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NESACS

THE NUCLEUS

February 1999 *Vol. LXXVII, No. 6*

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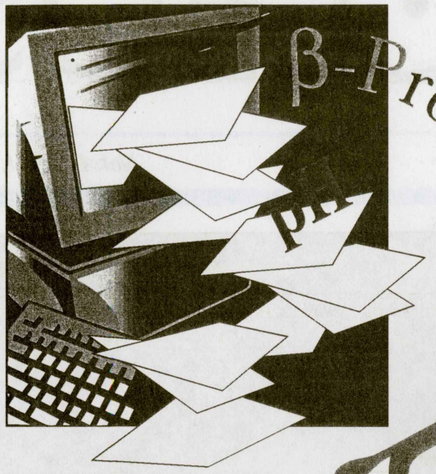

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May 1999 issue: March 25, 1999.

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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NERM 99

Call for Papers
Deadline for Abstracts:
March 15, 1999.
Clarkson University, Potsdam, N.Y.
June 22-25, 1999
Registration materials will be mailed in March.
General technical papers or contributed symposium papers are invited. *(Standard ACS form, original and 2 copies to: Dr. B.K. Lavine, Dept. of Chemistry, Clarkson University, Potsdam, NY 13699-5810.*

Symposia Topics
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Immunosensors, Nucleic Acid Biosensors and Receptor Based Sensors
Analysis of Heavy Metals, Pesticides, and other Hazardous Compounds
Electro-catalytic Processes

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Directions

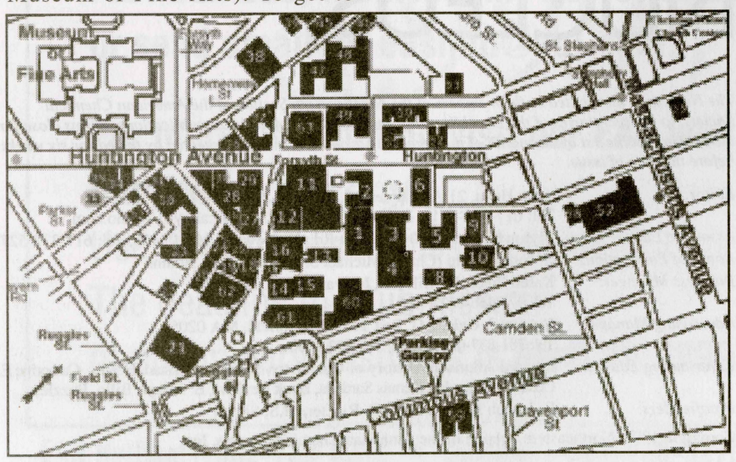
Northeastern University
Recommendation: Take the T!
By Public Transportation:

Orange Line: Change from the Green Line at North Station or Haymarket, or via Red Line at Downtown Crossing. Take Forest Hills car to Ruggles Station. The Raytheon Amphitheater is only a few steps from the T entrance. OR Green Line, E-train to Northeastern stop, walk on Huntington Ave. outbound to Forsyth St. turn south and walk to the dead-end of Forsyth where the Amphitheater is located.

From the West: Take Rte. 9 East, which becomes Huntington Ave. Turn right onto Ruggles St. (just before the Museum of Fine Arts). To get to Columbus Ave., turn left onto Tremont St. (third light), next left, then right onto Columbus Ave. Proceed two blocks to Visitor Parking.

From the North: (via Rte. I-93 or 1) Take the Storrow Drive exit. Proceed to the Fenway exit, following signs to Boylston St. inbound. Bear right onto Westland Ave., turn right onto Massachusetts Ave., proceed to the third light. Turn right onto Columbus Ave. Parking is about 3 blocks along Columbus Ave.

From the South (via Rt3. 3, SE Expressway)**:** Take Exit 18 (Massachusetts Ave.) and proceed onto Melnea Cass Blvd. Continue for ~ two miles, turn right onto Columbus Ave. Visitor parking is about 3 blocks along Columbus Ave. ◇



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NESACS

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*elected or ex-official

Monthly Meeting

The 803rd Meeting of the Northeastern Section of the American Chemical Society

Thursday, February 11, 1999

Raytheon Amphitheater, Northeastern University, 120 Forsyth St. Boston, Mass.

5:30 pm Social Hour; a table of Career Services Literature and Aids will be available

6:30 pm Dinner

8:00 pm Evening meeting, Dr. Donald O. Rickter, Chair, presiding

Dr. Robert Langer, M.I.T. *Advances in Drug Delivery and Tissue Engineering*

Dinner reservations should be made no later than February 4, noon. Please call or fax Marilou Cashman at 800-872-2054. Reservations not canceled 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. Parking: Visitor's Parking Lot, enter from Columbus Ave. (Free voucher issued).

Next Meeting: *March 11, 1999, Wellesley College, Social hour and dinner 5:30, Faculty Club; Evening Meeting at 8:00, Science Center; Dr. Charles E. Kolb, Aerodyne Research, "Atmospheric Chemistry: Basic Principles and Analytical Challenges."*

Biography

Dr. Robert Langer is the Kenneth J. Germeshausen Professor of Chemical and Biomedical Engineering at M.I.T. He received a B.S. from Cornell University in 1970 and a ScD from M.I.T. in 1974, both in chemical engineering. He has written 550 articles, 390 abstracts, 320 patents, edited 12 books, and has received over 60 major awards including the 1998 Lemelson-MIT Prize (the world's largest prize, $500,000, for invention and innovation) and the Gairdner Foundation International Award (49 of the recipients of the Gairdner Award subsequently received the Nobel Prize). Dr. Langer is a member of the FDA's Science Board, the FDA's highest advisory board. Dr. Langer was elected to the Institute of Medicine of the National Academy of Sciences and to the National Academy of Engineering and the National Academy of Sciences. He is the only active member of all 3 United States National Academies. ◇

Abstract

Advances in Drug Delivery and Tissue Engineering

By Robert Langer
Massachusetts Institute of Technology

Over the past two decades, increasing attention has been paid to development of systems to deliver drugs for long time periods at controlled rates. Such systems have been developed for the treatment of eye diseases and birth control. Some of these systems can deliver drugs continuously for over 1 year. However, little attention has been given to developing systems for the controlled release of large molecules (M.W. > 1000) such as polypeptide hormones. In early studies, we discovered that small pellets made of hydrophobic polymers could release many different macromolecules in bioactive form for over 100 days in vitro and in vivo. By using these techniques, a variety of systems for releasing polypeptides such as insulin, epidermal growth factor, angiogenic factors, interferon, anti-sense oligo-nucleotides, and protein vaccines have been designed. In order to provide increased release rates on demand, a polymer-drug delivery system containing small magnetic beads was designed. Release rates were controlled by an oscillating external bar magnet. When exposed to the magnetic field, polymer matrices release up to 30 times more of the drug.

Bioerodible polymers, in particular polyanhvdrides have been synthesized as vehicles to release both large and small molecules. These polymers are unique in that they show surface erosion and lead to near constant release rates of incorporated drugs. By altering the hydrophobicity of the polymer backbone, release time from 1 week to 6 years can be achieved. They have been approved by the FDA in novel drug delivery systems.

In addition, a new approach involving the application of bioerodible polymers to serve as implantable scaffolds for mammalian cells to create new organ transplants is being studied. This approach has been used to create a variety of tissues such as liver, skin, and cartilage in animals and humans. ◇

Section News

1998 National Medal of Science to Prof. George Whitesides

Dr. Whitesides received this distinction for his innovative and far-ranging research in chemistry, biology, biochemistry and material science that has brought break throughs to transition metal chemistry, heterogeneous reactions, organic surface chemistry, and enzyme-mediated synthesis.

1998 National Medal of Technology to Biogen, Inc.

Biogen, Inc. of Cambridge, MA received this distinction for the development of drugs that help large, previously underserved patient populations throughout the world and for the development of hepatitis B vaccines, the first vaccine using genetic engineering.

The Boston Globe, December 9, 1998, p. A20. ◇

Undergraduate Summer Research

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 interaction between undergraduate students and faculty.

Research awards of $ 3250 will be given for the Summer of 1999. 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 5, 1999 for publication in The NUCLEUS. They are also expected to participate in the Northeast Student Research Conference (NSCRC) in April 2000.

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, 1999.

Application: Application forms are available from departmental chairs and the NESACS office (508) 653-6329 or 1-800-872-2054. Completed applications with two photocopies are to be submitted no later than March 26, 1999, to the Chair of the Selection Committee:

Prof. Edwin Jahngen
Department of Chemistry
University of Massachusetts Lowell
Lowell, MA 01854

Notification: Applicants will be notified of the results by April 24, 1999. ◇

Mentoring Your Peers

Be Part of This New Paradigm

In early Fall 1998, two members of the Northeastern section of the ACS, Jean Fuller-Stanley and Patricia Hamm, attended a "Mentoring for Success" workshop in Washington DC conducted by the Minority Affairs Office of National ACS. The goal of the ACS Peer Mentoring Program is two-fold:

- To develop a Peer Mentoring Program at the local section level designed to attract, recruit, and retain women and under-represented minorities
- To create an environment at the local section level that will seek out and encourage active participation by under represented minorities and women members in local section activities

What is Peer Mentoring?

There is greater recognition that the mentee makes valuable contributions to the mentorship relationship. In this context, mentoring becomes a *two-way street*. The mentor introduces and guides the mentee with respect to the nuances of the local section. In turn, the mentee assists the mentor in gaining new insights and appreciation of different ways that the local section can broaden its appeal base. During the process both mentor and mentee participates in learning and building skills in the areas of leadership, cross-cultural communication, coaching, listening, and empowering from view different than their own.

Prescription for the Future: Dynamic Equilibrium!

The Northeastern Section of ACS is to be commended for its continued commitment to diversity and inclusivity. Since the early history of this section, there has been participation of women and minority members at the leadership level. However, despite good intentions, the number of new and different members in leadership role has been somewhat static. As chemists, we are well aware of the onset of equilibrium. Equilibrium is not something to be feared — it is inevitable. The Peer Mentoring Program is one concrete way that we, as a section, can ensure that this equilibrium is dynamic rather than static.

The Peer Mentoring Program seeks to act as a catalyst to revitalize the local section and ensure that the Northeastern Section continues to provide vibrant leadership sustained by participation of a more involved and diverse membership.

Setting-up a Local Section Mentoring Program

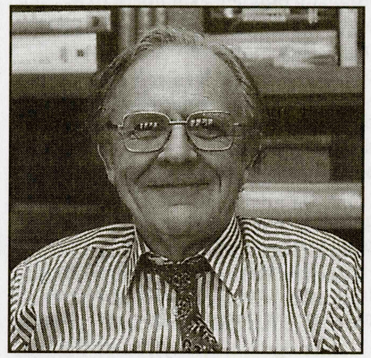
- Wanted: Advisory Committee Members
- Wanted: Peer Mentors
  Long-term or short-term (this is not a life-long commitment)
- Wanted: Mentees
- Wanted: "Hospitality Buddies"

We will train mentors and mentees! For further information, please contact:
Jean Fuller-Stanley, 781 283-3224, e-mail:jstanley@wellesley.edu
Patricia Hamm, 781 344-4636 ◇

NESACS History

Geoffrey Wilkinson 1921-1996

Based on an article by M.L.H. Green (University of Oxford, England) and W.P. Griffith (Imperial College of Science, Technology and Medicine, London, England) in Platinum Metals Review **1998**, *42* (4), 168-173, *the house organ of Johnson Matthey Co. Condensed by Arno Heyn.*
For the original article, see the website http://www.matthey.com.



Sir Geoffrey Wilkinson was born in Todmorden, Yorkshire. He was one of the greatest international inorganic chemists, making noted contributions in transition metal chemistry, homogeneous catalysis, organometallic chemistry, and coordination chemistry. In 1973, when he shared the Nobel Prize with E.O. Fischer, the award was made for the discovery of ferrocene and similar "sandwich compounds", work he did jointly with R.B. Woodward, while Wilkinson was an Assistant Professor at Harvard from 1951 until 1955.

Wilkinson, the first of three children of Henry and Ruth (Crowther) Wilkinson spent his childhood in Todmorden. His parents, as was usual at the time, left school at age 12 to enter the working world; Henry as a house painter and decorator, Ruth as a weaver. His interest in chemistry arose early, partly because an uncle managed a factory in Todmorden which produced Glauber's salt and Epsom salt. On Saturday mornings he was allowed to tinker in the small factory laboratory. He won a County fellowship in 1931 to attend Todmorden Secondary School (later "High School"), and because of his excellent progress, a Royal Scholarship to attend Imperial College of Science and Technology at London University.

At Imperial College he studied both chemistry and geology. In 1941 he graduated with a B.Sc. degree, first class honors, and continued his studies toward a Ph.D. under H.V.A. Briscoe, the only Professor of Inorganic Chemistry in Britain. His thesis was on: "Some Physicochemical Observations

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on Hydrolyis in the Homogeneous Vapour Phase", a title to disguise the fact that the compound studied was phosgene.

In 1942 he was selected by the Joint Recruiting Board as a scientific officer at the Atomic Energy Project in Canada. He worked at the University of Montreal, and later at Chalk River, Ont. on nuclear fission. Many other celebrated scientists also worked there: John Cockroft (also from his old school in Todmorden), Bertrand Goldschmidt, Charles Coryell (later at M.I.T.), Alfred Maddocks (later at Cambridge University), Jules Guéron, and Pierre Auger, and also two scientists who were later convicted for being spies for the Soviet Union: Alan Nunn May and Bruno Pontecorvo.

Shortly after the war Wilkinson joined the staff at the Lawrence Livermore Laboratory, working with Glenn T. Seaborg on the production of neutron-deficient isotopes of the transition elements and lanthanides. Seaborg has stated that Wilkinson had made more artificial isotopes than anyone has ever made, a total of 89. Here he also started amassing his vast knowledge of descriptive inorganic chemistry: At the time the separation and isolation of isotopes had to be done by chemical means, requiring an intimate knowledge of the chemical behavior of target elements and others from which they were to be separated. One of the nuclear transmutations he accomplished was that of platinum into gold. The report of this resulted in a headline in the *San Francisco Chronicle*: "Scientist discovers gold mine in the cyclotron."

In 1950-51 he received a faculty appointment at M.I.T. to conduct research in coordination chemistry, then, in 1951 he was appointed Assistant Professor of Chemistry at Harvard University where he did the research on ferrocene and other cyclopentadienyl compounds.

The recognition by Wilkinson and Woodward of the unique "sandwich structure" of ferrocene (*bis*-(cyclopentadienyl)iron, Cp_2Fe) was a crucial point in his career, which started the emphasis on organo-transition metal chemistry, still an active field today. Twenty years later Wilkinson wrote a personal account of this discovery.[1] From 1952-1953 he extended this work to *bis*(cyclopentadienyl) complexes of ruthenium, rhodium, iridium, and others. He used the new technique of nuclear magnetic resonance (NMR) to show that covalent metal hydrides (in this case Cp_2ReH) gave high-field ^1H NMR shifts.

In 1955 Wilkinson was appointed to Briscoe's old chair at Imperial College, still the only chair in inorganic chemistry in Britain. He was one of the youngest professors Imperial College ever had. Here at Imperial he did most of the work on platinum group chemistry. This interest was probably sparked by the recognition that these metals had many oxidation states, resulting in a rich body of chemistry.

His interest in platinum metals chemistry led to an early association with the Johnson Matthey Company, the prime marketer of platinum metals. He had a consulting relationship and received the supply of platinum metals needed for his research program on a "loan" basis, i.e. Johnson Matthey received back the spent materials for recycling.

Wilkinson turned his interest to the catalytic activity of platinum metal compounds. The work of one of his students, Fred Jardine, isolated the compound $RhCl(PPh_3)_3$, known as "Wilkinson's catalyst".[2] This catalyst is very effective for the hydrogenation of alkenes and alkynes and of hydroformylated hex-1-yne to *n*-heptaldehyde and 2-methylhexaldehyde. $RhCl(PPh_3)_3$ was a chance discovery, it was the product obtained when it was attempted to make $Rh(Cl_3PPh_3)$, and was discovered to be a very powerful catalyst. $RhCl(PPh_3)_3$ can be made readily by reacting $RhCl_3.nH_2O$ in ethanol with excess triphenylphosphine.[3]

Wilkinson later showed that

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though $RhCl(PPh_3)_3$ was a very effective hydrogenation catalyst, it was not a hydroformylation catalyst. The agent responsible for hydroformylation catalysis was $RhH(CO)(PPh_3)_3$. Most of the butyraldehyde used for the synthesis of bis(2-ethyl-hexyl)phthalate, a plasticizer for PVC, uses $RhH(CO)(PPh_3)_3$ as the catalyst. It is likely that Wilkinson's work on catalysis was an important factor in his being chosen for the 1973 Nobel Prize in chemistry, although the "sandwich" compounds were noted in the citation.

In subsequent years Wilkinson and his students worked in Rhodium, Ruthenium, Osmium, Iridium , Platinum and Palladium chemistry.

Wilkinson the Man

Wilkinson was the academic supervisor for the two authors of the *Platinum Metals Review* article on which this piece is based. In their joint obituary of Wilkinson they wrote: "The spirit in his research group was more like that of an urgent gold rush in the West than the scholarly and disciplined calm expected in academia."[4] He worked hard, six or even seven days a week, from early morning to late evening., and he expected his students to do the same. However, he was not a slave driver and was not put off by eccentric behavior. He freely used expletives when thwarted or stirred and had a great sense of fun. He was able to inculcate others with his enthusiasm. He would wander from one to the other in his lab in the late afternoon and inquire "What's new" and make suggestions for altering conditions if a reaction did not work as hoped for. He had no great sympathy for theoretical chemistry and would quote examples when theoretical predictions were proved wrong by subsequent findings.

He was in a hurry to publish results, sometimes resulting in errors. So, at one time, he announced the product of the reaction between thiophene and iron pentacarbonyl as thiopheneiron tricarbonyl, when it was later shown that there was no sulfur in the product, and that it was the unexpected butadieneiron tricarbonyl, a fact which Wilkinson accepted without being greatly disturbed.

Wilkinson was a staunch fighter for the recognition of the importance of chemistry by government in Britain, communicating his views bluntly to prime ministers, ministers of education, vice chancellors and others who held the purse-strings of research funds, people he would refer to as "the apparatchiks."

Geoffrey Wilkinson had a lasting influence on his former students, and on chemistry and the Northeastern Section can be proud that a small, but decisive part of his career was spent in our midst.

---

[1] G. Wilkinson, *J. Organomet. Chem.*, **1975, *100,*** 273.
[2] F. Jardine, *Rhodium Express*, **1997**, *16,* 4; *Progr. Inorg.Chem.* **1991,** *28,* 63.
[3] J.A. Osborn *et al., J. Chem. Soc.* A, **1966,** 1711.
[4] *The Independent,* October 1, 1996.◇

Meeting Report

Bioinformatics: A New World of Restriction and Modification Enzymes

By Richard J. Roberts, New England Biolabs, Inc.
Submitted by Dr. Roberts as an extension of his address at the October 16, 1998 Centennial Meeting

DNA sequence is fast becoming the hottest commodity sought by the contemporary biologist. With fifteen genomes already sequenced and twice as many underway, we are gaining a new view of what is required to catalyze life. An important finding is that in most organisms more than 40% of the genes cannot be assigned a function and a many as 30% appear unique to each organism. This is true even of *E. coli*, which is the best studied of all

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organisms. Bioinformatics is playing a key role in assigning function to many genes usually by gauging their similarity to genes encoding proteins whose function is well-characterized. Restriction enzymes and their associated methyltransferases (MTases) pose a particularly interesting challenge for bioinformatics because predictions on the basis of similarity are only of limited value.

Typically, a restriction enzyme recognizes a specific DNA sequence and cleaves it, while the associated MTase recognizes the same sequence and methylates a key residue within that sequence, thereby preventing cleavage of the host DNA by its own restriction enzyme.[1] DNA MTase genes; are easily spotted because they contain coding sequences for many characteristic protein sequence motifs of 6- 12 amino acids. [2,3] Their most valuable property, the DNA sequence with which they interact, has so far proved difficult to predict unless an especially close homolog is present in GenBank. Restriction enzymes pose an even greater challenge. Typically, they are found very close to their cognate MTase genes,[4] but now can only be identified unambiguously when they show very close sequence similarity to another sequenced restriction enzyme gene of the same specificity. More often they are best described as an open reading frame, lying next to a DNA MTase gene, but which lack any similarity to other sequences present in GenBank.

We have screened the known genomic sequences to locate DNA MTase genes and the results are summarized in Table 1. The table contains many surprises. In *Haemophilus influenzae*, the very first sequenced genome,[5] four DNA MTases had previously been characterized using biochemical approaches,[6,7] but in the genome there are at least seven genes. Since we are especially interested in the Type II restriction enzymes, the subset that produces useful biochemical reagents, our first goal was to identify the genes for *Hind*II and *Hind*III This was easy since *Hind*III and *Hind*II had already been cloned and sequenced independently.[8,9] Of the other MTase genes, one was clearly the DNA MTase of *H. influenzae* and three were associated with non-Type II restriction systems. But one seemed clearly to be part of a Type II restriction enzyme system never previously seen by biochemical analysis of *H. Influenzae* This latter system called *Hind*V could be identified because both its restriction enzyme and MTase genes showed close similarity to the genes encoding the known restriction-modification (RM) system, *Hgi*DI.[10] By cloning the MTase gene, we now know that indeed it is a functional DNA MTase and has the same specificity as *Hgi*DI.[11] So far the adjacent gene encoding the putative restriction enzyme has proved refractory to cloning, a trait commonly associated with restriction enzyme genes.

Another sequenced genome me is that of *Methanococcus jannaschii*[12] and it too held a number of surprises. Biochemically, two Type II restriction enzymes had been reported,[13] but the genome contained no less than twelve MTase genes four of which appeared to be part of Type I or Type III systems, while the remaining eight were candidates for Type II systems. Of these eight, one could clearly be identified on the basis of sequence similarity with *Mth*ZI[14] as encoding one of the biochemically characterized restriction enzymes, *Mja*I. Two others had predictable specificities on the basis of sequence similarity and these have subsequently been confirmed. Five more are currently bring examined. The distribution of these systems are shown in Figure 1. The greatest surprise of all came from the genome of *Heliobacter pylori,*[15] the causative agent of human ulcers. No less than twenty-three Mtase genes could be identified, of which fourteen ere candidates to form part of Type II RM systems. In this case, little biochemistry had been carried out on this pathogen before the sequence became available and just a single MTase gene[16] and two restriction enzymes[17] had been identified.

What are the lessons that can be learned from these surprising findings? The first is that biochemistry alone is an inefficient way to find RM systems. One early hint that this might be the case for restriction enzymes came from studies of *Neisseria gonorrhoeae.* For many years, Drs. D. Stein, A. Piekarowicz and their coworkers have been cloning restriction systems from *N. gonorrhoeae* and have made some extraordinary findings.[18] Growth of *N. gonorrhoeae* in the laboratory and examination of cell extracts for restriction enzymes typically show that only one or two restriction enzymes are present in sufficient quantities to isolate and characterize.[19] Furthermore, different isolates frequently seem to express enzymes with different recognition specificities.[20] However, the genomes of *N. gonorrhoeae* and its plasmids are modified at many sites,[21] suggesting the pres-

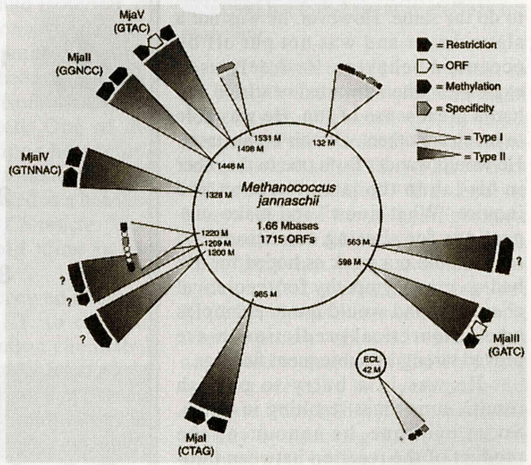

Figure 1: Circular map of *Methanococcus jannaschii* showing the Type I and II restriction-modification (RM) system genes.

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ence of many more active MTase genes than active restriction enzyme genes. As a result of selective cloning for MTase genes, it is now known that every strain of *N. gonorrhoeae* so far examined has genes for at least twenty different RM systems, most of which can be activated when the genes are transferred into *E. coli.* It now appears that the picture that had emerged from *N. gonorrhoeae* may not be as exceptional as had been thought. RM systems are probably more widespread than had been imagined, but they are not always expressed. One reason for this lack of expression may be the phenomenon of phase variation. In both *H. influenzae* and *H. pylori*, several of the RM genes have short repeat sequences within their coding regions of the type prone to replication errors.[22] Thus, within a population of bacteria, some individuals may have a functional gene while others may not. If RM systems commonly switch between active and inactive states by this and other mechanisms, it leads to some interesting possibilities. First, many of the potential restriction enzyme genes may be present in inactive forms. If cloned into *E. coli* they would need to be "fixed" before active enzyme could be expressed. Furthermore, it suggests that these genes have the potential for very rapid evolution by constantly going through active and inactive states, a situation that could account for the absence of observable sequence similarity between restriction enzyme genes. This is exemplified by *Bam*HI and *Eco*RI, two restriction enzymes that appear structurally related[23] and have somewhat similar recognition sequences (GGATCC and GAATTC, respectively). Both features suggest a common ancestor and yet at the sequence level they are completely dissimilar. If many of the restriction enzyme genes, and perhaps even their associated MTase genes, are frequently oscillating between active and inactive states, then the selfish gene hypothesis proposed to explain their persistence looks less appealing.[23a] This model still might apply to systems that were constantly expressed but could nor explain the phase variable systems. While the restriction of foreign DNA within a subset of the population where a gene is active is still tenable, it is difficult to imagine that organisms such is *Heliobacter* and *Neisseria* need more than 20 such systems to ward off infection. With *H. pylori* devoting more than 1% of its total genome to RM genes, there seems a good chance that some new biology is waiting to be discovered. There is also the question of how these systems are controlled, particularly during transfer from one organism to another. We have some hints that specific control genes are used in a few cases, but these represent a small

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Type I restriction enzymes recognize a specific sequence, but cleave randomly. They contain three subunits: a specificity subunit (S) responsible for sequence recognition, a methylation subunit (M) which in all known cases forms N^6-methyl adenine, and a restriction subunit (R). When a Type I enzyme encounters hemi-methylated DNA, it acts as a methylase. With unmodified DNA, it acts predominantly in the restriction mode but occasionally will methylate. These enzymes require ATP, Mg^{++} and S-adenosylmethionine to cleave DNA.

Type II restriction enzymes are the best known of the restriction enzyme systems. They produce specific fragments of DNA and are key to the production of recombinant DNAs. They consist of one protein which acts as a restriction enzyme and a second protein that acts as a methylase. Typically, the restriction enzyme requires only Mg^{++} as a cofactor. Most of the known enzymes recognize symmetric sequences and the dimeric restriction enzyme cleaves symmetrically. The methylase is a monomer. Several subtypes of these enzymes are recognized; best known are the Type IIS enzymes, which recognize asymmetric sequences and generally cleave a few nucleotides away from the recognition sequence. A typical Type IIS enzyme has two methylases, one specific for each strand of the recognition sequence.

Type III restriction enzymes have properties intermediate between Type I and Type II. They are multisubunit enzymes, recognize specific sequences, but typically cleave 20 to 25 nucleotides away from that sequence and rarely give complete cleavage. The restriction activity requires ATP and is enhanced by S-adenosylmethionine. Only five such enzymes have been characterized.

Organism	Genome Size (Mb)	Type I	Type II	Type III	Orphans R	Orphans M	Orphans S
Aquifex aeolicus	1.55	no clear candidates					
Archaeoglobus fulgidus	2.18	1	2	–	–	–	–
Bacillus subtilis	4.21	–	2	–	–	1	–
Borrelia burgdorferi	1.44	–	1	–	–	–	–
Escherichia coli	4.60	2	–	–	–	2	–
Haemophilus influenzae	1.83	2	3	1	–	1	–
Helicobacter pylori	1.66	3	14	2	–	1	2
Methanobacterium thermoautotrophicum	1.75	1	2	–	–	–	–
Methanococcus jannaschii	1.66	3	6	–	–	2	1
Mycobacterium tuberculosis	4.40	1	1	–	–	–	–
Mycoplasma genitalium	0.58	1	–	–	–	1	–
Mycoplasma pneumoniae	0.81	1	1	–	1	–	6
Pyrococcus horikoshii	1.74	–	3	–	–	–	–
Synechocystis species	3.57	1	1	–	–	1	1
Treponema pallidum	1.16	–	–	–	–	1	–

Table 1: PotentialRestriction-modification (RM) systems in fully sequenced genomes. Genes labeled as orphans are those which cannot he unambiguously assigned as part of a restriction-modification system. They are categorized by restriction subunit (R), methylation subunit (M) and specificity subunit (S).

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Meeting Report

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minority, Once again, the RM systems, often viewed merely as cold reagents that emerge occasionally from freezers, are providing hot topics for research.

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Puzzle Column

By Paris Svoronos

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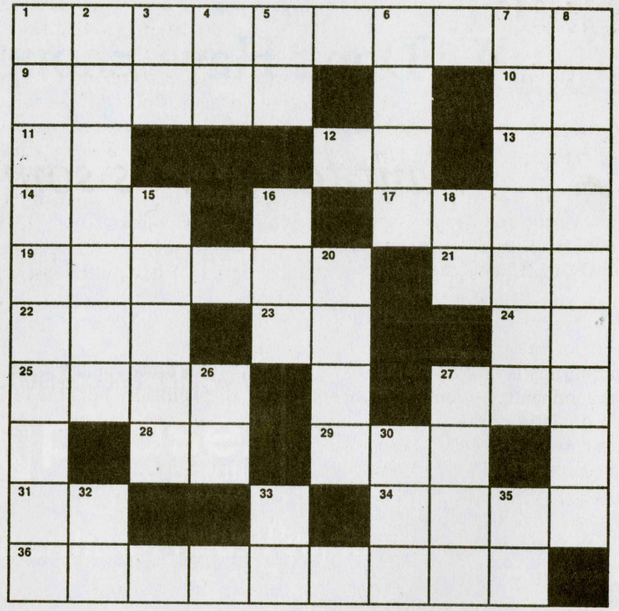

ACROSS

__ synthesis: reaction of an alkoxide with an alkyl halide to yield ethers
9. Product of the reaction of a carbonyl with a primary amine
10. Noble gas
11. The lowest atomic number metal
12. Arabic prefix
13. Two-thirds of an ion
14. Lithium diisopropyl amide's initials
17. Wyatt ___
19. __'s reagent: forms a water-soluble hydrazone
21. Persian Gulf country
22. Alkene's suffix
23. Element atomic number 63
24. Two-thirds of inn
26. __ Descartes: Related science and philosophy
27. Common in volleyball and tennis
28. Element atomic number 99
29. Enemy
31. Element atomic number 105
34. Other term used to describe Christmas
36. Common name for 2-hydroxytropone

DOWN

1 . __reaction: conversion of an aryl alkyl ketone to the amide via ammonium polysulfide
Product of the reaction of straight-chain dinitriles with
Ammonia
3. Same as 11 across
4. Letters surrounding M
5. Shorthand notation .for "in other words"
6. Has Avogadro's number in molecules
7. Cyclic ether
8. Five-carbon alkyl group
15. Side-chained alkane
16. Natural mineral
18. Expensive element
20. __ reaction: Reaction of phenol with hexamethylene tetramine
26. Element atomic number 34 (reversed)
27. Noble gas (atomic number 10)
30. Yoko
32. Halogen
33. Element discovered by Marie Curie
35. There are such government savings bonds

The solution will be published next month and will be put on the NESACS Website about Feb. 5. (http://www.tiac.net/users/obermayr)

Summer Scholar Report

Recognizing the Bimorphism of the Human Transferrin Receptor.

By Irene Chen* and Gregory Verdine, Harvard University, Department of Chemistry and Chemical Biology

Introduction.

Current cancer therapies, such as chemotherapy and radiation therapy, are predominantly systemic treatments which destroy cells based on their rapid growth rate rather than actual malignancy. In addition to killing cancer cells, these treatments cause a widespread devastation of healthy cells which normally grow rapidly (e.g. epithelial and bone marrow cells), leading to serious side effects and placing limits on the tolerable drug dosage. A proposed alternative strategy is to selectively target cancer cells by taking advantage of their abnormal karyotypes. In particular, a segment of chromosome 3 (3q26.2-qter) is known to be lost in cancers such as non-small cell lung cancer, ovarian cancer, and sarcoma.[1] Although normal cells are diploid, containing two distinct copies of each gene, the loss of a chromosome segment renders a cell monozygous for the genes located on the lost segment. Thus, a cell which normally expresses two different alleles of these genes would express only one after such an event. Therefore, molecules that are able to specifically bind the remaining allele would selectively target transformed cells, since normal cells would be protected by their heterozygosity.

The transferrin receptor (TfR) gene maps to chromosome 3q26.2-qter.[2] TfR is a cell surface receptor which binds to and mediates the uptake of the iron-transport protein transferrin. Due to increased iron requirements in rapidly growing cells, the expression of TfR in some cancer types is up to 104 times the normal expression level [3] and it has been shown that antibodies binding to TfR will inhibit iron uptake and thus slow the proliferation of cancer cells.[4] Importantly, there are two alleles of the TfR gene which differ at residue 142 (serine/glycine), and the frequencies of these alleles are nearly equal in the human population.[5] Potentially, a cancer patient who is heterozygous for TfR (ser/gly) may have monozygous cancer cells, and antibodies directed against the appropriate TfR allele would specifically inhibit the growth of these cells.

The goal of this project is to produce antibodies which can distinguish the two alleles of TfR. Past attempts to make such antibodies by injection of a relevant TfR fragment into mice have been frustrated by the diversity of the immune response against TfR; [6] the probability of generating and isolating an antibody which binds at the polymorphic residue is vanishingly small

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*1998 Norris Richards Summer Scholar

Summer Scholar

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given the large size of the protein (672 amino acid extracellular domain [7]). One way to overcome this obstacle is to direct the immune system toward residue 142 by attaching a small molecule hapten, nitrophenyl azide, to this residue, thus making the area highly immunogenic. Use of this modified TfR fragment as an immunogen should elicit a population of antibodies biased toward recognition of the desired bimorphic site. These antibodies may then be cloned and screened for the ability to bind around residue 142. Semirational back-engineering of the resulting antibody (e.g. phage display library) may yield an antibody with the desired ability to distinguish serine and glycine at residue 142.

The region surrounding residue 142 is rich in charged amino acids and is accessible to protease digestion, indicating that it is likely to lie on the surface of the protein.[6,8] Since we plan to bioconjugate a hapten specifically to this residue by its mutation to a nucleophilic cysteine residue, it is important to note that there are four other cysteine residues in the extracellular TfR domain. However, these are believed to be involved in disulfide bridges in the folded protein, and thus exhibit significantly less nucleophilic reactivity.[9]

Experimental section.

TfR construct. A Cys142 mutant was generated by site-directed PCR mutagenesis of the human TfR gene [10], and the soluble fragment (residues 121-760) was cloned into a baculovirus expression vector (pAcGP67) for protein overexpression and secretion. The TfR(Cys142) vector was transfected into Sf9 insect cells using the BaculoGold system (PharMingen), and a high titer stock of TfR(Cys142) baculovirus was obtained after viral amplification.

Protein expression and purification.[11,12] High Five cells (Invitrogen) were cultured in serum-free media and infected with TfR(Cys142) baculovirus.[13] The media were collected three days after infection and incubated overnight with transferrin-sepharose resin. The resin was washed with phosphate-buffered saline solution. Elution of bound TfR(Cys142) protein was effected by 1M NaSCN, 50 mM HEPES, pH 7.5. Conditions for scale-up and downstream purification of TfR(Cys142) are currently being optimized.

Results and Future Plan.

A nucleophilic thiol group has been introduced into the TfR protein at the bimorphic residue by mutation to cysteine-142. Preliminary results demonstrate the feasibility of overexpression and purification of TfR(Cys142) in the baculovirus/insect cell system. The identity of the TfR(Cys142) construct has been verified by DNA sequencing. TfR(Cys142) protein produced by infected High Five cells is immunoreactive toward a polyclonal antibody raised against wild-type TfR produced in mammalian CHO cells[14] (figure 1, lane 3). This protein also has the same apparent molecular weight as wild-type TfR produced in High Five cells by other investigators,[15] (figure 1, lane 4) as assessed by denaturing polyacrylamide gel electrophoresis (SDS-PAGE). The presence of secreted TfR(Cys142) in the media of infected High Five cells and its subsequent purification through transferrin affinity have also been verified by SDS-PAGE (figure 2b, lane 2).

Nitrophenyl azide has been chosen as the hapten, because it is immunogenic and contains a photocleavable affinity label which may be activated by UV irradiation, thus facilitating future antibody mapping (figure 3).[16] Its small size will minimize potential perturbations of the TfR structure. It has been shown that nucleophilic aromatic substitution will occur specifically with a protein cysteine free thiol at pH ~6 under native conditions.[17] TfR is also known to be stable at low pH (~5).[18] Thus, reaction of 4-fluoro-3-nitrophenyl azide (Aldrich) with the Cys142 mutant TfR should specifically label residue 142 with the hapten to afford the desired immunogen.

If the plan described above is successful, the nitrophenyl azido Cys-142 TfR immunogen will be used to immunize mice to obtain a biased library of monoclonal antibodies against TfR. This library will be screened for antibodies having the desired ability to bind the region containing residue 142, and the photoaffinity labeling of these antibodies via *in situ* generation of a nitrene will be used to construct a rough map of the antibody binding site. This information may then allow us to engineer the antibody to increase affinity and specificity for the natural serine and glycine 142 variants of TfR.

Acknowledgements.

I would like to thank the Northeastern Section of the American Chemical Society for supporting this summer project, M. Lawrence, J. Olson, J. Lebron, and J. Huang for invaluable help in the baculovirus expression system and purification of the transferrin receptor, and Li Jing Sun and Gregory Verdine, without whom this research would not have been possible.

Figure 1. Western blot of media supernatant from High Five cells.
Lane 1: molecular weight markets; molecular weights in kiloDaltons are indicated to the left.
Lane 2: wild-type TfR produced in CHO cells, provided by J. Olson.
Lane 3: media supernatant from High Five cells infected with TfR(Cys142) baculovirus.
Lane 4: media supernatant from High Five cells infected with wild-type TfR baculovirus, provided by J. Lebron.

Figure 1

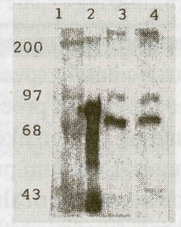

Figure 2. SDS-PAGE of fractions containing TfR(Cys 142). Gels were silver stained.
(a) SDS-PAGE of media supernatant from High Five cells.
Lane 1: molecular weight markers.
Lane 2: media supernatant from High Five cells infected with

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TfR(Cys 142) baculovirus.
Lane 3: media supernatant from High Five cells infected with TfR(Cys142) baculovirus, after overnight incubation with transferrin- sepharose resin,
(b) SDS-PAGE of protein purification.
Lane 1: molecular weight markers.

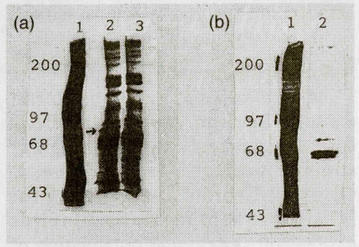

Figure 2

Lane 2: elution of TfR(Cys 142) from transferrin-sepharose by I M NaSCN.

Figure 3. Proposed covalent addition

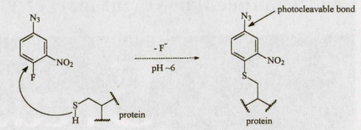

Figure 3

of a hapten to TfR(Cys 142). Photolysis of the azide should result in a nitrene species, thereby facilitating the mapping of antibody interactions.

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Pharmaceutical Process Research and Development
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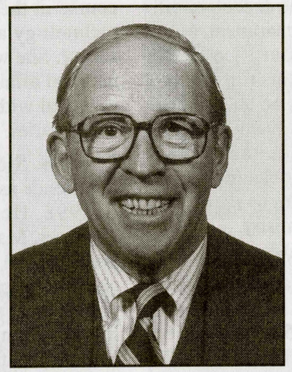
Historical Notes

We continue the biographical sketches of chemical scientists whose deaths have been reported to us.

by Edward R. Atkinson

George H. Büchi
Written by Glenn Berchtold (Prof.emer., M.I.T.) and Louise Foley (Ph.D.1970, M.I.T., with Prof. Büchi).



MIT Professor Emeritus George H. Büchi of Cambridge, MA, and Jackson, NH, one of this century's foremost organic chemists, died of heart failure while hiking with his wife in his native Switzerland on August 28, at the age of 77. He was an avid hiker, hunter, skier and fisherman.

Professor Büchi born, on Aug. 1, 1921, in Baden, received a diploma in chemical engineering in 1945, from Eidgenossische Technische Hochschule in Zurich and the DSc in organic chemistry in 1947, working in the laboratory of Professor Leopold Ruzicka. He was a Firestone Postdoctoral Fellow in the Laboratory of Professor M. Kharasch at the University of Chicago for three years before accepting a faculty appointment from the Massachusetts Institute of Technology in 1951.

He was promoted to associate professor at MIT in 1956, and to full professor in 1958. He was appointed the Camille and Henry Dreyfus Professor of Chemistry in 1971, a position he held until his retirement in 1991. During his tenure at MIT, Professor Büchi trained 70 PhDs and more than 100 postdoctoral students. Many of his former coworkers have gone on to leadership positions in academia and industry around the world.

Professor Büchi's research, reported in over 200 publications, made significant contributions in diverse areas of organic chemistry. His work in the 1950s in organic photochemistry was instrumental in converting this latent field into an understandable and useful synthetic tool, and it laid the groundwork for what is now modern organic photochemistry. Over a period of ten years the structural work in Büchi's laboratory and his mechanistic insights provided a detailed understanding of several fundamental photoreactions all of which were unprecedented at the time. The light-catalyzed addition of carbonyl compounds to alkenes and alkynes is known as the Paterno-Büchi reaction.

Professor Büchi's structural work in natural products chemistry led to the structure determination of more than 55 natural products. During this era prior to the routine utilization of X-ray crystallographic methods for organic structure determination, his accomplishments are among the finest examples of structure elucidation by classical degradation and spectrometric techniques. The structures of the sesquiterpenes patchouliol (with J. Dunitz), maaliol, aromadendrene, valerenic acid, calarene and copaene (with P. de Mayo), all containing novel skeletons, were disclosed in succession. Work on the complex alkaloids, uleine, flavocarpine and aconitine (with K. Wiesner), led to the structures through ingeniously conceived degradative studies. A study on the bis-indole alkaloid voacamine suggested that the antitumor alkaloids vinblastine and vincrystine were similarly bis-indoles. This suggestion was confirmed in collaboration with K. Biemann (MIT) and N. Neuss and M. Gorman (both of Eli Lilly).

The synthesis of over 75 complex natural products came from Professor Büchi's laboratory. His syntheses were considered creative, elegant and original. Typically his syntheses were very efficient in producing quantities of the target compound in very few steps. The first syntheses of many sequiterpenes (e.g., patchouliol, maaliol, aromadendrene, agarofuran), iboga alkaloids, iridoid glucosides (loganin), aflatoxins and their metabolites were accomplished. Both vindoline and catharanthine first yielded to synthesis in his laboratory; these two alkaloids were subsequently combined by Potier to produce the antitumor drug, vinblastine. Neolignans (burchellin, guianin, futoenone) and the zoanthoxanthins, a group of marine pigments, were synthesized by elegant biomimetic routes. Throughout his career Professor Büchi maintained a strong interest in flavor principles, and many were synthesized in his laboratory. They include damascones (rose), methyl jasmonate (jasmine), muscone (musk deer), sinensals (orange), khusimone (vetiver), khaweofuran (coffee), furaneol (strawberry), and muscopyridine.

Many important contributions to synthetic methodology were developed in Professor Büchi's laboratory. They include numerous methods for new and convenient preparations of olefins, carbonyl compounds, macrocycles, tropolones, and heterocycles. A new synthesis of allylic sulfones and their conversion to polyolefins provided for a novel synthesis of betacarotene from vitamin A.

Professor Büchi, in collaboration with MIT colleague Professor Gerald N. Wogan, established molecular toxicology as an important scientific discipline. Their experimental evidence concerning carcinogenesis provided fundamental chemical, biological, and epidemiological correlations which are a paradigm for modem toxicological studies. They were first concerned (in 1963) with establishing the structures of the aflatoxins, fungal metabolites which had been isolated from spoiled peanuts and found to be responsible for a mass outbreak of poultry disease. The structure of aflatoxin B1, the

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Historical Notes

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major metabolite, was deduced by Büchi by ingenious application of spectroscopic information. It is a potent carcinogen, and its consumption is associated with primary liver cancer. Subsequent work resulted in the isolation and structure identification of other aflatoxins (including M_1, the metabolite from milk) and a number of other mycotoxins (rubatoxins, tryptoquivalines, mollicellins, malformin C). In a series of brilliant synthetic studies, he devised methods for their total synthesis. The synthetic methods provided the quantities of aflatoxin metabolites needed for essential toxicological investigations. Later work established the structure of aflatoxin Q a metabolite of aflatoxin B_1 in human liver, and identified the structure of the major adduct formed between aflatoxin B_1 and DNA. The isolation and identification of one DNA-aflatoxin-derived. adduct as a 3-hydroxyaflatoxin linked *via* C-2 to the N-7 atom of a guanine, of DNA was a milestone in toxicology: it provided the first totally convincing molecular structure for a carcinogen-induced covalent modification of a mammalian DNA.

Elected to the National Academy of Sciences in 1965, he was recognized throughout his career with numerous awards, honorary degrees and lectureships from around the world. Professor Büchi was a consultant for Hoffmann-La Roche Inc. in both the US and Switzerland and for Firmenich SA in Switzerland. He held more than 30 US patents with these companies and on his own.

Professor Büchi is survived by his wife of 43 years, Anne Barkman Büchi of Cambridge, MA and Jackson, NH; a brother, Heinrich, of Berne, Switzerland; and three nephews, all of whom live in Switzerland.

John W. Irvine, Jr., 84, died on February 23, 1998 at his home in Tucson, Arizona. He received the S.B. in chemistry at MIT in 1939. While working for the Ph.D. he was a research associate in the department of physics and was involved in the then classified research project that used radioactive iron to determine the shelf life of blood stored for the armed forces. He joined the chemistry department faculty in 1943, became full professor in 1958, and retired in 1979. At the time of his retirement Jack was the executive officer of the chemistry department, a successor to the legendary Leicester Hamilton. One of Hamilton's books that Jack inherited was an autographed copy of the Tenney L. Davis two-volume treatise on powder and explosives. Jack gave the books to me and, years later, I gave them to the Center for the History of Chemistry.

Richard Mahanna, 62, died on May 27, 1998. After graduating from Brockton High School he served in the U.S. Army for the 1958-1960 period, then received the S.B. from MIT in chemical engineering in 1961. For over 20 years he was a plant manager for Reichold Chemicals in Andover, Mass. and then was a self-employed consultant. He was active in the affairs of the Sigma Phi Epsilon fraternity and the Cystic Fibrosis Foundation of Natick, Mass. He served as a eucharistic minister at St. Catherine's Church in Westford, Mass.

David P. Kidger, 70, died at his home in Danvers, Mass. on April 28, 1998. He was a native of Newton and after service in World War II received the B.S. from Illinois Wesleyan University in 1953. In the subsequent 20 years he was employed as a chemist in the production of edible fats and oils by Swift Co., Lever Brothers, and Nabisco. In retirement he worked as a cabinet maker and enjoyed membership in the American Rose Society.

Margaret Miller, 51, died on April 21, 1998 after a year's struggle with cancer. She was a native of New York and was raised in Tomkins Cove, N.Y. and Craigville, Mass. After graduating from Wells College in Aurora, N.Y. she joined the biological research staff at Arthur D. Little, Inc., received the M.S. in information science at Simmons College (1981), and became director of the ADL Life Science Library. She was a specialist with whom ADL staff consulted in the field of pharmaceutical, biochemical, food, and agriculture business. She was an expert in government regulatory procedures in these areas. She also served as the corporate quality control assurance officer for six years. She taught a course in the literature of science and technology at the Simmons graduate school. She was active in the local and national affairs of several associations involved with quality control and special libraries.

Loren S. Sjöstrom, 85, known to all his friends as "Johnnie", died on May 1, 1998. He was a native of North Andover, Mass., a graduate of Searls High School in Methuen, and a 1935 chemistry graduate of Northeastern University. From 1936 until retirement in 1977 Johnnie was a member of the technical staff at Arthur D. Little, Inc. and served as a vice president of the company for the last 15 years. He became director of the extensive ADL work in the fields of foods and flavors. He and his associate, Ernest Crocker, invented the well-known flavor profile which served as the basis for the development of hundreds of food products. For his service to the profession Johnnie became president of the Northeast Section of the Institute of Food Technologists, was awarded professional status by the American Institute of Chemists, and was honored by ASTM. His family teased him when a planned appearance on the cover of *Time Magazine* was cancelled by the death of Pope John, whose picture was used in place of Johnnie's.

Johnnie was active in the Gordon conferences on food and nutrition held at Colby-Sawyer College in New London, N.H. where he owned a summer residence on the shores of Little Sunapee lake. At the conferences he hosted informal gatherings on the beach. Those of us who attended them, all of us who knew him well at ADL and the fellow members of his Masonic lodges and church, remember him with affection. Johnie promised me that he would write a biography of Ernest Crocker for this column, but fate intervened

to be continued

National Chemistry Week News

Poster Contest

Reported by Michael E. Strem

A national poster contest for elementary school students, categories K-2, K3-5, and K6-8 was held. Local Sections were encouraged to hold their own contest, winners to compete at the Anaheim ACS meeting in March. Prizes to be awarded are $1000 US Savings Bonds or a computer to the winners, $500 Savings Bonds to each Honorable Mention . Teachers of winners will receive a computer for use in their classrooms.

In the Northeastern Section, Luke Arcovio of Newbury Neck Middle School has won the Section's contest in the K3-5 category, the only category in which there were entries. His poster is entitles "Cool Chem and the Gang", done in cartoon style.

Congratulations to Luke and his science teacher, Ms. Debra Phinney and good luck for Anaheim. ◇

Correction

In the January Issue, on page 14, the photos were credited erroneously to "Robert" Phillips. We apologize to **James** Phillips, who was the photographer at the Centennial Meeting and took these pictures. ◇

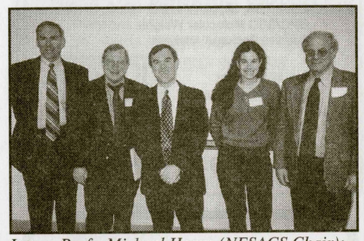
Member News

Michael E. Strem, ACS Director of Region I, is one of the four Directors elected to serve on the Executive Committee. The Executive Committee acts for the ACS board on matters of urgency arising between meetings of the Board and handles staff matters. ◇

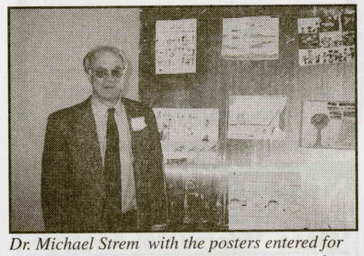
Pictures from the Seventh Annual Northeast Regional Undergraduate Chemistry Day

(photos by M.Z. Hoffman)

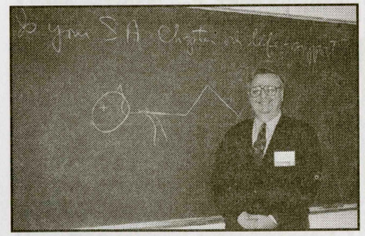
(See story at the left)



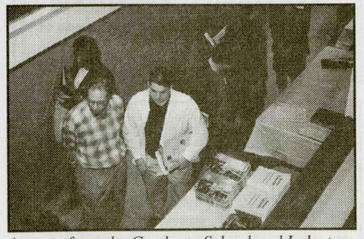
L to r: Profs. Michael Hearn (NESACS Chair); Warren Giering (B.U., organizer of the Undergraduate Day); Thomas Tullius (B.U., keynote speaker); Ms. Hilary Plake (B.U., president of Chemia); Dr. Michael Strem (Strem Chemicals, Director, ACS Region I).



Dr. Michael Strem with the posters entered for the poster contest. The winning entry is on the upper right



Prof. Morton Hoffman of B.U. presenting a workshop on "Reviving a Shallow-Breathing Student Affiliate Chapter".



A scene from the Graduate School and Industry Fair.

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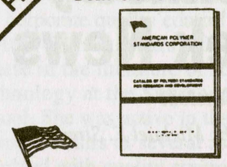

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Jan. 26

Prof.. Kai Johnsson (Univ. Bochum, GER)
"Free Radical Reactions of Isoniazid; Implications for Isoniazid Sensitivity and Resistance in M. Tuberculosis"
Tufts University
Pearson Hall, Room 106, at 4:30 PM

Jan. 26-28

Prof. Maurice Brookhart (Univ. NC, Chapel Hill)
Karl Pfister Visiting Lecturer
Mass. Inst. of Technology
Room 6-120, at 4 PM

Jan. 28

Prof. Nadian Seeman (New York Univ.)
Title TBA
Dartmouth College
Steele Hall, Rm. 107, at 10:30 AM

Feb. 2

Prof. Don Wiley (Harvard Univ.)
Title TBA
Tufts University
Pearson Hall, Room 106, at 4:30 PM

Feb. 3

Prof. Philip DeShong (Univ. MD, College Park)
"Silicon-Based Strategies for the Synthesis of Natural Products"
UMass, Dartmouth
Science & Eng. Bldg., Rm. 305, at 4 PM

Feb. 4

Prof. William Chameides (Georgia Inst. Tech.)
Title TBA
Boston College
Merkert Chem. Ctr., Rm. 127, at 4 PM

Prof. Jeff Nagle (Bowdoin College)
Title TBA
Dartmouth College
Steele Hall, Rm. 107, at 10:30 AM

Dr. Mike Gilson (C.A.R.B)
Title TBA
Mass. Inst. of Technology
Room 6-120, at 4 PM

Feb. 8

Prof. William Lipscomb (Harvard Univ.)
Title TBA
Harvard Univ.
Pfizer Lecture Hall, at 4:15 PM

Feb. 9

Prof. Daniel Nocera (Mass.Inst.Tech.)
"Two-Electron Mixed Valency - An Untraveled Road in the World of Energy Conversion Chemistry"
Tufts University
Pearson Hall, Room 106, at 4:30 PM

Feb. 10

Prof. Malcolm Chisholm (Indiana Univ.)
"The Chop-Chop Reaction (a la Schrock and Cummins): Further Studies Aimed at Elucidating Mechanisms"
Mass. Inst. of Technology
Room 6-120, at 4 PM

Prof. Graham Jones (Northeastern Univ.)
"Designed Enediynes as Targeted Antitumor Agents"
UMass, Dartmouth
Science & Eng. Bldg., Rm. 305, at 4 PM

Feb. 11

Prof. Joe Bruno (Wesleyan Univ.)
Title TBA
Dartmouth College
Steele Hall, Rm. 107, at 10:30 AM

Prof. Craig Wilcox (Univ. Pittsburgh)
Title TBA
Mass. Inst. of Technology
Room 6-120, at 4 PM

Feb. 16

Prof. Ted Cohen (Univ. Pittsburgh)
"Novel Synthetic Methods Using Organosulfur and Organolithium Chemistry"
Tufts University
Pearson Hall, Room 106, at 4:30 PM

Feb. 17

Prof. Karen Goldberg (Univ. Washington)
"Reductive Elimination and Oxidative Addition Reactions Involving C-C, C-H, and C-X Bonds at Pt(IV)/Pt(II)"
Mass. Inst. of Technology
Room 6-120, at 4 PM

Prof. James Rusling (Univ. Conn.)
"Functional Films of Enzymes and Nucleic Acids on Electrodes"
UMass, Dartmouth
Science & Eng. Bldg., Rm. 305, at 4 PM

Feb. 18

Prof. Wenbin Lin (Brandeis Univ.)
Title TBA
Dartmouth College
Steele Hall, Rm. 107, at 10:30 AM

Prof. Barry M. Trost (Stanford Univ.)
Prof. Joanne Bronson (Bristol-Myers Squibb)
Bristol-Myers Squibb Lectures in Organic Synthesis
Mass. Inst. of Technology
Room 6-120, at 4 PM

Dr. William King (Abbott Labs)
"Futuristic Cardiac Markers"
Northeast AACC Meeting
Doubletree Guest Suites Hotel, Waltham, 6-9 PM
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dedrum@bics.bwh.harvard.edu

Prof. Anne Mayes (Mass. Inst. Tech.)
"Modifying Biomaterials Surfaces"
Univ. Mass, Lowell
Olney Hall, OH-428, at 3:30 PM

Feb. 22

Prof. Gregory Van Duyne (Univ. PA Med. Sch.)
"A Structural Framework for Understanding Cre-loxP Site-specific Recombination"
Harvard Univ.
Pfizer Lecture Hall, at 4:15 PM

Feb. 23

Prof. Richard Friesner (Columbia Univ.)
Arthur D. Little MIT Seminar
Mass. Inst. of Technology
Room 2-105, at 4pm

Feb. 23

Prof. Ingrid Fritsch (Univ. Arkansas)
Title TBA
Tufts University
Pearson Hall, Room 106, at 4:30 PM

Feb. 24

Prof. Martin Taubman (Forsyth Dental/Harvard)
"Glycosyl Transferases in the Etiology and Amelioration of Dental Caries"
Boston Glycobiology Discussion Group
MIT Faculty Club, at 6:30 PM
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Prof. Matthew Zimmt (Brown Univ.)
"Solvent as Wire? Solvent-Mediated Electronic Coupling in Electron Transfer"
UMass, Dartmouth
Science & Eng. Bldg., Rm. 305, at 4 PM

Feb. 25

Dr. Jerry Skotnicki (Wyeth-Ayerst Labs.)
Title TBA
Dartmouth College
Steele Hall, Rm. 107, at 10:30 AM

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