**Molecular Motion and Heteronuclear Relaxation Part I – Lecture Outline**

**Chris Brosey, 11/16/2010**

**Overview**

**Why study biomolecular dynamics?**

**Brief survey of protein motion:**

*Global rotational diffusion – the diffusion tensor*

*Local NH bond fluctuations – the model-free formalism, extended model-free formalism*

*Bringing all motions together – the spectral density function*

**Finding a way to study motion with NMR – how motion stimulates relaxation of excited nuclei**

**How can we measure protein motion by monitoring NMR relaxation?**

*Expressions for relaxation rates in terms of spectral density values at transition frequencies, J(w)*

**Molecular Motion and Heteronuclear Relaxation Part II – Lecture Outline**

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**Measuring relaxation rates – R1, R2, and NOE pulse sequences and data analysis**

**Spectral density mapping**

*Full versus reduced approaches*

**Analysis of Motion**

*Diffusion tensor extraction*

*Model-Free analysis*

*Brief overview of different schools of thought – ModelFree (Palmer), relax (d’Auvergne)*

**Examples from our lab and the literature**

**Up and coming areas for biomolecular dynamics and NMR relaxation**

**Molecular Motion and Heteronuclear Relaxation**

**References and Further Reading**

**Reviews**

Korzhnev, D.M., Billeter, M., Arseniev, A.S., and Orekhov, V.Y. NMR studies of Brownian tumbling and internal motions in proteins. *Proj. Nuc. Mag. Res. Spec.*, **38**: 197-266 (2001).

Palmer, A.G. NMR probes of molecular dynamics: Overview and comparison with other techniques. *Annu. Rev. Biophys. Biomol.*, **30**: 129-55 (2001).

Luginbuhl, P. and Wuthrich, K. Semi-classical nuclear spin relaxation theory revisited for use with biological macromolecules. *Proj. Nuc. Mag. Res. Spec.*, **40**: 199-247 (2002).

Palmer, A. NMR characterization of the dynamics of biomacromolecules. *Chem. Rev.*, **104**: 3623-3640 (2004).

Morin, S. A practical guide to protein dynamics from 15N spin relaxation in solution. *Prog. NMR Spec.* (in press).

Kleckner, I.R. and Foster, M.P. An introduction to NMR-based approaches for measuring protein dynamics. *BBA - Proteins and Proteomics* (in press).

Boehr, D.D., Dyson, H.J., and Wright, P.E. An NMR perspective on enzyme dynamics. *Chem. Rev.* **106**: 3055-79 (2006).

**Diffusion tensor calculations**

Bruschweiler, R., Liao, X., Wright, P.E. Long-range motional restrictions in a multidomain zinc-finger protein from anisotropic tumbling. *Science*, **268**: 886-80 (1995).

Tjandra, N., Feller, S.E., Pastor, R.W., and Bax, A. Rotational diffusion anisotropy of human ubiquitin from 15N NMR relaxation. *JACS*, **117**: 12562-66 (1995).

Fushman, D., Xin, R., and Cowburn, D. Direct determination of changes of interdomain orientation on ligation: Use of the orientational dependence of 15N NMR relaxation in Abl SH(32). *Biochemistry*, **38**: 10225-30 (1999).

Walker, O., Varadan, R., and Fushman, D. Efficient and accurate determination of the overall rotational diffusion tensor of a molecule from 15N relaxation data using computer program ROTDIF. *J. Mag. Res.*, **168**: 336-45 (2004).

**Model-free formalism (MF) and Extended model-free formalism (EMF)**

Lipari, G. and Szabo, A. Model-free approach to the interpretation of nuclear magnetic resonance relaxation in macromolecules. I. Theory and range of validity. *JACS*, **104**: 4546-59 (1982).

Lipari, G. and Szabo, A. Model-free approach to the interpretation of nuclear magnetic resonance relaxation in macromolecules. II. Analysis of experimental results. *JACS*, **104**: 4559-70 (1982).

Clore, G.M., Szabo, A., Bax, A., Kay, L.E., Driscoll, P.C., Gronenborn, A.M. Deviations from the simple two-parameter model-free approach to the interpretation of nitrogen-15 nuclear magnetic relaxation of proteins. *JACS*, **112**: 4989-91 (1990).

**Classic examples of heteronuclear relaxation studies and model-free analysis**

Palmer, A.G., Rance, M., and Wright, P.E. Intramolecular motions of a zinc finger DNA-binding domain from xfin characterized by proton-detected natural abundance 13C heteronuclear NMR spectroscopy. *JACS*, **113**: 4371-80 (1991).

Mandel A.M., Akke, M., Palmer, A.G. Backbone dynamics of *Escherichia coli* ribonuclease HI: correlations with structure and function in an active enzyme. *J. Mol. Biol.*, **246**: 144-63 (1995).

**Hydrodynamic R1 and R2 prediction software**

De la Torre, J.G., Huertas, M.L., and Carrasco, B. HYDRONMR: Prediction of NMR relaxation of globular proteins from atomic-level structures and hydrodynamic calculations. *J. Mag. Res.*, **147**: 138-46 (2000).