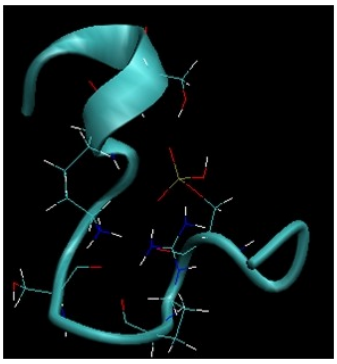
IT Services

Case Study

BlueBEAR provides a substantial computing resource that properly supports the research work of research staff and students at Birmingham. It provides a cost effective facility that optimises the effectiveness of research and ensures the University continues to be a world-class academic learning and research environment.

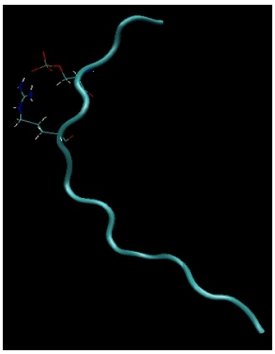
Using Molecular Simulation to Interpret Phospho-Peptide Structure from Mass Spectrometry



Challenges & Background

Proteins are the work horses of biology, being the machines responsible for most cellular processes. Once a protein has been initially made by a cell it may undergo further modifications. Phosphorylation is one such modification, being particularly important for cellular message passing, as indicated by the publication of more than 14,000 academic articles on the subject every year. Malfunction of this regulatory process leads to many disease states including cancer, and thus kinase inhibitors, drugs that block phosphorylation, have a market value of about 50 billion dollars annually. Currently, the structural consequences, and hence the mechanisms of action, of protein phosphorylation are poorly defined. If we look more closely at the structural changes associated with phosphorylation, and develop a rule set for how it changes protein structure and function then we will model better the biology of phosphorylation and the diseases associated with the dysregulation of phosphorylation.

Mass spectrometry (MS) has the potential for rapidly probing protein and peptide structures. MS is a technique for identifying the chemical constitution of a protein by fragmenting it and "weighing" the components. More precisely, the ionised fragments are separated according to their mass-to-charge ratios. Since the fragmentation process is dependent on the structure of the protein or peptide, the observed fragments also depend on the structure. Thus, MS is a potential tool for telling us about the structure of proteins, peptides, phosphopetides and phosphophorylated proteins. MS is a particularly appealing technique since it does not have the problems of protein crystallisation inherent in X-ray crystallography or of protein size inherent in NMR, the usual methods used to probe protein structure. This project is developing the application of computational modeling for the interpretation of MS data. Despite the use of simple physical models this is still a computationally intensive process. The aim is to characterise the structural changes induced by phosphorylation.



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