**Chemistry, Fluctuations and Consistency**

July 19, 2013

Bob Eisenberg

Chemistry is about chemical reactions that convert reactants to products described nearly always by some version of the law of mass action. A reactant in a chemical reaction has been described by a single concentration—independent of spatial location—for what seems centuries, indeed from before physicists believed that molecules existed. Chemical reactions have been described by the law of mass action for all that time without saying where the reactants and products were located.

Not worrying about the locations of reactants was a necessary approximation when the effects of location could not be simulated or computed. Chemists ignored spatial dependence so they could make progress even without the necessary mathematics. The spectacular success of chemistry would not have been possible (in my opinion) if chemists of the last centuries had to deal with both the atomic/electronic details of the reactions and the spatial dependence of reactants and products.

Chemical reactions are today resolved on an atomic scale of distance (say 10-10 meters) and an attosecond 10-18 sec time scale, smaller by some eight orders of magnitude and faster by some eighteen orders of magnitude than the resolution available when the law of mass action was introduced. The question we deal with is a modern one: can the law of mass action deal with reactions on such fast and small scales?

**Reactions and fluctuations in liquids.** The difficulty with fast time scales is seen clearly in reactions in liquids, for example in reactions in complex fluids derived from the ionic mixtures of sea water that make the chemistry of life. When the solutions of life are viewed with sufficient resolution, thermal fluctuations in concentration are obvious in both experiments and simulations. Roughly speaking such fluctuations occur in times of nanosecond 10-9 sec and shorter. Thermal fluctuations of concentrations like these cannot be removed by stirring because they can be too large, too localized, and too brief.

Fluctuations sometimes produce regions of high concentration. High concentrations produce fast rates of reactions in many cases. In these reactions, electron flow occurs very quickly in the regions that happen to fluctuate to a large concentration. Where concentrations are near their average value, reactions will occur much more slowly. One imagines that an attosecond 10-18 sec reaction quickly starts and reaches completion when a local concentration fluctuates to a value much larger (say 10×) than the spatial average.

**Chemical Reactions in Complex Fluids do not occur in a Spatially Uniform System** (for the most part). It seems likely that chemical reactions in fluids occur mostly at concentrations very different from the (spatial) average concentration of classical descriptions. They occur mostly in local regions of the complex fluid that have high concentrations of reactants, that have lifetimes long compared to attosecond 10-18 sec but short compared to nanoseconds 10-9 sec. After all, local concentrations fluctuate thermally to values much larger than the spatial average for very long times indeed compared to the time scale of attosecond 10-18 sec reactions. What is actually happening in such reactions has only a faint resemblance to the classical image of a chemical reaction in a spatially uniform system.

What actually happens in a fluctuating coupled system like this can be horribly complex, because it depends on the ***interactions*** of the fluctuating concentrations of reactants and products and the surrounding solvent and solute molecules of the complex fluid. And let us not forget interactions with the boundary conditions that allow the reaction to be contained, controlled and studied.

The fluctuations in concentrations have a direct effect through the law of mass action but they also have change the energetics of the chemical reaction itself and thus the rate ‘constants’. For example, fluctuating concentrations of charged reactants change the electric field and thus the motion of electrons and electrical component of the energetics of the reaction itself.

**Most reactants and products in a chemical reaction are polar and have significant electrical charge;** many have net charge. Most chemical reactions occur in complex fluids containing ions or significantly polar reactants or solvent. All reactions important for biology occur in complex fluids (like extracellular ‘Ringer’ solutions) that are ionic mixtures derived from seawater.

In ionic solutions, fluctuations in the number density of reactants and ions produce fluctuations in electric forces. These interact directly with the electrons moving in the chemical reaction itself. ‘Everything’ electrical interacts with ‘everything else’ because of the long range of electric forces. (Electric forces can extend to the boundaries before screening can occur. Many fluctuations and all attosecond reactions are too fast to be attenuated by screening.) The flow of electrons in the reactants (as they change into products) is coupled to the electrodiffusion of the surrounding solutes. Quantum chemistry of the chemical reaction is coupled inseparably (in an ionic complex fluid) to electrodiffusion of ions. Analysis and simulation must use mathematics that allows interactions of the ‘laws’ of quantum chemistry and ‘everything’ else.

**Quantum Chemistry is coupled widely in a complex fluid.** If quantum chemistry is to deal with this coupled system, all flows and forces must be dealt with consistently. (‘Consistently’ means that the each of the types of forces must satisfy physical laws established in experiments, e.g., electrical potential must be consistent with the charges present, according to Maxwell’s equations or their appropriate simplifications. Hydrodynamic flows must be consistent with Navier-Stokes equations. The influence of charge flows on hydrodynamic flows must satisfy Newton’s laws. Classical Brownian motion theory cannot be used, unfortunately, because it does not allow electrical forces to fluctuate as concentrations of ions fluctuate.)

In particular, chemical reactions in complex fluids need to be analyzed with theories and simulations that allow spatial fluctuations in concentration. Assuming spatial uniformity has been highly productive and appropriate in our history but that assumption is inappropriate (in my opinion) as we seek understanding on atomic scales of space and time.

**Reactions in ionic solutions are likely to occur in small spatial domains with concentrations of reactants very different from the spatial average**. Analysis will require theory and simulations that couple the electron flows (that make a chemical reaction) to fluctuations in the concentration of charges in the surrounding fluid (that make diffusion) The Schrödinger equation (or whatever) description of electron flow in the reacting molecules will need to be coupled to the Maxwell equations of the electric field in the solution (pun intended) itself (on the time scale of attosecond 10-18 sec) and then to the simulation or field equations of electrodiffusion and convection.

A consistent, fully coupled variational treatment seems to be needed to couple quantum, electrodiffusion, and hydrodynamic fields although other approaches may be possible that I don’t know about. In any approach, the fields must be interact consistently and correctly. It is very hard to guess all the interaction terms needed to enforce consistency. Consistency must be an output, a result of the mathematics, enforced by algebra not argument, in my view.

**Variational Methods Enforce Consistency.** The integro-differnetial equations derived in a variational treatment are automatically consistent, as long as the algebra is done right. For example, reactants and products in a reaction in a complex fluid could be described by an Energetic Variational description of electron flow in the chemical reaction that also includes the (free) energy and dissipation of electrodiffusion and convection. Ad hoc treatments of interaction are unlikely to be robust enough to be useful, or transferable from one set of conditions to another, particularly in the special crowded conditions in and near active sites of enzymes so important in biology and biochemistry.

Consistent treatments of reactions and ionic solutions are not well developed. Almost everything remains to be done before we can understand when the classical description of chemical reactions is a satisfactory approximation for reactants in complex fluids.

