

ChemLetter

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Dear Alumni and Friends,

We are pleased to provide to you another issue of the *ChemLetter*. As usual, the stories herein describe a tiny fraction of the goings on. Indeed, this issue carries several sad stories that must be reported—the losses of two former chairs (Professors Emeritus Ed Lingafelter and Norman Gregory) and the spouses of two former chairs (Roberta Lingafelter and Irene Cady). We elected not to provide in this issue a next installment in the saga of how the State of Washington is funding higher education. That too would have been a sorry tale.

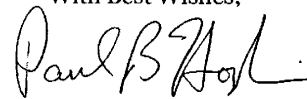
Instead, let me use this brief message to relate some of the more uplifting tales of the recent past. At this year's commencement, the Chemistry faculty gathered to honor nearly two hundred undergraduates who during the past year have earned a bachelor degree in chemistry or biochemistry. This is surely an all-time record for this Department, the combined result of the baby boom echo wending its way through higher education and the popularity of our biochemistry degree option—they outnumber the chemists nearly two to one! Our graduate program, too, is the largest in its history (with 225 graduate students studying with us). It is funded by federal grants and contracts that in magnitude top the list for the College of Arts and

Sciences (apologies to Biology, Physics, and Psychology, the other power-house units in our College). The success of Chemistry faculty at winning these grants and contracts sets yet another new record for the Department.

So our programs are big, but are they any good? They are great! Our undergraduate and graduate students are winning national awards for their work. They are securing the next educational or employment opportunity that they seek. One heads to Stanford for graduate work in Chemistry, another to Mt. Sinai Medical School for the M.D.-Ph.D. program, another joins the faculty of the University of Southern California, and yet another will begin a career at Dupont Central Research. UW Chemistry is for these students the stepping-stone to their own success and to giving back to society through their future contributions.

I hope this letter finds you and your loved ones in good health and working toward accomplishing your own dreams.

With Best Wishes,



Paul B. Hopkins
Professor and Chair

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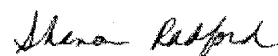
New Faculty Profiles

Keck Young Scholar Award

EDITOR'S NOTE

The *ChemLetter* has a new look again, or rather, we've updated an older look. Modern technology has advanced to the point that printing the *ChemLetter* in-house is considerably more cost-effective than sending it out to a traditional print house, but it hasn't advanced enough to allow us to do all of the fancy things a print house can do. You'll notice that lines and shading do not "bleed" off the page, and there is no longer a self-mailing insert. Eliminating the insert was a particularly difficult decision, as many of you use it to keep in touch and, of course, to make donations. However, the savings (an estimated 75%!) and convenience of having complete control over the number of copies run, in our minds, outweighed the potential disadvantage of a mailer-free *ChemLetter*. We hope you will appreciate our fiscal responsibility and continue to keep in touch with us!

Sincerely,



Shanon Radford

Ironing Out the Details

The role of cysteine residues in promoting the function of non-heme iron enzymes.

Professor Julia A. Kovacs

Non-heme iron enzymes promote a number of important biological reactions, including serotonin, leukotriene, and DNA synthesis. Most of these enzymes contain iron ligated by oxygen and/or nitrogen ligands, and their main function is to create highly reactive iron-peroxo ($\text{Fe}^{\text{III}}\text{-OOH}$ $\text{Fe}^{\text{III}}\text{-O}_2^-$), or iron-oxo ($\text{Fe}^{\text{IV}}\text{=O}$ or $\text{Fe}^{\text{V}}\text{=O}$) oxidation catalysts. In the mid-1980s, a new class of non-heme iron enzymes containing cysteine sulfur(s) coordinated to the iron was discovered. These include nitrile hydratase (NHase), superoxide reductase (SOR), and peptide deformylase (PDF).

An obvious question concerns the role that the cysteine sulfur ligand(s) play in promoting the function and determining the properties of these enzymes. Cysteine sulfur ligands form highly covalent bonds to transition metals and facilitate electron transport in biology. Research in the Kovacs group has shown that cysteine sulfur ligands also help to (1) make iron redox inactive, thereby avoiding unwanted side reactions that could damage DNA and/or protein backbones; (2) stabilize low-spin iron, even in a non-heme environment (it was previously thought that porphyrins were the only biological ligands capable of stabilizing low spin iron); and (3) make an otherwise inert metal ion, such as low-spin Fe^{III} (or Co^{III}), reactive with respect to product release.

The molecular-level details regarding metalloprotein function are typically revealed using several complementary lines of study at the interface of chemistry, biology, and physics. Protein structure and function can be probed using high resolution (synchrotron) X-ray crystallography and site-directed mutagenesis. Application of biophysical techniques (such as EXAFS, RR, MCD, EPR, ENDOR, and Mossbauer), which specifically probe the metal ion and its surroundings, reveal details about electronic and geometric structure of the active site (the metal ion and its surroundings).

Systematic alteration of the active site structure allows one to correlate structure with properties and function. This is readily accomplished with synthetic models. Small molecular analogues reproducing key spectroscopic features help to fine-tune details regarding active site structure and mechanism by providing, for example, parameters needed to interpret biophysical data. Details regarding key bond lengths (for example, the O-O distance of an activated O_2 intermediate), the presence or absence of protons, or the identity of intermediates, can be "fuzzy" or lacking due to limitations imposed by either the biological system or physical technique. Quite often these details can be revealed via synthetic models, as has been demonstrated by Kovacs' research involving analogues of nitrile hydratases (NHases) and superoxide reductases (SORs).

The function of cysteine-ligated non-heme iron enzymes varies enormously from nitrile hydration by NHases, to peptide hydrolysis by peptide deformylase, to superoxide reduction by SORs. NHases are metalloenzymes that convert nitriles to less toxic amides cleanly and rapidly under mild conditions. SORs remove potentially toxic superoxide from anaerobic organisms without forming O_2 as a side-product.

Oxidations mediated by superoxide are implicated in a number of important neurological and degenerative diseases, such as Parkinson's and Alzheimer's, and cell death and tissue damage that occurs following a stroke. Some types of cancer are thought to arise

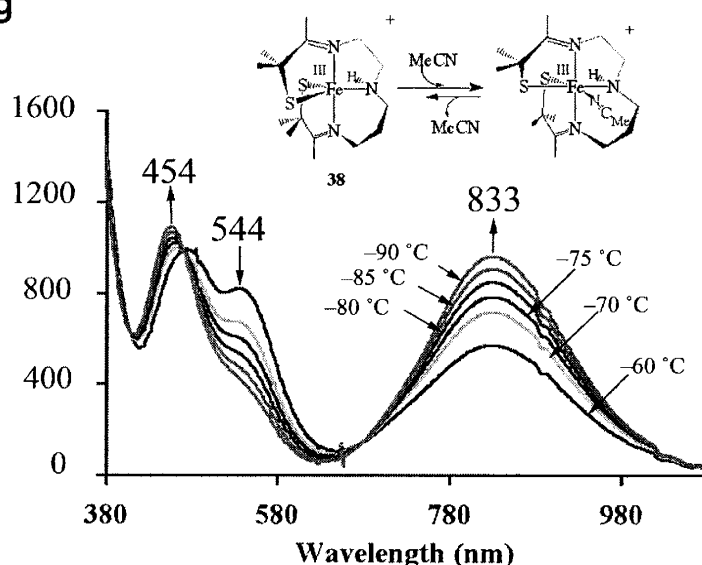


Fig 1. An electronic absorption spectrum showing one of Kovacs' nitrile-binding NHase models.

from oncogene mutations caused by superoxide-induced oxidative damage to DNA. The mechanism by which SORs are proposed to reduce superoxide involves superoxide binding to the reduced Fe^{II} state followed by the transfer of an electron from the metal ion to the bound substrate, via an inner sphere pathway, to afford an Fe^{III} -peroxide intermediate.

Much progress has been made by the Kovacs group in the biomimetic modeling of cysteine-ligated non-heme iron active sites in biology and developing our understanding of the roles played by cysteine sulfur ligands in promoting biological metalloenzyme function. Kovacs has shown that as long as two *cis* thiolates are incorporated into the coordination sphere, the spectroscopic and magnetic properties of the resulting model complexes closely resemble those of NHase. The electronic spectral properties of Kovacs' synthetic analogues are remarkably similar to that of the NHase enzyme and display an intense low-energy band determined to be $\pi\text{S-to-Fe}$ charge transfer in character. From the intensity of this band it is clear that the Fe-S bonds of NHase and these models are fairly covalent. The Fe-S bonds are extremely short (2.21 Å), reflecting the low spin-state and a high degree of covalency. The delocalization of electrons within these covalent Fe-S bonds reduces the energy required to pair electrons (the nephelauxetic effect).

In order for synthetic models and metalloenzyme sites to display reactivity, there must be an open or labile coordination site. With M^{III} ($\text{M} = \text{Fe}, \text{Co}$) six-coordinate, octahedral structures are highly favored and tend to be less reactive than, for example, five-coordinate structures, especially if the M^{III} ion is low-spin. Five-coordinate structures are difficult to isolate, however, in the absence of a protective protein pocket or ligand constraints. A coordinatively unsaturated five-coordinate Fe-NHase intermediate is observed, by Mossbauer and EPR, upon flash photolysis of NO from the NO-inactivated form at low-temperatures. In 1998, Kovacs' group synthesized a five-coordinate synthetic analogue of this NHase intermediate, that displays Mossbauer and EPR parameters that compare well with those of the NHase intermediate. Nitric oxide (NO) and azide (an NHase inhibitor) binds to Kovacs' synthetic analogue, *trans* to a thiolate sulfur, to afford models for the NO-inactivated and azide-inhibited forms of NHase. Both the azide-bound and NO-

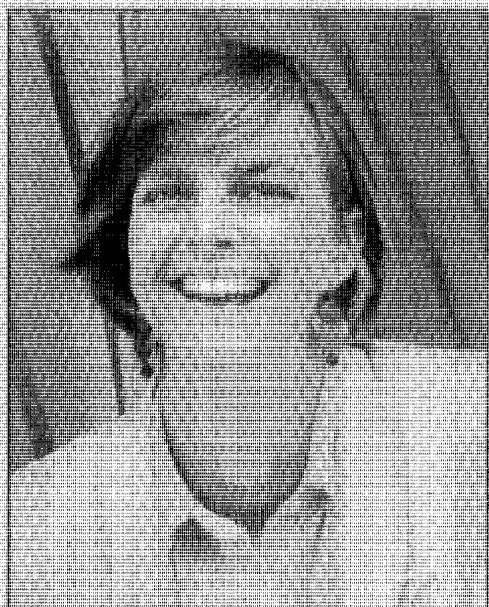


Photo: Mary Levin, University Photography

Julia A. Kovacs joined the Department of Chemistry faculty in 1988, moving through the professorial ranks to become, in 1994, the first woman in Department history to achieve the rank of full professor.

Professor Kovacs' fascination with iron enzymes began during graduate school at Harvard, where she worked with Richard H. Holm modeling nitrogenase, an iron-sulfur cluster enzyme that, under ambient conditions, creates natural fertilizer by reducing atmospheric nitrogen to ammonia.

Post-doctoral work with Robert G. Bergman at Berkeley focused on carbon-sulfur bond cleavage within hetero-bimetallic systems and allowed Dr. Kovacs to augment her experience in mechanistic chemistry and reactivity. She then turned her attention to the role of cysteine in bioinorganic chemistry, which she continues to study today.

In the past decade, Professor Kovacs has established herself as one of the foremost experts on cysteine ligated non-heme iron enzymes (see article for an in-depth look at Professor Kovacs' research). She has had steady support from the National Institute of Health, has recently written invited reviews and perspectives for *Science*, *Chemical Reviews*, and the *Proceedings of the National Academy of Sciences*, among others, and she has accepted an invitation to be first speaker of the 2003-04 MIT-Harvard inorganic lecture series.

bound synthetic analogues reproduce key magnetic and spectroscopic features of NHase, as well as average metal-sulfur bond lengths. The NHase substrates (nitriles) also bind to Kovacs' models if ligand constraints causing the reactive site to open up are incorporated into the ligand design (Fig 2). Competitive binding experiments show that when in an environment resembling that of NHase, iron has a higher affinity for nitriles vs. water or alcohols. This has important implications regarding the NHase mechanism of catalysis.

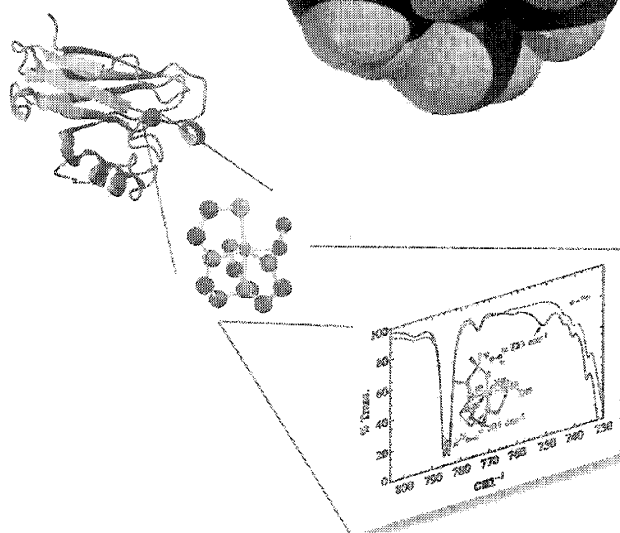
The spectroscopic characterization and isolation of Fe^{III} -peroxo complexes is extremely difficult owing to their high reactivity and photolability. Only recently have biomimetic analogues of reactive metal-peroxide or -superoxide species been generated and characterized at low temperatures. Kovacs recently showed that when a thiolate ligand is incorporated into a multidentate ligand, biomimetic SOR reactivity is observed. At low temperatures ($\leq 90^\circ\text{C}$), a transient peroxide intermediate is detected by electronic absorption, EPR, IR, and XAS spectroscopies. Addition of D_2O causes the ferri doublet in the vibrational (IR) spectrum to collapse to a single $\nu_{\text{O-O}}$ stretch at 784 cm^{-1} , indicating that the peroxide intermediate is protonated. Peroxide is released from this intermediate at a rate of $65(1)\text{ sec}^{-1}$ (at 298 K)—a rate comparable to that of the SOR enzyme. Together these data imply that, like the enzyme, oxidation of Kovacs' synthetic analogue proceeds via an inner-sphere electron transfer pathway to afford an end-on $\text{Fe}^{\text{III}}(\eta^1\text{-OOH})$ intermediate.

The non-heme iron active site of SOR resembles the heme iron site of cytochrome P450. Both contain a cysteine ligand *trans* to an open coordination site, with the four equatorial histidines of SOR resembling a broken-up porphyrin ring. The P450 analogy goes even further in that both SOR and cytochrome P450 have been proposed to form end-on hydroperoxide ($\text{Fe}^{\text{III}}\text{-OOH}$) intermediates during their catalytic cycle. The major difference is that the O-O bond is cleaved with P450, whereas the Fe-O bond is cleaved with SOR.

It has been proposed that the *trans* cysteine sulfur plays an important role in promoting O-O bond cleavage. How this O-O bond cleaving chemistry is avoided with SOR remains to be determined. It is likely that the spin-state of the intermediate peroxide plays an important role in determining whether the Fe-O or O-O bond cleaves.

If we wish to fully understand how the electronic structure of

Fig 2. (right) Ligand constraints incorporated into the design of one of Kovacs' molecules. Fig. 3. (below). To fully understand metalloenzyme function, several complementary methodologies at the interface of chemistry, biology, and biophysics are required. This integral connection is illustrated here in a synthetic model for the active site (i.e., the metal ion and its coordinated ligands) of the metalloenzyme superoxide reductase (SOR) and its molecular-level characterization using vibrational spectroscopy.



SOR contributes to its function, then a systematic study that correlates Fe-O (vs. O-O) bond cleaving properties in iron thiolate/peroxide complexes with spin-state and the positioning of the thiolate sulfur (*cis* vs. *trans* relative to the peroxide) is needed.

These are just a few of the ongoing questions the Kovacs group continues to explore.

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Donations fund vital Departmental activities, such as fellowships, scholarships, recruiting, and research symposia.

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Eric C. Brown, *Computational studies on the effects of heteroatom substitution in delocalized π systems*; Prof. Weston Borden; Autumn 2002

Jasmine Rae Bryant, *Mechanistic studies of the oxidations of hydrocarbons by manganese and Ruthenium transition metal complexes*; Prof. James Mayer; Autumn 2002

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Rebecca Lee Hoenigman, *Theoretical and experimental investigations of diradicals, pyramidalized alkenes, and bent alkynes*; Prof. Weston Borden; Autumn 2002

Irene Yuk Man Kung, *Part I: Cobalt thiolate complexes modeling the active site of cobalt nitrile hydratase. Part II: Formation of inorganic nanoparticles on protein scaffolding in Escherichia coli glutamine synthetase*; Prof. William Atkins; Summer 2002

Craig Michael Schulz, *Microsequential injection systems for the real-time monitoring of glucose metabolism of live cells by enzymatic assay*; Prof. Jaromir Ruzicka; Autumn 2002

Jennifer Sue Shumaker-Parry, *Quantitative aspects of SPR spectroscopy and SPR microscopy: Applications in protein binding to immobilized vesicles and dsDNA arrays*; Prof. Charles Campbell; Autumn 2002

John William Tomaszewski, *Structure and dynamics of small proteins by NMR*; Prof. Niels Andersen; Summer 2002

Jennifer Wightman Tonkin, *Metal partitioning in the aqueous environment: Field, laboratory and modeling studies*; Profs. James Murray and Laurie Balistreri; Summer 2002

Renee Melissa Van Ginhoven, *Self-trapped exciton, defects, and water impurities in silica*; Prof. Hannes Jonsson; Summer 2002

MASTER OF SCIENCE

Andri Arnaldsson, Winter 2003

Chung-Jen James Chou, Summer 2002

Marci M. Deleon, Autumn 2002

Katherine J. Ellison, Autumn 2002

Kimberly A. Firestone, Summer 2002

Emily Marijke Gussenhoven, Winter 2003
Thesis: Hydrocarbon oxidation and self-exchange studies using iron coordination complexes.

Janiece Louise Hope, Winter 2003

Darcy A. Kennedy, Summer 2002

Kristopher Alan Kilian, Winter 2003

Jennifer Mei-An Popham, Autumn 2002

James Patrick Shelby, Winter 2003

Wayne Yoshikazu Shinoki, Autumn 2002
Thesis: Gadolinium porphyrin and referenced pressure sensitive paint.

Derek J. Thirstrup, Autumn 2002

Guangtao Zhang, Autumn 2002

UNDERGRADUATE HONORS

Sophomore Medalist: David E. Moilanen

Phi Beta Kappa National Honor Society:

Peter B. Allen	Benjamin A. Paulson
Nena C. Bonn	Heidi A. Perry
Melanie C. Francisco	Thong D. Pham
Thinh D. Ho	Sean M. Snyder
Devon Livingston-Rosanoff	James A. Troy

Baccalaureate Honors:

The top 10% of each UW college's or school's graduating class is awarded a series of distinctions based upon cumulative grade point averages.

<i>Summa Cum Laude</i> , 3.95+	<i>Cum Laude</i> , 3.75-3.85
Noel S. Fitzgerald	Peter B. Allen
David E. Moilanen	Angela A. Asemota
Sean M. Snyder	Serine Avagyan
	Nena C. Bonn
<i>Magna Cum Laude</i> , 3.86-3.94	Damien N. Dombrowski
Kevin M. Moore	Dylan J. Hargreaves
Paul A. Temkin	Benjamin A. Paulson
	Lee E. Peterson
	Gretchen J. Smith
	Cristina L. Swanson

Jim Billigmeier (MS, 1967) retired in May, 2000. He has been traveling to Alaska and the Caribbean, volunteering, and playing golf. **Marian Boehr** (B.S., 1946) served as an American Baptist missionary doctor in India for 38 years. Since her retirement in 1992, Dr. Boehr has been a popular mission speaker nationwide. Her new book, *Medicine and Miracles Amid the Multitudes*, is available through International Ministries at 1-800-222-3872 x2196. Dr. Boehr has received many prizes and honors for her humanitarian work. **Walter G. Boyle** (Ph.D., 1956) is enjoying his retirement traveling and hiking. Dr. Boyle retired from the Lawrence Livermore Laboratory. **John R. Cort** (Ph.D., 1997) is a senior research scientist at Pacific Northwest National Laboratory (U.S. Department of Energy.) **Anthony Esposito** (Ph.D., 1991) is a postdoctoral fellow in Chemistry and Materials Science at Lawrence Livermore National Laboratory doing single-molecule spectroscopy for biological applications. **Kevin E. Johnson** (Ph.D., 1991), Associate Professor of Chemistry at Pacific University in Oregon, spent the 01-02 school year collaborating with Jeanne Pemberton at the University of Arizona, Tucson, on an NSF-funded project to develop and implement emission infrared spectroscopy for interfacial studies of electrolytes at electrode surfaces under potential control. During the collaboration, two IR cells were constructed—one for the Pemberton group, and one for research with undergraduates at Pacific University. **Frank E. Karasz** (Ph.D., 1958), the Silvio O. Conte Distinguished Professor of Polymer Science & Engineering at the University of Massachusetts, Amherst, received the Herman F. Mark Medal for 2002 from the Austrian Research Institute for Chemistry for his research in polymer physics and Chemistry. **Colin Kennard** (Post-Doc, 1963-64) worked in Ed Lingafelter's crystallography group from 1963-64, after which he returned to Australia as a lecturer at the University of Queensland in Brisbane. During his career, he produced over 500 internationally accepted scientific papers. Since his retirement in 1999, he has remained active by working as an explainer at the Queensland Science Centre, (similar to the Pacific Science Center in Seattle), producing teaching material for distance education on difficult chemical subjects, and helping the local primary school, Ironside State School, with its Centre of Excellence in Science. **Lanny Replogle**

Send in your updates!

If you or someone you know was a student or post-doctoral fellow in the UW Department of Chemistry, we want to hear from you. Send the name, year(s) attended, and a brief description of current activities to:

ChemLetter Editor
University of Washington
Department of Chemistry
Box 351700
Seattle, WA 98195-1700

Have interesting news to share or want to hear about particular goings-on in the Department? Send inquiries or suggestions to the address above.

(Ph.D., 1960) retired from teaching at San Jose State University in 1992, the same year his son Eric received a Ph.D. in Chemistry from Carnegie-Mellon University. He is the owner of and winemaker at Fenestra Winery in Livermore, CA, which he started in 1976. **Richard R. Roesler** (Ph.D., 1969) applications chemist at the Bayer Corporation, was appointed adjunct professor in the department of polymers and coatings at North Dakota State University. The appointment was made in recognition of Dr. Roesler's contributions to the department's curriculum and seminars. **John M. Rusin** (Ph.D., 1973) received his Ph.D. from the College of Engineering, but still remembers his P-chem classes with Eggers, Rabinovitch, and Halsey and enjoys receiving the *ChemLetter*. He now directs a \$1.05 million NSF grant to train high school teachers in how to incorporate materials science into their classes. **W. Alan Sweeney** (Ph.D., 1954) has written a book for the general public entitled, *Happy and Healthy in a Chemical World*. The book is intended to increase awareness and

understanding of the roles of chemicals in our lives. Dr. Sweeney is the author of numerous publications, and he holds dozens of patents, many relating to infrared and ultraviolet spectroscopy, BTX processing, and biodegradability of detergents. *Happy and Healthy in a Chemical World* is available in bookstores and online at www.1stbooks.com and www.amazon.com. **Isiah M. Warner** (Ph.D., 1977) was named one of the first Howard Hughes Medical Institute (HHMI) Professors. Dr. Warner is one of only 20 researchers nationwide to receive one of the million dollar, four-year grants. HHMI created these professorships to encourage scientists to "bring the creativity they have shown in the lab into the undergraduate classroom." Dr. Warner is also Boyd Professor and Philip W. West Professor at Louisiana State University. **Ron Yates** (Ph.D., 1977) is a senior program manager in the External Technology Department at The Dow Chemical Company. Dr. Yates is responsible for university cooperative research projects and U.S. Federal Government contract research and development.

Obituaries:

Agnes Irene Hoving-Cady, wife of the late Professor Emeritus George H. Cady, died on March 15, 2003. She was an artist and art teacher, and she remained involved in Department functions long after her husband's death.

Lillian V. Gregory (Wife of the late Professor Emeritus Norman W. Gregory) died June 25, 2003 from natural causes.

Norman W. Gregory (BS/BA 1940, Professor of Chemistry 1946-89, Professor Emeritus 1989-2003) died May 25, 2003 from cancer-related complications. A story about Professor and Mrs. Gregory will appear in the next issue of the *ChemLetter*.

James Law (Ph.D., 2001) died May 29, 2003 at his home in Mountain View, CA after an acute illness.

Edward Lingafelter (Post-Doc, 1939-41, Instructor 1941-45, Professor of Chemistry 1945-84, Professor Emeritus 1984-2003) died April 7, 2003 (see p. 8 for story).

Roberta Lingafelter, wife of the late Professor Emeritus Edward Lingafelter, died April 6, 2003 (see p. 8 for story).

James A. Young (Ph.D., 1967) died from Parkinson's disease on January 5, 2001.

Chemistry Staffer Recognized for Outstanding Contributions

Vince Stricherz

Republished courtesy of *University Week*

As James Gladden concluded his undergraduate career at the University of Washington, little did he realize he was about to encounter a big “detour” sign. He received his psychology degree in 1972, then three

“...if you want to
accomplish something
very complicated you
can't do it by yourself.”

years later went to work for his alma mater full time—as an engineering technician in the Chemistry Department.

Now, nearly 28 years after being hired, he is the technical services manager in chemistry, a key player in the department's administrative team, and the 2003 recipient of the UW Distinguished Staff Award.

“It's just one of those journeys,” he said. “I had a childhood interest in science and technology and electronics. I was an electronics hobbyist as a kid, but that's when electronics were a lot simpler, in the pre-personal computer days.”

Gladden worked electronics jobs, including a stint with the Physics Department research group of Nobel Prize winner, Hans Dehmelt, to help pay his way through college.

“By the time I graduated, it was the path of least resistance, and it was something I was interested in doing,” he said.

After graduation, he worked in various electronics jobs around Seattle until he got a call inviting him to go to work for a chemistry research group. The job was temporary at first, but his value became apparent as he worked on a grant proposal for a large mini-computer, the department's first large computer. When that proposal succeeded, he took over as computer manager.

In the mid-1990s he worked on another grant, this one for a powerful spectrometer. The magnet alone cost in the neighborhood of \$2 million, but Gladden could have put his own brand on the electronic controls. To meet the department's needs, he devised a console so advanced that a leading vendor

of such equipment studied and replicated parts of his design. His work in that instance saved the department about \$1 million, said Paul Hopkins, chemistry chairman.

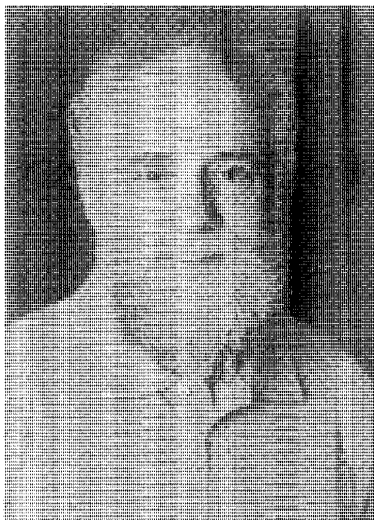


Photo: Kathy Sauber, UW Photography

“In his current role as a member of my staff leadership team, Jim now meets weekly with the small group of faculty and staff that oversee the department. The issues we face range from personnel to technical,” Hopkins wrote in a letter supporting Gladden's nomination for the staff award.

“When Jim speaks, I listen very carefully. He is intensely analytical, he is creative, and he is humane.”

Gladden grew up in Pasco, came to Seattle to attend the UW, and then stayed. His coursework included more math than he needed for his bachelor of science degree, he said, and he also took courses in physics and computer programming. But now he finds himself in management, supervising more than a half-dozen people.

He says his psychology degree has probably come in handier as a parent than as a manager.

“I never thought of myself as a manager. I'm not a natural manager, but I'm a detail person and that's what matters in management, to keep track of details,” he said.

“It's not my first love. I prefer the engineering more, but there's always a natural tension there, because if you want to accomplish something very complicated you can't do it by yourself.”

Grad Club Corner

Jason Benedict

With the relocation of president and co-founder, Shaun Dunnick, to South Carolina, I was elected to lead the Chemistry Graduate Student Club through another prosperous year. The success of the club is evidenced by the large turnouts of graduate students, as well as faculty and staff, at the organized social gatherings. Attendance of the quarterly parties exceeded 200 members of the department, along with their families and friends.

In December, the club sponsored an evening of bowling at the HUB, which managed to bring smiles to the faces of grads who would otherwise have been working diligently in lab (it's good to get out every now and then). While these social gatherings have been, and undoubtedly will continue to be, a tremendous success, the other various committees of the grad club have been just as successful.

The Catalyst Committee, which advocates for under-represented chemists in society, held monthly meetings and continues to bring speakers, both industrial and academic, to discuss their workplace experiences. This winter, the colloquia featured a talk by Dr. Debra Rolison, followed by discussion with a panel consisting of UW deans, NSF members, and representatives from various other funding agencies. The Catalysts enjoyed a tremendous turnout, as the event was additionally co-sponsored by ADVANCE and AWIS (Association of Women in Science).

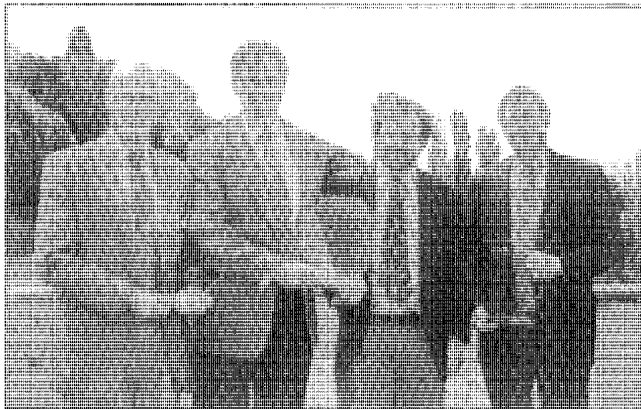
The latest addition to the CGSC structure is the Chemistry Graduate Recruitment Committee. This four-member committee was established to provide cooperative collaboration with the faculty committee responsible for organizing recruiting activities. Together they ensured, and will continue to ensure, that prospective graduate students perceive the department and the university as a top-tier research facility that remains loyal to the interests of the graduate students that serve it.

All in all, this past year proved to be yet another successful one for the Chemistry Graduate Student Club and the department in general. We are glad to have had the opportunity to help keep our department strong, productive, and in high spirits, and we hope we may continue to do so for many years to come.

MMV Project of the Year 2002

Protein farnesyltransferase inhibitors (Pf-PFT): from novel concept to potent new leads

The MMV Project of the Year 2002 Award was presented to key Pf-PFT project team members Wesley Van Voorhis and Michael Gelb of the University of Washington (Seattle), Andrew Hamilton of Yale University, and David M. Floyd of Bristol-Myers Squibb (BMS) during MMV's 3rd Annual Stakeholders' Meeting on 18 May 2003.



Team members (left) with their awards on the World Economic Forum's terrace overlooking Lake Geneva. From left to right: Andrew Hamilton, Professor and Chair of Chemistry, Yale University; Wesley Van Voorhis, Professor of Medicine, and Michael Gelb, Departments of Chemistry and Biochemistry, University of Washington (Seattle); David M. Floyd, Vice-President, Bristol-Myers Squibb (BMS),

Since its introduction into the Medicines for Malaria Venture (MMV) portfolio in 2001, the protein farnesyltransferase inhibitors (Pf-PFT) project has moved from strength to strength, earning it MMV's Project of the Year 2002 Award. In its first year, the project advanced from "lead discovery" to "lead optimization," a process which normally takes two years. Experts consider the Pf-PFT protein to be a novel target for the development of new antimalarial drugs. Having scanned more than 300 compounds known to inhibit PFT, the project team now has compounds that show great promise for drug therapy for malaria (*On-line news, University of Washington School of Medicine, Vol. 7, Number 20, May 23, 2003*).

Wes Van Voorhis and Mike Gelb of the University of Washington (Seattle) summed up reasons for the project's rapid progress in its first year:

- The availability of the *P. falciparum* genome as a facilitator of drug research and development;
- "Piggy-backing" on the human-PFT inhibitors that Bristol-Myers Squibb (BMS) is developing for cancer chemotherapy;
- Strong collaboration between private sector and academia;
- Expert advice from MMV staff and Expert Scientific Advisory Committee (ESAC); and
- MMV funding.

In his presentation to stakeholders, Mike Gelb gave MMV kudos for its ability to not only foster projects but to terminate them when a dead end is reached, something which happens rarely in the academic world. He cited MMV's ESAC as a key force in getting the academic members of teams to "listen" and even admit that academics "don't really understand how to make a drug."

Gelb also said that ESAC, which includes a number of people who have made drugs for a living, acted as the catalyst that pushed their project forward in the right direction.

Solomon Nwaka, MMV Scientific Officer managing the project said, "This is a good project, a good team, a good partnership. It exemplifies how the MMV approach can facilitate development of new drugs for diseases of the poor." For more information on this project and to read the full press release, visit www.mmv.org.



Mike Gelb presents background on the Pf-PFT project to MMV stakeholders during the 18 May meeting.



Wes Van Voorhis explains how the Pf-PFT project was able to rapidly develop from a novel concept to potent new leads.

Congratulations to the entire Pf-PFT project team: University of Washington (Wes Van Voorhis, Mike Gelb, Pravin Bendale, Kohei Yokoyama, Laxman Nahlen, Kasey Rivas, Kevin Bauer, Fred Buckner, Christophe Verlinde); BMS (David Floyd, David Williams, Lou Lombardo); Yale University (Andy Hamilton, Erin Pusateni, Dora Carrico, Jeff Lockman, Zheng Zang); University of South Florida (Said Sebti); University of Central Florida (Debopam Chakrabarti, Shelly Patterson); Paragon Biomed (Marie Hanley); MMV (Solomon Nwaka, J Carl Craft)

Lifelong Chemistry

Shanon Radford
Professor Ronald Stenkamp

After 64 years of service to the University of Washington, Edward Clay Lingafelter ('Ling') died on April 7, 2003, at the age of 88.

Born on an Ohio farm in 1914, Ling was the oldest of three children. His family relocated first to Chicago, then to San Francisco, where his father worked for the Remington-Rand Corporation.

He received Ph.D. from Berkeley under the tutelage of G.N. Lewis, then he and his new bride, Roberta, packed up and moved to Seattle in 1939 for what was supposed to be a one-year post-doc position at the UW. They both fell in love with the natural beauty of the area.

At the same time, Ling found his life's work teaching chemistry and studying crystal structures and, later, metal complexes. His first research problems in Seattle were physical chemistry characterizations of components of soaps, such as long-chained fatty acids. The research was carried out in conjunction with Professor Tartar's group and had a strong connection with the research division at Proctor & Gamble.

Into the 1950s, Ling and colleagues studied a range of physico-chemical properties of these molecules, including their conductivity, their solubilities, and their surface tension properties. He began his crystallographic research on these compounds.

Ling's first graduate student, Lyle Jensen, started working with him in 1939, and together they measured and analyzed X-ray diffraction patterns of several organic sulfonates. These molecules were too large for complete structure determinations at that time, but these studies were the first in a large number of crystallographic analyses carried out by Ling, Jensen, and other colleagues.

In the early 1950s, Ling's research program started shifting from solution studies of soap-like molecules to crystal

structure analyses of small organic and inorganic molecules. By 1960, nearly all of his research activity was focused on structure determinations and analyses of inorganic compounds. Some of these were purely inorganic, such as Cs_2ZnBr_4 , and some were metals complexed with organic ligands.

As crystallographic methods and techniques became more powerful, Ling's group used them to provide structural information for better understanding the chemical properties of compounds. His group made good use of developments in computer technology to probe the structures of many metal complexes. Their approach was to study sets of complexes with variations in the metals and in the ligands.

One group of ligands that kept Ling's attention into retirement were the acetylacetonates. Careful study of the interatomic distances and angles in the



Left: Edward Lingafelter; Right: Roberta Lingafelter. Circa 1940.

metal complexes with these ligands provided fundamental information about the stereochemical and geometrical restraints that dictate how ligands interact with metals.

Similar analyses were carried out by



Newlyweds Edward & Roberta Lingafelter pose with best man Williston Lingafelter, Ed's younger brother, and Maid of Honor Grace Kneedler, Roberta's younger sister, on their wedding day, April 30, 1938.

Ling and colleagues on other types of ligands such as ethylenediamine and salicylaloximine. The emphasis in their structure determinations was to understand the structural and functional properties of small molecule ligands that would allow them to chelate metals.

Other types of compounds that attracted the attention of Ling's group were the Tutton's salts and guanidinium salts. The latter possess ferroelectric properties, and determining the structural correlates of those were important considerations in that research. Collaborations with Professor Norman Rose and other inorganic chemists also yielded many crystal structures of interesting metal complexes.

In later years, Ed collaborated with Verner Schomaker. They shared an office, and this undoubtedly helped to foster conversations between them. They worked with others on a number of crystallographic projects, but they also addressed physical chemical issues of importance in chemical education. Ling's last published paper concerned a mix of structural and functional issues.

During his tenure at the UW, Ling moved through all the professorial ranks, and he was Associate Dean of the Graduate School from 1960-69. He served as acting Department Chair from 1976-78, while Alvin Kwiram was on

sabbatical, and did a term as Chairman of the Undergraduate Curriculum Committee. Though a talented administrator, his first love was teaching, and he is remembered as a kind and generous mentor.

After his retirement in 1984, he continued to fill in in the classroom, and he kept office hours 2-3 days a week so that freshman chemistry students could drop by for assistance.

He believed strongly in the notion that knowledge should be shared, and in that spirit, he always published his research results as quickly as possible. During the 1960s and '70s, when computer time was expensive and the machines themselves took several minutes to perform a single calculation, Ling shared valuable computer time with members of other research groups, both within and without the Department of Chemistry.

Ling published over 100 peer-reviewed papers spanning more than fifty years (1941-1993). He was a member of the American Crystallographic Association, Phi Beta Kappa, and the American Chemical Society, among others. He was very active in the local ACS section, presenting papers, chairing committees, and attending meetings.

Ling gave dozens of invited lectures at meetings and universities all over the world. One of his more unusual accomplishments was an exchange program he developed with world-renowned inorganic chemist Luigi Sacconi from the University of Florence

in Italy. Ling and Dr. Sacconi took turns sending graduate students to each other's institutions, and Ling would often accompany students to Italy. He also taught himself the language so he could deliver lectures in Italian.

In addition to his teaching and research accomplishments, Ling was a loving and devoted husband and father of five sons—Bob, Tom, Jim, Dick, and Dan. After a day on campus, he would come home for a lively dinner with his family, often returning to his lab with one or two of the boys, who amused themselves playing with molecular structures and IBM cards. He was passionate about the Boy Scouts, earning a Silver Beaver for his work as Scoutmaster in Troops 158 and 171.

Ling's wife, Roberta Kneedler Lingafelter, the oldest of four children, was born on the Kneedler family's Oklahoma homestead in 1915. The family moved to the Bay area when Roberta was a child, and she met Edward Lingafelter at Berkeley while studying math and teaching.

During WWII, she taught at an all-girls college for a while before she and Ling started their family. She continued to tutor occasionally, but focused most of her attention on her family and volunteer work.

Roberta, too, was active in the Scouts and served many times as den mother. She volunteered with the League of Women Voters researching and disseminating information about



Ed & Roberta on Ed's 79th Birthday, March 28, 1993.

candidates and issues, and she was an enthusiastic member of the Women's Guild at Assumption Church. At a diminutive 5'2", Roberta was, nonetheless, "the steel behind the framework" who, according to son Tom, "could whip five boys into shape and keep [them] in line with just a look."

The Lingafelters weathered terrible heartache when their eldest son, Bob, died from cancer in 1996. Then Roberta had a heart attack and stroke in 2000 and needed access to 24-hour care. Though it was difficult for them to give up their home, Ed and Roberta couldn't bear to be apart and moved together into an adult care facility.

In the last few years of his life, Ed suffered from Alzheimer's disease, and so devoted was he to Roberta that he became uncharacteristically irritable when they were separated. When she died on April 6, he followed her a scant 29 hours later. They would have celebrated their 65th wedding anniversary this year.

Ed and Roberta are survived by four sons, five daughters-in-law, and seven grandchildren, and their legacy of lifelong love and devotion will be remembered by countless friends and colleagues.



Edward and Roberta Lingafelter with their five sons on their 50th Wedding Anniversary, April 30, 1988. From left to right: Richard, James, Edward, Daniel, Thomas, Robert, and Roberta Lingafelter.

Remembrances in honor of the Lingafelters may be made to Everett Providence Hospital, The American Alzheimer's Association, or the University of Washington Department of Chemistry. Please contact Shanon Radford (206/543-1611) for more information.

Putting Science Into Science Fiction: Science at the Movies

Mary Harty

How possible are those sci-fi ideas we see on the big screen? "Science at the Movies," a free film and lecture series hosted by the Department of Chemistry, aims to answer this question. The series, inaugurated in autumn of 1999, was established to create a fun and approachable venue in which the general public can access, understand, and discuss scientific endeavors at the University of Washington. We have been pleased with the turnout (standing room only!) and the diversity of our audiences, which have included high school and college students, university staff and faculty, as well as Seattle families. Many students later write a class essay about the topic.

The series couples movies with presentations by UW professors and students designed to encourage audiences to think critically about the science portrayed in media. Recent events include:

•**Frankenstein** with Dr. David Kimelman (Biochemistry), who presented "Creating Monster Tadpoles." Both the book and the movie *Frankenstein* confront the ethical dilemma of whether certain scientific questions should be pursued. Dr. Kimelman shared his perspective on the latest possibilities in his research and some of the surrounding ethical issues.

•**Chain Reaction** with Dr. Larry Crum (Applied Physics), who presented "Science and Hollywood: An Oxymoron (or how Hollywood ruined a perfectly good scientific discovery-sonoluminescence)." Dr. Crum actually consulted on this movie, and they still portrayed the science completely wrong!

•**The Matrix** with Dr. Hunter Hoffman (Human Interface Technology Lab), who presented "Eating Virtual Chocolate." Dr. Hoffman's research employs virtual reality in order to lessen the pain that burn victims suffer. He also uses the technology to aid people with phobias.

•**Men in Black** with Dr. Donald Brownlee. "The Possibility of Alien Life." In his book *Rare Earth*, Dr. Brownlee (Astronomy) contends that alien life is pretty unlikely. On the other hand, *Men in*



Gene Wilder as the both mad and absent-minded Dr. Frederick Frankenstein. Twentieth Century Fox, 1974.

Black suggests that Elvis Presley is an alien life form—maybe both are right!

•**Gattaca** with Dr. Maynard Olson (Human Genome Project), who presented "To What Extent Does Our DNA Determine Our Fate?" *Gattaca* depicts a near-future society in which one's personal and professional destiny is determined by one's genes. Dr. Olson gave the audience insights into the contributions and possible dangers that genetic mapping has given society.

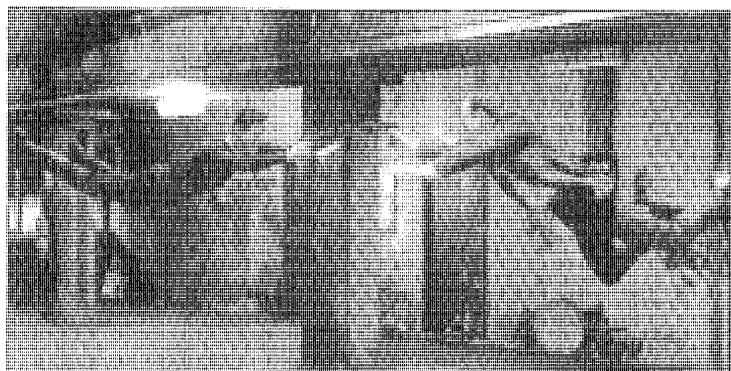
•**Young Frankenstein** with presentations by freshman Chemistry students. Our own students donned laboratory coats and goggles and presented various chemistry demonstrations. They also discussed stereotypes promoted by media, such as the "mad scientist" or the "absentminded professor."

•**Vertical Limit** with Mt. Everest climber Dr. Thomas Hornbein (Anesthesiology), who presented "The Limits of Vertical Limit." Dr. Hornbein was a member of the first American expedition to summit Mt. Everest. Who better to comment on the vision of Mt. Everest portrayed in the film *Vertical Limit*? Dr. Hornbein's research includes studies of the long term effects of high altitude on brain function. He assured the audience that there was no way the Chris O'Donnell character would be running and jumping at 26,000 ft. of elevation.

•**Blade Runner** with Dr. Henry Kautz (Computer Science and Engineering), who presented "Will Androids Dream of Electric Sheep? Present and Future Progress Toward Artificial Intelligence." Dr. Kautz gave the audience an update on the uses of robots in our society, including the potential use of nurse robots that might aid our aging baby-boomer population.

Future events may see us branching out of the sci-fi/action genre and into drama. The compelling portrait of the life of mathematician and Nobel Laureate John Nash in the film *A Beautiful Mind* is tentatively set for February 23. In May, we hope to screen *The Official Story*, a heart-wrenching tale of Argentine revolutionaries. Please join us!

For more information, contact Mary Harty by telephone at 206/543-8698 or by e-mail at harty@chem.washington.edu.



Neo (Keanu Reeves) and Agent Smith (Hugo Weaving) wage virtual battle in 1999's *The Matrix*. Copyright © 2002 Warner Brothers.

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