Molecular and Electro Dynamics: Merging the Methods

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Abstract

Plasma physics and molecular dynamics deal with electrodynamics in very different ways. This paper seeks to catalyze their fusion.

Molecular dynamics has used periodic boundary conditions that are not compatible with electrodynamics. Periodic boundary conditions destroy long-range fields. Plasma physics has used the particle-in-cell method to avoid periodic boundary conditions. I suggest that the particle-in-cell methods may be able to replace the Coulomb law terms in the 'potentials' of molecular dynamics. Other terms are needed to deal with the finite diameter of atoms in molecular dynamics. Periodic boundary conditions can be used with these higher-order terms if periods are large, as in modern computations. Molecular dynamics has difficulty dealing with the nearly vanishing concentrations of calcium and cofactors that are important controllers of much biological function. Collisions lasting femtoseconds are thought to be important inside ion channels. Molecular dynamics uses Coulomb's law to analyze these collisions but Feynman points out that "Coulomb's law is true only in statics. It is false in general."

This paper seeks to catalyze the fusion of plasma physics and molecular dynamics so electrodynamics can be computed realistically in proteins. Molecular dynamics [1-3] is one of the most important methods in molecular biology. It brings to life the magnificent structures [4] of the more than one hundred thousand proteins with measured atomic coordinates [5]. Many biological functions are controlled or executed by just handfuls of atoms in these structures, as seen in thousands of laboratories that create mutations every week [6]. Understanding how these proteins work has been one of the most important tasks of biology since the chemical identity and importance of proteins was discovered in the 1930's by Cohn and Edsall [7].

Electrodynamics [8-10] is described by the Maxwell equations on all scales [11], certainly including the time scale of gamma rays $\sim 10^{-21}$seconds. Once the dielectric approximation is removed [12, 13], the Maxwell equations contain no adjustable parameters. Polarization in this formulation is dealt with as compressibility is dealt with in fluid mechanics [14], perhaps with a variational energy formulation. An empirical description of polarization is needed to complement the theory in the range of interest in a particular application. The empirical description could be a giant look-up table of the data itself, using interpolation to fill in gaps. Nowadays, computers have enough memory to make such a table with the help of artificial intelligence.

Without material constants, electrodynamics might be thought to be useless in describing material systems. But that is not the case [15]. Circuits are material systems that describe some of the most important applications of electrodynamics, from telegraphs to logic bringing power to our lives and information to our computers.

Circuits are analyzed by current laws [16-19]. The Maxwell Ampere law implies a Maxwell current law for the total current that is as general as the Maxwell equations themselves.

$$\mathbf{J_{total}} = \mathbf{J} + \varepsilon_0 \, \partial \mathbf{E} \, / \, \partial \mathrm{t} \tag{1}$$

$\mathbf{J_{total}}$ is defined, as Maxwell did, as the 'true current' needed for computations [20] Vol. 2 Section 610 p. 232; [21]. Maxwell could not have chosen a stronger adjective or name than 'True Current' to emphasize the importance of $\mathbf{J_{total}} = \mathbf{J} + \varepsilon_0 \, \partial \mathbf{E} \, / \, \partial \mathrm{t}$. $\varepsilon_0 \, \partial \mathbf{E} \, / \, \partial \mathrm{t}$ is the universal displacement current.

We use the Maxwell-Ampere law

$$\mathbf{curl\ B} = \mu_0(\mathbf{J} + \varepsilon_0 \partial\mathbf{E} / \partial t) = \mu_0 \mathbf{J_{total}} \tag{2}$$

Take the divergence and apply the identity $\mathrm{div}\ \mathrm{curl} = 0$. The result is

$$\textbf{Maxwell Current Law} \qquad \mathbf{div\ J_{total}} = \mathbf{0} \tag{3}$$

Kirchhoff's current law

$$\textbf{Kirchhoff Current Law} \quad \mathbf{div\ J} = \mathbf{0} \quad \text{when } \mathbf{J} \gg \varepsilon_0 \partial\mathbf{E} / \partial t \tag{4}$$

This is an appropriate approximation when $\partial\mathbf{E} / \partial t$ and displacement current are small at long times or low frequencies.

The current laws above do not depend on material parameters in this formulation. Traditional formulations that crudely approximate polarization replace the universal displacement current term of eq. (1) - (4) with $\varepsilon_r \varepsilon_0 \partial\mathbf{E} / \partial t$ where ε_r is the dielectric constant a single real dimensionless number.

Molecular dynamics involves electrodynamics because most of the atoms of proteins are charged [22-26]. Molecular dynamics uses the laws of electrodynamics to compute the movement of the charged atoms of proteins. For historical reasons, molecular dynamics has used Coulomb's law as its version of electrodynamics and has implemented its calculations in periodic systems even though proteins are not periodic. Using Coulomb's law avoided the computationally expensive solution of Poisson's equation (or Gauss' law) and boundary conditions. Periodic systems could be computed in the early days of molecular dynamics when real systems could not be handled by the computer systems of those times.

Long-range fields are destroyed by periodicity. Periodicity replaces physical boundary conditions with artificial constraints. These artificial constraints significantly distort the physical system.

Coulomb's law ignores boundary conditions. Boundary conditions are not widely discussed in the molecular dynamics literature, but they are essential components of a theory of biological systems. Boundary conditions are also crucial in engineering science. Inputs and outputs are found in almost all engineering systems. Engineering devices depend on boundary

conditions for the very definition of their inputs and outputs. Inputs and outputs are also found throughout biology and characterize many physiological systems on all scales, from organ to protein. The inputs and outputs of biological systems that often satisfy the engineering definition of devices. Boundary conditions are needed to define biological devices like ion channels and transporters. They also define metabolic machines like the electron transport chains of mitochondria.

Periodic systems imply periodic boundary conditions. These cannot be reconciled with Coulomb's law in general. The difficulties are easily shown by a computation with standard MD software of the potential produced by a ***SINGLE*** charge. The computation does not give a result compatible with Coulomb's law. The difference in behavior is clearest at distances far from the charge. The potential in a periodic system does not always go to zero at the boundary. The potential field goes to zero far from the charge if only Coulomb's law is used. ***ONLY*** when the period is very large does the standard practice of molecular dynamics agree with its own treatment of electrodynamics. Large periods are an artificial constraint that defeats the original purpose of using periodic approximations.

These difficulties may seem inherent in any calculation of charged particles. They are not. I write to point out that these issues have been dealt with by plasma physicists in a mature literature [27-31] that is apparently unknown to biologists.

The particle-in-cell method deals with particle dynamics without assuming periodic boundary conditions. Particle-in-cell methods calculate long-range fields correctly while dealing with particle-particle interactions. The literature of the particle-in-cell method includes many packages of computer programs. Some twenty-five packages are specifically cited in its Wikipedia entry on June 20, 2025. Indeed, Wikipedia has separate articles for different variants of particle-in-cell, e.g., 'colored-particle-in-cell' and 'multiphase particle in cell'. Other packages can be found by search engines. Repositories of programs are numerous, including EPOCH https://epochpic.github.io/documentation.html and the UCLA PICKSC programs https://picksc.physics.ucla.edu/index.html. Tutorials are available in book [28] and online forms are available.

Particle-in-cell methods are not restricted to the electrostatic interactions described by Coulomb's law. Molecular dynamics simulations occur on the time scale of 10^{-15} sec. Random thermal motions are on the much slower time scale of the speed of sound. Randomness is overwhelmingly obvious in visualization of molecular dynamics. The rapid thermal motions that dominate the simulations of molecular dynamics should not be analyzed as if they are static when they are in fact remarkably dynamic.

Collisions inside ion channels have been a central subject—indeed, an organizing theme [32]—of research from billiard balls in 1955 [33] to present day molecular dynamics [34, 35]. The collisions occur in handfuls of femtoseconds but they are simulated in molecular dynamics with Coulomb's law, not the Maxwell equations. Coulomb's law is electrostatic and is in fact false on rapid time scales. Feynman is outspoken on the subject [10], devoting much of Section 15-6 to it. He could hardly use stronger language: "Coulomb's law is true only in statics. It is false in general."

The large number and high-speed motions of charges in proteins can discourage analysis. It may seem impossible to do better than using Coulomb's law. Using the full Maxwell equations may seem out of the question. However, engineers routinely analyze circuits that switch in nanoseconds or faster using a circuit approach [15, 36, 37]. Circuit methods are remarkably successful at very short time scales, although their limitations appear on the microwave time scale: current is no longer confined to branched one dimension beyond microwave frequencies.

Total current in ion channels can be computed using the Maxwell current law eq. (3) and the circuit approach because the total current is nearly one dimensional [38]. Total current is independent of location in such systems and the complexity of collisions is avoided in the analysis of total current. Total current is the output of channels important for most of their biological functions (like the action potential [39, 40] so the circuit approach using total current is of practical biological importance as well as being part of classical electrodynamics.

Biology can benefit by the circuit analysis methods in other ways. All biological systems satisfy the Maxwell equations and those imply strong constraints on charge movements in organelles and short cells. These constraints can be formulated as circuits laws very helpful in

understanding atomic scale behavior of mitochondria, for example [41]. Some biological systems are naturally circuits [39] like nerve cells. Skeletal muscle is a good example.

Circuit methods use quite simple mathematics because circuits greatly restrict the behavior of current flow compared to what is possible in electrodynamics (and the Maxwell partial differential equations) in general.

Circuit methods are best understood using Maxwell's current law [42] as a generalization of the classical Kirchhoff law (see eq. (3)-(4) above). It may be possible to extend the circuit method to molecular dynamics using the particle-in-cell methods. Extending molecular dynamics with circuit methods will be needed to combine the chemical description of ion channels [43] to their electrical function [44, 45]. The number of atoms involved in a propagating action potential prevents direct computation unless circuit ideas—like the Maxwell current law—are used. The particle-in-cell methods may allow application of the Maxwell current law to atomic detail simulations of ions in solutions and proteins and thus simulations of the circuits involved or the function of cytochrome c oxidase [41] and the generation of ATP in mitochondria [37, 46] as well as in propagation of the action potential [39].

The particle-in-cell method originally dealt with point particles that are good representations of electrons. Ions in electrolytes have finite diameter and the variation of diameter from one type of ion to another is very important in determining their biological and chemical properties. Selectivity in biology and chemistry can be understood in large measure by physical effects of ion diameter that do not depend on specific chemical binding. Selectivity is present in physical systems without binding. See [47-49] for the biological application of standard ideas in solution chemistry to the crowded charges of biological systems [47]. See the comprehensive review [50]. Recently, particle-in-cell methods have been extended to finite-size particles [51, 52] and other approaches have been used for stationary finite particles in computational electronics [53, 54] but those methods are not likely to include the chemical type interactions described by the higher order terms of classical force fields of molecular dynamics.

Molecular dynamics has developed elaborate force fields to deal with nonideal finite size chemical effects. Elaborate force fields with staggering numbers of parameters are needed to deal

with the wide variety of atomic interactions in proteins and the wide range of conditions in which details of the interactions are biologically important. It is important to preserve this detail in any revised methods.

I suggest here that the Coulomb term in the force fields of classical MD can be replaced with the particle-in-cell method without changing the periodic treatment of other higher order terms in the potentials of molecular dynamics. The effects of finite-size ions in molecular dynamics come primarily from other terms in the force fields and 'potential' functions. It is safe to retain the periodic treatment of the other terms of the force fields of classical MD if those terms fall off with distance rapidly enough in periods used routinely in modern computers.

Discussion

This paper seeks to catalyze the fusion of plasma physics and molecular dynamics so electrodynamics can be computed realistically in proteins. In my view, these methods will eventually succeed just as they have in plasma physics and computational electronics.

The traditions of plasma physics and molecular dynamics differ in more than their treatment of electrodynamics. Plasma physics was developed in the tradition of 'physics as usual'. In that tradition, models are made and equations are written from fundamental physical principles. Conservation laws play a prominent role. Those equations are solved by methods of numerical analysis, that are always checked for accuracy by comparison with known systems of a few charges. Simulations are checked the same way, by comparison with simplified systems with known properties. Those checks are extensive and are an essential part of the analysis, often requiring revision of previous work.

Molecular dynamics was developed as a qualitative science. In the beginning, computers were so limited that even charge could not be computed. No one imagined that the full complexity of charge in a protein could be computed at all, let alone on the biological time scale, that is some fourteen orders of magnitude slower than the time step used in simulations of atomic motion [55].

The qualitative tradition means, however, that many crucial parts of simulations have not been checked by comparison with other relevant and well-known systems. Qualitative models are hard to check or falsify. It is difficult to choose between competing metaphors [56]., particularly if they are subjectively pleasing. The community of molecular dynamics seems comfortable with qualitative standards. A tenfold error in the computation of current through a single open ion channel [57, 58] was only recently brought to general attention [35].

The qualitative tradition has led to the avoidance of many glaring quantitative problems in traditional molecular dynamics. The conflict of periodicity and Coulomb's law is one example. Another is the lack of focus on the properties of ionic solutions. An enormous literature describes the free energy per mole of ionic solutions of various composition and concentrations [50, 59-70]. Force fields should be required to fit this data in solutions with a range of compositions and concentrations that occur in biological systems, in organelles, cells and extracellular space.

The computation of effects of calcium ion concentrations is particularly important. Most proteins function inside cells where the calcium concentration is very small, $\sim 10^{-8}$ molar. The intracellular calcium activity has large effects on enzyme rate constants and changes the function of most intracellular or membrane proteins, as documented in many chapters of textbooks of biochemistry. Indeed, calcium acts as a cofactor that controls many enzyme and protein functions, the way a gas pedal controls the speed of a car. Molecular dynamics cannot cope with the enormous number of water molecules (or their interactions) needed to simulate $\sim 10^{-8}$ molar calcium concentrations inside cells in atomic detail. The same difficulty plagues molecular dynamics simulations of any of the many cofactors controlling enzyme rates and protein function. I mention to the non-biologist that the analysis of these cofactors is one of the main topics of medical biochemistry because so many diseases and drugs act on these systems. Medically motivated biochemistry is supported lavishly for this reason by government agencies and private pharmaceutical companies.

Coarse-graining methods are needed to deal with these nearly vanishing cofactor concentrations. These methods may well succeed in dealing with vanishing concentrations once they are developed systematically. A special feature of proteins may make coarse-graining easier.

Surprisingly large concentrations of ions are found near ion channels, binding sites, and nucleic acids [71] because of the large densities of acid and base side chains. The concentrations can be as large as those in solid NaCl. These concentrations are buffered because they are controlled by the permanent (i.e., fixed) charge of the acid and base side chains (as they are controlled by fixed charges in classical ion exchangers [72]). Coarse-graining methods for this environment should be easier to develop because of the buffering, i.e., the total concentrations of salt ('ionic strength') do not change very much under normal conditions.

Conclusion

Quantitative molecular dynamics is needed to understand and control biological function of proteins in health and disease. The quantitative traditions of physics are needed to supplement the qualitative traditions of structural biology.

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References

1. Frenkel, D., and B. Smit. 2001. Understanding Molecular Simulation. Academic Press, New York.
2. Rapoport, D. C. 1997. The Art of Molecular Dynamics Simulations. Cambridge University Press, New York.
3. Schlick, T. 2002. Molecular Modeling and Simulation. Springer Verlag, New York.
4. Curry, S. 2015. Structural Biology: A Century-long Journey into an Unseen World. Interdiscip Sci Rev 40(3):308-328.
5. Bank, P. D. 2025. World Wide Databank. In https://www.wwpdb.org/.
6. Walquist, M. J., and M. R. El-Gewely. 2018. Mutagenesis: Site-Directed. eLS, pp. 1-14.
7. Cohn, E. J., and J. Edsall. 1943. Proteins, Amino Acids, and Peptides. Reinhold, New York.
8. Griffiths, D. J. 2024. Introduction to electrodynamics. Fifth Edition. Cambridge University Press.
9. Zangwill, A. 2013. Modern Electrodynamics. Cambridge University Press, New York.
10. Feynman, R. P., R. B. Leighton, and M. Sands. 1963. The Feynman: Lectures on Physics, Vol. 2. Mainly Electromagnetism and Matter. Addison-Wesley Publishing Co., also at http://www.feynmanlectures.caltech.edu/II_toc.html, New York.
11. Eisenberg, B. 2025. True on All Scales: A Tribute to Stuart Rice. DOI: 10.13140/RG.2.2.11167.47522.
12. Eisenberg, R. S. 2019. Dielectric Dilemma. preprint available at https://arxiv.org/abs/1901.10805.
13. Eisenberg, R. S. 2021. Maxwell Equations Without a Polarization Field, Using a Paradigm from Biophysics. Entropy 23(2):172, also available on arXiv at https://arxiv.org/ftp/arxiv/papers/2009/2009.07088.pdf and 07010.03390/e23020172.
14. Eisenberg, B., C. Liu, and Y. Wang. 2022. On Variational Principles for Polarization Responses in Electromechanical Systems. Communications in Mathematical Sciences 20(6):1541-1550.
15. Eisenberg, R. 2023. Circuits, Currents, Kirchhoff, and Maxwell. Qeios Qeios ID: L9QQSH.2.
16. Balabanian, N., and T. A. Bickart. 1969. Electrical network theory. Wiley.
17. Weinberg, L. 1975. Network analysis and synthesis. Krieger Pub. Co.

18. Gray, P. R., P. J. Hurst, S. H. Lewis, and R. G. Meyer. 2009. Analysis and Design of Analog Integrated Circuits. Wiley.

19. Ayers, J. E. 2018. Digital Integrated Circuits: Analysis and Design, Second Edition. CRC Press.

20. Maxwell, J. C. 1865. A Treatise on Electricity and Magnetism (reprinted 1954). Dover Publications, New York.

21. Eisenberg, R. S. 2024. Maxwell's True Current. Computation 12(2):22-46 see arXiv 2309.05667.

22. Brooks, B. R., R. E. Bruccoleri, B. D. Olafson, D. J. States, S. Swaminathan, and M. Karplus. 1983. CHARMM: a program for macromolecular energy minimization and dynamics calculations. J. Comput. Chem. 4:187-217.

23. Huang, J., and A. D. MacKerell Jr. 2013. CHARMM36 all-atom additive protein force field: Validation based on comparison to NMR data. Journal of Computational Chemistry 34(25):2135-2145.

24. Christen, M., P. H. Hünenberger, D. Bakowies, R. Baron, R. Burgi, D. P. Geerke, T. N. Heinz, M. A. Kastenholz, V. Krautler, C. Oostenbrink, C. Peter, D. Trzesniak, and W. F. van Gunsteren. 2005. The GROMOS software for biomolecular simulation: GROMOS05. J Comput Chem 26(16):1719-1751.

25. Pettersen, E. F., T. D. Goddard, C. C. Huang, G. S. Couch, D. M. Greenblatt, E. C. Meng, and T. E. Ferrin. 2004. UCSF Chimera—A visualization system for exploratory research and analysis. Journal of Computational Chemistry 25(13):1605-1612. https://doi.org/10.1002/jcc.20084.

26. Chimera. downloaded March 2022. Chimera.

27. Verboncoeur, J. P. 2005. Particle simulation of plasmas: review and advances. Plasma Physics and Controlled Fusion 47(5A):A231.

28. Pritchett, P. L. 2003. Particle-in-cell simulation of plasmas—A tutorial. Space Plasma Simulation:1-24.

29. Birdsall, C. K., and A. B. Langdon. 1991. Pasma Physics via Computer Simulation. Institute of Physics, London.

30. Wolf, E. M., M. Causley, A. Christlieb, and M. Bettencourt. 2016. A particle-in-cell method for the simulation of plasmas based on an unconditionally stable field solver. Journal of Computational Physics 326:342-372.

31. Wolf, E. M. 2015. A particle-in-cell method for the simulation of plasmas based on an unconditionally stable wave equation solver. Michigan State University.

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

33. Hodgkin, A. L., and R. D. Keynes. 1955. The potassium permeability of a giant nerve fibre. J. Physiol. 128:61-88.

34. Mironenko, A., U. Zachariae, B. L. de Groot, and W. Kopec. 2021. The persistent question of potassium channel permeation mechanisms. Journal of molecular biology 433(17):167002.

35. Hui, C., R. de Vries, W. Kopec, and B. L. de Groot. 2025. Effective polarization in potassium channel simulations: Ion conductance, occupancy, voltage response, and selectivity. Proceedings of the National Academy of Sciences 122(21):e2423866122.

36. Ferry, D. K., X. Oriols, and R. Eisenberg. 2025. Displacement Current in Classical and Quantum Systems. Computation 13DOI 10.3390/computation13020045v2(arXiv preprint arXiv:2408.13268):45-76.

37. Eisenberg, R. S. 2023. Maxwell's Current in Mitochondria and Nerve arXiv **2309.05667**. arXiv **2309.05667**:http://arxiv.org/abs/2309.05667.

38. Eisenberg, R. S. 2020. Electrodynamics Correlates Knock-on and Knock-off: Current is Spatially Uniform in Ion Channels. Preprint on arXiv at https://arxiv.org/abs/2002.09012.

39. Huxley, A. 1972. The Quantitative Analysis of Excitation and Conduction in Nerve. From Nobel Lectures, Physiology or Medicine 1963–1970. Elsevier, Amsterdam.

40. Neher, E. 1997. Ion channels for communication between and within cells Nobel Lecture, December 9, 1991. Nobel Lectures, Physiology or Medicine 1991-1995. N. Ringertz, editor. World Scientific Publishing Co, Singapore, pp. 10-25.

41. Xu, S., R. Eisenberg, Z. Song, and H. Huang. 2023. Mathematical Model for Chemical Reactions in Electrolytes Applied to Cytochrome c Oxidase: An Electro-Osmotic Approach. Computation 11(12):253.

42. Eisenberg, and R. S. 2025. Current Laws and the Maxwell Equations. DOI: 10.13140/RG.2.2.34171.63524

43. Catterall, W. A., T. M. G. El-Din, and G. Wisedchaisri. 2024. The chemistry of electrical signaling in sodium channels from bacteria and beyond. Cell Chemical Biology 31(8):1405-1421.

44. Bezanilla, F. 2018. Gating currents. The Journal of General Physiology 150(7):911-932.

45. Eisenberg, R., L. Catacuzzeno, and F. Franciolini. 2022. Conformations and Currents Make the Nerve Signal. ScienceOpen Preprints.

46. Eisenberg, R. 2024. Current Flow in Nerve and Mitochondria. DOI: 10.14293/PR2199.001212.v1.

47. Eisenberg, B. 2003. Proteins, Channels, and Crowded Ions. Biophysical Chemistry 100:507 - 517.

48. Liu, J. L., and B. Eisenberg. 2020. Molecular Mean-Field Theory of Ionic Solutions: a Poisson-Nernst-Planck-Bikerman Model. Entropy 22:550 Preprint available at https://arxiv.org/abs/2004.10300.

49. Boda, D., M. Valiskó, and D. Gillespie. 2020. Modeling the Device Behavior of Biological and Synthetic Nanopores with Reduced Models. Entropy 22(11):1259.

50. Vera, J. H., and G. Wilczek-Vera. 2016. Classical Thermodynamics of Fluid Systems: Principles and Applications. Crc Press.

51. Nguyen, V. P., A. de Vaucorbeil, C. Nguyen-Thanh, and T. K. Mandal. 2020. A generalized particle in cell method for explicit solid dynamics. Computer Methods in Applied Mechanics and Engineering 371:113308.

52. Bai, J., Y. Cao, Y. Chu, and X. Zhang. 2018. An improved immersed finite element particle-in-cell method for plasma simulation. Computers & Mathematics with Applications 75(6):1887-1899.

53. Gross, W. J., D. Vasileska, and D. K. Ferry. 1999. A novel approach for introducing the electron-electron and electron-impurity interactions in particle-based simulations. Electron Device Letters, IEEE 20(9):463-465.

54. Ramey, S. M., and D. K. Ferry. 2003. A new model of including discrete dopant ions into monte carlo simulations. IEEE transactions on Nanotechnology 2(4):193-197.

55. Eisenberg, B. 2010. Multiple Scales in the Simulation of Ion Channels and Proteins. The Journal of Physical Chemistry C 114(48):20719-20733.

56. Hull, P., and A. Lampert. 2025. Using metaphorical considerations to benefit research on the sodium channel fast inactivation mechanism. Journal of General Physiology 157(4):e202413683.

57. Piana, S., J. L. Klepeis, and D. E. Shaw. 2014. Assessing the accuracy of physical models used in protein-folding simulations: quantitative evidence from long molecular dynamics simulations. Current opinion in structural biology 24:98-105.

58. Shaw, D. E., P. Maragakis, K. Lindorff-Larsen, S. Piana, R. O. Dror, M. P. Eastwood, J. A. Bank, J. M. Jumper, J. K. Salmon, and Y. Shan. 2010. Atomic-level characterization of the structural dynamics of proteins. Science 330(6002):341-346.

59. Hovarth, A. L. 1985. Handbook of aqueous electrolyte solutions: physical properties, estimation, and correlation methods. Ellis Horwood,, New York.

60. Barthel, J., and R. Neueder. 1997. Electrolyte Data Collection: Viscosity of nonaqueous solutions. I. Alcohol solutions. DECHEMA.

61. Barthel, J., and R. Neueder. 1992. Electrolyte Data Collection: Tables, Diagrams, Correlations, and Literature Survey. DECHEMA.

62. Barthel, J., R. Buchner, and M. Münsterer. 1996. Electrolyte Data Collection: Dielectric properties of nonaqueous electrolyte solutions / J. Barthel ; R. Buchner ; M. Münsterer. Pt. 2a. Scholium International.

63. Barthel, J., R. Buchner, and M. Münsterer. 1995. Electrolyte Data Collection Vol. 12, Part 2: Dielectric Properties of Water and Aqueous Electrolyte Solutions. DECHEMA, Frankfurt am Main.

64. Barthel, J. 1997. Dechema Chemistry Data Series. Deutsche Gesellschaft für Chemisches Aparatewesen.

65. Kontogeorgis, G. M., and G. K. Folas. 2009. Thermodynamic Models for Industrial Applications: From Classical and Advanced Mixing Rules to Association Theories. John Wiley & Sons.

66. P. Meissner, H., C. L. Kusik, and J. W. Tester. 1972. Activity Coefficients of Strong Electrolytes in Aqueous Solution.

67. Pitzer, K. S. 1991. Activity Coefficients in Electrolyte Solutions. CRC Press, Boca Raton FL USA.

68. Pytkowicz, R. M. 1979. Activity Coefficients in Electrolyte Solutions. CRC, Boca Raton FL USA.

69. Zemaitis, J. F., Jr., D. M. Clark, M. Rafal, and N. C. Scrivner. 1986. Handbook of Aqueous Electrolyte Thermodynamics. Design Institute for Physical Property Data, American Institute of Chemical Engineers, New York.

70. Anderson, H. L., and R. H. Wood. 1973. Thermodynamics of aqueous mixed electrolytes. Water. F. Franks, editor. Plenum Press, New York.

71. Jimenez-Morales, D., J. Liang, and B. Eisenberg. 2012. Ionizable side chains at catalytic active sites of enzymes. European Biophysics Journal 41(5):449-460.

72. Helfferich, F. 1962. Ion Exchange. McGraw Hill, New York.