**Flux Ratio**

**Bob Eisenberg**

**March 23 2014**

There is an enormous literature in physiology, starting basically with Hodgkin [[2](#_ENREF_2)] that classifies membrane transport systems (that do NOT use ATP) into channels and ‘transporters’, using as a criteria the ratio of unidirectional fluxes (that I define below).

The motivation is that the ratio of unidirectional fluxes in bulk solutions can be characterized by an exponent of one (in the classical expression, see below) but is less than one in transporters and greater than one in channels.

The classical treatments did not include a description of the electric field created by the permanent or polarization charges of the channel, or by mobile charges themselves in the bath, for that matter. The classical treatments ignored the Poisson equation. Thus, it is not clear whether the classical separation is valid or not.

I think it is of the greatest importance to evaluate the flux ratio using self consistent theories that include ion size and resulting saturation phenomena, along with the electric field computed from all the charges present. A number of these are available, e.g., [[1](#_ENREF_1), [3](#_ENREF_3), [5-8](#_ENREF_5)] and a number of other procedures and simulations to the same end.

Unidirectional fluxes were introduced to describe the flow of tracer amounts of isotopes from one side of a membrane (or channel) to another side where the concentration of tracer (but NOT the main species) is negligible.

Tracers are defined by two properties. They have ***all*** parameters (diameter, diffusion coefficient, etc etc) exactly the same as the main species. They have negligible concentration and (of course) they can be traced, usually because they are radioactive since they are a different isotope with a different atomic weight.

I illustrate the properties with a particular system, using three isotopes of sodium, 24Na, 22Na, both radioactive (and easy to tell apart because they decay differently) and the main stable isotope 23Na.

The set up that DEFINES unidirectional flux ratios is shown in the Table below. The thick vertical line represents the membrane.

**[Na]** is the concentration of **Na**

**Unidirectional Flux Setup**

|  |  |  |
| --- | --- | --- |
| *Role* | *Outside ‘east’* | *Inside ‘west’* |
|  |  |  |
| **23Na *is theMain Species*** | **[23Na]out**, e.g., 0.3 M | **[23Na]in**, e.g., 0.1 M |
|  |  |  |
| ***Components of* 23Na *Main Species*** |  |  |
| ***Influx of Main Species*** | **[23Na]out**, e.g., 0.3 M | **[23Na]out exactly zero always** |
| ***Outflux of Main Species*** | **[23Na]out exactly zero always** | **[23Na]in**, e.g., 0.1 M |
|  |  |  |
| **24Na *is the Tracer of Influx*** | **[24Na]out** typical 10-12M | **[24Na]out** **exactly zero, always** |
|  |  |  |
| **22Na *is the Tracer of Outflux*** | **22[Na]out****exactly zero, always** | **22[Na]out**typical 10-12M |
|  |  |  |

The net flux of the main species is **Jnet**(**23Na)** and is customarily decomposed into

 

The flux RATIO is defined as the left hand side

 

where  is the electrical potential across the membrane (inside minus outside),  is the gradient of chemical potential of Na, in electrical units, given by the ‘Nernst equation’  and  is the driving force, the gradient of electrochemical potential.

The right hand side is the ‘independence principle’ of Hodgkin and Huxley, see eq. 8-12 of {Hodgkin, 1952 #466}

The flux ratio can be estimated from the ratio of tracer fluxes. For convenience we assume the ‘specific activity’ *s* of the two isotopes is the same.

 

Then for an ideal situation in bulk

 

What is found across membranes is almost never ideal. Rather, a flux ratio exponent ***K*** is found, not equal to one

 

The flux exponent is defined by

 

The second equality defines the flux exponent from experimental measuremetns.

It is widely believed (p. 81 of Keener and Snyd [[4](#_ENREF_4)] does it well) that channels have , ideal solutions have , and transporters have .

**The question is what are the values of *K* in consistent theories?**

**What formula defines *K* in PNPF?**

**References**

1. Eisenberg, B., Y. Hyon, and C. Liu, Energy Variational Analysis EnVarA of Ions in Water and Channels: Field Theory for Primitive Models of Complex Ionic Fluids*.* Journal of Chemical Physics, 2010. **133**: p. 104104

2. Hodgkin, A.L., The ionic basis of electrical activity in nerve and muscle*.* Biological Reviews, 1951. **26**: p. 339-409.

3. Hyon, Y., B. Eisenberg, and C. Liu, An energetic variational approach to ion channel dynamics*.* Mathematical Methods in the Applied Sciences, 2013.

4. Keener, J. and J. Sneyd, *Mathematical Physiology*. 1998, New York: Springer.

5. Lin, T.C. and B. Eisenberg, A new approach to the Lennard-Jones potential and a new model: PNP-steric equations*.* Communications in Mathematical Sciences, 2014. **12**(1): p. 149-173.

6. Liu, J.-L., Numerical methods for the Poisson–Fermi equation in electrolytes*.* Journal of Computational Physics, 2013. **247**(0): p. 88-99.

7. Liu, J.-L. and B. Eisenberg, Correlated Ions in a Calcium Channel Model: A Poisson–Fermi Theory*.* The Journal of Physical Chemistry B, 2013. **117**(40): p. 12051-12058.

8. Mori, Y., C. Liu, and R.S. Eisenberg, A model of electrodiffusion and osmotic water flow and its energetic structure*.* Physica D: Nonlinear Phenomena, 2011. **240**(22): p. 1835-1852.