Bob Eisenberg <bob.eisenberg@gmail.com>

Re: "markov" models, gating, and electrostatics

Bob Eisenberg <bob.eisenberg@gmail.com> Mon, Apr 7, 2014 at 8:12 AM
Reply-To: bob.eisenberg@gmail.com
To: Chun Liu <liu@math.psu.edu>, Bob Eisenberg <beisenbe@rush.edu>
Cc: Pancho <FBezanilla@uchicago.edu>, Nani Ana Correa <nanicorrea@uchicago.edu>, Wolfgang Nonner <wnonner@med.miami.edu>

Dear Chun

This comment applies I suspect to all Master Equation models.

We need not to hide the fact:

ALL chemical reactions in water solutions involve LARGE amounts of charge.

Even liquid argon is held together by STRICTLY electrical forces (fluctuating induced charges produced by quantum scale fluctuations of charge denisty)

So models that ignore the electric field are ignoring a central and universal REALITY.

Of course, such models might be decent approximations, but THEY MUST ACTUALLY SHOWN TO BE APPROXIMATIONS (by experimentation or theory or simulation .....) and not just assumed to be a good approximation, when they ignore a reality.

Even worse, it is really very unlikely that a model that does not involve charge can work under more than one condition (e.g., ionic strength of background solution, or divalent concentration of background salt, or, most of the time, concentration of reactant and product). Even if an UNcharged model is parameterized to work correclty under one set of conditions, how could it possibly work under different conditions that change the electric field as would changes in ionic strength of background solution, or divalent concentration of background salt, or, most of the time, concentration of reactant and product.

Most experimentation is done by changing conditions and thus often by changing the electric field.

As ever
Bob

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On Mon, Apr 7, 2014 at 7:14 AM, Bob Eisenberg <bob.eisenberg@gmail.com> wrote:

> Dear Chun
>
> I have been thinking about gating models, and what I am thinking applies to lots of 'state' models made of a sequence of first order ode's.
>
> Imagine, to make the discussion easiest and most concrete, that the different states involve different spatial locations even though no spatial location or equation for spatial translation is involved in the equations. This is CERTAINLY true for Markov models of gating which are supposed to be described confromation changes involving (usually) substantial motions of (often) thousands of atoms in a protein.
>
> I think it obvious that these models cannot satisfy "Kirchoff's current law" which is a restatement of Maxwell's equations.
>
> Because these Markov models do not involve charge at all (in an explicit way: no forces or potentials are computed from the charges in the models), they cannot possibly account for currents correctly. INDEED, IT IS A TRIVIAL MATTER TO CONSTRUCT COUNTER EXAMPLES SINCE THE FLOWS IN THESE MODELS ARE THE SAME WHATEVER THE CHARGES BEING TRANSPORTED. For example, in a multi state Markov model A goes B goes to C goes to D one can simply make one transition charged and another uncharged, and Kirchoff's current law is not satsified.
>
> It is a harder matter to know if there is an easy low resolution way to fix this.
>
> One way would be to put potential dependence in each rate constant AND COMPUTE THE POTENTIAL from the charge transfer in that one step USING THE ASSUMPTION OF A FIXED 'CAPACITANCE' i.e., ratio of self energy to charge.
>
> What do you think?
>
> I am sending a copy of this email to Pancho Bezanilla and to Wolfgang Nonner who may very well have a different and more constructive perspective than I have.
>
> As ever

Bob

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