Re: Ionic Interactions and Chemical Reactions

Richard Moxley <rmoxley@rochester.rr.com> **Thu, Jul 28, 2011 at 6:35 PM**
To: beisenbe@rush.edu

Dear Bob,

Thanks for your explanation and for the additional information. As always, it is very helpful to me as well as educational.

I do remember our conversations at Harvard when you spoke about your concerns about the general lack of application of ideal solution assumptions to the work we were and are carrying out in biological systems. I also remember from our college days your concern about the validity of the assumptions that went into the application of thermodynamics (especially irreversible thermodynamics and non-equilibrium thermodynamics) to biological systems.

I hope we have a chance to get together sometime within the next year to discuss some of your insights and experimental results.

At present I am consumed by the possibility that we may be on the verge of actually discovering a partial or largely complete treatment for myotonic dystrophy type 1. Much of our research is pursuing clinical and bench to bedside studies to prepare for future (next 2 years) investigation of antisense oligonucleotide therapy of DM1.

We can discuss our DM1 research as well as the exciting work you are pioneering.

Let me know if you plan to go to our 50th Harvard Reunion. Joan and I will go because it gives us an excuse to visit Donna's family and to see our grandsons. If you and Ardyth are going, Joan and I will want to make time for us to get together with the two of you.

Warmest regards,

Mox

> ----- Original Message -----
> **From:** Bob Eisenberg
> **To:** Richard Moxley ; Bob Eisenberg
> **Sent:** Thursday, July 28, 2011 7:22 AM
> **Subject:** Re: Ionic Interactions and Chemical Reactions
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> Dear Mox
>
> Good to hear from you.

I hope you smile as you read the paper. It is meant to be amusing.....not mystifying.

The story is a remarkable one.
Edsall et al knew (from the days of Debye Huckel) that ionic solutions did not even approximate the properties of ideal solutions.

> Here is a quote from the present day leading experimentalist in the field:
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> > "It is still a fact that over the last decades, it was easier to fly to the moon than to describe the free energy of even the simplest salt solutions beyond a concentration of 0.1M or so."
> >
> > Kunz, W.; Neueder, R. An Attempt at an Overview. In "Specific Ion Effects"
> > Kunz, W., Ed.; World Scientific Singapore, 2009; pp 11.

What Edsall et al did not realize is that the entire edifice of allostery, and of complex chemical reaction schemes, was built on the assumption that ionic solutions were ideal!

We have recently shown that enzymes, like ion channels have ion concentrations of many molar (20 to be precise in some 570 enzymes of known structure in the databank) in and near the active site. They more closely resemble ionic liquids (e.g., melted NaCl) than ideal infinitely dilute solutions.

The crucial point is that in nonideal solutions the activity of one ion depends on the concentrations of ALL ions, not just its own concentration. So 'coupling' and interactions occur for physical reasons, in addition to what may occur in the enzyme and reaction schemes themselves.

This means that the literature of Enzyme Kinetics must be reworked since a substantial fraction of what is attributed to the enzyme is occuring between the ions and reactants. The same is probably true of chemical kinetics itself but that is a bit trickier to explain.

The needed revision is essential (in my opinion) to be able to get the control of chemical and enzymatic reactions that we have of semiconductors. You and I have seen what happens when we really do get full control of the physics of a technology: all of digital and computer technology is a direct result. Imagine what would happen if we could have equivalent control of chemistry and biochemistry!!!

The key additional step is a mathematical framework that can handle the interactions naturally without arbitrary approximations. That is now available thanks to Chun Liu (see attached, which IS hard going but just read the Abstract, which we tried very hard to make clear). He has solved the problem that Onsager, Katchalsky, Prigogine, Kirkwood, et al tried to solve. The problem was mathematical not scientific which means that one can PROVE it is is solved. There is a tiny pre-echo of this in my undegraduate thesis (I knew the problem existed and had not been solved but had no clue of how to solve it.)

I imagine Edsall would be pleased but not amused at this contribution.

As ever
Bob

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On Wed, Jul 27, 2011 at 6:27 PM, Richard Moxley <rmoxley@rochester.rr.com> wrote:

> Dear Bob,
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> Congratulations on another very interesting and challenging article. I will continue to do my best to digest it. But, no doubt you have tackled another problem area in scientific investigation that deserves new light and discussion.
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> Keep up the excellent work and thought.

Warmest regards,

Mox

----- Original Message -----
From: Bob Eisenberg
To: Bob Eisenberg
Sent: Monday, July 25, 2011 9:06 AM
Subject: Ionic Interactions and Chemical Reactions

Dear Friends and Colleagues,

I hope you will find that the attached article provides ideas and opportunities for future work. The article shows that the free energy of an ionic species depends on the concentrations of all types of ions, not just its own concentration.

The reason is that Ionic solutions are rarely ideal: they contain charges that interact with each other and form an ionic atmosphere with large effects. But the Law of Mass Action assumes ideal solutions.

Interactions of ions are easily mistaken for complexities in chemical reactions or multiple states of enzymatic catalysts.

The existence of strong interactions in bulk ionic solutions is an experimental fact known 'forever' and directly measured by many methods. This is not theory. Ionic interactions are documented in many experiments reported in books, reviews and papers cited in the article.

The reality of ionic interactions has not found its way into the common consciousness, the conventional wisdom of most of us. Certainly I was unaware of them for many decades. The reality of ionic interactions has been known, however, to the physical chemistry community for a long time, including the editor who invited this paper, and the referees who reviewed it.

Dealing with ionic interactions presents a wide range professional opportunities and I am sending this email hoping that you share that view.

There is an enormous need to include ionic interactions realistically in our descriptions of bulk solutions, enzymes, ion channels, and chemical reactions in bulk and near electrodes. I for one think that quantitative understanding and design of channels, transporters, enzymes, and catalytic reactions require the realistic treatment of ionic interactions because 'everything' interacts with everything else in these systems, through the electric field and (usually) steric repulsion. Of course, this is an opinion that others may not share, and will only be proven by the successful design of these molecules.

I hope you share my view of the opportunity this gives all of us to make useful contributions. Much more needs to be done than any one (group) of us can do.

All questions, comments, suggestions, and criticisms are most welcome!

As ever

Bob

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