

A magazine highlighting research at the **University of Oregon**

Spring 1998, Volume III, Number 2

A Message About Research

Inventing Tomorrow's Technologies

UO Scientist Invents Small, Plastic Electronic Device-Research Continues

Cracking the Code

Researcher's Know-how Turns Jellyfish Protein Into Tool for Medical Science

Stopping the Crab

Battling Cancer-Molecule by Molecule-in the Chemistry Lab

• Drawing a Blueprint for Architects of the 21st Century

Educator Creates A New Kind of Training for a Rapidly Evolving Profession

Making Schools a Better Place for Learning

Reducing Discipline and Behavior Problems Leaves More Time for Teaching and Learning

Harnessing a Renewable Resource

UO Researchers are Tapping into the Sun's Free and Abundant Energy

Back Issues

About INQUIRY...

Return to University of Oregon News and Calendar Page.



A Message About Research From



STEADMAN UPHAM

Vice Provost for Research and Graduate Education and Dean of the Graduate School

If I have seen farther than others, it is because I was standing on the shoulders of giants.

--Sir Isaac Newton

Cutting-edge research follows from the purposeful accumulation, assembly, and application of facts, information, knowledge, and wisdom. Yet breakthroughs in research often occur serendipitously in brilliant flashes of insight. The researchers featured in this issue of *Inquiry* illustrate both principles. They have carefully built their research programs on the results of others in their field to move to the next level of achievement. And each has been motivated by an "aha! experience," the flash of insight that allows one to connect previously disparate facts and information in novel and important ways.

 PAGE ONE--Materials scientist <u>Mark Lonergan</u> explores the molecular structure of new materials, seeking ways to utilize their singular properties in next-generation electronic applications.

- PAGE TWO--The discoveries of chemist <u>Bruce Branchaud</u> and molecular biologist <u>Jim</u> Remington are leading to important biomedical applications.
- PAGE THREE--<u>Educators Rob Horner and George Sugai</u> develop and implement a new and
 practical program for grades K-8 to reduce discipline problems and significantly improve school
 learning environments. <u>Architect Nancy Cheng</u> prepares today's students for success by exposing
 them to cutting-edge telecommunications technologies.
- PAGE FOUR--<u>Energy researchers Frank Vignola, Dave Cohen, and John Reynolds</u> work to expand our abilities to harness the world's most important renewable energy resource, the sun.

Like Newton, these University of Oregon researchers are committed to learning from those who preceded them. They value and respect this tradition through their living example and by training and educating the next generation of scientists and educators for our world.

Back to INQUIRY home page

©1998 University of Oregon

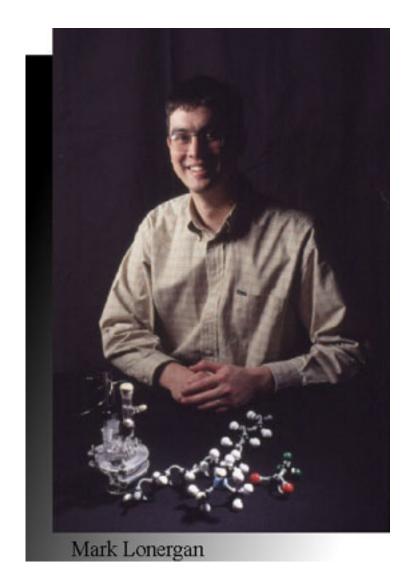
Inventing Tomorrow's Technologies

UO Scientist Uses Exotic Material to Create New Electronic Device--Research Continues

Electrical engineers may soon have a new tool for controlling currents in electronic circuitry, including computer chips, thanks to the pioneering research of Mark Lonergan, a University of Oregon assistant professor of chemistry.

As reported in a recent issue of *Science* magazine, Mark Lonergan has created a "tunable diode," a new type of device for manipulating electricity. Lonergan's realization of the tunable diode relies on the special properties of a relatively new class of materials known as conducting polymers. While his invention doesn't look like much--a glass beaker, some tubes and wires held together with epoxy--it possesses beneficial characteristics not found in devices made of more conventional materials.

"The unique properties of this device should open new avenues in the design of circuitry for the control and manipulation of electrical energy," Lonergan says. "It will be a useful new addition to the electrical engineer's toolbag."



The manipulation of energy in electrical circuits can be likened to controlling concertgoers seeking admittance to Portland's Rose Garden. In each case, specialized structures exert control over the system's traffic flow. Conventional diodes can be viewed as a kind of turnstile for electricity (diodes convert alternating current into one-way direct current). Lonergan's innovation--the "tunable" part of the tunable diode--adds another dimension of control to the turnstile. In essence, it gives engineers the ability to regulate not only the direction of flow but, in addition, the pressure required to pass through the turnstile. If the diode is tuned high enough, only those fans who are willing to exert a lot of energy on the turnstile will get to hear the concert.

"We do our work somewhat in the spirit of inventors." Engineers have yet to devise specific applications exploiting the unique characteristics of the tunable diode. Lonergan notes, however, that "if the tunable diode proves practical, it may one day join the transistor, resistor, and capacitor as a common component found in a myriad of new electronic devices. It is a new tool, and the advent of any new tool opens up new possibilities."

Since inventing the tunable diode, Lonergan and members of his laboratory have been steadily refining it, bringing closer the day of its application to real-world engineering problems. But Lonergan is also interested in exploring further, seeking to unravel the fundamental mysteries surrounding conducting polymers and to discover other new applications.

From the technological viewpoint, conducting polymers interest Lonergan because they blend the versatile structural and mechanical properties typical of plastics with the electrical properties required of active elements in microelectronic devices. This unique synergy may lead to exciting new technologies such as computer video displays as thin as a *Time* magazine and just as flexible.

"At present, we are investigating the feasibility of making all-plastic versions of the microelectronic devices commonly found inside computers," he says.

Another area of Lonergan's interest in conducting polymers is their application in nanotechnology--the rapidly evolving world of extraordinarily small devices. He notes that conducting polymers are long chainlike molecules only a few atoms in width; to some, these structures, with their attractive electrical

Electronic Legacy at UO

Mark Lonergan's invention comes 50 years after the invention of the transistor by three researchers, one of whom, the late Walter Brattain, earned a master's degree from the University of Oregon in 1926. Brattain and his collaborators, John Bardeen and William Shockley, jointly received the 1956 Nobel Prize in physics.

properties, hold the promise of being used as tiny wires. At a size a thousand times smaller than the smallest connections on today's best computer chips, they could be part of the answer to the continuing

effort to make smaller chips.

"We do our work somewhat in the spirit of inventors," Lonergan says. "We are really seeking to understand the most fundamental principals that govern the actions of conducting polymers, but we keep

Back to INQUIRY home page

practical applications in mind."

©1998 University of Oregon



FACULTY Profiles	GRADUATE Studies	UNDERGRAD Studies	HOME
FACILITIES	Research PROGRAMS	Research INSTITUTES	SEMINARS

Member, <u>Materials Science Institute</u> <u>Lonergan Lab</u>

B.S., University of Oregon, summa cum laude, 1990. Ph.D., Northwestern University, 1994 (Mark A. Ratner and Duward F. Shriver). Postdoctoral: California Institute of Technology, 1994-96 (Nathan S. Lewis). Honors and Awards: National Science Foundation Predoctoral Fellow, 1990-93; A.A. Noyes Postdoctoral Fellow, 1995; ACS/Proctor Gamble Graduate Award in Physical Chemistry, 1995; Dreyfus New Faculty Award, 1996; National Science Foundation CAREER Award, 1997. At Oregon since 1996.

Research Interests:

Our research program is based on the discovery and quantitative understanding of interfacial electron transfer processes that depend on applied bias in a complex, nonlinear and often asymmetric way. This pursuit is at the heart of efforts to identify and control novel systems that enhance and/or mimic the behavior of conventional semiconductor interfaces, which form the basis for nearly all present day microelectronic devices. An important element of our approach is to understand how the unique chemistry of "new" materials manifests itself in interfacial charge transfer processes. Our studies over the past five years have focused on conjugated or "conducting" polymers where we have been working on three major projects that all draw in some way on the unique redox (doping) chemistry of conjugated polymers relative to more traditional inorganic conductors. Three major areas of research are: (1) Electron transfer at inorganic semiconductor | conjugated polymer interfaces; (2). Polyelectrolyte mediated redox chemistry and inter-faces between dissimilarly doped conjugated polymers; (3) Electron transfer at nanostructured semiconductor interfaces. For more information, see the lab web site at http://www.uoregon.edu/~Inrgn

Selected Publications

- M. C. Lonergan, "A Tunable Semiconductor Diode Based on an Inorganic Semiconductor | Conjugated Polymer Interface," Science 278, 2103-2106 (1997).
- F. E. Jones, B. P.Wood, J.A. Myers, C. Daniels-Hafer, and M. C. Lonergan, "Current transport and the Role of Barrier Inhomogeneities at the High BarrierÊ n-InP | Poly(pyrrole) Interface," J. Appl. Phys. 86, 6431-6441 (1999)
- B. L. Langsdorf, X. Zhou, M. C. Lonergan, "Kinetic Study of the Ring Opening Metathesis Polymerization of Ionically Functionalized Cyclooctatetraenes," Macromolecules 34, 2450-2458 (2001).
- M. C. Lonergan and F. E. Jones, "Calculation of Transmission Coefficients at Non-Ideal Semiconductor Interfaces Characterized by a Spatial Distribution of Barrier Heights," J. Chem. Phys. 115, 443-455 (2001).
- C. Daniels-Hafer, M. Jang, S.W. Boettcher, R. Danner, and M.C. Lonergan, "Electrochemical Tuning of Charge Transport at the interface between Indium Phosphide and a Polypyrrole-phosphomolybdate Hybrid", J. Phys. Chem. B 106, 1622-1636 (2002).
- M.C. Lonergan, C.H. Cheng, B.L. Langsdorf, X. Zhou, "Electrochemical Characterization of Polyacetyelene Ionomers, and Polyelectrolyte Mediated Electrochemistry Toward Interfaces Between Dissimilarly Doped Conjugated Polymers", J. Am. Chem. Soc. 124, 690-701(2002).

To Contact Dr. Lonergan:

Phone: 541-346-4748 lonergan@uoregon.edu



WEBMASTER
lynde@oregon.uoregon.edu

Mark C. Lonergan

Associate Professor Physical & Materials Chemistry



FACULTY Profiles GRADUATE Studies UNDERGRAD Studies HOME
FACILITIES Research PROGRAMS Research INSTITUTES SEMINARS

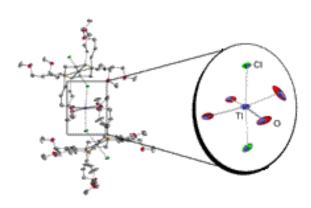
- < Welcome
- < Apply
- < Contact Us
- < Media Coverage
- < Visit Information
- < Newsletters
- < Chemistry Purchasing

Department Email / Phone List

1253 University of Oregon Eugene, OR 97403-1253 541-346-4601

Photo of Mt. Hood by Bernd Mohr. **WEBMASTER:** lynde@uoregon.edu

UO Home Page



UO Lab Discovers Method to Assemble 1-D Coordination Polymers

Researchers in the Tyler lab recently demonstrated how "arrested" chloride abstraction reactions can be used to assemble 1-D coordination polymers.

PDF: Arrested chloride abstraction from trans-RuCl₂(DMeOPrPE)₂ with TIPF₆; formation of a 1-D coordination polymer having unusual octahedral coordination around Thallium(I). Nathaniel K. Szymczak, Fusen Han and David R. Tyler, Dalton Transactions, 2004, 3941 - 3942.

Learn More...

http://www.ocean.udel.edu/extreme2002/ is s int



Cracking the Code

Researcher's Know-how Turns Jellyfish Protein Into Tool for Medical Science

In the cold ocean current off the San Juan Islands, a graceful Pacific Northwest jellyfish, Aequorea victoria, hypnotically undulates like a shaggy parasol, softly emitting a green, otherworldly glow. The cause of the glow--green fluorescent portein, or GFP--is the only known spontaneously fluorescent protein in all of nature. In the past five years, thousands of biomedical researchers around the world have begun using this exotic jellyfish protein (now cultured in bacteria) as a tiny lantern illuminating important biological processes previously hidden from view. Groundbreaking work to expand dramatically the usefulness of this remarkable protein is taking place at the University of Oregon in the lab of molecular biologist Jim Remington.

."This unique characteristic of GFP makes it extremely useful for biomedical researchers," says Remington, an associate professor of physics. "It gives them a window through which to peer at the inner workings of any type of living cell."

For example, by using genetic engineering techniques researchers can splice GFP onto other proteins of interest--say, a therapeutic hormone--so



Jim Remington

that where the hormone goes, the GFP goes. Shining a certain kind of light on the cell causes the GFP to

glow and allows a scientist to see where the hormone lodges and where it has the most potent effect. Similarly, a researcher studying a particular gene can replace part of that gene with GFP so that when the gene "turns on" the GFP also lights up.

."Scientists were finding new uses and even more interesting properties of the protein on nearly a daily basis," Remington asserts. "But curiously, no one knew exactly how the GFP worked--they didn't know how it hung together."

An expert in cracking the molecular codes of complex proteins, Remington decided to decipher the enigmatic molecule. In a concentrated nine-month effort, he and two fellow UO researchers determined GFP's structure. They discovered the <u>elegant assemblage</u> is composed of 238 amino acids arranged in a stable birdcage-shaped structure with a small glowing strand of matter suspended within like an incandescent parakeet on a perch.

."Now that we know the structure, we can begin modifying it for additional uses," Remington says. His research team has already changed one of GFP's 238 amino acids to create a protein with a yellow glow; now they are working on a blue-green variant. Other labs have created blue- and red-glowing versions of GFP.

.What use are these differently glowing GFPs?

."By itself, GFP provides a simple on-off test," Remington explains. "But researchers could use a variety of colored GFPs to test for a number of different possibilities at one time. This makes it a much more useful tool."

Remington's team is working on one version of the protein that responds to changes in pH--the chemical scale of alkalinity and acidity--that are associated with a wide range of cellular activities.

Another modified version under study signals changes in calcium concentration. Calcium levels fluctuate just before a nerve cell fires, so an indicator of when this takes place could be very useful in research into nerve tissue regeneration.

...THE ELEGANT ASSEMBLAGE IS COMPOSED OF 238 AMINO ACIDS ARRANGED IN A STABLE BIRDCAGE-SHAPED STRUCTURE WITH A SMALL GLOWING STRAND OF MATTER SUSPENDED WITHIN LIKE AN INCANDESCENT PARAKEET ON A PERCH.

Remington also notes that since GFP fluorescence can be turned on and off with light, it is easy to envision using it as a bio-optical data storage device. A CD-sized storage disc, Remington calculates, could potentially hold ten thousand times the data of one of today's CD-ROMs.

."This protein is a key," he says. "It is already unlocking many doors, and it promises to unlock others that we've been well aware of but have been unable to open."

Back to INQUIRY home page

©1998 University of Oregon



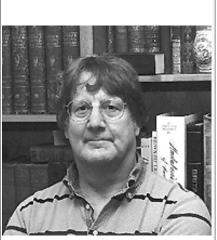
S. James Remington

GRADUATE STUDIES ADMISSIONS SEMINARS

FACILITIES

CAMPUS & OREGON LIFE

HOME



Professor of Physics

B.S., Oregon State University; Ph.D., University of Oregon

Member of:
Institute of Molecular Biology

Office: Willamette Hall Room 377

Telephone: 541-346-5190

Lab: Willamette Hall Room 355

Telephone: 541-346-5192

Webpage:

http://www.uoxray.uoregon.edu/welcome.html

Email: <u>iremington@uoxray.uoregon.edu</u>

Research Interests

Our group uses an interdisciplinary approach in applying physical techniques to the study of biological molecules, especially the structure, function, and interaction of enzymes and fluorescent proteins. The primary technique we use is x-ray crystallography, but occasionally we do computer modeling of enzyme active sites and other properties of proteins. In the laboratory, chemists and biologists collaborate with physicists to achieve a broader intellectual basis for the research.

Green Fluorescent Protein

The newest and most exciting project in the laboratory involves a protein that spontaneously rearranges itself to become fluorescent, absorbing blue light (or UV) and re-emitting green light, hence the name Green Fluorescent Protein (GFP). GFP was discovered in the Pacific Northwest jellyfish Aequorea victoria and has become enormously popular as a visible tag for proteins of interest or as a marker for gene expression. It is nontoxic and has been expressed in essentially all types of organisms ranging from bacteria to mice. No host factors are required for the transformation to a fluorescent protein. If GFP is linked to a protein of interest, the cellular location of that protein in the living cell is revealed by a glance in the fluorescence microscope. We determined the structure of the protein in 1996 and have since embarked on a large project to generate a variety of biosensors by taking advantage of the fact that most forms of the protein actually have two absorption maxima that are sensitive to changes in the protein structure. Using genetic engineering techniques we have successfully

constructed visual pH indicators, halide (chloride) concentration indicators and redox potential sensors. The color of the protein can also be modified by changing the environment or internal structure of the chromophore, which is derived from the primary sequence Ser(Thr)65-Tyr66-Gly67. We reported a yellow mutant in 1996 based on substitution of Thr203 with Tyr, but subsequently a Russian group has discovered related proteins from coral that fluoresce yellow and red, enabling multicolor reporting of a variety of cellular processes. It is fascinating that these different fluorescent proteins are nevertheless based on the same Xaa-Tyr-Gly peptide, and suggests that additional autocatalytic chemistry is involve in maturation of the protein. Crystals of a red variant are now on hand and work is well under way to determine the structure.

Enzyme Structure-Function Relationships

For many years we have worked to determine detailed structure function relationships in citrate synthase, which is at the entry to the citric acid cycle and is found in every organism examined. Citrate synthase, in its rate-determining step, abstracts a proton from the methyl group of acetylCoenzyme A to form a carbon-carbon double bond. The side chain which accomplishes this task is Asp375 working in concert with His274 (sequence numbering of pig heart enzyme). This equilibrium for this seemingly simple reaction is disfavored in solution by 12-15 orders of magnitude, and proposals for how an enzyme can do this are extremely controversial. Several publication have resulted from our studies, but the answer remains elusive. Recently, we determined the crystal structure of an enzyme that catalyzes an essentially identical reaction (malate synthase) in order to compare their respective mechanisms. It was fascinating to discover that the underlying chemistry is essentially the same in the two enzymes, but all of the details with the exception of an aspartic acid acting as a base are different. Evidently, Nature has discovered only one solution to this fundamental problem in chemistry, but the machinery is almost totally different! These studies are ongoing.

In the last few years, we have defined the first structures of two new families of enzymes, glycerol kinase and serine carboxypeptidase and may continue studies in these areas in the future. However, they are now "back burner" projects in favor of other exciting developments. Both enzymes are members of newly discovered superfamilies that are very diverse. For example glycerol kinase, actin and the heat shock cognate chaperonin (HSC70) are all ATPases with the same basic fold that utilize conformational changes upon hydrolysis of ATP to drive otherwise unrelated and extremely diverse biological processes.



Selected Publications

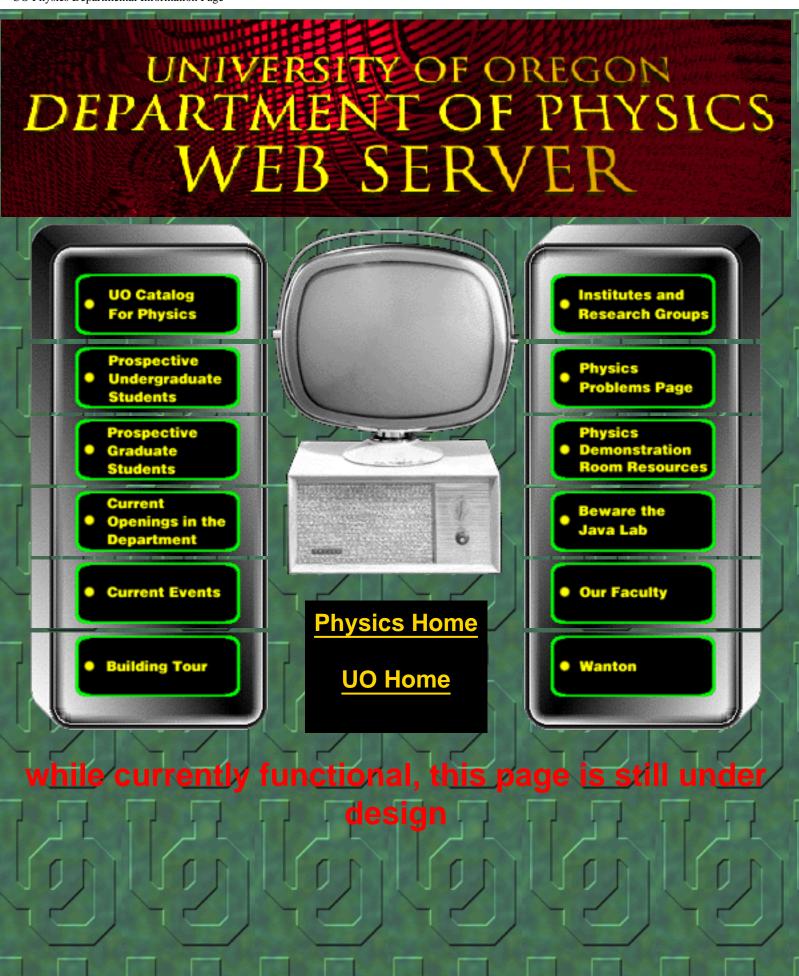
- Remington S.J., R.M. Wachter, D.K. Yarbrough, B. Branchaud, D.C. Anderson, K. Kallio, and K.A. Lukyanov. (2005) zFP538, a yellow-fluorescent protein from Zoanthus, contains a novel three-ring chromophore. Biochem **44**:202-12.
- Dooley C.M., T.M. Dore, G.T. Hanson, W.C. Jackson, S.J. Remington, and R.Y. Tsien (2004) Imaging dynamic redox changes in mammalian cells with green fluorescent protein indicators. J Biol Chem Feb 25 [Epub ahead of print]
- Rossignol R., R. Gilkerson, R. Aggeler, K. Yamagata, S.J. Remington, and R.A. Capaldi (2004) Energy substrate modulates mitochondrial structure and oxidative capacity in cancer cells. <u>Cancer Res</u> **64**:985-93.
- Hanson G.T., R. Aggeler, D. Oglesbee, M. Cannon, R.A. Capaldi, R.Y. Tsien, and S.J. Remington (2004) Investigating Mitochondrial Redox Potential with Redox-sensitive Green Fluorescent Protein Indicators. J Biol Chem **279**: 13044-53.
- Anstrom D.M., K. Kallio, and S.J. Remington (2003) Structure of the Escherichia coli malate synthase G:pyruvate:acetyl-coenzyme A abortive ternary complex at 1.95 A resolution. Protein Sci 12:1822-32.
- McAnaney T.B., E.S. Park, G.T. Hanson, S.J. Remington, and S.G. Boxer (2002) Green fluorescent protein variants as ratiometric dual emission pH sensors. 2. Excited-state dynamics. <u>Biochem</u> **41**:15489-94.
- Hanson G.T., T.B. McAnaney, E.S. Park, M.E. Rendell, D.K. Yarbrough, S. Chu, L. Xi, S.G. Boxer, M.H. Montrose, and S.J. Remington (2002) Green fluorescent protein variants as ratiometric dual emission pH sensors. 1. Structural characterization and preliminary application. <u>Biochem</u> **41**:15477-88.
- Capaldi, R.A., R. Aggeler, R. Gilkerson, G. Hanson, M. Knowles, A. Marcus, D. Margineantu, M. Marusich, J. Murray, D. Oglesbee, S.J. Remington, and R. Rossignol (2002) A replicating module as the unit of mitochondrial structure and functioning. Biochim Biophys Acta **1555**: 192-5.
- De Giorgi F., L. Lartigue, M.K. Bauer, A. Schubert, S. Grimm, G.T. Hanson, S.J. Remington, R.J. Youle, and F. Ichas (2002) The permeability transition pore signals apoptosis by directing Bax translocation and multimerization. FASEB J 16:607-9.
- Remington, S.J. (2002) Negotiating the speed bumps to fluorescence. Nat Biotechnol **20**: 28-9.
- Yarbrough, D., R.M. Wachter, K. Kallio, M.V. Matz, and S.J. Remington (2001) Refined crystal structure of DsRed, a red fluorescent protein from coral, at 2.0-A resolution.

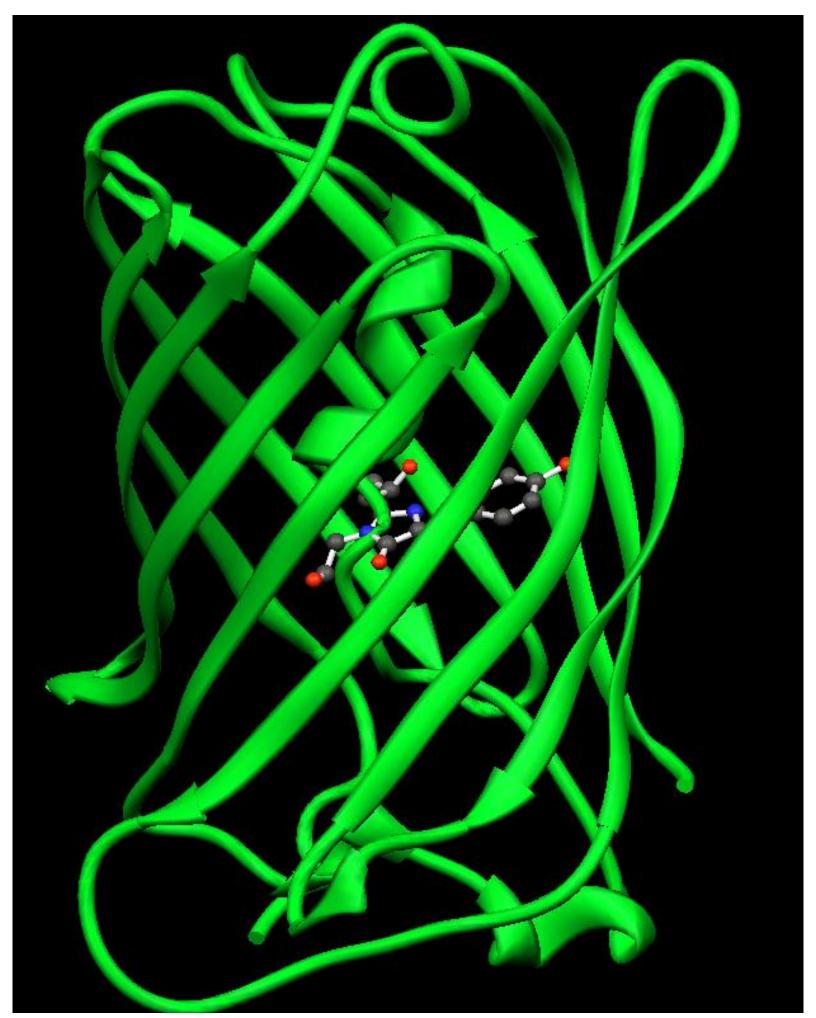
PNAS 98: 462-7.

- Wachter, R. M., D. Yarbrough, K. Kallio, and S.J. Remington (2000) Crystallographic and energetic analysis of binding of selected anions to the yellow variants of green fluorescent protein. <u>J Mol Biol</u> **98**:462-7.
- Howard, B. R., J.A. Endrizzi, and S.J. Remington (2000) Crystal structures of *Escherichia coli* malate synthase G complexed with magnesium and glyoxylate at 2.0 A resolution: Mechanistic implications. <u>Biochemistry</u> **39**:3156-68.
- Jayaraman, S., P. Haggie, R.M. Wachter, S.J. Remington, and A.S. Verkman (2000) Mechanism and cellular applications of a green fluorescent protein-based halide sensor. <u>J Biol Chem</u> **275**: 6047-50.
- Wachter, R.M. and S.J. Remington (1999) Sensitivity of the yellow variant of green fluorescent protein to halides and nitrate. Current Biology **9**: R628-9.
- Elsliger, M.A., R.M. Wachter, G.T. Hanson, K. Kallio, and S.J. Remington (1999) Structural and spectral response of green fluorescent protein variants to changes in pH. Biochemistry **38**:5296-301.
- Bystrom, C.E., D.W. Pettigrew, B.P. Branchaud, P. O'Brien, and S.J. Remington (1998) Crystal structures of *Escherichia coli* glycerol kinase mutant S58W in complex with non-hydrolyzable ATP analogs reveal a putative active conformation of the enzyme as a result of domain motion. Biochemistry **38**:3508-18.
- Usher, K.C., I.F. De la Cruz, F.W. Dahlquist, R.V. Swanson, M.I. Simon, and S.J. Remington (1998) Crystal structures of CheY from Thermotoga maritima do not support conventional explanations for the structural basis of enhanced thermostability. Protein Science **7**:403-12.
- Ormo, M., C.E. Bystrom, and S.J. Remington (1998) Crystal structure of a complex of *Escherichia coli* glycerol kinase and an allosteric effector fructose-1,6-biphosphate. Biochemistry **37**: 16565-72.
- Usher, C., L.C. Blaszczak, G.S. Weston, B.K. Shoichet, and S.J. Remington (1998) Three-dimensional structure of AmpC beta lactamase from Escherichia coli bound to a transition-state analogue: possible implications for the oxyanion hypothesis and for inhibitor design. Biochemistry **37**:16082-92.

Updated: March 2005 Contact: webmaster

Copyright© 2000-2004 Institute of Molecular Biology





http://comm.uoregon.edu/inquiry/s98/images/gfp.jpg (1 of 2) [3/6/2005 8:13:06 AM]

http://comm.uoregon.edu/inquiry/s98/images/gfp.jpg					



Stopping the Crab

Battling Cancer--Molecule by Molecule--in the Chemistry Lab



While modern medical science has a spectacular track record of diagnosing, treating, and in many cases eradicating diseases that once killed or debilitated millions, still no cure is in sight for many of cancer's most common and deadly forms. University of Oregon chemistry professor Bruce

Branchaud (Bran-show) is one of the thousands of scientists worldwide working to stop the crab.

What does chemistry have to do with fighting

cancer?

.BB: Many promising anticancer compounds are known to exist in nature. But extracting even a small amount of a naturally occurring compound can sometimes be difficult, prohibitively expensive, or might not produce enough of the compound to be practically useful. It can make more sense to produce the compound in a chemistry laboratory. Cancer researchers need a ready supply of a potentially useful compound before they can assess its potency and clinical value.

Are there other applications of chemistry to cancer research?

.BB: An equally critical contribution of chemistry is the creation of variations, or analogs, of a promising compound. The difference in chemical structure between a compound and an analog of it may be slight, but the difference in action--for example in its ability to stop the growth of a tumor--may be profound. Part of my work is developing new strategies and methods to efficiently create analog compounds, many of which have never existed before.

Would you describe some of your cancer-related research?

.BB: One piece of work comes with an interesting history. Plants related to daffodils have been used in folk medicine as a cancer treatment as far back as the fourth century B.C. Modern science has isolated several potent anticancer compounds from a particular daffodil. The most potent compound is called pancratistatin.

.Unfortunately, extracting pancratistatin is difficult--one process takes forty days of work--and the yield is skimpy. One-hundred-and-fifty pounds of daffodil bulbs can yield just a little more than a thumbtack's weight of pancratistatin.

We are developing a relatively straightforward synthesis of pancratistatin from a simple and inexpensive sugar, D-glucose. The goal of this project is to make the creation of much larger amounts feasible and to allow the production of analogs of pancratistatin for testing as improved anticancer agents.

In these days of highly competitive research funding, why do funders support your work?

.BB: Granting agencies are interested in supporting chemists who are developing fundamentally new methods to synthesize organic compounds, and especially those researchers whose methods might help solve practical problems. That's us.

THE DIFFERENCE BETWEEN A COMPOUND AND AN ANALOG MAY BE SLIGHT, BUT THE DIFFERENCE IN ACTION - FOR EXAMPLE IN ITS ABILITY TO STOP THE GROWTH OF A TUMOR - MAY BE PROFOUND.

What is the most satisfying part of your work?

.BB: Creating new compounds that, to our knowledge, have never previously existed is "going where no one has gone before." I like that. Also, training the next generation of scientists is satisfying. Students trained in my lab have gone on to become university professors, research scientists at pharmaceutical and biotech firms; they have earned fellowships from the National Institutes of Health. As the years go by, society will reap the rewards of their work.

What's ahead in the world of organic synthesis?

.BB: There are things we can do today that couldn't be done ten years ago. In another ten years additional fundamental advances in the area of organic synthesis will yield new medicines and useful new materials, to name just a few things with a big payoff for society.

Back to INQUIRY home page

©1998 University of Oregon



FACULTY	Profiles	GRADUATE Studies	UNDERGRAD Studies	HOME
FACILI	TIES	Research PROGRAMS	Research INSTITUTES	SEMINARS

Associate Member, <u>Materials Science Institute</u>
Associate Member, <u>Institute of Molecular Biology</u>

B.S., University of Massachusetts, North Dartmouth, 1976. Ph.D., Harvard University, 1981 (R. B. Woodward). Postdoctoral: Massachusetts Institute of Technology, 1981-83 (Christopher Walsh). Honors and Awards: NIH Postdoctoral Fellow, 1981-83; Alfred P. Sloan Fellow, 1987-89; Visiting Professor, Phillips Universitat, Marburg, Germany, 1991; Visiting Professor, Harvard University, 1992, 1993. At Oregon since 1983.

Research Interests

Single-Molecule Molecular Motors

In Nature there are many spectacular examples of nanoscale molecular devices. Molecular switches are common. Molecular motors are also widespread. We are working on creating synthetic non-biological molecular motors. Part of the inspiration for this project comes from biology. Part comes from recent developments in nanochemistry and nanotechnology. We are focusing on rotary motors. Our approach will use energy-driven diastereoselective reactions in chiral molecules to drive repeated 360-degree bond rotation in a preferred direction.

Oxidatively-Activated Self-Regulating Antioxidants

Many common antioxidants also have pro-oxidant activity. For example, when vitamin E is at highconcentration vitamin E radical can act as a pro-oxidant initiator of lipid peroxidation. We are designing and testing new synthetic antioxidants which have the antioxidant and pro-oxidant activity blocked by an oxidatively-removable protecting group. When autoxidation chain reactions are occurring, the protecting group should be oxidized then removed to release a standard antioxidant, such as vitamin E, which can

suppress autoxidation chain reactions. The overall result should be low concentrations of active antioxidant/pro-oxidant molecules yet have the ability to respond to, and suppress, autoxidation reactions by sensing them then releasing antioxidant molecules.

In addition to antioxidant activity, the molecules we are designing and testing should be useful for several fundamental and applied areas of study. The oxidatively-released blocking group could be used to mask a fluorescent probe, producing a fluorescent signal when oxidative activity is detected. Tumors and infections are often sites of elevated oxidative activity forming so-called reactive oxygen species (ROS). The oxidatively-released blocking group could be used to mask potent anticancer agents or antibiotics, for oxidatively-mediated site-specific release at the tumor or site of infection.

Enzyme-Mimetic Molecularly-Imprinted Polymers as Oxidation Catalysts

Oxidase enzymes oxidize substrates using molecular oxygen. Synthetic non-biological oxidases could be useful catalysts in organic chemistry. Molecularly imprinted polymers imprinted with redox-active cofactors and a binding site for substrates could become important new oxidation catalysts. Polymer-bound catalysts provide easy workup of reactions by simple filtration. Catalyst selectivity can be custom-tailored in the imprinting process. The catalysts should be environmentally-friendly with molecular oxygen as the oxidant. The only by product is H_2O_2 which is easy to disproportionate to molecular oxygen and water.

Oxidase reaction: RR'CHOH + O₂ => RR'C=O + H₂O₂

Catalase or catalase-mimetic reaction: $H_2O_2 => 1/2 O_2 + H_2O$

Overall Reaction: RR'CHOH + O_2 => RR'C=O + 1/2 O_2 + H_2O

Design, Synthesis and Testing of Malate Synthase Inhibitors as New Types of Antibiotic

The glyoxylate shunt pathway is used by microorganisms to metabolize acetate or long chain fatty acids as a source of carbon. It diverts intermediates away from the tricarboxylic acid (TCA) cycle when the organisms are exposed to low oxygen conditions.

The glyoxylate shunt pathway has recently been recognized as new target for the design of antibiotics. Yeast and bacteria contain the pathways but humans do not. Thus, inhibitors of enzymes in the glyoxylate shunt pathway might be effective new types of antibacterial and antifungal agents. This is an especially timely topic because many deaths in AIDS patients are caused by yeast infections with Candida albicans and by bacterial infections with Mycobacterium tuberculosis. A recent summary of this topic can be found on the website of the journal Nature: http://www.nature.com/nsu/010705/010705-10.html.

Two of the five enzymes in the glyoxylate shunt pathway are unique to that pathway and are not found in humans. Those enzymes are isocitrate lyase and malate synthase. The Remington group at Oregon has previously solved the structure of malate synthase. Recently they have solved the structure with substrates or substrate analogs bound. This result is significant because that structure can be used to guide the design of potent inhibitors of malate synthase. Such inhibitors can be expected to be selective agents against fungi and bacteria, targeting their glyoxylate shunt pathway, without (ideally) significantly affecting any human enzymes and pathways.

The collaboration between the Branchaud and Remington groups involves the design, synthesis and evaluation of malate synthase inhibitors. This project will involve molecular modeling, organic synthesis, testing of enzyme-inhibitory properties, protein crystallography of enzyme-inhibitor complexes, and testing of antibiotic activity. It is unlikely that any single person could do all of those things, but organic chemists and biochemists can play major roles in different aspects of the project. Recently a couple of good lead compounds have been discovered.

Selected Publications:

"ATP Analogs with Non-transferable Groups in the g Position As Inhibitors of Glycerol Kinase", Bystrom, C. E.; Pettigrew, D. W.; Remington, S. J.; Branchaud, B. P. Bioorganic & Medicinal Chemistry Letters 1997, 7, 2613-2616.

"b-Haloethanol Substrates As Probes For Radical Mechanisms For Galactose Oxidase", Wachter, R. M.; Montague-Smith, M.; Branchaud, B. P. The Journal of the American Chemical Society 1997, 119, 7743-7749.

"A Synthesis of (-)-Tashiromine and Formal Synthesis of (+)-Tashiromine Utilizing a Highly Enantioselective Pyrrole/Cobaloxime ¼-Cation Cyclization", Gage, J. L..; Branchaud, B. P. Tetrahedron Letters 1997, 38, 7007-7010.

"Cross Coupling of Alkyl Cobaloximes With Maleic Anhydrides. Basic Studies and Applications to the Synthesis of Chaetomellic Acid A And C-Glycoside Maleic Anhydrides", Slade, R. M.; Branchaud, B. P. The Journal of Organic Chemistry 1998, 63, 3544-3549.

"An Approach to (+)-Pancratistatin from D-Glucose: A Conformational Lock Solves A Stereochemical Problem", Grubb, L. M.; Dowdy, A. L.; Blanchette, H. S.; Friestad, G. K.;; Branchaud, B.P. Tetrahedron Letters 1999, 40, 2691-2694.

Additional Publications

To Contact Dr. Branchaud:

Phone: 541-346-4627

bbranch@oregon.uoregon.edu



WEBMASTER

lynde@oregon.uoregon.edu

Bruce P. Branchaud

Professor Organic & Bioorganic Chemistry



Drawing a Blueprint for Architects of the 21st Century

Educator Creates A New Kind of Training for a Rapidly Evolving Profession

It used to be difficult enough for an architect trying to mediate between the often conflicting needs of clients, builders, and engineers; but things are only getting more complicated. Now, with increasing ease of telecommunication--from the Internet to video conferencing--and the evermore-interconnected global economy, an architect's partners might not even be on the same continent.

."Architecture firms are either embracing these new technologies or dying," observes Nancy Cheng, an assistant professor of architecture at the University of Oregon.

Architecture schools are facing a similar challenge as they struggle to integrate into their courses the computer tools and skills training appropriate to the profession as it will be practiced in the early twenty-first century.

."A lot of manufacturing has moved from America to parts of the world where labor costs are much lower. The same thing is happening in architecture," she says. "If the U.S. wants to



remain competitive in this rapidly changing environment, our architecture students must be able to use the most advanced techniques."

.To accomplish this, Cheng is exploring new ways to teach that cornerstone of architectural education, the design studio. Traditionally, students enrolled in the design studio work in teams to develop architectural designs from inception and first sketches all the way through to detailed plans. Cheng has expanded the idea of teams to include students in other parts of the world--British Columbia, Hong Kong, Taiwan.

In her "virtual design studio," the far-flung team members collaborate face-to-face in live video conferences and shuttle their designs back and forth over the Internet. In one assignment, students in different countries individually develop component parts of a larger project. Then they work collaboratively on creating and designing an element integrating the two parts.

."Today, merely becoming adept with the tools of the trade is not enough," Cheng says. "It is essential for success in this profession to learn how to collaborate with peers."

Cheng is using the virtual design studio as a laboratory in which she conducts research into new forms of design communication. She explores such questions as the optimum size for virtual group collaborations and the strengths and weaknesses of various telecommunications technologies. After analyzing these data, she publishes the results in professional journals where others can benefit from her findings.

" IT IS ESSENTIAL FOR SUCCESS IN THIS PROFESSION TO LEARN HOW TO COLLABORATE WITH PEERS." Cheng notes that the pace of change, both of teaching strategies and the profession in general, does not appear to be slowing down. The past fifteen years have seen a sea change in the profession, as it has moved into the world of computer-aided design (CAD), she explains. But the mouse and keyboard are very clunky design tools, says Cheng, who expects that developments in the area of virtual reality will be the next great advance that the profession and educators need to assimilate.

."There are currently in development various virtual reality-based design tools that allow an architect to enter the virtual world and shape spaces and structures with the movement of a hand," Cheng says. "Improvements in computer interfaces will allow us to shape and think about new types of environments."

Because of forward-looking teachers such as Nancy Cheng, architecture students at the University of Oregon get advanced training in the tools they will be using as architects of the twenty-first century.

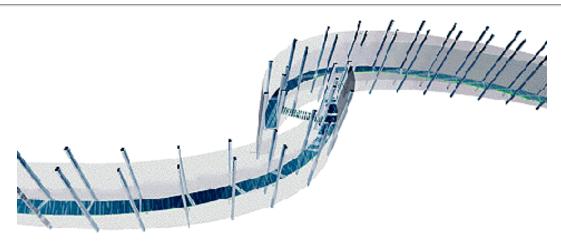
Back to INQUIRY home page

©1998 University of Oregon

department of architecture, university of oregon

Virtual Design Studio

Sharing ideas over the Internet



Teaming up students from different schools to work on the same design project.

Reseach Goals

- Optimizing the use of new media for remote design collaboration
- Understanding how to facilitate groups using telecommunication tools

Teaching Goals

- **Design:** Sharing and comparing design methods
- **Technology:** Working together to make the tools perform
- Culture: Opening eyes to different ways of working together.

Learning Benefits

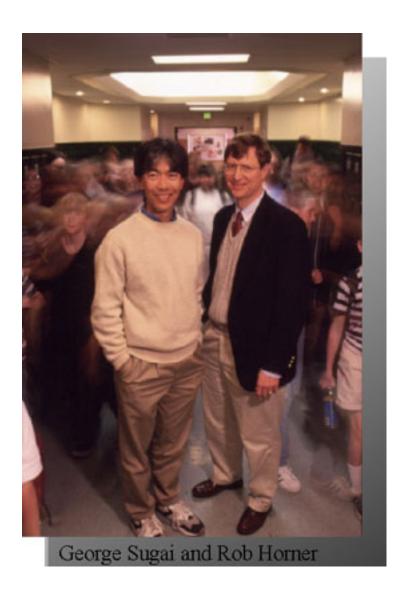
- Motivation of mysterious foreign partners
- New role for students as readors, editors
- Fairness of more tutors, anonymous presentation, peer feedback

| next | nywc home |



Making Schools a Better Place for Learning

Reducing Discipline and Behavior Problems Leaves More Time for Teaching and Learning



The problem is simple to describe. Schools where discipline and behavior problems are rampant are not good places for students to learn, for teachers to teach and for parents to send their kids. Solving this problem, however, is not as easy.

Improvements in discipline do not come about by dealing with one student or one class at a time but by making widespread and fundamental changes in how schools function as systems, say Professors Rob Horner and George Sugai of the University of Oregon College of Education.

To bring about this change, they devised a schoolwide approach called Effective Behavior Support, or EBS, which is designed to define, teach and encourage appropriate student behavior in grades kindergarten through the eighth grade. More important, EBS creates a school environment in which teaching, not discipline, is the focus of attention.

"Our program is based on the fact that 85 percent of students have the social skills to do

quite well if placed in a reasonable environment,"

Horner says. "If an effective school environment can be established, teachers are freed to devote special attention to the students who have larger behavioral problems."

On the first days of the school year, teachers in EBS schools teach their students school-wide and classroom expectations with fast-paced, interactive instruction. One school using EBS established five basic expectations of student behavior: be respectful, be responsible, be there and be ready, follow directions, and keep your hands and feet to yourself. Teachers work to make sure that students understand these expectations as they might apply to six school areas: classroom, hallway, gym, cafeteria, open common areas, and school bus.

."By treating the whole school as a system, we create a culture with widespread student support for socially appropriate behaviors," Sugai says. "In this kind of positive environment, teachers have more resources to spend with the one to seven percent of students who display the most severe problem behaviors."

"CREATING A LIVABLE
SOCIETY WITHIN THE
SCHOOL IS A KEY
ELEMENT FOR A
GOOD EDUCATION."

One pillar of the EBS approach is matching the intensity of the intervention to the intensity of the problem. Research shows that students who have the most problem behaviors respond well to increased amounts of adult supervision and contact. To help these students, Horner and Sugai recommend establishing strong adult-child relationships that take place daily and foster academic and social success.

One EBS school has the 30 students with the most severe problem behaviors attend daily morning check-in and afternoon check-out sessions. There the students interact, either one-on-one or in small groups, with an adult who helps them stay focused, prepared, caught up, and out of trouble.

Horner and Sugai carefully track the results of EBS programs in 67 schools, mostly in Oregon-including Tigard and Tualatin, Eugene, Roseburg, and Bend--but also in Hawaii, Texas, and British Columbia.

The results?

."Astronomically successful," Horner says.

In one school, after using EBS for only a year, office discipline referrals fell dramatically from 2,628 to 1,525--a 42 percent reduction. More important, these improvements were maintained over the next two years.

."Education is a key element in creating a livable society," says Sugai. "And conversely, creating a livable society--in this case, within the school--is a key element for a good education."

Back to INQUIRY home page

©1998 University of Oregon



Harnessing a Renewable Resource

Researchers Are Tapping into the Sun's Free and Abundant Energy

It's spring. We're seeing more of the sun and daydreaming about its warm rays shining on our gardens and summer vacations. Researchers at the University of Oregon are also focused on the sundevising methods to harness its abundant energy to benefit humanity. UO solar researchers are working in areas ranging from the cost and availability of the energy we use to the comfort and efficiency of the buildings in which we live and work. Here are three of their stories.

... For Clean Energy Production

.What contribution can solar energy make to the Northwest's energy needs?

That is the question Frank Vignola has been exploring since 1977. Vignola is a senior research associate in the <u>University of Oregon physics</u> department and director of the <u>Solar Radiation Monitoring</u> Laboratory (SRML).

"Our work is dedicated to producing the most accurate solar radiation data possible. In simple terms, we keep track of exactly how much sunlight is coming our way. Half of our <u>13 monitoring stations</u> are concentrated in Oregon,

but the network extends into Idaho, Utah, and Wyoming," he says. "Gathering this information is a

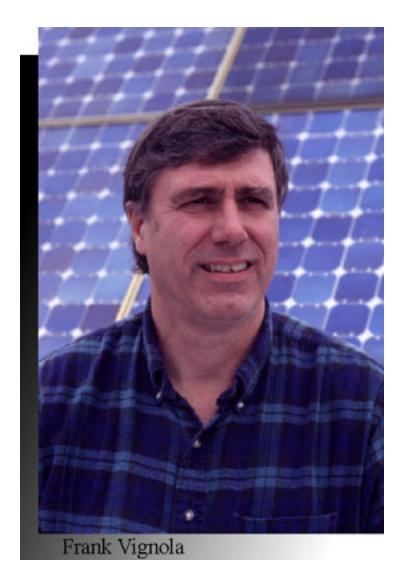
"THE NEXT CENTURY
WILL BE THE
BEGINNING OF
THE SOLAR AGE. "

fundamental step toward a future where we make significant use of this clean, abundant,

and renewable energy resource."

And how big a resource might it be? Vignola's research indicates that prime sites in eastern Oregon could produce four times the region's energy needs, or the equivalent output of sixty power plants--each with a thousand megawatts of generating capacity.

In the same way that stream flow data are necessary for an accurate calculation of the productivity and cost-effectiveness of a proposed hydroelectric dam, accurate solar "flow" data are necessary for planners to weigh the costs and benefits of adding solar power generation to the region's energy mix.

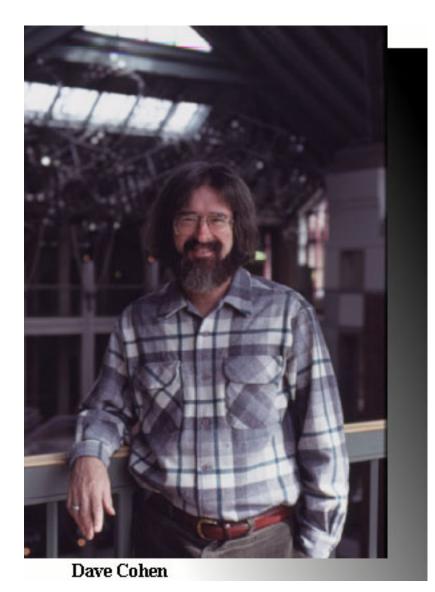


."Solar energy is not science fiction," Vignola asserts. "Right now, solar facilities in California with over 350 megawatts of generating capacity are successfully marketing solar electricity."

.Vignola is using his massive database of solar radiation measurements to help other researchers. One project will enable more accurate information to be extracted from satellite sensing devices. In another, Vignola used the database to determine the amount of solar energy available to photovoltaic cells mounted on east-west oriented roofs as compared to those with the assumed-to-be-superior southern orientation. His calculations show that, in fact, the difference between the two orientations is less than previously believed.

."The next century will be the beginning of the solar age," Vignola asserts. "Solar resource assessment is an essential element of the infrastructure that will bring that age about."

... For New Technology



There are no gas stations on Mars. So when NASA's Mars rover was tooling around the surface of the Red Planet, it relied on photovoltaic (PV) cells to gather energy from the sun and keep its "tank" on the F side of E.

."NASA wasn't concerned about cost with the rover's cells, which were made of super-efficient but very costly materials," says <u>Dave Cohen</u>, a professor of <u>physics at the University of Oregon</u>. "Here on earth, where we've got to balance both efficiency and cost, the number-one contender for a workable PV that could be mass-produced and have a real effect on our energy needs is a material called <u>amorphous silicon</u>."

"OUR WORK WILL CONTINUE UNTIL THOSE TECHNOLOGICAL ADVANCES ARE ACHIEVED."

Amorphous silicon is cheap, abundant and

easily fabricated, says Cohen, who is playing an important role in a national effort to develop economically viable PV cells. Fixed on a substrate of glass or stainless-steel foil, a layer of amorphous silicon one ten-thousandth of an inch thick can efficiently capture energy from the sun and transform it into usable electricity.

But there is a snag. The impressive electrical properties of amorphous silicon diminish with long-term exposure to light. This "stability problem" is one of the most serious challenges facing researchers seeking to improve this technology.

Work in Cohen's laboratory is focused on determining the fundamental mechanisms of this instability and overcoming their limiting effects on solar cell performance. In addition, he coordinates the research for a nationwide group of about fourteen scientists (funded through the National Renewable
Energy Laboratory in Golden, Colorado) who experiment with various ways to overcome the stability problem. When one of these scientists devises a potential improvement, they often send a test sample to Cohen, who uses his twenty years of experience with amorphous silicon to analyze its electrical properties and stability.

"PV-produced energy is going to play an increasingly important role as technological advances make cheap, highly efficient PVs available for both commercial power generation and home energy needs," Cohen says. "Our work will continue until those technological advances are achieved."

... For Better Buildings

."An architect who is not keeping the sun in mind is an architect who is not doing his job," says John Reynolds, a University of Oregon professor of architecture and director of the UO Solar Energy Center. "The sun is a vital element of any architectural design. It gives you light and heat and, if you do it right, it will even cool your building."

This passionate belief in the importance of "passive solar architecture" has guided Reynolds's career since he joined the UO architecture faculty in 1967. Over the years, more than 3,000 students have studied with Reynolds. He teaches Environmental Control Systems, a course required for all architecture students, as well as advanced seminars in passive solar heating and cooling. He helped write Inside Out: Design Procedures for Passive Environmental Technologies, an influential book inf the field of passive solar architecture.

."There are many different ways to address the architectural questions of heating, cooling, lighting, acoustics, water, and waste,"



Reynolds says. "In my classes, I've tried to teach my students that the most elegant and environmentally integrated path to this end is to make the most of the principles of passive solar architecture."

Two of the most noticeable characteristics of solar buildings are lots of south-facing glass, to let in the sun's strongest rays, and lots of thermal mass (a brick wall, for example) behind the glass, to store the sun's energy for use at night.

Reynolds has recently studied the solar dynamics of courtyard architecture and the cooling--and pleasant aesthetic--effect it can provide a building.

."The concept of wrapping each building around a garden, as is common in Spain, for example, is

"THE MOST ELEGANT
AND ENVIRONMENTALLY
INTEGRATED PATH IS TO
MAKE THE MOST OF THE
PRINCIPLES OF PASSIVE
SOLAR ARCHITECTURE."

the opposite of the pattern of the North American residential neighborhood, where the garden is wrapped around the building," he observes.

His next project is compiling the information and insights he gathered during his courtyard research project into a book.

The American Solar Energy Society presented Reynolds with its 1997 Passive Pioneer Award for his work in the field of

passive solar energy.

For additional information about solar-related work at the UO and around the world, visit the student-operated UO Solar Information Center on the World Wide Web at http://darkwing.uoregon.edu/~sic/.

Back to INQUIRY home page

©1998 University of Oregon



National Renewable Energy Laboratory

innovation for Our Energy Future

► About NREL

All about us: Contacts, organization, management, jobs, procurement, visitor information, and phone book.

NREL's Research & Technology Development

Explore our cutting-edge research & technology development and find out how to get involved.

Applying Technologies

We partner with international, environmental, and government agencies to apply renewable energy and energy efficiency solutions. We help license and transfer technologies into the marketplace, and help clean energy entrepreneurs succeed.

Learning About Renewables & Energy Efficiency

All about renewable energy and energy efficiency, plus information for homeowners, businesses, students & teachers, inventors, electricity providers, and farmers.



NREL — Keeping Up with the Rapidly Growing **Wind Industry**

Wind energy — it's the fastest growing electricity-generating technology in the world. And thanks to the successful research and development partnerships between industry and DOE's Wind Program at NREL and Sandia National Laboratories, it's breaking U.S. records as well. Full Story

Major R&D Areas



Solar





Wind









Hydrogen & **Fuel Cells**







Advanced Electric Vehicles & Fuels Infrastructure Systems



Energy Analysis



Basic Sciences

NREL is operated by Midwest Research Institute • Battelle



Need Help? | Security & Privacy | Disclaimer

Content Last Updated:

NEWS

Manning School Triumphs in Middle School Science Bowl

January 29, 2005

New Lab Delves Into Plants for Fuels

January 19, 2005

NREL and Colorado School of **Mines Sign Cooperative Agreement**

December 21, 2004

▶ Newsroom

EVENTS

POWER-GEN Renewable Energy Conference

March 1-3, 2005 Las Vegas, NV

Basler Distributed Generation School

March 8-10, 2005 St. Louis, MO

More Events

RESOURCES

Publications

Photo Library (PIX)

Renewable Resource Maps & Data