7:22-28.

76. Monod, J., and A. Wainhouse. 1997. ***Chance and Necessity: An Essay on the Natural Philosophy of Modern Biology***. Penguin.

77. Jacob, F., and B. E. Spillmann. 1993. ***The Logic of Life: A History of Heredity***. Princeton University Press.

78. Shockley, W. 1976. The path to the conception of the junction transistor. Electron Devices, IEEE Transactions on 23:597-620.

79. Shockley, W. 1950. ***Electrons and Holes in Semiconductors to applications in transistor electronics***. van Nostrand, New York.

80. Eisenberg, B. 2018. Asking biological questions of physical systems: The device approach to emergent properties. Journal of Molecular Liquids 270:212-217. Preprint available on arXiv as https://arxiv.org/abs/1801.05452.

81. Li, S., N. Liu, X.-h. Zhang, D. Zhou, and D. Cai. 2014. Bilinearity in spatiotemporal integration of synaptic inputs. PLoS computational biology 10:e1004014.

82. Li, S., D. Zhou, and D. Cai. 2015. Analysis of the dendritic integration of excitatory and inhibitory inputs using cable models. Communications in Mathematical Sciences 13:565-575.

83. Neudeck, G. W. 1989. ***The Bipolar Junction Transistor***. Addison-Wesley.

84. Neudeck, G. W. 1989. ***The PN Junction Diode***. Addison-Wesley.

85. 2019. History of Radio. https://en.wikipedia.org/wiki/History_of_radio#Crystal_sets.

86. Eisenberg, B., X. Oriols, and D. Ferry. 2017. Dynamics of Current, Charge, and Mass. Molecular Based Mathematical Biology 5:78-115 and arXiv preprint https://arxiv.org/abs/1708.07400.

87. Eisenberg, R. S. 2019. Updating Maxwell with Electrons, Charge, and More Realistic Polarization. arXiv preprint available at https://arxiv.org/abs/1904.09695.

88. Jonnes, J. 2004. ***Empires of light: Edison, Tesla, Westinghouse, and the race to electrify the world***. Random House Trade Paperbacks.

89. Mott, N. F. 1939. The theory of crystal rectifiers. Proc Roy Soc A 171:27-38.

90. Goldman, D. E. 1943. Potential, impedance and rectification in membranes. J. Gen. Physiol. 27:37–60.

91. Hodgkin, A. L., and B. Katz. 1949. The effect of sodium ions on the electrical activity of the giant axon of the squid. J. Physiol. 108:37–77.

92. Hille, B. 1972. The permeability of the sodium channel to metal cations in myelinated nerve. J Gen Physiol 59:637-658.

93. Hille, B. 1975. Chapter 4: Ionic Selectivity of Na and K Channels of Nerve Membranes. In ***Membranes: a series of advances Volume 3 Lipid Bilayers and Biological Membranes: Dynamic Properties***. G. Eisenman, editor. Marcel Dekker, New York. p. 256-323.

94. Hille, B. 2001. ***Ion Channels of Excitable Membranes***. Sinauer Associates Inc., Sunderland.

95. Eisenberg, R. S. 1996. Computing the field in proteins and channels. Journal of Membrane Biology 150:1–25. Preprint available on physics arXiv as document 1009.2857.

96. Valiskó, M., B. Matejczyk, Z. Ható, T. Kristóf, E. Mádai, D. Fertig, D. Gillespie, and D. Boda. 2019. Multiscale analysis of the effect of surface charge pattern on a nanopore's rectification and selectivity properties: from all-atom model to Poisson-Nernst-Planck. arXiv preprint arXiv:1902.07117.

97. Matejczyk, B., M. Valisko, M. T. Wolfram, J. F. Pietschmann, and D. Boda. 2017. Multiscale modeling of a rectifying bipolar nanopore: Comparing Poisson-Nernst-Planck to Monte Carlo. The Journal of chemical physics 146:124125.

98. Hato, Z., M. Valisko, T. Kristof, D. Gillespie, and D. Boda. 2017. Multiscale modeling of a rectifying bipolar nanopore: explicit-water versus implicit-water simulations. Phys Chem Chem Phys 19:17816-17826.

99. Ható, Z., D. Boda, D. Gillespie, J. Vrabec, G. Rutkai, and T. Kristóf. 2016. Simulation study of a rectifying bipolar ion channel: Detailed model versus reduced model. Condensed Matter Physics 19:13802.

100. Shurkin, J. N. 2006. ***Broken Genius: The Rise and Fall of William Shockley, Creator of the Electronic Age***. Macmillan, New York.

101. Riordan, M., and L. Hoddeson. 1997. ***Crystal Fire***. Norton, New York.

102. Arns, R. G. 1998. The other transistor: early history of the metal-oxide semiconductor field-effect transistor. Engineering Science and Education Journal 7:233-240.

103. Seitz, F., and N. G. Einspruch. 1998. ***Electronic Genie The Tangled History of Silicon***. University of Illinois Press, Chicago.

104. Gertner, J. 2012. ***The idea factory: Bell Labs and the great age of American innovation***. Penguin.

105. Buderi, R. 1996. ***The invention that changed the world: How a small group of radar pioneers won the Second World War and launched a technological revolution***. Simon and Schuster.

106. Shockley, W. 1949. The Theory of p-n Junctions in Semiconductors and p-n Junction Transistors. Bell System Technical Journal 28:435-489.

107. Chen, D., L. Xu, A. Tripathy, G. Meissner, and R. Eisenberg. 1997. Rate Constants in Channology. Biophys. J. 73:1349-1354.

108. Eisenberg, B. 1998. Ionic Channels in Biological Membranes: Natural Nanotubes. Accounts of chemical research 31:117-125.

109. Eisenberg, B. 1998. Ionic channels in biological membranes. Electrostatic analysis of a natural nanotube. Contemporary Physics 39:447 - 466.

110. Eisenberg, R. S. 1999. From Structure to Function in Open Ionic Channels. Journal of Membrane Biology 171:1-24, available on arXiv at https://arxiv.org/abs/1011.2939.

111. Eisenberg, B. 2000. Permeation as a Diffusion Process. In ***Biophysics Textbook On Line "Channels, Receptors, and Transporters" http://www.biophysics.org/Portals/1/PDFs/Education/eisenberg.pdf http://www.biophysics.org/AboutUs/Committees/Education/EducationalResources/BiophysicalMechanisms/tabid/546/Default.aspx*** L. J. DeFelice, editor. Published in physics ArXiv as arXiv:0807.0721.

112. Wang, Y., C. Liu, P. Liu, B. Eisenberg, and (2020). 2020. Field Theory of Reaction-Diffusion: Mass Action with an Energetic Variational Approach. Preprint available on the physics arXiv at https://arxiv.org/abs/2001.10149.

113. Scharfetter, D. L., and H. K. Gummel. 1969. Large signal analysis of a silicon read diode oscillator. IEEE Trans Electron Devices:64-77.

114. Gummel, H. K. 1964. A self-consistent iterative scheme for one-dimensional steady-state transistor calculations. IEEE Trans. Electron Devices ED-11:445-465.

115. Bazant, M. Z., K. Thornton, and A. Ajdari. 2004. Diffuse-charge dynamics in electrochemical systems. Physical Review E 70:021506.

116. Kilic, M. S., M. Z. Bazant, and A. Ajdari. 2007. Steric effects in the dynamics of electrolytes at large applied voltages. II. Modified Poisson-Nernst-Planck equations. Phys Rev E Stat Nonlin Soft Matter Phys 75:021503.

117. Coster, H. G. L., E. P. George, and R. Simons. 1969. The Electrical Characteristics of Fixed Charge Membranes: solution of the Field Equations. Biophysical Journal 9:666-684.

118. Zook, J. M., R. P. Buck, J. Langmaier, and E. Lindner. 2008. Mathematical model of current-polarized ionophore-based ion-selective membranes. The journal of physical chemistry. B 112:2008-2015.

119. Johannesson, B. 2010. Development of a Generalized Version of the Poisson– Nernst–Planck Equations Using the Hybrid Mixture Theory: Presentation of 2D Numerical Examples. Transport in Porous Media 85:565-592.

120. Voukadinova, A., M. Valisko, and D. Gillespie. 2018. Assessing the accuracy of three classical density functional theories of the electrical double layer. Phys Rev E 98:012116.

121. Gillespie, D. 2015. A review of steric interactions of ions: Why some theories succeed and others fail to account for ion size. Microfluidics and Nanofluidics 18 717-738.

122. Boda, D., R. Kovacs, D. Gillespie, and T. Kristof. 2014. Selective transport through a model calcium channel studied by Local Equilibrium Monte Carlo simulations coupled to the Nernst-Planck equation. Journal of Molecular Liquids 189:100-112.

123. Berti, C., S. Furini, D. Gillespie, D. Boda, R. S. Eisenberg, E. Sangiorgi, and C. Fiegna. 2014. Three-Dimensional Brownian Dynamics Simulator for the Study of Ion Permeation through Membrane Pores. Journal of Chemical Theory and Computation 10:2911-2926.

124. Barcilon, V., D. P. Chen, and R. S. Eisenberg. 1992. Ion flow through narrow membranes channels: Part II. SIAM J. Applied Math 52:1405-1425.

125. Chen, D. P., and R. S. Eisenberg. 1993. Charges, currents and potentials in ionic channels of one conformation. Biophys. J 64:1405–1421.

126. Chen, D., R. Eisenberg, J. Jerome, and C. Shu. 1995. Hydrodynamic model of temperature change in open ionic channels. Biophysical Journal 69:2304-2322.

127. Hollerbach, U., D. P. Chen, D. D. Busath, and B. Eisenberg. 2000. Predicting function from structure using the Poisson-Nernst-Planck equations: sodium current in the gramicidin A channel. Langmuir 16:5509-5514.

128. Hollerbach, U., D.-P. Chen, and R. S. Eisenberg. 2002. Two- and Three-Dimensional Poisson-Nernst-Planck Simulations of Current Flow through Gramicidin-A. Journal of Computational Science 16:373-409.

129. Kerkhoven, T. 1988. On the effectiveness of Gummel's method. SIAM J. Sci. & Stat. Comp. 9:48-60.

130. Bank, R. E., J. Burgler, W. M. Coughran, Jr., W. Fichtner, and R. K. Smith. 1990. Recent Progress in Algorithms for Semiconductor Device Simulation. International Series of Numerical Mathematics 93:125-140.

131. Bank, R. E., D. J. Rose, and W. Fichtner. 1983. Numerical Methods for Semiconductor Device Simulation. IEEE Transactions on Electron Devices ED-30:1031-1041.

132. Bazant, M., R. Bennewitz, L. Bocquet, N. Brilliantov, R. Dey, C. Drummond, R. Dryfe, H. Girault, K. Hatzell, K. Kornev, A. A. Kornyshev, I. Kratochvilova, A. Kucernak, M. Kulkarni, S. Kumar, A. Lee, S. Lemay, H. Medhi, A. Mount, F. Mugele, S. Perkin, M. Rutland, G. Schatz, D. Schiffrin, E. Smela, E. Smirnov, M. Urbakh, and A. Yaroshchuk. 2017. Electrotunable wetting, and micro- and nanofluidics: general discussion. Faraday Discuss 199:195-237.

133. Peters, P. B., R. van Roij, M. Z. Bazant, and P. M. Biesheuvel. 2016. Analysis of electrolyte transport through charged nanopores. Phys Rev E 93:053108.

134. Rashid, M. H., K. Afridi, J. M. Alonso, I. Batarseh, A. Bryant, J. Carrasco, L. Chaar, A. K. Chattopadhyay, M. Chow, and H. S. H. Chung. 2010. ***Power Electronics Handbook: Devices, Circuits and Applications***. Elsevier Science.

135. Baliga, B. J. 2010. ***Fundamentals of Power Semiconductor Devices***. Springer US.

136. Burger, M. 2011. Inverse problems in ion channel modelling. Inverse Problems 27:083001.

137. Burger, M., R. S. Eisenberg, and H. Engl. 2007. Inverse Problems Related to Ion Channel Selectivity. SIAM J Applied Math 67:960-989

138. Arning, K. 2009. Mathematical Modelling and Simulation of Ion Channels. In ***Radon Institute for Computational and Applied Mathematics***. Johannes Kepler University Linz, Linz. 139.

139. Eisenberg, R. S. 2019. Dielectric Dilemma. preprint available at https://arxiv.org/abs/1901.10805.

140. Catacuzzeno, L., L. Sforna, F. Franciolini, and R. Eisenberg. 2020. Why are voltage gated Na channels faster than K channels: a multi-scale hierarchical model. bioRxiv:2020.2005.2011.088559.

141. Wright, M. R. 2007. ***An Introduction to Aqueous Electrolyte Solutions***. Wiley, New York.

142. Han, S., J. Lapointe, and J. E. Lukens. 1993. Thermally Activated Barrier Crossings in Superconducting Quantum Interference Devices. In ***Activated Barrier Crossing: Applications in Physics, Chemistry and Biology***. G. Fleming, and P. Hänggi, editors. World Scientific Publishing, New Jersey. 241-267.