# Leon Bruner and the Dawn of Biophysics at UCR

**1931 - 2003**

Leon did his graduate work at the University of Chicago with Andy Lawson, the founding chair of the Department of Physics, UCR



PHYSICAL REVIEW
LETTERS

VOLUME 3 NOVEMBER 1, 1959 NUMBER 9

## INTERNAL FRICTION IN IRON AT LOW TEMPERATURES

L. J. Bruner
Institute for the Study of Metals, University of Chicago, Chicago, Illinois
(Received September 10, 1959)

We wish to acknowledge the support and encouragement of Professor A. W. Lawson throughout the course of this work. The zone-refined iron was obtained through the courtesy of J. W. Halley, K. K. Fetters, and G. W. Rengstorff; it was purified by the latter under the project supported by the American Iron and Steel Institute.

[1]P. G. Bordoni, J. Acoust. Soc. Am. 26, 495 (1954).
[2]D. H. Niblett and J. Wilks, Phil. Mag. 2, 1427 (1957).
[3]H. L. Caswell, J. Appl. Phys. 29, 1210 (1958).
[4]D. O. Thompson and D. K. Holmes, J. Appl. Phys. 30, 525 (1959).
[5]A. Seeger, Phil. Mag. 1, 651 (1956).
[6]L. J. Bruner (to be published).

Leon worked at the IBM Watson labs in Poughkeepsie for three years, 1959 to 1962.

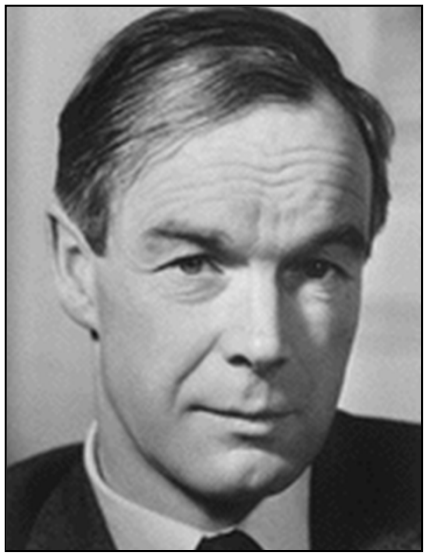
He was appointed to the UCR Physics Department in July 1962 as an Assistant Professor II just two years after Riverside became a general campus of the University of California. Here he decided to dramatically change the focus of his research to biophysics.

Leon was an albino, a person who cannot synthesize melanin, an essential pigment for, among many other things, retinal development, so he was legally blind and was also afflicted with poor hearing. But he never let this interfere with his science or his friendships. I suspect his albinism kindled his interest in biology.

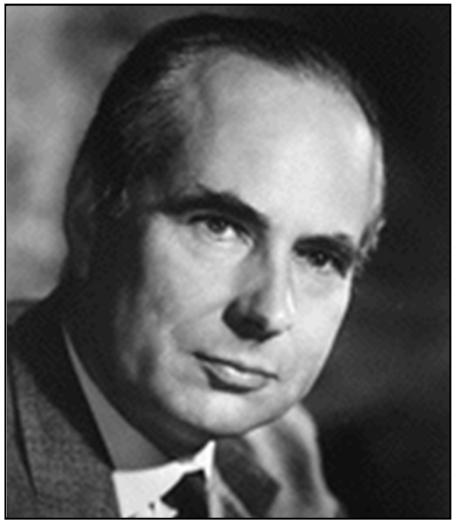
# 1963-64
# How I came to work for Leon.
# (And how he lifted the scales from my eyes.)

The Croonian Lecture: Ionic Movements and
Electrical Activity in Giant Nerve Fibres
Alan Hodgkin *Proc R Soc B 1958 148 (930), p. 1*

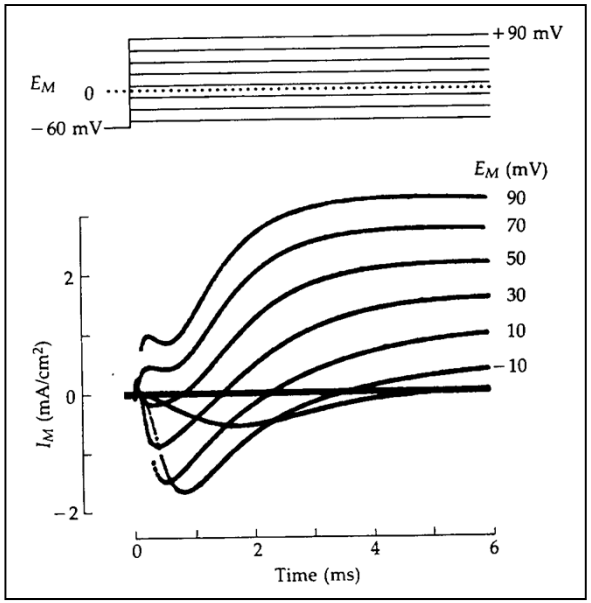
# Hodgkin and Huxley: Voltage-Clamp Currents and Model for the Action Potential 1948-1952

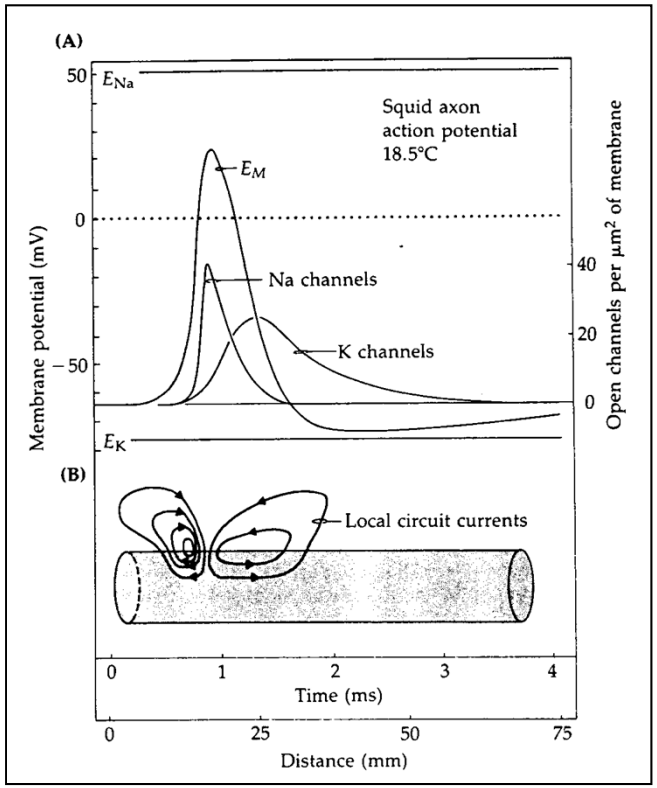


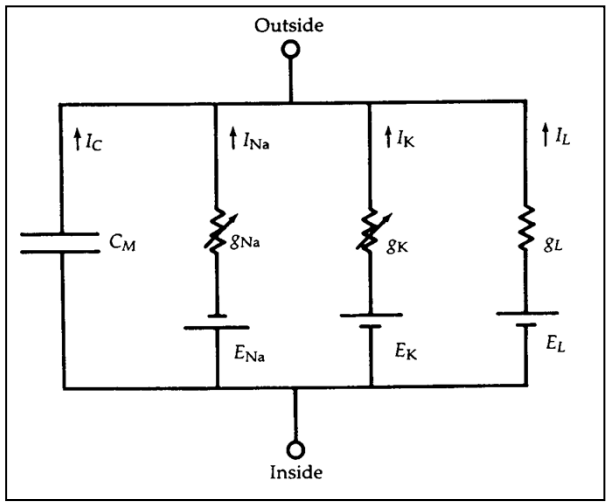
Alan Hodgkin



Andrew Huxley



# Leon's biophysical debut!

BIOPHYSICAL JOURNAL VOLUME 5 1965

Pages 867 -908

## THE ELECTRICAL CONDUCTANCE OF SEMIPERMEABLE MEMBRANES

### I. A FORMAL ANALYSIS

L. J. BRUNER

*From the Department of Physics, University of California, Riverside*

ABSTRACT A kinetic analysis of membrane conductance under conditions of stationary flow is presented. The semipermeable membrane is idealized as a homogeneous laminar phase separating ionic solutions on either side. It is assumed, without consideration of the mechanisms involved, that some ion species permeate the membrane while others do not. The flux of a given species is taken to be linearly related to the gradient of its concentration and to the electric field. The resulting flow equations, when combined with Poisson's equation, permit the formulation of the conductance problem in terms of a set of non-linear differential equations. They describe the spatial variation of the electric displacement and contain the ion current densities as parameters. Their integration, subject to appropriate boundary conditions, fixes the values of these parameters and of the corresponding transmembrane potential. The solution of the conductance problem cannot, however, be carried through in analytic form. The numerical analysis of a number of special cases will be presented in subsequent publications.

## THE ELECTRICAL CONDUCTANCE OF SEMIPERMEABLE MEMBRANES

### II. UNIPOLAR FLOW, SYMMETRIC ELECTROLYTES

L. J. BRUNER

*From the Department of Physics, University of California, Riverside*

We are indebted to Mr. J. E. Hall for valuable assistance in the preparation and processing of computer programs. Our extensive use of the facilities and services of the Western Data Processing Center, Graduate School of Business Administration, University of California at Los Angeles, is also gratefully acknowledged. Assistance with the numerical analysis was provided by the Computing Center of the University of California at Riverside as well. This work was supported by the Office of Naval Research.

*Received for publication, May 11, 1965.*

REFERENCES

JEFFREYS, H. and JEFFREYS, B. S., 1956, Methods of Mathematical Physics (third edition), Cambridge, The Cambridge University Press.

SMIRNOV, A. D., 1960, Tables of Airy Functions and Special Confluent Hyergeometric Functions (translated from the Russian by D. G. Fry), Oxford, Pergamon Press.

# These papers attracted the attention of Max Delbrück, a physicist turned biologist, who called up Leon and invited him to lunch and discussion at Caltech.

Because Leon couldn't drive, I was enlisted as chauffeur for Leon and, for Delbrück, an object of curiosity.

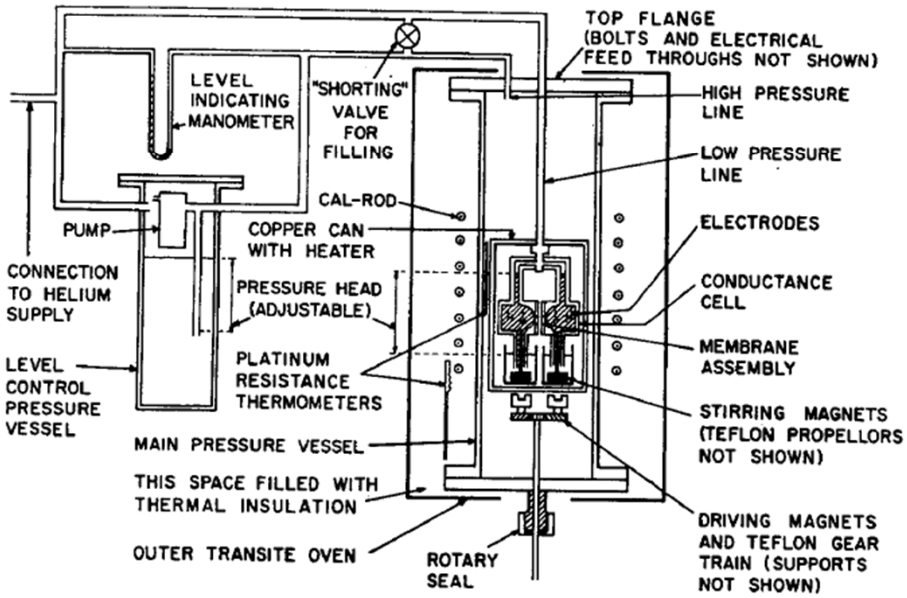
Max at the time he was awarded the Nobel Prize with Luria and Hersey in 1968.

Leon's Delbrück connection eventually lead to my post doc at Caltech.

THE JOURNAL OF CHEMICAL PHYSICS VOLUME 50, NUMBER 4 15 FEBRUARY 1969

# Electrical Conductivity of Silver Bromide Membranes and the Diffuse Double Layer*

J. E. HALL† AND L. J. BRUNER
*Department of Physics, University of California, Riverside, California*
(Received 22 May 1968)



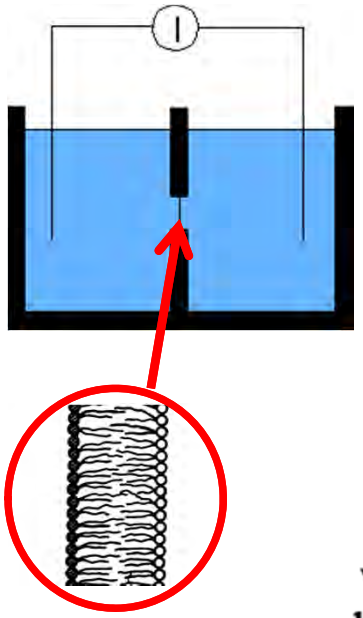

A great learning experience, but a better system was on the way….

J. Membrane Biol. 14, 143–176 (1973)

# The Nature of the Voltage-Dependent Conductance Induced by Alamethicin in Black Lipid Membranes

Moisés Eisenberg*, James E. Hall and C. A. Mead

California Institute of Technology,
Division of Biology and Department of Electrical Engineering,
Pasadena, California 91109



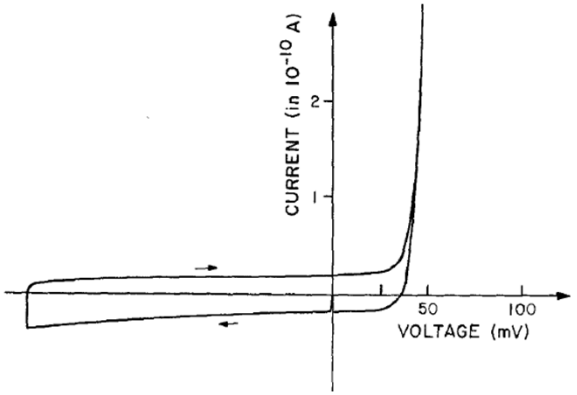
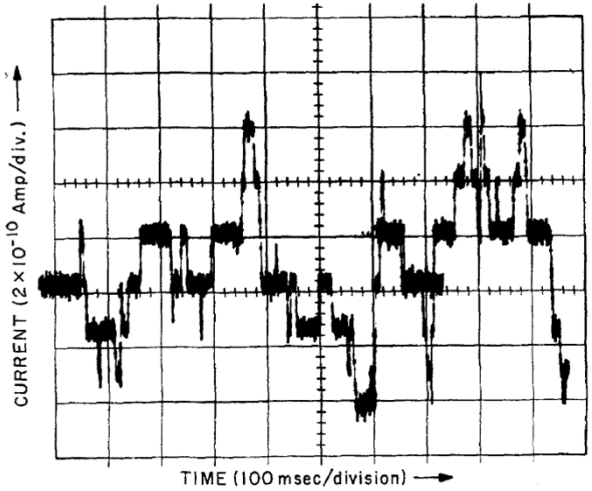



Fig. 2. Voltage-current curve of a PE-decane membrane $8.5\times10^{-3}$ cm² in area, with 0.1 M NaCl front and back and $3\times10^{-6}$ g/ml alamethicin *front only*. $dV/dt=4.5$ mV/sec. Arrows show direction of voltage sweep




We thank Professor Max Delbrück for many useful suggestions and for critical readings of the manuscript. We are grateful to Dr. Ed Lipson for suggesting the simple derivation of Eq. (17) and to Professor Leon Bruner for suggesting the glycerol experiments. We also thank Mr. H. M. Simpson for the skillful design and construction of several membrane cells.

# The paper that got me my first faculty job, Assistant Professor at Duke!

## The Permeability of Thin Lipid Membranes to Bromide and Bromine

JOHN GUTKNECHT, L. J. BRUNER, and D. C. TOSTESON

From the Department of Physiology and Pharmacology, Duke University Medical Center, Durham, North Carolina 27710. Dr. Bruner's present address is the Department of Physics, University of California, Riverside, California 92502.

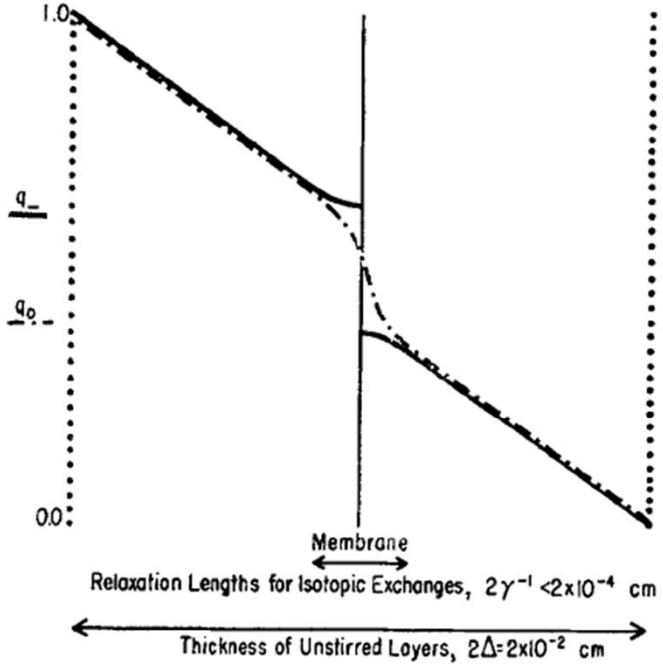



FIGURE 6. Model for Br transport across bilayers with isotopic exchange between $Br_2$ and $Br^-$. Similar to Fig. 5 except that isotopic exchange between $Br_2$ and $Br^-$ is assumed to occur *both* in the bulk bathing solutions *and* in the unstirred layers. $\gamma^{-1}$ is the mean distance which a $^{82}Br_2$ atom can diffuse before it is destroyed by an isotopic exchange reaction with $Br^-$. For details see text and Appendix.

Published April 1, 1972

BIOPHYSICAL JOURNAL VOLUME 44 1983

# PRESSURE EFFECTS ON ALAMETHICIN CONDUCTANCE IN BILAYER MEMBRANES

L. J. BRUNER
*Department of Physics, University of California, Riverside, California 92521*

J. E. HALL
*Department of Physiology and Biophysics, University of California, Irvine, California 92717*

ABSTRACT We report here the first observations of the effects of elevated hydrostatic pressure on the kinetics of bilayer membrane conductance induced by the pore-forming antibiotic, alamethicin. Bacterial phosphatidylethanolamine-squalene bilayer membranes were formed by the apposition of lipid monolayers in a vessel capable of sustaining hydrostatic pressures in the range, 0.1–100 MPa (1–1,000 atm). Principal observations were (*a*) the lifetimes of discrete conductance states were lengthened with increasing pressure, (*b*) both the onset and decay of alamethicin conductance accompanying application and removal of supra-threshold voltage pulses were slowed with increasing pressure, (*c*) the onset of alamethicin conductance at elevated pressure became distinctly sigmoidal, suggesting an electrically silent intermediate state of channel assembly, (*d*) the magnitudes of the discrete conductance levels observed did not change with pressure, and, (*e*) the voltage threshold for the onset of alamethicin conductance was not altered by pressure. Apparent activation volumes for both the formation and decay of conducting states were positive and of comparable magnitude, namely, ~100Å$^3$/event. Observation *d* indicates that channel geometry and the kinetics of ion transport through open channels were not affected by pressure in the range employed. The remaining observations indicate that, while the relative positions of free-energy minima characterizing individual conducting states at a given voltage were not modified by pressure, the heights of intervening potential maxima were increased by its application.

We had lots of fun doing this paper! Can't resist showing a few tidbits!

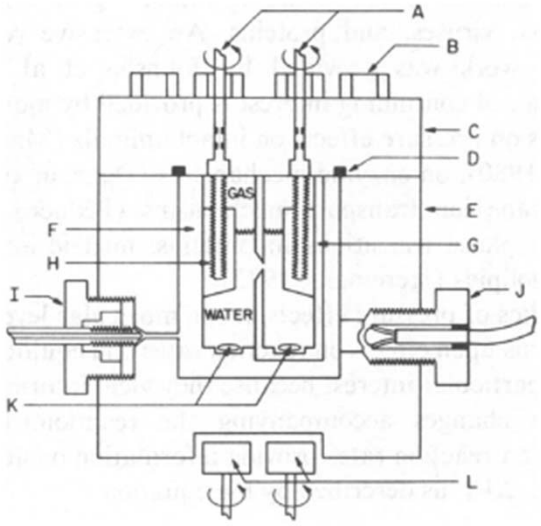
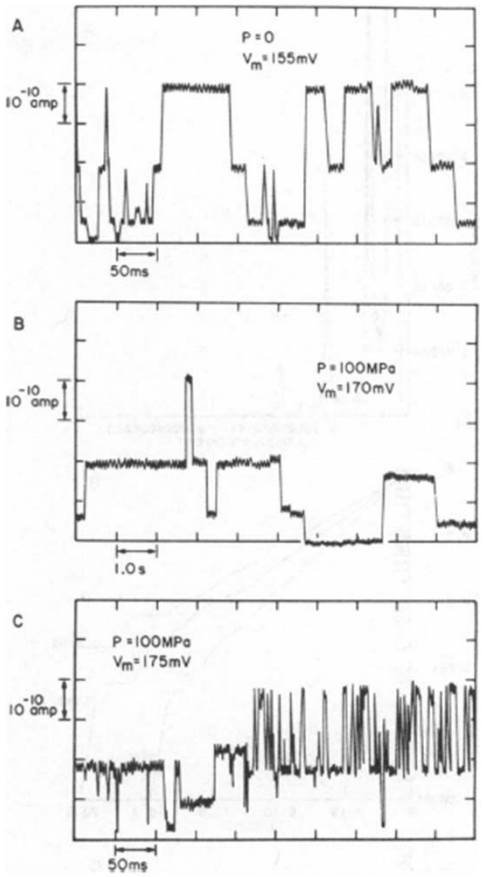
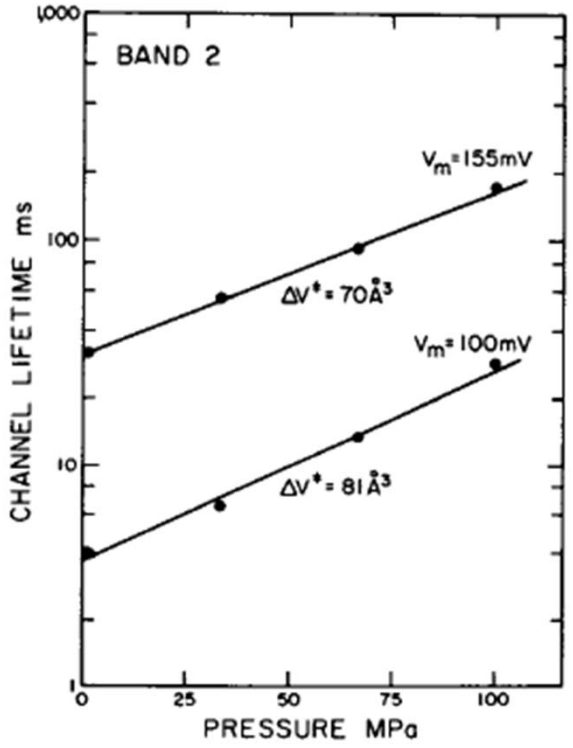



FIGURE 2 The cell for membrane measurements at elevated pressure is illustrated. The essential components are as follows. *A*, rotary feedthroughs for plunger drive; *B*, retaining bolts for pressure vessel cap; *C*, Stainless steel vessel cap; *D*, O-ring pressure seal; *E*, stainless steel pressure vessel body; *F*, Teflon block (membrane cell); *G*, Teflon cup with membrane aperture; *H*, plungers for liquid level control; *I*, high pressure gas inlet; *J*, silicon strain gauge transducer; *K*, Teflon-coated stirring bars; *L*, stirring bar drive magnets; electrodes and electrical feedthroughs are not shown.




(Just in case you don't remember 10 atm = 1 MPa!)
OK, 10 atm = 1.01325010000438 MPa to be precise.

# Leon left a lasting influence on biophysics

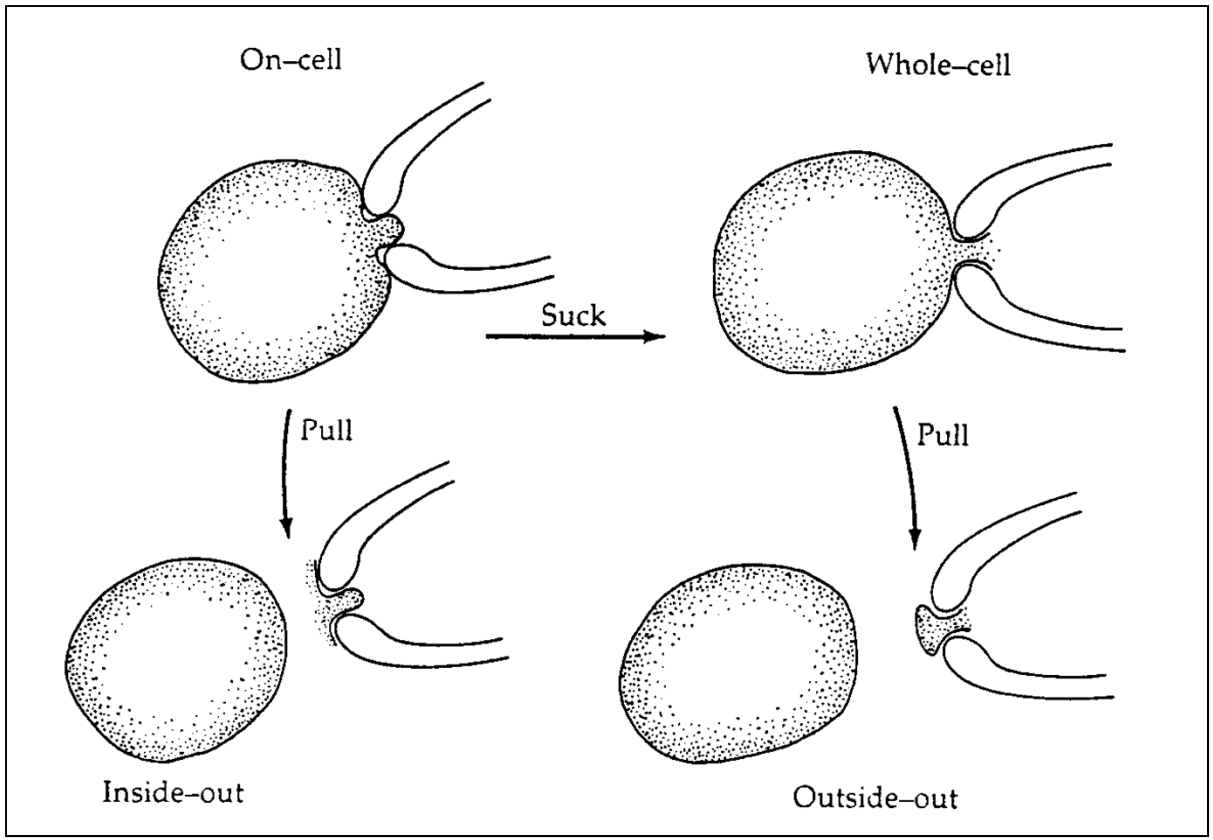
June 1, 1999 JGP vol. 113 no. 6 763-764
The Rockefeller University Press

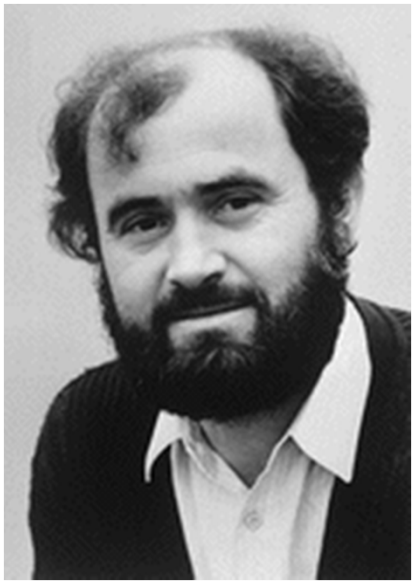
# Perspectives on Ion Permeation

Olaf Sparre Andersen, Editor

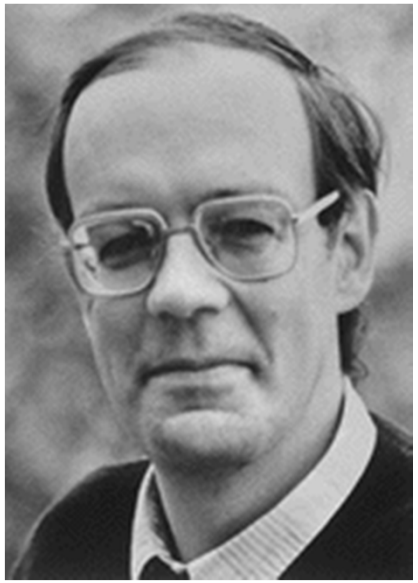
Following the lead of Julius Bernstein, who almost 100 yr ago used electrodiffusion theory to describe the resting membrane potential of muscle and nerve, ion movement across biological membranes has traditionally been described using the Nernst-Planck electrodiffusion equations. Beginning in the mid-1950's, however, descriptions of ion movement through membranes moved beyond the conventional implementation of the Nernst-Planck analysis. First, it was found that $K^+$ movement through voltage-dependent potassium channels could not be described by the Nernst-Planck electrodiffusion equations, as the flux-ratio exponent describing the $K^+$ tracer flux was much larger than the expected value of 1. This led to the notion of single-file flux (Hodgkin and Keynes. 1955. *J. Physiol. 128:61–88). Second, ion–ion interactions within the membrane were introduced explicitly into the Nernst-Planck flux equations via the Poisson equation (Bruner, L.J. 1965. Biophys. J. 5:867–886). Third, it became apparent that ion channels were not simple aqueous pores: they could concentrate ions and exhibit saturation behavior. The latter property was not readily accounted for by the Nernst-Planck equations, which led to the development of rate-theory models of ion permeation (Läuger, P. 1973. Biochim. Biophys. Acta. 311:423–441).*

# Neher and Sakmann: Patch-Clamp Recording,1976-1981

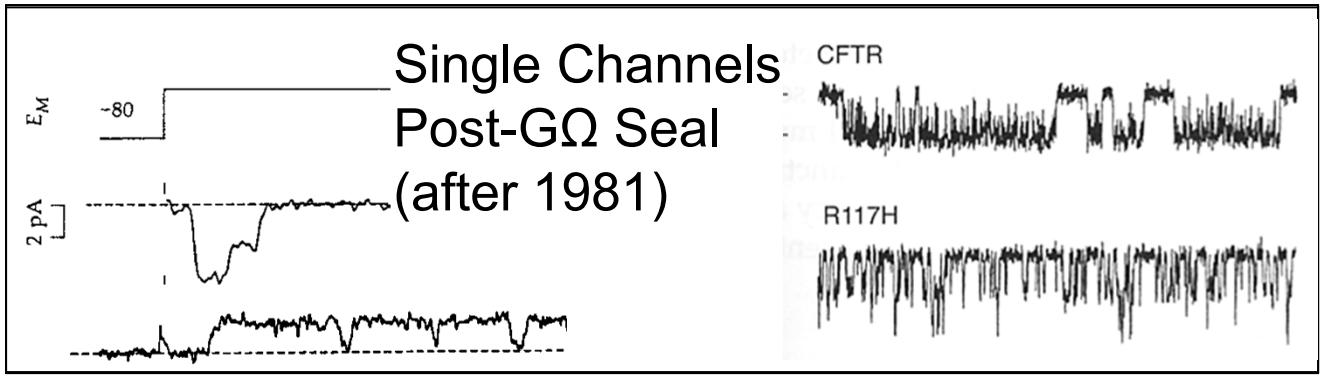


Erwin Neher



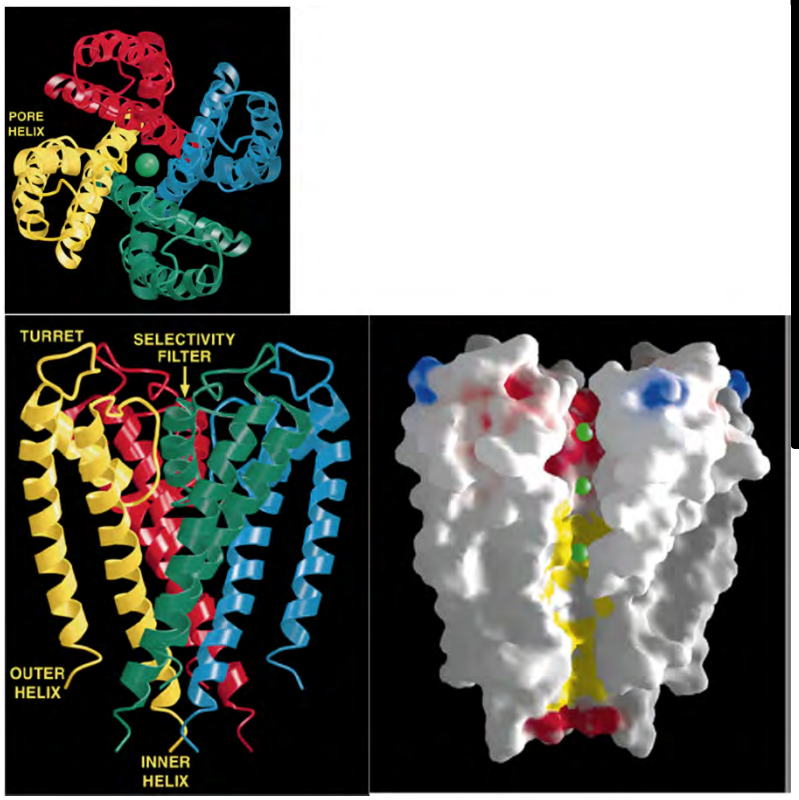
Bert Sakmann



# Membrane Biophysics: then and now

## 1965

# of ion channels known: 0
#of molecular diseases 1
(sickle cell anemia)
# of ion channel diseases 0
# of drugs targeting ion channels 0




## 2011

# of ion channels known: > 100
Na channels, Ca channels, Cl channels
#of molecular diseases: *many*
# of ion channel diseases: *many*
e.g. diabetes, cysitic fibrosis, long QT, epilepsy…
#of drugs targeting ion channels: *many*
(and many more on the way!)
A very few examples:
Orinase (K channel blocker for diabetes)
beta blockers.
Ca channel blockers
etc. etc.

**The Structure of the Potassium Channel: Molecular Basis of $K^+$ Conduction and Selectivity**
Declan A. Doyle, *et al.*
*Science* **280**, 69 (1998);

# Leon and Pat Bruner at their house in Riverside circa 1990

Photo from  Anna Bruner Rudd

# Hodgkin and Huxley Model: Gating Parameters and Computed Action Potential