2000 PROGRAM

8:30 a.m. **Registration and Continental Breakfast**
Atrium (Room 1-65), William T. Young Library

9:00 a.m. **Welcome by Dr. Fitzgerald Bramwell, Vice President for Research and Graduate Studies, University of Kentucky - Auditorium (Room 1-62), William T. Young Library**

9:05 a.m. **Introductory Remarks - Dr. Anne-Frances Miller, University of Kentucky**

9:10 a.m. **Dr. Michael F. Summers, University of Maryland Baltimore County**
"NMR Studies of HIV-1 Genome Recognition and Retrovirus Assembly"

Progress made toward understanding the molecular determinants of HIV-1 genome recognition and packaging will be presented. Current studies focus on interactions between the HIV-1 nucleocapsid protein and the stem loop recognition elements of the Psi-packaging signal, including RNA stem loops SL2 and SL3. In addition, structural studies of the capsid proteins of the HIV-1 HTLV-I and RSV retroviruses suggest a new mechanism for capsid assembly that involves oxidation of conserved cysteines, triggered as the assembly virus enters the oxidizing environment of the bloodstream.

10:10 a.m. **Break**

10:30 a.m. **Dr. David E. Wemmer, University of California at Berkeley**
"A Structure Based Approach to Design of Sequence Specific Minor Groove Ligands"

Some years ago we began structural studies of the natural product distamycin-A, which binds to A-T rich sequences in DNA, using NMR spectroscopy. With a minimum binding site of four consecutive A-T pairs the distamycin bound in the center of a region of narrow minor groove. As we looked at other combinations of A-T pairs we identified a new type of complex, one in which two distamycin molecules bound side-by-side and antiparallel, in a region of wider groove. This structure lead us to consider groove width as a major factor in determining binding affinity, and allowed the successful implementation of a hydrogen-bond based recognition of G-C base pairs. To maintain high sequence specificity, and to enhance affinity, it was logical to tether the ligands together. With a combination of these ideas it is now possible to design a ligand to bind almost any DNA sequence of interest with high affinity (dissociation constants in the nanomolar range) and good specificity (incorrect sequences being bound 10-100 fold less tightly than correct ones). The evolution of this design, and the current state of our understanding of the binding modes will be described in this talk. Examples of the uses of such ligands in a biological context will also be given.

11:30 a.m. **Dr. H. Peter Spielmann, University of Kentucky**
"NMR Spectroscopy of Novel Materials"

Fullerenes are a new allotrope of carbon with new uses, properties and possibly, new synthetic rules. Therefore, we are using ^{13}C NMR spectroscopy and theoretical calculations to correlate chemical shifts, pyramidalization, and hybridization with observed regiochemistry of addition in fullerene derivatives. Thus, we are developing a theory of fullerene reactivity.

12:00 p.m. **Buffet Lunch, Faculty Club [Please return registration card by March 31, 2000 for reservations. Cost to be paid in advance or at registration: Faculty/ Guest ($10.00); Graduate Student ($5.00).]**

2:00 p.m. **Dr. Stanley J. Opella, University of Pennsylvania**
"NMR Spectroscopy and Functional Genomics"

The structures of individual proteins and their complexes with small molecules, peptides, and nucleotides are being determined at an increasingly rapid rate. However, most biological functions are carried out in a coordinated fashion by groups of proteins from a single operon or large complexes organized as supramolecular structures, such as membranes or viruses. As a result, the structures of only a fraction of the proteins can be solved using currently available high throughput methods. Only in exceedingly rare cases will all the structural and regulatory proteins of an operon or virus crystallize in forms suitable for x-ray diffraction or reorient rapidly in solution for NMR approaches. Further, proteins in complexes typically aren't soluble or, if they are soluble, don't reorient rapidly in aqueous solution. Fortunately, solution NMR methods can be adapted and solid-state NMR methods are well suited for studies of slowly reorienting, immobile or insoluble molecules. Examples of how NMR can be used to characterize the structures and dynamics of many proteins found, or soon to be discovered, in the course of sequencing genomes will be discussed.

3:00 p.m. **Break**

3:20 p.m. **Dr. Ad Bax, National Institutes of Health**
"Nuclear Magnetic Resonance of Weakly Aligned Proteins"

Weak alignment of molecules results in incomplete averaging of dipolar interactions. Provided the alignment is extremely weak (~10^{-3}), the NMR spectrum retains the simplicity and high resolution of regular liquid state NMR spectra, but nevertheless permits measurement of one- and two-bond dipolar interactions. These provide information on the orientation of internuclear vectors, which complements the conventional NOE and J coupling parameters. Such measurements not only make structure determination more robust, they also promise to expedite the process and to extend the size of proteins whose structure can be studied by NMR.

4:20 p.m. **Dr. Anne-Frances Miller, University of Kentucky**
"Insights Into Redox Catalysis from NMR Spectroscopy"

Essentially all of the chemical reactions in our bodies, and in biology, are mediated by enzymes which catalyze and control each reaction. Most of the reactions involved in respiration and primary metabolism involve gain or loss of electrons and are thus "redox" reactions. We are using NMR spectroscopy to learn how relatively large, slow and flexible molecules such as proteins can control the activities of individual tiny, fast, delocalized electrons, for such control is crucial to life.

5:00 p.m. **Optional Tour of the New NMR Facilities**

(http://www.chem.uky.edu/seminars/naff/welcome.html)

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Twenty-Sixth Annual Symposium on

Chemistry & Molecular Biology

established in the memory of
Anna S. Naff

NMR Spectroscopy in Biological Chemistry

SPEAKERS
Ad Bax
Stanley J. Opella
Michael F. Summers
David E. Wemmer

Friday, April 7, 2000

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