STRATEGIES II

Exactly what constitutes chemistry or, more specifically, experimental chemistry is defined by the tools available. That is to say, what chemists do is controlled by the reactions which are available to them and the instruments that exist. There is, however, a more basic constraint, i.e., the wave function of any molecule being studied.

If we accept Quantum Mechanics, we subscribe to the belief that any and all information about a molecule is contained in the wave function. Everything that happens to a molecule is determined by the wave function, which is, in essence, the court of last resort. A wave function determines any reaction a molecule takes part in; the wave function determines all aspects or characteristics we measure about a molecule. Indeed, what we can know about any given molecules — and about chemistry in general — is contained in some wave function.

It is fair to say, at least in principle, that if we had the ability to calculate with a high degree of accuracy the complete wave function for any molecule, we could very possibly bring chemistry as a field into the age of computer simulation. This is essentially the task confronting the computational chemist.

Another aspect of this field is often overlooked, i.e., the question of interpreting and manipulating these wave functions. Historically, the emphasis has been on accurately calculating the wave function, usually to obtain one or two pieces of information for purposes of comparison with experiment. We have now reached the point at which we can undertake the systematic interpretation of all aspects of the wave function in order to extract *all* information useful to the practice of chemistry. We will deal with this aspect at a later date.

Of course, before we can do anything in chemical analysis or prediction, we need to confront the calculation of a wave function. The first question one should ask is, "How accurate a wave function do I really need?" One is often gratified and surprised to learn that the accuracy need not be all that great.

Once one has established the level of accuracy required, the next question must relate to what tools are available to produce a sufficient wave function. And it is at this point at which the constraints imposed by the various calculational tools must be considered.

Constraints and Strategies

Many of the problems in computational chemistry require the optimization of a geometry. In areas such as pharmaceuticals, one usually has structures containing several rings. There are many bond lengths, bond angles and dihedral angles to be optimized — and you doubtless do *not* want to optimize all possible variables! One learns fairly quickly that very stable structures (benzene rings, for instance) do not tend to undergo bond-length changes easily. Hence, when working with a structure containing benzene, one should first consider those elements which are most likely to undergo change. This is where one's chemical intuition comes into play in developing a strategy. Above, all, one needs a *strategy*.

If one is dealing with a structure containing some exotic element (often as not a transition metal), there is little recourse. Of the four systems described in Strategies I, only the Extended Hückel Method is easily capable of generating any kind of wave function. This is especially true if the structure is of any size. EH will not optimize geometries, so will need to obtain experimental coordinates to generate the wave function.

In dealing with large hydrocarbon structures (or any structure amenable to Molecular Mechanics), a new strategy is emerging that may prove to be most effective. If one needs a high-quality wave function for a very large structure, it is clear that running a large enough Ab Initio calculation will be impossible. What one *can* do is optimize the structure using Molecular Mechanics, then take this structure and run a single SCF calculation using a good basis set with some Ab Initio system. This strategy will generate a wave function over a good geometry and is an approach which is proving useful.

Undoubtedly, situations will arise when one find it necessary to carry out a large Ab Initio calculation. Strategies to approach this problem is some optimal fashion are also employed routinely. In doing an Ab Initio calculation, one would like to bring to bear a high-quality basis set such as 6-31G*. Although this basis set gives good geometries and energies, it is usually prohibitive to optimize a geometry with it. Now, however, we know that STO-3G (a relatively inexpensive basis set) gives good geometries if not such good energies. The first step, then, is to optimize your geometry at the STO-3G level and *then* use the resulting geometry as a starting point for a 6-31G* refinement run.

One could easily produce a book in which are outlined the many strategies of the type mentioned above.

How to Pose a Computational Question

There is no algorithmic method for rearranging all questions of chemical interest into computationally askable questions. At best, I can offer simple guidelines.

When confronted with a chemically interesting question one must immediately relate it to a wave function. What analysis or manipulation of the wave function can be related to the question? When dealing with reactions and reactivity of molecules, one calls upon the body of research known as Frontier Orbital Theory. In dealing with questions of measured quantities (such as spin densities, dipole moments, etc.), one must appeal to the technique which is known to yield the desired results most fully. Perspective and experience are required, but there is now a significant body of research from which to draw.

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