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Research Interests: Enzyme mechanisms, protein detection and spectroscopy, natural product chemistry and biosynthesis.

The central theme in our work is the integrated application of chemical, physical and biochemical techniques to solve problems in biological systems.

Enzyme Mechanisms: Research over the past ten years has focused on the enzymes of biotin biosynthesis in bacteria and this has led to the elucidation of the mechanisms of all of the enzymes involved. Current work, in collaboration with Dr Campopiano's group, builds on the techniques developed in this project and is extending these studies to key enzymes of lipid biosynthesis and biotin utilising pathways.

Specific Protein Detection: A significant number of problems in cell biology and medical diagnostics require the development of protein-specific labelling and detection methods. This is particularly problematic where distinction has to be made between isoforms of the same protein. We have recently been working on two approaches based on different types of chemistry. One project, relevant to studies in apoptosis in cancer cells, involves the development of substrate-based suicide inhibitors for labelling and inactivation of human caspase enzymes. The second ongoing project tackles the difficult task of development of reagents which selectively bind to the eight different isoforms of the 14.3.3 signalling protein, the levels of which can be used to diagnose neurodegenerative disease. Here we are using selective enrichment (SELEX) techniques to identify and isolate single ssDNA sequences which bind strongly to the individual isoforms.

Protein Measurement on Surfaces: Quantitative measurement of biological molecules on surfaces is relevant to problems in surgical instrument reprocessing and food hygiene but the techniques currently employed are relatively insensitive. In collaboration with Dr Jones's team we are developing a new approach to fluorescent probes for proteins which are fluorescent after reaction and have negligible background fluorescent. In parallel, our collaborator Dr Barton (Optical Physics, Heriot-Watt) has constructed a surface scanning fibre optics based spectrofluorimeter. Using this approach the limit for protein detection on stainless steel has been pushed to a level of a few pg/mm^2, comparable with the current limit for solution detection.

New Methods for Decontamination of Surgical Instruments: The fact that the infective agent of variant Cretzfeld-Jacob Disease (vCJD) cannot be destroyed by normal cleaning and sterilisation processes has caused grave public and professional concern. We are developing decontamination methods, based on RF gas-plasma chemistry, which allow surface biomolecule destruction to levels 1000 to 10,000 fold better than current practice and have shown that these effectively remove infectivity in a model system. We are now developing this technology, together with industrial collaborators, with the aim of introducing it to hospital practice.

Selected Recent References

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