THE NUCLEUS

January 1997 *Of the Northeastern Section of the American Chemical Society* *Vol. LXXV, No. 5*

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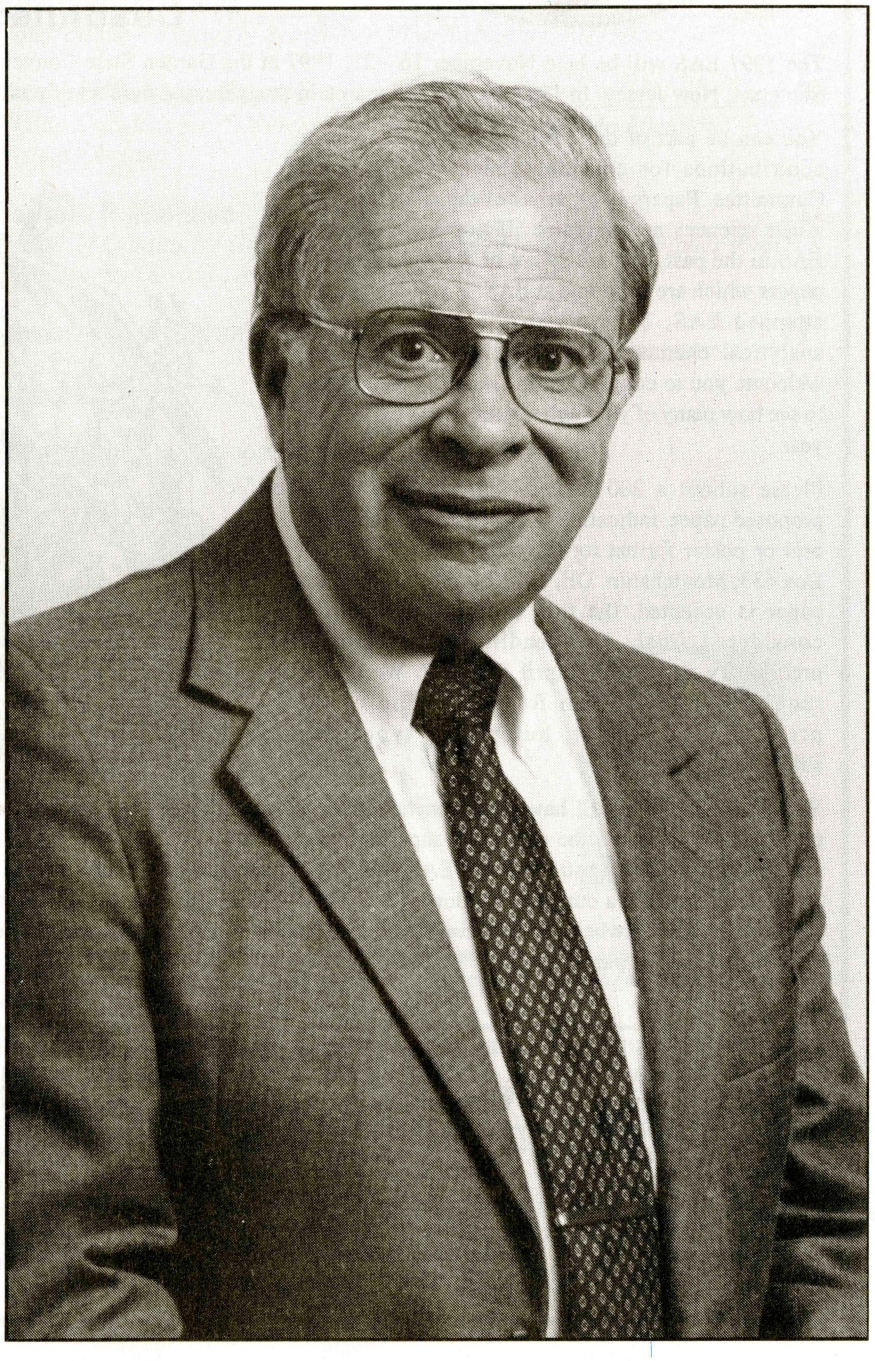
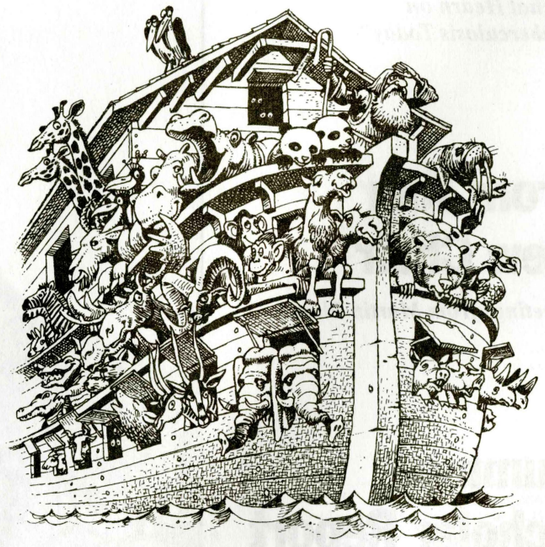


Unfortunately, no one can hold back the course of time. While November 1997 may seem like a long way off, now is the time to submit your abstracts for papers to be presented in 1997

Call for Papers
Deadline: April 15, 1997

The 1997 EAS will be held November 16 - 21, 1997 at the Garden State Convention Center and the DoubleTree Hotel in Somerset, New Jersey. In 1997, we hope to maintain the increased number of contributed papers submitted in 1996.

You can be part of the 1997 EAS. We solicit your contributions for consideration by the Program Committee. Papers in all areas of the analytical and allied sciences are welcome. If you have attended EAS in the past, you are aware of the wide range of papers which are welcome at EAS. If you have never attended EAS, but work in the general area of analytical chemistry and the allied sciences, we welcome you to come aboard. You will be surprised to see how many of your colleagues attend EAS every year.



Please submit a 200 to 250 word abstract of the proposed paper, indicating your preference for either oral or poster format to: Program Committee, P.O. Box 633, Montchanin, DE, 19710-0633 U.S.A. If the paper is accepted, the title and author(s) will be considered final. The deadline for receipt of preliminary abstracts is April 15, 1997. We do not require a special form for submission of the preliminary abstract, but please type your submission.

While you may not still have a typewriter, you are probably connected to the electronic superhighway. You may FAX your abstract to the EAS FAXLINE (302-738-5275), or submit it as an electronic file in any major word processing format via our Bulletin Board (302-738-5968) or our Web site; please include the name of the word processor in the file description when downloading to our BBS. In May 1997, authors of proposed papers will be notified regarding the acceptance of their paper.

EAS FACTS IN BRIEF: EAS is a non-profit [501(c)(3)] scientific organization run totally by volunteer scientists. 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 the Delaware Valley; the New York Microscopical Society; and the Delaware Valley, New England, and New York Sections of the Society for Applied Spectroscopy. The **1996** EAS attracted 5000 attendees and included over 640 Technical Papers, 14 CONFERENCES-IN-MINIATURE, 23 EAS Short Courses, 24 EAS Exhibitor Workshops, 9 Seminars, 9 Tutorials, and 318 exhibit booths. In **1997,** we expect the advance Registration fee to remain at a low $65. For more information, call the **EAS HOTLINE (302-738-6218),** send a FAX to the **EAS FAXLINE (302-738-5275),** send e-mail to EASINFO@AOL.COM, or write to EAS, P.O. Box 633, Montchanin, DE 19710-0633. EAS also maintains a Home Page on the Internet at the URL: "http//www.eas.org/~easweb/".

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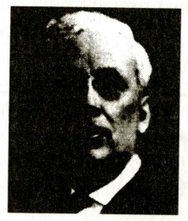

The Nucleus is distributed to the members of the Northeastern Section of the American Chemical Society, to the secretaries of the Local Sections, and to editors of all local publications. Forms close for advertising on the 1st of the month of the preceding issue. Text must be received by the editor six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

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From the New Chair

Greetings and best wishes for a happy, healthy and prosperous New Year.

It is a great honor to be Chair of the Northeastern Section of the American Chemical Society for 1997. With that honor comes the responsibility to continue the excellent agenda of NESACS. To make this happen requires the assistance and cooperation of members, the committees and the officers. I encourage those of you who are not actively engaged to take a personal role in the activities of your Section.

The Nucleus editor, the Chairs of the award committees and the Continuing Education committee deserve special appreciation for the highly visible results of their efforts. But appreciation is also due to less visible people who donate their time and energy to making arrangements for meetings, dinners and other events like Summerthing.

This year is especially exciting. We must prepare now for two major

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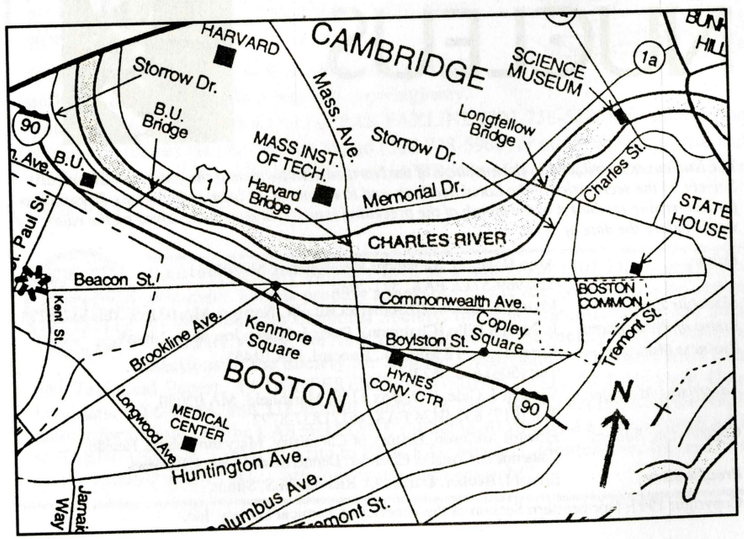
Nominations

Philip L. Levins Memorial Prize

Nominations for the Philip L. Levins Memorial Prize for outstanding performance by a graduate student on the way to a career in chemical science should be sent to the Executive Secretary, NESACS, 23 Cottage St., Natick, MA 01760 by March 1, 1997. The graduate student's research should be in the area of organic analytical chemistry and may include other areas such as environmental analysis, biochemical analysis, or polymer analysis. Nominations may be made by a faculty member, or the student may submit an application. A biographical sketch, transcripts of graduate and undergraduate grades, a description of present research activity and three references must be included. The nomination should be specific concerning the contribution the student has made to the research and publications (if any) with multiple authors. The award will be presented at the May 1997 Section Meeting. ◇

Directions



From the West: Take the Mass. Turnpike (I-90) to Exit 18. Exit left, follow signs to Cambridge. At the second set of lights turn right onto Storrow Drive. Exit at the Kenmore Exit. Follow * below.

From the South or North: Take Route I-93 to Boston. Exit onto Storrow Drive at Exit 26. Continue on Storrow Drive to the Kenmore Exit. Follow * below.

***From Kenmore Exit off Storrow drive:** At first set of lights turn right onto Beacon St. In Kenmore Square stay in center lane and take the center road which is Beacon St. The Holiday Inn is about 0.6 M on the right at St. Paul St. Park in metered spaces on Beacon St. or in the garage (enter from St. Paul St.)

By Public Transportation: Take, or chage (at Park St. or Government Center) to the Green Line, "C" train. Exit at the St. Paul St. exit, directly across from the Inn. ◇

Monthly Meeting

The 785th Meeting of the Northeastern Section of the American Chemical Society

Thursday, January 9, 1997
Holiday Inn at Brookline
1200 Beacon St., Brookline, Mass., Whitney B Room

5:30 Social Hour

6:30 Dinner

7:45 Evening Meeting, Dr. Martin Idelson, presiding
Introduction of the Speaker, Dr. P. Samuel
Michael Hearn, Ph.D., Wellesley College,
Tuberculosis Today: Chemical Perspectives on the Resurgence of the White Plague

Refreshments will be served after the program.

Dinner reservations should be made no later than noon, January 2. Please call or fax Marilou Cashman at (800) 872-2054. 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** on a space available basis in the garage.

Next meeting on February 13, 1997 at Bridgewater State College, Bridgewater, Mass. ***Speaker:*** *Dr. Christopher Martin, National Marine Fisheries, on "Marine Biotoxins", 5:30pm Social Hour and Dinner, 8:00pm Evening meeting.*

Abstract

Tuberculosis Today: Chemical Perspectives on the Resurgence of the White Plague

Combination therapy involving the "miracle drug" isonicotinic acid hydrazide (INH) was largely responsible for the abandonment of quarantine practices in the control of tuberculosis infection in the years immediately following the Second World War, enabling thousands of sanitarium patients to return home and lead normal lives. In spite of the efficiency of INH and other tuberculostatic drugs, researchers have recently observed a sharp rise in the number of new cases of tuberculosis world-wide and the emergence of drug-resistant strains of *Mycobacterium tuberculosis*. This has led to the urgent need for the development of newer and more effective drugs, the re-examination and re-evaluation of older drugs, as well as the exploration of the modes of action of antimycobacterial compounds in general.

Recent disclosures in the research literature have pointed out the key role of certain anti-tubercular Schiff bases in preventing the biosynthesis of the chemical components of the cell wall of the bacillus, thus entraining death of the tuberculosis pathogen. In this vein, we have developed a simple and general procedure for the preparation of Schiff base derivatives of INH on such a scale and in such purity as to be convenient for subsequent biological evaluation. In particular, we have found that an appropriate choice of structural elements in the Schiff base synthesis increases compound lipophilicity by several orders of magnitude, which may signify better permeation of the bacterial lipid domain and better drug action.

Near-infrared spectroscopy (NIR) provides an opportune method for monitoring our preparations. NIR constitutes a robust and dependable means of analysis of INH and its congeners with minimal technical effort. During the formation of the tuberculostatic Schiff bases, for example, it is possible to readily follow the loss of the first overtone band of the N-H stretch at 1558 nm in INH. Estimates of pseudo-first order rate constants obtained from NIR are useful in categorizing reactions and adjusting preparative conditions. Thus the formation of tuberculostatic compounds in the aromatic series would appear to require less vigorous conditions than the synthesis of the related aliphatic ketomycolate mimics.

Biography

After receiving his undergraduate degree in chemistry with highest honors and highest distinction at Rutgers College, Michael Hearn took his Ph.D. degree in organic chemistry at Yale. Since that time, he has taught at Wellesley College. A member of the American Chemical Society for more than twenty-five years, Professor Hearn has served on the Board of the Northeastern Section since 1985 and was recently voted Chair-Elect. His professional involvements include memberships in the Organic and Polymer Divisions of the ACS, the National Science Teachers Association, the Council on Undergraduate Research, the Coblentz Society, the American Society for Microbiology and the Council on Near-Infrared Spectroscopy. He is a Fellow of the American Institute of Chemists and serves as Associate Editor of Organic Preparations and Procedures International. Professor Hearn's research efforts include the synthesis and reactions of organic hydrazines, the development of new tuberculostatic compounds and the use of vibrational spectroscopy in the analysis of these materials. He is especially interested in working with research students across disciplines to help them to make the intellectual connections between chemistry and their other scientific endeav-

Board of Directors

Notes of Meeting of September 19, 1996

(From the Minutes of M. Hearn)

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

Officers' Reports:

Chairman: P. Samuel reminded the Board that the Section's Centennial will occur in 1998.

Treasurer: J. Piper presented the current budget report. It was VOTED and PASSED to accept the report.

Committees:

Publication: E.J. Billo MOVED that the Board ratify contracts for the Editor, Business Manager and Advertising Manager of the *NUCLEUS*. PASSED. It was the sense of the Board that the *NUCLEUS* be distributed on a trial basis to members of the Rhode Island and Central Massachusetts Sections.

Education: M.Hoffman announced the Annual Undergraduate Day, to be held at Boston University on November 9.

Constitution and Bylaws: A. Heyn, reporting for T. Light, stated that the ACS C&B Committee had recommended some editorial changes to the amendment of Article VIII, Sec.1. It was the sense of the Board that these editorial changes be accepted.

NERM: E.J. Billo, reporting for T. Gilbert, announced that an Oversight Committee had been established to insure good forward planning for future NERM meetings.

National Chemistry Week: V. Wilcox announced via P. Samuel that the ACS Satellite Program Telecast "Teaching Chemistry, 1996" will be held at the University of Mass. Lowell on November 4. Dr. Tanner has planned an excellent program, including laboratory demonstrations and hands-on experiments to fit the theme: Integrating General and Organic Chemistry.

Old Business: It was determined that the actual "birthday" of the Section will be March 7, 1998.

Notes of Meeting of October 10, 1996

Officer's Reports:

Treasurer: M. Hearn reported for J. Piper on the budget report, which was ACCEPTED. It was MOVED and VOTED that James U. Piper, Treasurer, is authorized to sign checks on Fidelity Investment Accounts which are not part of the Trustee holdings. A. Heyn, Chairman of the Awards Committee, requested that separate expense item lines be developed for the NESACS Hill Award expenses and the Hill Lectureship awards, which are sponsored by but not administered by the Section.

Archivist: M. Simon introduced David Adams who will chair the Chemical Landmarks Subcommittee.

Committees:

Awards: A. Heyn reminded the Board that the evening program will include the presentation of the Henry A. Hill Award to Dr. A. Viola.

Chemistry Education: M. Hoffman announced the program for the November 9, 1996 Annual Undergraduate Chemistry Day. P. Brauner voiced her concern regarding the status of Chemistry departments in the State Colleges. The Board referred this matter to the Chemistry Education Committee for formulating a motion in opposition to a loss of departmental standing based on the number of graduates.

Medicinal Chemistry Group: M. Singer mentioned that the September meeting had been very successful. Plans are going forward for the December meeting.

Old Business: A. Obermayer discussed the Section's Web Site. An *ad hoc* committee was formed to bring recommendations back to the Board.

The Board discussed the upcoming 1998 Centennial of the Section. A Centennial Committee is to be formed to plan the observance. ◇

Summer Scholar Report

Overexpression of E. coli EcoRI Modification System Enzymes

Phillip Stephan Cuculich†, Advisor: Evan R. Kantrowitz
Boston College, Merkert Chemistry Center

Escherichia coli RI (EcoRI) DNA restriction and modification enzymes are responsible for host specificity of *E. coli*. The restriction endonuclease enzyme recognizes a hexanucleotide repeat (5'- GAATTC -3') and cleaves double-stranded DNA in a staggered fashion between the guanine and first adenine residues. The methyltransferase enzyme, or methylase, adds a methyl group to the second adenine, nearest the axis of symmetry, leaving the site resistant to endonuclease cleavage. The endonuclease and methylase are two independent proteins which are coded for by distinct genes, and will be referred to collectively as the EcoRI modification system.

Both enzymes have proven useful for analysis and manipulation of DNA molecules. Catalytic requirements are relatively simple: the endonuclease, active as a dimer, requires unmodified DNA and a divalent cation, preferably Mg^{+2}, while the methylase, active as a monomer, requires unmodified DNA and S-adenosyl-L-methionine (1). Although both enzymes recognize the same sequence, it has been shown that the interactions are distinct for each enzyme. The limited recognition sequence size makes these enzymes attractive for investigation of sequence-specific DNA-protein interactions.

An effective method that can be used to study relationships between protein structure and function is site-specific mutagenesis (2). This method substitutes specific amino acids in an enzyme to determine its effect on specific activity. To better study DNA-protein interactions, site-specific mutagenesis will be used to modify the EcoRI restriction endonuclease.

The genes for the EcoRI modification system have been sequenced and cloned into the plasmid vector pKC30(7), downstream from the bacteriophage lambda p_L promoter, yielding plasmid pSCC2 (3). Although it has been reported to be a good overproducing system, the heat activated system has some drawbacks. First, for site-specific mutagenesis studies, one needs a plasmid with a bacteriophage origin of replication, or phagemid, to produce the required single-stranded DNA. Second, pSCC2 has not proven to be stable in certain *E. coli* strains, making storage and manipulation difficult. Therefore, the objective of this research project was to clone the EcoRI modification system into an effective overproducing expression system that can be easily mutated. The two expression systems are the pET System (Novagen) (5), using the T7 promoter and the *E. Coli pyrB* promoter system (9).

†1996 Norris/Richards Summer Scholar

Results

A schematic diagram of the procedure for cloning the EcoRI DNA modification system into both the T7 and *pyrB* promoter systems is shown in Figure 1. An Nde I restriction site was introduced into the first codon of the endonuclease gene and a Sac I site was introduced into the region immediately downstream from the methylase gene to better facilitate DNA manipulation. The Polymerase Chain Reaction (PCR) technique allowed for rapid and accurate amplification of the genes using specifically mismatched primer sequences to introduce the Nde I and Sac I restriction sites (4).

(a) Amplifying Eco RI endonuclease and methylase by PCR and corresponding introduction of Nde I and Sac I sites

Using the aforementioned pSCC2 as a template, the Eco RI endonuclease and methylase genes were amplified using PCR techniques. Primers complementary to the beginning of the endonuclease gene and end of the methylase gene were synthesized, with specific mismatches present. The amplification was performed by heating pSCC2 to 94°C for double strand DNA denaturation. This was followed by cooling the reaction to 50°C to allow the single-stranded primers to anneal to the single-stranded DNA template. After this step, the reaction was heated to 72°C, allowing Taq Polymerase to extend primer sequences. This process was repeated for 25 cycles, yielding several micrograms of double-stranded DNA containing the endonuclease and methylase genes with an Nde I site in the beginning and a Sac I site at the end. These sites facilitate the cloning of the Eco RI modification system into other expression vectors.

(b) Cloning PCR product into pET23a and subsequent overexpression

The 1823 base pair PCR fragment (1823PCR) was separated by agarose gel electrophoresis and purified using GeneClean (US Biochemicals). Because the restriction sites on 1823PCR were so close to the termini of the fragment, it was necessary to clone the fragment into a vector before digesting the fragment with restriction enzymes. A unique characteristic of *Taq* polymerase is that it adds one adenine to the 3' termini of the extended PCR fragment in a non-template-dependent manner. pBluescript II SK (Stratagene) was restricted with EcoRV and separated and purified using the same agarose gel/GeneClean technique. EcoRV restricts bluntly, leaving no "sticky ends" on the cleaved fragment. The linear pBluescript fragment was then treated with *Taq* DNA polymerase and deoxyTTP to yield a fragment with one thymidine on each of the 3' termini. Then, 1823PCR and the T-tailed pBluescript fragments were treated with DNA ligase. The resulting plasmid contained the two genes

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Summer Scholar Report

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of interest inserted into the EcoRV site in the multiple cloning region of pBluescript. This vector, along with the T7 expression vector, pET23a, was digested with Nde I and Sac I. The fragment containing the Eco RI modification system (1823pBlue) and the fragment containing the T7 expression system were then separated and purified. These two fragments were treated with DNA ligase, yielding the plasmid pNUT1 (Figure 1). This plasmid was digested with various restriction enzymes to confirm that the Eco RI system had been inserted into the multiple cloning region of pET23a, between the Nde I and Sac I sites.

pNUT1 was transformed into both BL21(DE3) [F⁻*ompT* r_B^- m_B^-] and BL21(DE3)pLysS, containing a plasmid encoding for a T7 lysozyme (8). These host cells contain a chromosomal copy of the gene for T7 RNA polymerase and are lysogens of bacteriophage DE3 (5). Addition of isopropyl-ß-D-thiogalactopyranoside (IPTG) induces T7 RNA polymerase, which transcribes the target DNA in pNUT1. The T7 lysozyme in the pLysS host inhibits transcription by binding to the T7 RNA polymerase, providing a tighter control of overexpression (6).

(c) Cloning PCR product into pEK164 and subsequent overexpression

The plasmid pEK164 contains the *pyrB* and *pyrI* genes and the production of these proteins is controlled by the *pyrB* promoter. This promoter has been shown to overexpress *E. coli* and non-*E. coli* proteins to approximately 50% total soluble cell protein (9). Plasmid pEK164 was digested with Nde I and Sac I and fragments were separated by agarose gel electrophoresis. The larger fragment was selected and purified by GeneClean, removing the two *pyr* genes. The 1823pBlue fragment, digested previously with Nde I and Sac I, was added to the pEK164 fragment and treated with DNA ligase. The structure of the resulting plasmid, pNUT2, was confirmed by treatment with various restriction enzymes. Thus pNUT2 contains the Eco RI genes under the control of the pyrB promoter. pNUT2 was transformed into EK1104 [F⁻*ara, thi,* Δ*pro-lac,* Δ*pyrB, pyrF*±*,rpsL*] and EK005 [F⁻*his, pyrF*±] for overexpression. The *pyrB* promoter is activated when uracil levels are low. Thus, by regulating the concentration of uracil in the growth media, overexpression quantities are controlled.

(d) Site-directed mutagenesis for optimum methylase and mutant endonuclease expression

Site-directed mutagenesis was performed by the Kunkel method (2). The phagemid pNUT1 was transformed into CJ236 [*dut-1 ung-1 thi-1 relA-1*/pCJ105 (Cm^r)] to produce uracil-containing plasmid. The transformed cells are then superinfected by the filamentous helper bacteriophage M13K07, and the uracil-containing single stranded DNA is extracted from the phage. The rest of the procedure involves annealing a mutagenic oligonucleotide primer, extending the primer with DNA polymerase, and completing the circular plasmid with DNA ligase. The first mutagenesis introduced an Nde I site at the beginning of the methylase gene. Using Nde I to delete the endonuclease gene, this mutation will allow the methylase to be overexpressed alone, perhaps increasing methylase production. The structure of the resulting plasmid, pNUT3, was confirmed by a digestion with Nde I. The second mutagenesis introduced a mutation at the Asn-141 of the restriction endonuclease. Asn-141 was the only residue to show hydrogen bonding with the 6-amino group of the inner adenine of the recognition site, the methylation site of the methyltransferase. The polar asparagine was substituted with a nonpolar valine, which also has a slightly smaller van der Waals surface than asparagine. With this mutation, it is believed that the endonuclease might better recognize and bind to a methylated recognition sequence. The resulting plasmid, pNUT4, awaits sequencing to confirm proper mutagenesis.

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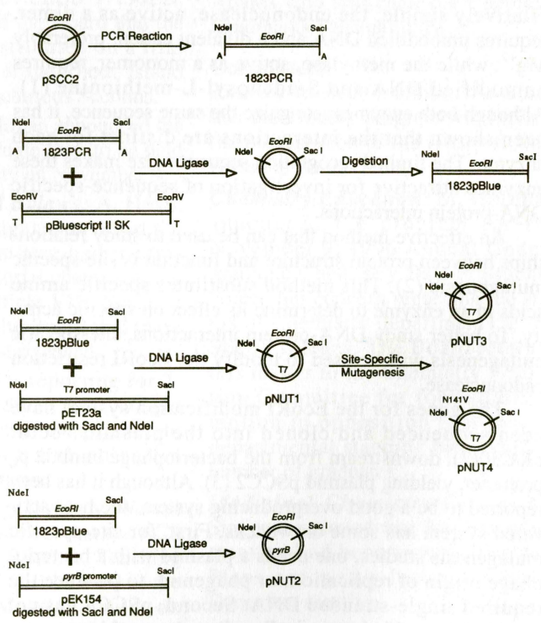

Figure 1. *Schematic of the protocols used to amplify the E. coli EcoRI endonuclease and methyltransferase genes by PCR, to clone EcoRI genes into a linear "T-tailed" pBluescript vector, to clone EcoRI genes into pET23a, an expression vector using the T7 promoter (5) and subsequently to mutate the pNUT1 phagemid by site-specific mutagenesis, and to clone the Eco RI genes into pEK154, en expression vector using the pyrB promoter.*

Phillip Cuculich

by Prof. Evan R. Kantrowitz

Mr. Phillip Cuculich, originally from Chicago, is a senior biochemistry major at Boston College. He began his independent research project last spring and is continuing his project as a Scholar of the College this year. In addition to his passion for biochemistry, Phillip has a keen interest in medical public policy and is heavily involved with the Bands Program at BC.

The Norris and Richards Summer Scholarship has a profound effect on Phillip. He has developed into a more mature scientist as the summer progressed. In addition, Phillip was able to understand first-hand the material he had learned about in biochemistry lectures. As a result of the Norris and Richards Summer Scholarship, his interests now lie in academic medicine and biochemical research. In fact, Phillip has applied for admission into a number of MD/PhD joint degree programs, where I have no doubt he will find success. He wishes to continue study of protein structure and function relationships as they relate to human disease. ◇

Summer Scholar

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(e) Future directions

The summer research on the cloning and overexpression of the *E. coli* EcoRI restriction and methyltransferase genes will continue as a Senior Scholar of the College Project. The EcoRI modification system sequencing primers have been made, and the genes will be sequenced shortly to insure the PCR reaction did not introduce new mutations as well as to confirm mutagenesis results. The two proteins will be separated and purified using a two column procedure (3). To further investigate the mechanism of DNA-protein recognition and activity, characterization studies will be done on both wild-type and mutant endonucleases.

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Samuel P. Mulliken

Father of Qualitative Organic Chemistry and of Nobel Prize Winner Robert S. Mulliken

by David L. Adams, Ph.D.,
Babson College

"While I was growing up, my father was writing his lengthy well-known treatise on *A Method for the Identification of Pure Organic Compounds*, in four volumes. This was the standard work in the field for many years. The first volume contains a set of two standard color charts which were prepared through home labor by myself and my sister. We had small gummed squares of all the various colors; one of each color had to be stuck in its proper place in the chart. We were paid for each completed chart. Another activity which I carried on was proof-reading of my father's books" (*1*).

This quote, written by Samuel Parsons Mulliken's son Robert S. Mulliken in his book *Life of a Scientist*, provides insight to the two great passions which shaped his father's life - his family and qualitative organic analysis. These two devotions often crossed paths as evidenced in the opening paragraph. Samuel P. Mulliken, called Sam by family and friends, was the father of both the 1966 Chemistry Nobel Prize winner Robert S. Mulliken and qualitative organic analysis (*2, 3*). Sam Mulliken spent the better part of his academic life developing the first classification scheme for qualitative organic analysis. Virtually all his professional activities were closely connected with this effort. As for his family, it always drew him back to his hometown of Newburyport, Massachusetts. He taught at the University of Cincinnati; did graduate research in Leipzig, Germany; taught at Clark University in Worcester, MA and at Bryn Mawr; and conducted private research in Rhode Island. Yet, after each of these assignments he returned to his hometown. In 1895 he returned to stay. The opening quote provides a vivid example of Sam Mulliken pursuing his professional goals in qual organic while at the same time including family members in his activities.

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Early Life in Newburyport, Massachusetts

Sam Mulliken was born in Newburyport on December 19, 1864 at 46 High Street. The house in which he was born stands today in much the same shape as then. Sam's early interest in

Samuel P. Mulliken

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chemistry grew from his reading "Conversations on Chemistry" by Jane Marcet, the same book that his father, Moses Mulliken, had read, and which his son, Robert, would read. In prior times, Michael Faraday had been motivated by this same book. Sam graduated from Newburyport High School in 1881 and thereafter worked for two years in a Newburyport apothecary shop. He subsequently received one of the first scholarships from the Wheelwright Scientific Fund for "the assistance of such Protestant young men of the city of Newburyport . . . in obtaining a scientific education" (4). With the help of this scholarship, Sam enrolled in MIT in the Fall of 1883, having been excused from the first year chemistry requirements. The Wheelwright Scientific Fund continues to award two to four scholarships to Newburyport High School graduates to this day and many continue to enter MIT. Sam entered MIT with another Newburyport High graduate, Arthur A. Noyes, who also received a Wheelwright scholarship and studied chemistry. The two were long time friends. As youngsters, they performed chemical experiments together at both the Noyes and Mulliken family homes, sometimes to the dismay of their parents (5).

Higher Education and Marriage

After graduation from MIT in 1887 in Course V, the chemistry program, Sam taught chemistry at the University of Cincinnati for one year as an Assistant in Chemistry. Sam, together with fellow MIT graduates Arthur A. Noyes, Augustus H. Gill, and Frederick F. Bullard, then traveled to Germany. He originally intended to work in Adolf von Baeyer's lab in Munich but when he arrived the lab was full and he had to seek lab openings elsewhere. After some time enjoying Germany, Sam finally enrolled at the University of Leipzig to work on the preparation and characterization of the chlorocinnamic acid geometric isomers under the direction of Johann Wislicenus. Mulliken received his Ph.D. degree in chemistry in 1890 and returned to America (6, 7).

Sam obtained a position as a Fellow in Chemistry at the newly established Clark University in Worcester, Massachusetts for the Spring of 1891. During the 1891-92 academic year he worked at Bryn Mawr College as Associate in Chemistry, then returned to Clark to work as both Instructor in Organic Chemistry and Acting Head of the Chemistry Department from 1892–94. Subsequently, he worked for a year as a Research Assistant at the private laboratory of Oliver Wolcott Gibbs in Newport, Rhode Island. In the Fall of 1895 he accepted an appointment as Instructor in the Chemistry Department at MIT (8, 9). While at MIT Sam was promoted to Assistant Professor in 1905, Associate Professor in 1913, and Professor in 1926 (10).

In 1893 Sam married his distant cousin, Katherine Wilmarth Mulliken. Their first son, Robert Sanderson, was born in 1896. Sam and Katherine had two more children, Katherine Freeman and Samuel Gyles. The family never left Newburyport, though they moved from 46 High Street to 51 Bromfield Street, then to 6 Harris Street and finally up the road to 10 Harris Street.

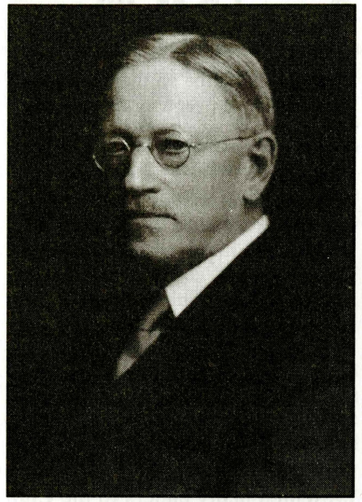
MIT – The Early Years

In the 1890's Arthur Noyes, Augustus Hill and Sam, all of whom received their Ph.D.'s in Germany in 1890, were reunited in the MIT chemistry department. In 1896 Mulliken collaborated with Noyes on a book titled *Laboratory Experiments on the Class Reactions and Identification of Organic Substances* (11). This was the first published, systematic treatment of qualitative organic analysis and was used for many years at MIT. This would be Sam's first brief foray into a succession of treatises outlining the laboratory identification of pure organic compounds spanning the next 26 years. From 1895 to 1897 Mulliken and Noyes introduced experiments in the identification of organic compounds in MIT's third year organic chemistry course (12). Sam later developed a graduate course in qualitative organic analysis in which students employed his method of using physical properties and chemical reactions to identify pure substances and components of a mixture.

Sam continued his interest in organic compound identification and eventually turned his entire professional activities in this direction. He developed and taught a course in qualitative organic analysis, his thesis students worked on associated laboratory techniques, and he limited his writing and speaking activities to the qualitative organic analysis texts he was researching and about to publish.

Qual Organic – A Method . . .

In 1904, after several years of painstakingly detailed laboratory work, Mulliken published *A Method for the Identification of Pure Organic Compounds – Volume I* (13). This volume contained descriptions of about 2300 pure organic compounds containing carbon and hydrogen or carbon, hydrogen and oxygen and a method for their systematic classification based on chemical reactions primarily and physical properties. This was followed by a series of "Methods" publications: Volume III (14) in 1910 dealing with commercial dyestuffs, Volume II (15) in 1916 describing organic compounds containing nitrogen, and Volume IV (16) in 1922 describing organic compounds containing elements other than carbon, hydrogen, oxygen and nitrogen. The "Mulliken scheme", as it came to be called, developed in these books was the first systematic scheme established to identify organic compounds. It was extensively used by academic and industrial chemists in America and Europe well into the era of spectroscopic methods. The Mulliken scheme was based on the use of chemical reactions and physical properties to categorize unknown organic compounds into groups, sub-groups, and genera after which additional identification tests could be performed. Prior to this time the identification of organic compounds was accomplished by determination of elemental composition and molecular weight, and reference to



Samuel P. Mulliken

M.I.T. Chemistry Faculty with Ellen Swallow Richards, about 1900.

(Photos: MIT Museum)

compilations of compounds known to have the same molecular formula. Mulliken's publications were renowned for the extensive compilations of properties of organic compounds, the thoroughness with which all the qualitative schemes were described and tested, and the care taken to precisely describe the results (17).

In 1935 Shriner and Fuson developed an alternative scheme for qualitative organic analysis based on solubilities in their text *The Systematic Identification of Organic Compounds* (18) which is still used in some colleges. As other schemes and instrumental methods of identification became available, the Mulliken scheme, passed on to his MIT colleague Ernest Huntress after Mulliken's death, began to lose popularity. In the early 1950's Huntress gave the rights to the "Mulliken/Huntress" qual organic scheme to his former graduate student and Sam's former MIT lab assistant, Edward R. Atkinson of Amherst, Massachusetts (19).

Sam had opportunities to leave MIT during this time. The most significant offer came from his friend and early collaborator Arthur Noyes who worked at the California Institute of Technology in Pasadena. Sam turned down the offer, probably, so his son Robert speculates, to remain close to his family in order to better support them. Robert claims that the lack of money around the Mulliken household in the early 1900's was likely due to the fact that Sam partially supported his mother and sister who still lived in the family home at 46 High Street (20).

The CWS and Dye Chemistry

During World War I, Sam directed research on the production of noxious gases at MIT. On May 11, 1918, at the age of 53, Mulliken was appointed a Major in the Chemical Warfare Service (CWS). He was chief of the Confidential Technical Section at the headquarters of Major-General Siebart, Chief of the CWS, in Washington, DC. He was honorably discharged on January 6, 1919 (21, 22).

Mulliken was very interested in the chemistry of dyes and consulted in the dye industry. This interest likely developed because of the importance of the textile industry in Newburyport at that time, the applied nature of chemistry taught at MIT, and the fact that many MIT students got jobs in the textile industries. The nearby cities of Lowell and Lawrence were renowned for their textile mills and Lowell was home to the Lowell Textile Institute and the famous textile dye authority, Louis Olney. Sam developed and taught a course in dye chemistry at MIT and he regularly took students on field trips to textile companies in Lawrence as part of the course. His long-standing interest in dyes is also evidenced in Volume III of his Methods series dealing with the qualitative analysis of commercial dyestuffs. Mulliken had no intention of writing a volume on the identification of commercial dyestuffs (14) but was apparently persuaded that this venture was of sufficient importance to put aside his work on completing Volume II. Thus it happened that Volume III appeared six years before Volume II.

Dr. Edward Atkinson was Sam's graduate assistant the last time Sam taught the dye chemistry class in the Fall of 1933. Ed remembers the day he accompanied Sam and the class on a mill trip to Lawrence. Since Ed had a car he asked Sam if he would like a ride to Newburyport from Lawrence. Sam declined, opting instead to return to Cambridge and take the Boston and Maine Railroad train home to Newburyport, thus illustrating Mulliken was fond of commuting by train (23). Toward the end of his life Sam received a special award from the

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Samuel P. Mulliken

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Boston and Maine on the occasion of his riding it for over a million miles!

The Tuesday Night Club and Outdoor Activities

Although Sam spent most of his time either at or traveling to and from MIT, he was also involved in his community. He was an active member of the Tuesday Night Club of Newburyport from 1922 until his death in 1934. The Tuesday Night Club was, and remains, a close knit, dedicated small group of members and invited guests. It regularly meets on Tuesday nights for victuals and member presentations, followed by discussions. Sam presented many papers to the Club members at their meetings. The titles and topics were varied and included: "Gas" – Sam brought in samples of noxious gases and gave the members a whiff; "In the Days of Kaiser" – Sam reminisced about his student days in Germany; "Metawamkeetook" – Sam expounded on his ancestor John Giles who allegedly was abducted by Indians; "A Nice Little War" – Sam relayed accounts of his ancestor General Samuel Parsons of the Revolutionary War; and "Hitler" (24, 25). The circumstances surrounding Sam's talk on Hitler presented on February 6, 1934 provide a contemporary view of Sam's life and times. Meeting notes state that the "conclusion of the evening was that Things in Germany and perhaps elsewhere are going straight to Hell" — very prophetic indeed. Also, Sam could not find his written paper which he brought with him. Two other club members returned to the Mulliken house to retrieve the paper but couldn't find it. When they returned to the meeting, they found the paper in the chair where Sam was sitting. The minutes record Sam as being an "absent-minded professor."

Sam was very fond of the outdoors and went on many hiking and fishing expeditions with family members, graduate students and faculty colleagues. Sam enjoyed extended stays at a cottage in Pemaquid, Maine and often took rides in a 30-foot motor boat along the scenic Maine coast. In 1932, he organized an all day fishing trip to Ipswich Bay for the MIT chemistry department. The trip was expanded in 1933 and an annual fishing expedition soon became a tradition. Sam also took family members on boating trips up the Merrimack and Parker Rivers and hikes through the White Mountains of New Hampshire (6, 7).

The Later Years

During his 39 years of teaching at MIT, Sam taught undergraduate organic chemistry, qualitative organic analysis, chemistry of dyes and dyestuffs, and heterocyclic chemistry at various times. Sam also occasionally accepted administrative responsibilites. One such position was Head of MIT's Undergraduate Organic Chemistry Division from 1925 to 1934. As Division Head, he directed the undergraduate instructional work (26, 27). In 1933, Sam was asked by an MIT undergraduate seeking a waiver from the organic chemistry requirement. Sam was reluctant to grant such a waiver, but after meeting with the student, allowed him to take the course final exam. After passing the exam Sam approved the waiver (28). The student was Robert Burns Woodward – no one would deny that Sam's decision in this case was indeed warranted!

Sam was active both professionally and personally, but by the Spring of 1934 he was getting old and tired, regularly falling asleep in his Morris chair in his office in Room 4-440 at MIT. He last taught during the 1933–34 academic year and because of failing health was granted a leave of absence from MIT for the Fall of 1934. During the Summer of 1934 he contracted rheumatic fever and spent some time in the Anna Jacques Hospital in Newburyport. He died at home of a coronary thrombosis on October 24, 1934 and was buried at the Oak Hill Cemetery in Newburyport. The funeral was attended by many Tuesday Night club members and faculty of the MIT chemistry department. Ten MIT faculty acted as pall bearers including Frederick G. Keyes, Augustus H. Gill, James F. Norris, Arthur A. Blanchard, Avery A. Ashdown, Tenney L. Davis. Avery A. Morton, Ernest H. Huntress, N. A. Milas and Robert T. Armstrong (29, 30). On his grave marker Sam's professional achievements are listed incuding his Ph.D. at Leipzig and posts he held at MIT. Also present at the Mulliken funeral was Dr. Edward R. Atkinson, then a graduate student at MIT. Ed remembers Sam as a kind, almost shy man who by 1933 was weary and burned out (28).

Upon his death in 1934, Mulliken's professional belongings in Room 4-440 at MIT passed into the possession of his faculty colleague and qualitative organic analysis collaborator Ernest H. Huntress. Over the next several years Huntress gradually disposed of the voluminous chemical samples Sam stored in his office. Today, after renovations at MIT, no trace of Mullikens office and laboratory space remains. There is, however, a photograph of the 1899–1900 MIT Chemistry Department on the first floor of Building 4 in a lobby honoring Ellen Swallow Richards. Samuel Parsons Mulliken is in the second row, 3rd from the right, directly behind Mrs. Richards (31).

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From the New Chair

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events that will occur in 1998: the National Meeting in Boston during August and the 100th anniversary of the Section's founding. I would like those of you who wish to take part in preparing for these events to contact me by telephone (617-527-8880), FAX (617-527-3222) or e-mail (actingup @tiac.net).

If engaging in preparations for the National Meeting or the 100th Anniversary does not appeal to you there are many other volunteer activities from which to choose. A list of committees and their chairs will appear in the February issue of the *Nucleus*. Please feel free to call any of these people or myself for more information on how you can be of help. Your assistance will be most welcome. The more people who participate, the easier it is for all.

Supplementing the *Nucleus* is the new NESACS home page on the web (www.tiac.net/users/obermayr/nesacs) This site began last November. It will provide meeting information as well as other material of interest to ACS members.

I look forward to an exciting year and to seeing you at our monthly meetings. ◇

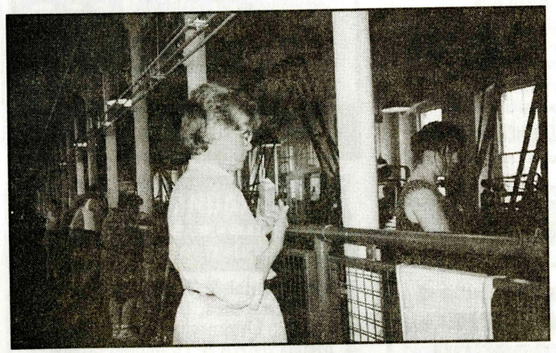
Please donate your copies of *THE NUCLEUS* to your local High School when you no longer need them.

Pictures from Summerthing 1996

August 17, 1996 at Lowell, Mass.

Organizers of Summerthing: (l. To r.) Janet Perkins, Arlene Light, Ted Light, Mary Burgess

Mary and Dick Lania registering



In the Boott Building weaving room

NESACS Group in the Canal boat.

(photos by Michaeline Chen and Janet Perkins)

Nomination

Aula Laudis

The Northeastern Section annually honors teachers of Chemistry at the secondary level in our region by choosing several for selection to AULA LAUDIS, an honorary society to reward teachers who have shown unusual skill in the classroom in any of several ways:

a. Active involvement in teacher groups, conferences, NEACT or such.

b. Many years of successful teaching, current or past.

c. Success of their students in interscholastic chemistry competitions.

d. Pioneering new curriculum developments.

Nominations, including a one-page summary of the nominee's relevant accomplishments, are due **February 15, 1997**, to be sent to:

David Olney, P.O. Box 559
Mattapoisett, MA 02739. ◇

Henry A. Hill Award

Nominations for the Henry A. Hill award for Outstanding service to the Northeastern Section should be sent to the Administrative Secretary, NESACS, 23 Cottage Street, Natick, MA 01760 by June 1. A resume of professional activities and description of the candidate's contributions to the Northeastern Section should be included. ◇

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