NMR studies of protein-small molecule and protein-peptide interactions

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Stellingen

Behorende bij het proefschrift:

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1. Although three paramagnetic NMR studies on protein-ligand complexes using 1D ^{1}H-NMR have been published, limited practical information concerning the applicability and limitations is available and therefore this area still requires further development. – This thesis, chapter 2

2. Chemical shift perturbations (CSPs) caused by direct contact with ligand and indirect conformational changes cannot be distinguished by simply mapping of CSPs on FKBP12. – This thesis, chapter 3

3. With two-armed probes, the magnetic susceptibility tensor can be predicted with sufficient accuracy to provide a low-resolution model of the ligand orientation and the location of the binding site without resonance assignments of the protein. – This thesis, chapter 4

4. In the complex of plastocyanin with charged peptides, the latter interconvert between many different orientations in fast exchange on NMR time scale. – This thesis, chapter 5

5. Paramagnetism, once considered a severe drawback in NMR, has now contributed significantly in structural biology and complemented existing NMR tools.
   – Bertini, I. et al. *Chem. Rev.,* **1993,** *93(8),* 2833-2932.
   – Otting, G.. *Annu. Rev. Biophys.,* **2010,** *39,* 387–405.

6. In ligand-observed NMR experiments, it is now possible to obtain information about the location of the binding site and the binding mode of the ligand.
   – Sledz, P.; Abell, C.; Ciulli, A. In *NMR of Biomolecules: Towards Mechanistic System Biology*; pp. 265–280.

7. The excellent predictability and rich information in pseudocontact shifts from a paramagnetic center in a protein allow the simultaneous determination of the conformation, orientation, and location of the bound ligand.
   – This thesis, chapter 4; John, M. et al. *J. Am. Chem. Soc.*, **2006**, *128*, 12910–12916.

8. Although there is a variety of *in vitro* approaches that can address particular interactions, there is always a need for new techniques.
   – Wienken, C. J. et al. *Nat. Commun.*, **2010**, *1:100.*

9. Nature can do more than scientists. Therefore scientific advances are often inspired by Nature and findings discovered from Nature.

10. Diversity is the art of bonding individualities together in a seemingly random and chaotic but actually purposive and organized way.

Jia-Ying Guan, Leiden, 2nd December 2013