Date: 5/25/2001 4:49 AM From: Bob Eisenberg To: holdenerj@kenyon.edu Copy: bob@aix550.phys.rush.edu, eisenbergs@kenyon.edu Subject: Direct Simulations

Dear Judy

Glad to hear that you and the baby are doing so well. You have exciting times ahead of you! Enjoy!

Indeed, you catch me at a busy time, but that is fine. It is what I want to do.

I will send along some papers next week, meanwhile I attach a couple of things to get acquainted.

About simulations: I have not written the following up in a formal paper yet, but it shows the essential problem

Consider the problem of predicting the motion of 10,000 iron atoms in a solid at room temperature, all given an initial velocity at time zero and moving in a vacuum. We know the answer, if the initial velocity is not too high, Newton's laws describe the motion to many significant figures.

If the velocity is very high, Einstein special relativity describes the motion with no known error (i.e., something like 12 or 15 significant figures, I have not kept up with the literature)

The last two paragraphs should be viewed as experimental facts: I do NOT invoke them as "laws"

Consider the simulation problem. First consider a direct calculation (without mathematics, just a computation of all trajectories).

If standard simulation packages are used, the trajectory of the Fe ball is not computed at all, because gravitation is not included in the equations.

Then just add gravitation. We do and find that the gravitational force is some 10^{-36} times the the interatomic forces in the simulation.

The result of the gravitational force cannot be calculated then in any computer with finite word length. (Of course, averaging procedures can be used to separate the small non zero mean

force from the large random fluctuating force. The fact that they are absolutely required is the point of these paragraphs)

What is striking is that the sum of the random motions is identically zero!!! Otherwise, the ball would not follow special relativity and it does. The direct simulation cannot recover this fact: anyway, that is my assertion.

What is needed instead is a hierarchy of analysis. Atomic detail is very much needed, but only some parts of it. We do not want all the detail of random motions that add to zero. We DO need certain measures of atomic detail, namely the mass of each atom and the number of atoms. Those measures absolutely can NOT be found from a direct macroscopic calculation. Those measures are, however, ALL we need from the simulation.

Of course, what we need in way of atomic detail depends on what we want to know. The "measures" depend on what we choose to measure (to make an accurate and not confusing pun, at least I hope it is one of those).

This is NOT a contrived example. If we replace the gravitational force with a long range electric field (created by charge placed on electrodes in salt water, i.e., biological plasma, for example) we have the problem I and other biophysicists (and electrochemists and molecular biologists) have every day when we study movement of substances in electrolytic cells, or across membranes, or through ionic channels (proteins with holes down their middle).

My point is that simulations are an invaluable irreplaceable component of the hierarchy of models needed to understand condensed matter (the physicists' name for liquids and solids) like biological systems.

But the hierarchy of models is absolutely needed. Direct simulations have tremendous difficulty reproducing the macroscopic phenomena of 19th century physics, e.g., they have tremendous difficulty reproducing the macroscopic experimental phenomena called "Ohm's law", Fick's law, etc. Direct simulations are needed to determine the parameters of those models. Mathematics (e.g., singular perturbation theory, in its multiple scale techniques) is needed to create a hierarchy of simulation and theory to describe experimental phenomena.

Some experimental phenomena will in fact depend on atomic detail in a crucial way and can be dealt with only by simulation. Other experimental phenomena (Iike the trajectory of the iron ball) will depend mostly on conservation laws and long range fields and need only a few measures of atomic detail. Still other phenomena will need both.

The fun is to pick important phenomena, do the analysis, and get understanding and control. For those of us dealing with proteins, e.g., ion channels, of immense biological and medical importance (1/3 of the human genome codes membrane proteins; about the same fraction of all drugs act directly or indirectly on membrane proteins), the goal of control is of great human significance to us, our families, and our babies to be!

Please let me know anything you wish about this discussion.

Attached is a CV and a few bio documents and papers as a way of getting to know each other.

As ever Bob

********** REPLY SEPARATOR **********

On 5/23/2001 at 3:43 PM Judy Holdener wrote:

>Dear Bob, > >Hello to you and Sally. Great to hear from you. >Gambier is much quieter these days with everybody >gone, and I am recovering from the school year. >The baby is fine; he seems to be pushing his limits >already in his movements. They are becoming more >prevalent and I am feeling them in all sorts of strange >places. > >Please do send the papers when you get a chance. >I look forward to reading them. And please call >me Judy! > >Have a good trip. You sound very busy! > >Judy > > > > >Bob Eisenberg wrote: > >> Dear Dr. Holdener >> >> Sally is standing next to me and I am >> reminded that I have not yet said "Hello!" >> by email. >> >> Hello! >> >> I have not forgotten that I owe you a couple >> of papers and a paragraph or two about the >> inherent limitations of simulation. >> >> I am off to Washington to review grants and >> solicit grants for a couple of days (NASA and >> DARPA) but will surely be able to do this before >> the end of the Memorial Day weekend. >> >> Hope you have recovered from the stresses (and strains?) >> of the end of the semester. >> >> Hope the baby is doing well with and by you. >> >> Sally says Hello too! >> >> Ever yours >> Bob >> >> ================================ >> >> aka RS Eisenberg >> Bard Professor and Chairman >> Dept. of Molecular Biophysics >> Rush Medical Center >> Chicago IL 60612 >> >> Email: beisenbe@rush.edu >> Department WebSite: www.rushu.rush.edu/molbio/ >> Personal WebSite: www.rushu.rush.edu/molbio/physioeis.html >> Voice: (312)-942-6467 >> FAX: (312)-942-8711 >>

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