THE NUCLEUS

March 1994 *Of the Northeastern Section of the American Chemical Society* *Vol. LXXII, No. 7*

Monthly Meeting

Richards Medal awarded to Richard H. Holm for work in bioinorganic chemistry

1994 NESACS Candidates

Historical Notes

Murder at Harvard

Summer Scholars

Two aspects of enzyme chemistry

The Northeastern Section of the American Chemical Society, Inc.

Office: Marilou Cashman, 23 Cottage St., Natick, MA 01760. 1-800-872-2054 (Voice or FAX) or (508) 653-6329. Any Section business may be conducted via the business office above. Washington, D.C. ACS Hotline: 1-800-227-5558

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Cover: *Prof. Richard H. Holm*
(photo by Kopy-Antupit Studio)

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THE NUCLEUS

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Editor:	Arno Heyn, 21 Alexander Rd., Newton, MA 02161, Tel: 969-5712, FAX: 527-2032
Associate Editor:	Myron S. Simon, 20 Somerset Rd., W. Newton, MA 02165, Tel: 332-5273
Board of Publications:	Michael E. Strem (Chair), Joseph A. Lima
Business Manager:	Karen Piper, 19 Mill Rd., Harvard, MA 01451, Tel: (508) 456-8622
Advertising Manager:	Vincent J. Gale, 56 Bartlett Island Way, Marshfield, MA 02050, Tel: (617) 837-0424
Contributing Editors:	Edward Atkinson, History of Chemistry, Book Reviews; Maryann Solstad, Health; Chris Arumainayagam, Calendar.
Proofreaders:	Ernest I. Becker, Donald Rickter, M.S. Simon

1994 NESACS Candidates for Election

Chairman-Elect *(one to be elected)*
Doris I. Lewis *(Suffolk Univ.)*, Patricia L. Samuel *(Boston Univ.)*
Treasurer *(one to be elected)*
James U. Piper *(Simmons College)*
Trustee *(one to be elected)*
G. Richard Handrick *(retired)*
Councilor/Alternate Councilor *(4 Councilors and 4 Alternate Councilors to be elected)*
Catherine E. Costello *(M.I.T.)*, Reen D. Gibb *(Brookline H.S.)*, James A. Golen *(U. Mass. Dartmouth)*, Arno H.A. Heyn *(retired)*, Esther A. H. Hopkins *(Mass. Dept. of EPA)*, Cynthia B. McGowan *(Merrimack College)*, Janet S. Perkins *(retired)*, Dorothy J. Phillips *(Waters Chromatogr.)*, Norman W. Rice *(ORYZA)*, Donald O. Rickter *(Polaroid)*, Patricia L. Samuel *(Boston Univ.)*, Irwin A. Taub *(U.S. Army Natick R&D Ctr.)*, Alfred Viola *(Northeastern Univ.)*, Valerie R. Wilcox *(Nat'l Plastics Center & Museum)*
Nominating Committee *(two to be elected)*
James N. Lepage *(W.R. Grace & Co.)*, Joseph A. Lima *(Houghton Chemical Co,.)*, Debra J. Saez *(Technically, Inc.)*, J. Donald Smith *(U. Mass Dartmouth)*
Norris Award Committee *(two to be elected)*
Charles L. Braun *(Dartmouth College)*, Saul G. Cohen *(Brandeis Univ.)*, Dudley R. Herschbach *(Harvard Univ.)*, Robert S. Umans *(Boston College)*

Petition Candidates: In accordance with the Northeastern Section Constitution, Article VIII, Sec. 3, "Any group comprising 2 percent or more of the membership of the Northeastern Section may nominate candidates for any elective office provided that such nomination (accompanied by the signatures of the nominating group) shall be presented in writing to the Chairman of the Nominating Committee not more than ten days following the March meeting of the Northeastern Section." Accordingly, such petitions are due March 20, 1994 and should be sent to Dr. Dorothy J. Phillips, Waters Chromatography, Inc., 34 Maple St., Milford, MA 01757. At least 100 valid signatures are required. Preferably, the petition should be sent by certified mail.

Nominating Committee: Dorothy J. Phillips (chairman), E. Joseph Billo, Phyllis A. Brauner, Morton Z. Hoffman, Michael E. Strem. ◇

Call for Papers

Undergraduate Research Poster Session
at the
Twenty-fourth Northeast Regional ACS Meeting (NERM-24)
Burlington, Vermont
June 19–22, 1994

The organizers of NERM-24 invite undergraduate students, including graduating seniors to submit abstracts for presentation at the Undergraduate Research Poster Session, which will be part of the extensive programming for undergraduates at this regional meeting. Send abstracts on standard ACS forms to the organizer of the session: Prof. Edward J. Miller, Dept. of Chemistry, SUNY-Plattsburgh, Plattsburgh, NY 12901. **Deadline for receipt of abstracts: March 4, 1994.**

Annual Undergraduate Research Symposium
Saturday, April 30, 1994

The Northeastern Section of the ACS is soliciting the submission of poster papers for this symposium, which will be hosted by the Student Affiliates of Boston University. Send abstracts on standard ACS forms to the organizer, Prof. Patricia L. Samuel, Department of Chemistry, Boston University, Boston, MA 02215. Tel: 617-353-2124; fax: 617-353-6466; e-mail: psamuel@chem.bu.edu. **Deadline for receipt of abstracts: April 15, 1994.** ◇

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Esselen Forum

April 13, 1994

A Forum is planned for April 13, 8 p.m. at the Science Center, Harvard University. The general topic will be the polymerase chain reaction which has been used to replicate small pieces of DNA many times. This is a basic technique used in sequencing the human genome, in genetic engineering, in forensic analysis and in studying DNA in ancient tissues. The technique is the scientific basis, carried to fictitious extremes, in the movie *Jurassic Park.* Watch for the detailed announcement in the April issue. ◇

Board of Directors

by Michael J. Hearn

NOTE: Board meetings are held on the meeting day at 4:30 p.m. On March 10, 1994 it will be held in the Cabot Room of the Mallinckrodt Chemistry Building (opposite the Science Center). **Section members are invited to attend.**

Condensed Minutes, Meeting of December 9, 1993
Officer's Reports:
Chairman's Report: Dr. Phillips reminded board members to submit their annual reports on time.

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Monthly Meeting

The 760th Meeting of the Northeastern Section of the American Chemical Society

Theodore William Richards Meeting

Thursday, March 10, 1994

Harvard University Faculty Club

5:30 Social Hour

6:30 Dinner

Harvard University Science Center, Lecture Hall B

8:00 **Award Ceremony**
Reflections on Theodore William Richards — Dr. Dudley R. Herschbach, Harvard University
Introduction of the Medal Recipient — Dr. Jeremy Knowles, Harvard University
Presentation of the Medal to Professor Holm — Dr. James A. Kaufman, Chairman, Northeastern Section
Richards Medal Address: *Research in Biologically Related Inorganic Chemistry* — Dr. Richard H. Holm, Harvard University

Refreshments will be served after the program.

Dinner reservations should be made no later than March 4, 1994. Please call Marilou Cashman at (800) 872-2054. Reservations not cancelled at least 24 hours in advance must be paid. Members, $21.00; Non-members, $23.00; Retirees, $12.50; 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: Broadway Street Garage, 3rd level. Enter via Cambridge St. and Felton St.

Next meeting: Thursday, April 14, 1994 at Harvard University. Esselen Award to be presented to Kary B. Mullis (La Jolla, CA) for work in Biochemistry related to Genetics. His topic is ***The Polymerase Chain Reaction****. Social Hour 5:30 pm followed by dinner (Faculty Club), Evening meeting at 8:00 pm, Science Center. Also note that on Wednesday, April 13 at 8:00 pm, there will be an* ***Esselen Forum*** *at the Harvard University Science Center. See preliminary announcement on page 4.*

Abstract

Several current problems in biologically related inorganic chemistry will be considered. The structures and functions of metal binding sites in a number of enzymes have been investigated by the synthetic analogue approach. Recent results relevant to molybdooxotransferases, sulfite reductase, nitrogenase, and cytochrome *c* oxidase will be presented, with emphasis on the fundamental chemistry underlying the functions of mononuclear or polynuclear metal sites in these enzymes. ◇

Biography

Richard H. Holm was born in Boston, Massachusetts on 24 September, 1933. He holds a B.S. degree from the University of Massachusetts and the Ph.D. from Massachusetts Institute of Technology (1959). He started his academic career as an assistant professor at Harvard University and subsequently served on the faculties of the University of Wisconsin, M.I.T., and Stanford University. He returned to Harvard in 1980 to revive inorganic chemistry at that institution, and in 1983 became Higgins Professor of Chemistry. He was Chairman of the Department during the period 1983-86.

His research interests are in the inorganic chemistry of the transition elements. Among the research contributions of the Holm group are those in the areas of static and dynamic molecular stereochemistry, applications of paramagnetic NMR to problems of structure and reactivity, multi-electron transfer series, tetraazamacrocycles, inorganic synthesis of mono- and polynuclear molecules, oxygen atom transfer reactions, magnetic properties of solids, metal-thiolate, dithiolene, and thiometallate complexes, and bioinorganic chemistry with emphasis on synthetic analogues and reaction systems of the active sites of cytochrome P-450, iron-sulfur proteins and enzymes, nickel hydrogenases, molybdenum hydroxylases, and the Mo- and V-containing sites of nitrogenases. Over 50 students have received Ph.D. degrees based on this research, which has also involved over 75 postdoctoral associates.

He has served on numerous advisory and visiting committees and has been on the editorial boards of several journals. He has held over 50 lectureships, including the Baker Lectureship at Cornell University and the Miller Professorship at the University of California-Berkeley. Professor Holm has received a number of awards, including the Bailar Medal, the American Chemical Society Award in Inorganic Chem-

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MCG Officers 1994

Chairman: Dr. N. Laxma Reddy
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Secretary: Dr. Craig Siegel, Genzyme Corp., (617) 252-7657
Treasurer: Dr. Michael Singer, Organix, Inc., (617) 932-4142 ◇

Molecular Modeling:

The Small-Molecule Approach

A Satellite TV Seminar produced by the American Chemical Society, sponsored by the Medicinal Chemistry Group and U. Mass. Lowell

Tuesday, March 29, 1994, 1-4 p.m.
University of Massachusetts Lowell
Olney 150. **Free parking available**

The seminar has been organized by Dr. J. Phillip Bowen of the Univ. of Georgia. The three-hour seminar will include the following presentations:

Garland R. Marshall, Director of the Center for Molecular Design and Prof. of Molecular Biology and Pharmacology, Washington Univ., on the conceptual framework for drug design.

Yvonne C. Martin, Senior Project Leader, Computer-Assisted Molecular Design, Abbott Laboratories, on molecular modeling in the design of potent and selective D1 agonists.

Daniel F. Ortwine, Research Associate, Parke Davis Pharmaceutical Research Division, Warner-Lambert Co., on the use of pharmacophore models in the design of N-methyl-D-aspartate.

Following the Satellite seminar will be a local site panel discussion on molecular modeling including local experts in this field.

Advance registration is encouraged as there will be limited seating. Please mail a registration fee of $30 ($20 for students and high school teachers) to Michael Singer, c/o Organix Inc., 65 Cummings Park, Woburn, MA 01801. Checks payable to: MCG-NESACS. Participants will receive a booklet of the material presented during the satellite seminar.

For information call Michael Singer at (617) 932-4142.

Directions to the Univ. of Massachusetts Lowell, North Campus: Follow I 495 to the Lowell Connector. Take Exit 5N, Thorndike St. Turn LEFT at light beyond underpass. Go straight at two lights to the end of Fletcher St. Turn RIGHT onto Pawtucket St., STRAIGHT at blinking light at hospital, LEFT at next light, over bridge onto University Ave. Follow Univ. Ave. to traffic light. Turn RIGHT, parking is on your right beyond Olney Hall. ◇

Board of Directors

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Treasurer's Report: Dr. Piper presented the itemization for November. His report was ACCEPTED.

Councilors' Report: Dr. Phillips congratulated Dr. Gilbert on his appointment to the Standing Council Committee on Meetings and Expositions and M. Burgess on her appointment to the Standing Council Committee on Professional Relations.

Committee Reports:

Awards: Dr. Foye reported that the recipient of the Henry A. Hill Lectureship Award has been selected. He urged the Board to consolidate the write-up on awards in the Section's Annual Report to give it more prominence.

Hospitality: Dr. Howell confirmed the locations of the upcoming meetings: January at Curry College, February at Regis College, March and April at Harvard, May possibly at Brandeis.

Publications: Dr. Costello indicated that planning for the *NUCLEUS* in 1994 was on track. Dr. Heyn, Editor, stated that the January issue would be 12 pages, the February issue to be 16 pages.

Public Service: Dr. Handrick conveyed the message from Dr. Brauner that fresh volunteers for working with the committee would be welcome, especially in connection with the Holiday Lectures.

Richards Medal Committee: Dr. Kaufman relayed the information that the Awardee has been selected and will receive the award at the March Section Meeting. Dr. Green, Chairman of the Committee will soon offer suggestions concerning staffing of the committee in a manner to assure a greater degree of continuity.

Other Committees:

National Chemistry Week: Dr. Phillips relayed information received from Bert Paul summarizing the MIT program *Forum for Young Chemists* on Saturday, November 13, 1993 at which Dr. Phillips addressed the group of 8th to 11th graders on careers in chemistry. V. Wilcox described her experience in bringing hands-on chemistry to 150 children in rural Georgia, a venture supported by the National Plastics Museum and the Section.

NERM 23: Dr. Gilbert announced that the meeting, in addition to being scientifically successful, was financially successful, as well, resulting in $13,000 after expenses which will be distributed to Sections in proportion to their attendance. Therefore, a large part will be going to this Section. Dr. Hopkins suggested that a part of this be used as seed money for the next NERM meeting in this Section.

Old Business: Dr. Hopkins reviewed the procedure to be followed at this evening's Section meeting for voting on an amendment of the Constitution and Bylaws.

New Business: Dr. Kaufman stated the value of obtaining copies of the Annual Reports of other Large Sections.

Annual Meeting, January 13, 1994

Officer's Reports:

Chairman's Report: Dr. Phillips reviewed highlights of the past year and thanked board members for their efforts to make the programs successful, such as: Project SEED, the Education Task Force Workshop, the ACS Short Course, the MIT Young Chemists Forum, the ACS Satellite programs at the University of Massachusetts - Dartmouth and Lowell.

Chairman-Elect: Dr. Kaufman mentioned the strong Section Meeting talks presented during the year and hoped for an even better 1994.

Secretary: Dr. Hearn, while preparing the Annual Report was struck by the number of projects undertaken by the Section in Awards, Education, and Public Awareness.

Treasurer's Report: Dr. Piper presented the financial report for 1993 which was ACCEPTED.

Trustees: Dr. Handrick presented a preliminary report. The final report will be prepared as soon as the year's data are received from the banks and stockbroker.

Committee Reports:

Hospitality: Dr. Howell reported that total dinner attendance at meetings was about 500.

Publications: Dr. Costello reported that 1993 was a successful year for the *NUCLEUS*. Advertising income has exceeded the budgeted amount significantly, thanks to the efforts of Advertising Manager Vincent Gale. It is planned to increase the number of pages published in 1994. Dr. Phillips thanked the Board of Publications for the excellent Summer issue given out at the NERM-23 meeting.

Membership: New members have been invited to attend meetings of the Section and a number of them have done so. L. Rubin mentioned the excellent work of Arlene and Ted Light in developing the local Employment Clearing House.

Other Committees:

Public Service: Dr. Brauner discussed the several activities of this committee. She extended thanks to several members who helped in making the Holiday Lectures at the Science Museum a great success.

Speakers' Bureau: Dr. Michael Dube has joined Mary Ann Solstad and will, in time, take over the Speakers' Bureau.

Summerthing: V. Wilcox described this successful August program with its three venues in central Massachusetts.

Dr. Phillips thanked all committees for their work and referred to the upcoming Annual Report of the Section for details about their activities.

Old Business: None

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Consulting Chemists' Meeting

March 17, 1994
An ISO-9000 Workshop

What is it? How is it implemented? Will it benefit the smaller-scale technical business?

Speakers: Mr. William Noz, Mr. Harold Greenberg, Ms. Lesley Enos, Principals in the ISO-9000 Network.

Sheraton Tara Lexington Inn
Lexington, MA
727 Marrett Rd., Exit 30B, Rte.128, Rte. 2A West 1/4 mile to Hotel
Dinner at 5:30 p.m.
Workshop 6:30-9:00

The Professional Consulting Chemists' Group of the Northeastern Section and Pernix, Inc. of Wayland, MA are co-sponsors.

Call Debra Saez at (508) 521-1327 by March 15, 1994

Cost: $ 50, which includes the dinner, workshop and all hand-out materials.

Description of the Workshop

Smaller-scale and start-up technical manufacturing and service-providing companies need to be familiar with the Quality Management and Quality Assurance guidelines developed by the international Organization for Standardization (ISO) if they are to remain competitive on domestic and international business fronts. This Workshop is designed to provide general but substantive information to small technical businesses on the requirements contained in the ISO-9000 guidelines. This Workshop is important to any technical business which develops, designs, produces, installs services, or supplies a product or service. ◇

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

Board of Directors

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New Business: Dr. Singer, Treasurer of the Medicinal Chemistry Group, stated that active officers were guiding the group for the coming year. He hoped for closer coordination with the Board of Directors. The feeling was expressed that any of the officers of the group, just as any Section Members, are welcome to attend Board meetings.

After parting remarks expressing her appreciation for the cooperative spirit of the Board of Directors and members of the Section, Dr. Phillips recessed the Annual Meeting.

Condensed Minutes, Meeting of January 13, 1994

Officer's Reports:

Chairman's Report: Dr. Kaufman, thanking Immediate Past Chairman Dorothy Phillips for her guidance of the Section's activities in 1993, presented her with the ACS Past Chairman's pin. Dr. Kaufman stated his hopes for the Section for 1994. He especially invited members to attend Board of Directors Meetings.

Treasurer's Report: Dr. Piper presented the December 1993 summary which was APPROVED.

Committee Reports:

Budget: Dr. Piper presented the proposed 1994 budget which is to be voted at the February meeting.

Constitution and Bylaws: Dr. Hopkins invited members who were interested in serving on this committee to contact her.

Publications: Dr. Strem thanked outgoing chair Dr. Costello for her able leadership of the Board of Publications. 1994 is expected to be a successful year for the *NUCLEUS*. Dr. Heyn, editor, stated that the February issue would be 16 pages and the March issue expected to be 20 pages.

Public Relations: L. Charpentier was welcomed as the 1994 chairman of the committee.

Other Committees:

Project SEED: Dr. Phillips stated that there is a February 11th deadline for

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Historical Notes

Nineteenth Century Harvard Murder

For our column this month we are indebted to *Paul R. Jones*, chairman of the Department of Chemistry, University of New Hampshire and 1994 chairman of the ACS Division of History of Chemistry. The letter from Eben Horsford to Justus von Liebig (printed below) is part of an enormous volume of printed matter, much in the public press, describing a sorry event in the history of Harvard's chemistry department. Concise biographies of both Horsford and Webster can be found in the W.D. Miles treatise, "American Chemists and Chemical Engineers" American Chemical Society, Washington, D.C. 1976.

Paul Jones writes: *In 1991 I was digging through an archival collection related to Liebig in the Bavarian State Library in Munich. My goal was to find material on Johannes Wislicenus who had spent a few months working in Horsford's laboratory at Harvard when Wislicenus was only 18 years old. The thought was that I might find some reference to Wislicenus in correspondence to or from Horsford. The search uncovered a dozen or so letters written by Horsford to Liebig, the first few before 1860 and the remainder in the 1860's. The latter letters dealt largely with the manufacture of baking powder (see P.R. Jones, "Justus von Liebig, Eben Horsford, and the Development of the Baking Powder Industry", Ambix, 40, Part 2, 65(1993). The letter printed here came in the earlier period. I am certain that what is printed here is the original letter as Liebig received it. Any irregularities in the English would then be Horsford's own doing." The bibliographic reference for the letter is SBLIEB03.H0R Liebigania II B Letter # 3.*

Cambridge, August 31, 1850

My dear friend,

Day before yesterday perished on the gallows my former friend Dr. Webster. I have thought to give you a summary of his case, knowing the interest you have taken in his trial—and thinking you might like to know the points upon which his fate hinged, divested of all the rubbish of a fortnight's record of testimony.

You have probably seen his confession—or seen some allusion to it. The drift of it was that he had invited Dr. Parkman to his laboratory in Boston, in the hope of inducing him to postpone his claims which had long before matured, that Dr. Parkman came as invited, that Dr. P. was exceedingly insolent, overbearing, and threatened him with social and professional ruin, at the same time thrusting his fist in his face; that thereupon in the height of his passion he caught a block of wood, and struck him a blow that killed him instantly. He immediately attempted his recovery by application of ammonia to his nostrils but after ten minutes became satisfied that life was totally extinct. He then thought only of concealment. It never occurred to him to go out and proclaim the fact of the quarrel and state the circumstances—only to destroy as rapidly as possible every virtue of the body. He took it to a sink and there dismembered it, at the same time burning the clothes in a furnace. The head, feet and hands as most likely to be recognized he first destroyed the trunk and a part of the limbs he attempted to conceal. The imperfection of the execution of this plan led to his detection and arrest.

His contradictory stories to his friends and counsel rendered them almost powerless before the trial came on, and a most elaborate scheme of circumstantial and direct testimony on the part of the government proved his guilt. The little pamphlet I sent you contains a tolerably fair summary of the testimony as rendered.

The substance of the testimony adduced by the government showed that Dr. Parkman was last seen entering Dr. Webster's rooms, that the body dismembered and partially destroyed was found in these rooms, that on Dr. Webster's person and in his house were articles of Dr. Parkman's property, and finally that there were known to be difficulties between him and the deceased, which had almost brought the parties at an earlier period to a personal collision. In view of all these things the jury rendered a verdict of guilty—a verdict in which the community have about acquiesced generally, but which the whole country abroad from one end to the other, thought was not sustained by the published testimony. An appeal was made to the governor for pardon or commutation, supported by petitions from all parts of the country. It was supported moreover by the most solemn asservations of Dr. Webster of his entire innocence of the crime of which (word missing) had been condemned. This petition was not granted. I should have stated that there was a suit for a new trial on the grounds of certain informalities in the prosecution of this case. This was not granted. Before the final consideration of his case by the governor and council, he sent in a confession of what I have told you. It availed nothing. He confessed the homicide although he denied the premeditation—he had by his previous protestation of his innocence and by the confession deprived his statements of all reliance whatsoever.

Such was the strong desire of the jury to bring him in not guilty that had Dr. Webster made the confession while the trial was in progress, they would have rendered the mildest verdict which the law permits a verdict that would have shut him up in the state prison at the utmost but a few years. So that he has really been hung on a falsehood. The character of Dr. Parkman was marked by eccentricities. He was distinguished for his benevolence and at the same time known to be exacting in the very last degree. The knowledge of this—fact by the technical community prepared them to believe Dr. W's statement.

A number of quite unimportant and totally irrelevant circumstances

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Historical Notes

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were made to bear against the Dr. That is, I suppose, uniformly the case where a community is as deeply excited as ours has been.

Had the Dr. been more careful to have his expenditures and his income bear a due relation to each other this infamy would never have come upon him. He has never been a man of principle or of self control. His history which has recently come to the more general knowledge of the friends of family show him to have been guilty in early life of deeds which merited all he has just received.

But let him rest. He was buried in Mt. Auburn without a funeral on the day succeeding his execution.

His family in all their temptations have done nothing to withdraw from them the respect, confidence and affection of the circle with which they have so long mingled.

I have just returned from a vacation of six weeks, a part passed among mountain shooting, fishing, camping in the woods etc., a part on Shetten Island shooting and fishing along the sea shore—and a week at the meeting of the association of which I was last year the secretary. We had an exceedingly interesting meeting. I presented a paper on the ammonia in the air—some of the results of which I will enclose to you, with the request however that no publicity be given to them till I shall have still extended them. The results are more surprising than I supposed when I wrote you and Dr. Breed. Yet I want more time. I had also four other lesser papers of which but two were presented.

The chemical section furnishes about sixty papers altogether.

Within the last few weeks Porter has been called to a chair something like my own at Brown University—an appointment in the highest degree flattering. Prof. Norton who visited Giessen during Mr. Porter's stay has also been called to the same institution.

My school never opened so well. I have I believe twenty-seven; a number quite appalling to me, especially when I consider that I have a course of about seventy lectures to deliver at the Medical College in Boston during the coming fall and winter. I had hoped to have this part filled by Mr. Porter but he has done better, and I retain it temporarily till someone shall be found who has done something in Chemistry and who will work as well as lecturer.

Mr. Soldan who was with you two years ago is now my assistant. He wishes to be remembered to you.

I have today commenced my determination of ammonia for this year—

The balance of the letter was never found. The letter included a table of Horsford's analyses of ammonia in air, rain, and snow, covering the period December 1849-July 1850. In 1856 Horsford declared these earlier results to be in error. ◇

1993 Summer Scholars' Reports

Cloning of E. coli Fructose 1,6-Bisphosphatase into an Expression Vector

by Gayle Phadungchai[†]

Boston College, Merkert Chemistry Center, Department of Chemistry

Advisor: Evan Kantrowitz

Of all the metabolic pathways, gluconeogenesis, the biosynthesis and degradation of glucose may be the most important for glucose is the primary energy source of the brain. In fact, survival depends on the ability of the body to synthesize glucose after only one day of food deprivation. Fructose 1,6-bisphosphatase (FBP) from *E. coli* catalyzes an essential reaction in the gluconeogenesis pathway and also regulates the pathway. A detailed study of fructose 1,6-bisphosphatase may provide valuable insight into the catalytic mechanism of the enzyme and the allosteric interaction of its subunits. The reaction catalyzed converts fructose 1,6-bisphosphate to fructose 6-phosphate and inorganic phosphate which is essential for the growth of *E. coli* on substances such as glycerol, succinate, and acetate[1]. In addition, the regulation of fructose-6-bisphosphatase production is a major control point in gluconeogenesis[1].

Over the past fifty years the enzyme has been studied by various biochemical and biophysical methods. FBP from *E. coli* has been sequenced and the gene has been cloned[2]. Although the X-ray structure of mammalian FBP has been determined, the X-ray structure of *E. coli* FBP has not. However, *E. coli* FBP and pig kidney FBP have 70% homology at the active site region from residues 240-290. Consequently parallels can be drawn between the two enzymes.

One powerful tool that can be used to study the relationship between structure and function of FBP is site-specific mutagenesis which substitutes specific amino acids in the enzyme[3]. Site-specific mutagenesis will be used to directly modify FBP from *E. coli* in order to investigate its catalytic and regulatory mechanisms. Before, site-directed mutagenesis can be used the *E. coli fbp* gene on the plasmid pJS54 must be moved into an expression vector such as pET3a[4]. The pET3a vector controls expression of the insert DNA by a T7 promoter inserted into the BamHI site of the multicopy pBR322 plasmid[4]. Over expression produces enough enzyme for characterization studies. Once the gene is cloned into pET3a and over expressed a procedure must be devised to purify the enzyme. Thus the objective of this research project was to clone the *fbp* gene from *E. coli* into the vector pET3a and develop a protein purification procedure for the enzyme.

[†]1993 Norris Summer Scholar

Results

A schematic diagram of the procedure for the cloning of *E. coli fbp* gene into the pET3a plasmid is shown in *Figure 1*. In order to clone the *fbp* gene in pET3a a NdeI restriction site had to be introduced at the first codon of the *fbp* gene and a second NdeI site, located in the protein coding region, had to be removed in such a fashion that the amino acid sequence of the protein was not altered. Site specific mutagenesis was used for the addition and eradication of these NdeI restriction sites.

(a) Amplifying FBP by PCR

The *fbp* gene must be single stranded for site-specific mutagenesis. Thus the first step required cloning the *fbp* gene into a vector that can replicate itself as single-stranded or double-stranded DNA. The vector used was pUC118 which carries a phage origin of replication. Before the *fbp* gene could be cloned into pUC118 enough FBP DNA needed to be accumulated. The Polymerase Chain Reaction (PCR) was used to amplify the DNA[5]. Primers complementary to the beginning and end of the gene were synthesized. The PCR procedure involved heating pJS54 to 94°C to separate the DNA strands and then cooling to 55°C to allow for the single stranded primers to anneal to the DNA template. In the presence of nucleotides the primers were extended with Taq polymerase at 72°C. This PCR cycle was repeated 30 times to produce between 1 to 5 micrograms of double stranded DNA which carried the *fbp* gene. Each PCR primer contained mismatches to the DNA target sequence so that the PCR reaction would introduce an EcoRI restriction site at the beginning of the gene and a BamHI restriction site at the end of the gene. These restriction sites are necessary to clone the *fbp* gene into the plasmid vector pUC118.

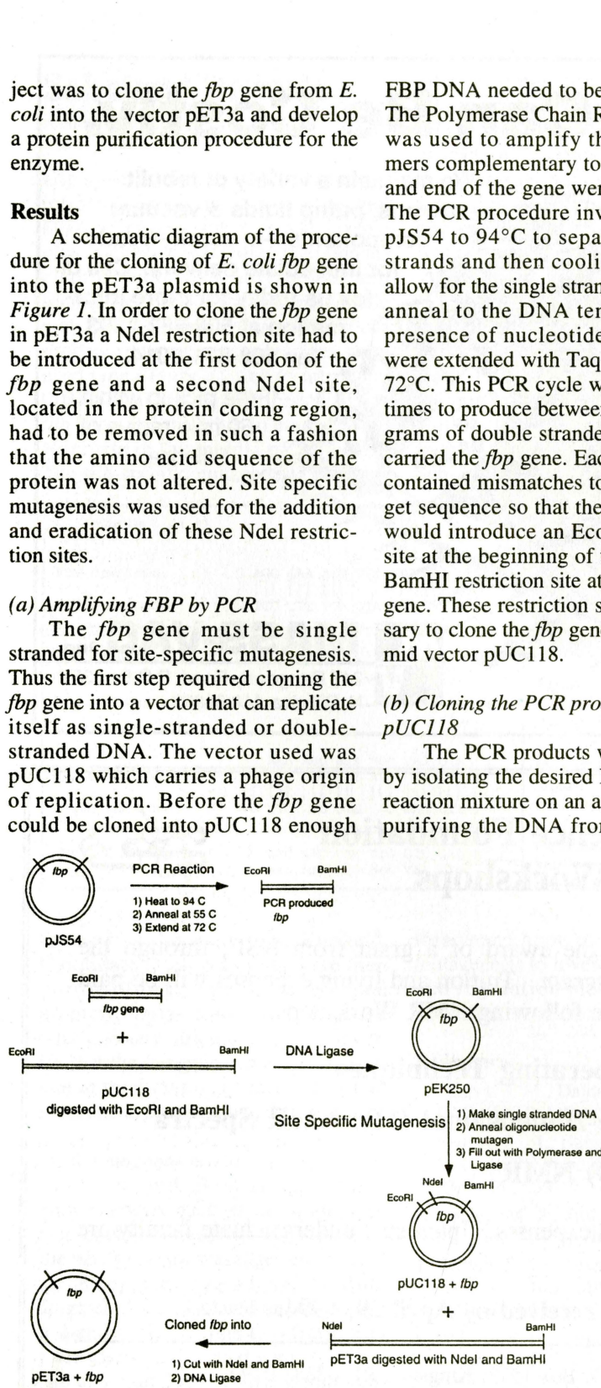

Figure 1. *Schematic of the protocols used to amplify the* ***E. coli*** *fructose 1,6-bisphosphatase gene by PCR, to clone fructose 1,6-bisphosphatase gene into pUC118, to mutate the pEK250 plasmid by site-directed mutagenesis, and to clone the fructose 1,6-bisphosphatase gene into the expression vector, pET3a.*

(b) Cloning the PCR product into pUC118

The PCR products were separated by isolating the desired DNA from the reaction mixture on an agarose gel and purifying the DNA from the agarose using Gene Clean (US Biochemicals). The PCR product and pUC118 were digested with the restriction enzymes EcoRI and BamHI (*see Figure 1*) and the digested fragments were isolated and again purified by agarose gel electrophoresis and Gene Clean. The PCR fragment and pUC118 fragment were treated with DNA ligase (*see Figure 1*). The cloned pUC118 with the PCR product (now named pEK250) was then digested with various restriction enzymes to verify that the *fbp* gene was inserted into the pUC118 plasmid (*see Figure 2*). The experimental fragment sizes were the expected sizes, thus pEK250 is pUC118 with the fbp gene inserted between the EcoRI and BamHI sites.

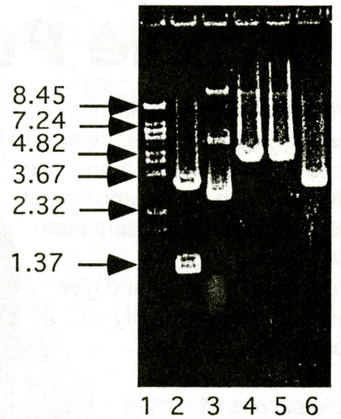

Figure 2. *Analysis of restriction fragments of the* ***fbp*** *gene cloned into the pUC118 plasmid by agarose gel electrophoresis. The following samples were run in each lane respectively: (1) molecular weight standards of λ DNA digested with BstEII, (2) the* ***fbp*** *gene cloned into pUC118 digested with EcoRI and BamHI, (3) the* ***fbp*** *gene cloned into pUC118, (4) the* ***fbp*** *gene cloned into pUC118 digested with BamHI, (5) the* ***fbp*** *gene cloned into pUC118 digested with EcoRI, and (6) pUC118 alone digested with EcoRI and BamHI. The numbers on the left hand side of the gel correspond to the number of kilobase pairs of each fragment of the λ DNA.*

(c) Site-specific Mutagenesis

The pEK250 plasmid was transformed into strain XL1-Blue MRF and M13K07, a filamentous helper bacteriophage, was used to induce production of the single-stranded DNA. The

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Scholars' Reports

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site-specific mutagenesis procedure involves using the single-stranded DNA of interest, annealing a mutagenic oligonucleotide, extending the oligonucleotide with DNA polymerase, and sealing the 5' end of the oligonucleotide with DNA ligase (*see Figure 1*). In our procedure two oligonucleotides were used (*see Figure 3*), one to introduce the NdeI site at the first codon of the *fbp* gene and the other to eradicate the NdeI site in the middle of the gene[3]. The site-specific mutagenesis was performed by the method of Kunkel[6]. Candidate DNA plasmids were then purified from colonies that grew on ampicillin plates and were digested with various restriction enzymes to verify that the *fbp* gene contained an NdeI site at the first codon and had lost an NdeI site in the middle of the gene.

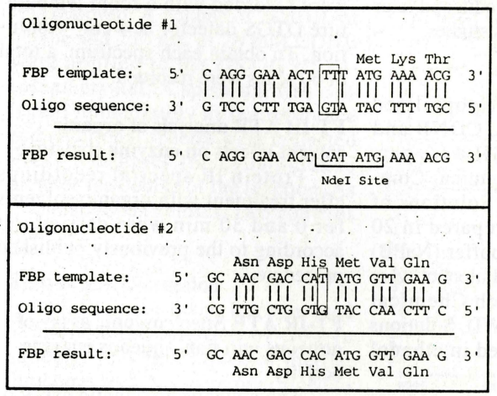

Figure 3. *Sequences of the two oligonucleotides used to introduce and remove the NdeI sites within the* ***fbp*** *gene needed for the cloning into pET3a. The sequences of the wild type* ***fbp*** *template, the oligonucleotide used for the mutagenesis, and the sequence of the resulting mutation within the* ***fbp*** *gene are shown.*

(d) Cloning into pET3a

NdeI and BamHI restriction enzymes were used to digest the purified plasmid to remove the *fbp* gene, the pET3a vector was digested with the same enzymes (*see Figure 1*). Both fragments were isolated on an agarose gel and purified. The two fragments were mixed and treated with DNA ligase and transformed into competent DF657 [tonA22, λ_r-, ompF627(T_2^R), relA1, pit-10, spoT1, Δ(fbp)287][1] cells which lack the *fbp* gene. Use of these DF657 competent cells prevents recombination between the *fbp* gene in pET3a and the chromosomal *fbp*. The candidate plasmids were purified by the alkaline lysis method and then treated with a variety of restriction enzymes to verify that the *fbp* gene was cloned into pET3a plasmid.

(e) Future Directions

The next step will be to purify the fructose 1,6-bisphosphatase from *E. coli*. This summer project on the cloning and overexpression of the *E. coli* fructose 1,6-bisphosphatase gene will be continued as part of a Senior Scholar of the College Project. During this year I hope to use site-specific mutagenesis to investigate the catalytic and regulation mechanisms of this important metabolic enzyme.

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Gayle Phadungchai

1993 Norris Summer Scholar

Dr. Evan Kantrowitz, Gayle's research supervisor comments: "Gayle Phadungchai began working in my laboratory at Boston College during her freshman year, at which time she helped with a variety of experiments and computer related projects. However, her real introduction to independent research came as a result of her work during the summer of 1993 as a Norris Summer Scholar. ...She devoted full time to a research project and this concentrated period gave her the chance to combine and apply the knowledge that she had gained from lectures to the research project. I believe that learning to combine lecture material and to perform independent laboratory work has allowed Gayle to develop during this period into a mature research scientist, something that may not have been possible without the Norris Summer Scholarship." ◇

Richard H. Holm

continued from page 5

istry, the Harrison Howe Award, the Centenary Medal of the Royal Society, the Dwyer Medal of the Australian Chemical Society, the American Chemical Society Award for Distinguished Service in the Advancement of Inorganic Chemistry, the Polyhedron Prize for Creativity in Inorganic Chemistry, the Alfred Bader Award in Bioorganic or Bioinorganic Chemistry, and the National Academy of Sciences Award in Chemical Sciences. He is a member of the American Academy of Arts and Sciences and the National Academy of Sciences. Recently he was awarded the honorary Doctor of Science from the University of Chicago. ◇

Enzymatic Activity of Glutathione-S-Transferase in Non-Aqueous Solvents

by Michelle A. Poirier†

Department of Chemistry, University of Massachusetts Dartmouth, North Dartmouth, MA 02747

Advisor: Dr. Bal Ram Singh

Introduction

Glutathione-s-transferase (GST), a two-substrate ubiquitous enzyme, is one of the liver's several detoxification enzymes. This enzyme catalyzes the reaction between γ-glutamylcysteinylglycine (glutathione, GSH) and electrophilic xenobiotics including drugs, chemicals, or carcinogens, such as polycyclic aromatic compounds.[1,2] For reasons ranging from function to diversified presence, GST remains an important macromolecule for biochemical study.

Until quite recently, it was believed that enzyme catalysis in general was possible only in aqueous media (except for those enzymes located in biological membranes). In the last few years, however, observations have been made which contradict this conventional wisdom. In particular, α-chymotrypsin and subtilisin, two proteases which are not membrane bound, were found to display activity in several organic solvents.[3] Of particular interest to this research is the fact that novel properties have been observed from non-aqueous enzyme catalysis. These properties include thermal stability, significantly different substrate specificities, and, in some cases, the ability to catalyze a totally different reaction.[3,4] In most cases non-polar solvents have been observed to be favorable for non-aqueous enzymology.

The non-aqueous enzyme catalysis of GST has been investigated in this study. Previous work has demonstrated that GSH can be non-covalently bound to the enzyme and the free glutathione separated from the enzyme/substrate complex by gel filtration.[5] This work provided a means of combining the water soluble substrate with the enzyme before the enzyme was utilized to increase the chance of non-aqueous catalysis. Fourier-transform infrared spectroscopy (FT-IR) ATR (attenuated total reflectance) technique has been used in this research to study the effect of organic solvents on the structure of GST, with octane and amyl alcohol as model hydrophobic and hydrophilic solvents on a relative scale. The catalysis of GST was also analyzed by FT-IR ATR technique using 1-chloro-2,4-dinitrobenzene (CDNB) as the model electrophilic substrate. An assay system was first established in aqueous media and later modified for non-aqueous studies.

†1993 Norris Summer Scholar

Materials and Methods

Equine liver GST (lyophilized powder, EC. 2.5.I.18), CDNB and crystalline reduced GSH were purchased from Sigma Chemical Company (St. Louis, MO). Solutions of GST and GSH were prepared in 20 mM sodium phosphate buffer (NaPB) pH 6.5. Octane and amyl alcohol were purchased from Aldrich Chemical Company (Milwaukee, WI). Solutions of CDNB were prepared in ethanol immediately prior to use.

Spectrophotometric assay of aqueous enzyme activity

Each protein solution was assayed for enzymatic activity using a Beckman DU Model 2400 Spectrophotometer. To perform this assay, 50 µL of 20 mM GSH was added to a 1 mL reaction mixture containing 50 µL of 20 mM CDNB and 10 µL of 1mg/mL GST and the absorbance at 340 nm was monitored.

FT-IR Spectroscopy-ATR Technique

FT-IR Spectra were recorded on a Nicolet Model 8210 spectrophotometer equipped with a 60° horizontal zinc selenide crystal ATR (attenuated total reflectance) accessory.[6,7] All spectra were recorded with a room temperature DTGS detector at 4 cm^{-1} resolution. To obtain each spectrum, a total of 50 scans were recorded.

FT-IR ATR analysis of organic solvent effects on enzyme structure

Protein IR spectral recordings after treatment with organic solvents for 0 and 30 min were carried out according to the previously published procedure.[7]

FT-IR ATR Spectroscopic assay of aqueous and non-aqueous enzyme activity

The aqueous enzymatic assay of the GST-catalyzed conjugation of CDNB to GSH was accomplished by adding 100 µL of 20 mM GSH and 100 µL of 20 mM CDNB to a 1800 µL solution of buffer layered on the crystal. A volume of 10 µL of 1 mg/mL GST was added to the solution and a spectrum was collected immediately as a reference. Spectra were collected every 5 minutes for 20 minutes to monitor the course of the reaction. Two controls were run in addition to the first assay. The first control, "GSH &CDNB", was a repeat of the first run, omitting the addition of the enzyme. The second control, "CDNB only", was a repeat of the first, omitting the GSH.

The non-aqueous enzymatic catalysis was completed according to the following procedure. Volumes of 100 µL of 1 mg/mL GST and 500 µL of 20 mM GSH were added to 1800 µL of buffer layered on the crystal. The solution was allowed to incubate on the crystal for 30 minutes before the bulk was removed. A volume of 1800 µL of octane and 250 mL of 20 mM CDNB were applied to the GST/GSH adsorbed crystal. A spectrum was collected immediately as the reference and additional spectra were collected every 5 minutes for 20 minutes to monitor the course of the reaction. As in the aqueous studies, two controls were run.

Results and Discussion

FT-IR Spectroscopy has been used to analyze the function of GST in aqueous and non-aqueous media. Structural analyses were performed to provide insight into possible non-aqueous enzymatic activity. FT-IR ATR technique has previously been demonstrated to be a useful method of studying protein structure because of its high sensitivity as a technique.[7] More recent work has expanded use of the technique to include the effect of organic solvents on the structure of proteins. In this study structural analysis of GST was performed in buffer, octane, and amyl alcohol. *Figure 1* represents the spectrum of the enzyme in buffer. The peak at 1650 cm^{-1} is the amide I band and Amide II band is represented by the peak at 1550 cm^{-1}. The ratio of the amide I to amide II peak height represents the enzyme in its native form. *Figure 2* depicts GST upon exposure to (**A**) octane and (**B**) amyl alcohol for 30 minutes. The results of the analysis are summarized in Table I. It can be seen from the table that the ratio of amide I to amide II decreases 15.8% upon exposure of GST to octane. In contrast, this ratio increases 26.3% upon exposure of the enzyme to amyl alcohol.

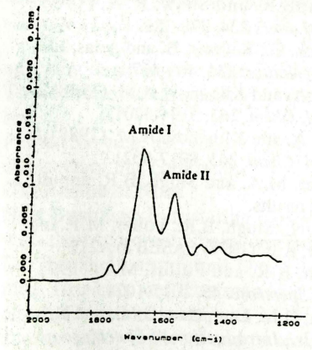

Figure 1. FT-IR spectrum of glutathione-s-transferase (GST) enzyme in buffer

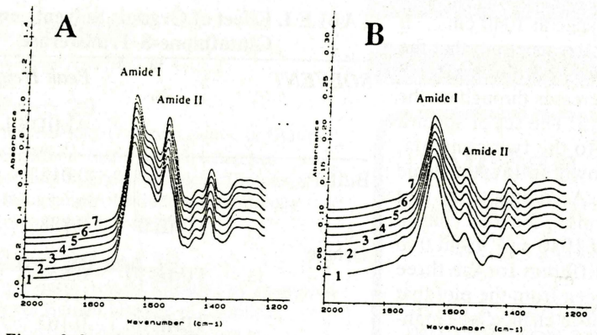

Figure 2. Spectrum of GST enzyme on exposure to (A) octane, (B) amyl alcohol

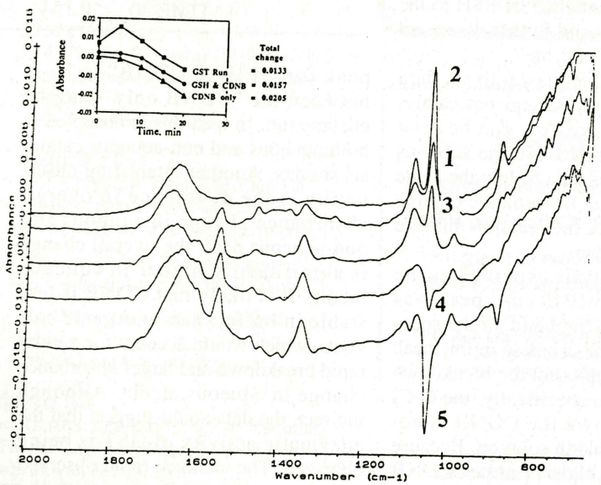

Figure 3. Spectrum of the GST-catalyzed reaction in aqueous medium

The structural analysis seems to indicate a larger change in structure from the native form for amyl alcohol exposure. According to previous studies with α-chymotrypsin, a change in structure was observed upon exposure to amyl alcohol but not octane.[6] This enzyme was also shown to retain its activity in octane and not in amyl alcohol.[3] The structural studies of GST may suggest that the enzyme retains its activity in octane.

The spectrum of the GST-catalyzed reaction in aqueous medium is depicted in *Figure 3*. The set of peaks in the region of 1040-1100 cm^{-1} is believed to represent the CDNB molecule. Chlorine, when bound to a carbon on a benzene ring, has a very

strong IR absorbance at 1040 cm^{-1}.[8] It is apparent from the spectrum that the peak at 1040 cm^{-1} increases after 5 minutes, then decreases throughout the remaining spectra. The set of spectra corresponding to the two controls, although not shown, follow the same decreasing trend. According to the plot shown in Fig. 3 inset, the total change of absorbance at 1040 cm^{-1} from 0 to 20 minutes is different for the three runs. It can be seen from the plot that the total absorbance change was highest for "CDNB only". This change decreased upon addition of GSH to the reaction contents and further decreased upon addition of enzyme.

The non-aqueous catalysis data are compared with the aqueous catalysis data in *Figure 4*. It can be seen from the two graphs that the aqueous and non-aqueous data follow the same trend: the lowest absorbance change was observed for the reaction mixture containing enzyme.

In the catalysis experiments the decrease in the 1040 cm^{-1} peak was observed in *Figure 3* and all the spectra collected. The decrease in this peak is believed to represent the breakdown of CDNB, more specifically, the C-Cl bond. It is known the CDNB is not particularly stable in solution. Because the decrease is highest in the "CDNB only" data, the breakdown seems to be occurring more rapidly without the enzyme. Perhaps the binding of substrates to the enzyme and the reaction itself is preventing the immediate breakdown in solution. Because the reaction occurs without the enzyme, although very slowly, one would expect the decrease in the 1040 cm^{-1} peak for "GSH & CDNB" to be in between the "CDNB only" and the enzyme run. In fact, this is observed in both aqueous and non-aqueous catalysis studies. Another interesting observation is the difference in overall absorbance change in aqueous and non-aqueous data: the overall change is significantly higher in aqueous media. It is likely that CDNB is less stable in buffer than in organic solvents, which would account for a more rapid breakdown and larger absorbance change in aqueous media. Although indirect, the data could suggest that the enzymatic activity of GST is being observed. The identical trend observed in octane, in combination with the structural data of GST in octane, may suggest that the enzyme retains its activity in organic solvents. In order to better understand the FT-IR spectra, it will be necessary in the future to analyze the breakdown products of CDNB closely by gas chromatography-mass spectrometry.

TABLE I. Effect of Organic Solvents on Structure of Glutathione-S-Transferase

SOLVENT		*Peak Heights*		*Ratio*	*Rel. % Change*
		AMIDE I	AMIDE II		
Buffer		0.012	0.0087	1.379	—
Octane	TIME 0	0.838	0.722	1.161	–15.8%
	TIME 30	0.834	0.717	1.163	–15.7%
Amyl Alcohol	TIME 0	0.162	0.093	1.742	+26.3%
	TIME 30	0.154	0.092	1.674	+21.4%

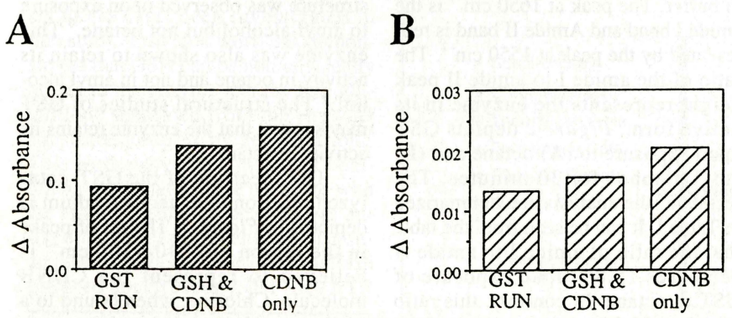

Figure 4. *Comparison of aqueous and non-aqueous catalysis data of the GST-catalyzed reaction*

Non-aqueous enzyme catalysis of GST has both biochemical and biotechnological applications. This study, in combination with others of its type, may provide a better understanding of the mechanism of non-aqueous catalysis, including the role of the solvent in catalysis. Biotechnological applications of non-aqueous GST catalysis include the degradation of environmental pollutants, most of which are only soluble in non-aqueous media.

Acknowledgements

The author would like to thank the Northeastern Section of the American Chemical Society (James Flack Norris Summer Scholarship) for providing the support to conduct this research. The author would also like to thank Dr. Bal Ram Singh for his helpful advice.

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Michelle A. Poirier

Dr. Singh writes: (condensed)

Michelle, currently at the U. of California-Berkeley, was one of the top students in chemistry at UMass Dartmouth. She entered as a liberal arts major, but enjoyed science courses and so changed her major to biology and soon realized that "to understand biology, it was important to know chemistry." So she changed her major to chemistry (biochemistry option). In 1991, she contacted me regarding doing biochemical research in my laboratory. She got interested in an enzyme that may be relevant to local problems, so we decided on glutathione-S-transferase with a goal of getting it to work in non-aqueous solvents. Then, the water insoluble PCBs could be a substrate. PCB is a major pollutant in the Acushnet River.

After summer research in 1991, funded by Pfizer Corp., she continued the research in the summer of 1993 as a Norris Scholar. Michelle showed a very strong dedication to this project. In addition to learning several research techniques, she learned how to design a relevant project applicable to local problems. She developed a very strong confidence in planning research and deriving conclusions from her results. ◇

Board of Directors

continued from page 8

applying as preceptor of the program. Those interested are invited to contact her.

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New Business: In fostering closer ties with the Medicinal Chemistry Group, Dr. Kaufman appointed Drs. Gleekman, Hopkins and Kaufman to a special committee to work with M. Singer and his fellow officers and to seek the advice and expertise of Dr. J. Neumeyer. ◇

Calendar

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March 29
Prof. Michael D. Morse (Univ. of Utah)
"Electronic Structure and Chemical Bonding in Transition Metal Diatomics"
Massachusetts Institute of Technology
Room 2-105 at 4:00 pm

March 29 and 30
The Fourth Annual Science Day sponsored by the Barnett Institute of Chemical Analysis and Materials Science at Northeastern University

March 29
Prof. Charles R. Cantor (Boston Univ.)
"Implications of the Human Genome Project"
356 Ell Center at 4:00 pm

March 30
Prof. Charles R. Cantor (Boston Univ.)
"Sequence-specific DNA Purification"
356 Ell Center, 9:00 am – 12:15 pm

The Science Day Poster Session
Ell Center Ballroom, 1:00–3:00 pm

The DeVivo Lecture in Materials Science
356 Ell Center at 4:00 pm

March 30
Dr. Kenneth G. Mann (Univ. of Vermont)
"The Assembly of Blood-Clotting Enzymes on Membranes"
UMass Dartmouth, Rm. 305, Science & Engineering Bldg (Group II) at 4:00 pm

March 31
Prof. Jack W. Szostack (Harvard Medical School)
"Isolation of New Ribozymes from Large Pools of Random RNA Sequences"
Boston College, Rm. 127,
Merkert Chemistry Center at 4:00 pm

Notices for the Nucleus Calendar should be sent to:
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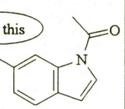

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March 1

Prof. Dennis Jacobs (Univ. of Notre Dame)
"State-to-State Reaction Dynamics in Molecular Ion/Surface Scattering"
Massachusetts Institute of Technology
Room 2-105 at 4:00 pm

March 2

Prof. Steve Adelman (Purdue University)
"Energy Transfer and Reaction Processes Occurring in Liquid Solution"
Harvard University, 12 Oxford Street
Mb-23 at 4:00 pm

March 3

Prof. Gerald S. Manning (Rutgers Univ.)
"An Attractive Force Between Like-Charged Particles"
Boston College, Rm. 127,
Merkert Chemistry Center at 4:00 pm

March 7

Prof. W. Clark Still (Columbia Univ.)
"Combinatorial Approaches to Problems in Molecular Recognition"
Harvard University, 12 Oxford Street
Mb-23 at 4:00 pm

Dr. David Kaplan (U.S. Army Natick Research Center)
"Biosynthesis and Processing of Silk Proteins"
Tufts University, Room 136, STC,
4 Colby St., Medford at 2:30 pm

March 9

Prof. Erkang Wang (Chinese Academy of Sciences)
"Recent Developments in Electroanalytical Chemistry"
Northeastern University
Rm. 129, Hurtig Hall at 4:00 pm

Dr. Gordon T. Wallace (UMass, Boston)
"Metals in Boston Harbor, Massachusetts Bay and Gulf of Maine: Sources, Transport and Fate"
UMass Dartmouth, Rm. 305, Science & Engineering Bldg (Group II) at 4:00 pm

March 10

Prof. A. Busu (Univ. of Connecticut at Storrs)
"Understanding the Relationship Between Chemicals and Cancer"
Northeastern University
Rm. 129, Hurtig Hall at 4:00 pm

Prof. Michael Fayer (Stanford University)
"Vibrational Dynamics in Liquids and Glasses: ps IR Photon Echoes and Other ps Techniques"
Harvard University, 12 Oxford Street
Mb-23 at 5:00 pm

March 14

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"From Bridged Annulenes to Fe(IV)-Metalloporphyrinoids"
Harvard University, 12 Oxford Street
Mb-23 at 4:15 pm

March 15

Prof. David Zax (Cornell University)
"Probing Structures (Electronics and Otherwise) in a One Dimensional Conductor — the Metal Molybdenum Selenides"
Massachusetts Institute of Technology
Room 2-105 at 4:00 pm

March 16

Dr. James Wang (Harvard University)
TBA
Brandeis University
Gerstenzang 122 at 4:00 pm

March 17

Prof. P. Davidovitz (Boston College)
"How Do Gas Molecules Enter Liquids and What do They do There?
Northeastern University
Rm. 129, Hurtig Hall at 4:00 pm

Prof. Sidney M. Hecht (Univ. of Virginia)
"RNA Cleavage by Activated Fe-Bleomycin"
Boston College, Rm. 127,
Merkert Chemistry Center at 4:00 pm

March 21

Prof. JoAnne Stubbe (MIT)
TBA
Harvard University, 12 Oxford Street
Mb-23 at 5:00 pm

March 23

Dr. Iwao Ohmine (Institute for Molecular Science, Japan)
"Liquid Water Dynamics: Fluctuation, Relaxation and Chemical Reactions"
Harvard University, 12 Oxford Street
Mb-23 at 5:00 pm

Dr. John T. Welch (SUNY – Albany)
"Stereocontrol, the Carbon-Fluorine Bond and Biologically-Active Compounds"
UMass Dartmouth, Rm. 305, Science & Engineering Bldg (Group II) at 4:00 pm

March 24

Prof. Robert I. Cukier (Michigan State U.)
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Merkert Chemistry Center at 4:00 pm

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Prof. Robert Squires (Purdue University)
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Harvard University, 12 Oxford Street
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