UNIVERSITY OF RHODE ISLAND
Department of Chemistry

GRADUATE STUDENT HOSTED SEMINAR

Room 234 Pastore Hall
3:00 p.m, Monday, Oct. 5, 2015

Prof. Robert G. Griffin

Chemistry Department
MIT
Cambridge, MA

"Amyloid, Membranes, Microwaves and the Magic Angle"

HOSTS

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Amyloid, Membranes, Microwaves and the Magic Angle

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This presentation will selectively cover three closely related topics that employ magic angle spinning (MAS) NMR, dynamic nuclear polarization (DNP) or both.

In the first we determine the atomic resolution structure of amyloid fibrils. Many peptides and proteins form amyloids whose structures are of considerable pathological as well as functional importance. However, these assembles do not diffract to high resolution and are insoluble, and therefore the two primary tools of structural biology, X-ray diffraction and solution NMR, are not applicable. We therefore have developed a ensemble of MAS experiments that permit, together with cryoEM, the determination of high resolution fibril structures. We demonstrate the methodology with studies of the polymorphic fibrils prepared from the small peptide YTIAALLSPYS ($TTR_{105-115}$) derived from the protein transthyretin. In addition, we demonstrate the applicability of this approach to disease related amyloidiogenic proteins – β_2m and Aβ, the proteins associated with dialysis related amyloidosis and Alzheimer's disease, respectively.

Second, we discuss structural studies of the voltage dependent anion channel (VDAC) a 283 amino acid membrane protein in 2D crystalline bilayers that utilize PAR and PAIN dipolar recoupling sequences and photocycle intermediates of bacteriorhodopsin, a 248 amino acid membrane protein, that incorporate recoupling and DNP.

Finally, we discuss dynamic nuclear polarization (DNP) which utilizes subterahertz microwaves (~150-600 GHz) generated by gyrotron microwave sources together with paramagnetic polarizing agents to enhance the sensitivity of MAS NMR experiments. Specifically, we irradiate electron-nuclear transitions that transfer the large electron polarization to nuclear spins. We have obtained enhancements up to $\varepsilon\sim400$ in recent CW experiments and $\varepsilon\sim300$ with pulsed microwaves. DNP is easily incorporated into structural studies of both amyloid and membrane proteins.