



Medical University of Graz

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Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging
Molecular Biology and Biochemistry

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SEMINAR

"Protein Complexes in Cell Regulation"

Prof. Dr. Rolf Boelens

*Bijvoet Center for Biomolecular Research
Utrecht University, The Netherlands*

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NMR spectroscopy has developed to an invaluable tool to investigate the structure and dynamics of biomolecules. It provides unique detailed information on the interactions between biomolecules which can be weak and transient, that cannot be easily obtained by other methods. This progress is due to technical advances in NMR spectroscopy (multidimensional NMR and high-field NMR instruments), in protein production and $^{13}\text{C}/^{15}\text{N}/^2\text{H}$ isotope labeling, and considerable advances in computing.

At Utrecht, we use NMR spectroscopy to study structure and dynamics of protein-protein and protein-DNA complexes involved in signaling, transcription and DNA repair. Studied examples are (i) E.coli Lac repressor,¹ (ii) the human XPF-ERCC1 DNA repair complex,² (iii) the Rad6-Rad8 ubiquitination complex,³ (iv) nucleosome structure and dynamics,⁴ and (v) Hsp90 chaperone complexes.⁵ $^{13}\text{C}/^{15}\text{N}$ isotope labeling was required for all NMR studies, and in several cases complemented with ^2H labeling. Many complexes were modelled using our docking procedure Haddock.⁶ In many cases the NMR studies were complemented with biophysical data and results from complimentary structural biology techniques.

The different examples demonstrate the strength and flexibility of NMR for studying the structure and dynamics of proteins and complexes involved in cellular regulation.

1. Kalodimos CG et al, Chem Rev **2004**, 104, 3567-86; Loth K et al, J Biomol NMR **2013**, 56, 41-49
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3. Huang A et al, J Mol Biol **2011**, 410, 424-35; Hibbert RG et al, PNAS 105 **2011**, 5590-95
4. van Nuland R et al, Epigenetics & Chromatin **2013**, 6:12;
5. Karagoz GE et al, PNAS **2011**, 108, 580-85 ; Karagoz GE et al, Cell **2014**, 156, 963-74
6. Dominguez C et al, JACS **2003**, 125, 1731-37; van Dijk AD et al, FEBS J **2005**, 272, 293-312