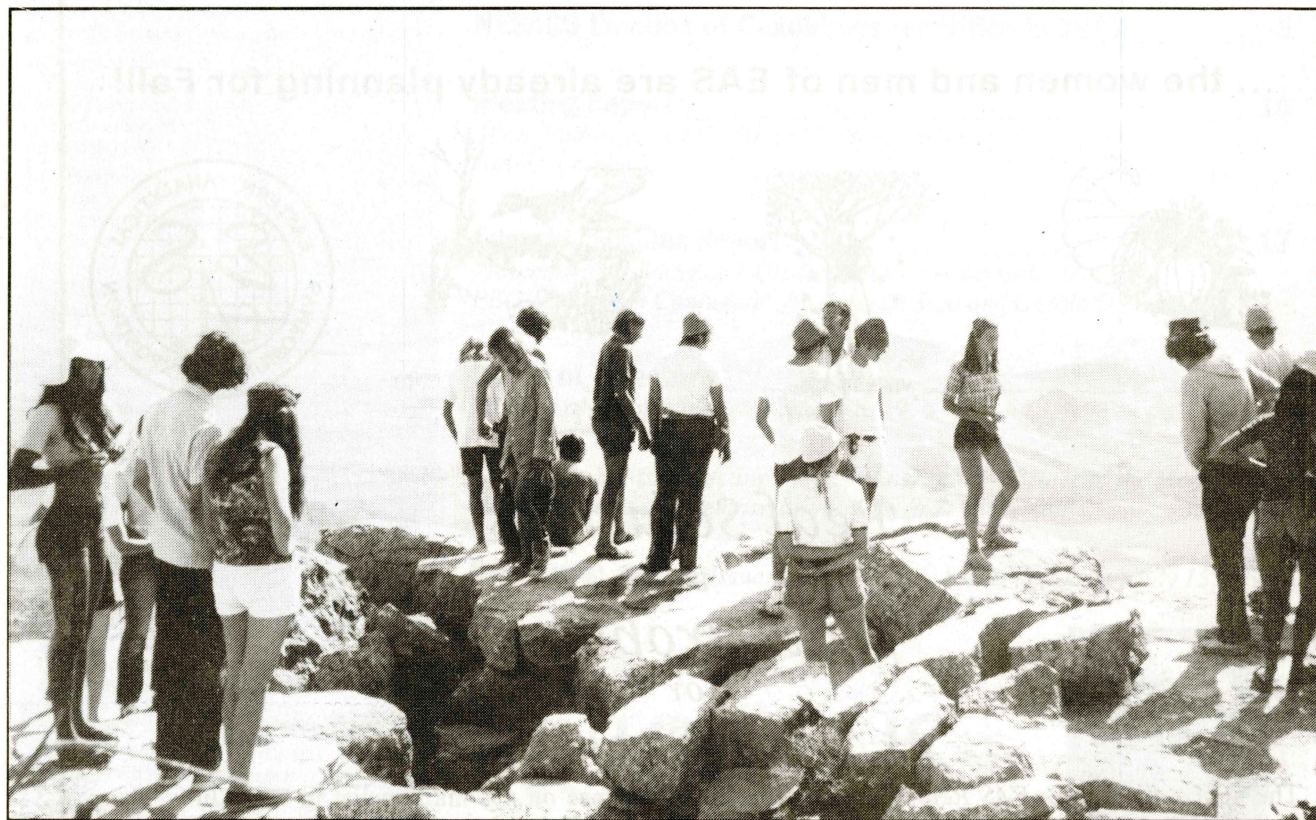


THE NUCLEUS

May 1996

Of the Northeastern Section of the American Chemical Society

Vol. LXXIV, No. 9



Monthly Meeting

Education Night
"Adventure in the Sinai"

Meeting Report

Free Radicals: Bane or Boon?
Richards Award Address of JoAnne Stubbe

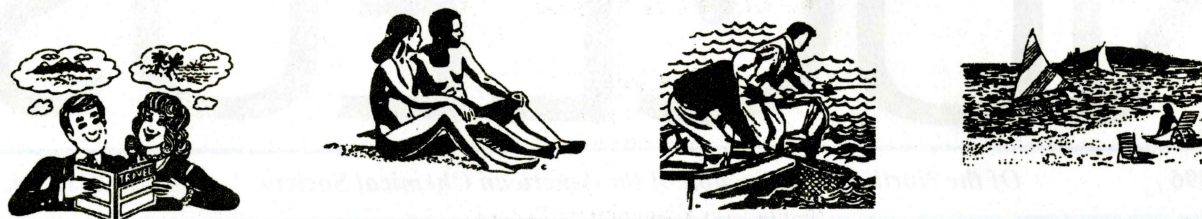
Candidates' Statements

*Election of 1997 Officers
and Committee members*

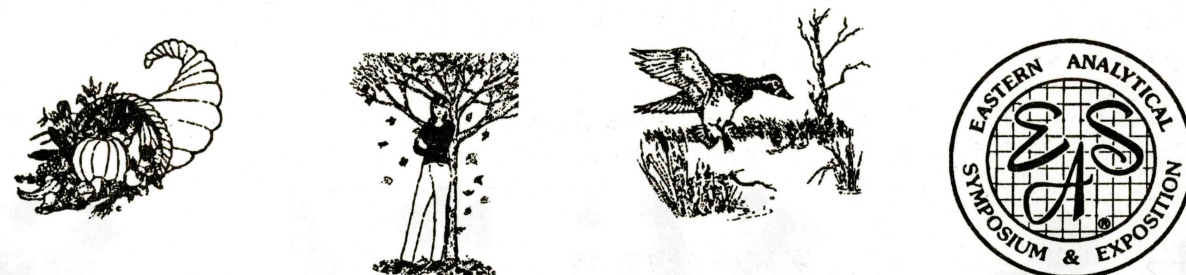
Summer Scholar's Report

Rona D. Sadia and Gerald D. Fasman
"Attempted Refolding of 9-Cis-Retinal"

While you are planning your summer vacation ...



... the women and men of EAS are already planning for Fall!



Real Solutions
to
Real Problems
for
Real People

The next issue of *The EAS Retort* newsletter will reach those on our mailing list in early July. There they will find information about an expected 600 technical papers (in 60 invited and 30 contributed Technical Sessions), 25 EAS Short Courses, 30 EAS Workshops, 15 EAS Tutorials, 5 EAS Seminars, Housing information, a Registration form, a listing of the Exhibitors which will occupy 325 booths, and much, much more! In 1996, the advance Registration fee will be a low \$65.

What? You aren't already on our mailing list? You say you simply can't wait to find out more about the 1996 EAS? Don't despair, more information is available now! Contact: the EAS HOTLINE at 1-302-738-6218, the EAS FAXLINE at 1-302-738-5275, request information via e-mail to EASINFO@AOL.COM, or set your Web browser to view our Home Page at <http://www.eas.org/~easweb/>

EAS FACTS IN BRIEF: EAS is a non-profit [501(c)(3)] scientific organization run totally by volunteer scientists. The 1995 EAS attracted almost 4800 attendees and included 467 Technical Papers, 7 CONFERENCES-IN-MINIATURE, 23 EAS Short Courses, 27 EAS Exhibitor Workshops, 5 Seminars, 8 Tutorials, and 301 exhibit booths. EAS is proudly sponsored by the Analytical Division and the North Jersey and New York Sections of the American Chemical Society; the American Microchemical Society; the Chromatography Forum of Delaware Valley; the New York Microscopical Society; and the Delaware Valley, New England, and New York Sections of the Society for Applied Spectroscopy.

The Northeastern Section of the American Chemical Society, Inc.

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All Chairmen of standing Committees, the editor of *THE NUCLEUS*, and the Trustees of Section Funds are members of the Board of Directors. Any Councilor of the American Chemical Society residing within the section area is an ex officio member of the Board of Directors.



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Deadlines: <i>Summer Issue: June 10, 1996; September Issue: July 15, 1996.</i>	

THE NUCLEUS



The Nucleus is distributed to the members of the Northeastern Section of the American Chemical Society, to the secretaries of the Local Sections, and to editors of all local publications. Forms close for advertising on the 1st of the month of the preceding issue. Text must be received by the editor six weeks before the date of issue.

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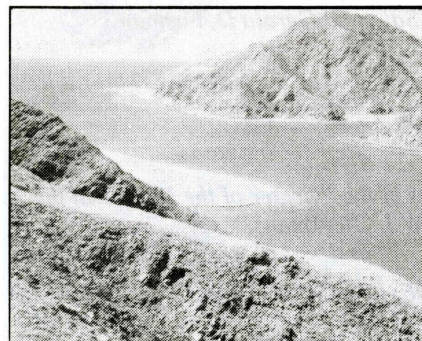
Abstract

This illustrated adventure takes us into the Sinai peninsula along with a group of students from the American International School in Israel. We travel along the shores of the Dead Sea, investigating both the northern and southern edges, as well as the fresh water springs along its western shore. We then travel south to Eilat, visit the oceanographic laboratories, and then proceed along the eastern shoreline of the Gulf of Eilat to the tip of the Sinai peninsula at Ras Muhammed and the Red Sea.

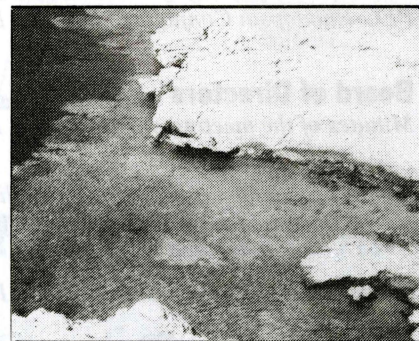
During their travels, students had an opportunity to study the geological

formations which have been carved in the wilderness. Students also had a chance to explore the shoreline and study the endemic flora and fauna. In the offshore areas, students were able to swim out to the coral reefs and observe the many different forms of marine animals inhabiting the reef. A representative sample of the type of specimens observed is shown. Water samples at a depth of 0–0.5 meters were gathered by students for later analysis in the school chemistry laboratory.

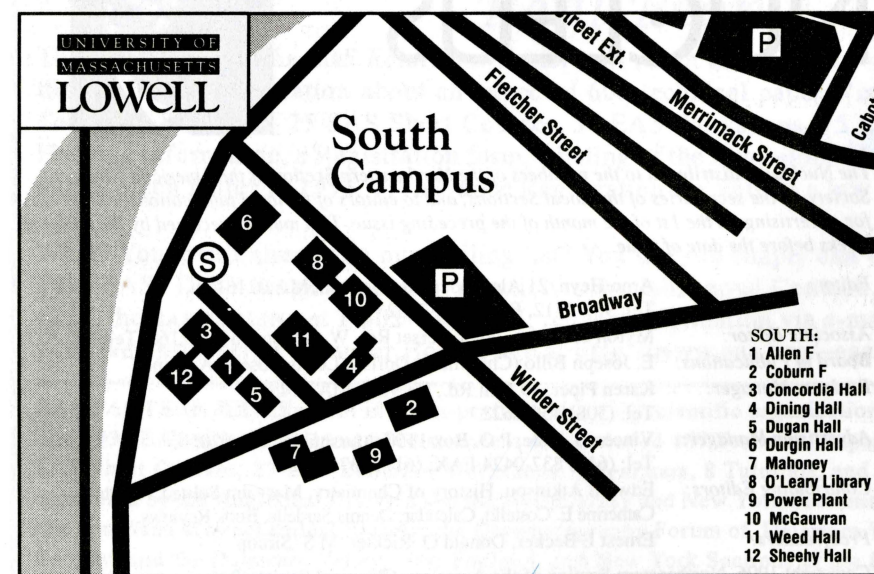
Water samples were taken from Ein Gedi, Pools of David, Sodom, Eilat, Pool of the Sun, Coral Beach, Nueba, Dahab, Ras Nitzrani, Sharm-el-Shiek, and Ras Muhammed. An analysis and commentary on the results obtained are presented. ♦



South of Eilat, color variations of the water indicate depths at "The Fjord".



Swimmers along the edge of the coral reef at Ras Muhammed where water suddenly drops 300 meters straight down.



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Directions

May Meeting

Take **Route 3 North** from either Rte. 128/95 or 495 and exit at **Exit 32** to a rotary. At the top of the exit ramp, take the *first* right off the rotary (Sign: "Westford Rd., Lowell 3 miles").

Proceed for 1 mile, past a Burger King and McDonalds on the left, and a Ford/Nissan dealership on the right. Go to the fourth set of traffic lights, one mile from the rotary. (Caution: At the second light, bear left). The road heads toward a bridge crossing the Merrimack River. *Do not cross the bridge.* Turn right into **Middlesex Street**, with the river on your left. Proceed about one mile along Middlesex Street to the first traffic light. Stay left at the light and cross a railroad bridge. Almost immediately after the bridge, bear right onto **Broadway**. There is a red brick building, Humane Society, on the left. Proceed several hundred feet. The south campus buildings are on both sides of the street. At the first set of lights, corner of **Broadway and Wilder Street**, park in the large parking lot. ♦

Monthly Meeting

The 780th Meeting of the Northeastern Section of the American Chemical Society

Education Night

Thursday, May 9th, 1996
University of Massachusetts Lowell, South Campus

5:00 Social Hour, Courtyard, South Campus (next to Dining Hall)
In case of inclement weather: Dining Hall, West Wing

6:00 Dinner Dining Hall, West Wing, South Campus

7:30 Evening Meeting, Concert Hall in Durgin Hall, South Campus
Dr. Patricia Samuel, Chairman, Northeastern Section, presiding

Address *Chemical Oceanography: Adventure in the Sinai*
Dr. Wallace J. Gleekman

Presentation of Awards

Philip L. Levins Memorial Prize
James Flack Norris/Theodore William Richards Undergraduate Research Fellowships
Undergraduate Grants-in-Aid
Undergraduate Research Symposium
1995 Project SEED Students
Excellence in Teaching at the Secondary School Level
Induction of New Members into Aula Laudis
Avery A. Ashdown Chemistry Examination;
Simmons College Prize

Refreshments will be served after the program.

Dinner reservations should be made no later than noon, May 2. Please call or fax Marilou Cashman at (800) 872-2054. There will be a choice of beef roulade, salmon, or pasta primavera (vegetarian) entrees. Reservations not cancelled at least 24 hours in advance must be paid. Members, \$25.00; Non-members, \$28.00; Retirees, \$15.00; Students, \$8.00. **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 available, see map on p. 4.

Plans are under way for Summerthing 1996. Place and date to be announced.



Biography

Born in Boston, Gleekman received an undergraduate degree from Bridgewater State College, and after graduate work at Boston University, Union College and Harvard University, he received a Ph.D. from Walden University.

After military service in the Far East, he began his teaching career at Wrentham, Mass. High School and the King Philip Regional High School,

Mass. as a science teacher and department head. In 1958 he moved to Brookline, Mass. High School where he taught courses in chemistry, biology, physics, oceanography, environmental science, and general and physical science. He also served as Housemaster (assistant principal) at Brookline High School, as well as Director of the Brookline Summer School. He retired from Brookline High School in 1995. In addition, he was an instructor of

oceanography and administrative assistant at the U.S. Naval Reserve Officers School in Boston.

He was elected to the Board of Directors of the Norfolk County and Massachusetts Teachers Association. He is currently serving as an Adjunct Professor of Sciences at Emerson College in Boston.

Dr. Gleekman spent a sabbatical year at the American International School, in Israel as science consultant and coordinator and compiled a series of slide presentations for scientific, religious, and citizen groups. He has been a speaker at local, regional and national meetings of the American Chemical Society and National Science Teachers Association.

In his spare time he is an avid sailor and is currently the varsity sailing coach at Brookline High School and the Commonwealth School. He has served as officer and on the Board of Directors of several interscholastic sailing associations in New England. The New England Schools Sailing Association has recently honored him by naming its fall sailing regatta as the "Gleekman Trophy Regatta" in recognition of his contributions to high school sailing.

Gleekman was selected as a General Electric Science Fellow and has received a number of honors, recognizing his excellence in science and/or chemistry teaching: the Lyman C. Newell Award for Chemistry Teaching, the Northeastern U. S. Regional Award in High School Chemistry Teaching, the James Bryant Conant National Award, and the John A. Timm Award. Gleekman was elected to the Aula Laudis Society, the High School Chemistry Teachers' "Hall of Fame", by the Northeastern Section. He was also given the Distinguished Service Awards for Distinguished Service to the Teaching Profession by Norfolk County and by the Massachusetts Teachers Association.

He has served as Chairman of the Northeastern Section and for many years as chairman of its Committee on Chemistry Education. He received the Henry A. Hill Award for Distinguished Service to the Northeastern Section,

continued on page 7

TRACE ELEMENT ANALYSIS

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- Spark Source Mass Spectrometry (SSMS)
- Graphite Furnace Atomic Absorption Spectrometry (GFAAS)



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Fax 603-429-9471

Medicinal Chemistry Group Symposium

High Speed Techniques in Drug Discovery

Thursday, May 23, 1996
Boston College, Chestnut Hill, MA

Lectures in Merkert Chemistry Building, Room 127
Reception and Dinner in Shea Room, Conte Forum, Third Floor

- 3:00** Coffee and Refreshments
- 3:30** Dr. Val S. Goodfellow, Cortech, Inc.
"Rationally Designed Piperazine Combinatorial Libraries for the Discovery of Bradykinin Antagonists"
- 4:30** Dr. Michael Boisclair, Mitotix, Inc.
"High Throughput Screening Against Novel Therapeutic Targets"
- 5:30** Social Hour/Wine and Cheese
- 6:15** Dinner
- 7:45** Dr. Joseph C. Hogan, Jr., ArQule Inc.
"High Speed Synthesis of Thematic Arrays for Small Molecule Drug Development"

From I-90/Massachusetts Turnpike: East to Exit 17 (Newton/Watertown). Take the first right onto Centre Street. Proceed 1.5 miles to Commonwealth Avenue (Route 30). Take a left onto Commonwealth Avenue and follow east for about one mile. Chestnut Hill campus is on the right

From Route 128/I-95: Commonwealth Avenue (Route 30), five miles. Chestnut Hill campus is on the right.

From Downtown Boston: Commonwealth Avenue (Route 30), west into Newton. Chestnut Hill campus is on the left.

Dinner reservations should be made **no later than Thursday, May 16**. Please call or fax Marilou Cashman at (800) 872-2054 or (508) 653-6329. Reservation not cancelled at least 24 hours in advance must be paid in full. Members \$25.00; Non-members, \$28.00, Retirees, \$15.00, Students, \$12.00. Anyone who needs special services or transportation, please call a few days in advance so that suitable arrangements can be made.

Abstracts

Rationally Designed Piperazine Combinatorial Libraries for the Discovery of Bradykinin Antagonists

Dr. Val S. Goodfellow, Cortech Inc.,
Denver, Colorado

Combinatorial chemistry is incorporated into a drug discovery program that involves integrating knowledge of natural and synthetic ligands with computer-aided design of appropriate scaffolds and pharmacophores. Structural

features favoring *in vivo* stability and oral absorption are emphasized. The optimization of lead structures then progresses using an integrated mix of combinatorial and traditional structure based medicinal chemical techniques. An initial lead, CP-2458 ($IC_{50} = 4 \mu M$), was carefully selected from this library

continued on page 17

Member News

Speakers at Waters Symposium, Pittcon; Other Awards

The Waters Symposium at the 1996 Pittsburgh Conference on Analytical Chemistry on March 4 featured three local scientists who had been invited to present papers on Ion Selective Electrodes. Each year a special topic is selected, and a few experts in the field are selected to make presentations at the half-day symposium. James L. Waters, the founder of Waters Associates, has sponsored these annual symposia since 1989. The focus is to "explore the origin, development, implementation and commercialization of scientific instrumentation of established and major significance."

The three chemists from this area were **Martin S. Frant**, Orion Research, Inc., speaking on: *Where Did Ion Selective Electrodes Come From?*, **Truman S. Light**, retired from the Foxboro Company, who spoke on *Industrial Use and Applications of Ion Selective Electrodes* and **C.C. Young**, Nova Biomedical Corp., whose topic was *Evolution of Blood Chemistry Analyzers Based on Ion Selective Electrodes*. The other Symposium speaker was Jaromir Ruzicka of the University of Washington who spoke on *The Seventies - The Golden Age for Ion Selective Electrodes*.

Peter T. Landsbury Jr., an Associate Professor of Chemistry at M.I.T. is one of two awardees of the Excellence In Chemistry Award sponsored by the Zeneca medicinal chemistry department for his work on protein aggregation processes in human disease, such as in Alzheimer's disease. The award includes an unrestricted research grant of \$30,000. ◇

Biography

continued from page 5

and recently he has received the Theodore William Richards Award for Excellence in High School Teaching. ◇

ACS Short Course

How to Develop and Troubleshoot Capillary GC Methods

A One-Day Short Course Sponsored by the Northeastern Section, ACS, Committee on Continuing Education

National ACS is making top-rated ACS Short Courses available to local sections at tuition fees greatly reduced from the normal \$425. The NESACS Committee on Continuing Education is pleased to sponsor this newly developed course, which is being presented by one of the program's most experienced instructors.

Date and Time: Wednesday, May 15, 1996, 8:30 a.m. - 5:00 p.m.

Place: Frost Lounge, Ell Building, Northeastern University, 360 Huntington Ave

Program Agenda:

The Approach: Systematic, structured approaches to problem solving and method development; how to choose a chromatographic separation technique.

Specifics of "How to" ...: Effect of column parameters on separation and resolution; Optimization of methods for performance and/or productivity; Cost reduction methods; Selection of sample preparation/concentration techniques; How to get the results you want from your injector(s) and sample inlet systems; Achieving the required accuracy and precision; Selection of GC detectors; Handling "dirty" samples; Minimizing the cost of methods development and analysis; High productivity methods.

Troubleshooting: Eliminating the bottlenecks in laboratory operation; Method diagnostics and preventative maintenance; How to troubleshoot methods and results.

The Newest Technologies: Programmable temperature injection; Large sample volume injection for sensitivity; Flow programmed injection techniques; Cool on-column injection for quantitation; Columns for very high resolution and fast analysis; Highly selective detectors.

Practical Examples: Examples of how methods are developed, tested, and documented.

Instructor: Stuart F. Cram, Worldwide Marketing Manager, Hewlett-Packard Chemical Analysis Group. Formerly Research Manager for Varian's Instrument Division and Chief of Chromatographic Analysis at the National Institute of Standards and Technology. He has been one of the highest rated instructors in the A.C.S. Short Course Program since 1977.

Pre-registration Required - Registration Fees:

ACS Members if mailed before May 1 \$125.00; after May 1 ... \$175.00
Non-ACS Members if mailed before May 1 ... \$175.00; after May 1 ... \$225.00

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

Parking Fee \$3.00/day

University cafeterias will be available for lunch.

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

Registration form for Short Course:

How to Develop and Troubleshoot Capillary GC Methods

Name: _____ Mail with remittance to: (*Please make checks payable to NESACS*)
Address: _____ Prof. Alfred Viola, Chair
NESACS Committee on Cont. Ed.
Department of Chemistry
Northeastern University
Boston, MA 02115

Affiliation: _____
Telephone: _____

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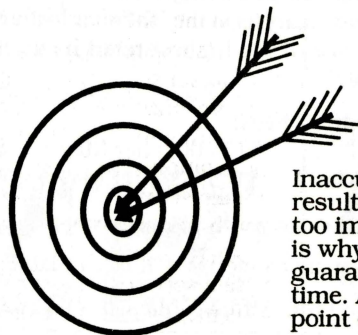
Location:

Availability:

Registration limit 10 Participants/Session

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Northeastern Section

Election of Candidates for 1997

In the interest of providing maximum information and expression of opinions by the candidates for election in 1996, the Nominating Committee has prepared this section of the Nucleus for mailing concurrently with the ballots. All candidates were asked to submit biographical material and, with the exception of committee member nominees, position statements. Except for correcting typographic errors, and minor changes to attain uniformity in format these statements have been reproduced without change. An official ballot along with a ballot envelope and a return envelope have been provided. The election and balloting are being carried out in conformance with Article VIII of the Constitution of the Northeastern Section. The order of candidates on the ballot was determined by lot. Comments regarding the election or election process may be addressed to the Nominating Committee Chair, Ms. Valerie Wilcox.

BALLOT DIRECTIONS: Vote for the candidate(s) of your choice, insert your ballot into the ballot envelope, insert the ballot envelope into the return envelope, *sign your name on the return envelope only*, affix postage, and mail.

**THE BALLOT MUST BE
RECEIVED BY JUNE 1, 1996.**

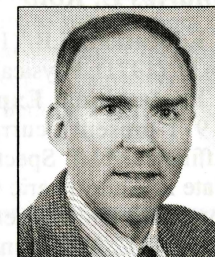
**Please donate your copies of
THE NUCLEUS to your local
High School when you no
longer need them.**

Chairman-Elect

Michael J. Hearn

Education and Experience: B.A., Chemistry, Rutgers College (1971), Phi Lambda Upsilon, Phi Beta Kappa; M.S., M.Phil., Ph.D. Yale University (1976); Instructor in Chemistry/Postdoctoral Associate, Yale University (1976-77); Assistant to Full Professor, Wellesley College (1977-present); Senior Visitor, School of Chemical Sciences, University of East Anglia, Norwich, England (1980-81); Assistant to Associate Editor, *Organic Preparations and Procedures International* (1985-present); Numerous papers in chemical research journals and conferences; Awards in teaching.

Professional Activities: ACS member since 1971. Board of Directors, Northeastern Section, A.C.S. (1985-present); Chairman, NESACS Education Committee (1985-90); NESACS Secretary (1990-present); AAAS; Sigma Xi; N.Y. Academy of Sciences; American Society for Microbiology; Fellow, American Institute of Chemists; NSTA; Member of ORG and POLY Divisions of ACS.



Statement: A number of significant challenges currently face our field, and as members of the Northeastern Section, we have important opportunities to begin to meet these challenges. Some of the challenges are matters of substance and some are matters of public perception of our discipline, but nearly all can be met by renewing our efforts in professional understanding, public awareness, and chemical education. The strong traditions of the committees and activities of the Northeastern Section provide effective ways in which to make these efforts.

We must, for example, better define our own role as chemical professionals. We can begin to do this through establishing clear standards and agreed-upon guidelines for the proficient and responsible practice of our discipline. As a professional organization, we need in turn to describe more fully the expectations we have of employers of chemists. Much good work in this area of professional understanding has already been accomplished within our Section, but with current economic uncertainties we can truly say that much more remains before us.

Public awareness of the positive impact of chemistry on daily life is a goal that must in large part be achieved through patient and sustained efforts. The successful alleviation of the human condition which chemistry has brought about over many decades is not a headline-grabbing story, but it is a vital and compelling one. Public lectures, seminars and other activities stressing chemistry in the public interest foster communication between the chemical profession and the average citizen. Such programs help to reduce the negative perception of science elitism in our society. Outreach programs to state and local government representatives

assist those in decision-making roles by serving as resources of information about chemistry. A number of committees in our Section are actively contributing to these significant public awareness issues.

Efforts in chemical education within the Section provide great opportunities for involvement. The Section sponsors programs and activities over a wide range of educational needs: from hands-on experiments for elementary school children to short courses in new topics for mature professionals. One major direction for the future will be the welcoming into our ranks of new chemists from groups traditionally underrepresented, and this begins with chemical education.

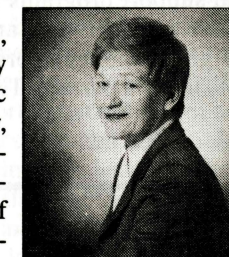
In sum, my chief goal as Chairman would be renewed participation by Section members in these important areas of professional understanding, public awareness and chemical education.

Ruth Tanner

Education and Experience: B.S., Purdue University, Ph.D., University of Cincinnati (Physical Organic Chemistry). Senior Teaching Fellow, University of Cincinnati; Postdoctoral Fellow, Physical Organic Chemistry, Duke University; Professor of Chemistry, University of Massachusetts Lowell; Visiting Professor, Physical Organic chemistry in Food Engineering, Mass. Institute of Technology. Societies: American Chemical Societies: Iota Sigma Pi; Institute of Food Technologists.

Statement: The American Chemical Society provides services and programs to chemists and to the chemistry profession, and recently, has become involved in tailoring a role for chemistry and the chemical society in public affairs and government policy. Probably the most valuable aspect of the Society, however, is its existence as a professional organization that offers the sense of community which extends to the local section organizations. It is the local section which can, in turn, be influential in the programs and policies of the parent organization. The local sections also have the responsibility to take steps to extend this sense of community to students, both graduate and undergraduate, who are the future of the society.

Among the many important services and programs which the ACS has arranged for its members is the continuing education program, through short courses, has been particularly valuable for helping chemists stay on the cutting edge. This, in turn, has made these chemists more valuable to their employers. Such programs have been focused to build skills vertically. However, the employment security picture has changed dramatically, and so should the focus of chemistry programs. Chemists now, and certainly in the foreseeable future, need to broaden their skills horizontally to remain employable. For instance, the ACS could, and probably should, run short courses and seminars, and even sponsor



six month programs in, for example, managing a business, or owning a consulting firm. This change in direction needs to be reflected in the curriculum of the undergraduate and graduate programs in chemistry, and it requires a major emphasis at the national level. The Northeastern Section should be instrumental in influencing these changes.

There are a number of programs offered by the Northeastern Section and by the national ACS for undergraduate chemistry majors. These programs encourage the students to participate in events sponsored by the organization, but they require the students to take the initiative. The undergraduate chemistry majors are the future of the organization, and the Northeastern Section should extend the sense of professional community to them. This could be begun by inviting one or two student affiliate chapters to each monthly meeting as guests of the Section. The students could be made especially welcome by assigning individual ACS members as hosts for individual students.

As Chair, I would see it as my responsibility to encourage and support programs and activities of the Section which benefit its members and future members, and to use the weight of the membership of the Section to influence the policies of the national ACS.

Treasurer

James U. Piper

Education and Experience: B.S., M.I.T.; M.S., Ph.D., Emory University; Research appointments at Yale University (1963-66), M.I.T. (1966-67 and 1972-73), Worcester Foundation for Experimental Biology (1979-80); Teaching appointments, at New Haven College (1963-66), Simmons College (1966-present).

NESACS Activities: Treasurer, (1977-present).

Statement: The Treasurer chairs the Budget Committee, is responsible for all Section funds, except those of the Trust Accounts, and prepares reports to the Board of Directors, National ACS, and state and federal agencies. The Section currently operates with a budget of \$160,000 of which 40% comes from Trust Funds and 30% from local and national dues. About 35% of all expenditures are related to awards which recognize achievements in chemistry at all levels, from high school students to professional chemists. This also includes programs that encourage young people to enter the profession. Administrative expenses constitute 20% of expenditures. The remaining 45% is used for services to the membership, such as the *NUCLEUS*, monthly meetings, continuing education programs and workshops, professional relations activities, and public relations. The quality of these programs is high, and the major budgetary problems involve setting priorities among them.

Auditor

Anthony L. Rosner

It has been my pleasure to have served and grown as Auditor for the Northeastern Section of the ACS over the past six years and to have had the experience of working with Jim Piper. Since 1986, I have developed my accounting, computing, and administrative skills to the level of having managed over 120 research grants totaling \$10M at several universities and colleges nationwide. In a changing economic and political climate, I relish the opportunity of being able to continue as Auditor and would welcome your suggestions and support.

Trustee

Charles E. Kolb

Education: S.B. (1967), Chemistry, M.I.T.; M.A. (1968), Ph.D. (1971), Physical Chemistry, Princeton University.

Professional Experience: Aerodyne Research, Inc. (1971-present), currently President and CEO; Research Affiliate, M.I.T. Spectroscopy Laboratory (1981-95); Associate in Atmospheric Chemistry, Harvard University Center for Earth and Planetary Physics, (1976-85); numerous NAS/NRC, NASA and DoD committees and panels. Editor of *Geophysics Research Letters* (1996-98).

ACS Northeastern Section: Chairman-Elect and Program Committee Chairman (1990); Chairman (1991); Co-Chairman, Elementary Education Task Force (1991-95); Chairman, Nominating Committee (1992); member, Budget Committee (1990-92); Trustee (1993-96).

Statement: I have been privileged to play a leadership role in the Northeastern Section for several years. I would be honored to continue that effort as a Trustee of the Section's financial endowment. It is vital that the Trustees protect and enhance the Section's current financial assets of over 1.5 million dollars while ensuring that sufficient income is available to fund the Section's important work in chemistry education, professional services to members and recognizing and rewarding outstanding work in chemistry, chemical engineering and chemical education. I believe what I have learned during the last three years as a Trustee and in over ten years of experience leading a successful corporation will help me ensure that the Section remains on firm financial footing.

Michael E. Strem

Education: A.B., Brown University (1958), M.S. (1961), Ph.D. (1964), University of Pittsburgh

Professional Experience (last ten years): Strem Chemicals, Inc., President (1964-present)

Service in National ACS: Committee on Committees (1993-96); Society Committee on Budget and Finance (Associate, 1994-96); service on numerous other committees 1987-1992. Division of Small Chemical Businesses, Councilor (1986-96), Chairman (1982-3, 1985).

Northeastern Section: Chairman-Elect (1988); Chairman (1989); Board of Publications, Chairman (1991, 1994); Chairman, Nominating Committee (1990-92); Northeast Regional Meeting, Exhibits Chairman (1993).

Related Activities and Honors: Member: Royal Soc. of Chemistry, Gesellschaft Deutscher Chemiker, Société Française de Chimie; Materials Research Society. Henry A. Hill Award for Distinguished Service to the Northeastern Section (1995).

Statement: Many years of experience have taught me much about the finances of the Northeastern Section. I am aware of the fiscally conservative attitudes prevalent within our membership and will act accordingly if you elect me as your Trustee. I promise also to work actively with the officers and board members in fiscal matters to support them in reaching the goals they have set for the Section. I feel that being president of a corporation for over 30 years has provided me with the skills to manage the Section's funds properly, and I look forward to your support.

Councilors and Alternate Councilors

Charles J. Bardsley

Retired
No statement received

Charles A. Blank

Education: B.A., M.A., Brooklyn College of the City of New York; Ph.D., Physical-Inorganic Chemistry, Syracuse Univ; Certificate in Biotechnology, Boston University School of Medicine-Metropolitan College.

Professional Experience: National Research Corp. Fellow, Syracuse University (1948-51); Research Chemist, E.I. DuPont de Nemours, Inc., Buffalo, N.Y. (1951-52); Lieutenant, U.S. Navy, Scientific and Technical Intelligence Analyst (1951-52); member, Technical Staff, Bell Telephone Laboratories (1952-54); Staff Chemist, IBM Corp. (1954-56); Staff Physicist, Melpar, Inc., Falls Church, VA (1956-59); Physical Scientist, Dept. of Defense, Washington, D.C. (1960-78; early retirement 1978); Lecturer and Laboratory Instructor, Organic and General Chemistry, Assumption College (1984-85); Lecturer of Physics, Northeastern University (1985-86); Instructor of Physics and Laboratory Instructor, Worcester State College and Curry College (1986-87); Instructor for Physics and Tutor for Chemistry, Manatee Community College, Bradenton, Fla. (1988-90); Lecturer for General Chemistry, Curry College (1988-90); Health and Safety Instructor, American Red Cross (1995-present);

Service in ACS: Member since 1948; member of ChemEd, Inorganic, and Physical Divisions; Executive Council, Binghamton New York Section (1957-59); Joint Board on Science Education member, Northern Virginia Section (1967-70).

Northeastern Section: Senior Chemists Group Representative, Board of Directors (1994-present).

Related Activities: American Institute of Chemists, Emeritus Fellow; Member, New York Academy of Sciences; Fellow, Washington Academy of Sciences.

Statement: I believe that my more than 40 years of combined employment experience in industry, government and academia as a professional scientist and chemist will continue to prove most useful in serving and representing all members of NESACS. Currently, as a semi-retired chemist, I continue to maintain active affiliations with several other professional organizations, which provides a useful means for "networking" in support of NESACS goals and activities. Additionally, I am most sensitive not only to the career and employment problems of the student and younger chemists, but also to the reemployment challenges facing the older and more experienced chemists. Consequently, I am a strong advocate of ACS-supporting/providing continuing education opportunities, scholarships, and fellowships which permit the enhancement/updating of scientific knowledge and special skills as an aid to those actively seeking employment. If you choose to elect me as Councilor/Alternate Councilor, I will be pleased and look forward to devoting my best efforts to serve members of NESACS.

Mary T. Burgess

Education: B.S., Simmons College.

Northeastern Section Activities and Statement: I have been a member of the Northeastern Section, ACS, during my entire career in chemistry. I have been involved in programs related to Education and Professional Relations including the development of the Student Awards Program and the Henry A. Hill Award. As Hospitality Chairman, I participated in NERM 1978, National ACS Meeting in Boston 1990, NERM 23, Boston 1993 at Northeastern University, ACS Pops programs and Summerthing. I have been a member of the national ACS Committee on Professional Relations and Liaison to the Women Chemists Committee at the same time.

I am currently working with the Program Committee of the Northeastern Section. I have been active in both local and national affairs and will be proud to continue to represent our Section as Councilor of the Northeastern Section. I ask for your continued support and hope that you will vote for me for Councilor of the Section.

Michaeline F. Chen

Education: B.A., Clark College; M.S., Boston College.

Professional Experience: Currently, Research Chemist, Armor/Structural Ceramics Team, Ceramics Research Branch, U.S. Army Research Laboratory. During the previous

10 years, conducted work in advanced materials synthesis and processing, and surface science and materials characterization at the Army Research Laboratory, Watertown, Mass.

Service in ACS: Member since 1976. Public Relations Committee (1987-88); Associate (1988), Member (1989-93) Economic Status Committee; Member, Economic and Professional Affairs Committee (1994); Associate, International Activities Committee (1995-present).

Northeastern Section: Served and chaired Summerthing/Fallfest Committee (1982-92); Chairman, Hospitality Committee (1984-87); Chairman, Hospitality Committee, IUPAC Meeting in Boston (1986); Board of Directors (1984-present); Councilor (1988-96); Professional Relations Committee (1988-present), Chairman (1988); Nominating Committee (1988, 1995); Organizing and Planning Committee, Chairperson of Public Relations, National ACS Meeting, Boston (1990);

Statement: I shall continue to broaden our Section's influence on national policy decisions, increase interaction between the Northeastern Section and the National Society, promote new and interesting programs, and increase the involvement of members in section activities. I would sincerely appreciate your support and your vote so that I may continue to serve you as Councilor.

Michael J. Dube

Education: B.Sc., Southeastern Mass. University; Ph.D., Brown University (1993)

Professional Experience: Visiting Asst. Prof., Brown University (Spring 1993); Lecturer, Rhode Island College (Spring-Summer 1993); Assistant Prof., Wellesley College, (Fall 1993-present)

Northeastern Section: Chairman, James Flack Norris Speakers' Bureau (1994-present).

Statement: Recently I have begun serving the NESACS as Chairman of the James Flack Norris Speakers' Bureau. I am currently aware of the activities and functions of the Section and the dedication necessary to play an active role in its affairs. I feel that serving as Councilor will allow me to attain experience that will prepare me to better serve the Section now and in the future. If elected, I will represent the Section's interest and participate in the various forums at both the local and national levels. I would faithfully serve the Section, offering fresh, new insights that will reflect the changing interest of the chemical community. Several issues that continue to warrant attention are the role the chemical community plays in society, increasing the quality of chemical education in our institutions, exposing students to chemistry by supporting programs that allow students to perform research, and increasing minority enrollment in chemistry. If given the chance, I would effectively voice and communicate the concerns and needs of the Section to the best of my ability.

Patrick M. Gordon

Education: B.Sc., University of Guyana; M.Sc., University of New South Wales; Ph.D., University of Manitoba.

Professional Experience: Post Doctoral Research Associate, Kansas State University (1987-88), Organix, Inc. (1988-91); Scientist, Polaroid Corp. (1991-present).

Northeastern Section: Treasurer, Program Chair, Chairman and immediate Past Chairman, Medicinal Chemistry Group, NESACS; Organizer of the Medicinal Chemistry Symposium at the 1993 NERM meeting in Boston.

Statement: I have been involved with the Medicinal Chemistry Group of the Northeastern Section of the ACS since 1989. During that time I participated in holding all the officer positions within the group. That allowed me, with the help of my colleagues, to make a significant impact in reviving the Medicinal Chemistry Group. Today, as many of you have witnessed, the group has provided the scientific community in the Boston area with topical seminars and symposia. Moreover, the experience gained during my tenure helped me to appreciate what more can be, and needs to be, done at the local level.

For example, the ACS has shown a commitment to raising the level of involvement of minorities in science by establishing a Committee on Minority Affairs. One such program of that committee is the *Minority Scholars Program*, which is in need of local involvement. Furthermore, the National Organization of Black Chemists and Chemical Engineers (NOBC-ChE) is also working with the national ACS to develop programs to meet some of their mutual objectives. As a Councilor, one of my goals would be to aid in those efforts, particularly since I am involved with the local chapter of NOBCChE. I firmly believe that we have to reach more potential scientific leaders at a young age. Therefore, another goal would be to work at using, for example, the *Volunteer in Public Outreach Program* as a means of getting high schools that traditionally do not have a strong science program, to build one. Finally, if elected, I would always welcome ideas from you and would be willing to work with you to make our Local Section one that we can all be proud of.

Richard P. Johnson

Education: B.S. (1972), Ph.D. (1976) from Syracuse University. Postdoctoral studies at the University of Geneva, Switzerland, and the University of Wisconsin, Madison.

Professional Experience: Iowa State University, University of New Hampshire since 1985, currently Professor of Chemistry. Research Interests: photochemistry, highly strained organic molecules, applications of theoretical methods.

Service in ACS: Member since 1972; Ames Section, Chairman, 1982-1983.

Statement: Challenging times and opportunities lie ahead for science, both in industry and education. We should all work harder to demonstrate the fundamental importance of chemistry. As a candidate for councilor, I have no fixed agenda beyond that. I would do my best to represent both the section and the discipline of chemistry.

Doris I. Lewis

Education: B.S., Duke University (1965); Ph.D. Tufts University (1972).

Professional Experience: Newton College of the Sacred Heart (1970-75); Suffolk University (1975-present); Currently Professor and Chair of Chemistry.

Service in ACS: National Science Funding Network (1991-present). Member of Chemical Education and Analytical Divisions.

Northeastern Section: Continuing Education Committee (1979-81); Student Affiliate Coordinator (1978-90); National Meeting Committee (1990); Alternate Councilor (1991-93); Councilor (1994-96); Board of Publications (1995-97).

Statement: The local section should be the front line of the American Chemical Society in delivering services to members and representing the chemical profession in the community. Serving the Section as Councilor and as a member of the Board of Publications, I have tried to represent our many constituencies fairly. Industrial and academic chemists, those employed or seeking employment, younger chemists or retired chemists, and the chemists of the future, our Student Affiliates, all should be represented and served by the programs of the Section. Honored traditions of our historic Section, like the *NUCLEUS* and our awards for excellence in chemistry and chemical education need our continuing support, but we need to look to our current needs and opportunities, as well. Most recently, I have been involved in helping those who are attempting to start a home page for the Section on the Web, and to upgrade our services in matching prospective employers with job seekers by using the Internet. Throughout my involvement with the Northeastern Section I have been honored to work with the many dedicated and talented chemists whose efforts have resulted in successful programs of service to chemists and outreach to the community. I would appreciate your vote, and promise that if elected, I will continue to do my best to represent you and to serve the needs of the membership of the Northeastern Section.

Truman S. Light

Education: S.B., Harvard University (1944); M.S., University of Minnesota (1949); Doctor of Chemistry, University of Rome (Italy) (1961).

Professional Experience: Assistant Professor, Boston College (1949-59); Senior Scientist, AVCO R&D (1959-64); Principal Research Scientist (1964-88), Consultant (1988-present), The Foxboro Co.; Adjunct Professor, Chemical Instrumentation, Boston College (1987), Suffolk University (1992), Aquinas College, Newton (1994-95).

Awards: Natl. Science Foundation Faculty Fellowship (1995-61); Henry A. Hill Award for Service to the Northeastern Section (with Arlene Light) (1993); Waters Symposium Award (Ion Selective Electrodes), Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy (1966).

Service in ACS: Committee service: Local Section Affairs, Constitution and Bylaws, Membership Affairs, Employment Services Advisory Board, Copyrights.

Northeastern Section: Councilor (1976-1995); Chairman (1978); member and chairman of various committees: Student Affiliates, Constitution and Bylaws, Esselen Award, Professional Service, Employment Services.

Statement: I am a candidate for Councilor because I am an Alternate Councilor, at the present time, and I can accomplish much more for the Northeastern Section as a full Councilor. To refresh your memory, the Council of our Society (analogous to the Congress of the US) is its governing body. Councilors are appointed to Committees to suggest and evaluate changes and make and control budget appropriations. Councilors need to be in attendance at both National Meetings each year (why are there so many National Meetings—that's a separate story—no room here to discuss it). Some Councilors cannot afford the time or expense to attend both meetings, hence we have Alternate Councilors who are appointed, meeting by meeting, to substitute. As a Councilor for many years, I have been fortunate to be able to attend both National Meetings and be appointed to and served on several committees (see above). In my semi-retirement I am able to continue this attendance, but the uncertainty of being an Alternate Councilor precludes most committee appointments. We (Arlene Light and I) have become particularly active volunteers in the National Employment Clearing House, training the volunteers and helping applicants and employers to find their way through this hectic process.

So, to conclude my statement: I seek your vote for Councilor to be able to continue my involvement in several of the facets of the national ACS that make it one of the premier scientific and publishing professional societies in the world. Thank you!

John L. Neumeyer

Education: B.S., Columbia University (1952); Ph.D. (Medicinal Chemistry), University of Wisconsin (1961).

Professional Experience: Research Chemist, Ethicon (Div. of Johnson & Johnson) (1952-57); Senior Research Chemist, FMC Corp. (1961-63); Senior Staff Scientist, Arthur D. Little, Inc. (1963-69); Distinguished University Professor, Medicinal Chemistry and Chemistry, Northeastern University (1969-92); Visiting Professor of Chemistry, University of Konstanz, Germany (1975-77); Visiting Scientist, McLean Hospital, Harvard Medical School (1985-86); Scientific Director, Chairman and Co-Founder, Research Biochemicals International (1980-present)

Service in National ACS: Councilor and Executive Committee (1971-81), Vice Chairman (1981), Chairman (1982), Councilor (1983-87), Division of Medicinal Chemistry; Society Committee on Publications (1991-94).

Northeastern Section: Founder and Chairman, Medicinal Chemistry Group (1964-65); Councilor (1988-present); Trustee (1989-93).

Statement: Having served the American Chemical Society in a variety of functions over the past 32 years, most recently as a Councilor and Trustee of the Northeastern Section, I have become keenly aware of the problems and concerns of its members, both on the local and national scene. If re-elected, I will continue to devote my time, energies and experience in academia and industry to carrying out my responsibilities as Councilor, both nationally and at the local level.

Directors-at-Large

Anthony C. Bevilacqua

Withdrawn

Leisa Corbett

Education: B.S. Chemistry, Boston College (1985)

Experience: Chemist, Houghton Chemical Co. (1986-88); Technical Sales Chemist, HNU Systems (1988-90); Chemical Product Manager, Houghton Chemical Co. (1991-present), managing a line of industrial water treatment chemicals.

Memberships: ACS, Association of Water Technologists.

Yigong Gao

Education: B.S., M.S., Beijing Medical University; Ph.D., Medicinal Chemistry, Northeastern University (1991)

Experience: Postdoctoral Fellow, Research Triangle Institute, North Carolina (1992); Synthesis Group Leader, Research Biochemicals, Intl. (1992-present).

Awards: Marie Curie Award, European Nuclear Medicine (1992).

Statement: If elected as Director-at-Large I pledge to devote my energies and experience as a working chemist to the needs of the Society.

James A. Kaufman

Education: B.S., Tufts University (1965); Ph.D., W.P.I. (1971); Post-Doctoral Fellow, W.P.I. Chemical Engineering Department (1971-73).

Experience: Instructor, W.P.I. (1966-69); Research Associate, Holy Cross College (1970-71); Senior Research Chemist, Dow Chemical Co. (1973-77); At Curry College: Associate Professor (1977-82), Professor (1982-present), Director, Health Safety & Environmental Affairs (1991-93); Laboratory Safety Consultant (1980-present); Founder/President The Laboratory Safety Workshop (1981-present).

American Chemical Society: Member, Council Committee on Chemical Safety (1979-88); Division of Chemical Health and Safety: member (9 years), Editor of Division Newsletter (one year), Membership Committee (6 years), Chairman (1986); Developed letter on lab safety from ACS President to college/university presidents; developed national awards for college/university lab safety programs;

organized and chaired several DCHAS symposia; ACS Tour Speaker (1991-present).

Northeastern Section: Councilor (1982-87); Alternate Councilor (1981); Auditor (1981); Chairman, Health and Safety Committee (1978-91, 1996); Contributing Editor, *NUCLEUS* safety column (2 years); Chairman, Safety Symposium for NERM-8, Safety Symposia for Mass. Safety Council Annual Meeting (1978, 1981); Moderator, Hazardous Waste Symposium at Simmons College (1984); Nominating Committee (1985); Workplace Chemicals Conference (May 1086); helped to develop and organize Academic Lab Safety Council (1989); Participated in symposia on lecture demonstrations, home chemical safety, and lab safety; Chairman-Elect (1993); Chairman (1994); Past-Chairman (1995).

John O'Gara

Withdrawn

Mary Ann Solstad

Education: B.S. Chemistry, Pomona College; M.S. Chemistry, Mount Holyoke College.

Experience: Scripps Institute (one year); Consultant on Chemical Health and Safety

American Chemical Society: Division of Chemical Health and Safety: Social Chair, Councilor (six years), Member-at-Large of Executive Committee; Joint Board-Council Committee on Chemical Safety (nine years), Subcommittee on Safety Videos (six years); Technical Advisor on a laboratory safety practices film (1995-96); Liaison between chemists and industrial hygienists for developing an ACS program to certify Chemical Hygiene Officers, a position mandated for every laboratory by OSHA Laboratory Standard. Northeastern Section: Chairman, James Flack Norris Speakers Bureau (1980-94); Contributing Editor on Chemical Health and Safety, The *NUCLEUS* (1980-present); Councilor/Alternate Councilor for about 10 years.

Nominating Committee

Henry Brown

Education: A.B., University of Michigan (1941); M.D., University of Pennsylvania (1944).

Experience: U.S. Navy (1942-44 and 1954-56): Nutrition Unit, Naval Research Institute, Oakland Naval Hospital Metabolic Research Unit; Runyon Cancer Fellow, University of Cambridge (1952-53); Department of Surgery, University of Wisconsin (1957-63); Harvard Surgical Unit and Sears Surgical Laboratory, Boston City Hospital (1963-present) Assistant Director until 1976; moved with the unit to New England Deaconess Hospital in 1976. Current researches are concerned with the molecular biology of wound healing with the Brigham and Women's Hospital

Plastic Surgery Research Group and anatomic studies with the Anatomic Institute of the University of Paris. He also directs hand surgery and rehabilitation medicine for the Deaconess teaching rotation at the Manchester, N.H. Veterans Administration Hospital.

Northeastern Section: Esselen Award Committee (1996).

Statement: I would like to see our Section of the ACS foster closer interaction and ties between the pharmaceutical, biotechnology and industrial firms and the academic community through our meetings and symposia. Together, rather than as individuals, we have much more to contribute to enrich chemical knowledge and progress.

Catherine E. Costello

Education: A.B., Chemistry, Emmanuel College (1964); M.S. (1967), Ph.D. (1970), Organic Chemistry, Georgetown University.

Experience: Associate Director, M.I.T. Mass Spectrometry Resource; Director of the BUSM Mass Spectrometry Resource, Dept. of Biophysics, Boston University School of Medicine (1995-present)

American Chemical Society: Currently a member of the Constitution and Bylaws Committee; Committee Associate, International Activities Committee. ACS Tour Speaker.

Northeastern Section: Board of Publications (1988-1993), Chairman (1990, 1993); Nominating Committee (1982, 1983, 1987, 1992).

Arabinda Dey

Education: M.Sc., Patna University (India); Ph.D., Calcutta University.

Experience: Staff Scientist, Duracell, Inc. (formerly P.R. Mallory & Co.), Chief Scientist in the R&D Department of the Duracell Worldwide Technology Center, Needham, Mass. (1966-1995), retired in 1995. Research on lithium batteries as primary and rechargeable systems, resulting in over fifty papers and sixty U.S. patents. Received the Battery Research Award of the Electrochemical Society (1990).

James A. Golen

University of Massachusetts Dartmouth
No statement received

Norris Award Committee

Saul G. Cohen

Education: A.B., summa cum laude (1937), Ph.D. (1940) Harvard University.

Professional Experience: Instructor (1940-41), Research Associate (1941-43), Harvard University; Natl. Research Council Fellow, Lecturer, U.C.L.A. (1943-44); Research

Chemist, Pittsburgh Plate Glass Co. (1944-45); Polaroid Corporation (from 1945); Chief Chemist (1948-50), Consultant (1950-present); At Brandeis University: Associate Professor (1950-52), Professor (1952-73), University Professor (1973-86), University Professor Emeritus (1986-present), Chairman, School of Science (1950-55), Dean of Faculty (1955-59), Chairman, Dept. of Chemistry (1959-64, 1967-72); Visiting Professor: Harvard Medical School (1965), Hebrew University of Jerusalem (1972).

Related Activities and Honors: Director, Manhattan Fund (1972-95); Board of Overseers of Harvard College (1983-89), served on several committees of the Board of Overseers; Member of Phi Beta Kappa, Sigma Xi, American Chemical Society, The Royal Chemical Society, London, American Society of Biological Chemists, European Photochemical Association, Inter-American Photochemical Society.

Honors: Guggenheim Fellowship, Fulbright Senior Research Scholar in U.K., 1958-1959; American Academy of Arts and Sciences, Fellow 1956-, Councilor 1967-1971; Fellow, American Association for Advancement of Science. James Flack Norris Award, American Chemical Society, 1972 Centennial Medalist, Harvard University Graduate School of Arts and Sciences, for Contributions to Society, 1992.

Northeastern Section: Trustee and Director (1976-84)

Research and Publications: Research in mechanisms of organic reactions, photochemistry, enzymology, free radicals, vinyl polymerization, high polymers, photographic processes, and radiation chemistry. Numerous publications in refereed American and international journals.

Cynthia B. McGowan

Merrimack College
No statement received

Patricia L. Samuel

Boston University
Chairman, Northeastern Section (1996)
No statement received

Robert S. Umans

Education: A.B., Columbia University (1962); M.S. (1963), Ph.D. (1966), Yale University.

Professional Experience: NIH Postdoctoral Fellow, Johns Hopkins University (1966-68); Postdoctoral Fellow, University of Paris (1968-69); Assistant Professor of Chemistry, Boston University (1969-75), Boston College (1976-77), Wellesley College (1977-79); Research Fellow and Research Associate, Harvard School of Public Health (1980-86); Assistant Professor of Chemistry, Wellesley College (1986-90); Faculty in Residence in Biochemistry, University of New Hampshire (1991-93); Adjunct Associate Professor of Chemistry and Assistant Director of Undergraduate Laboratories, Boston College (1993-present).

Related Activities: ACS member since 1969. ◇

Meeting Report

Radicals: Bane or Boon?

Report of the March 1996 Richards Award

Address by JoAnne Stubbe

Manuscript supplied by Dr. Stubbe

"Free radicals" have long been associated in the popular press with alteration of our genetic blueprint, DNA. If the lesions go unrepaired, they ultimately lead to diseased states and contribute to the aging process. Free radicals are thus associated with chemical reactivity that is uncontrolled, whose reactions lead to destruction. "Nature", however, has evolved sophisticated systems to harness the reactivity of radicals to execute difficult, exquisitely specific, transformations in key steps in metabolism and to play key roles in the survival of the organism. Tinkering with these fine-tuned systems, however, leads to loss of control and destruction of the natural system.

In the past few years it has become apparent that organic paramagnetic species are much more relevant in biological systems than previously appreciated. Figure 1 summarizes the amino acid radicals now known to function as essential components of enzymes involved in metabolism. Tyrosyl radicals (Fig. 1a) play a key role in oxidation of H_2O to O_2 catalyzed by a putative tetramanganese cluster associated with photosystem II. They play a key role in prostaglandin biosynthesis catalyzed by PGH synthetase and in nucleotide metabolism catalyzed by ribonucleotide reductases. Substituted tyrosine radicals play roles in oxidation of alcohols to aldehydes (Fig. 1b), aldehydes to acids (Fig. 1b) and amines to imines (Fig. 1c). Tryptophan cation radicals play an essential role in a peroxidase catalyzed reaction and glycyl radicals play essential roles in acetyl-CoA formation and nucleotide metabolism under anaerobic conditions. Finally, very recently cysteinyl radicals have been shown to play an essential role in nucleotide metabolism, specifically nucleotide reduction.

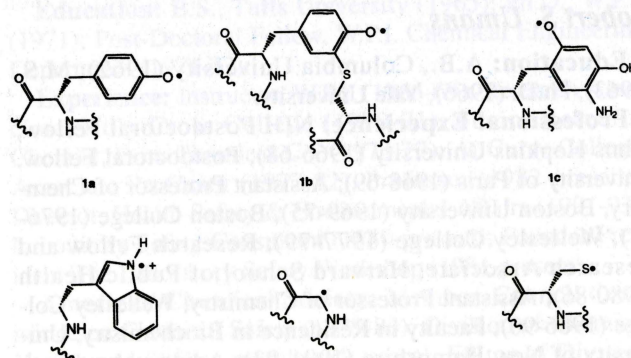
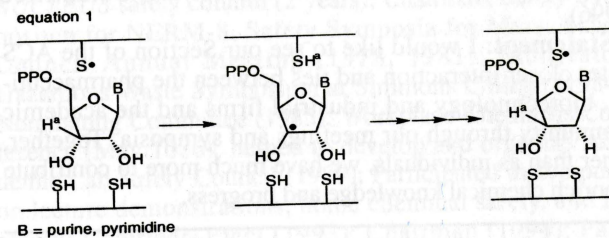


Figure 1 Amino Acid Radicals identified as playing a catalytic role in a variety of enzyme-catalyzed reactions.

One example will be presented that demonstrates the importance of controlled radical based reactions in biology: the ribonucleotide reductases (RNRs). These proteins catalyze the rate determining step in DNA biosynthesis: the conversion of nucleotides to deoxynucleotides (eq. 1).



The enzymes reduce both purine and pyrimidine nucleotides in an exquisitely regulated fashion, as controlling the relative ratios of the deoxynucleotide pools is essential for the fidelity of DNA replication. This central role in metabolism makes them a prime target for design of anti-tumor and antiviral agents. What is surprising about RNRs is that despite this central role in metabolism, the primary and quaternary structures and the unusual metallo-cofactors have not been evolutionarily conserved (Fig. 2). Our laboratory has focused on understanding the mechanism of nucleotide reduction, using three complementary approaches. The first approach uses the wild-type enzyme, the normal substrate and physical organic methods. The second uses substrate analogs: mechanism-based inhibitors. The third uses protein analogs: site-directed mutants. An example of each approach is outlined subsequently and demonstrates the amazing specificity of this system and the fragility of the system to minimal alterations.

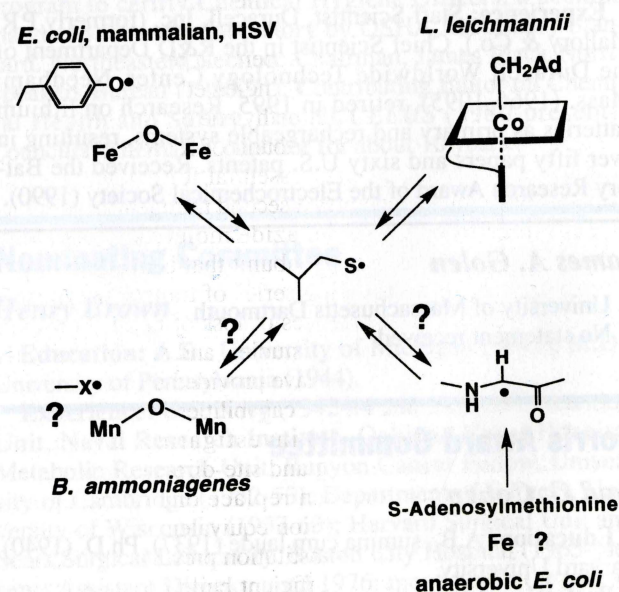
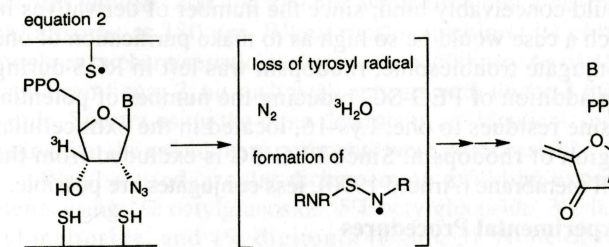


Figure 2 The cofactors identified in ribonucleotide reductases isolated from different sources.

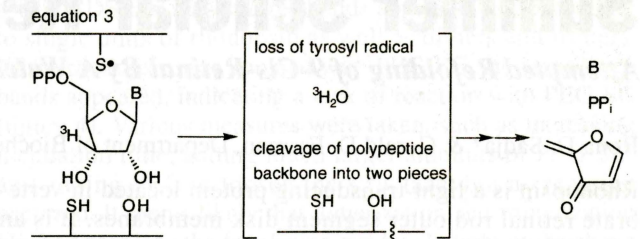
As indicated in eq. 1, a key step in catalysis is 3'-hydrogen atom abstraction by a thiyl radical. To test this hypothesis [$3'-^2H$] or [$3'-^3H$] nucleotides were synthesized and an isotope effect on the reduction process measured. These results establish the importance of 3' carbon hydrogen bond cleavage. Given the molecular biological revolution, gram quantities of RNRs can now be obtained, allowing us to look for intermediates along reaction pathways using rapid kinetic methods (millisec time scale). In the case of the adenosyl-cobalamin enzyme from *L.leichmannii* (Fig. 1), rapid freeze quench EPR experiments have revealed an intermediate composed of cob(II)alamin and a thiyl radical, generated with an apparent rate constant of $250 s^{-1}$. The turnover number of this RNR is $\sim 2 s^{-1}$, demonstrating that this intermediate is generated in a kinetically competent fashion.

The second approach uses mechanism-based inhibitors to better define the catalytic capabilities of these enzymes. An example is shown in eq. 2.



2'-Azido-2'-deoxynucleotides are stoichiometric mechanism-based inhibitors of the tyrosyl radical-dependent RNRs. The inhibitors require 3' carbon-hydrogen bond cleavage (as does the normal reduction process) to initiate the enzyme inactivation. When the 2'-hydroxyl group of a nucleotide is replaced with an azide moiety, the normally exquisitely controlled radical-dependent reduction process is dramatically compromised. As indicated in eq. 2, the entire substrate is decomposed to 2-methylene 3-(2H) furanone that alkylates and inactivates one subunit of RNR and the tyrosyl radical on a second subunit, essential for catalysis, is lost. Loss of one radical generates a second nitrogen-centered radical derived from the initial azide moiety and covalently attached to a cysteine of the subunit that is alkylated by the furanone. This is an amazing series of transformations and demonstrates the consequences of loss of control of a radical-dependent process. These studies, and studies with other mechanism-based inhibitors have provided us with important information about the catalytic capabilities of RNRs.

The third approach to investigating mechanisms involves protein engineering and site-directed mutagenesis. In the case of RNR, one can replace one of the cysteine residues providing the reduction equivalents to make dNTP (eq. 1) with a serine. This substitution prevents the reduction process, perhaps allowing sufficient build up of an intermediate such that it can now be detected experimentally. The results of such a substitution are summarized in eq. 3.



The normal substrate becomes a mechanism-based inhibitor. The process is initiated by 3' carbon-hydrogen bond cleavage. The tyrosyl radical on one subunit is destroyed and the polypeptide of the second subunit is cleaved into two pieces, the consequence of radical chemistry gone astray.

These types of studies have allowed us to formulate a mechanism for the nucleotide reduction process involving a number of reactive radical intermediates. The RNRs can catalyze 500,000 turnovers without making a mistake, initiated by hydrogen atom abstraction uniquely at 3'-position of the sugar. Tinkering with the system, by altering the substrate or protein (eq. 2 and 3), however, results in complete destruction of the system.

RNRs are just one of many examples of nature's ability to control free radical chemistry and use the reactivity of these species to its advantage. We now have examples of specific radical-based reactions that occur at every position of the deoxyribose ring of nucleotides in exquisitely controlled reactions. Thus, while free radicals can clearly be associated with destruction and lack of control, it is important to remember that they also can be very effectively controlled, allowing difficult chemistry to occur in essential steps in metabolism. \diamond

Abstracts

continued from page 16

based on receptor specificity. Structure activity relationships for this initial library lead were rapidly explored using multiple parallel synthesis techniques to produce lead compound CP-2550 ($IC_{50} = 120 nM$). This non-peptide bradykinin antagonist is undergoing further optimization by traditional and combinatorial methods. This directed combinatorial approach compares very favorably with random natural products screening or chemical file screening approaches for the discovery of new leads for bradykinin antagonists.

High Throughput Screening Against Novel Therapeutic Targets

Michael Boisclair, Mitotix, Inc., Cambridge, MA

An immediate challenge faced by drug discovery programs involving novel therapeutic targets is to quickly identify lead compounds. The process has been greatly aided in the last

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Summer Scholar Report

Attempted Refolding of 9-Cis-Retinal By A Water-Soluble PEG-Rhodopsin Conjugate

Rona D. Sadjia* & Gerald D. Fasman, Department of Biochemistry, Brandeis University

Rhodopsin is a light-transducing protein located in vertebrate retinal rod outer segment disk membranes. It is an insoluble integral membrane protein consisting of seven α -helices (figure 1) which interweave through the membrane of rod cells, comprising approximately 90% of the protein found in the bilayer. The chromophore 11-*cis*-retinal is covalently bound to rhodopsin through a protonated Schiff base at Lys-296. When light enters the eye and reaches the chromophore, it isomerizes to all-*trans*, initiating a series of photointermediates. The final intermediate, metarhodopsin II, activates the G-protein transducin and an enzymatic cascade begins which results in a neural signal.

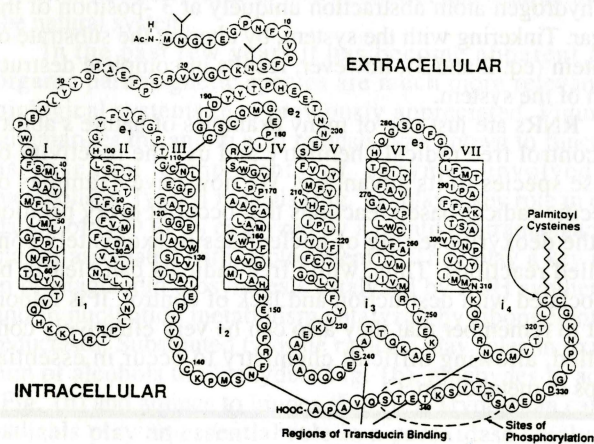


Figure 1. Model of the secondary structure of bovine rhodopsin indicating lysine residues, one of which (Lys-16) is extracellular and particularly susceptible to chemical modification with PEG-SC (Hargrave & McDowell 1992).

Rhodopsin is a very interesting protein to study due to its key role in vision. Furthermore, it was discovered that mutations in rhodopsin are responsible for autosomal dominant retinitis pigmentosa (Dryja 1990). Being an integral membrane protein, however, limits direct observation of rhodopsin, as X-ray crystallography is extremely difficult for such water-insoluble proteins.

It was discovered that polyethylene glycol succinimidyl carbamate (PEG-SC; molecular weight = 5,000 Da) could react with exposed lysine residues on exterior loops of membrane proteins to form water-soluble conjugates (Wei and Fasman 1995). Previous work with PEG-porin has resulted in crystallization, although growth is presently too modest to submit to X-ray crystallography. Attempts were

made to link rhodopsin in rod outer segment (ROS) to PEG-SC, isolate and purify PEG-rhodopsin, and submit the conjugate to tests which would ascertain that PEG-rhodopsin has, indeed, retained its native form and function.

Attempts to refold PEG-rhodopsin with 9-*cis*-retinal, a less expensive and more common analog to 11-*cis*-retinal, have thus far been unsuccessful. A variety of detergents such as dodecyl maltoside, octylglucoside, lauryl maltoside, and digitonin were used to facilitate refolding, and 2 M guanidine hydrochloride was added to loosen the lipid structure and allow easier access of PEG-SC to lysine residues. There are ten lysine residues in rhodopsin to which PEG-SC could conceivably bind; since the number of derivatives in such a case would be so high as to make purification of one conjugate troublesome, rhodopsin was left in ROS during the addition of PEG-SC, reducing the number of potential lysine residues to one, Lys-16, located in the extracellular region of rhodopsin. Since PEG-SC is excluded from the cell membrane (Arnold 1990), less conjugates are possible.

Experimental Procedures

Bovine ROS enriched in rhodopsin (0.36 mg/mL) was a generous gift from Dr. D. Oprian (Brandeis University). PEG-SC with a molecular weight of 5000 kDa was synthesized by Wei (Wei and Fasman 1995). A 1:0.9 ratio of ROS to PEG-SC was mixed in 0.1 M sodium tetraborate buffer, pH 9.3 for one hour at room temperature. This was followed by centrifugation in a Beckman 50.2Ti rotor for 25 min at 45 000 rpm and 4°C. The pellet was resuspended in a minimal volume of deionized water and washed twice more. The sample at this point contained rhodopsin, PEG-rhodopsin, diPEG-rhodopsin, as well as a small amount of other proteins. (Di-PEG-rhodopsin appeared as a faint band and was presumably the result of damage to ROS cells, allowing PEG-SC access to the nine intracellular lysines.) PEG-rhodopsin was purified from ROS using a 3 mm SDS-PAGE slab gel, 10% polyacrylamide. The second band was cut out and electro-eluted, then run through a Pierce Extracti-Gel D detergent removing column to eliminate any remaining SDS. The concentration of PEG-rhodopsin was determined using a Pierce micro BCA assay. The ratio of PEG to rhodopsin was then calculated to be 0.96 using the method of Skoog (1979).

Refolding experiments were conducted using 1% dodecyl maltoside, n-octylglucoside, lauryl maltoside, and digitonin. Two methods were utilized for each detergent. 9-*cis*-Retinal was dissolved in 95% ethanol to 1.9 mM. In the first procedure, the detergent was added to 50 μ L PEG-

rhodopsin to make a 1% solution. 6 μ L retinal in ethanol was added to PEG-rhodopsin and incubated half an hour in the dark at 4°C while gently rotating. The second procedure reversed the order of mixing: retinal in ethanol was added to PEG-rhodopsin, followed by incubation as above. After this, detergent was added to make 1% and again allowed to incubate. Circular dichroism spectra from 400 to 200 nm were taken of these attempts at refolding using a Jobin Yvon Auto-Dichrograph Mark V instrument (see Prevelige and Fasman 1987).

Purification of rhodopsin from ROS using concanavalin A affinity chromatography followed the method of Oprian (1993).

Results and Discussion

We attempted to refold 9-*cis*-retinal with PEG-rhodopsin using 1% dodecyl maltoside, octylglucoside, lauryl maltoside, and digitonin. An absorbance spectrum from 650 to 250 nm was taken for each experiment. PEG-rhodopsin absorbs between 300 and 280 nm, while unfolded 9-*cis*-retinal absorbs at 380 nm. When rhodopsin binds its chromophore, a characteristic peak appears at 500 nm. As can be seen from figure 2, no such peak appears with dodecyl maltoside. Spectra using the other detergents are identical, indicating that the refolding experiments were unsuccessful.

We also used circular dichroism on refolding experiments using 1% octylglucoside, 5% octylglucoside, 3% lauryl maltoside, and 1% digitonin (figure 3). None of the samples refolded into the α -helical form; rather, all indicated a random structure.

It should be noted that PEG-rhodopsin was isolated from PEG-ROS through electrophoresis and subsequent electroelution, and it was thought that the sample might not have been as pure as desired. Therefore, attempts were made to use a more efficient purification method using a concanavalin A affinity column, which strongly binds carbohydrate moieties, of which rhodopsin has two. The protein is then eluted using α -D-mannopyranoside. The strategy was to first attempt such a purification on unbleached rhodopsin and then PEGylate

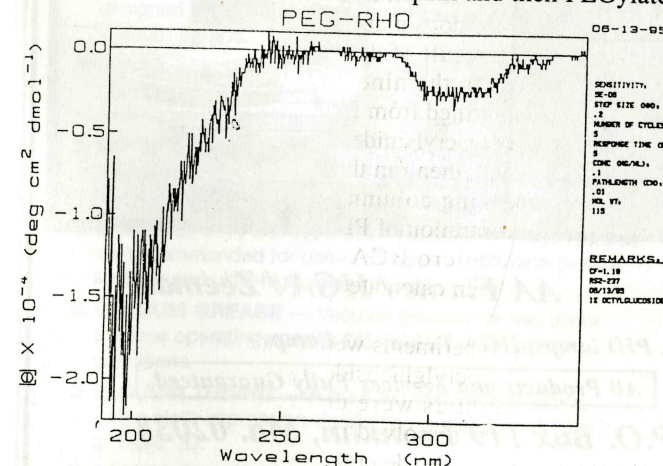


Figure 3. Circular dichroism spectrum of PEG-rhodopsin in 1% octylglucoside. A random structure is indicated.

dark-adapted rhodopsin. When purified rhodopsin was run on a 10% SDS-PAGE gel, three bands appeared, corresponding to single units of rhodopsin as well as dimers and trimers. When rhodopsin was coupled with PEG-SC, the same three bands appeared, indicating a lack of reaction with PEG-SC (figure 4). Various measures were taken, such as increasing incubation time, adding much larger amounts of PEG-SC, and adding PEG to loosen the structure; but no reaction occurred. It seems likely that dimerization and trimerization blocked access to the free lysine residue. In light of the above information, it appears that in the future methods must be taken to prevent dimerization. With purified PEG-rhodopsin, it should then be possible for refolding experiments to continue. If it follows that PEG-rhodopsin can refold 9-*cis*-retinal, it will then be necessary to show that refolding occurs with the natural chromophore, 11-*cis*-retinal. Experiments to verify that PEG-rhodopsin has the same activity as rhodopsin would then proceed, followed by attempts at crystallization.

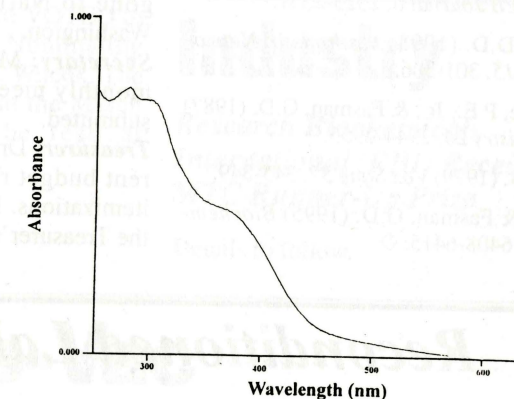


Figure 2. Absorbance spectrum of 6 μ L of 1.9 mM 9-*cis*-retinal in ethanol incubated with 50 μ g PEG-rhodopsin in 1% dodecyl maltoside. Had retinal bound to rhodopsin, there would be an absorbance maximum at 500nm.

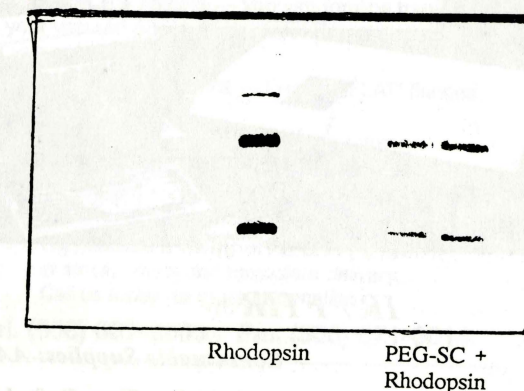


Figure 4. 10% polyacrylamide SDS-PAGE gel of rhodopsin purified using a concanavalin A-sepharose 4B affinity column and samples of PEG-SC with rhodopsin, in which no reaction occurred.

*James Flack Norris/Theodore William Richards Summer Scholar

Summer Scholar

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Acknowledgements

We thank Dr. Daniel Oprian, Jeanne Rim and Vik Rao for providing us with samples of rhodopsin and excellent advice and Jiang Wei and Mythili Suntharalingam for their assistance.

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Board of Directors

Minutes of the Meeting of February 8, 1996

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

(The order of items has been rearranged to conform to the usual NUCLEUS format)

Officer's Reports:

Chairman: Dr. Samuel indicated that the Annual Report of the Section has gone to National Headquarters in Washington.

Secretary: Minutes for the previous monthly meeting were approved as submitted.

Treasurer: Dr. Piper presented the current budget report, including recent itemizations. It was VOTED to accept the Treasurer's Report.

Archivist: Dr. Simon expressed the hope that an area institution will come forward with permanent space for the archives.

Editor: Dr. Heyn indicated that the March issue of the NUCLEUS comes to sixteen pages and is ready to go to press. Dr. Heyn made a call for manuscripts of interest to readers concerning the activities and history of the Section and its members.

Committee Reports:

Board of Publications: Dr. Billo reported that the needed financial supplement for operating the NUCLEUS is down substantially, in large part due to the good success of V. Gale in obtaining advertising.

Budget: See under Old Business.

Chemical Education: Dr. Hoffman communicated to the Board through the good offices of Dr. Samuel the call for Papers of the Annual NESACS Undergraduate Research Symposium (Abstracts due 12 April; Symposium 27 April at Boston University) and the National Undergraduate Research Sym-

posium in August (Orlando, Florida). Announcement was also made of the upcoming Norris/Richards Summer Student Research Scholarships.

Constit. and Bylaws: Dr. Simon, on behalf of the committee, stated that an amendment will be brought to a future Board meeting to regularize election and terms of office for certain committees.

Continuing Education: Dr. Viola indicated that a second session of the Microsoft Excel course was offered in January. Another short course will be offered in the spring; it is an experimental course which National is asking us to try. National has essentially guaranteed that the Section will take no loss, should enrollments be unfavorable.

Esselen Award Committee: Dr. Browner reminded the Board that the ceremonies would be on 15 April at Harvard.

Minority Affairs: Dr. Phillips indicated that NESACS has some truly good applicants for this year's undergraduate minority scholarships.

Nominating: V. Wilcox stated that the required slate of candidates would be

presented in the new business portion of today's agenda.

Public Relations: Dr. Howell asked for more information about events, speakers, and activities for inclusion in hometown newspapers.

Safety: M. Solstad made the Board aware of the intention of Dr. Heindel to propose at the New Orleans Meeting ACS certification for Chemical Hygiene Officers. Concern was expressed over competition with current certification of industrial hygiene officers now offered by the American Industrial Hygiene Society. Cooperation should be stressed, rather than competition.

Old Business: The Board VOTED to accept the Budget Proposal of the Budget Committee.

New Business: The Board VOTED to accept the report of the Nominating Committee as given by V. Wilcox. The slate is to be published in the March NUCLEUS and will be read at tonight's Section Meeting.

Respectfully submitted,
M. J. Hearn, Secretary ◇

Hospitality Anyone?

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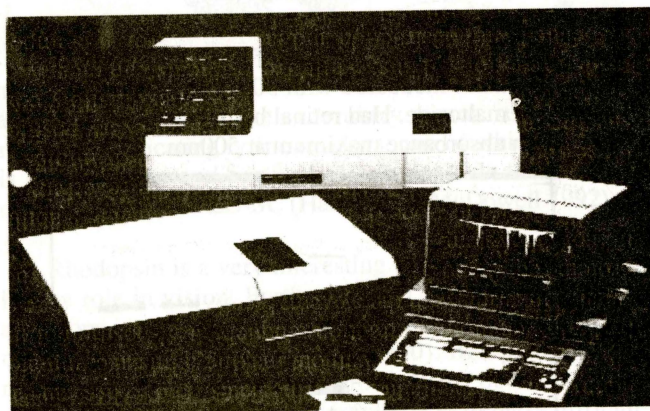
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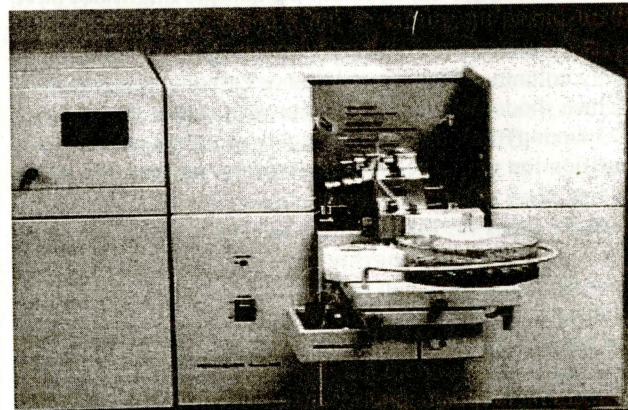
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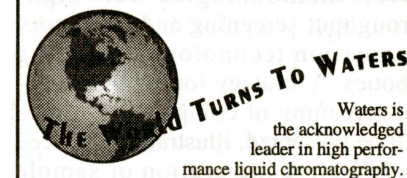
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few years by the development of novel methodologies for high-throughput screening and laboratory automation technology, including robotics. A strategy for high-throughput screening of compound libraries will be presented, illustrating the need for effective integration of sample acquisition, laboratory automation, hierarchical screening and high-volume data management.

High Speed Synthesis of Thematic Compound Arrays for Small Molecule Drug Development

Dr. Joseph C. Hogan, Jr., ArQule Corp., Medford, MA

ArQule has developed an integrated modular synthetic chemistry technology which enables the accelerated development of molecular recognition agents for a wide variety of applications in drug discovery, drug delivery, separations, diagnostics and catalysts design. This development process incorporates and combines useful features from both the structure-guided ("rational") approach to ligand design and the high volume screening approach using large numbers of molecules obtained from natural sources, from libraries of peptides or oligonucleotides or from the combinatorial synthesis of collections of small organic molecules. ◇

Calendar

April 16

Prof. Daniel Kahne (Princeton Univ.)
"Carbohydrates as DNA Binders: Structure, Function and Design"
Tufts Univ., Rm. 104, Pearson Hall, 4:30 pm

April 18

Prof. Rachel Klevit (Univ. Washington, Seattle)
"Structure and Dynamics of a Zinc-Finger-DNA Complex"
Boston College, Merkert Chemistry Ctr., Rm. 127, 4:00 pm

Prof. S. Gellman (Univ. of Wisconsin)
"Biopolymer Folding and Refolding: From Model Studies to the Real Thing"
Northeastern Univ., Rm. 129, Hurtig Bldg., 4:00 pm

Prof. Myron Rosenblum (Dept. of Chemistry, Brandeis Univ.)
"Polymers from Cofacial Metallocenes"
UMass Lowell, Olney Hall, Rm 428, 3:30 pm

April 22

Prof. Barry Sharpless (Scripps Research Inst.)
Title TBA
Harvard University
12 Oxford St., Mb-23 at 4:15 pm

Prof. Joseph Wang (New Mexico State Univ.)
"Field Monitoring of Trace Metals - Bringing the Laboratory to the Field"
Tufts Univ., Rm. 104, Pearson Hall, at 3:30 pm

Dr. Harold H. Kung (Northwestern Univ.)
"Removal of NO_x Pollutants from Automobile Exhaust"
Tufts Univ., AV Room, STC Building, 2:30 pm

April 24

Prof. Wolfgang Ketterle (M.I.T.)
"Bose-Einstein Condensation of an (Almost) Ideal Gas"
Harvard Univ., 12 Oxford St., Mb-23, 4:00 pm

April 25

Prof. Evan Kantrowitz (Boston College)
"Global Energy Changes as the Means of Allosteric Control in Aspartate Transcarbamoylase"
Boston College, Merkert Chemistry Ctr., Rm. 127, 4:00 pm

April 30

Prof. Ken Feldman (Pennsylvania State Univ.)
"Ellagitannin Chemistry"
Boston College, Merkert Chemistry Ctr., Rm. 130, 2:00 pm

May 1

Minisymposium "Chemical Mechanisms in Atmospheric Chemistry"
2:00 pm Prof. Paul Wennberg (Harvard Univ.)
3:00 pm Prof. Roger Miller (Univ. N. Carolina)
4:00 pm Coffee Break
4:30 pm Prof. Mario Molina (M.I.T.)
Harvard Univ., Science Center D

May 13

Dr. James Wells (Genentech)
"Prospects for Shrinking Proteins to Peptides"
Harvard University
12 Oxford St., Mb-23, 4:15 pm

May 17

Prof. Julius Rebek (M.I.T.)
"Molecular Assembly and Recognition"
Boston College, Merkert Chemistry Ctr., Rm. 130, 4:00 pm

May 20

Prof. Gary Posner (The Johns Hopkins Univ.)
"Designer Drugs for Healthier Living"
Tufts Univ., Rm 104, Pearson Hall, 3:30 pm

May 30

Prof. Roger Giese (Northeastern Univ.)
"Mass Tag DNA Sequencing"
Northeastern Univ., Rm 129, Hurtig Bldg, 4:00 pm

June 18

Prof. Ern Della (Flinders Univ., Adelaide, Australia)
Title TBA
Boston College, Merkert Chemistry Ctr., Rm. 130, 2:00 pm

Notices for the Nucleus Calendar should be sent to:

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