

Viewpoint paper

Qualitative thinking in the age of modern computational chemistry—or what Lionel Salem knows¹

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Abstract

A personal assessment is given of the present state of computational chemistry, and in particular of the persistent need for qualitative orbital thinking at a time when exceedingly accurate calculations are possible. The need for the qualitative view arises, it is claimed, from the inherent difference between predictability and understanding, from certain potential impediments to chemical understanding intrinsic to human–computer interactions, from the peculiar yet productive way that experiment and theory interact in chemistry, and lastly from some special features of theory in science in general. © 1998 Elsevier Science B.V.

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The achievements of modern computational chemistry are astounding. It is reasonable today to handle billions of configurations, and to achieve chemical accuracy, kilocalories say, in calculating binding energies and geometries, in ground and transition states of reasonably complex molecules. There is no question that the enterprise of computational theoretical chemistry is successful.

Now Lionel Salem and I grew up and developed scientifically in the climate of the very same computer which made all this possible. Russ Pitzer taught me to punch cards; I still miss the sound of the key punch. The extended Hückel method, which several of us developed in the Lipscomb group, would have been impossible without modern computers. But I took a different turn, moving from being a calculator in the framework of semiempirical theory, to being an

explainer, the builder of simple molecular orbital models. I was and am still doing calculations, but my abiding interest is in the construction of explanations; and also in thinking up moderately unreasonable things for experimentalists to try.

In existing as a scientist, meaning that my work was of continuing interest to other chemists. I was helped in that I moved into whatever part of chemistry I did, just a little ahead of the heavy guns of computational chemistry. So I switched from organic to inorganic molecules just when organic molecules become reasonably calculable. Recently I've been less fortunate, for when I moved to solids and surfaces I came back into heavy fire: physicists had been doing calculations on these materials for a long time; and they were (are) hardly likely to believe that one-electron calculations and a chemical viewpoint are of value.

I want to make some observations on computational quantum chemistry, perforce influenced by

¹ Dedicated to Professor Lionel Salem on the occasion of his 60th birthday.

my prejudices. Given the advances in the field, any molecule I can calculate (without geometrical optimization), with the simplest extended Hückel approximation, can be done so much better by most computational chemists. So why don't I feel threatened; why is there a role for people of my ilk? Or for Lionel.

Actually, I do feel threatened and bypassed! But that's just an emotional reaction, and my aging figures in it. But when I think about it quasi-rationally, I don't feel very threatened. Or maybe I put on a brave face, for here...

It's even more complicated: part of me feels bypassed, and it feels so good, for the knowledge that a calculation is reliable and can predict the anomalous, weird geometry of, say, Si_2H_2 before the molecule is made, that is really great! Part of me is bypassed, and it doesn't feel good, because something I said may be just wrong, not supported by better calculation.

However, in general while I am bypassed, I feel that actually there is a deeper need than before for the kind of work I or Lionel Salem do. The factors I see shaping this need are many: at least four. The first, I would claim, is the difference between predictability and understanding. A second has to do with human-machine interactions; a third with the peculiar dialogue of experiment and theory in chemistry; and a fourth with the special features of theory in science in general.

Let me discuss these in turn, and I will do so in a personal way, as provocatively as I can, asking you to disagree.

'Understanding' means different things to different people. First of all let me say that I do not accept a strict reductionist way in science. By reductionism I mean the idea that there is a hierarchy of sciences, with an associated definition of understanding and an implied value judgment about the quality of that understanding. That hierarchy goes from the humanities, through the social sciences to biology, to chemistry, physics, and mathematics. In a caricature of reductionism one aspires to the day when literature and the social sciences will be explained by biological functions, biological ones by chemical ones, and so on. We probably owe the beginnings

of this philosophy to Descartes, and its more explicit statement to Auguste Comte and the French rationalist tradition. Notice my readiness to blame the French.

Scientists have bought the reductionist mode of thinking as their guiding ideology. Yet this philosophy bears so little relationship to the reality within which scientists themselves operate; and it carries potential danger to the discourse of scientists with the rest of society.

I think the reality of 'understanding' is the following. Every field of human knowledge or art develops its own complexity of questions. The problems facing chemistry are in some ways more complex than the ones in physics. Much of what people call understanding is a discussion of questions in the context of the complexity or hierarchy of concepts which are developed within that field. If you wanted to deprecate this way of thinking, you could call it quasi-circular. I wouldn't deprecate it; I think this kind of understanding is quintessentially human and has led to great art and science.

There are vertical and horizontal ways of understanding. The vertical way is by reducing a phenomenon to something deeper: classical reductionism. The horizontal way is by analyzing the phenomenon within its own discipline and seeing its relationships to other concepts of equal complexity.

Let me illustrate the futility of reductionism with a *reductio ad absurdum*. Suppose you receive an anonymous letter, in that letter is a sheet of paper with a four-line poem, 'Eternity', by William Blake:

He who binds to himself a joy
Does the wingèd life destroy
But he who kisses the joy as it flies
Lives in eternity's sun rise.

Knowing the sequence of firing of neurons when the poet wrote those lines, or in your mind when you read it, or in the mind of the person who sent the letter, knowing the fantastic, beautiful complexity of biochemical actions behind the firing of neurons and the physics and chemistry behind that, that knowledge is incredible and desirable, that knowledge is going to get you a lot of Nobel Prizes, I want that knowledge, but... it has nothing to do with understanding the poem, in the sense that you and I understand a poem, or drive a car, or otherwise live in this terrible

and wonderful world. The ‘understanding’ of Blake’s poem is to be sought at the level of the language in which it is written, and the psychology involved in the writing and reading of it. Not in the firing of neurons.

If you are willing to accept a leap between the humanities and science, I tell you that even in two ‘hard natural science’ fields as close to each other as chemistry and physics, even there, there are concepts in chemistry which are not reducible to physics. Or if they are so reduced, they lose much that is interesting about them. I would ask the chemist to think of ideas such as aromaticity, acidity and basicity, the concept of a functional group, or a substituent effect. Those constructs have a tendency to wilt at the edges as one tries to define them too closely. They cannot be mathematicized, they cannot be defined, unambiguously (I know Richard Bader would disagree!), but they are of fantastic utility to our science.

I actually think understanding in chemistry is part vertical, part horizontal.

Even if we were to accept the vertical mode as dominant, I think there is a problem that modern computational approaches to chemistry face. Let me explain by putting forward one definition of understanding in physics and chemistry that most people I think will agree on, and which follows the reductionist programme: we understand an observable if we know the mix of different physical mechanisms leading to it (there may be more than one) and can make a semi-quantitative estimate of the contributions of each mechanism.

In thinking about explanations this way, experimentalists invoke contributions or factors with a venerable history: electrostatics (charges, dipoles), donor–acceptor interactions, orbitals. The computational chemist, on the other hand, is content with getting the Hamiltonian right and then proceeding as expeditiously and accurately as possible to a solution of the wavefunction and a calculation of the desired observable. The calculations, whatever formalism is followed, are elaborate. What happens next is an imaginary dialogue between the experimentalist and the theorist.

The experimentalist asks: ‘What is the bond angle of water?’ You, the theorist, plug it into the best programs available and you get it right to three significant figures. Everyone is happy. Then the experimentalist asks the same question for TeH_2 .

You say ‘Wait a minute, I have to calculate it...’, and you get that right; and you get right Li_2O and F_2O as well. But if that’s all you do, no matter how well you do it, the experimentalist will grow increasingly unhappy. Because you haven’t provided him/her with a simple, portable explanation, one based on electronegativity, or relative energies of s and p orbitals, or donor or acceptor character or whatever set of factors he or she feels comfortable with. The experimentalist will think ‘This theorist is only good at simulating experiments’; or, less charitably, ‘The computer understands, this theorist doesn’t’. Which is not too bad. Sometimes that predictability is needed, sometimes it’s quicker, or as Fritz Schaefer so aptly calls it in a paper, ‘odorless’. Sometimes it even gets the facts right before experiment: the story of the ground and excited states of Si_2H_2 is an exemplary case. In many interesting areas of chemistry we are approaching predictability, but... I would claim, not understanding.

Let me digress here to give here a simple pedagogic strategy which I teach for eliciting understanding. This is to alternate the computational and the ‘understanding’ roles. I define understanding (operationally, if faced with a really good computer program and a complex problem), as being able to predict qualitatively (this forces you to think before) the result of a calculation before that calculation is carried out. If the calculation’s result differs from what your understanding gives you, well then its time to think again, do numerical experiments until you rationalize (that’s also to ‘understand’) the results. Until the explanation is so clear that you could kick yourself in the butt for not having seen why. But don’t stop, iterate the process, go on. Understanding will build if you follow this way of analysis.

Back to the program with perfect predictability. Does it, or you, its programmer, understand chemistry? I would say that no, it doesn’t, it simulates it. It is capable of making predictions, but it is not capable of telling you trends (because the human being defines, probably in a horizontal way of thinking, what makes for a trend: donor, acceptor, base acid, etc.). The program also lacks the most human and chemical quality of intelligence, of seeing connections, relationships, metaphors. I ask you to think about what you consider intelligence in a person, a student or mentor. Is it the ability to calculate or make connections?

I realize full well that I tread a minefield full of angry controversy, namely that of artificial intelligence, of what thought and consciousness mean. Francis Crick, Roger Penrose, Marvin Minsky, Joseph Weizenbaum will not agree with me or each other. I just give you my view: one reason I survive is that I build explanations (deceptive, oversimplified, as they may be); in doing so I answer the desperate pleas from the experimentalist, a spiritual plea, for understanding and not simulation.

Now let me talk about another problem of computational molecular science. This is the psychology of man–machine interactions. From such interactions arise non-trivial psychological barriers to successful chemical theory. For instance there is the inherent game-playing aspect of debugging, which enthralls and eventually enslaves. As you try to make that program work, as you curse and cajole it, you may get so involved with it that you lose contact with chemical reality, the problem to be solved.

Another concern is a giving in to fancy graphics. The computer can spew out a near infinity of contour diagrams of orbitals. If you put 20 of them in a paper, noone is going to read the paper; it's absolute folly to think that anyone will be impressed! Reporting research has an abiding pedagogical component; those 20 overly detailed diagrams clearly serve as a sign that you don't want anyone to understand or worse, maybe you think this is a way to hide lack of understanding, which is usually, like revelation, bright and intense.

In my opinion, graphical presentation has actually deteriorated with the advent of computers. For the ornery software never gives you what you want, and eventually we accept compromises we never would accept in a human drawing. Often the published lettering on the axes of a graph, or the scale markings, is weird. This is a give-away of a compromise born of laziness or desperation.

However, these are trivia. More important is the inherent complexity of the enterprise of computational chemistry. Suppose you have that perfect program. It does require an incredible effort to write the code. The results have oscillated before with increasingly faithful accounts of correlation. Now

you are sure the problem is solved. For any molecule the code will give you the correct geometry, polarizability, spectrum. That's the grail to which we have aspired.

But it's complex. It has to be complex, for nature is (only the wild dreams of theoreticians of the Dirac school make nature simple). It is our minds that are simple, not nature. Given that complexity, there is a natural tendency on the part of the computational theorist to think that there can be no single, simplified explanation (in a way a curious conclusion for a reductionist who believes in Dirac's dictum), and to be loathe to give such an explanation to experimentalists, especially in their own language, based as it is on vague, time-honored contexts which may bear no relation to what you calculate.

I can only give you the advice: try, please try. Take the existential plunge, the hazard of providing an explanation. Do numerical experiments to probe your wild notion, to be sure, but don't be afraid, forward a simple explanation.

I know that I am not consistent in advocating a complex universe, but simple explanations.

A third reason why I'm not too worried about being bypassed has to do with the curious dance of experiment and theory.

Chemistry is an experimental subject (85% of the chemists in academia and 99.5% of those in industry are experimentalists). So is physics, which has a real psychological problem, a kind of schizophrenia, for it is an experimental field but (because of its buying whole-hog reductionist logic) one which has opted to have theoreticians as its heroes (the only exceptions are Fermi and Rutherford). Experimentalists use theory or theoretical frameworks in certain ways and they use them a lot; there are no facts without a framework to think about them. The theories experimentalists use are often simple: often so simple they're ashamed to put them into print, so they invent grander reasons than those that initially moved them.

One such theory is the orbital model, learned not without pain by experimentalists, taught to them by great English teachers such as Coulson and Orgel. Orbitals have served chemistry well: I have lived off this model, and pushed it on. One does need to go beyond orbitals, that is clear. A problem that I see in

with modern CI methods is that people have not sufficiently stressed why certain configurations mix. Actually VB ideas are helpful here. Much more conceptual work is needed in just this area.

There is also a real problem with density functional theory, in that the originators of the method, and most of its first generation implementors, have denied the attribution of any significance to the Kohn–Sham orbitals. This is now being repaired, but there is a difficulty here in that experimentalists are being denied a part of their intuition; and nothing is offered in exchange except ‘Trust me’; and why should they trust theoreticians?

Now I want to mention some special features of theory in science and ask how modern computational chemistry fares with respect to taking advantage of these. Let me enumerate some of the circumstances in which chemical or physical theory just might have an inherent advantage over experiment:

1. Theory allows calculations on unstable molecules, unstable conformations of stable molecules, transition states for reactions not followed, to be performed with as little or as much difficulty as the corresponding computations on stable molecules. The purpose of such calculations is not merely to quantify the energetic misery of these unstable species, but to discern from the calculations what are the factors responsible for their instability. If we understand these factors, we will be able to devise a strategy for moving the molecules to lower energy. Theory serves uniquely here, for the constraint of the Boltzmann factor makes unlikely the experimental probing of such metastable species.
2. Chemistry is discontinuous, but theory allows and often dictates continuous variation. One example is the Karplus curve for vicinal proton–proton coupling constants, derived theoretically as a continuous function, probed experimentally by discrete conformationally fixed molecules. Another example is the concept of a continuously varying dimensionality in the advances in critical phenomena, contrasted with the reality of three dimensions and the modeled ‘reality’ of one or two dimensions.
3. Observables in chemistry may be the result of several simultaneously operative physical mechanisms. A measurement cannot resolve these mechanisms (though a series of observations on related molecules may provide that resolution: witness the elegant dissection of through-space and through-bond interactions in Heilbronner’s photoelectron studies). However, theory has no problem in resolving mechanisms. One can calculate the contribution of each physical factor, or if all factors are already in the calculation one can throw away certain matrix elements and keep others, thus manipulating the theory to isolate the separate effects.
4. Theory can simplify. The strong dictates of thermodynamics often prevent the observation of the simplest version of a reaction type or of a molecule. Substituents may modify a reaction path very slightly, and yet the parent reaction with no substituents may be masked by an entirely different process. Theory is not hampered by the reactions observed and can, in fact, examine the simplest variant of a reaction. Of course, this is a curse as well as a blessing. Substituents may be what makes an important reaction go, but the theoretician has an innate tendency to throw away those perturbations and to idealize the problem to the soluble stage. On occasion, the explicitly soluble may be totally impractical. The stage is set for a classical dialectical contest between the practical experimentalist and the oversimplifying theorist. Both will gain if they persist in their struggle.

The most important role of theory is to make connections. I do believe that to see ‘my nature singing in me is your nature singing²’ (to quote Archie Ammons) is our purpose. There is no greater joy and no greater contribution than to make people see the unity of this world (which is what connections form), and yet be at peace with the diversity and richness of the universe.

² From A.R. Ammons ‘Singing and Doubling Together’, in A.R. Ammons Selected Poems, expanded ed., Norton, New York, 1986, pp. 114–115.

Publication history: this contribution was originally given as a lecture at a Cambridge meeting honoring two great pioneers of computational quantum chemistry, Frank Boys and Isaiah Shavitt. At that time, the paper was entitled 'How Nice to Be Bypassed by What Boys and Shavitt Have Wrought'. At the urging of the organizer of the conference, my friend Fritz Schaefer, the paper was submitted to the *Journal of Physical Chemistry*, where the other papers presented at the Cambridge meeting were published.

However, the style of the paper proved too much for the editors and reviewers of the *Journal of Physical Chemistry*, who rejected it because it was not a typical scientific paper.

Portions of this paper have been published in my book 'The Same and Not the Same', Columbia University Press, 1995, and in 'Theory in Chemistry', *Chemical and Engineering News*, 72(30), p. 32, July 29, 1974.