Approved 10/6/09

Prov Council 10.06.09

Center Recharter Proposal
August 2009

Center for Supramolecular Studies
College of Science and Mathematics
California State University at Northridge

Name: The name shall be: **The Center for Supramolecular Studies** and will be referred to herein as the **Center**.

Mission Statement: The Center exists to further the knowledge of the physicochemical properties of supramolecular assemblies. To fulfill this mission, we believe in the following values:

Values:

1. Commitment to high precision analysis including multiple spectroscopic methods. At present, this is made possible by recent advances in methodology and computer data fitting techniques of electron paramagnetic and time-resolved fluorescence quenching data.

2. Commitment to the design, synthesis, and use of strategically functionalized reporter molecules. An integral part of the Center's activities is a strong organic synthesis program incorporating spectroscopic labels through covalent derivatization of supramolecular constituents.

3. Commitment to employ techniques capable of reporting the dynamic aspects of supramolecular assemblies in the appropriate frequency range at relevant temperatures.

4. Commitment to involve students as well as faculty in all activities including teaching, learning, researching, and disseminating new knowledge.

Purposes: In keeping with the University's Mission statement affirming a "Commitment to Teaching, Scholarship, and Active Learning", the purposes of Center is to

1. Assist faculty and students in the development of research projects and grant proposals,

2. Form a group of teachers, researchers, and students committed to keeping abreast of scientific advancements in the field as well as disseminating new knowledge,

3. Assist faculty in the publication of important new knowledge arising from their research,

4. Promote the offering of seminars, workshops, and scientific meetings,

5. Serve as a focal point for inquiries from external funding agencies and the public with interest in supramolecular research.

Organization: The Center shall be a special purpose center. Participation in the Center will be open to interested faculty and students from all departments of the University.

The Center shall be administered by a Director and an Advisory Committee. The Director shall be appointed by the Dean of the College of Science and Mathematics with the advice of the Advisory Committee.

The Director shall be responsible for the general operation and administration of the Center, allocating funds, staffing programs and administrative operations, and promoting synergistic relationships among members of the Center. The Director shall prepare a yearly report of the Center's activities that will be distributed to the Dean of the College of Science and Mathematics and the Associate Vice President of Graduate Studies, Research, and International Programs.

The responsibilities for specific activities may be delegated by the Director with the advice of the Advisory Committee.

The Advisory Committee shall be composed as follows:

1. Director of Research and Sponsored Projects

2. Associate Vice President of Graduate Studies, Research, and International Programs

3. Dean of the College of Science and Mathematics

4. Two faculty members, one from the College of Science and Mathematics and another faculty member from outside the College, nominated each year by the Director and approved and appointed by the Dean of the College of Science and Mathematics.

5. The Director of the Center

The Advisory Committee will meet as needed to conduct business. It shall establish bylaws and operating procedures to ensure that the Center's activities promote the University's teaching and research missions. These bylaws and operating procedures shall be consistent with the policies of the University and the laws of the State of California.

Finances:

The Center shall be self-supporting through donations; grants and contracts from public or private organizations; proceeds from workshops, meetings, or clinics; and funds allotted through the Strategic Planning Initiatives of California State University at Northridge. The Director, with the advice of the Advisory Committee, shall be responsible for all financial functions of the Center and will assure the the fiscal soundness of the Center. Surplus funds will be disbursed by the Director to promote the purposes of the Center with the approval of the Advisory Committee. The Director shall include a financial statement in the yearly report of the Center's activities.

Resources:

No office or laboratory space outside that assigned to members of the Center shall be needed. Equipment and other property purchased by the Center will be managed according to the usual practices of the University.

The Dean of the College of Science and Mathematics will be responsible for the oversight of all funds.

Outline of Report:

Publications of the members of the Center
Grant Applications of the members of the Center
Grant Awards to the members of the Center
Funds accrued to the Center.
Financial statement.
Summary of seminars, workshops, and scientific meetings

Period of Operation:

The Center shall be dissolved as of June 30, 2014 unless this charter is renewed prior to that date.

Appendix: Charter membership and current focus.

Current Focus: A. Self assembling aggregates such as micelles and vesicles. B. Bimoleculare collisions in liquids.

A. Why micelles are important: Micelles have long been the subject of intense world-wide scientific investigation with, among others, the following goals: (1) to better understand colloidal physicochemical phenomena; (2) to elucidate the role of micelles formed in lipoproteins and as substrates of lipid metabolizing enzymes; (3) to provide models to test theoretical predictions of the behavior of compartmentalized liquids; and (4) to exploit the fact that micelles can act as unique reaction media. The study of micelles encompasses a wide range of disciplines interested in problems that range from the highly theoretical to the practical. Theoretical problems such as micelle structure and dynamics and statistical distribution of additive molecules remain to be solved. Practical concerns such as the elimination of environmental pollutants, viscosity control, oil recovery, drug delivery, decontamination after chemical warfare, and solar production of energy are in need of further study. In addition to their use as models, micelles are directly exploited by nature to solve the problem of transporting water-insoluble molecules in biological systems, for example, in blood and the digestive system. The structure and dynamics of these naturally occurring aggregates are not well understood at the present.

Problems curently being addressed in the study of micelles

1. Micelle size and size dispersion. A satisfactory theoretical understanding of the aggregation numbers of ionic micelles is not available to this day despite claims to the contrary. The growth of these micelles with increasing surfactant concentration and/or added salt cannot be predicted at present by any available theory. The problem in the past has been a lack of precision data against which to test theory. A newly developed EPR technique (Bales, et al., 1998) is capable of detecting relative micelle aggregation numbers in SDS with a precision of about one molecule. By combining our own measurements and literature results, we have derived (Quina et al., 1995) an empirical equation for the case of the often studied sodium dodecyl sulfate (SDS). Such formulations are important because they offer not only precise tests of theory but also foundations to design new experiments and methods to compare existing data taken under different experimental conditions. This type of careful study needs to be extended to other types of micelles.

We have chosen the well established method of time-resolved fluorescence (TRFQ) quenching together with emerging electron paramagnetic resonance (EPR) techniques to study aggregation numbers. These were chosen because of their ability to study simultaneously the dynamics in the frequency range pertinent to micelles. Our approach is to study the same system using both techniques in order to eliminate the need for assumptions about the statistical distribution of additive molecules.

2. Collision frequency of additive molecules. Collision rates in membrane mimetic systems such as micelles and vesicles are typically of order 3×10^7 s^{-1} thus a technique sensitive to collisions on this time scale is required and thus far only two have been successful: TRFQ and EPR. Both techniques employ an indicator (e.g. pyrene for TRFQ and a nitroxide free radical for EPR) and both rely upon measuring the effect of added molecules (quenchers or paramagnetic broadeners). Since nitroxide free radicals and a number of other paramagnetic molecules effectively quench fluorescence, it becomes possible to design a wide variety of experiments to study essentially the same system using both techniques, substantially increasing the information available. TRFQ has been used to study dynamics in micelles for many years and is highly developed, while EPR has only recently been developed (Bales and Stenland, 1993) for this purpose. In recent work (Bales and Almgren, 1995; Bales and Stenland, 1995), we have demonstrated that EPR and TRFQ give results that are consistent with one another in a model system provided that the statistics of the distribution of the quencher/broadener is properly treated. This means that EPR may be used to extract collision rate information that previously was only available from TRFQ. In experiments using micelles as model membranes, we strive to use probes that mimic the structure of actual membrane components; thus, we are conducting a program involving the synthesis of spectroscopically labeled lipids, especially phospholipids.

3. Statistical distribution of additive (guest) molecules. Additive molecules are distributed among host micelles statistically, thus, the signal is a superposition of signals due to compartments containing zero, one, two, three, etc. additives. Either these component signals must be separated or the superposition must be interpreted under testable assumptions. So far, the separation has been effected in neither the TRFQ nor the EPR experiment; therefore, the superposition must be interpreted. Crucial to this interpretation is a correct understanding of the statistics because each component signal must be weighted properly. Almost all work to date in the literature has assumed a random distribution leading to the Poisson distribution even in the face of evidence that this assumption was inadequate. This unsatisfactory situation prevailed because, outside of a few attempts to treat special cases, no general statistical theory was available until 1993 (Bales and Stenland, 1993). We provided such a statistical theory in our 1993 paper and went on to test it using the tandem methods of TRFQ (Bales and Almgren, 1995) and EPR Bales and Stenland, 1995).

4. Location of additive molecules. Most of the work in this area has been carried out on frozen samples of micelles under the hope that the host micellar structure and location of the additive are preserved upon freezing. Micelles are highly dynamic structures, so, to understand micelles as reaction media, the location must be determined in a dynamic sense; i.e., in terms of the frequency with which a molecule encounters a certain position within the aggregate. We approach this problem operationally by measuring the collision frequency of collision with another molecule in a given location. This leads to a determination of the probability that one molecule encounters another. Obviously this is a bootstrap procedure in which

the relative locations of molecular pairs is postulated within a given model and then tested. As an example of the procedure, one could begin with a molecule that is most likely confined to the aqueous phase, measure the collision frequency with, e.g., a hydrophobic molecule, and define the location of hydrophobic molecule relative to the aqueous phase. Then one defines the location of a second hydrophobic molecule relative to the first.

B. Bimolecular Collisions in Liquids

Understanding bimolecular collision rates in liquids is fundamental to understanding chemical reactions in those media and has a vast literature extending over the last century. We have succeeding in modeling collision rates using nitroxide spin probes studied by EPR analyzing the data using software developed in the Center over the past several years. An important problem was solve in 2009 when we learned to separate spin exchange and dipolar interactions opening the way to directly measure both the encounter and re-encounter rates. Over the next 5 years, we shall concentrate on improving the theory which has not seen any major advances since the 1980's, primarily due to the fact that adequate experiment methods have not be available.

Personnel and Resources of the Center for Supramolecular Studies

Personnel: The current members of the Center are as follows. It is anticipated that other faculty members representing related fields will join the Center in the future.

Dr. Barney Bales is an EPR spectroscopist with experience using spin probes in liquids, liquid crystals, and micelles. He developed the statistical theory of additives in micelles and showed that EPR and time-resolved fluorescence quenching may be used as complementary techniques for structural studies and elucidation of dynamics of micelles.

Dr. Joseph Hajdu is a bioorganic chemist with experience in elucidation of metal catalysis in enzyme models including metal-binding antibiotics and the biochemistry of phospholipases. He has developed synthetic techniques to prepare molecules with spectroscopic labels (fluorescent or nitroxide) at a wide variety of positions. His role is to synthesize functionalized surfactant probes carrying reporter groups to be used in the physical measurements to be added to the micelles for spectroscopic measurements. His focus to date has been on phospholipids, due to their importance in the biological membranes, lipoproteins, and related structures.

Dr. Miroslav Peric is an EPR spectroscopist with experience using spin probes to form images in living mice. He is an expert in computer analysis of EPR spectra which allows the extraction of the experimental parameters with high precision. Recent developments in the interpretation of spin exchange (Bales and Peric, 1997) allow high precision determinations of molecular collision rates even at rather low concentrations of probes.

Dr. Radha Ranganathan is a laser physicist who recently turned to studies using time-resolved fluorescence quenching and now runs our TRFQ facility. She has developed her expertise in this area working with Mats Almgren of Uppsala University in Sweden and Frank Quina of Universidade de São Paulo, Brazil.

Resources

State-of-the-art EPR (Bruker 300ESP) and TRFQ (Edinburgh flash-lamp) spectrometers are housed in adjacent labs. The same labs contain a Sigma 701 automatic tensiometer capable of a wide range of surface chemistry measurements including computer controlled automatic critical micelle concentration determinations with temperature control. Sample preparation and computing facilities are in these same labs as is liquid nitrogen; thus the majority of the physicochemical experiments and analysis are performed in the same rooms. The standard range of modern equipment for organic chemical work, as well as a new Radiometer,PHM 290 pH-stat assembly, scintillation counter, Cary 3E UV-vis spectrophotometer, HPLC's, two Nicolet FT-IR, and one Perkin Elmer FT-IR-1600, 200-, and 400 - MHz Bruker FT-NMR spectrometers with multinuclear probes, a Perkin Elmer 243B polarimeter, and a Nonius CAD-4 X-ray diffractometer are available. Inert-atmosphere solvent purification apparatus, vacuum oven and freeze-drying apparatus are available. Organic synthesis is carrying out in two adjacent labs containing 8 fume hoods and totaling 1500 ft^2. When needed, the NMR Regional Facility at Caltech with a 500-MHz spectrometer and the Mass Spectrometry Center at UC Riverside are available by appointment.

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