

Chemistry is traditionally an experimental science. However, recent advances in computer technology and the development of highly efficient computer algorithms have opened the way for a viable alternative approach to chemistry: chemistry by computer. We use such computer calculations to determine the structures of molecules and to help understand how molecules react with one another. The procedure employed is called *ab initio* molecular orbital theory, the term *ab initio* signifying that the calculations are carried out from first principles using the laws of quantum mechanics. No experimental data other than values of fundamental physical constants are used. An important feature is that the calculations can be carried out as readily for reactive or hazardous species as for normal, stable molecules. They are therefore particularly useful in cases where experimental studies might be difficult or impossible. Properties that may be examined include molecular structures and reaction pathways, as well as many thermodynamic and spectroscopic properties.



During the year, we enjoyed a stimulating visit from Professor Mark Gordon from Iowa State University and four of the members of his research group, namely senior research associate Dr Mike Schmidt and three PhD students, Jamie Rintelman, Heather Netzloff and Ryan Olsen. This collaborative venture was funded by the US National Science Foundation, and included Professor Michael Collins and Dr Alistair Rendell on the ANU side. Greg Sandala joined the research group in March from the University of Windsor, Canada, having won an IPRS scholarship. We were delighted in November when Dr Michelle Coote was appointed Rita Cornforth Fellow.

Free Radical Chemistry

Radicals are ubiquitous in chemistry, biology, and polymer science. Because they are reactive species, they are often difficult to study experimentally and therefore theory has a potentially useful role to play in their characterisation. We have been using theory to determine radical stabilisation energies, with the important aim of seeing how individual substituents stabilise or destabilise a radical centre. We have also been examining the details of radical addition reactions and radical abstraction reactions, both of which are very important in biological chemistry and polymer chemistry. A particularly important application has been concerned with gaining a better understanding of the RAFT polymerization process with the ultimate aim of improved process control. (*with M.L. Coote, D.J. Henry, R. Gomez-Balderas, G.P.F. Wood, and H. Fischer [U. Zurich], M.W. Wong [U. Singapore]*)

Oxidative Damage to Proteins

An understanding of the oxidation of proteins by free radicals is of great importance because of its implication in a number of human disorders such as Alzheimer's disease, atherosclerosis, and diabetes, as well as aging. We have been using *ab initio* molecular orbital calculations to address the problem. Initial targets have included the cleavage of the peptide backbone following radical formation, and migration of the radical site within the peptide. (*with G.P.F. Wood, M.L. Coote, R. Jacob, C.J. Easton, and M. Davies [Heart Research Inst., Sydney], R.A.J. O'Hair [U. Melbourne], A. Rauk [U. Calgary, Canada]*)

Oxides and Hydroxides of Alkali and Alkaline Earth Metals

We have been examining the alkali metal oxides and hydroxides as a preliminary to investigating their interesting acid and base properties. Reliable experimental data are very sparse for these molecules. Their theoretical description is not entirely straightforward either and has necessitated incorporation of several new features and the development of new basis sets. (with M.B. Sullivan, A.P. Scott, T. Büsgen, and B.J. Smith [Walter and Eliza Hall Inst., Melbourne], J.M.L. Martin [Weizmann Inst. Israel], L.A. Curtiss [Argonne Nat. Lab. USA], S.R. Kass [U. Minnesota USA])

Enzyme-catalysed Reactions

Vitamin B₁₂ is one of nature's essential vitamins. We have used *ab initio* calculations to model reactions mediated by coenzyme B₁₂. Although these reactions have been extensively studied experimentally, there is certainly no consensus as to how they proceed. We find that protonation and/or deprotonation at appropriate sites facilitates the reactions, and that reactions that are facilitated by protonation (or deprotonation) are facilitated by the partial-proton-transfer that enzymatic hydrogen bonding can provide. Supporting evidence for our proposals has come from site-directed mutagenesis experiments. This and other recent examples provide strong encouragement for the use of computer calculations in a predictive manner in the study of enzyme reactions. Our most recent studies are being directed at the abstraction steps in these B₁₂-mediated reactions. (with G.M. Sandala, M.L. Coote, and B.T. Golding [U. Newcastle upon Tyne], D.M. Smith [Ludwig Maximilians U. Munich], S.D. Wetmore [Mount Alison U. Canada])

Development of Improved Theoretical Procedures

The ability to predict reliable thermochemistry represents a very important application of *ab initio* molecular orbital theory. We have recently been designing and assessing methods that are suited for predicting accurate thermochemistry for free radicals because these represent particular challenges for theoretical investigation. Our latest work has been concerned with methods that we have designated G3-RAD, G3X-RAD, G3(MP2)-RAD and G3X(MP2)-RAD. (with D.J. Henry, M.B. Sullivan)

Interaction of Metal Ions with Biological Systems

Metal ions are of great importance in biological function. We have embarked on a theoretical study to probe the interaction of metal ions with prototypical biological molecules. Our initial studies have focussed on the interaction of calcium dications with simple model systems in order to establish suitable theoretical procedures that can be applied to larger molecules. (with I. Corral, and O. Mó, M. Yáñez, Autonoma University of Madrid, Spain)

<http://rsc.anu.edu.au/research/radom.php>