Biochemical Reactions and Molecular Recognition
Professor Chris Easton

One theme of our research involves the analysis of chemical reactions, particularly those occurring in biological systems. Our objectives in this area are: i) to develop methods to regulate biochemical processes associated with disease states, ii) to produce physiologically active compounds with potential as pharmaceuticals, and iii) to develop biomimetic synthetic methods and catalysts. The other main field of research is in the area of supramolecular chemistry and molecular recognition, and involves the design, synthesis and evaluation of molecular hosts. Applications of this chemistry in the development of catalysts, molecular reactors and devices, and photochemical and thermal switches are being pursued.

Highlights of our recent results include the development of:

(i) enzyme inhibitors to down-regulate, and prohormones to up-regulate, the biosynthesis of peptide hormones;

(ii) models to predict the susceptibility of amino acids and peptides towards free radical processes associated with disorders such as Alzheimer's and cardiovascular disease;

(iii) molecular ratchets, sensors, shuttles, tweezers and switches;

(iv) molecular reactors to catalyse and control the regioselectivity of carbon-carbon bond forming reactions;

(v) novel spectroscopic techniques to analyse melamine-urea-formaldehyde and related resins, and improve the manufacture there of, and

(vi) compounds to inhibit and stimulate ion-flux through calcium ion channels.

Personnel highlights included the graduation of PhD students L Barr and M Gebara-Coghlan and MPhil student P G Dumanski. Dr H Onagi, who graduated in 2003, was awarded the 2004 J G Crawford Prize of the University for his PhD thesis, and the 2004 RSC Dean's Prize for best thesis. R Dawson received a prize for his presentation at the 20th Royal Australian Chemical Institute Conference in Cairns. A Philbrook received sponsorship from Orica (Australia) Pty Ltd to travel to Washington, USA, where she presented the opening lecture at the 38th International Wood Composites Symposium. Z Watts received an award from the National Institute of Biosciences to participate in the 9th International Symposium on Free Radicals in Corsica. Dr John Storey of the University of Aberdeen and Professor Keith Jones of Kingston University each visited for several months.

Free Radical Reactions of Amino Acids, Peptides and Proteins

Free radical reactions of amino acids and their derivatives are associated with a wide variety of disease states, including inflammation, and Alzheimer's and cardiovascular disease. They are also involved in the biosyntheses of many of the hormones that regulate biological activity, and are therefore intimately linked to the associated physiological and pathological conditions. This has prompted us to study aspects of the fundamental free radical reactions that are involved. Through this work we have developed models to predict the susceptibility of amino acids and peptides towards free radical processes associated with physiological disorders, and radical-resistant amino acids and peptides

have been designed and synthesised. We have produced enzyme inhibitors to down-regulate, and prohormones to up-regulate, the biosynthesis of peptide hormones. We are currently evaluating the potential of these compounds as pharmaceutical agents for treating human and animal disease states associated with hormone imbalances. *(With B J W Barratt, A Buchan, L Y F Chow, A J Herlt, I Li, A J Mortimer, L Radom, J S Simpson, Y-C Tsai, Z I Watts, A Wright)*

Supramolecular Chemistry and Molecular Recognition

This work exploits cyclodextrins as molecular hosts. Our early work in this area resulted in pharmaceutical formulations that are in everyday clinical use worldwide. In more recent studies modified cyclodextrins are being developed and exploited as molecular scaffolds for the construction of catalysts, molecular ratchets, shuttles, tweezers and switches, and photochemical devices. Another application of cyclodextrins involves their use to control the assembly of the components of chemical reactions, to facilitate the reactions and alter the outcomes. The cyclodextrins thereby act as reaction vessels, but at the molecular level. In this regard, we have developed demonstration systems to change the regio- and stereo-selectivity of reactions, and increase their rates by up to 100,000 times. We have also been exploring the synthesis of cyclodextrin rotaxanes, catenanes, knots and daisy chains of various topologies. These form the basis of molecular devices such as ratchets and motors, temperature and light sensors, photochemical frequency switches and molecular tweezers. Solid state and solution studies of cyclodextrin host-guest complexes and rotaxanes show that these assemblies may be designed to exploit the cyclodextrins as insulators of molecular filaments formed by the guests. This has potential, for example, in the development of microelectronic systems. *(With L Barr, S Bowen, M M Cieslinski, R Dawson, A J Herlt, J S Simpson, and S F Lincoln, J S Locke, B L May, J Patrick [U Adelaide])*

Other Collaborative Research

Other research involves studies of the structure of melamine-urea-formaldehyde resins, and the search for alternative reagents and improved manufacturing processes. Biochemical molecular recognition processes are also being studied, including the design and development of compounds to inhibit and stimulate ion-flux through calcium ion channels. *(With A Philbrook, J K Robinson, and A Dulhunty, M Casarotto [JCSMR, ANU], N Dunlop [Orica (Australia) Pty Ltd and the UnIChe program], A Ferrante, A Poulos [Adelaide Medical Centre for Women and Children])*

http://rsc.anu.edu.au/research/easton.php

The research group summit Mt Kosciusko in March