Dissertation abstract

The challenges of the post-genomic era call for an efficient automated study of proteins. NMR is a powerful tool capable of providing the information on protein structure, dynamics and interactions, yet its interpretation is today highly interactive. The present dissertation describes applications of three-way decomposition and molecular dynamics simulations to structural, dynamics and interaction studies.

Three-way decomposition is implemented in the MUNIN software and is used to extract structural data from a ^{15}N-NOESY-HSQC spectrum of azurin. Its performance is evaluated by comparison with an automated peak picker applied to the same spectrum and with a crystal structure, and the results are found to be correct and complete. This warrants the usage of MUNIN output in structure calculation. The program is also applied in the studies of protein dynamics by NMR relaxation experiments and is shown to be superior to conventional methods in resolving overlapped peaks, thereby significantly increasing the number of available dynamics probes in the protein. Interaction studies, such as often used in drug discovery by NMR, are treated by the three-way decomposition, which correctly identifies the spectra affected by ligand binding. The method is robust to usual spectral artefacts or mild changes in the experimental conditions.

Molecular dynamics simulations are the only tool which can give high resolution structural data in both space and time. It is used to study the mechanism behind the specificity of DNA recognition by the *Antennapedia* homeodomain. The mutation Q50K leads to a change in the recognised sequence from CCATTA to GGATTA. In both the wild type and altered complexes the entropic contribution is important for formation of the specific complex. It manifests itself, however, differently: with long lived water molecules in the former and by side chain mobility in the latter.

Keywords: three-way decomposition, 3D NOESY, NMR relaxation, drug discovery, DNA recognition, *Antennapedia* homeodomain

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