In this issue

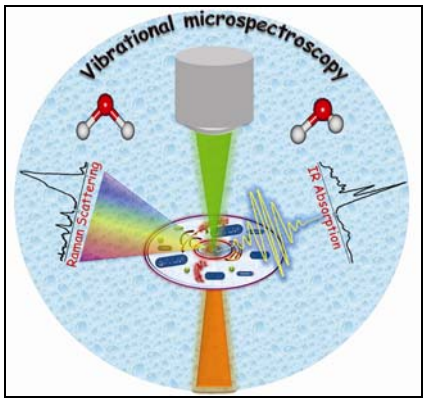
Chemistry and biology

The increasing interdisciplinarity in sub-divisions of science is evident in this issue of the journal as *Current Science* brings out a special section on research at the interface of chemistry and biology. This is part of the endeavour to celebrate 'chemistry' following the International Year of Chemistry 2011.

The remarkably beautiful architecture and shape of cells and cellular organelles are created by physical forces operating during the assembly of biological membranes from lipids and proteins. The business of cell is driven by the precise functional and structural compartments created by these membranes. One of the key features of the plasma membrane of eukaryotic cell is to provide mechanism for anchoring and integration of cell-surface receptors and proteins, and normally this is achieved by the intermediacy of hydrophobic transmembrane peptides with the ability to physically embed in the membranes. One exception to this mechanism was discovered in 1988 when it was found that a number of specialized proteins in African trypanosomes and mammalian brain are anchored to the plasma membrane by an altogether different architecture based on a complex glycolipid structure identified as glycosylphosphatidylinositol (GPI) anchor. This discovery of GPI anchor as an alternative mode of anchoring of proteins provided a new view of the plasma membrane organization. Since the first reports, a number of GPIs have been described, particularly from the parasitic protozoa and human biology, representing one of the most complex and biosynthetically expensive post-translational modifications in the cell. See **page 194**.

A central goal in chemical biology is to gain control over biological pathways using well-defined small molecules (ligands). The interactions of ligands with specific DNA sequences have provoked considerable interest in both basic research and medicine. Regulation of transcription machinery is one of the ways of achieving gene expression. The approaches towards transcriptional regulation show the possible strategies of manipulation of a few of these pathways using ligands. However, the critical information pertaining to the physical–chemical properties associated with ligand–DNA complexes with their biological effectiveness often remains unclear. Significant progress has been made towards the understanding of structural and dynamic properties of a number of ligand–DNA complexes. This provides key insights into the design of effective drugs. Interactions of ligands with DNA are studied using a variety of physical and biochemical methods in an attempt to determine the chemical and physical basis of novel binding phenomena such as DNA base sequence specificity, linkages between the geometry, correlation of structure–activity relationships and the thermodynamic properties. See **page 212**.

Bio-photonics is an emerging area in the modern research where the interaction of light with biological species is studied. Umapathy *et al.* (**page 232**) have mainly focused on the application of visible (for Raman) and infrared light to probe the molecular vibrations in biological species. Infrared and Raman spectroscopies have attracted great interest in the field of biology and medicine because of its ability to monitor cellular components based on their intrinsic chemical composition. The article covers the history, major developments and recent applications of vibrational spectroscopy on cells, tissues, biofluids and isolated biomolecules.



The practice of interdisciplinary sciences is best illustrated by the disappearance of boundary lines between the traditional disciplines of chemistry and biology. Although it is obvious that a deep understanding of biology requires knowledge of chemistry, these two disciplines of natural sciences have been guarded enthusiastically by most of the practitioners as independent areas. The advancement of science is rapidly breaking this unnecessary and unhealthy barrier. Krishnamoorthy (**page 266**) elaborates this point of view by taking a specific and important issue in biology, viz. how the biological activity is controlled by molecular dynamics and how this molecular dynamics can be observed by time-resolved fluorescence spectroscopy. While the activities addressed are biological in nature, the observation on molecular dynamics is a reflection of physical chemistry.

Traditionally, polyketide biosynthetic machinery paradigm has been primarily restricted to the biosynthesis of secondary metabolites that are not essential for the survival of the organism. Polyketide synthases (PKSs) are large multi-functional enzymes that are structurally and mechanistically related to fatty acid synthases. Genome sequencing projects revealed presence of a large number of PKS genes in organisms that are not traditionally known to produce secondary metabolites. A host of polyketide metabolites have now been shown to be essential for virulence and pathogenesis of *Mycobacterium tuberculosis* and pathogenic fungi. In *Dictyostelium discoideum*, an amoeba, PKS metabolites are

important for carrying out its complex life cycle. On the other hand, type III PKSs are believed to produce metabolites that could be functioning in their defense against environmental predators. Many of the PKS metabolites produced by different organisms also possess properties that make them commercially important for human beings. The varied functions and structures of PKS metabolites are contributed by concerted effect of subtle variations at genetic and biosynthetic level. Gokhale *et al.* (**page 277**) discuss the challenges in deciphering the '*pks* gene to PKS metabolite' path; tools employed by researchers in overcoming these obstacles; and the astounding versatility of these enzymes.

Kumar and Bachhawat (**page 288**) review current understanding of pyroglutamic acid. pyroglutamic acid or 5-oxoproline is the cyclic lactam of glutamic acid. The metabolite is ubiquitously present in living systems but its role is poorly understood. Pyroglutamic acid is found as an N-terminal modification in many neuronal peptides, most antibodies and many proteins. Pyroglutamate also exists as a free metabolite in living cells. In several genetic and certain metabolic disorders of humans, high levels of pyroglutamic acid are secreted in the urine in what is known as 5-oxoprolinuria. The precise reasons for the secretion of pyroglutamic acid in these disorders are still not clearly understood in many cases. The authors review the metabolism of this metabolite and how the role of this pyroglutamyl modification in proteins contributes to both the structural- and activity-related properties of the proteins, and how, as a free metabolite its role has gone beyond the mere description as an intermediary metabolite. The authors lament the paucity of research on pyroglutamate and indicate why far more research is needed in this area.

Enzymes are central to biological function and have been the subject of much research. Despite this, the mechanistic origin of the remarkable catalytic power of enzymes is still not completely understood. Karnawat *et al.* (**page 298**) discuss a fascinating aspect of enzymes, that of multi-substrate specificity – the ability of enzymes to catalyse the same chemical reaction on different small molecule substrates. This ability of enzymes is particularly interesting and relevant in nucleic acid binding enzymes. They illustrate this aspect of enzymes using four examples of enzymes that participate in nucleic acid metabolism and repair of damaged DNA. Structural studies have shown that an important requirement for function is complementarity of the enzyme and substrates. How multi-substrate binding enzymes retain catalytic efficiency while possessing complementarity remains to be understood. They also discuss various biophysical techniques that are being used to understand these properties with a special emphasis on vibrational spectroscopy. Vibrational spectroscopy is a relatively less used technique with enormous potential to provide detailed information on enzyme-substrate complexes in solution. Through sophisticated techniques such as ultraviolet resonance Raman spectroscopy, it is possible to selectively observe substrates within the active-sites of enzymes.