Bob Eisenberg <bob.eisenberg@gmail.com>

Re: query about voltage gating

Bob Eisenberg <bob.eisenberg@gmail.com> Sun, Jan 25, 2015 at 7:37 AM
Reply-To: bob.eisenberg@gmail.com
To: Wayne Saslow <wsaslow@tamu.edu>
Cc: "Bob Eisenberg beisenbe@rush" <beisenbe@rush.edu>, Bob Eisenberg <bob.eisenberg@gmail.com>

Dear Wayne

How good to hear from you!
AND with such a sensible question.

and what a coincidence. I have just finished the attached, and found your textbook and papers most most helpful. [All questions, comments, suggestions, and criticisms are welcome]

About voltage gating.

I am afraid the idle discussions of biophysicists are ill informed. YES I know that is extreme, but remember I am one of the few left who had extensive discussions about EXACTLY this subject with Cole, Hodgkin, and Huxley, and then Bezanilla and Armstrong.

1) Voltage dependence in the voltage activated sodium and potassium channels (studied by HH= Hodgkin & Huxley) is now known to be mediated by a SEPARATE MACHINE that is DISTINCT AND DIFFERENT from the pore through which sodium moves. This is all explained best on the website of Francisco (Pancho) Bezanilla. Just search for it at University of Chicago (google does better than the UofC search engine). Be sure you have lots of time. It is REALLY WONDERFUL science and fun!

2) H and Cole knew (they told me vociferously and often: I had many conversations with Cole in 1960 and 1961 and a few in 1962 on this subject and then innumerable, but not many, conversations with Hodgkin in the next decades) that the voltage dependent sodium channel responded to transmembrane potential and NOT current flow. (NOTE the voltage activated calcium channel which has a similar role in some cells to the voltage activated sodium channel is NOT NOT in this category). They both told me this was obvious from Cole and Curtis' impedance data (no change in capacitance, large change in conductance) but I have never understood it. It is in fact obvious from the Cole and Marmont voltage clamp

data and HHK voltage clamp, where they put a wire down the axon, changing currents enormously, and the action potential only changed a bit.)

3) ANY and I mean ANY model of THE OPEN CHANNEL will have voltage dependence that covaries (and in that sense depends on) current through the channel. It is inconceivable that current flow through the open channel does not change the PROFILE of potential inside the channel. Current through an open channel and potential within the channel interact strongly in any theory I believe. (In HH 'Voltage dependence' means dependence on transmembrane potential, of course. That transmembrane potential is a boundary condition for some model of current flow through the OPEN channel.)

Thus having a voltage sensor AWAY from the pore is a necessity if the channel is to respond to membrane potential and not current. I remember that H and C had some argument why it is best for biology that the channel respond to JUST voltage, but I do not remember what it is. I remember arguing with one or both of them that the voltage sensor had to be separate from and away from the pore, but no one (including me) took me seriously when I was 18 years old, an undergraduate, who knew nothing.

I also had this argument clearly with Bezanilla in 1974 or 1975 (I do not remember which) and by then I was on sound grounds. He and Armstrong fought me hard (privately) but Bezanilla has now with a magnficent series of experiments proven me right. I do NOT mean to be egotistical and memory is slippery but that is what I do in fact remember.

4) The really interesting question is what makes SINGLE channels switch from closed to open, with WELL DEFINED states, in which (ensemble mean) current flow does not vary at all with time, whether the channel is open for 10 microseconds or 10 seconds, or whenever the time is within the opening.

I believe (and Bezanilla) believes that the special voltage sensing machine works by modifying whatever process does (4) the spontaneous I REPEAT SPONTANEOUS opening and closing.

5) Other channels have voltage dependence that does NOT depend on a separate machine and that is a totally different story.

I hope this is some help

Please feel free to ask.

I attach our work on POSSIBLE explanations of spontaneous opening and closings.

As ever
Bob

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Return Address for email: beisenbe@rush.edu or bob.eisenberg@gmail.com

Bob aka RS Eisenberg
Bard Endowed Professor and Chairman
Dept of Molecular Biophysics & Physiology
Rush Medical Center
1653 West Congress Parkway
Chicago IL 60612 USA
Office Location: Room 1291 of
Jelke Building at 1750 West Harrison

Email: beisenbe@rush.edu
Voice: +312-942-6467
FAX: +312-942-8711
FAX to Email: +801-504-8665
Department WebSite: http://www.phys.rush.edu/
Personal WebSite: http://www.phys.rush.edu/RSEisenberg/

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New hospital tower at Rush

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On Sat, Jan 24, 2015 at 1:55 PM, Wayne Saslow <wsaslow@tamu.edu> wrote:

> Dear Bob,
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> As you recent article in JCP indicates, you continue to be active. I wish you continued good health!
>
> But I am writing with a simple question. Although I do no real biophysics -- I'm mostly doing magnetism and electronics now -- I do have an occasional beer with biologists with a physics inclination. They seem to be in awe of the idea of voltage-gated channels. Once I was too. But with time I came to ask why they are not electrochemical potential gated channels? What happened to the chemical differences between ions and atoms and molecules? Why should all channels seem to be voltage-gated (albeit with different voltages for different channels)?
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> If you could send me a reference on this I would be very appreciative. If I am to be a crank when I drink beer with biologists, I at least want to be a knowledgeable crank.
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> Best,
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> Wayne
>
> Professor Wayne M. Saslow
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Department of Physics
Texas A&M University
College Station, TX 77843-4242
office: 455 MPHY, 979-845-4841
wsaslow@tamu.edu

3 attachments

Lin Eisenberg Multiple solutions of steady-state Poisson-Nernst-Planck arxiv 1407.8252 (1) (1).pdf
603K

Coulomb Blockade Kaufman_arXiv_2014.pdf
176K

Mass Action and Conservation of Current January 23-2 2014 .pdf
760K