



Bob Eisenberg <bob.eisenberg@gmail.com>

Re: Y channels

Muhammad Ashraful Alam <alam@purdue.edu>

Mon, Jan 20, 2014 at 10:04 AM

To: bob.eisenberg@gmail.com

Thanks, Bob. I understand and completely agree with you. Also, I will read the paper you sent very carefully. If there is other review article from your group that you feel I should read, please send it to me.

Best regards,
Ashraf

On 1/20/2014 10:20 AM, Bob Eisenberg wrote:

Dear Ashraf

How good to hear from you!

Yes we share many interests and approaches and I hope we see a lot of each other here and at Purdue (and elsewhere too!)

The issue about MD is profound and social as much as logical.

The DNA issue that you cite focuses attention correctly because

a) it is an issue of obvious and profound importance (indeed in its RNA context the issue nucleic acid binding may be MORE important than DNA binding: most biologists believe life started with RNA based systems withOUT proteins in which RNA binding performed enzymatic functions. There are many traces of that left in biological systems today. There binding is the key to everything that happens. For a provocative question, ask yourself what held the "expensive molecules of life together, i.e., in the same vicinity, before cells were invented?)

b) the failure of MD to deal with DNA binding is diagnostic of both its logical and social (i.e., psychological) issues. Logically, the problem is that a lot of the free energy of DNA systems is in the ionic atmosphere around the permanent negative charges on its outside (what chemists call acid groups). Simple electroneutrality, and all sorts of direct measurements show that the concentration of monovalent salt within a Debye length of DNA is more than 5 Molar. I think in fact the figure is about 13 M but I might be wrong. (For Mark: solid NaCl is 37 M)

At concentrations like this MD is totally unable to get the free energy of any ionic solution right. This is an extreme statement. But it is also extremely easy to check.

Finally, it is possible (THIS IS A SPECULATION) that divalents (calcium and magnesium ions) are important in DNA binding and in the ionic atmosphere. I do not know whether this is true or not, but the correct experiments (using calcium buffer systems that have been ROUTINE in biology since the 1940s) can easily determine this.

Divalents control so much of biology that it is more than likely that they are involved in DNA and/or RNA binding.

c) the social and psychological question than arises, how could MD develop and be so generously supported despite this failing?

That should be pursued in talk more than writing.

But I will answer with a single word. Calibration.

Most MD'ers like most computer scientists do not understand the absolute necessity of calibrating one's calculations against experiments AND CONSERVATION LAWS.

Science in my view is Guess and Check. Without the ATTEMPT to check....things go horribly wrong, and science as a social process no longer converges towards useful explanations let alone towards building things that work.

As ever
Bob

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On Mon, Jan 20, 2014 at 8:53 AM, Muhammad Ashraful Alam <alam@purdue.edu> wrote:
Dear Bob:

My students and I enjoyed your talk at the Math department. I understand your emphasis of salt and strong correlation in confined spaces. In a recent course at nanohub-U, I have tried to emphasize both points. Also, I echo your sentiment about MD -- I was surprised to find that to this day, there is no MD model that can predict the stability of a pair of DNA molecules and we are forced to use empirical 'Santa-Lucia' type models to calculate melting temperatures. When I asked around, everyone said that it is too difficult. If this the case, MD studies of protein-antibody interaction -- in the presence of salt solution -- is perhaps out of question.

Thanks for visiting us. Since you know so much, I hope you will not mind if I come back to you

often with elementary topics that I want to understand more deeply!

Regards,
Ashraf

On 1/18/2014 5:54 AM, Bob Eisenberg wrote:

Dear Mark and Ashra and Supriyo,

Here is the paper I wrote discussing branched channels a VERY long time ago. It was naive but I hope sets the science. Just search for "branched" and you will find my specualtions. The name "atomic biology" is of course appropriate for a subject in which the main players are the current carriers sodium, potassium, calcium, and chloride ions.

I also attach the structural paper. Fig. 4 shows the branched structure.

I spare you the experimental papers by Don Hilgemann but am glad to send them annotated if you wish any time. The first main reference is J Gen Physiol-1992-Hilgemann-905-32.

Let me know if I can help in ANY way!

As ever
Bob

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