



Bob Eisenberg <bob.eisenberg@gmail.com>

Fundamental Issues you have uncovered

1 message

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Wed, Oct 22, 2014 at 7:44 AM

Reply-To: bob.eisenberg@gmail.com

To: Per Nissen <per.nissen@nmbu.no>, "Bob Eisenberg beisenbe@rush" <beisenbe@rush.edu>

Dear Per

Good to hear from you.

I fear we face here a breakdown in the scientific process and method and that is a very hard thing to face and deal with.

By the way, I too am a grandpa, am also chairman of an academic department for 38 years, etc so this is not just an angry radical young man/woman (although one should not disparage them too much as agents of change).

The basic issue is shown in slides I attach written for a talk to my department this week.

Also in the zip file of a recent article and its supporting arXiv document.

Fundamentally, chemical analysis has been based on two assumptions which are so seriously wrong that they undercut the possibility of chemistry being an "exact" science.

An exact science, in this language, is a science that can predict what will happen in conditions quite different from those in which measurements are made, with zero adjustable parameters. Exact sciences allow devices to be built that actually work reasonably robustly.

Examples are semiconductor devices, indeed almost any device of our electronic technology, and much of physics.

The two assumptions of chemistry that are dreadfully wrong are

a) Cavalier treatment of the electric field, i.e., ignoring the fact that conservation of matter does NOT guarantee conservation of charge. This is extremely serious because conservation of charge forces flows of CURRENT (not flux of matter) to be 'perfectly' correlated (1 part in $1e17$ or so) in systems of chemical reactions. If these correlations are not in the theory, or more specifically the theory will produce artifactual charge densities that can have huge effects

b) Ignoring the EVER PRESENT three dimensional nature of chemical reactions (in the condensed phase). This issue can be seen in the following real but somewhat exaggerated example, a counter example to use

math speak, designed to illustrate the essential issue.

Consider a chemical reaction that occurs in say $1e-19$ sec that is a classical covalent bond change that is steeply dependent on concentration.

In a condensed phase like an ionic solution, fluctuations of concentration occur on time scales longer than let's say $1e-9$ seconds as can be seen from any MD simulation, or many types of theories.

These fluctuations produce regions of concentration of substantial size (I actually do not know the size, and it is important to know it, but they must be more than 10's of nanometers than tenths of angstroms).

In these regions, the covalent bond change will occur VERY much quicker than in regions of average concentration.

Thus the AVERAGE properties of the chemical reaction (averaged over all space and time as is done in classical chemistry that assumes perfect stirring) will be VERY different with QUALITATIVELY different properties from what happens in the fluctuating regions.

The duration of these fluctuating regions is VERY MUCH LONGER ('infinite') compared to the time scale of the chemical bond change itself so there is LOTS of time for the reaction at high concentrations and VERY high rates to occur.

I believe in fact that in many cases most of the chemical reaction will occur in these regions with properties very very different from the average.

Thus theories only involving averages will fail QUALITATIVELY.

Furthermore, the 'real theory' i.e., something that has the ingredients necessary to make chemistry an exact science, will of course involve electrodiffusion, in which 'everything interacts with everything else' and electrical current flow, diffusion, and perhaps even convection and heat flow are all coupled one to another.

Mathematics to handle that is now known. And simulations can deal with some of these issues IF THEY ARE DONE HONESTLY WITH REAL CALIBRATION.

But these have not been done yet and so the experiments you cite and discuss cannot be dealt with in this tradition.

What is clear is that discrete phenomena can arise from such systems.

I hope this is some help

As ever
Bob

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On Wed, Oct 22, 2014 at 6:01 AM, Per Nissen <per.nissen@nmbu.no> wrote:

Dear Bob,

Attached is a reanalysis of some recent ITC data for binding to a channel. The data are precise, and the profile can be well represented as multiphasic.

As previously mentioned (in connection with my 2011 poster which I hope you have received), ITC data are better represented by multiphasic profiles than by the conventional curvilinear profiles. The same goes for binding as studied by other means, see my reanalysis, also in the poster, of data of Fersht and coworkers. Extensive reanalyses of pH data do also give, so far apparently without exception, multiphasic profiles (provided that the data are sufficiently detailed and precise). What is puzzling to me is the finding that pH profiles for non-biological systems also quite often can be well represented as multiphasic. Extremely strange is the finding that the mere injection of methanol or propanol into water or of propanol into methanol also gives what appears to be multiphasic profiles, at least there are parallel or roughly parallel lines. These experiments should of course be repeated, it seems that there must be an artifact of some kind, but I have no ready access to an ITC instrument. Do you have any comments on these strange findings?

Do the recent findings by Köpfer et al. (Science 346: [352-355](#). 2014), see also the comment by Hummer (p. 303 in the same issue), have any bearing on the interpretation or explanation of the profile for potassium channels (and channels for other ions)? I cannot evaluate this.

From November 6 to 17 my wife and I will be in Burma for a cruise on Irrawaddy. After that I should be able to work full time preparing for the Baltimore meeting, except for a few days around Christmas when we will be with children and grandchildren in the Bergen area.

Best regards,

Per

2 attachments



Perspectives ASBMB Today.zip

1008K



Physics of Electricity Department Talk October 24 2014.pptx

1987K