Monthly Meeting
Richards Medal to Stephen J. Lippard

Meeting Report
What Is Different about Fluorocarbons?
by David M. Lemal

Summer Scholar Report
Toward a Small-Molecule Activated Protein Splicing System

Book Review
Having Faith, an ecologist’s journey to motherhood
by Sandra Steingraber
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For Additional Information contact: Department of Chemistry
102 Hurtig Hall
Northeastern University
Boston, MA 02115
Tel: (617) 373-2822
Monthly Meeting


Who Was Theodore William Richards?

Pictures on pp. 24-25

Meeting Report


ACS Short Course

Interpretation of Mass Spectra, May 2 and 3, 2002

Section Business

Candidates for 2003, Board of Directors Meeting of December 6, 2001

Summer Research Report


Book Review

Having Faith, an Ecologist’s Journey to Motherhood, by Sandra Steingraber; reviewed by Dennis Sardella

Puzzle Column

Solution to the February Puzzle: p. 21

Cover: Stephen J. Lippard in the Saddle

Deadlines:

May 2002 issue: March 14, 2002
Summer Issue: June 28, 2002 (National Meeting Issue)
Stephen J. Lippard is the Arthur Amos Noyes Professor of Chemistry and Head of the Chemistry Department at the Massachusetts Institute of Technology. He was born in Pittsburgh, Pennsylvania and educated in the Pittsburgh public schools. He studied at Haverford College (B.A., magna cum laude, 1962) and the Massachusetts Institute of Technology (Ph.D, 1965). After a postdoctoral year at MIT during 1965-66 he joined the faculty of Columbia University as an Assistant Professor of Chemistry, being promoted to Associate Professor with tenure in 1969 and to Professor in 1972. In January of 1983 he moved to MIT. He has taken sabbatical leaves at the University of Göteborg in Sweden, the MRC Laboratory of Molecular Biology in Cambridge, England, the Anorganisch-Chemisches Institut der Technischen Universität München, Garching, Federal Republic of Germany, and the University of California, San Diego.

Professor Lippard has held fellowships from the Woodrow Wilson Foundation, the National Science Foundation, The Alfred P. Sloan Foundation, The Camille and Henry Dreyfus Foundation, the Guggenheim Foundation, and the John E. Fogarty International Center.

He is a member of the American Chemical Society, The Royal Society of Chemistry, The American Crystallographic Association, The Biophysical Society. He was elected to Phi Beta Kappa (junior year), Sigma Xi, and the American Society of Biological Chemists, and a Fellow of the American Association for the Advancement of Science.

He was editor of the well-known series “Progress in Inorganic Chemistry” from Volume 11 to 40, w as an Associate Editor of the journal Inorganic Chemistry, is now an Associate Editor of the Journal of the American Chemical Society, was a Founding member of the Editorial Advisory Board for Chemical Research in Toxicology, and serves or has served on the editorial boards of Accounts of Chemical Research, Anticancer Drug Design, Bioorganic & Medicinal Chemistry, Bioorganic & Medicinal Chemistry Letters, ChemBioChem, Chemical and Engineering News, Chemical Research and Technology, Chemistry & Biology, Inorganic Chemistry, Inorganic Chemistry Concepts, Inorganica Chimica Acta, Journal of Biological Inorganic Chemistry, Journal of Inorganic Biochemistry, and Topics in Biological Inorganic Chemistry. He is the author or co-author of over 550 publications in the fields of inorganic and coordination chemistry, organometallic chemistry, and biological chemistry.

He has co-authored a book with Jeremy Berg entitled “Principles of Bioinorganic Chemistry.” He holds several US. and foreign patents. He has chaired several symposia at American Chemical Society national meetings, was Alternate Councilor for the Division of Inorganic Chemistry, was Chairman of the Bioinorganic Subdivision, and Chairman of the Inorganic Division. He has given over 50 named lectureships at universities both in this country and abroad, served as a panel member of the Medicinal Chemistry Study Section B and BMT Study Section of the National Institutes of Health, and has been a consultant for Engelhard Corporation, Exxon Corporation, Johnson Matthey Co., Procept, Smith Kline & Beckman, Suntech and John Wiley & Sons, Inc. He is currently Chairman of the Scientific Advisory Board of NAXCOR. He was Chairman of the 1985 Gordon Conference, Johnson Matthey Co., Procept, Smith Kline & Beckman, Suntech and John Wiley & Sons, Inc. He is currently Chairman of the Scientific Advisory Board of NAXCOR. He was Chairman of the 1985 Gordon Conference.
Abstract

Three Avenues in Bioinorganic Chemistry

The interface between inorganic and biological chemistry is broad and expanding. Metal ions are extensively applied in diagnostic and therapeutic medicine. The simple coordination compound cis-diamminedichloroplatinum(II), also known as cis-platin, has contributed significantly to the management of testicular cancer, formerly a leading cause of death of young males. This and related platinum anticancer drugs kill cancer cells through a multifactorial mechanism. The first step is activation to facilitate DNA binding. Structures of the major platinum-DNA adduct reveal distortions of the double helix that trigger the interaction of proteins involved in gene activation. Inhibition of the key cellular processes of transcription and nucleotide excision repair ensues. The discovery of a means of applying this information has afforded a new treatment for ovarian cancer, currently undergoing a phase I clinical trial in Boston.

Metal ions are also key components of enzymes. In methanotrophic bacteria, which use methane as their sole source of carbon and energy, a hydroxylase enzyme (MMOH) housing a carboxylate-bridged non-heme diiron unit activates dioxygen for the selective conversion of methane into methanol. This remarkable reaction proceeds in a stepwise fashion, the details of which have been delineated through structural studies of the enzyme and its partner proteins required for activity, mechanistic studies of intermediates, and experimental and theoretical analyses of the C-H bond activation step. Analogs of the active site have been synthesized that afford insight into the structures and chemistry of MMOH.

Neurochemistry is similarly replete with inorganic ions essential for function. New fluorescent sensors for zinc and nitric oxide have been obtained that have the potential to map neural networks in the hippocampus, the center of learning and memory.

Section News

January Section Meeting speaker David M. Lemal, as announced earlier, will be receiving the 2002 ACS Award for Creative Work in Fluorine Chemistry at the Orlando Meeting. There is an extensive write-up about his work in C&ENews 2002, Jan. 21, 54.

The following students will be receiving Fellowships of the Organic Division, ACS (name of the mentor and institution in parentheses):

David J. Guerin (Scott J. Miller, Boston College)
Rebecca T. Ruck (Eric N. Jacobsen, Harvard Univ.)
Jennifer V. Schaus (James S. Panek, Boston Univ.)

Our congratulations and best wishes to these Award/Fellowship recipients.

The Public is Invited.

Anyone who needs special services or transportation, please call Marilou Cashman a few days in advance so that suitable arrangements can be made.

Free Parking: in the Broadway St. Garage (3rd level or higher), enter from Cambridge St. via Felton St.

Next Meeting: April 18, 2002, Gustavus J. Esselen Award to Dr. Ronald Breslow, Columbia University. 5:30 Reception and Dinner, Harvard Faculty Club; 8:15 Award Meeting, Pfizer Lecture Hall, Mallinckrodt Building, 12 Oxford St. Dr. Breslow: "Chemistry Lessons from Biology and Vice-versa"
Who was Theodore William Richards?

by M.S. Simon

Adapted from The NUCLEUS, 1996 (3) 4 ff

The presentation of the Theodore William Richards Medal to Stephen J. Lippard this month recognizes ‘conspicuous achievement in the advance-ment of chemistry’, and we can take pride not only in the choice this year, but also in the many distinguished chemists who have won this honor in past years. [See the listing in THE NUCLEUS, 1998 (2) 24]. But as we honor Prof. Lippard, we are also honoring the memory of Richards himself. Who was this man?

The first award of what, at that time; was known as the Theodore William Richards Gold Medal (the medal is still gold, with a silver replica for informal display) was made to Arthur Amos Noyes in 1932. The Section Chairman, William Ryan, introduced the occasion with the following quotation by Henry Watterson:

A mound of earth a little higher graded
Perhaps upon a stone a chiselled name,
A daub of printer’s ink soon blurred and faded
And then — oblivion. That — that is fame.

Ryan went to point out that Watterson, as an observer in national politics, had developed a cynical attitude toward self-seeking politicians, and Ryan contrasts the impermanence of reputation of such with the seekers of truth for truth’s sake for whom true fame is imperishable. With reference to Richards he said, “True fame ... lives on, not merely to perpetuate the name of the individual and his accomplishments, but rather to inspire and encourage others who are serving similar ends.”

But in our age, when only “fifteen minutes” of fame are allowed, it behooves us to keep alive the names and accomplishments of our predeces-sors in chemistry. The Northeastern Section has many great chemists, but the earliest of the internationally renowned was Theodore William Richards. His Nobel Prize in Chemistry, awarded in 1914, was the first given an American chemist.

He was born in Germantown in 1868, was educated at home by his mother, a poet, and his father a marine artist. He became interested in science at the age of six when he was shown the rings of Saturn through a four inch telescope by Professor Josiah Parsons Cooke, Jr. of Harvard while the family was at Newport, R.I. At ten he was making Pharaoh’s Serpents with mercuric thiocyanate and coloring flames with various salts. He obtained money to set up a chemistry laboratory when he was 13 by printing on a hand press, copywriting, and selling an edition of his mother’s sonnets. He was allowed to attend chemistry lectures at the University of Pennsylvania, and at 14 entered and studied chemistry at Haverford. He received the Bachelor of Science at 17. He went to Harvard to study under Cooke and received a Bachelor of Arts and, at 20, after a year of very difficult research in which he demonstrated exceptional experimental skills in determining the atomic weight ratio of oxygen to hydrogen in water, earned the Ph.D. degree. A year in Europe on a Harvard fellowship gave him the opportunity of studying analytical techniques at Göttingen and visiting important laboratories in Germany, France, England, and Switzerland. He returned to Harvard in 1889 as an assistant and remained there for the rest of his years. When Cooke died, in 1892, Richards, already an assistant professor, was sent to Ostwald at Leipzig and Nernst at Göttingen to prepare himself to become the instructor...
Who Was TWR?
Continued from page 6

in physical chemistry. His rise to full professorship at Harvard in 1901 came quickly, when Göttingen attempted to recruit him.

His early work centered one what at the time was one of the major scientific problems, that of determining exact atomic weights. He explained his choice, “not merely because I felt more competent in that direction than in any other, but also because atomic weights seemed to be one of the primal mysteries of the universe. They are values which no man by taking thought can change. They seem to be independent of place and time. They are silent witnesses of the very beginnings of the universe, and the half-hidden, half-disclosed symmetry of the periodic system of the elements only enhances one’s curiosity about them. Moreover, among the many properties possessed by an element, the atomic weight seems one of the most definite and precise. Hence in trying to satisfy a desire which had as its object the discovery of more knowledge concerning the fundamental nature of thing’s, one naturally assigns to the atomic weights an important place.”

In the following years Richards and his students (if we include independent work of Baxter and Höngschmid, who had been trained by him) determined the atomic weight of 55 of the 92 known elements, in many cases in parts per ten thousand, in some, parts per hundred thousand. All of the elements whose atomic weights were the basis for determining the atomic weights of other elements were determined. His work on lead from uranium and from non-radioactive sources advanced acceptance of the theory of isotopes, the only conclusive evidence until the development of the mass spectograph.

He was always respectful to those on whose shoulders he was standing, J.J. Berzelius and J.S. Stas, pioneers in atomic weight determination, but when his superior methods showed that the Stas values had to be revised, he took the mantle on his own shoulders. A modest man, only after searching diligently for his own possible errors would he conclude that the Stas work had to be superseded.

He was guided to success by “his ability to foresee all sources of error and possible calamities which the average investigator would have overlooked completely”, reported his son-in-law, James B. Conant.

Richards put it thus, “Every substance must be assumed to be impure, every reaction must be assumed to be incomplete, every method of measurement must be assumed to contain some constant error, until proof to the contrary can be obtained. As little as possible must be taken for granted.”

It is illuminating to consider that much of his work was conducted in Boylston Hall, where his laboratory had been a stockroom, where the iron sashes of the fume hood rained rust, and a flood on the floor above caused the ceiling to collapse on him; where fumes from elsewhere in the building could ruin his experiments. Finally, the Wolcott Gibbs Memorial Laboratory, a gift of Dr. Morris Loeb, was built in 1912 and Richards had the facilities his work deserved.

The concentration on atomic weights suggests that Richards was solely an analytical chemist. Indeed, he was a superb analytical experimentalist, but his work in other areas of physical chemistry formed an important part of the total picture. His work began at the period when physical chemistry was aborning; van’t Hoff, Arrhenius, Ostwald, Nernst were the new names and the Zeitschrift für Physikalische Chemie was founded in 1887. Richards’ first student in physical chemistry was G.N. Lewis, to whom he assigned the study of the electrochemistry and thermochemistry of amalgam cells. Richards rejected the belief of that day that atoms were incompressible, developed evidence that atomic volumes change, and, according to Lewis, very nearly discovered the third law of thermodynamics in his studies of the relationship of changes in free energy and total energy accompanying a reaction. His inven-

Have you looked at the NESACS website?
WWW.NESACS.org
Meeting Report

What Is Different About Fluorocarbons?

An address delivered at the January 10, 2002 meeting of the Northeastern Section by David M. Lemal, Dartmouth College

Of all the elements in the Periodic Table, only fluorine can fully replace the hydrogens in virtually every kind of organic molecule.1 The properties and chemical reactivity of the resulting fluorocarbons and fluorocarbon derivatives are dramatically different from those of the parent compounds. From the inert, uniquely slippery polymer Teflon® to the liquids that carry oxygen in blood substitutes and breathing liquids, perfluorinated substances enjoy an abundance of uses, for many of which they are without equal. Fluorinated drugs and agrochemicals are also very important, but these compounds generally contain at most a few fluorines. The account that follows is focused on fundamental aspects of fluorocarbon chemistry, with emphasis on the relationship between perfluorinated compounds and their hydrocarbon counterparts.

Contrasts between these classes of compounds are traceable principally to three key differences between hydrogen and fluorine. The great disparity in electronegativity is of central importance, and fluorine’s ~20% greater van der Waals radius and bond length to carbon give rise to large steric effects in highly fluorinated molecules. In addition, lone pairs give fluorine π donor ability that hydrogen lacks.

The remarkable volatility and low refractive indices of fluorocarbons are attributable to fluorine’s status as the most electronegative element, for its tightly bound electrons resist polarization. The consequently weak London forces between fluorocarbons are largely responsible for their peculiar solubility properties. Immiscibility of fluorocarbon liquids with many other solvents forms the basis for fluororous biphase technology,2 which facilitates the separation of reaction mixtures.

Fluorine’s schizophrenic character as π donor but σ acceptor is clearly revealed in relative acidities. For example, pentafluorocyclopentadiene 13 (13 < pKα < 16) differs in acidity only modestly from the parent hydrocarbon (pKα = 163) because of opposing σ and π effects; but the perfluoropentamethyl derivative 25, with no lone pair-π repulsion in its anion, is at least 18 orders of magnitude more acidic than the parent (pKα ≤ -2). Further illustration of the interplay between σ and π effects is found in the relative gas phase stabilities of CH₃F₃₆ ions. The most stable of the four cations, and therefore the best compromise between stabilizing π and destabilizing σ effects, is CHF₂₆6.

Call For Papers

Northeast Student Chemistry Research Conference 2002

Open to undergraduates, graduates, and postdoctoral fellows in all areas of chemical research

Saturday, April 27, 2002

Boston University, Science Building

Visit the NESACS YCC website at http://people.bu.edu/nycc for details.

Abstracts will be accepted on this site. There is no registration fee.

Students are invited to present a poster or a 15 minute oral presentation.

Deadlines:

Oral presentations: April 5, 2002
Poster presentations: April 12, 2002

Undergraduate Research Poster Session

224th National Meeting of the American Chemical Society Boston, Massachusetts, August 18–22, 2002

The ACS invites undergraduate students to submit abstracts of their research papers for presentation at the Undergraduate Research Poster Session, which will be part of the program for undergraduates at this national meeting.

Abstracts must be submitted electronically:

• Go to the meeting web site: http://chemistry.org/portal/Chemistry?PID=acsdisplay.html&DOC=meetings%5Cboston2002%5Cindex.html
• Click on “Submitting a Paper”
• Click on “CHED” (Division of Chemical Education)
• Go to “Undergraduate Research Posters”

For further information, contact:
LaTrease E. Garrison, Undergraduate Programs American Chemical Society 1155 Sixteenth Street, NW Washington, DC 20036 Tel: (202)872–6166; Fax: (202)833–7732 e–mail: l_garrison@acs.org

Deadline for receipt of abstracts: April 8, 2002
Electron withdrawal by fluorine tends to lower in energy all of the molecular orbitals in a fluorocarbon, but the effect is much greater on $\sigma$-type than on $\pi$-type orbitals because of the compensating $\pi$ donor effect of the fluorine lone pairs (the “perfluoro effect”). Whereas the first ionization potentials ($\pi$) of ethylene and tetrafluoroethylene are virtually identical, the second ($\sigma$) differ by more than 3 eV. Another manifestation of the perfluoro effect is found in the hexafluorobenzene radical anion (3), wherein the half-filled LUMO is a $\sigma^*$ instead of a $\pi^*$ orbital.

Perfluoroalkyl substituents markedly stabilize strained carbon skeletons (the “perfluoroalkyl effect”), making possible the isolation and study of ring systems whose parent molecules are unknown or extremely unstable. Steric protection is responsible in part for the effect, but strengthening of skeletal C-C bonds is apparently also significant. As an example, Dewar thiophene (4) has been observed only in cryogenic matrices,10 but perfluorotetramethyl Dewar thiophene (5) has a half-life for aromatization of 5.1 hours at 160 °C.11 Isomerization of hexamethyl Dewar benzene (6) to the benzene is highly exothermic ($\Delta H \approx -57$ kcal/mol12), yet at 400 °C perfluorohexaethylbenzene is transformed in good yield into its Dewar isomer 7.13 This amazing reversal illustrates the importance that steric effects can assume in fluorocarbons, as the reaction is driven by relief of nonbonded repulsion in the benzene.

Ketones are strongly destabilized by fluorine substitution because of electron withdrawal from an already electron-deficient carbonyl carbon. In contrast to typical enols, perfluorenols are strikingly stable kinetically, resisting ketonization even in the presence of powerful acids.14 In some cases they are thermodynamically stable as well.15 Heptafluorocyclopentenol (9) is a case in point, as $K_{enol}$ for its formation from the cyclopentanone 8 is $\sim$130 even in carbon tetrachloride (cf. cyclopentanone itself, $K_{enol} = 1.1 \times 10^{-8}$ in H$_2$O16). Equilibrium constants for enolization of 2 $H$-perfluoroketones are far higher in Lewis basic solvents such as ether, THF and acetonitrile than in carbon tetrachloride because of the powerful hydrogen bond donor ability of perfluorenols.
The strain energy of hexafluorocyclopropane is greater than twice that of the parent hydrocarbon (~70 vs. 27.6 kcal/mol).¹⁷ The large amount of s character in the exocyclic carbon orbitals results in especially strong bonds to hydrogen, thus lowering the energy of cyclopropane, but electronegative fluorine atoms prefer bonding to carbon orbitals with more p character (Bent’s Rule¹⁸). Destabilization of 3-membered rings by fluorine is evident in the contrasting behavior of quadricyclane (10) and its perfluoro counterpart. The hydrocarbon has a half-life of 4 hours at 154 °C for ring opening to norbornadiene,¹⁹ but octafluorquadricyclane (11) rearranges to a tricycloheptene at temperatures just above 0°C.²⁰ Incidentally, the ¹⁹F NMR spectrum of octafluorquadricyclane spans more than 100 ppm, thus illustrating the great dispersion available in fluorine NMR that enhances its value as a structural tool.²¹

Other evidence for fluorine’s preference for sp³ over sp² hybridization at carbon includes the much greater heat of polymerization of tetrafluoroethylene as compared with ethylene: ΔH = -37.2 vs -22.7 kcal/mol.²² It is apparent as well in the thermal cyclization of perfluorodiene and –trienes. For example, decafluorohexa-1,5-diene (12) rearranges cleanly to the strained bicyclo[2.1.1]hexane 13,²³ a reaction that proceeds completely in the opposite direction with the parent hydrocarbons.²⁴ Cope rearrangement of perfluoro-1,5-dienes takes place via biradical transition states,²⁵ not concerted as with hydrocarbon dienes,²⁶ again in large part because of fluorine’s preference for p-rich carbon orbitals.

In contrast to cyclopropanes, fluorine substitution significantly stabilizes cyclobutanes, presumably because it reduces repulsion between nonbonded carbons by diminishing electron density in the center of the ring.²⁷ This helps to explain why the highly strained and reactive alkene 14 is stable at elevated temperatures²⁸ while the parent hydrocarbon dimerizes or polymerizes rapidly below 0 °C,²⁹ and why [2.2.2]propellane 15³⁰ ring opens a great deal slower at room temperature than the only previously isolated derivative of this very strained ring system (16).³¹
Meeting Report

Continued from page 10

Whereas the fragile central bond of 16 is cleaved electrophilically in an instant by bromine at –70 °C, 15 is stable even to sulfuric acid in acetonitrile at room temperature. The electron withdrawal by fluorine that makes 15 stoutly resistant to electrophilic attack renders it very susceptible to attack by nucleophiles, for all of the halide ions cleave its central bond under gentle conditions.32

We hope the above catalog of contrasts, though hardly complete, serves to highlight the special nature of fluorocarbons and their derivatives, and to help the reader understand why they continue to fascinate the researchers who study them.

Acknowledgement. The author is greatly indebted to the coworkers whose names appear in the references, and to the National Science Foundation, the Air Force Office of Scientific Research and the donors of the Petroleum Research Fund of the American Chemical Society for support of the work carried out in our laboratory.

References


14 For a concise summary of this work of Bekker, Knuyants et al., which encompasses 19 papers, see: Hart, H.; Rappoport, Z.; Biali, S.E. in The Chemistry of Enefs; Rappoport, Z., Ed.; Wiley: Chichester, 1990; p 502.


21 Emsley, J.W.; Feeney, J.; Sutcliffe, L.H. High Resolution Nuclear Magnetic Resonance Spectroscopy; Pergamon: Oxford, 1966; Vol. 2, Chap. 11. The range of 19F chemical shifts is ~300 ppm for organofluorine compounds and ~1000 ppm overall.


32 Smith, J.R., Ph.D. Dissertation, Dartmouth College, 1999

Nominations

Henry A. Hill Award for Outstanding Service to the Northeastern Section

Nominations for the Henry A. Hill Award for Outstanding Service to the Northeastern Section are invited. Nominations should be sent by August 8, 2002 to the Administrative Secretary, NESACS, Marilou Cashman, 23 Cottage St., Natick, MA 01760. A resume of professional activities and description of the nominee’s service to the Northeastern Section should be included. The Award is to be presented at the October meeting of the Section.

Michael J. Dube, Chair, Awards Committee
Applications Invited

The James Flack Norris and Theodore William Richards Undergraduate Summer Research Scholarships

The Northeastern Section of the American Chemical Society (NESACS) established the James Flack Norris and Theodore William Richards Undergraduate Summer Scholarships to honor the memories of Professors Norris and Richards by promoting research interactions between undergraduate students and faculty.

Research awards of $3250 will be given for the summer of 2002. The student stipend is $2750 for a minimum commitment of ten weeks of full-time research work. The remaining $500 of the award can be spent on supplies, travel, and other items relevant to the student project.

Institutions whose student/faculty team receives a Norris/Richards Undergraduate Summer Research Scholarship are expected to contribute toward the support of the faculty members and to waive any student fees for summer research. Academic credit may be granted to the students at the discretion of the institutions.

Award winners are required to submit a report (~5-7 double-spaced pages including figures, tables, and bibliography) of their summer projects to the NESACS Education Committee by November 8, 2002 for publication in The Nucleus. They are also required to participate in the Northeast Student Chemistry Research Conference (NSCRC) in April 2003.

Eligibility: Applications will be accepted from student/faculty teams at colleges and universities within the Northeastern Section. The undergraduate student must be a chemistry, biochemistry, chemical engineering, or molecular biology major in good standing, and have completed at least two full years of college-level chemistry by summer, 2002.

Application: Application forms are available on the NESACS web site at http://www.nesacs.org. Completed applications are to be submitted no later than March 22, 2002 to the Chair of the Selection Committee:

Professor Edwin Jahngen,
University of Massachusetts Lowell
Chemistry Department, Room 520
265 Riverside Street, Olney Hall
Lowell, MA 01854-5047

Notification: Applicants will be notified of the results by e-mail on April 26, 2002. Written confirmation will follow.
ACS SHORT COURSE

Designed to improve the skills and marketability of practicing B.S., M.S., and Ph.D. chemists.

The NESACS Committee on Continuing Education is pleased to sponsor this newly updated National ACS Two-Day Short Course, at a registration fee less than half of that charged at National and Regional ACS Meetings.

INTERPRETATION OF MASS SPECTRA

This Short Course is designed for chemical scientists who require the knowledge and skill of mass spectral interpretation. The course does not require expertise in advanced mathematics, physics, or theoretical chemistry. Registrants should have a basic knowledge of chemistry, and course work in organic chemistry is desirable. Participants should bring a basic calculator to the course.

DATES and TIME: Thursday, May 2, 2002; 8:00 a.m. – 5:00 p.m.
and Friday, May 3, 2002; 8:30 a.m. – 5:00 p.m.

PLACE: Snell Library, Room 90, Northeastern University, 360 Huntington Ave., Boston, MA

PROGRAM AGENDA:

Introduction to Chemical Bonding in Organic Molecules as it Pertains to Mass Spectrometry


Naturally Occurring Stable Isotope Abundances and Their Role in Peak Intensity

The Molecular Ion
   Odd-electron ions; the nitrogen rule; logical losses.

Fragmentation as it Relates to Structure, Elemental Composition, and Compound Type.

Mass Spectra of High Molecular Weight Compounds.

MS/MS Mass Spectra – What Are They and How Do We Deal With Them?

Fragmentation of Specific Compound Types – Aliphatic and Aromatic Hydrocarbons, Alcohols, Amines, Acids, Aldehydes, and Ketones.

Library Searches and Mixed Spectral Data

Chemical Ionization and Electron Ionization Spectra Used Together to Determine the Identity and Structure of an Unknown.

COURSE BONUS!

Bring your own mass spectra to the course for analysis. The instructor will help you to interpret your spectra and use them as examples for class discussion if appropriate.

INSTRUCTOR:

O. David Sparkman is an Adjunct Professor of Chemistry at the University of the Pacific in Stockton, Cal., and a consultant to the National Institute of Standards and Technology Mass Spectrometry Data Center. At the University of the Pacific he teaches courses in mass spectrometry and analytical chemistry and manages the mass spectrometry facility. He is on the Editorial Advisory Boards of the Journal of the American Society for Mass Spectrometry and the HD Science GC/MS Update – Part B. He is the author of Mass Spectrometry Desk Reference, and with J. Throck Watson developed the Mass Spectral Interpretation Quick Reference Guide. Professor Sparkman is one of the highest rated instructors in the ACS Short Course program.

PRE-REGISTRATION REQUIRED – Registration Fees:

ACS Members if received before Apr 17 ............... $450.00; after April 17 .......$525.00
Non-ACS Members if received before April 17 ....$550.00; after April 17 .......$625.00

There will be a limited number of scholarships for unemployed ACS Members on a space-available basis.

Parking Fee: about $14.00/day

University cafeterias will be available for lunches.

For further information contact: Prof. Alfred Viola at (617) 373 2809

Registration form for Short Course: Interpretation of Mass Spectra. May 2-3, 2002

Name: ____________________________________ Business Affiliation: ________________________________
Mailing Address: __________________________________ Telephone: ________________________________

Mail with remittance to:

(Please make checks payable to NESACS.
Sorry, we cannot accept credit cards or purchase orders.)

Prof. Alfred Viola, Chair
N NESACS Committee on Cont. Ed.
Department of Chemistry
Northeastern University
Boston, MA 02115
Board of Directors

Notes of Meeting of December 6, 2001

NOTE: Board Meetings are held on the monthly meeting day at 4:30 p.m. Section members are invited to attend.

Officers’ Reports:
Chair: T. Frigo announced that NESACS has received a mini-grant of $500 from the ACS Office of Diversity for the February 2002 joint meeting with NOBCChE.
T. Frigo relayed Dr. Shakhashiri’s appreciation for having been awarded lifetime membership to NESACS. He also sent a video-tape of the Holiday Lecture, to be kept by D. Lewis and to be made available on loan.
A meeting with officials of the Boston Museum of Science is to be held for planning for NCW 2002.
He reminded board members that annual reports are due.
Chair-Elect: M. Hoffman stated that for the February 14 Meeting (Valentine’s Day), in honor of the occasion, members’ “Special Valentines” are to be invited to the reception and dinner as guests of the Section.
Treasurer: J. Piper presented the November 2001 Treasurer’s Report. After some discussion, it was MOVED and VOTED to accept the report.
Standing Committees:
Bd. Of Publications: MIT is starting a Program in Science Writing which may offer an opportunity for cooperation.
The reader survey has been completed and results are being tabulated for later presentation.
A revised budget has been presented to the Budget Committee.
Help from YCC is sought for improving the website appearance.
Editor: The January issue is to be 24 pages, with the first summer scholar report to be in the issue.
Membership: M. Chen stated that two new members will be at tonight’s dinner.
Chemistry Education: R. Tanner stated several issues for next year’s “Connections to Chemistry” meeting: How to accommodate the increased number of applicants, how to maintain current costs per person, whether there can be industrial sponsorship.

Also, Chemmatters has been sent to all attendees of the 2001 “Connections” with a label stating “compliments of NESACS.”

Norris Richards Scholar papers have been submitted to the NUCLEUS. Only one of the Scholars has asked for support to attend the Orlando ACS Spring Meeting. The other three expect to present papers at the Boston ACS Fall Meeting.

The issue of section and personal liability was raised. Clarification of Section responsibility, such as for Section-supported travel to ACS Meetings is to be sought by the Chair with help from M. Strem.

Esselen Award: J. Koob reported (written report) that four nominations have been received and a committee meeting has been scheduled for December 18, 2001 to make a final selection. Six or seven members are expected to be present, one of them by speakerphone from California. Ways are to be sought for trimming the costs of the award meeting.

Other Committees:
Natl. Chemistry Week: D. Lewis MOVED as the sense of the Board for making a $2000 donation to the Bassem Shakhashiri Science Foundation in lieu of giving Dr. Shakhashiri an hono- rarium. So VOTED unanimously.

Summerthing: D. Lewis stated that Summerthing 2002 will again be at the Boston Red Sox, with the date to be determined after the game schedule is available. If it is possible to schedule this event during the August 25-29, 2002 National ACS Meeting in Boston, 1000 tickets will be ordered, otherwise 200 if the game is in June or July.

Younger Chemists: A. Tapper reported that the February 14, 2002 Career event is all set with 5 speakers from 3:00-5:30 pm, preceding the regular monthly NESACS meeting.

She stated that volunteers are needed for the April Research Symposium Organizing Committee.

Government Affairs: M. Hearn stated that the National OLGA is planning the 2002 State House Day. The State’s newest Congressman is to be contacted. The ACS Chemistry and Public Affairs Committee is modifying the Grass Roots Awards to recognize recipients on both the national and local level.

New Business: A. Heyn stated that it is time to activate a National Meeting Committee for the August 2002 ACS Meeting in Boston. M. Hof fman agreed to chair this committee.

From the minutes of M. Singer
The ability to perturb the activity of intracellular proteins in a specific, dose-dependent fashion with small molecules represents a significant boon to clinical and basic medical research. One general approach, chemical induction of dimerization (CID), uses small molecules to dimerize two different proteins, bringing these proteins in close proximity to one another. This approach has proven fruitful in the modulation of various important catalytic and signaling events, namely Fas-mediated apoptosis, eukaryotic gene transcriptional regulation, and activation of receptor tyrosine kinases (Belshaw et al., 1996, Amara et al. 1997, Rivera et al. 1996). Although CID’s have been useful in many biological processes, this approach has not been extended to the post-translational modification of protein levels. In this research, we aim to construct a ligand-activated intein that allows small molecule-dependent induction of protein levels using CID technology.

Protein splicing involves the excision of non-coding peptides called inteins that interrupt the coding extein sequences of a given polypeptide. This autocatalytic activity has sparked several structural and mechanistic studies (for review, see Perler, 1998). The intein structure is modular, with conserved N- and C-terminal regions and nucleophilic residues at splice junctions responsible for the acyl transfer reactions leading to extein ligation (Fig.1 Mills et al., 1998). Recent work in protein splicing has focused on the use of trans splicing elements, with each extein fused to either the N- or C-terminal half of the minimal intein. Splicing activity is then dependent on association between the two intein termini to form the active site (Mills et al., 1998; Evans et al., 2000).

Recently, Ozawa et al. have engineered a trans splicing system of the VDE intein from S. cerevisiae that is dependent on protein-protein interactions (Figure 2A; Ozawa et al. 2000). The authors split the VDE intein and an EGFP reporter in half (VDE N, VDE C; EGFP N, EGFP C) and coexpressed protein fusions of EGFP N, VDEN-calmodulin and M13 peptide-VDE C-EGFP C in E. coli. Splicing was shown to be dependent on the interaction between calmodulin and M13 peptide in E. coli, as constructs lacking these binding partners did not splice in trans to produce an EGFP signal.

† 2001 Norris/Richards Summer Scholar Boston, MA 02115
These results suggest that the reconstitution of the intein active site is a proximity-driven process, wherein the association of the N- and C-terminal intein fragments leads to \textit{trans} splicing. In this research, we sought to apply the CID system to protein splicing, by replacing the calmodulin and M13 peptide with FKBP (FK-506-binding protein) and FRB* (FKBP-rapamycin bonding domain), two proteins that interact in the presence of the macrolide rapamycin (Figure 2B, Liberles \textit{et al.} 1997).

**Experimental Plasmid construction.** Standard PCR cloning methods were used to construct the fusions EGFP\textsuperscript{N}-VDE\textsuperscript{N}-Linker-FKBP and FRB-Linker-VDE\textsuperscript{C}-EGFP\textsuperscript{C}. The mutant EGFP “m125” (E125I, I129C) used by Ozawa \textit{et al.} (2000) was used in this research. EGFP\textsuperscript{N} (EGFP\textsubscript{1-128}) was amplified from the pCI-EGFP plasmid (Clontech, Palo Alto, CA) and VDE\textsuperscript{N} (VMA\textsubscript{1-184}) was amplified from genomic DNA extracted from strain BY4741 (MAT\textit{a}, \textit{his3D1} \textit{leu2D0}, \textit{met15D0}, \textit{ura3D0}, \textit{fpr1::kanMX4}; Research Genetics, Huntsville, AL) using the Qiagen genomic DNA extraction kit (Qiagen, Inc., Valencia, CA). These two PCR products were ligated via mutually-primed PCR with external primers containing \textit{BamH}I and \textit{XhoI} sites, and cloned into the \textit{BamH}I-\textit{XhoI} sites of the galactose-inducible yeast expression vector pESC-Leu (Clontech). FKBP (FKBP\textsubscript{1-107}) amplified from plasmids available in the laboratory (Nyanguile \textit{et al.} 1997) was cloned into the \textit{XhoI}/NheI sites of pESC-Leu (Clontech). (The full construct is referred to as pESC-Leu-NTERM.) Similar techniques (mutually primed PCR followed by cloning) were used to clone VDE\textsuperscript{C} (VMA\textsubscript{1389-454}) and EGFP\textsuperscript{C} (EGFP\textsubscript{129-239}) into the \textit{SalI}/\textit{XhoI} sites of the galactose-inducible yeast expression vector pESC-His (Clontech). FRB* was amplified from plasmids already available in the laboratory (Liberles \textit{et al.} 1997) was cloned into the \textit{BamH}I-\textit{SalI} sites of pESC-His. (The full construct is referred to as pESC-His-CTERM.) The “Linker” residues were derived from Ozawa \textit{et al.} (2000) and incorporated into PCR cloning primers to confer flexibility to the signal tripartite fusion protein. The amino acid sequence of the N-terminal linker was ASNLENGRNG; the continued on page 18.
The Nucleus March 2002

sequence of the C-terminal linker was GNNDNNDV. For in vitro studies, the full N-terminal intein construct was subcloned from pESC-Leu-NTERM into the BamHI-EcoRI sites of bacterial expression vector pET-28b (called pET-28-NTERM; Novagen, Madison, WI); the C-terminal construct was subcloned from pESC-His-CTERM into the BamHI-XhoI sites of pET-28b (called pET-28-CTERM). Sequence confirmation of all constructs was performed by Seqwright, Inc. (Houston, TX).

Expression and solubility testing. Each pET-28b construct (pET-28b-CTERM and pET28b-NTERM) were transformed into BL21(DE3) lysogen competent cells (Novagen). The levels of expression at 25, 30, and 37°C for both constructs were assessed by growing one colony from each BL21(DE3) transformation in kanamycin (30 µg/mL)-supplemented Luria-Bertani medium (LB) to an optical density (OD600) of 0.4-0.7, inducing transcription via addition of isopropyl-β-D-thiogalactopyranoside (IPTG, final concentration 1 mM; control was uninduced), and allowing expression for 4 h. A 1 mL aliquot of induced and uninduced cells were pelleted; the supernatant was removed; the cell pellet was resuspended and lysed by boiling at 100°C for 10 min in SDS loading buffer (2% SDS, 0.25% bromophenol blue, 10% β-mercaptoethanol). The resulting lysates were subjected to SDS-PAGE on a NuPAGE 4-12% Bis-Tris gradient gel in MES electrophoresis buffer (Invitrogen, Carlsbad, CA). Experiments to assay the solubility of the expressed proteins were run in a similar manner, lysing cells via sonication in Lysis Buffer (500 mM NaCl, 50 mM Tris-HCl pH 8.0) and pelleting the lysates. Both the supernatant (soluble) and pelleted cell debris (insoluble) fraction were boiled in SDS loading buffer and subjected to SDS-PAGE as above.

Protein overexpression. One colony of the appropriate BL21(DE3) transformant was inoculated into a 1 L culture of kanamycin-supplemented LB, and grown at 37°C (pET-28b-NTERM) or 25°C (pET-28b-CTERM) overnight. A 50 mL aliquot of the stationary phase overnight culture was reinoculated into fresh 1 L kanamycin-supplemented LB, grown to OD600 0.4-0.7, and induced at the optimal temperature (25°C for C-terminal, 30°C for N-terminal) for 24 hr and 4 hr, respectively. Cells were pelleted, resuspended in 20 mL Lysis Buffer, and mechanically lysed via French press. Lysates were centrifuged at 15,000g for 20 min. The pET28b vector encodes hexahistidine tags at the N- and C-terminal ends of the recombinant proteins, and these His tags were used to purify the proteins via Ni2+ affinity chromatography. As such, the resulting supernatant was loaded onto an affinity column charged with 2 mL Ni2+ TALON resin (Clontech) and pre-equilibrated with 20 mL Lysis Buffer. The supernatant-containing column was incubated for 1 hr at 4°C under gentle shaking. Supernatant was allowed to flow through the column (“flow through”), and the column was subsequently washed 4 x 10 mL of Lysis Buffer (“wash”). The bound proteins were eluted from the column by addition of Elution Buffer (500 mM NaCl, 50 mM Tris-HCl pH 8.0, 100 mM imidazole) in 1 mL aliquots. Fractions were collected and assayed for protein using the Bradford assay (Bio-Rad, Hercules, CA), and protein-containing fractions were pooled (“eluant”).

Construction of yeast strain. In yeast cells, the FKBP ortholog Fprlp binds rapamycin to form a complex that binds Torlp, ultimately leading to growth arrest in G1 (Zheng et al., 1995). In order to overcome the problem of rapamycin cytotoxicity in yeast cells, an fprlp knock-out yeast strain mutant for Torlp had to be constructed. It is known that a mutation in the non-essential tor1 allele (S1972R) renders yeast rapamycin-resistant (Zheng et al. 1995). The Tor1 wild-type allele was cloned from yeast genomic DNA, appropriately mutated, and gel purified.

We first transformed the FKBP-containing pESC-Leu-NTERM into the BY4741 strain and selected on Leu-deficient, geneticin (30 µg/mL)-containing agar (Leu’ gen) with glu-
cose as a carbon source. Although the yeast fpr1 had been deleted, the FKBP from our transformed pESCLeu-NTERM construct will participate in a deleterious FKBP-rapamycin-TOR interaction. A colony from the first transformation (BY4741 with pESC-Leu-NTERM) was grown in Leu- media supplemented with galactose to induce the expression of the N-terminal intein construct containing FKBP. Homologous recombination of our mutant tor1 allele into the genome of these cells is currently being conducted, and selection will be performed on Leu-, gen agar plates supplemented with galactose and 1 μg/mL rapamycin. Transformations were completed as described by the S.C. EasyComp Transformation Kit (Invitrogen).

**Results and Discussion.**

**Protein expression.** High levels of protein expression of the N-terminal construct were obtained at both 30°C and 37°C (Figure 3). The absence of a strong band in the soluble fraction at 37°C for the N-terminal construct (Figure 4) indicates that the overexpressed N-terminal intein product is not soluble and well-folded at 37°C; we therefore conducted a large-scale expression and purification of the pET-28b-NTERM at 30°C to yield the ~50kD product in reasonable purity (Figure 5). Since our NTERM and CTERM constructs consist of several segments of proteins (EGFP and VDE) that may not fold correctly outside the context of the full peptide, it is possible that the peptides co-purifying with our target may be molecular chaperones responsible for re-folding proteins in *E. coli*.

The C-terminal intein construct posed more difficulties with respect to soluble expression and purification. Again, the C-terminal intein express at high levels at both 30°C and 37°C (Figure 3), but solubility experiments showed that a significantly higher fraction of the C-terminal fusion protein was solubly expressed at 37°C than at 30°C (Figure 4). However, attempted purification of large-scale preparations of the fusion protein at 37°C failed (Figure 5). In order to increase solubility, we attempted overexpression at a lower temperature, with favorable expression results (data not shown). Although we did not attempt a solubility test at this temperature, the large-scale preparation of the fusion protein at 25°C was partially successful, yielding small amounts of the impure protein (Figure 6). Interestingly, a similar pattern of bands co-eluted with the C-terminal intein as with the N-terminal intein. This may be a further indication of a cellular unfolded protein chaperone response or simply that we are eluting constitutively expressed ubiquitous proteins that have affinity for the Ni column. We are currently looking into other expression systems (for example, different bacterial cell lines may increase soluble expression) and more extensive purification for yielding a target free of contaminants for in vitro studies.

**Future goals.** The difficulties inherent in soluble expression and purification of the C-terminal intein fragment have led us to pursue *in vivo* studies in yeast and mammalian cells. We are currently attempting the Torlp recombination and yeast transformations as discussed (Zheng et al. 1995), and will select for recombinants resistant to rapamycin. After transforming the rapamycin-resistant strain containing the N-terminal intein construct with our C-terminal construct, we will induce

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**Figure 3.** N and C-terminal intein fusion expression. The arrows indicate the band corresponding to the overexpressed product (~50 kD for N; ~30 kD for C).

**Figure 4.** Solubility test of N- and C-terminal inteins. (Note: lane for “37 uninduced” not loaded in N-terminal constructs)

**Figure 5.** Purification of N- and C-inteins. FT = flow of lysate through column; WA = wash; EL = elution. Boiled induced cells and Ni²⁺ resin also included.

**Figure 6.** Purification of C-intein. Legend as in Figure 5.

continued on page 21
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expression of both N- and C-terminal fragments with galactose and assay for in vivo splicing activity upon addition of rapamycin. We are also in the process of subcloning the N- and C-terminal intein fusions into pCMV-Script mammalian expression vector (Stratagene, La Jolla, CA). Instead of relying on FKBP and FRB dimerization with rapamycin, our new system involves a small molecule-dimerizer with rapamycin, our new system relies on FKBP and FRB dimerization. We are also in the process of subcloning the N- and C-terminal intein fusions into pCMV-Script mammalian expression vector. The development of this synthetic dimerizer for the regulation of protein-protein interactions. *PNAS USA* **1997** 20, 10618-10623.


Book Review

Having Faith. An Ecologist’s Journey To Motherhood


Reviewed by Dennis J. Sardella, Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, MA 02467

Phil Cousineau, in his book The Art of Pilgrimage, says, that “The difference between pilgrim and tourist is the intention of attention, the quality of the curiosity.” From this perspective, Sandra Steingraber’s book, Having Faith. An Ecologist’s Journey To Motherhood, qualifies as a pilgrimage through pregnancy, with Steingraber serving up an enjoyable blend of experience, scientific reflection, and writing that verges on the poetic.

Now a book chronicling the ten months of a pregnancy and the first year of infancy may not, admittedly, be an obvious choice for a review in a periodical aimed at chemical professionals. Certainly, I would not have expected to be interested in reviewing it. When it came across my desk (unsolicited), my initial reaction was “Here’s one that was clearly misdirected,” rather like my reaction when my wife and I are trolling the aisles of the local video store and she picks up a film whose jacket blurb describes it as “heartwarming”. For some reason, however, I glanced through the first few pages of “Having Faith” and was drawn into it, so here I am, recommending that you read a book which is not about chemists, or the chemical profession, but which illustrates beautifully what can happen when an artist and a scientist inhabit the same body.

Sandra Steingraber, who currently teaches at Cornell, can flat out write. Someone, during her scientific apprenticeship, obviously forgot to tell her about the importance of writing in the third person and/or the passive voice. The result is a style that is a kind of extended meditation on her experimental observations in the laboratory of her pregnant body.

In the very early stages of her pregnancy, during the time when, to quote Psalm 139, “when I was growing in secret in my mother’s womb”, there is not much that Steingraber can actually observe. She nonetheless imagines the changes taking place, such as the proliferation of blood vessels, in imaginative parallels between external observations as a naturalist with the processes taking place within her:

“Plant physiologists still can’t explain why maple sap runs in the spring. It’s a mystery that secretly pleases me. All trees stockpile sugar during the winter, and in most species simple capillary action can account for its ascent from roots to branches in the early spring. This is the same adhesive force that draws a drop of water through a paper napkin. But this principle cannot account for the ten to twelve gallons of 4 percent sucrose solution that your average sugar maple can pull up its trunk and pour into a bucket...
during the month of March. Injure any other tree and sap will merely ooze from the wound. But the complex hydraulics of maples somehow generates an interior force that exceeds the outside air pressure. Sap spurts from every gash and broken branch.” (p. 30)

“My botanical reverie soon turns obstetrical. In fact, the internal anatomy of a human placenta resembles a maple grove: the long columns of cells sent out by the embryo into the uterine lining during the first few weeks of pregnancy quickly branch and branch again until, by the third month of pregnancy, the treetops of an entire forest press up against the deepest layers of the womb. Meanwhile, the open taps of the uterus’s spiral arteries send jets of blood spurting between these arboreal structures.” (p. 31)

As the book advances along with her pregnancy, Steingraber’s attention moves beyond the confines of her body to the interactions linking the mother, the developing fetus and the environment. Along the way, she discusses the effects of teratogens such as diethylstilbestrol (DES), mercury and lead, exploring and challenging some time-honored ideas such as the notions of threshold toxicity limits and the placental barrier that supposedly protects the unborn child from exogenous contaminants (both now known to be incorrect). She provides information on the various ways in which data on birth defects is (and often is not) catalogued throughout the United States. She employs data from the *Toxics Release Inventory* to describe the release of toxins into the environment as a result of both natural processes and human activity, highlighting the ways in which government and business have often chosen to ignore data far decades. Her discussion of lead contamination ranges widely, covering

continued on page 24
the known toxicity of lead compounds, the introduction of organolead compounds as antiknock additives in gasolines and their continued use for decades in the face of incontrovertible evidence of lead toxicity, arguably because the alternative, ethanol, was nonpatentable, and therefore less profitable,

• the promotion of lead-based pigments by the paint industry, the consequence being that their banning in the United States trailed that in Europe by decades,

• the fact that coal-based power plants, the single greatest emitters of lead into the biosphere, were until relatively recently exempt from environmental regulations governing lead emission,

eventually connecting again with her personal story linking lead pollution in the starting point of her and her husband’s journey from a leave in her home state of Illinois (one of the major US areas of combustion-based lead release) to Somerville, her husband’s home city, where she and her husband then resided.

In all the back and forth movement between the intricate process taking place within her and the potential environmental assaults that could derail or terminate it, though, Stein-graber’s narrative; while informative thought provoking and sobering, never became hysterical. There are even laughs along the way, such as when she speaks of feeling herself isolated, in transit between two worlds:

“Being pregnant is like walking over a plank-and-cable bridge. Behind me, on one bank, is the tribe of women who are not mothers. They drink wine, stay up late, skip meals, change lovers, study Sanskrit, and write grant proposals for a five-year study of tropical cloud forests. In front of me, on the other bank, is the tribe of mothers. They arrive at meetings late, leave parties early, are badly in need of haircuts, know way too much about the care

Book Review
Continued from page 23

Pictures of T.W. Richards
from Harvard University Archives

T.W.R. in 1888

Asst. Prof. T.W.R. with his Harvard Chem 4 Class in 1892 (back row, center)

T.W.R. in 1907
and feeding of guinea pigs, and have to hang up now.” (p. 94)

The well-established correlation between brain size and gestational period suggests that human pregnancies should last about twenty-two months. However, the size of the human pelvis makes this impossible, the result being that the first year of life can be regarded as the last twelve months of pregnancy. This provides a rationale for Steingraber’s devoting the last third of her book to her first year of motherhood, and in particular to an extensive discussion of nursing and mother’s milk. Steingraber provides a vivid contrast between the extensive benefits provided by mother’s milk and the alarming fact that biomagnification (a process which she links to conservation of mass as one moves up the food chain) concentrates toxins in mother’s milk, making it among the most contaminated of foods.

This, in a way, brings me back to where I began - to the question of why a middle-aged male chemist should be enthusiastically recommending a book on the pregnancy of an ecologist, and why I think you should consider reading it. There are, in fact, quite a few reasons, beginning with the quality and vitality of Sandra Steingraber’s writing, which many scientists could benefit from imitating at some level. Next is her ability to integrate the personal and professional perspectives in a way that respects the integrity of both. Thirdly, there is simply a lot to learn about the interlocking nature of biological and biochemical processes and the way in which they are inextricably intertwined with the world in which we live and move. Finally, because the demographic shift in the profession in recent decades makes it extremely likely that in the near future (if it has not already happened) you, or someone in your laboratory or department, will be experiencing these remarkable changes, or be married to someone experiencing them, or working with or supervising someone negotiating them, the ability to appreciate the magnitude and the majesty of what is happening could prove very useful. ♦
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March 5
Prof. John A. Gerlt (Univ. of Illinois, Urbana-Champaign)
"Does Sequence or Structure Determine Enzyme Function? Different Reactions Catalyzed by the 'Same' Active Site"
Tufts Univ., Pearson Chem. Building, 62 Talbot Ave., Medford, Room 106, 4:30 pm

March 6
Prof. Richard Eisenberg (Rochester Univ.)
Harvard/MIT Inorganic Chemistry Seminar @ Harvard
Harvard Univ., MB-23 Pfizer Lecture Hall, 4:15 pm

March 7
Prof. Bryan Coughlin (U Mass Amherst)
TBA
Dartmouth College, room 101 Fairchild, 10:30 am
Prof. Ron Shen (Univ. of Calif., Berkeley)
Harvard/MIT
Harvard Univ., MB-23 Pfizer Lecture Hall, 4:15 pm
Prof. Alex Pines (Univ. of Calif., Berkeley)
Harvard/MIT
Physical Chemistry Seminar at MIT
"NMR and MRI at a Distance"
MIT, Room 2-105, 4 pm

March 11
Prof. David Walt (Tufts Univ.)
"Optical Sensor Microarrays; from Molecular Biology to Artificial Olfaction"
Boston Univ., 590 Commonwealth Ave., Science Center Auditorium, SCI 107, 4:00 pm

March 12
Prof. Eric Bakker (Auburn Univ. & Ecole Normale Superieure, Paris)
"From Extremely Selective Ion Sensors to Smart Microspheres"
Tufts Univ., Pearson Chem. Building, 62 Talbot Ave., Medford, Room 106, 4:30 pm

March 14
Prof. Jennifer Doudna (Yale Univ.)
"Splicing with a twist: Unexpected structure around the branch point of a group II intron"
Boston College, Merkert Chemistry Center, Room 130, 2609 Beacon St. 4:00 pm
Prof. Jeff Gelles (Brandeis Univ. Dept. of Biochemistry)
Harvard Univ., MB-23 Pfizer Lecture Hall, 4:15 pm
Dr. Erik J. Sorensen(Scripps Research Institute)
Seminar in Organic Chemistry TBA
MIT, Room 6-120, 4 pm

March 15
Dr. John E. Blume (Vice President, Strategic Technologies, Metabolex Inc.)
"Genomics as a Viable Approach for Therapeutic Target Discovery"
CURRENT TOPICS IN MEDICAL CHEMISTRY -- A DISTINGUISHED LECTURE SERIES, Boston Univ., 595 Commonwealth Ave., Room 228 Rafik B. Hariri Building, 2:00 pm

March 18
Prof. Bill Tolman (Univ. of Minnesota)
"Using Synthetic Chemistry to Understand Copper and Iron Active Sites in Proteins"
Boston Univ., 590 Commonwealth Ave., Science Center Auditorium, SCI 107, 4:00 pm
Jennifer Stone, Stern Group (MIT)
Biochemistry Seminar Series
"Molecular Mechanisms of T cell Triggering"
MIT, Room 6-120, 4pm

March 19
Prof. Erick M. Carreira (ETH, Zurich)
Novartis Lecture in Synthetic Organic Chemistry
MIT, Room 6-120, 4 pm

March 20
Prof. Dev Arya (Clemson Univ.)
"Neomycin-Nucleic Acid Interactions"
Boston College, Merkert Chemistry Center, Room 130, 2609 Beacon St. 4:00 pm
Prof. Donald Daresbourg (T.A.M.U)
Harvard/MIT Inorganic Chemistry Seminar @ MIT
MIT, Room 6-120, 4 pm

March 22
Dr. Barrie J. Carter (Executive Vice President & CSO, Targeted Genetics Corp.)
"Developing Therapeutic Applications of Gene Delivery"
 CURRENT TOPICS IN MEDICAL CHEMISTRY -- A DISTINGUISHED LECTURE SERIES, Boston Univ., 595 Commonwealth Ave., Room 228 Rafik B. Hariri Building, 2:00 pm

March 25
Prof. Marina Petrukhina (SUNY-Albany)
"Rh2(O2CCF3)4 Adducts with Polycyclic Aromatic Hydrocarbons: Discrete Molecules, 1D Polymers and 2D Networks"
Boston College, Merkert Chemistry Center, Room 130, 2609 Beacon St.4:00 pm
Prof. Dennis Curran (Univ. of Pittsburgh)
"An Introduction to Fluorous Techniques for the Synthesis of Organic Molecules"
Boston Univ., 590 Commonwealth Ave., Science Center Auditorium, SCI 107, 4:00 pm

March 26
Prof. William R. Roush (Univ. of Michigan)
TBA
Boston College, Merkert Chemistry Center, Room 130, 2609 Beacon St. 4:00 pm
Prof. Milan Mrksich (Univ. of Chicago)
"A Surface Chemistry Approach to Studying Cell Adhesion"
Tufts Univ., Pearson Chem. Building, 62 Talbot Ave., Medford, Room 106, 4:30 pm

March 27
Drs. Lijuan Zhang and Robert Rosenberg (MIT)
"Heparan Sulfate: A Glycobiology Frontier in the Post-genomic Era"
The Boston Glycobiology Discussion Group, 6:00 pm dinner, MIT Faculty Club, 50 Memorial Drive, Cambridge; reservation is required: contact David Newburg (781-642-0025)
Prof. Allan J. Jacobson (Univ. of Houston)
Inorganic Chemistry Seminar TBA
MIT, Room 6-120, 4 pm