Bob Eisenberg

(more formally, Robert S. Eisenberg

Curriculum Vitae

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Maintained with loving care by John Tang, all these years, with thanks from Bob!

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Education

Elementary School: New Rochelle, New York

High School, 1956-59. Horace Mann School, Riverdale, New York City, graduated in three years with honors and awards in Biology, Chemistry, Physics, Mathematics, Latin, English, and History. An interviewer of J.R. Pappenheimer, Professor of Physiology, Harvard Medical School, on American Heart Sponsored television program, ~1957.

- Undergraduate, 1959-62. Entered Harvard College with Advanced Placement as a sophomore, concentrated in Biochemical Sciences, Prof. J.T. Edsall tutor and mentor; advisor in Physiology Prof. J.R. Pappenheimer; graduated in three years A.B., *summa cum laude*.
- Summer work, 1960-61. Nerve Muscle Program at Marine Biological Laboratory directed by Prof. S.W. Kuffler.
- Doctoral work: University College London 1962-65 (Ph.D. in Biophysics: B. Katz, Chairman); Supervisor, P. Fatt; External Examiner, A.L. Hodgkin. Mentor (over several decades): A.F. Huxley.

Academic Positions

Main Positions

Rush Medical College, Chicago IL. Rush Employee ID 010207

- 2015 ... Chairman emeritus, Physiology & Biophysics (Department renamed again)
- 1995-2015 Chairman of Molecular Biophysics and Physiology (Department renamed)
- 1976 -... Endowed Chair "The Francis N. and Catherine O. Bard Chair of Physiology "
- 1976-1995 Chairman of Physiology: first and founding Chairman

University of California at Los Angeles

1975-1976	Professor of Biomathematics and Physiology,
	Chairmen: Carol Newton, W. Mommaerts
1970-1975	Associate Professor, Department of Physiology
1968-1970	Assistant Professor, Department of Physiology

Duke University, Durham NC

Associate, 1965-1968. Dept. of Physiology, Duke University, Chairman: D. Tosteson. Postdoctoral fellow of P. Horowicz, along with P. Gage, C. Armstrong, etc.

Secondary Positions

- Adjunct Research Professor, Department of Applied Mathematics, Illinois Institute of Technology, 2017, ID A20413703
- Research Professor, Department of Chemistry, Illinois Institute of Technology, 2022. ID A20413703
- Adjunct Professor, Dept of Bioengineering, then Biomedical Engineering (July, 2021) University of Illinois Chicago 2007- ... UIN 658809751
- Affiliate, Department of Mathematical Sciences, University of Wisconsin Milwaukeer Campus Email address is <u>eisenber@uwm.edu</u> Campus ID is **991532774**.

Affiliate Member, National Institute for Theory and Mathematics in Biology Chicago Zu Chongzhi Distinguished Lecturer Duke Kunshan University 2020

MOST Chair Professor (Minstry of Science and Technology). National Tsin Hua University, Institute of Computational and Modeling Science, Hsinchu Taiwan 2018, ID V01609–0; Taiwan ID# OC30049593

Visiting Scientist, long term. Mathematical Biology Institute. Ohio State University (2015)

Miller Institute Professor, University of California, Berkeley, October, 2012-February 2013, sponsored by Department of Chemistry, Rich Saykally in particular. ID 012503669

Visiting Scholar, Dept of Mathematics, Pennsylvania State University 2011. ID 9 82583348

Senior Scientist, Argonne National Laboratory (Mathematics and Computer Science Division, 2005 – 2011 Badge number B0 56980 A

Schlumberger Visiting Professor, University of Cambridge (UK) 2002

Visiting Fellow, Corpus Christi College, University of Cambridge (UK) 2002

Visiting Professor, 2000-2003 Computational Electronics, Beckman Institute, University of Illinois, Urbana Champaign

Visiting Scientist, 1991-1995. Physics, Brookhaven National Laboratory, Upton, NY.

Honors

Editorial Board of Computation Journal

- MOST Chair Professor (Ministry of Science and Technology). National Tsin Hua University, Institute of Computational and Modeling Science, Hsinchu Taiwan, Host: Jinn-Liang Liu, 2018.
- Distinguished Scientist in Residence, supported by a Fields Research Fellowship, Fields Institute for Research in Mathematical Sciences, University of Toronto, 2017, 2018.

Visiting Scientist, long term. Mathematical Biosciences Institute. Ohio State University

- Lakeside Lecture, Academia Sinica, Dept of Math., National Taiwan University, 2013. Organizers: Y-Chiuan Chen, Chen-Yu Chi, Chun -Chung Hsieh, Jeng-Daw Yu
- Keynote Speaker, Science Week, Loyola University (Chicago), 2013.
- Miller Visiting Professor, Miller Institute for Basic Research in Science and Department of Chemistry, University of California, Berkeley, October-February, 2012-2013.
- Keynote and Summary Speaker, National Taiwan University Taipei "Workshop on Mathematical Models of Electrolytes Applied to Molecular Biology", January, 2012; December, 2013. Tai-Chia Lin 林太家 Organizer)

Keynote Speaker, Lancaster University: Conference on Fluctuations and Coherence. (2011) see www.physics.lancs.ac.uk/FluctuationsConference2011/talks.htm

Keynote Speaker, Oak Ridge National Laboratory and University of Tennessee, Knoxville. Summer School on Biophysics: Computational and Theoretical Challenges (2010).

Institute of Medicine of Chicago

Senior and Life Member of the IEEE

Argonne National Laboratory: Director's Seminar

Fellow, American Physical Society (Division of Biological Physics)

Member Executive Board, American Physical Society (2002-2004)

Plenary Lecture at European Mathematics Society/AMAM 2003

Schlumberger Medal, Physical Chemistry, University of Cambridge, UK

Schlumberger Visiting Professor, University of Cambridge (UK)

Visiting Fellow, Corpus Christi College, University of Cambridge (UK)

Associate Editor, News in Physiological Sciences, 1988-1992

Associate Editor, Comments on Theoretical Biology, 1987-1992

Editorial Board, Journal of General Physiology, 1970-1991

Editorial Board, Journal of Computational Electronics, 2001-2013

Senior Common Room Award for "Most Promising Scholar"

L.J. Henderson award for thesis in Biochemical Sciences

A.B. received *summa cum laude*, after three years at Harvard College.

Harvard College Scholarship

Phi Beta Kappa: member of "Senior Sixteen", in second year at Harvard College.

Personal

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Born in Brooklyn, New York, April 25, 1942: Citizen of the United States. Social Security Number 075-xx-xxxx. Married Ardyth Eisenberg, 1991.

Children (mother, Brenda Russell, formerly Brenda R. Eisenberg, from 1964 to 1988): Benjamin Russell Eisenberg, born March 17, 1969. *Grandchild, mother Angelle Moutoussamy* Crystal Lynn Moutoussamy, born March 19, 1994
Emily Ruth Eisenberg, born February 8, 1973. Husband, Benjamin Taylor Jill Anna Trowbridge (born Eisenberg) *Grandchildren, father John Trowbridge* James Louis Trowbridge, born August 15, 1997. Holly Sophia Trowbridge, born July 11, 2000. Henry Samuel Trowbridge, born January 15, 2004. Alastair Solomon Trowbridge, born January 10, 2006
Sally Lynn Eisenberg, born June 20, 1979. *Family Christmas Letters:* [2001] [2002] [2003] [2004] [2015] [2006] [2007] [2008] [2009] [2010] [2011] [2012] [2013] [2014] [2015] [2016]

[2017] [2018] [2019] [2020] [2021] [2022] [2023] [2024]

Family Photos (unedited) from many years are at *Family photos* or https://picasaweb.google.com/111845037112506820480

Life Glimpsed through Ion Channels

A Super Short Scientific Biography

See <u>Living History</u> <u>https://www.youtube.com/watch?v=wj7QiLAv61E</u>

I have been interested in how physical things work as long as I can remember, and in how living things work nearly as long, from the day my father (a physician and then psychiatrist) showed me that was the best way to mold my interests to his approval.

At Harvard John Edsall was my tutor, and he did in fact tutor me, biweekly at first and then (nearly) weekly, nominally in biology, but really in the wisdom of science. (John Edsall was born the son of a Dean of Harvard Medical School, and was a fulcrum for the pivotal change from macroscopic to molecular biology at Harvard and elsewhere, training Bruce Alberts, David Eisenberg, and Jared Diamond among many other distinguished scientists.) My coursework was in physics, chemistry, applied mathematics, and electrical engineering, but, if my memory serves me correctly, not in biology at all. (I actually love evolutionary and descriptive biology as I love collecting classical CD's but those loves are hobbies more than anything else.) My undergraduate thesis solved the cable equation of physiology (the transmission line equations of engineering) with a Green's function, reproducing in an elegant but useless way what I had learned from Morse & Feshbach about heat equations.

My graduate work was experimental at University College London, where my department chairman Bernard Katz was to win the Nobel Prize a few years later. Fortunately, Andrew Huxley (Chair of Physiology at UCL, winner of the Nobel Prize with Alan Hodgkin in 1964 a year or two before Bernard Katz, if I remember correctly) had solved the cable equations the way I had, but much earlier and much more originally and insightfully, and so was happy to spend many hours teaching me, on the side, as if he didn't have enough else to do. My experimental work measured the spread of current in crab muscle fibers over a range of frequencies, using impedance spectroscopy, as it is now rather pretentiously named.

I will not bore you with the many decades of experimental work I did analyzing the flow of current in muscle fibers and then the lens of the eye. I became a Department Chairman at Rush Medical College in Chicago in 1976: the temptation of an Endowed Chair was enough to make a 34 year old move from the perpetual spring of Brentwood (LA) to the recurrent vagaries of midwestern weather. In the 1980's, I started thinking about the theoretical problem of describing ion movement through the water filled tunnels of charge we call ionic channels.

The ionic channel is where we still are; but gazing through this narrow hole has proven to be rather like looking through a keyhole in a door. The closer you get to it, the further you can see, even glimpsing the horizon (of knowledge) occasionally, even seeing a star or two, when all else seems dark.

Scientific Biography

I received my A.B. (summa cum laude) at Harvard College after three years of study with John Edsall as tutor. I started studying electrical properties of cells at Harvard Medical School (Physiology) with John Pappenheimer and at his recommendation I was accepted into Steve Kuffler's Nerve Muscle Training Program at the Marine Biological Laboratory, Woods Hole. At the MBL for three summers, I got to know Alan Hodgkin, Bob Taylor, K.C. Cole, John Moore, and too many others to name. I went to University College London for my Ph.D. with Paul Fatt as supervisor, where Bernard Katz was Chairman. Alan Hodgkin was my external examiner (and scientific hero!) and Andrew Huxley my mentor, for many years. My Ph.D. thesis and later work for a decade or two used engineering methods (impedance measurements: dielectric spectroscopy of single cells) to determine the electrical structure of cells and tissues (skeletal muscle, cardiac muscle, lens of the eye). I developed mathematical models to describe the electrical and physical structure mostly using methods of singular perturbation theory (working with Julian Cole, Victor Barcilon, and Art Peskoff). I helped Brenda Eisenberg use statistical sampling methods of stereology to measure the structure. As a postdoc at Duke (Physiology), Brenda and I showed that glycerol treatment disconnected the T-tubular system of skeletal muscle, and Peter Gage and I studied the electrical properties of the resulting detubulated preaparation. I rose through the academic ranks at UCLA, and was appointed the first Chairman of the Department of Physiology at Rush Medical College in Chicago when I was 33 years old, a position I held for 39 years.

I served as Chairman of the Physiology Study Section of the NIH for several years, and Director of Research (etc) for the American Heart Association (Chicago Branch). After single channel recording was discovered, I introduced Alan Finkel (Axon Instruments), Rick Levis, and Jim Rae to the patch clamp technique, and invented the integrating headstage after thinking hard about how to increase the impedance and reduce the noise of the feedback element in a current to voltage converter. Together we designed the Axopatch amplifier that is used by thousands of channologists to this day.

I have spent many years working on ion channels, which are protein nanovalves that control an enormous range of biological function. I am trying to understand the current that flows through the channel, in a range of solutions of different composition, over a range of voltages. Working with Zeev Schuss, I showed how the flux over a potential barrier of any shape could be evaluated analytically, starting from a description of the stochastic trajectories of diffusion. 'Eyring models' of transition state theory arise as a special case of very high symmetrical barriers and it is hardly easier to compute than the general formulas.

Zeev Schuss, Boaz Nadler, Amit Singer, and I went on to show how mean field models can be derived from a model of the stochastic trajectories of ions in solution, using the techniques of probability theory and a classical closure approximation.

I adopted the drift diffusion equations of semiconductor physics, introduced them with their use of doping to represent the permanent charge of side chains of proteins (e.g., the acidic and basic side chains glutamate and lysine), and gave them the nickname PNP to remind people that proteins could have charge distributions like those of transistors and might (conceivably) function that way.

Working with Wolfgang Nonner, then Dirk Gillespie, Dezső Boda, Doug Henderson and others, I showed how the properties of concentrated electrolytes (as summarized in the primitive model of ionic solutions) can account for selectivity of two important types of channels, the L-type calcium channel of the heart and the voltage activated Na⁺ channel of nerve.

I also

(1) helped design and build selective channels using nonselective bacterial channels (ompF porin) as the 'substrate' (with Hank Miedema, et al, from Groningen),

(2) helped design abiotic ionic channels (which Zuzanna Siwy builds),

(3) helped Weishi Liu apply geometric perturbation theory to ion channels,

(4) used the mathematics of inverse problems to design the selectivity and permanent charge of channels, assisting Heinz Engl and Martin Burger. This paper is particularly unusual since it is one of the few cases in which an inverse problem of significance to biology could be solved in detail and with quite robust results.

(5) worked with Dezső Boda, Doug Henderson, Dirk Gillespie and Wolfgang Nonner to extend the crowded charge model of selectivity from calcium channels to the Na channel of nerve, showing that the same model can explain both (very different) types of channels *without changing any parameters*, just by reproducing the mutation (known from experiment) to change one channel type into another, EEEA \leftrightarrow DEKA, i.e. Glu-Glu-Glu-Ala \leftrightarrow Asp-Glu-Lys-Ala. This work shows that a single model with just one set of never changing parameters can account for the selectivity properties of two very different types of channels (Na channel of nerve and Ca channel of muscle). When the side chains in the channel protein are changed in the model, the protein changes selectivity just as it does in life. This work also reveals control parameters for the Na channel: the dielectric coefficient changes the contents of the channel, and has almost no effect on Na⁺ vs. K⁺ selectivity. The diameter of the selectivity filter changes the Na⁺ vs. K⁺ selectivity and has almost no effect on the contents of the channel.

(6) showed (with the same collaborators) that calcium selectivity does not arise from models of the L-type Ca channel that do not allow Glu residues to mix with ions.

(7) suggested that the simple model of selectivity works so well because it computes the important structures of the selectivity filter. These models put the 'side chains' into their optimal position (with minimal free energy) and thus determines the 'optimal' relation of side chains and permeating ions. These methods compute a self-organized selectivity filter in which the induced fit of side chains and ions is determined by the positions of the ions and side chains at thermodynamic equilibrium. The model computes the structure of the selectivity filter and that structure changes significantly from one solution to another.

(8) started to apply the energy variational principle developed by Chun Liu and collaborators to problems in ion permeation, selectivity, gating (with YunKyong Hyon and Chun) and to new subjects of water movement (with Yoichiro Mori and Chun) and vesicle formation and fusion (with Fred Cohen, Rolf Ryham, and Chun). The variational principle allows the coupling of different interacting structures and different physical properties of a single system in a mathematically well defined and (automatically) self-consistent way. It produces different partial differential equations and boundary conditions depending on the structures, physics, and coupling included in the underlying model. It thus seems ideally suited to the complexity of ions and water in solution, channels, and tissues, as well as to the interactions of multiple systems and physics that produce flow of ions and water and movement of membranes and cells and tissues in biological systems.

(9) Along the way, I helped Amit Singer (working with Zeev Schuss) show why the charge distribution of table salt (NaCl) does not produce sparks and electrocute those who touch it. Safety in salt is a consequence of probability theory, among other things, as all salt eaters should be glad to know.

(10) Moving to new methods and questions, I grew curious about the density of charged amino acids in active sites. The density of charge is enormous in ion channels and I wondered if it was also high in active sites of enzymes in general. Jie Liang, David Jimenez-Morales and I have used some wonderful search algorithms designed and implemented by Jie and David and found huge densities of acid (presumably negative) and basic (presumably positive) side chains in active sites, some 20 Molar (for comparison solid sodium chloride is 37 Molar). This very special charged environment seems likely to have been selected by evolution for a particular physical reason that we do not know.

(11) The traditional laws of chemistry do not apply well in environments as crowded as ion channels or active sites so I looked up the derivation of the classical 'law' of mass action that is taught to every graduate student in chemistry and most undergraduates as well. I found to my horror that the law is true (with constant rate constants) only when solutions are infinitely dilute and have no interactions between solutes. Since all ionic solutions have solutes that interact through the electric field, ionic solutions should not be described as they almost always have been in biochemistry and physiology. Ionic solutions do not obey the 'law' of mass action (with constant rate constants). Thousands of papers explain interactions by invoking conformation changes of enzymes and channels, or assuming complex reaction schemes and allosteric interactions (for example). Those explanations and schemes nearly always use rate constants that are constant. If they used variable rate constants that capture physical interactions of ions, the schemes and explanations would surely change dramatically, and might disappear altogether in some cases.

(12) Thinking about the law of mass action, I realized the obvious. It is incompatible with Kirchoff's current law which is nearly the same as Maxwell's equations. Maxwell/Kirchoff are about conservation of charge. (Indeed, 'charge'is an abstract quantity, unlike mass, that assumes different physical form in different settings. The charge flowing in a vacuum capacitor is not the charge flowing in a wire, or the charge flowing in an ionic solution. Maxwell's equations apply to the abstraction charge not just to electrons, ions, etc.) Maxwell and Kirchoff are global, involving

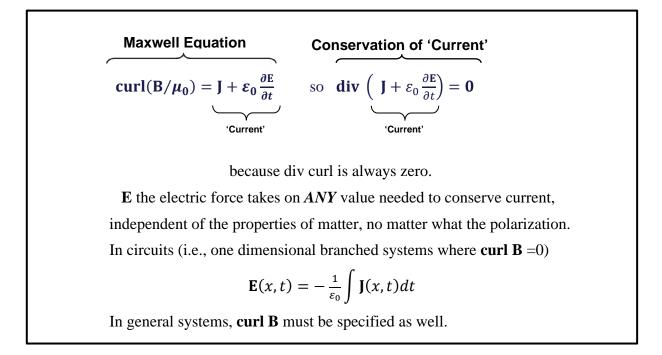
locations far apart. Mass action is about conservation of mass. Mass action is local involving only locations of reactants and products, close together. It is obvious once all this is stated, that the law of mass action (applied to a series of chemical reactions *at different physical locations* and with rate constants that are constant) is incompatible the Kirchoff's current law. It is easy to prove this by writing out the flux in such reactions and comparing it to the flow of current. They cannot be identical in general because one depends on the charge on the reactants (e.g., 'the valence') and one does not. The implications are profound because Maxwell's equations (nearly) always involve boundary conditions often far far away from a particular place. Chemical reactions are usually thought to be local, but if they involve charge movement from one place to another, they must satisfy Maxwell's equations and be described by global equations that usually depend on conditions far far away. The local law of mass action must be replaced then by chemical laws in which everything interacts with everything else according to Maxwell, and current flows in loops as described by Kirchoff's current law.

(12) Many of the properties of open channels are determined by the balance between electrostatic and steric forces among the ions and side chains crowded into a narrow space. 'Everything interacts with everything else' in systems like this and so the mathematics used to simulate or compute models must deal consistently with interactions. That is, every variable must satisfy every equation and boundary condition in all experimental situations. Such consistency is very difficult to satisfy in simulations that have full atomic detail and in fact very few checks of such consistency have been made and none (that I know of) in realistic ionic conditions, including the ionic mixtures (that involve calcium ions) actually found on either side of a channel.

Theories can ensure consistency if they are derived by the Energy Variational methods that include dissipation (i.e., friction) but those theories compute steric forces explicitly (in three dimensions) from Lennard Jones or Yukawa type models of atom atom interaction. Such computations are very difficult because the steric forces vary so steeply with location. Another approach is to replace those calculations with a careful treatment of the main consequence of steric forces. The main consequence is that ions cannot overfill a volume: there is a maxium number of ions that can fit in a volume. The concentration in a volume saturates. This approach depends on the calculation of the free energy of mixtures of spheres of any diameter in any concentrations. Jinn-Liang Liu has led the way in such calculations.

(13) Electricity is different from other force fields because it is universal. Electricity follows Maxwell's equations of electrodynamics exactly, in the nuclei of atoms and the nuclei of galaxies, from times much shorter than those of atomic motion (0.1 femtoseconds) to thousands of years. Electricity is different because it is so strong. One per cent charge imbalance (in an 80 kg object) produces a force enough to lift the earth. **Electrodynamics enforce the conservation of 'current'**

when 'current' includes Maxwell's vacuum displacement term $\varepsilon_0 \partial \mathbf{E}/\partial t$. The 'one line' proof is here for anyone who wants to see it.



Analysis shows that the **time rate of change of the electric field can take on whatever value is needed to ensure conservation of this current** <u>no matter what are the properties of matter or</u> <u>its polarization</u>. Properties of matter rearrange themselves to satisfy conservation of this current. The displacement current term $\varepsilon_0 \partial \mathbf{E}/\partial t$ is universal, inside matter and atoms, between stars, because it is a consequence of general physical laws, i.e., special relativity. Charge is relativistically invariant (i.e., it does not change as velocities approach the speed of light), unlike time, distance, and mass, all of which change dramatically at such velocities. The $\varepsilon_0 \partial \mathbf{E}/\partial t$ term makes charge satisfy the Lorentz transformation and be independent of velocity.

Theories of matter often treat electrodynamics cavalierly. Vacuum displacement current is usually ignored and so conservation of 'current' is not explicitly enforced. Theories and simulations without the vacuum displacement term $\varepsilon_0 \partial \mathbf{E}/\partial t$ are likely not to satisfy the laws of electrodynamics and do not satisfy conservation of current if polarization and dielectric properties are described realistically. Amending theories of matter to include electrodynamics is likely to produce significant improvement in applications to the real worlds of technology, biology, and medicine. Proofs and discussion are at https://arxiv.org/abs/1905.13574, 2019 version 4.

(15). The work on Kirchhoff's law and the Maxwell equations has taken many years. It is recorded in an embarrassing number of papers, I will not enumerate here.

The state of the work on Kirchhoff's law in December, 2022 is summarized in

a) Version 4 of "Kirchhoff's Law can be Exact." arXiv preprint available at https://arxiv.org/abs/1905.13574, 2019. The Addendum enumerates and discusses the crucial papers.

b) A Necessary Addition to Kirchhoff's Current Law of Circuits, Version 2. Engineering Archive EngArXiv, 2022. https://doi.org/10.31224/2234.

c) Eisenberg, R., X. Oriols, and D.K. Ferry, Kirchhoff's Current Law with Displacement Current. arXiv: 2207.08277, 2022.

Reference c) is of particular interest because Dave Ferry found a remarkable reference showing that Kirchhoff himself understood the need to include the time rate of change of the electric field in the currents he was describing.

I should add that the two senior authors (XO and DF) have worked on the design of high speed transistors of computers (that switch in 10^{-10} sec or less) using quantum mechanics of the Bohm flavor. Designers use Kirchhoff's law at these speeds, even though textbooks, Wikipedia, and derivations claim the law is an approximation valid only at slow speeds, say 10^{-3} sec and slower. Textbooks, Wikipedia and the literature ignore the gap of ~ 10^7 .

It is quite remarkable that the property of electricity used more than anything else (because it is used in every transistor of our computers, video screens, and mobile phones) is discussed incorrectly, and not derived in the literature, textbooks, or Wikipdia articles on electrodynamics.

This should be a particular embarrassment since the high speed circuits (designed by Kirchhoff's law) are abundant. There are something like 10^{11} high speed circuits in each computer, cell phone, and video device and something like 10^{10} such computers, phones, etc in the world (clearly much more: there are more than one device per person in China alone, making something > 1.4×10^9). So there are than 10^{20} high speed circuits in the world.

The lack of understanding of how conservation of current applies to the most important application of electricity is amazing.

The avoidance of the issue is a scandal, but not surprising given the realities of human behavior when people are caught making a mistake. Bottom line: scientists are people..

16) My collaborators (group leader: Huaxiong Huang; Shixin Xu, and Zilong Song) have used Kirchhoff's law, derived from the Maxwell equations, to analyze tissues of some complexity, using conservation laws, and using the real structures, from tissue to channels, with whatever resolution is needed to describe biological function. We worked on the lens of the eye first, and then moved to the optic nerve of salamanders that is part of the central nervous system. This material is motivated and reviewed in *Structural Analysis of Fluid Flow in Complex Biological*

Systems. see Review # 46. This review summarizes the work of many decades and builds on the contributions of many colleagues, over many years e.g., Rick Mathias (starting around 1975) and Dick Orkand (1960s).

(17) Moving to high resolution, we (group leader: Huaxiong Huang; Shixin Xu, and Zilong Song) have attacked one of the most important membrane systems in biology, namely the molecules (chiefly proteins) that use oxygen to generate ATP, motivated by most useful discussions with Oscar Juarez. ATP powers almost all the chemical reactions of life. No, that is not hyperbole, as unlikely as it sounds. The atomic details of the proteins are known, and several Nobel Prizes have been given in this area, but the *fundamental question of how does it work?* has not been answered or in my not so humble opinion even addressed. No equations are available to describe the flows of matter, electrons, and charge that produce ATP. The papers in the field discuss coupling and flow repeatedly but equations which define coupling and flow are notable for their absence

We believe that absence is caused by the absence of Kirchhoff's law in the analysis. Without Kirchhoff's law, one faces the impossible task of recreating macroscopic function that involves at least 10¹⁵ charges that interact in many ways with each other. **SCIENTISTS:** Imagine trying to compute an action potential without using Kirchhoff's law and the cable equation it implies! We have tried to fix that in Xu, S., et al., Mathematical Model for Chemical Reactions in Electrolyte Applied to Cytochrome c Oxidase: an Electro-osmotic Approach. 0.48550/arxiv.2207.02215 2022.

18) It seemed time, as I approached my 80th birthday, to do something altogether new, that would seem relevant to the present generation of molecular biologists, rightly obsessed with the (more than) one hundred fifty thousand structures of proteins they have at their fingertips.

Background: Modern molecular dynamics allows calculation of the motions of the $\sim 100,000$ atoms in each of these proteins, however approximately. And that resolution is needed to deal with the evident fact that a few atoms (in DNA, RNA, or proteins) controls macroscopic function. The implications for disease treatment cannot be overstated, as the mRNA vaccine THAT **DEPENDS** CRTICALLY design of the ON **UNDERSTANDING THE STRUCTURE OF A PROTEIN, should make clear.** See the general discussion in Asking biological questions of physical systems: The device approach to emergent properties. Journal of Molecular Liquids, 2018. 270: p. 212-217. Preprint available on arXiv as https://arxiv.org/abs/1801.05452.

The ideas have been actually implemented in a specific important protein in my papers led by Luigi Catacuzzeno.

1. Catacuzzeno, L., et al., Gating current noise produced by Brownian models of a voltage sensor. bioRxiv Biophysical Journal, 2021. **120**: p. 2021.01.13.426543.

Catacuzzeno, L., et al., Multiscale modeling shows that dielectric differences make NaV channels faster than KV channels. Journal of General Physiology, 2021. 153 DOI: 10.1085/jgp.202012706(2).

3. Eisenberg, R., L. Catacuzzeno, and F. Franciolini, Conformations and Currents Make the Nerve Signal. 10.14293/s2199-1006.1.sor-.ppd7mca.

Luigi and I worked together years ago with Wolfgang Nonner

4. Nonner, W., L., Catacuzzeno, and B. Eisenberg, Ionic selectivity in K channels. Biophysical Journal, 2000. **78**: p. A96.

5. Nonner, W., L. Catacuzzeno, and B. Eisenberg, Binding and selectivity in L-type calcium channels: a mean spherical approximation. Biophys J, 2000. **79**(4): p. 1976-92.

<u>New Work</u>. So..... I suggested to a brilliant undergraduate Stanley Nicholson, working with me in David Minh's group on molecular dynamics at the Illinois Institute of Technology, that we try to analyze atomic scale motions using the coherence techniques that Rick Mathias and I used in many papers some forty years ago.

As unlikely as it seemed when we started, it turns out the Hydrogen bond of the α -helix of a protein can be studied with the same mathematics as the equivalent circuit of a muscle fiber. This method makes no assumptions whatsoever about the properties of atomic motion and so **it promises a great deal as it is applied to other motions in proteins.** We already have shown that the layers of the α -helix interact with each other as more or less rigid bodies according to simple physical laws.

19) It is fun to show that an 80 year old can suggest radical approaches that his younger colleagues find useful! Now, this 82 year old suggests a radical approach to understanding circuits in general.

20) New approach to Circuits.

There are some ideas we (or anyway I) have taken granted for so long that it comes as a revelation that they need to be explained.

I am thinking of the idea of a circuit. As I do not have to tell you, circuits have been the backbone, the main application of electricity and electronics since the invention of the telegraph around 1840. Circuits deliver information and power to our lives. Nearly everything in a computer is done by circuits.

It came as a great surprise then when I found that circuits and circuit laws (like the Kirchhoff laws) are not mentioned in the two major textbooks of electrodynamics, Jackson and Griffiths. Jackson has been used as a required text in the great majority of physics departments for many decades. Griffiths is a beautifully written and widely used introduction that treats a great deal of advanced information (like the theory of relativity) so it can understood by undergraduates.

Jackson, J.D. 1999. Classical Electrodynamics, Third Edition (Wiley: New York).

Griffiths, D.J. 2017. Introduction to Electrodynamics, Fourth Edition (Cambridge University Press).

Why I asked myself are circuits not discussed in these books?

The reason is that (in my opinion) the authors did not know how to derive their analysis of circuits from the principles of electrodynamics.

There are no derivations of circuit laws that start from Coulomb's law or the Poisson equation.

The properties of circuits canNOT be derived from a treatment of charge by Coulomb's law or the Poisson equation because too many charges are involved.

The smallest circuit involves at least 10^{10} charges that interact. Even just the pairwise interactions are far larger than can ever be computed (something 10^{10} factorial, squared!).

The most important property of circuits is that current flows only in complete circuits. **Incomplete** circuits prevent current flow. This fact cannot be derived from Coulomb's law or the Poisson equation.

Of course, scientists might deal with very large numbers of charges by coarse graining but that is very hard and not exact on these scales. **It turns out however that one can deal with circuits by describing currents in them instead of charges**. And the description of current is exact as well as feasible. Few currents are needed to describe circuits compared to the number of charges and as we shall see below the current laws are exact.

After decades of foolishness on my part, I eventually saw the way to do this. The **Maxwell Ampere law provides exactly the coarse graining needed** and it has the extraordinary advantage of providing exact (not approximate) coarse graining because it involves extra physics not present in Coulomb's law or the Poisson equation.

One uses the Maxwell Ampere current law **curl B** = $\mu_0 J_{\text{total}}$ where total current is conduction of charges PLUS displacement current $\varepsilon_r \varepsilon_0 \partial \mathbf{E}/\partial t$ written here with the customary over approximated dielectric constant. The mathematics is explained in the paper <u>"Electrodynamics and Circuits, Version 2"</u>, see Publications list.

Then one takes the divergence of both sides to get **Divergence of total current is zero.** What this means physically is explained in the Electrodynamics paper.

You have to use total current here not just flow of ions because the displacement current is significant and usually very large in modern circuits because voltages change a lot in time.

This divergence equation written above defines the 'field' of total current (i.e., how total current behaves everywhere). The current field has strange properties because it is NOT created by sources and sinks in the normal meaning of those words. It is a field that comes ONLY from the circulation of magnetism (curl B). The lines of total current flow do not start or end. They rather make endless loops like the lines of force in a magnetic field. These are INESCAPABLE mathematical properties of any flow that has divergence zero.

In vivid language: Current loops through its solenoidal fields in circuits without beginning or end. The circuit loops are divergence free with no sources or sinks. **The circuit loops define the structure of current flow.**

The reason circuits work so well in electrical and electronic engineering is that they are built physically (i.e. they have a layout) designed to capture the NATURAL loops of current that are the UNAVOIDABLE property of any ANY field of total current. **CIRCUITS CAPTURE THE NATURAL LOOPS OF CURRENT FLOW.**

Capturing the lines of total current circuits enables each line of current to be quite (but not perfectly) independent of other lines of current. Individual circuits are then nearly independent. Electricians and electronic engineers can use circuits as if they are independent and they do not have to solve all of Maxwell's equations. Circuit design assumes each circuit is independent. Circuit implementation deals with how to approximate that situation with real components.

In one sentence circuits capture the natural and unavoidable loops in which current ALWAYS flows and allow their use by engineers and biology.

Internet Coordinates

Web Sites

Departmental Site: <u>https://www.rushu.rush.edu/rush-medical-</u> college/departments/department-physiology-biophysics leading to Personal Site <u>https://www.rushu.rush.edu/faculty/robert-eisenberg-phd</u> **Living History** <u>https://www.youtube.com/watch?v=wj7QiLAv61E</u>

FTP Sites

- 1) <u>Reprints</u> available on this <u>hyperlink</u>
 - or by anonymous ftp from <u>ftp.rush.edu</u>. (sign on as anonymous, for password; use your email address) Migrate to <u>/molebio/Bob_Eisenberg/Reprints</u> or just click on this hyperlink
- 2) *PNP* is available in various flavors,
 - a. from <u>ftp.rush.edu</u> at /<u>pub/PNP/;</u> <u>/pub/Hollerbach/; /pub/Nonner/,</u> thank you: D. Chen, U. Hollerbach, W. Nonner and S-W. Chiu.
 - b. See a much more modern (2008) version from Department of Chemistry, Northwestern University, Laboratories of Mark Ratner and George Schatz labs <u>https://www.nanohub.org/resources/2469</u>
- 3) Files of single channel currents with noise are in <u>/pub/Noise</u>, written in collaboration with Rick Levis (*deceased*, 2005).

Grant Support

Continuous Grant Support (without interruption) thanks to a combination of NSF, NIH, and DARPA from approximately 1970 to 2011. Miscellaneous additional grants from AHA, MDA, Chicago Heart, etc.

Scientific Administration

FIRST CHAIRMAN OF DEPARTMENT OF MOLECULAR BIOPHYSICS AND PHYSIOLOGY, 1976-2014,

see science at <u>https://www.rushu.rush.edu/faculty/robert-eisenberg-phd</u> and

https://www.rushu.rush.edu/research/departmental-research/physiology-and-biophysicsresearch/laboratory-robert-eisenberg-phd

AMERICAN PHYSICAL SOCIETY

Councilor (First term: 2000-2004) Councilor (Second term: 2005-2009) Member of Executive Board (2002-2004) Member, Committee on Committees (2003- 2006, 2009) Member, Audit Committee (2004 - 2007), Chair Audit Committee (2005 – 2006) Division of Biological Physics, Executive Board (2001- 2010)

BIOPHYSICAL SOCIETY

Member of U.S. National Committee International Union of Pure and Applied Biophysics (1978-1983)

Member of Council (1983-1986).

Member of Executive Board (1983-1986).

Member of Program Committee (1984).

Chairman of Nominating Committee (1985).

Chairman of Science Public Policy Committee (1985-1987).

CHICAGO CHAPTER OF SOCIETY FOR NEUROSCIENCE

Member of Council (1981-1984), Meeting Organizer, then President.

CHICAGO HEART ASSOCIATION

Member, Vice Chairman, then Chairman of the Research Council (1982-1986). Member, Vice Chairman, then Chairman of Research Review Committee (1976-1986; 1989).

NATIONAL ACADEMY OF SCIENCES

Chairman Proposal Review for Allocation of Supercomputer Time for the Study of Molecular Dynamics: 2015 (ANTON 1), 2016 (ANTON 2)

NATIONAL INSTITUTES OF HEALTH

Member (1979-1981), then Chairman (1981-1983) of Physiology Study Section. Member *ad hoc* (2004) Modeling & Analysis of Biological Systems Study Section. <u>NATIONAL SCIENCE FOUNDATION</u> Member, Steering Committee on Biology and Mathematics (1989, 1996).

PENNSYLVANIA MUSCLE INSTITUTE

Member (1980-1982; 1989-1990), then Chairman (1982-1987; 1989-1990) of the External Advisory Board, University of Pennsylvania, Director: A. Somlyo (1980-1987); Y. Goldman (1989-1990).

<u>SOCIETY OF GENERAL PHYSIOLOGISTS</u> Councilor; Chairman, Membership Committee.

UNIVERSITY OF MIAMI

External review of Graduate Program, Department of Physiology (1988).

Invited Lectures On-Line click here [PPTX] and/or

- (1) Miscellaneous slides at <u>SlideShare http://www.slideshare.net/</u>: search for Bob Eisenberg
- (2) Thanks to the Fields Institute, University of Toronto, a **three hour tutorial and lecture** with slides are available for viewing at links <u>Part 1a</u> or <u>Part 1b</u> and <u>Part 2a</u> or <u>Part 2b</u>.
- (3) Thanks to Joe Cychosz of Nanohub, Electrical and Computer Engineering ECE Purdue, lectures from January, 2014 in (1) <u>Chemistry</u>, [Slides: PDF] (2) <u>Mathematics</u> [Slides: PDF] and (3) a <u>Student Talk in Engineering</u>, [Slides: PDF], are all available at <u>https://nanohub.org/members/16305/contributions</u>
- (4) Thanks to Lancaster University Physics Department. Slides from Bob's lecture of July, 2011 at Lancashire July 2011. i.e., www.physics.lancs.ac.uk/FluctuationsConference2011/talks.htm
- (5) Thanks to the Mathematical Biology Institute, Ohio State University, my lecture (with slides) from April 2011 is available at <u>MBI April 2011</u>, i.e., http://beta.mbi.ohio-state.edu/video/player/?id=549&title=Ions+in+Channels%3A+important+biology+ready+for+mathematical+analysis
- (6) Thanks to Institute for Mathematics and its Applications, University of Minnesota, my lecture of December 2008 is available (with slides) at <u>[Talks and PDF]</u>, i.e., <u>http://www.ima.umn.edu/2008-2009/W12.8-12.08/abstracts.html#Eisenberg-Robert</u>
- (7) Thanks to Joe Cychosz of Nanohub, Electrical and Computer Engineering ECE Purdue, lecture from 2008 is available for viewing at <u>http://www.nanohub.org/resources/4726/</u> [Talk]: "Ionic Selectivity in Channels: complex biology created by the balance of simple physics." Nanotechnology 501 Lecture Series: Purdue University.
- (8) Thanks to Institute for Mathematics and its Applications, University of Minnesota, my lecture of July 2015 is available (with slides) at [Talks] and [PDF]. i.e.,

http://www.ima.umn.edu/videos/?id=3028

(9) Thanks to Shanghai Jiao Tong University, slides from 2016 short course are on Lectures <u>Day</u> <u>1</u>, <u>Day 2</u>, <u>Day 3</u>

Invited Lectures and Collaborations click here [PPTX]

(approximately 400 as of June, 2021)

- Academia Sinica and Depatment of Mathematics, Lakeside Lecture, National Taiwan University, 2013. Organizers: Yi -Chiuan Chen, Chen -Yu Chi, Chun -Chung Hsieh, Jeng -Daw Yu
- AGH University of Science & Technology: Faculty of Materials Science & Ceramics. Lecture Series: "From Atoms to Axons: Life as a Hierarchy of Devices" Robert Filipek, host.
- Albert Einstein College of Medicine, Department of Physiology. Host: MVL Bennett.
- Albert Einstein College of Medicine, Dept. Medicine: Cardiology, Ed Sonnenblick host.
- American Chemical Society, National Meeting, Division of Physical Chemistry
- American Chemical Society, National Meeting, 2008, Division of Physical Chemistry Symposium: Water Mediated Interactions, Dor Ben-Amotz, H. Asbaugh, Organizers.

American Heart Association

AMA Institute (1966)

- American Institute of Mathematics (AIM) meeting 2018-2021 SQuaRE (Structured Quartet Research Ensembles) "Analysis of ion transport in ion channels and biological tissues" Organizer Huaxiong Huang (6 paticipants, 1 week together, each of three years)
- AMaSIS 2018, Applied Mathematics and Simulation for Semiconductors, Weierstrass Institute, Berlin, Keynote Speaker, Juergen Fuhrmann Organizer.
- American Mathematical Society, 2012, Central Section, co-organizer (with Weishi Liu and Chun Liu) and speaker in "Special Session on Mathematics of Ion Channels: Life's Transistors"
- American Mathematical Society, 2015, Central Sectional Meeting, Lead-off speaker,
- American Mathematical Society, 2021, Section Meeting, Lead off speaker.

American Mathematical Society, 2023, Section Meeting.

American Physical Society (Division of Biological Physics) March Meeting, 2000

American Physical Society (Division of Biological Physics) March Meeting, 2006

American Physical Society (Division of Biological Physics) March Meeting 2009

American Physiological Society Meeting: 1978, 1979, 1983

Argonne National Laboratory Chemical Sciences

Argonne National Laboratory Material Sciences Division

Argonne National Laboratory Mathematics and Computer Sciences Division

Argonne National Laboratory Biology Division

Argonne National Laboratory: Director's Seminar

Association of Chairmen of Departments of Physiology

Australian National University (Canberra)

- Banff International Research Station BIRS "Ion Channels- Mathematical Modeling and Analysis" #16frg212, September 2016, Bob Eisenberg, Chun Liu and Huaxiong Huang, organizers
- Banff International Research Station BIRS, lead-off speaker at workshop "Ion Transport: Electrodiffusion, Electrohydrodynamics and Homogenization" #16w51, May 2016, Huaxiong Huang and Chun Liu, organizers
- Baylor University
- Beijing International Center for Mathematical Research, Zhennan Zhou, host, October 2020 Biological Chemists of the Federal Republic of Germany
- Biophysical Society, 1991: in Symposium on Ion Channels in Intracellular Membranes
- Biophysical Society, 1993. Workshop on "From Structure to Permeation in Open Ionic Channels."
- Biophysical Society, 2007: *in* Symposium on Modeling as a Tool in Biophysics; Sponsor American Physical Society (Division of Biological Physics)
- Biozentrum (Basel, Switzerland): Minicourse on Electrophysiology
- Biozentrum (Basel, Switzerland): Selectivity in Channels (Seminar in Structural Biology)
- Birkbeck College, London, Institute of Structural and Molecular Biology, Bonnie Wallace, host, May 2016.
- Boston University (Department of Mathematics)
- Brandeis University (Department of Biochemistry, Host: Chris Miller, 1986; Department of Chemistry, Host: Judy Herzfeld, 2008)
- Brigham Young University (Zoology), ~1998
- Brigham Young University (Chemistry), 2010

Brigham Young University (Computer Science), 2010

Brigham Young University (Zoology and Neuroscience), 2010

Brigham Young University (Henderson Symposium), 2014

Brookhaven National Laboratory (Department of Physics)

Brown University, Dept. of Applied Mathematics, 2001

Brown University, Computing Science Seminar Applied Mathematics, 2023. Slides in [PDF] and [PPTX]

California Institute of Technology (Biology)

- California Institute of Technology (Applied Mathematics)
- Cambridge University (England) Physiology: Foster Club
- Cambridge University (England) Chemistry, in the "Lennard Jones Lecture Series"
- Cambridge University (England) Pharmacology
- Cambridge (England): Schlumberger Lecture, 2002
- Cambridge University (England) Centre for Computational Chemistry
- Cambridge University (England), Department of Physics, Maxwell Centre, Ulrich Keyser, host, May 2016.
- Cambridge University (England), Department of Mathematics, Newton Centre, David Holcman, host, May, 2016.
- CCNY, Department of Physics, Mike Lubell Chairman
- CECAM: Ionic Transport: from Nanopores to Biological Channels (Organizers Mounir Tarek and Mark Sansom, Lyon (2007)
- Centro de Investigacion y de Estudios del Avanzados (Mexico City)
- Chicago Heart Association Cardiovascular Research Forum
- Chicago Medical School
- Chinese Academy of Sciences CAS (Beijing) Institute of Computational Mathematics (Benzhuo Lu, host, 2012)
- City of Hope, Duarte, California
- K.S. Cole Symposium (FASEB Federation of American Societies of Experimental Biology, 1974)
- Colorado State University (Fort Collins: Department of Chemistry)
- Columbia University, Department of Chemical Engineering
- Conference on Fluctuations, Escape, and Optimal Control Traverse City MI
- Conference of N.Y. Academy of Science, 1977
- Cornell University Medical School: Department of Physiology
- Cornell University: Department of Chemistry
- Courant Institute (NYU) Seminar "Mostly Biomathematics" (2004)
- Courant Institute (NYU) Joint Seminar with Chun Liu, Yoichiro Mori, "Mostly Biomathematics (2010)
- DARPA (Defense Advanced Research Projects Agency)
 - Many workshops.
 - Director's Seminar, 2001
- DSRC (Defense Sciences Research Council) Workshop on Biosensors
- Dominican University (River Forest IL)
- Draper Institute (September 2016) Dan Freeman, host.

Duke University Department of Physiology. Hosts Dan Tosteson and Paul Horowicz, 1964. Duke Kunshan "Zu Chongzhi Distinguished Lecture Series", September 2020.

DuPont Experimental Station, Wilmington DE

European Mathematics Society: Plenary Lecture at AMAM 2003 (Applied Math ...)

- Participant (not speaker) at EMBO Meeting in honor of retirement of Max Perutz at Kings College, Cambridge, 1980
- Emory University, Department of Physiology
- Faraday Discussion 160: Ion Specific Hofmeister Effects, Queen's College Oxford September, 2012, Pavel Jungwirth, Organizer
- Fields Institute, University of Toronto, Workshop on Transport of Ionic Particles in Biological Environments July, 2014, Organizer: Chun Liu, Maxx Metti . A **three hour tutorial and lecture** with slides are at hyperlinks <u>Part 1a</u> or <u>Part 1b</u> and <u>Part 2a</u> or <u>Part 2b</u>.
- Fields Institute Lecture, University of Toronto, November 2014
- Fields Institute Distingished Research Fellow Lecture series: "From Atoms to Axons" October 2017, Huaxiong Huang Host
- Fields Institute, Distringuished Resarch Fellow, April, 2018. Investigations of current flow in a resistor, transport in the lens of the eye, and spectral analysis of atomic trajectories in molecular dynamics simulations.
- Fields Institute, Lead off speaker, discussion leader, August 2019, "Ion Transport and Nanofluidics Modeling, Analysis and Numerics" organizers Nir Gavish and Huaxiong Huang.
- Fine Structure Society (Rosemont IL 1995)
- Flatiron Institute of the Simons Foundation "From Maxwell to Mitochondrion" Host Mike Shelley, March 10, 2020

Florida State University: Inaugural Workshop for Computational Science, 2000

FOCUS 2000, DARPA workshop, Session Leader, Speaker, Plenary Session

Fordham University, Biology and Mathematics Seminar October 2010

- Frontiers in Mathematical Biology: NSF-NIH Meeting, 2010 CSCAMM University of Maryland, Invited Speaker
- Frontiers in Applied and Computational Mathematics FACM, 2012, NJIT
- Free University of Berlin Instituteof Chemistry and Biochemical Modeling
- Fudan University, Shanghai, Department of Mathematics, Lectures on Biomathematics, 2011, organizer Chun Liu.
- Global Seminar on Mathematical Modeling and Applications, Molecular Mean-Field Theory of Ionic Solutions, Organizers Pei Liu, Arkadz Kirshtein, 2020 [PDF]
- Gordon Conference on Smooth Muscle, 1973

- Gordon Conference on Skeletal Muscle, 1980
- Gordon Conference on Skeletal Muscle, 1983
- Gordon Conference on Skeletal Muscle, 1985
- Gordon Conference on Solid State Ionics, 1990
- Gordon Conference on Ion Channels, 1998
- Gordon Conference on Ion Channels, 2000
- Gordon Conference on Water, 2010
- Grinnell College, Department of Biology
- Harvard University, Cambridge (Biology, Host Howard Berg)
- Harvard University, Medical School, Boston, (Neurobiology, Host Stephen Kuffler)
- Hebrew University, Jerusalem: Fritz Haber Lecturer in Physical Chemistry
- Hebrew University, Jerusalem: Bat Sheva (de Rothschild) Seminar
- Hebrew University, Jerusalem: Protein Dynamics and thermodynamics, participant and session chair.
- Henderson Symposium (Basic and Applied Statistical Mechanics of Condensed Matter, Brigham Young University, 2004)
- HRL (formerly Hughes Research Lab) Malibu: Physics Colloquium, 1999.
- HRL (formerly Hughes Research Lab) Malibu: Colloquium, 2005.
- ICIAM 6th International Congress on Industrial & Applied Mathematics Zurich 2007, Co-organizer, two minisymposia: Direct and inverse problems in channels and membranes. Organizer Martin Burger, Co-organizer Heinz Engl.
- IEEE International Conference on Pattern Recognition (1994), presented by Amir Averbuch and Moshe Israeli
- IIT (Illinois Institute of Technology) Department of Biological, Chemical and Physical Science (Hosts: Grant Bunker and Larry Scott)
- IIT (Illinois Institute of Technology) Department of Electrical and Computer Engineering (Host: Marco Saraniti).
- IIT (Illinois Institute of Technology) Department of Chemical and Biological Engineering (Host: Darsh Wasan)
- IIT (Illinois Institute of Technology) Department of Mathematics (Host: Shuwang Li)
- IIT (Illinois Institute of Technology) Department of Mathematics (Host: Chun Liu)
- IIT (Illinois Institute of Techology) Department of Chemistry (Host: David Minh)
- IIT (Illinois Institute of Technology), Colloquium in Department of Chemistry, 2021.
- IIT (Illinois Institute of Technology) Chicago Area SIAM Student Conference (CASSC) 2024

IIT (Illinois Institute of Technology) Department of Electrical and Computer Engineering (Host: Thomas Wong. 2025. Video at https://drive.google.com/file/d/1fsCuzqVugUam8p836xm8qzha6JNrIbvo/view?usp

<u>=sharing</u> and slides available at [PDF]

- Imperial College, London, Department of Chemistry, Alexei Kornyshev, host, May, 2016.
- Intel Workshop on Early Disease Detection (Sept 2002)
- Institue for Biomedical Sciences, Academia Sinica, Taipei, Taiwan, December 2013, (Host: Ru-Chi Shieh)
- Institute for Mathematics and its Applications (IMA), University of Minnesota, Solvation Workshop (December 2008) see link [Talks and PDF] or address http://www.ima.umn.edu/2008-2009/W12.8-12.08/abstracts.html
- Institute for Mathematics and its Applications (IMA), Univesity of Minnesota, Mathematics of Biological Charge Transport: Molecules and Beyond Workshop (July 2015) see link <u>Talks</u> and <u>PDF</u>
- Institute for Pure and Applied Mathematics, IPAM, UCLA, Ion Channels (2002)
- Institute for Pure and Applied Mathematics, IPAM, UCLA, Inverse Problems, Lecture and Workshop (2003)
- Institute for Pure and Applied Mathematics, IPAM, Lake Arrowhead UCLA Conference: Inverse Problems Reunion (2005)
- Institute for Pure and Applied Mathematics, IPAM, Lake Arrowhead UCLA Conference: Inverse Problems Reunion (2006)
- Institute for Theoretical Physics, University of California, Santa Barbara, Conference on Electrostatic Effects in Complex Fluids and Biophysics, 1998
- International Conference on Circuit/System Theory, Sydney, Australia (1970)
- International Conference on Computational Nanoscience
- International Conference on Unsolved Problems of Noise and Fluctuations in physics, biology, and high technology, Bethesda, 2002
- International Conference On Biological Oscillations and 9th EGSCO (European Study Group on Cardiovascular Oscillations) Joint Meeting, April 2016.
- International Filter Symposium, Santa Monica, CA, 1972

International Workshop on Computational Electronics: IWCE-5, 1997, Notre Dame.

- International Workshop on Computational Electronics, IWCE-6, 1998, Osaka
- International Workshop on Computational Electronics, IWCE-8, 2001, UIUC
- International Workshop on Computational Electronics, IWCE-9, 2003, Roma, Italia
- International Workshop on Computational Electronics, IWCE-11, 2006, Vienna, Austria
- International Workshop on Computational Nanotechnology, IWCN-20, 2019, Evanston IL

see http://www.iue.tuwien.ac.at/iwcn2019/wp-content/uploads/2019/06/IWCN-2019-Book-of-Abstracts.pdf

	IUPUI (Indiana University Purdue University Indianapolis), Department of Mathematical Sciences, May 2016, Giovanna Guidoboni and Julia Arciero, hosts.
	Jacobs University Bremen Germany
	Johns Hopkins (Department of Biology)
	Johns Hopkins (Department of Biomedical Engineering)
	Kansas University (Colloquia in Mathematics, 2005, 2007, 2015, Weishi Liu host)
	Kansas University, Mathematics Department, April, 2019, Weishi Liu, host. [PPTX]
	Kansas University, Mathematics Department, December, 2019, Weishi Liu, host. [PDF]
	Kavli Institute of Theoretical Physics, University of California Santa Barbara:
	Evolutionary Perspectives on Mechanisms of Cellular Organization 2010
	Laboratory of Molecular Biology, MRC, Cambridge England, Host Richard Henderson
	Lancaster University (Department of Physics, 2011, 2015)
	Lancaster University (Department of Biology, 2015)
	Lancaster University ('Kickoff Speaker, 2015, EPSRC (Engineering and Physical Sciences Research Council) Grant, PVE McClintock, Principal Investigator)
	Lancaster University: Keynote Speaker Conference on Fluctuations and Coherence, 2011. (organizer PVE McClintock) see <u>www.physics.lancs.ac.uk/FluctuationsConference2011/talks.htm</u>
	Lawrence Berkeley National Laboratory LBL Lecture to Molecular Foundry, June, 2013
	Liblice Conference (5 th) on Statistical Mechanics of Liquids, 1998
	Los Alamos National Laboratory (Center for Nonlinear Studies)
	Department of Cellular and Molecular Physiology, Stritch School of Medicine, Maywood IL, February 2017
	Loyola University, Department of Physiology, Maywood IL, ~2008, Don Bers, host.
	Loyola University (Chicago), Keynote Speaker, Science Week, October, 2013
	Loyola University (Chicago), Department of Chemistry and Biochemistry, Sam Cuikerman Host, January, 1997
	Marquette University, Milwaukee: Department of Biology
	Marquette University, Milwaukee: Department of Mathematics
	Marine Biological Laboratory, Woods Hole, Monday Night Seminar, 1968, host Mike Bennett "Three Dimensional Electric Field Problems in Physiology"
	MathBio22 Weierstrass Institute, Berlin, Organizer Barbara Wagner, September 2022
	Mathematical Biosciences Institute, Ohio State University, Speaker at "Modeling and computation of biomolecular structure and dynamics" April, 2011 <u>MBI 2011</u> , i.e.,
<u>htt</u> j	p://beta.mbi.ohio-state.edu/video/player/?id=549&title=Ions+in+Channels%3A+important+biology+ready+for+mathematical+analysis
	Mathematical Biosciences Institute, Ohio State University, Inaugural Speaker Visiting Scholars Program, September 2015

- Mathematical Biosciences Institute, Ohio State University, Speaker in workshop: Geometric and Topological Modeling of Biomolecules October 2015
- Mathematical Biosciences Institute, Ohio State University, "Wind Up Talk" for Workshop on "Multiple Faces of Biomolecular Electrostatics" October 2015
- Mathematical Biosciences Institute, Ohio State University, talk in Workshop "Modeling and Computation of Transmembrane Transport" November, 2015.
- Max Planck Institute (Goettingen: Erwin Neher. Am Fessberg series) 2007
- Max Planck Institute (Goettingen. MPI for Dynamics and Self-organization. Computational Neuroscience 2009)
- Max Planck Institute (Heidelberg: Ken Holmes)
- Max Planck Institute (Heidelberg: Bert Sakmann)
- Mayo Clinic, Pharmacology, John Blinks.
- Mayo Clinic, Physiology, Stuart Taylor.
- McMaster University: Department of Physics (Hamilton, Ontario)
- McGill University: Department of Biomedical Engineering, Jay Nadeau (March 2010)
- Medical College of Virginia
- Medical College of Wisconsin
- Medical Research Council, Mill Hill, England
- Merck, Sharpe, and Dhome
- Mesilla Conference on Physical Chemistry (2001), Las Cruces New Mexico
- Michigan State University (2011) Quantitative Biology and Mathematics, host Guowei Wei and Michael Garavito
- Miller Institute Lecture, October 2012
- Miller Institute Interdisciplinary Symposium, June 2013 (participant, not speaker)
- MIT Department of Applied Mathematics April 2006 Martin Bazant, host
- MIT Bio-Informatics Seminar (with the Whitehead Institute)
- MIT McGovern Institute for Brain Research September 2013 (Mark Thomas Harnett, host)
- MIT, Center for Enhanced Nanofluidic Transport (CENT), Webinar, Michael Strano, Host, October 2019 [TALK]
- Monash University, Australia: Electrical Engineering
- Monash University, Australia: Department of Physiology
- NASA Ames: Biomolecular Systems
- National Science Foundation (first MOBS Seminar: Modeling of Biological Systems)
- NATO Advanced Research Workshop. Ionic Soft Matter, Lviv, Ukraine

- National Taiwan University Taipei, Taida Institute for Mathematical Sciences. "Energetic Variational Approaches to Elastic Complex Fluids and Molecular Biology" January, 2010
- National Taiwan University Taipei "Workshop on Mathematical Models of Electrolytes Applied to Molecular Biology", January, 2012, December, 2013, Tai-Chia Lin 林太家 Organizer)
- National Taiwan University Taipei, December 2016, two lectures, Department of Mathematics & National Center Theoretical Science, Tai-Chia Lin 林太家, host
- National Taiwan University Taipei, December 2019, "Workshop on Mathematical Models of Electrolytes Applied to Molecular Biology", Lead-off Speaker, Session Chair, Department of Mathematics & National Center Theoretical Science, Tai-Chia Lin 林太家, host
- National Tsin Hua University, Institute of Computational and Modeling Science. MOST Chair Professor (Minstry of Science and Technology), Hsinchu Taiwan, Host: Jinn-Liang Liu, 2018.
- National Tsin Hua University: ICMS Workshop on Mathematics in Biological and Chemical Systems Host: Jinn-Liang Liu, 2020. Lead off Speaker.
- New Mexico Institute of Technology and Mining (Socorro)

Dept of Mathematics (host, Bxiang Wang), March 2011

- New Mexico Institute of Technology and Mining (Socorro)
 - Dept of Mathematics (host, Mingji Zhang), March 2016
- New York University Medical School (Physiology)
- New York University (Biology: Tamar Schlick's Group)
- NIH NINCDS
- NIH Arthritis Institute
- NIH GMS

NISTI-NIGMS Digital Biology Speaker (2003)

NIST Physical and Chemical Properties Division

NJIT (New Jersey Institute of Technology, Newark) Department of Mathematics, 2011

Northern Illinois University (Department of Mathematics, 2013, 2006

- Northwestern University: Chicago, Physiology
- Northwestern University: Evanston, Applied Mathematics
- Northwestern University Evanston Chemistry Colloquium
- Northwesern University Evanston Chemistry
 - George Schatz & Mark Ratner Laboratory (2010)
- Northwestern Univ Evanston, Mathematics "Conversations in Mathematics & Biology"

Northwestern University: Evanston, Neurosciences
Northwestern University Evanston, Physics and Engineering Sciences
Northwestern University, Evanston: Monica Olvera de la Cruz, host(ess): Materials Research Science and Engineering Center (MRSEC) July 2012
Notre Dame, Department of Electrical Engineering
Notre Dame, Department of Chemistry and Biochemistry
Novartis Foundation Symposium: Gramicidin and Related Peptides, 1998
Novartis Foundation Meeting: Physical Models of Ion Permeation, 2000
Oak Ridge National Laboratory and University of Tennessee, Knoxville. Summer School on Biophysics: Computational and Theoretical Challenges (2010).
Oberwolfach Workshop, The Mathematics of Mechanobiology and Cell Signaling, February 2018, organizer, Angela Stevens
Oregon Health Sciences University (Vollum Institute)
Oxford University (England) Department of Physiology (several times)
Oxford University (England) Department of Biochemistry (2011)
Oxford University Biochemical Society (England)
Oxford University Seminar in Physical and Theoretical Chemistry (England)
Oxford University Seminar in Chemistry (Hagan Bayley)
Oxford University OCIAM Mathematics in Medicine 5 th Study Group (October, 2005)
Oxford University OCIAM Mathematics in Medicine: Ion Channels (March, 2006)
Oxford University OCIAM Mathematical modelling of ion channels (September, 2011)
Oxford University OCIAM Lecture in Applied Mathematics, April, 2016, Jon Chapman, host.
PacifiChem (meeting of American Chemical Society, 2000)
PacifiChem (meeting of American Chemical Society, 2005)
Penn(sylvania) State University, Deptartment of Mathematics, IMA-PIP Workshop on Numerical Simulation of Complex Fluids and MHD
Chun Liu Laboratory Workshop, August 2012
Penn(sylvania) State University, Center for Neural Engineering; Physics, Engineering Science, and Mechanics. Steve Schiff organizer, July 2013)
Penn(sylvania) State University, Deptartment of Mathematics, Special Lecture, July 2014, organizer Tao Huang
Penn(sylvania) State University, Deptartment of Mathematics, CAM Lecture February 2015, organizers Chun Liu and Jinachao Xu

- Penn(sylvania) State University, Department of Mathematics, leadoff lecture in "Workshop On Transport And Dynamics In Complex Fluids And Biology", organizers Arkadz Kirshtein and Chun Liu. Abstract available at <u>https://sites.psu.edu/tdcfb16/abstracts/</u> Slides available with DOI: 10.13140/RG.2.1.2584.8569 at <u>https://www.researchgate.net/publication/306119626_Electricity_is_Different_August_2016_Penn_State_Mathematics_and_at_https://sites.psu.edu/tdcfb16/files/2016/08/PSU-TDCFB16-Eisenberg-1gmxsqg.pdf
 </u>
- Polytechnic University (Brooklyn, NYC) Department of Chemical Engineering (2010)
- Pierre & Marie Curie University (UPMC) Paris Department of Physical Chemistry (Pierre Turq, Jean-Pierre. Hansen) 2009
- Politecnico di Milano, Eight hours in lecture course, "A Mathematical Shuttle From Molecules To Neurons" organizer Riccardo Sacco and Giovanna Guidoboni
- Princeton University Program in Applied Mathematics (October 2009)
- Purdue University: Department of Biology (1967)
- Purdue University: Department of Electrical Engineering: Solid State Physics, Organizer: Mark Lundstrom
- Purdue University Physical Chemistry Seminar Series, 2008, Organizer Dor Ben-Amotz available at <u>http://www.nanohub.org/resources/4726/</u> [PDF]
- Purdue University Computational and Applied Mathematics Seminar, 2014, Host Jie Shen
- Purdue University Physical Chemistry Seminar Series, 2014, Organizer Dor Ben-Amotz
- Purdue University, Electrical and Computer Engineering, Graduate Seminar, 2014, Organizer: Gerhard Klimeck.
- Radon Institute (RICAM) EMS (European Mathematics Society) Linz, Austria (2006) Minicourse (3 days) Lectures on Ion Channels
- Radon Institute (RICAM), Linz, Austria, Special Semester on Quantitative Biology (2007) Ionic Channels
- **Rensselaer Polytechnic Institute Department of Mathematics**
- Rice University Colloquium in Computational and Applied Mathematics (March 2010)
- Rowland Institute (Cambridge MA)
- Rush Medical College (Physiology, 1975)
- Rush Medical College (Physiology and Biophysics, first Webinar, June 19, 2020) "Conformation, Currents, and Signals in the Action Potential"
- Rush Medical College, Journal Club [PPTX]
- Rush Medical College (Pharmacology, 2008)
- Salk Institute (Host: Steven Kuffler)
- Salk Institute (Host: C. Stevens)
- Sandia National Laboratory (Laura Frink/Grant Heffelfinger)

- Sandia National Laboratory Biophysical Discussion (Susan Rempe)
- Sapienza University of Rome, Dipartimento di Ingegneria Meccanica e Aerospaziale, Alberto Giacomello, host (November 2019), lecture and week of collaboration.
- Satellite Meeting (Debrecen) of International Physiological Congress, 1980
- Schlumberger Cambridge Research
- Scripps Research Institute La Jolla
- Shanghai Jiao Tong University (SJTU) "Recent Progresses on Coulomb Many Body Systems" (Xiangjun Xing and Wei Cai, 2012)
- Shanghai Jiao Tong University (SJTU) Seminar 2016
- Shanghai Jiao Tong University (SJTU) Short Course (8 lectures), 2016 SJTU Soft Matter Summer School 2016 see <u>Summer School</u>, Lectures <u>Day 1</u>, <u>Day 2</u>, <u>Day 3</u>
- Simon Fraser University (Vancouver) Department of Physics
- SISSA and ICTP Trieste, Italy Theoretical Biophysics and Structural Biology
- SISSA and ICTP Trieste, Italy. Challenge: correcting Einstein's mistake
- Society of Industrial and Applied Mathematics (SIAM)
- Invited lecture, Conference on Applied Probability in Science & Engineering Society of Industrial and Applied Mathematics
- Invited lecture, symposium on "Ionic Channels in Biological Membranes". Annual meeting, 1993
- Invited lecture, Symposium on Ionic Channels, 2001, Annual meeting
- Invited lecture, Symposium Electrodiffusion: Modeling, Analysis, Simulation, and Applications, 2005, Annual Meeting. New Orleans
- Invited lecture, Co-organizer Symposium Multiscale Modeling of Electrochemical Systems, 2006, Annual Meeting, Boston.
- Invited lecture, Symposium, Multiscale Nonlinear Problems in Biology, 2007, Conference on Dynamical Systems
- Lead-off Lecture, Workshop on Dimensional Reduction
- Invited Lecture, 2017, Symposium on Interactions in Coulomb Systems (Snowbird)
- Lead-off lecture, 2018, "Modeling and Computation in Molecular Biosciences and Biophysics" at the SIAM Conference on Life Science, organizers Dexuan Xu and Shan Zhao.
- Lead-off lecture, 2022, Eastern Spring Regional meeting "Mathematical Modeling in Biology and Medicine" Orgtanizers, Arkadz Kirshtein, Navid Mohammad Mirzae, Title: "Flushing Waste in the Central Nervous System"
- Society of Mathematical Biology (2013) Minisymposium "Modeling Ionic Flows in Biological Cells" Organizers, Carl Gardner and Steven Baer

- Society of Mathematical Biology (2021) Minisymposium "Workshop on Modeling and Analysis in Molecular Biology and Electrophysiology" Organizers Peter Bates, Weishi Liu, Mingji Zhang
- SPIE Annual Meeting (1994) *in* Symposium "Mathematical Imaging: Wavelet Applications" (presented by Amir Averbuch and Moshe Israeli)
- Stanford University (Department of Electrical Engineering)
- State University of New York (Albany)
- State University of New York (Stony Brook)
- Suzhou University (School of Mathematical Sciences) Mathematical Center for Interdisciplinary Research. "Modeling and analysis in molecular biology and electrophysiology" June 1-5, 2014. Organizers Chun Liu, Benzhuo Lu, Xingye Yue
- Suzhou University (School of Mathematical Sciences) Mathematical Center for Interdisciplinary Research. "Modeling and analysis in molecular biology and electrophysiology" June, 2016. Lead-off speaker. Organizers Chun Liu, Xingye Yue, Shenggao Xu
- Suzhou University (School of Mathematical Sciences) Mathematical Center for Interdisciplinary Research. "Modeling and analysis in molecular biology and electrophysiology" June, 2018. Lead-off speaker. Organizers: Minxin Chen, Chun Liu, Xingye Yue, Ling Yang, Shenggao Xu
- Swiss Federal Institute of Technology, Institute of Bioengineering EPFL Lausanne host Aleksandra Radenovic "Distinguished Lecture in Bioengineering" November, 2016,
- Taft School Centennial Symposium
- Technical University of Vienna (Mathematics)
- Technion, Department of Mathematics, February 2018, host Nir Gavish
- Telluride Science Research Center Symposium on Biological Ion Channels (2003)
- Telluride Science Research Center Symposium on Biophysical and Biochemical Properties of Ion Channels in Epithelia (2004)
- Telluride Science Research Center Symposium Biological Ion channels: Structure and Function (2005)
- Temple University, Philadelphia, Three Lecture Series including First Dean's Distinguished Lecture, Michael Klein Dean (April 2015)
- Texas Instrument Corporation (1966)
- Thomas Jefferson University: Daniel Baugh Institute
- TIDS12 Transport in Disordered Systems 12th Annual Meeting, Marburg, 2007
- TMR Meeting on Kinetics, Goteborg Sweden, 2000, Plenary Speaker
- Tsinghua Meeting Sanya Facility: "Mathematics Biophysics and Molecular Biosciences Workshop" December, 2016, organizers Guowei Wei and Bezhuo Lu.
- Tufts University Applied Mathematics Seminar, March, 2021 Recording at this link

Tulane University (1967)

Tunghai University, Ren Shiang Chen, host (December, 2016)

UCLA: Biology Department (1968)

UCLA: Jerry Lewis Muscle Disease Center

UCLA: Physiology Department

UCLA: Molecular Biology Institute

UCLA: Department of Anesthesiology

UCLA School of Engineering, Mechanics and Structures

UCLA Department of Bioengineering

Universidad del Valparaiso (Chile) Symposium in Honor to [sic] the 70th Birthday of Francisco Bezanilla, Centro Interdisciplinario de Neurosciencia de Valparaiso, September 25, 2014.

University of Calgary, Seminar, Centre for Molecular Simulation, Sergei Noskov, host. May 2016.

University College (London): Biophysics

University College (London): Physiology

University of Alabama, Department of Anesthesiolgy, Host Jiangquo Gu, 2024

University of Buffalo (SUNY) Department of Physiology and Biophysics

University of Buffalo (SUNY) Department of Electrical Engineering

University of California (Berkeley) Chemical Engineering, Chakraborty Group

University of California (Berkeley) Mathematics, Craig Evans Student Symposium, Partial Differential Equations (October 2012)

- University of California (Berkeley) Colloquium in Physics Department (Marvin Cohen)
- University of California (Berkeley) Seminar on Physical Chemistry (David Chandler) October 2012
- University of California (Davis) Department of Physiology (1969, Gene Renkin, host)
- University of California (Davis) Institute of Theoretical Dynamics, Joel Keizer, host (1998)

University of California (Davis) Department of Pharmacology, Don Bers host (2012)

University of California (Irvine) Miledi Group

University of California (Irvine) Colloquium in Physics

University of California (San Diego) McCammon Group

University of California (San Diego) Department of Mathematics (Bo Li, Host).

University of California (San Francisco, Biochemistry, ~1970)

University of California (San Francisco, Biochemistry, 2007)

University of Chicago: Applied Mathematics. Organizer Victor Barcilon

University of Chicago 'Computations in Science Seminars',

Organizers, L Kadanoff & Wendy Zhang

University of Chicago: Department of Biophysics. Organizer, George Eisenman University of Chicago: Department of Physics (Franck Institute), Leo Kadanoff University of Chicago: Department of Physiology Organizer, Harry Fozzard University of Chicago: Department of Chemistry Organizer, Graham Fleming University of Chicago Institute of Molecular Engineering, Matt Tirrell, Oct 2013 University of Colorado (Boulder): Applied Mathematics University of Colorado (Denver): Physiology University of Florida Department of Chemistry, Charles Martin's Nanogroup University of Gröningen, Netherlands (Department of Chemistry) University of Hawaii (von Bekesy Laboratory) University of Heidelberg Bioquant-Vorlesung Seminar, 2007 University of Heidelberg: Bioms-Bioquant Lecture in the Workshop on Transport, Signaling and Structure Formation in Cellular Systems: Mathematics Meets Experiments University of Illinois (Chicago): Department of Chemistry University of Illinois (Chicago): Department of Mathematics, 2016 University of Illinois (Chicago): Department of Physics University of Illinois (Chicago): Department of Bioengineering, 2007, 2009, 2019 University of Illinois (Chicago): Department of Biomedical Engineering, 2021, 2024 University of Illinois Medical School (Chicago): Department of Biochemistry University of Illinois Medical School (Chicago): Department of Ophthalmology University of Illinois Medical School (Chicago): Department of Physiology University of Illinois (Champaign-Urbana): Physiology University of Illinois (Champaign-Urbana): Biological Physics University of Illinois (Champaign-Urbana): Physics, Beckman Institute University of Illinois (Champaign-Urbana): Theoretical and Computational Biophysics Group, Klaus Schulten University of Illinois (Champaign-Urbana): Computational Electronics University of Iowa, Physiology and Biophysics (Hosts: Kevin Campbell and Chris Ahern, April 2014) University of Linz, Oesterreich (Austria). Johan Radon Institute of Applied Mathematics. University of Maryland (Baltimore): Physiology University of Maryland (Baltimore): Biochemistry University of Maryland (College Park): Electrical Engineering, Electrophysics Series University of Maryland (College Park): Institute for Physical Science and Technology

University of Maryland (College Park): CSCAMM
University of Massachusetts (Amherst) Department of Chemistry
University of Miami: Biophysics and Physiology
University of Michigan: Michigan Interdisciplinary Mathematics Meeting.
University of Michigan: Seminar in Applied and Interdisciplinary Mathematics
University of Münster, Westfälischen Wilhelms-Universität Germany,
Department of Applied Mathematics
University of New South Wales, Australia
University of Notre Dame (Department of Electrical Engineering)
University of North Carolina (Physiology) Host Gerry Oxford and Barry Palotta
University of North Caroloina (Chapel Hill) Dept of Biochemistry Host Gerhard Meissner.
University of North Carolina (Charlotte) Joint Seminar Mathematics and Bioinformatics
University of Oklahoma, Department of Physiology 1968
University of Pannonia (Veszprém Hungary): Department of Physical Chemistry Dezső Boda, 2009
University of Pennsylvania, Department of Physiology, Department of Chemistry, Department of Biology
University of Rochester (Physiology)
University of Rochester (Neurology)
University of Rochester (Neuromuscular Center)
University of South Carolina Dept of Mathematics and IMI (Interdisciplinary Mathematics
Institute), giving a lecture in the Applied and Computational Mathematics Seminar Series Nanoinstitute, February 2015, Qi Qang host.
Series Nanoinstitute, February 2015, Qi Qang host.
Series Nanoinstitute, February 2015, Qi Qang host. University of Sydney, Australia
Series Nanoinstitute, February 2015, Qi Qang host. University of Sydney, Australia University of Texas (Austin), Physics and Mathematics Seminar (Irene Gamba, host)
Series Nanoinstitute, February 2015, Qi Qang host. University of Sydney, Australia University of Texas (Austin), Physics and Mathematics Seminar (Irene Gamba, host) University of Texas (Austin), Colloquium in Physics (Harry Swinney, host) University of Texas (Austin) ICES/Computational Life Sciences and Biology Seminar:
Series Nanoinstitute, February 2015, Qi Qang host. University of Sydney, Australia University of Texas (Austin), Physics and Mathematics Seminar (Irene Gamba, host) University of Texas (Austin), Colloquium in Physics (Harry Swinney, host) University of Texas (Austin), ICES/Computational Life Sciences and Biology Seminar: "Ionic Selectivity: A Physical Analysis of Vital Chemistry" (Ron Elber, host)
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Series Nanoinstitute, February 2015, Qi Qang host. University of Sydney, Australia University of Texas (Austin), Physics and Mathematics Seminar (Irene Gamba, host) University of Texas (Austin), Colloquium in Physics (Harry Swinney, host) University of Texas (Austin) ICES/Computational Life Sciences and Biology Seminar: "Ionic Selectivity: A Physical Analysis of Vital Chemistry" (Ron Elber, host) University of Texas (Austin) Center for Nonlinear Dynamics (Harry Swinney, host) University of Texas (Austin) Center for Nonlinear Dynamics (Mark Raizen, host) University of Texas (Galveston) University of Texas (Southwestern: Dallas) University of Tokyo (Neuroscience)

University of Vermont

University of Vienna, Department of Mathematics
University of Vienna, Lecture "Mathematics and Molecular Biology", Wolfgang Pauli Institute; Christian Schmeiser, host (November 2016)
University of Washington
University of Wisconsin Madison (Electrical Engineering)
University of Wisconsin Madison (Contemporary Biochemistry)
University of Wisconsin Madison (Biochemistry, 2011, Julie Mitchell, host)
University of Wisconsin Milwaukee, 2010
University of Wisconsin, Milwaukee, 2024, Dept of Mathematics
USA-Japan Seminar Excitation-Contraction Coupling, Tokyo 1971
Vanderbilt University Colloquium on Physics
Washington University, St. Louis, Physiology
Washington University, St. Louis, Center for Computational Chemistry
Weierstrass Institute, Material Modeling Seminar, Host Barbara Wagner, Sept. 2022
Weierstrass Institute: Ion Channels, (three talks), Host: Manuel Landstorfer, Oct. 2024
Weizmann Institute, Rehovot: Bat Sheva (de Rothschild) Seminar.
Weizmann Institute, Rehovot: Chemistry Department
Western Nerve Net (San Diego)
Westfaelisch Wilhelms University Muenster Applied Mathematics
Westfaelische Wilhelms University Meunster Multiscale Simulation for Ion Channels (2009)
Workshop on Wavelets: 16 th International Conference of the IEEE Engineering in Biology and Medicine Society.
Workshop on Modeling and Analysis in Molecular Biology and Electrophysiology (2021) Duke Kunshan University. [PDF]
World Congress on Medical Physics and Biomedical Engineering, 1994.
Yale University (Department of Physiology)
Yale University (Section of Neuroscience)
Yale University (Department of Mathematics and Computational Science)
Xiamen University, Institute of Electromagnetics and Acoutstics, Lecture Series, 2013, Qing Liu, organizer.
Yangtze Conference on Fluids and Interfaces
Zhejiang University, Hangzhou. Symposium Department of Mathematics, 2011, organizer, Fang-Hua Li of the Courant Institute, NYU

Symposia Organized

- Chairman, Mini-symposium on **The Lens as a Syncytium**, Biophysical Society Meeting, 1980.
- Co-Chairman, with Brian Salzberg, **Symposium on Fine Processing in the Fine Processes** of the Nervous System, Biophysical Society Meeting, 1984.
- Chairman of Symposium and Luncheon Calcium Signals in Muscle, Biophysical Society Meeting, 1985
- Chairman of Symposium. Nerve Impulse: From Conduction to Channels by way of Conductance at the 100th Anniversary Meeting of the American Physiological Society, 1987.
- Chairman of Symposium. Skeletal **Muscle Physiology: an Update** at the 100th Anniversary Meeting of the American Physiological Society, 1987.
- Chairman of Minisymposium. **Moving through (Biological) Channels**, Society of Industrial and Applied Mathematics Conference on Applied Probability in Science and Engineering, New Orleans, 1990.
- Chairman of Minisymposium. **Ionic Movement through Biological Channels.** Society of Industrial and Applied Mathematics, Annual Meeting. Chicago, 1990.
- Organizer of Workshop: From Structure to Permeation in Open Ionic Channels. Biophysical Society Annual Meeting, Washington D.C., 1993
- Chairman of Symposium: **Ionic Channels: Natural Nanotubes**. American Physical Society Annual Meeting, 2000.
- Chairman and Organizer of Novartis Foundation Meeting: Physical Models of Ion Permeation, 2000
- Chairman and Organizer of **Symposium at International Conference on Computational Nanoscience, 2001:** Nanostructure Simulation from thin oxides to biological ion channels.
- Co-organizer of **Yangtze Conference on Fluids and Interfaces** (Chief Organizers Kwong-Yu Chan and D Henderson). Chairman, Ion Channels Session, 2001. see J. Colloid Interface Sci. 2002 246: p.222.
- Organizer and Chairman of Nanostructures: biological ion channels to thin oxides. Nanotech 2003, San Francisco.
- Co-organizer and Chairman (with Dirk Gillespie) of **Physical Models of Ion/Protein Interactions**, American Physical Society (Division of Biological Physics) March, 2003. Austin, TX.
- Chairman (Organizer Maria Kurnikova) **Physics of Ion Interactions with Proteins**, March, 2004, American Physical Society, Montreal Quebec Canada.

- Member, Organizing Committee, NATO Advanced Research Workshop. **Ionic Soft Matter** Lviv Ukraine, 2004.
- Helper to Andrij Trokhymchuk and David Busath, **Festschrift for Doug Henderson**, Brigham Young University, 2004.
- Co-organizer, with Heinz Engl, **RICAM Seminar on Ion Channels**, Johan Radon Institute of Applied Mathematics, University of Linz (Austria), 2004.
- Organizer and Chair, **Multiscale Analysis in Biology: Computation,** American Physical Society, March, 2005, Los Angeles.
- Organizer and Chair: MultiScale Analysis of Ions in Solutions, Proteins, and Channels: Analysis, American Physical Society, March, 2005, Los Angeles.
- Problem Presenter: Mathematics in Medicine Study Group, Mathematics Institute, Oxford University, Sept. 2005, March 2006
- Organizer and Chair: **Physical Models of Ion Channels**, American Physical Society, March 2006, Baltimore.
- Helper to Chris Breward: Oxford University OCIAM Mathematics in Medicine: Ion Channels, March, 2006.
- Member, Organizing Committee for <u>Special Semester on Quantitative Biology</u> analyzed by Mathematical Methods: RICAM (Radon Institute for Computational and Applied Math); (Oct 2007- Jan 2008: Johannes Kepler Univ of Linz, Austria) <u>http://www.ricam.oeaw.ac.at/ssqbm/</u>

Co-organizer (with Martin Burger, Peter Pohl, Heinz Engl) of Workshop on Ion Channels, Oct 8-12, 2007

- Co-organizer, with Martin Bazant of Symposium, **Multiscale Modeling of Electrochemical Systems** SIAM (Society of Industrial and Applied Mathematics), 2006.
- Organizer of ARO Sponsored Meeting, **Calibrating Simulations**, at Rush University Medical Center, January 2007.
- Facilitator of Annual Reciprocal Symposia between Biophysical Society and Division of Biological Physics of the American Physical Society, commencing 2007. Planned to be the first in a continuing series.
- Organizer of Symposium (Sponsored by American Physical Society Division of Biological Physics) **Modeling as a Tool in Biophysics**, at Biophysical Society Annual Meeting, 2007. Planned to be the first in a continuing series.
- Co-organizer: **Direct and inverse problems in channels and membranes,** ICIAM 6th International Congress on Industrial & Applied Mathematics Zurich 2007, Organizer Heinz Engl; co-organizer Martin Burger, pair of minisymposia.

- Lecturer Short course on **Channel Biophysics**, 10 hours, ICTP and SISSA Theoretical Biophysics and Structural Biology, Trieste, Italy, Organizer Paolo Carloni.
- Co-organizer: Symposium on **Inhomogeneous Electrolytes** Northwest and Rocky Mountain Regional Meeting American Chemical Society Co-organizer Douglas Henderson, June 2008.
- Organizer and Speaker: Workshop **Biophysics of Membrane Bound Channels** American Physical Society, Division of Biological Physics, March 2009.
- Co-organizer: National Taiwan University Energetic Variational Approaches to Elastic Complex Fluids and Molecular Biology January, 2010, Organizer Tai-Chia Lin
- Co-organizer Banff International Research Station BIRS **Ion Channels- Mathematical Modeling and Analysis** 16frg212, September 2016, Bob Eisenberg, Chun Liu and Huaxiong Huang, organizers.

Equipment and Software Designed

Wide band amplifiers for microelectrode recording (with several collaborators, see publications 3, 9, 11, 16, 22, and 24).

Software for computing and analyzing impedance measurements with wide band amplifiers *(ibid.)*

Axopatch Amplifier for patch clamp recording, with R. Levis, J. Rae, and A. Finkel, sold by Axon Instruments, Burlingame CA, now part of Molecular Devices Sunnyvale CA.

Perfusing Pipettes, a hardware kit available from ALA Scientific, for perfusing patch pipettes.

PNP Online <u>http://www.pnponline.org/</u> Interactive software for running Poisson Nernst Planck theory, with Brice Burgess

Patent Application, PCT/NL2003/000013 Liquid Based Electronic Device (from BioMade, Groningen, Netherlands.) Patent Application was subsequently withdrawn, but it is an interesting idea, nonetheless, in my biased view, PCT/NL2003/000013 Liquid Based Electronic Device (from BioMade, Groningen, Netherlands.) [PDF]

Patent Application, <u>U.S. Patent Application 12/297,179</u>: Mathematical Design of Ion Channel Selectivity via Inverse Problems Technology (with Heinz Engl and Martin Burger, from Rush University) [PDF]

Professional Societies

American Association for Advancement of Science American Mathematical Society American Physiological Society American Physical Society, Fellow American Society of Cell Biologists Biophysical Society Institute of Electrical and Electronic Engineering, Senior Member Mathematical Association of America New York Academy of Sciences Physiological Society, England (Associate Member) Royal Society of Chemistry (UK) Society of General Physiologists Society for Industrial and Applied Mathematics Society of Neuroscience Institute for Strategic Studies (London: 1963-1992)

Research Interests

1960's-1980's:

Electrical properties of cells and tissues. The relationship between the structure of biological tissues and the pathways for current flow: measurements of linear electrical properties to determine equivalent circuits of skeletal and cardiac muscle, nerve, the lens of the eye, and epithelia.

The modeling of tissues of complex geometry and the solution—in physically meaningful form—of the differential (or difference) equations which describe such tissues. Thus, models of the three dimensional spread of current in spherical and cylindrical cells; models of the spread of current in the random network of transverse tubules in skeletal muscle; models of current flow in the clefts of cardiac muscle; models of current flow in epithelia; models of current flow in dendritic trees.

The use of mathematics (ranging from singular perturbation theory to numerical simulation) to provide insight into the physical meaning of complex theory.

1960's-1990's:

Excitation-contraction coupling in skeletal and cardiac muscle; particularly, the junction between the tubular system and the sarcoplasmic reticulum and the mechanism of calcium release from the sarcoplasmic reticulum.

The electrical properties of the sarcoplasmic reticulum and its ionic channels as seen in patch clamp measurements from skinned muscle fibers.

1980's - 2000's:

Analysis of ionic channels, experimental and theoretical: properties of single channels in epithelia, particularly "pressure activated" channels. Single channels in sarcoplasmic reticulum of skinned muscle fibers.

Design of patch clamp amplifiers, headstage, holders with "zero excess" noise.

Optimal detection of single channel events using signal detection theory.

Measurement of open channel noise.

Theoretical analysis of ion movement through channels using an hierarchy of models from molecular dynamics to continuum electrostatics.

Simulations of the molecular dynamics of channel proteins.

Stochastic analysis of flux over barriers: first passage times, concentration boundary conditions and ionic fluxes.

PNP model of the open channel. Poisson-Nernst-Planck model of open channels, in which the potential distribution through the channel is calculated not assumed. PH model of the open channel, the Poisson Hydrodynamic model including temperature changes.

Coupling of fluxes, active transport, gating, and gating currents in a permanently open channel of one conformation as predicted by the PNP model in complex geometries and the PH model.

The stochastic generalization of the PNP model.

Simulations of the molecular dynamics of the entry process models of gramicidin.

2000 - 2010:

Design and construction of ion channels as useful devices.

Thus, building design tools for understanding current flow in bulk solution, ion channels, and proteins in general.

Computation of macroscopic properties of ionic solutions and channels from higher resolution models, using Langevin-Poisson, Monte Carlo Poisson, or Molecular Dynamics Poisson methods.

Mathematical analysis of macroscopic properties of ionic solutions and channels starting from higher resolution models, using Langevin-Poisson, Monte Carlo Poisson, or Molecular Dynamics Poisson methods.

Simulations and theories of gating and conformational change.

Construction of nonequilibrium statistical mechanics starting from the properties of chaotic trajectories computed with Poisson and molecular dynamics. Statistical mechanics as stochastic processes.

Crowded Charge model of protein function, specifically, ion selectivity and permeation in ion channels.

Variational Principles (built on the energetic variational approach of Chun Liu) applied to ions in channels, ions and water in solutions, cells, and macroscopic tissues, and to vesicles and viruses fusing with membranes.

2010 - ... :

Role of Crowded Charge in Enzyme Function. The density of acid and base side chains is so large at active sites that it appears to be a 'universal' feature that is a biological adaptation with an unknown function. Searching for that function, I ask a speculative question: what is the role of the high charge density and crossed conditions of at active sites? Does it significantly constrain solutions of the Schroedinger equation?

Field theory of ionic solutions. It seems clear that 'everything' interacts with everything else in ionic solutions, because of the range of the electric field, and often the effects of the finite size of ions on the shape of the electric field, and on entropy directly. Selfconsistent treatments are needed for such interacting systems in other areas of science and I suspect that the failures of classical theories of electrolytes arise because those classical theories are not selfconsistent. A field theory offers the additional substantial advantages of incorporating boundary conditions in a natural way. It thus can deal with nonequilibrium conditions arising from spatially nonuniform boundary conditions (e.g., the power supplies that make digital devices or biological cells work). It seems that a selfconsistent field theory of ionic solutions is needed. It is now practicable because of advances in applied mathematics. It should be clearly understood that ionic solutions are usually highly concentrated where they are most important, in and near the electrodes of electrochemical cells, in and near enzymes and enzyme active sites, ion channels, transporters, and binding proteins.

Field theory of chemical reactions. Chemical reactions usually occur in ionic solutions. Chemical reactions have been analyzed classically as if they occur in vacuum, or in ideal ionic solutions, at infinite dilution. It seems that a selfconsistent field theory of chemical reactions is needed. It is now practicable because of advances in applied mathematics. It seems that a selfconsistent field theory of chemical reactions is needed. It is now practicable because of advances in applied mathematics.

Administrative Work

UCLA

Member of Committee for Graduate Students.

First Year Advisor for Graduate Students.

Member of numerous review committees for promotions: received commendation from Vice Chancellor Saxon for work on review committees. Member of Advisory Committee for the Jerry Lewis Muscular Dystrophy Center.

Rush Medical College

As the founding chairman of the Department of Physiology, I helped build and maintain an outstanding basic research department, from 1976 to 2015 starting almost from scratch in a Medical Center not focused on such research. A measure of the success of the faculty was that nearly every faculty member with research space had NIH grants (almost always individual R01 grants) in different, nonoverlapping subjects. In 2015 the Medical Center chose to de-emphasize research, clinical and basic. For example, it abandoned such traditional, nearly universal features of a research institution as security of employment and put into place contracts that allow termination on a few months notice, even for Associate and Full Professors.

Chairman, Department of Physiology, then Department of Molecular Biophysics and Physiology. First holder of 'The Francis and Catherine Bard Chair of Physiology'

Department has approximately 19 faculty members and approximately 9,000 sq ft of usable research space. All faculty with research space have been well supported by the NIH, thanks to their significant personal productivity. Tenured faculty include (alphabetical order): Lothar Blatter (mitochondria in cardiac muscle), Fred Cohen (viral fusion); Tom DeCoursey (H⁺ ion channels); Mike Fill (Ryanodine Receptor); Dirk Gillespie (selectivity); Eduardo Rios (Ca⁺⁺ movement) Tom Shannon (excitation contraction coupling in cardiac muscle); Jingsong Zhou (mitochondrial defects in skeletal muscle disease). Wayne Chen, Visiting Professor, with a laboratory and Postdocs at Rush. Key members in Medical School Teaching: Tom Shannon, and Dirk Gillespie, formerly Joel Michael (nearly retired); in Nursing Teaching Jingsong Zhou and formerly Sue Donaldson and Joe Zbilut (deceased). Jingsong Zhou was in charge of our seminar series for many years. Elena Dedokova was responsible for the great success of our journal club, initiated by Eduardo Rios. Assistant Professors include Artem Ayuyan, Vladimir Cherny, Elena Dedokova, Griedrius Kanaporis, Rueben Markosyan, Deri Morgan, Josefina Ramos-Franco, and John Tang.

Academic Administration.

Member of College Councils.

Chairman of Promotions and Appointments Committee.

Member, Vice Chair, then Chair of Search Committee for Microbiology Chair.

Vice Chairman of Search Committee for Dean of the Medical College.

Member, Search Committee for Dean of the Graduate College.

Member, Search Committee for Pediatrics Chair.

Member, Search Committee for Microbiology Chair

Teaching

Undergraduate Students, leading to papers.

Chris Clausen (UCLA), see Publications 16-18 Clausen1 and Abstract 13 Clausen2

Stanley Nicholson (Illinois Institute of Technology) see Publication <u>228 Nicholson</u> winner of the "Karl Menger Undergraduate Award" leading to the award of an NSF GRFP (Graduate Research Fellowship Program)

Graduate students:

J. Leung, R. Mathias, E. Engel, R. Levis, R. Milton (with R. Mathias), J. Tang, P. Gates, J. Wang, A. Hainsworth (with R. Levis), P. Dull (summer student), Dirk Gillespie, Amy Del Medico (summer student), Boaz Nadler (in significant part: Zeev Schuss, supervisor); Amit Singer (in significant part: Zeev Schuss, supervisor), Janhavi Giri (Bioengineering, University of Illinois, Chicago), Claudio Berti, David Jimenez-Morales (Jie Liang, supervisor), Allen Flavell (Xiaofan Li, supervisor)

Post-doctoral fellows:

John Howell, Peter Vaughan, Bert Mobley, Art Peskoff, Richard Mathias, Eli Engel, Richard Levis, Richard Milton (with Rick Mathias), Kim Cooper, Peter Gates, Dunapin Chen, John Tang, Danuta Rojewska, Dirk Gillespie, Trudy van der Straaten (with Umberto Ravaioli), Sheila Wigger-Aboud (with Marco Saraniti), Jim Fonseca, Claudio Berti, David Jimenez-Morales

Community Activity

- AVENUE BANK OF OAK PARK: Director, Member, then Chairman of Audit Committee, Executive Committee, and Marketing Committee (1987-1992).
- AMERICAN HEART ASSOCIATION OF METROPOLITAN CHICAGO: Member, Board of Governors, Executive Committee, and President's Cabinet (1984-1986). Member Research Council (1989-1990) and Chairman, Committee on Human Experimentation.

TAFT SCHOOL (Connecticut): Speaker at Centennial Symposium, and Seminar Group.

PRESIDENT 7320 Condo Association. 1997-2003; 2007; 2009-2022.

TOWN TALK Telluride Science Research Center (part of Pinhead Lecture Series) 2003.

ARMY RESEARCH OFFICE talk to North Carolina Ventures Program for High Schools 2005.

LOYOLA UNIVERSITY Chicago. Keynote Speaker, Science Week, 2013.

ROBERT S. EISENBERG

PUBLICATIONS

(Last update: February 17, 2025)

<u>Reprints</u> available on this <u>hyperlink</u> or by clicking [<u>PDF</u>] here or below.

NIH maintained "My Bibliography: Bob Eisenberg"

at http://goo.gl/Z7a2V7

or

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47999805/?sort=date&direction=ascending

[Laboratory of Robert S. Eisenberg]

Publication List maintained for all these years with loving care by John Tang, with thanks from Bob!

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- 2. Eisenberg, R.S. Impedance of single crab muscle fibers. Ph.D. Thesis, University of London (1965). PMCID not available [PDF]
- 3. Eisenberg, R.S. The equivalent circuit of single crab muscle fibers as determined by impedance measurement with intracellular electrodes. J. Gen. Physiol. 50: 1785-1806 (1967). <u>PMCID: PMC2225735</u> [PDF]
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- Gage, P.W. and Eisenberg, R.S. Action potentials without contraction in frog skeletal muscle fibers with disrupted transverse tubules. Science 158: 1702-1703 (1967). <u>PMID:</u> <u>6059652</u> [PDF]
- Horowicz, P., Gage, P.W. and Eisenberg, R.S. The role of the electrochemical gradient in determining potassium fluxes in frog striated muscle. J. Gen. Physiol. 51: 193s-203s (1968). <u>PMCID: PMC2201208</u> [PDF]
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- Eisenberg, B. and Eisenberg, R.S. Selective disruption of the sarcotubular muscle: A quantitative study with exogenous peroxidase as a marker. J. Cell Biol. 39: 451-467 (1968). <u>PMCID: PMC2107525</u> [PDF]
- 9. Gage, P.W. and Eisenberg, R.S. Capacitance of the surface and transverse tubular membrane of frog sartorius muscle fibers. J. Gen. Physiol. 53: 265-278 (1969). <u>PMCID:</u> <u>PMC2202908</u> [PDF]

- Eisenberg, R.S. and Gage, P.W. Ionic conductances of the surface and transverse tubular membrane of frog sartorius fibers. J. Gen. Physiol. 53: 279-297 (1969). <u>PMCID:</u> <u>PMC2202906 [PDF]</u>
- Gage, P.W. and Eisenberg, R.S. Action potentials, after potentials, and excitation-contraction coupling in frog sartorius fibers without transverse tubules. J. Gen. Physiol. 53: 298-310 (1969). <u>PMCID: PMC2202907</u> [PDF]
- 12. Eisenberg, R.S., Howell, J. and Vaughan, P. The maintenance of resting potentials in glycerol treated muscle fibers. J. Physiol. 215: 95-102 (1971). PMCID: PMC1331868 [PDF]
- Vaughan, P., Howell, J. and Eisenberg, R.S. The capacitance of skeletal muscle fibers in solutions of low ionic strength. J. Gen. Physiol. 59: 347-359 (1972). <u>PMCID:</u> <u>PMC2203175</u> [PDF]
- Eisenberg, R.S., Vaughan, P. and Howell, J. A theoretical analysis of the capacitance of muscle fibers using a distributed model of the tubular system. J. Gen. Physiol. 59: 360-373 (1972). <u>PMCID: PMC2203177</u> [PDF]
- Leung, J. and Eisenberg, R.S. The effects of the antibiotics gramicidin-A, amphotericin-B, and nystatin on the electrical properties of frog skeletal muscle. Biochem. Biophys. Acta. Amsterdam 298: 718-723 (1973). <u>PMID: 4541500</u> [PDF]
- 16. Valdiosera, R., Clausen, C. and Eisenberg, R.S. Measurement of the impedance of frog skeletal muscle fibers. Biophys. J. 14: 295-315 (1974). <u>PMCID: PMC1334509</u> [PDF]
- Valdiosera, R., Clausen, C. and Eisenberg, R.S. Circuit models of the passive electrical properties of frog skeletal muscle fibers. J. Gen. Physiol. 63: 432-459 (1974). <u>PMCID:</u> <u>PMC2203561</u> [PDF]
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- Eisenberg, R.S. and Rae, J.L. Current-voltage relationships in the crystalline lens. J. Physiol. 262: 285-300 (1976). <u>PMCID: PMC1307644</u> [PDF]
- Mathias, R.T., Eisenberg, R.S. and Valdiosera, R. Electrical properties of frog skeletal muscle fibers interpreted with a mesh model of the tubular system. Biophys. J. 17: 57-93 (1977). <u>PMCID: PMC1473227</u> [PDF]
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