s8b.m4.o3 **Predicting function from protein structure comparison.** R. B. Russell, Bioinformatics SmithKline Beecham Pharmaceuticals New Frontiers Science Park (North) 3rd Avenue, Harlow Essex, CM19 5AW, UK
Keywords: structural genomics, bioinformatics

Structural Genomics experiments will provide many protein three-dimensional structures in advance of a clear understanding of protein function. If a protein is of known structure, but of unknown function, then functional insights typically come from comparison to other proteins of known structure. This talk will address two main areas relating to inferring function from structure comparison. The first area will deal with situations where a new structure shows obvious similarity to a protein adopting a similar fold. I will describe method of inferring evolutionary relationships (which are usually associated with functional similarities) from structural alignment, and discuss how functional details may be predicted even in the absence of evidence for homology. The second area covered will focus on instances where proteins show no overall similarity to other known protein structures. Specifically, I will describe a method for detecting local similarities at the main-chain or side-chain level that can imply a functional similarity. The talk will report several examples of functional insights gleaned by both methods of structure comparison.

s8b.m4.o4 **Systematics of Aromatic Hydrogen Bonds in Proteins.** T. Steiner*, G. Koellner *Institut für Chemie–Kristallographie, Freie Universität Berlin*
Keywords: protein, hydrogen bonding, data base survey

Hydrogen bonds with the electron-rich face of an aromatic ring acting as the acceptor, X–H···Ph, are commonly called 'aromatic hydrogen bonds'. Bond energies are typically about half as large as those of conventional hydrogen bonds X–H··O. Aromatic hydrogen bonds occur in crystals of many organic and biological molecules, and are particularly frequent in aromatic amines, tetraphenylborate salts, peptides and proteins (extensively surveyed in Ref. 1). In proteins, aromatic hydrogen bonds can be formed between suitable amino acids, between aromatic side chains and water molecules, and also between protein and bound ligand. In particularly rich systems like in acetylcholinesterase (AChE) complexes, various kinds of aromatic hydrogen bonds can be observed at the same time.[2]

To gain insight into the systematics of aromatic hydrogen bonding in proteins, we have performed a database analysis using 430 high resolution crystal structures (better than 1.5 Å) retrieved from the PDB. We consider aromatic hydrogen bonds in all possible configurations. Several repetitive structural motifs are identified, involving both main chain-to-side chain and side chain-to-side chain interactions. A considerable number of water-Ph contacts suggestive of aromatic hydrogen bonding is found. Because we use a large quantity of structural data, the geometrical characteristics of aromatic hydrogen bonds in proteins can be characterized with much better statistical significance than in previous studies.

[1] Desiraju, G. R., Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology*. Oxford University Press, 1999.
[2] Koellner, G., Kryger, G., Millard, C. B., Silman, I., Sussman, J. L., Steiner, T. Active-site Gorge and Buried Water Molecules in Crystal Structures of Acetylcholinesterase from *Torpedo californica*. J. Mol. Biol. (2000) 296, 713-735.