

A magazine highlighting research at the University of Oregon

Winter 1999, Volume IV, Number 1

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#### A Message About Research From



Tom Dyke Vice Provost for Research

If the twenty-first century is anything like the twentieth century, many major technological advances that benefit society will come from university research laboratories.

At the University of Oregon we are embarking on an ambitious effort to ensure that we remain at the forefront of scientific advance. We will accomplish this by bringing together a remarkable group of researchers working in exciting and productive areas of science. Together, they will address some of the most important questions we face today and in the coming decades. We are calling it the Brain, Biology, and Machine Initiative.

In the following pages you will meet some of the scientists involved in the initiative, learn about their work, and hear their thoughts about how the Brain, Biology, and Machine Initiative is vital for the UO, for our students, and for the state of Or egon.

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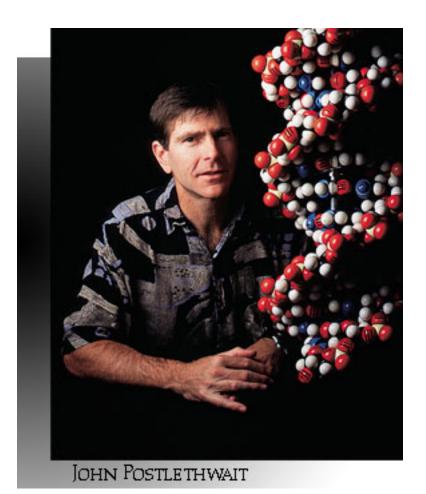
# **Fishing for Answers**

# DNA researcher uses tiny fish to understand human genetics

As you read this, thousands of scientists around the globe are forging ahead on one of the greatest scientific investigations ever conducted. The researchers are seeking nothing less than to fully understand DNA, the substance responsible for carrying hereditary information from one generation to the next in organisms as different as redwoods and rottweilers.

."In humans, we want to know how genes control the development of one cell--the fertilized egg--into the millions of cells that become a baby. We want to understand the mechanism that tells the cells to go to the right place and do the right thing--for example, to become an eyeball, a backbone, or a finger," says <u>University of Oregon</u> biologist <u>John</u>
Postlethwait.

.Conversely, researchers in this area are also discovering why cells sometimes don't go to the right place and don't do the right thing.



Such discoveries will have--and are already having--a dramatic impact on our understanding of the hundreds of developmental and genetic diseases that affect millions of Americans.

<u>Postlethwait's own research</u> is making a huge contribution to this effort. As unlikely as it may seem, his method of understanding the complexities of DNA and heredity is by investigating the genetic structure of a fish. The tiny tropical <u>zebrafish</u> has become an increasingly important biomedical research tool. First cloned at the UO in the early 1980s, the zebrafish has been at the heart of UO genetics

research ever since. Today, the UO has five major zebrafish laboratories staffed by 50 researchers; around the world, 200 labs work with zebrafish.

Postlethwait is the world's leading mapper of the genetic information in zebrafish DNA. A parallel research effort--the human genome project--is expected to achieve its goal of mapping human genetic information by 2003.

The task is monumental. If all the information contained in the DNA sequence of a human being were printed, it would require the equivalent of 200 volumes the size of a Manhattan telephone book (at 1,000 pages each). This information, in humans and all other species, is broken down into genes. Zebrafish have about 100,000 genes. Scientists have mapped a total of about 300 zebrafish genes--Postlethwait's group of researchers is responsible for 200 of these.

."Humans and zebrafish branched away from each other on the evolutionary tree about 420 million years ago," Postlethwait says, "but the amount of genetic information we hold in common is truly remarkable."

The more that is known about the DNA of each species, the more scientists can learn by crosschecking back and forth between the DNA maps.

The National Institutes of Health (a division of the U.S. Public Health Service that funds biomedical research) understands the value of teasing apart the mysteries of DNA. The NIH recently awarded Postlethwait's lab \$2.5 million to support research into the genetic correspondence between humans and zebrafish. In addition, it is funding a <u>zebrafish stock center</u> to be built at the UO under the direction of Postlethwait's colleague <u>Monte Westerfield</u>. The stock center will store thousands of genetically distinct strains of zebrafish--strains that Postlethwait calls irreplaceable--to be made available to researchers at the UO and around the world.

Looking to the future, Postlethwait believes that the next important step for nurturing science at the UO is the completion of the Brain, Biology, and Machine Initiative (see "Taking the Initiative").

."The BBMI would be a great help in recruiting talented grad students and postdocs," he says. "It calls for more and better facilities, and that equates with more and better students. Having more topnotch people in allied fields makes for increased <u>interdisciplinary collaboration</u>--already a hallmark of the research community here at the UO."

More top researchers also produce a greater number of important scientific publications, Postlethwait explains, and this can benefit undergraduates. For example, when he published his first major paper on zebrafish mapping in the prestigious journal *Science*, nine undergraduates were listed as coauthors. In late 1998, another Postlethwait paper in *Science* listed two undergraduate coauthors. Conducting important research side by side with a world-renowned researcher can provide an undergraduate with great experience, but publishing that research in a well-respected journal can also give a big boost to a budding student's career in this highly competitive field.

Postlethwait asserts that the BBMI will benefit society at large.

."People want to know how we got to be how we are. What regulates cell growth? Why are some individuals prone to alcoholism, schizophrenia, violence? How or to what extent are these conditions genetically determined?

."If society is interested in advancing its knowledge of human health in areas like these, or if society is concerned about birth defects, miscarriages, and infertility," Postlethwait insists, "then strong support for the Brain, Biology, and Machine Initiative is a terrific investment."

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# Faculty

# University of Oregon Institute of Neuroscience

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# John Postlethwait

Professor, Department of Biology B.S., 1966, Purdue; Ph.D., 1970, Case Western Reserve

#### Research Interests

Genetic regulation of animal development including development of the nervous system, the mechanisms of sex determination, the origin of novel morphologies in evolution and the evolution of the vertebrate genome.

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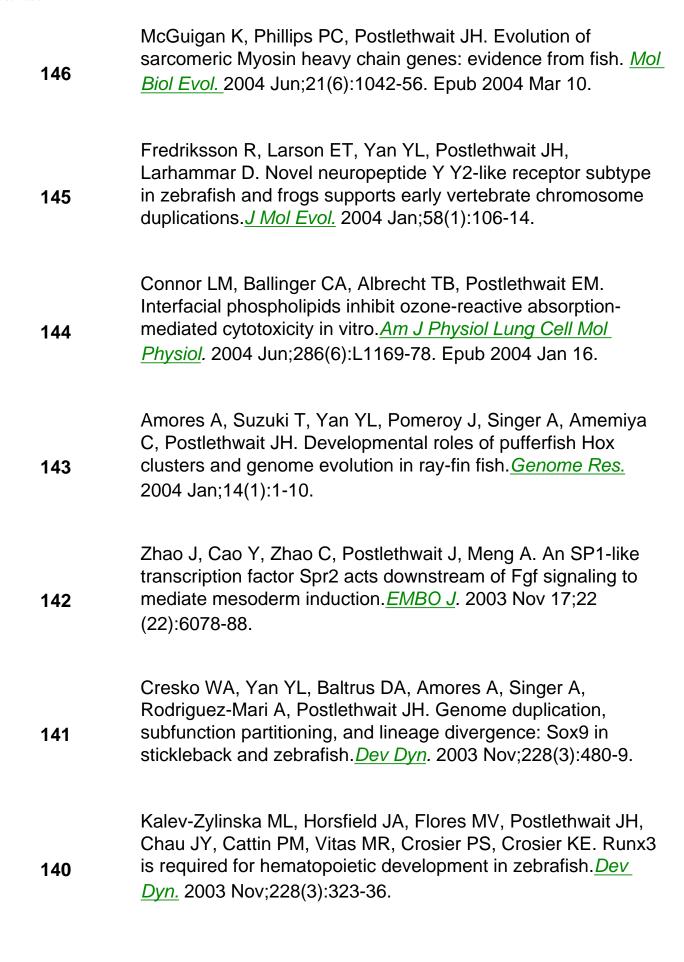
PostleLab.html

Vertebrates possess a variety of characters that distinguish them from their non-vertebrate chordate ancestors, including neural crest and epidermal placodes. What is the evolutionary genetic origin of the new molecular genetic functions that mold these novel morphologies? It has been suggested that gene duplication facilitates the evolution of developmental innovations, and vertebrates possess multiple copies of genes probably present in single copies in their chordate ancestors.

We have discovered a genome duplication in zebrafish lineage and have collected evidence that suggests that this duplication event may be shared by all teleost fishes. Additional large scale gene or genome duplications preceded the divergence of human and zebrafish lineages. We are investigating the possible roles of gene duplications in the origin of vertebrate innovations, working on the jawed fish zebrafish, the jawless fish lamprey, and a nonvertebrate chordate, the larvacean Oikopleura dioica. We aim to understand the developmental roles of genes related to those involved in making vertebrate developmental novelties by comparing their functions in the non-vertebrate chordate, zebrafish, and mammals.

# Publications **Complete list of publications**

152	Gloriam, D.E., Bjarnadottir, T.K., Yan, Y-L., Postlethwait, J.H., Schioth, H.B., and R. Fredriksson (2005) The repertoire of trace amine G-protein coupled receptors: Large Expansion in zebrafish. <i>Molecular Phylogenetics and Evolution</i> in press.
151	Papasani MR, Gensure RC, Yan YL, Gunes Y, Postlethwait JH, Pnugoti B, John MR, Juppner H, Rubin DA. Identification and characterization of the zebrafish and fugu genes encoding tuberoinfundibular peptide 39 (TIP39). <a href="mailto:Endocrinology">Endocrinology</a> . 2004 Aug 5 (epub).
150	Flores MV, Tsang VWK, Hu W, Kalev-Zylinska M, Postlethwait J, Crosier P, Crosier K, Fisher S. Duplicate zebrafish runx2 orthologues are expressed in developinskeletal elements. in press.
149	Cao Y, Shao J, Sun Z, Zhao Z, Postlethwait JH, and Meng A. <i>fgf1 7b</i> , a novel member of Fgf family, helps patterning zebrafish embryos. <u>Dev. Biol.</u> 2004 May, 271:130-143.
148	Naruse K, Tanaka M, Mita K, Shima A, Postlethwait J, Mitani H. A medaka gene map: the trace of ancestral vertebrate protochromosomes revealed by comparative gene mapping. <u>Genome Res.</u> 2004 May;14(5):820-8. Epub 2004 Apr 12.
147	Cresko WA, Amores A, Wilson C, Murphy J, Currey M, Phillips P, Bell MA, Kimmel CB, Postlethwait JH. Parallel genetic basis for repeated evolution of armor loss in Alaskan threespine stickleback populations. <i>Proc Natl Acad Sci</i> U S A. 2004 Apr 20;101(16):605



Rhinn M, Lun K, Amores A, Yan YL, Postlethwait JH, Brand M. (2003) Cloning, expression and relationship of zebrafish gbx1 and gbx2 genes to Fgf signaling. *Mech Dev.* 120(8):919-36.

Ruuskanen, J., H. Xhaard, A. Marjamaki, E. Salaneck, T. Salminen, Y.-L. Yan, J.H. Postlethwait, M.S. Johnson, D. Larhammar, and M. Scheinin (2003) Identification of duplicated fourth {alpha}2-adrenergic receptor subtype by cloning and mapping of five receptor genes in zebrafish. *Mol. Biol. Evol*. 10: prepublished on-line.

Rhinn, M., K. Lun, M. Werner, A. Amores, Y.-L. Yan, J. Postlethwait, and M. Brand (2003) Cloning, expression and relationship of zebrafish gbx1 and gbx2 genes to Fgf signaling during early brain development. *Mech. Dev.*, in press.

Fredriksson, R., E.T. Larson, Y.-L. Yan, J.H. Postlethwait, and D. Larhammar (2003) Novel neuropeptide Y Y2-like receptor subtype in zebrafish and frogs supports early vertebrate chromosome duplications. *J. Mol. Evol.*, in press.

Cresko, W., Y.-L. Yan, D. Baltrus, A. Singer, A. Rodríguez-Marí, and J.H. Postlethwait (2003) Genome duplication, subfunction partitioning, and lineage divergence: Sox9 in stickleback and zebrafish. Dev. Dyn., **in press.** 

#### **Books in Print**

- Postlethwait, John H. and Hopson, Janet (1989, 1992, 1995) The Nature of Life Third edition. McGraw Hill, New York, 700 pp. (An introductory biology textbook).
- Postlethwait, John H., Hopson, Jan, and Veres, Ruth (1991)
   Biology! Bringing Science to Life McGraw-Hill Publishing, New York, 600 pp. (An introductory biology textbook for non-biology majors).

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Gene Expression Search for gene expression patterns by gene name, developmental stage,

anatomical structure, developmental or physiological process.

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Generate graphical views of genetic, radiation hybrid or consolidated

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Mapping Panels

Summary listing of zebrafish mapping panels.

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Zebrafish Resource Center

Info, Strains, Probes Pathology Services Disease Manual



Development of the Zebrafish Database is generously supported by the NIH (P41 HG002659).

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#### **Resource Center Information**

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Lines ESTs/cDNAs
Monoclonal Antibodies
Pathology and Health
Services Guidelines For
Obtaining Fish Fees for
the materials we provide

#### Order

# Submit fish line to Resource Center

You can find strains available through the Resource Center by searching ZFIN for mutant and wild-type lines. You may also contact us with specific requests.

#### Acknowledging materials and services:

The Zebrafish International Resource Center is supported by grant P40 RR12546 from the NIH-NCRR. Please acknowledge the Zebrafish International Resource Center and this grant number in all publications resulting from the materials and/or services we are providing to you.

Thank you.

#### Guidelines for obtaining fish

• We prefer to ship embryos because they travel better than adults, but for some lines we may also be able to provide adult fish. We usually send 100-200 embryos but can send more if you make a special request. Fees are listed on another page.

- Note: ZIRC bleaches all embryos that are shipped. A tough chorion can be a byproduct of the bleaching procedure. If the embryos do not hatch on their own by 96
  hpf, the chorions will need to be removed manually. The procedure for removing
  the chorions can be found in the Zebrafish book or at the following web address:
  http://zfin.org/zf\_info/zfbook/chapt4/4.1.html.
- We want each shipment to be successful. We typically ship animals early in the week to avoid travel during a weekend. You will be notified of their expected time of arrival. Depending upon your location, you may need to obtain special permissions, make customs arrangements, or pick up the package at the airport or shipping service office. You should make these required arrangements before requesting shipment. Please inform us of any problems you have with the shipment.
- You should be ready to care for the fish, either embryos or adults, before they are shipped. Larvae (after about 5 days) must be fed paramecia and then baby brine shrimp for several weeks. Procedures for doing this are in *The Zebrafish Book, A guide for the laboratory use of zebrafish (Danio rerio)*, Monte Westerfield, ed. available on-line; or for a nominal fee, you can order hard copies from the Resource Center by web form or by telephone: (541) 346-6028.
- If you have not grown zebrafish before, you might want to practice before we ship you fish. You can obtain detailed information on maintaining and breeding adults and raising babies from the *The Zebrafish Book*. We can then send you fish with some confidence of their being grown and maintained properly.
- We encourage you to propagate the fish in your facility after you receive them from us because the Zebrafish Resource Center still has a limited capacity to fill orders.

#### **Materials**

Molecular probes including DNA libraries, cloned genes, antibodies etc. are available from the original sources or by contacting the Resource Center.

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Monte Westerfield, Professor

Westerfield Lab Alumni

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Tom Conlin, Scientific Curator

David Fashena, Scientific Curator

Ken Frazer, Scientific Curator

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Carrie Cleeton, Research Assistant

Ron Holland, Database Administrator

Michael Kent, Professor

Carrie Jones, Research Assistant

Jennifer Matthews, Veterinarian

Tim Mason, Programmer

David Lains, Research Assistant

April Mazanec, Research Assistant

Erin Quinn, Administrator

Jan Spitsbergen, Research Associate

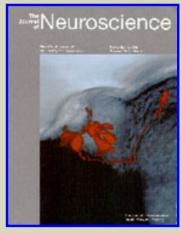
Norman Swanson, Research Assistant

Bill Trevarrow, Operations Director

Kelly Willius, Research Assistant

Zoltan Varga, Director

#### **Research Interests:**



Research in our laboratory focuses on understanding the mechanisms that regulate the differentiation of neurons and muscles. We would particularly like to understand how the specific properties of different kinds of cells are regulated. We study this question in zebrafish using a combination of anatomical, physiological, molecular, and genetic techniques.

We characterize the neurons and muscles that arise in the early embryo in terms of their detailed anatomy, physiology, development and genetics. Many of the cells in this system are individually identifiable and can be observed directly during growth of live embryos.

We use several approaches to elucidate the mechanisms that regulate the specification of these cell fates. We use fate mapping and lineage analysis to learn when and where different cell fates are established. We transplant cells to different locations in the embryo to learn when they are committed to particular fates. We identify genes that regulate fate specification by inducing mutations or by altering patterns of gene expression in transgenic zebrafish. The goal of our research is to provide a better understanding of the mechanisms regulating the establishment of specific neuronal and muscle cell fates during normal development.

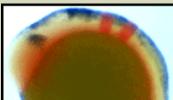
Our current projects include understanding the molecular genetics of muscle, ear and visual system development.

#### Lab Haiku from 2004 Institute retreat:

Mutant hunt is fun
Tangoing through the gene pool
Don't drink the water

#### **Some Recent Publications:**

• Hans, S., D. Liu and M. Westerfield. (2004) Pax8 and Pax2a function synergistically in otic specification, downstream of the Foxi1 and Dlx3b transcription factors. Development 131, 5091-5102.



- Hirsinger, E., F. Stellabotte, S.H. Devoto, and M. Westerfield. (2004). Hedgehog is required for commitment but not initial induction of slow muscle precursors. Dev. Biol. 275, 143-157.
- Jensen, A.M. and M. Westerfield. (2004). Zebrafish Mosaic eyes is a novel FERM protein required for retinal lamination and retinal pigmented epithelial tight junction formation. Curr. Biol. 14, 711-717.
- Liu, D, Chu, H., Maves, L., Yan, Y.-L., Morcos, P.A., Postlethwait, J.H., and Westerfield, M. (2003) Fgf3 and Fgf8 dependent and independent transcription factors are required for otic placode specification.

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- Sprague, J., Clements, D., Conlin, T., Edwards, P., Frazer, K., Schaper, K., Segerdell, E., Song, P., Sprunger, B., and Westerfield, M. (2003) The Zebrafish Information Network (ZFIN): the zebrafish model organism database. Nucl. Acids Res. 31:241-243.
- Yan, Y.-L., Miller, C.T., Nissen, R.M., Singer, A., Liu, D., Kirn, A., Draper, B., Willoughby, J., Morcos, P.
   A., Amsterdam, A., Chung, B.-C., Westerfield, M., Haffter, P., Hopkins, N., Kimmel, C., and Postlethwait,
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- Varga, Z.M., Amores, A., Lewis, K.E., Yan, Y-L., Postlethwait, J.H., Eisen, J.S. and Westerfield, M. (2001). Zebrafish smoothened functions in ventral neural tube specification and axon tract formation. Development 128:3497-3509.
- Jensen, A.M., C. Walker and M. Westerfield. (2001). mosaic eyes: a zebrafish gene required in pigmented epithelium for apical localization of retinal cell division and lamination. Development 128:95-105.
- Whitlock, K.E. and M. Westerfield. (2000). The olfactory placodes of the zebrafish form by convergence of cellular fields at the edge of the neural plate. Devel. 127:3645-3653.
- <u>Varga, Z.V., J. Wegner and M. Westerfield. (1999). Anterior Movement of Ventral Diencephalic Precursors</u>
  Separates the Primordial Eye Field in the Neural Plate and Requires cyclops. Devel. 126:5533-5546.

• Appel, B., A. Fritz, M. Westerfield, D.J. Grunwald, J.S. Eisen and B.B. Riley. (1999). Delta-mediated specification of midline cell fates in zebrafish embryos. Curr. Biol. 9:247-256.



#### Links:

- **ZFIN** (the zebrafish information network) the zebrafish model organism database.
- <u>The Zebrafish Database Project</u> status of ZFIN, the on-line database of zebrafish information.
- The Zebrafish International Resource Center resource and stock center for zebrafish.



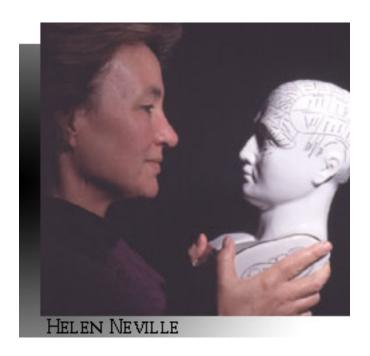
# Image is Everything

## Psychologist uses powerful new tool to explore the brain

Exactly what happens in the human brain as a person thinks, observes, remembers, or feels emotions? Using techniques developed in the past five years, scientists are now able to understand these activities as never before.

."This has been a dream for neuroscientists for many years and now, with fMRI--functional magnetic resonance imaging--we have the technology," says Helen Neville, a <u>University of Oregon psychology</u> professor who uses the fMRI in her research. "This advance is vastly important. It opens the doors to a whole new universe."

The fMRI is similar to the MRI machines used at hospitals which, like x-ray machines, produce



images of physical structures. But while an x-ray or an MRI primarily shows structure--where things are--the fMRI shows the activity taking place at a specific location. To accomplish this, it measures the oxygen in blood, which precisely indicates areas of activity. Research-grade fMRI machines can pinpoint activity in the brain to within one millimeter (about the thickness of a nickel) in humans, and down to a micron (about one-fiftieth the width of a human hair) in animals.

Before the fMRI, researchers had a comparatively sketchy sense of how the brain develops. With the new machine, scientists are able to observe the very finest wiring of an animal's nervous system while it's being strung together.

Neville uses this powerful tool to discover how the brain organizes itself as a child grows and how that organization affects the individual.

The answers to these fundamental questions promise to have profound implications. For example, a child's brain is most receptive to learning language during certain periods of his or her development.

Additional research is expected to specify similar windows of greatest opportunity for children to develop their skills in reading and mathematics. Such knowledge could lead educators to intensify certain kinds of teaching during the periods when the child is most ready to learn.

New understanding of the brain will also help doctors design treatments and rehabilitation therapies for people with brain damage and stroke as well as for children born deaf or blind or those deafened or blinded through accidents.

While the new brain-imaging technology is opening doors to important discoveries, research-grade fMRI technology is currently available in only a handful of facilities across the country.

."We have limited access to facilities at Georgetown University in Washington, D.C. and in Winnipeg, Manitoba, in Canada. We even have a student doing work in Germany," Neville explains.

Once they arrive at these far-flung locations, the Oregon researchers are only allowed access as "guests"--usually on weekends, sometimes at 2, 3 or 4 in the morning, when the machines are not ordinarily in use.

."Even then, we find ourselves getting bumped if there is a big traffic accident and the machines are needed for emergency use," Neville says.

She laments the inefficiency of this system and is enthusiastic about the benefits to Oregon and Oregonians of having a research-grade fMRI facility in the state (see "Taking the Initiative").

."It would give neuroscience a huge boost here at the UO. Our researchers study memory, visual perception, language acquisition, hearing, and attention. Access to a machine will give them all a huge advantage."

.She sees the investment in the Brain, Biology, and Machine Initiative as the beginning of a snowball effect.

."The return on such an investment for the citizens of Oregon comes in better health care; more federal dollars flowing into the state; more high-skill, higher-paying jobs and the additional taxes that are paid from those salaries. Perhaps most important of all, a first-class facility will draw first-class researchers and give Oregon students the best possible education, preparing them to become the next generation of top scientists."

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# Department of Psychology





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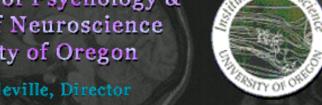
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Brain Development Lab



Department of Psychology & Institute of Neuroscience University of Oregon



Helen J. Neville, Director

Our broad goals are to study biological constraints and the role of input from the environment in the development of the human brain. We characterize the functional specializations of different neural systems in normal adults and take two broad approaches to the study of their development (normal adults):

- We compare cerebral organization in normal hearing, sighted, monolingual adults with that observed in adults who have had auditory or visual deprivation or who have had different language experience (neuroplasticity).
- We study the changes in functional cerebral organization that occur as normally and abnormally developing infants and children attain different ages and behavioural milestones. We employ the event-related potential (ERP) techniques and structural and functional magnetic resonance imaging (fMRI) in these studies (development).



Check out some research at the lab!

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Phone: (541) 346-4248 FAX: (541) 346-4271

e-mail: office@braindev.uoregon.edu

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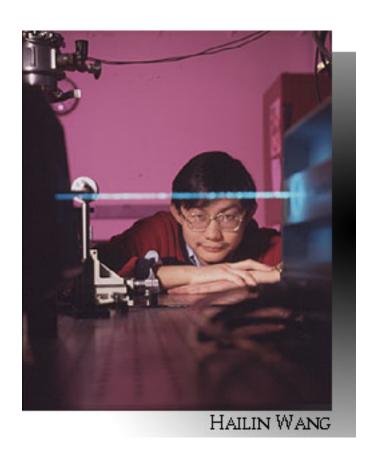
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# Lasers Dancing on the Head of a Pin

# Future technologies may be aglow with the light of tiny lasers



A laser is really not much more than a flashlight that emits a highly concentrated form of light. But the special properties of laser light have made it an extremely important tool, both in everyday applications such as CD players and at the most exciting frontiers of scientific research. University of Oregon physicist Hailin Wang is researching microlasers so small they may someday be commonly found by the hundreds or thousands on tiny computer chips.

."Optics, the field for studying lasers, is now the cutting edge of technological advance in the area of computers and information processing," asserts Wang. He is a member of the <u>Oregon Center for Optics</u>, a group of UO researchers that explores lasers and related technologies.

"Electronics has been vastly important for the past four decades, but now we are developing a whole

new set of technologies--*photonics*--that will take us far beyond the capabilities of electronic devices. We want to control how electrons, the components of electricity, interact with photons, the components of light," Wang says. "We want to be able to put this interaction to use in photonic devices."

The devices Wang and other optics researchers are investigating are almost unimaginably small-small enough for dozens to fit on the head of a pin. One way to control photons is to use a tiny glass sphere about one-fifth the diameter of a human hair. Wang shoots photons into the sphere, where they exhibit the "whispering gallery effect." This effect is familiar to visitors of large rooms with rounded ceilings, such as the rotunda of the U.S. Capitol. Due to the shape of the room, a person's voice, even a whisper, is transmitted with very little loss of volume around the arc of the dome.

Inside Wang's glass bead, photons exhibiting this same effect circle around the edge of the sphere. The reflecting characteristics of the sphere also increase the ephemeral lifetime of the photon. By exploring how to control photons in space and time, Wang is developing techniques that will advance photonics still further.

"We want to get to a place where a single photon can make a very big difference," he says.

"Computers will not always operate as they do now. A whole new class of photonic devices is emerging that will use optical switching and microlasers. Our work is helping lay the groundwork for those advances."

Hailin Wang came to the UO in 1995 from Bell Labs, one of the largest and most productive private research laboratories in the world.

."Oregon has an excellent optics program and I wanted to be part of it," he says.

He sees the creation of a critical mass of highly skilled researchers as one of the most important aspects of the Brain, Biology, and Machine Initiative (see "Taking the Initiative").

."Good people attract other good people. And when you have a lot of highly skilled researchers working together from the diversity of fields brought together by this initiative, they make exciting things happen. They make important advances."

These collaborations have a direct and important benefit on society, he notes.

."Researchers have an impressive track record for creating new and useful technology. In physics, our basic research has led to lasers, fiber optics, and super-sensitive sensors and detectors. A few of the practical applications of these advances are the Internet; laser surgery; and scanners used for warehouse inventories, the mail system, and even the supermarket checkout. Lasers have revolutionized the detection of minute amounts of pollutants or chemicals in our air and water.

."The Brain, Biology, and Machine Initiative supports the kind of research that made these advances possible," Wang says. "These are important advances for society, advances that have a big payoff."

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#### Welcome to the Oregon Center For Optics

The Oregon Center for Optics aims to promote and facilitate research and education in the sciences at the University of Oregon wherever optical science is involved in an essential fashion, in either its fundamental aspects or its technological applications, It promotes scientific interactions amongst the members of the center and between the members and the wider academic and industrial optics communities. The Oregon Center for Optics was founded in 1997 as an outgrowth of a 1985 Centers-of-Excellence Legislative Assembly to foster scientific activities that promote economic development.

<u>Optics Information</u>



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## On the Threshold

# Scientist sees basic research paying off big in treatments for physical and social problems

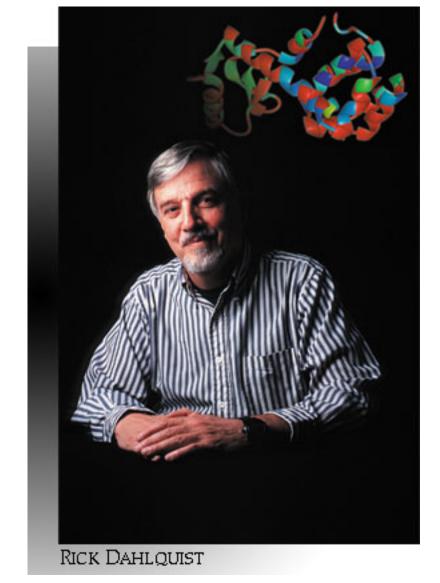
For many people an "ion-fueled proton turbine" might sound like something in the engine room on Star Trek. But when Rick

Dahlquist goes to work each day at the

University of Oregon Institute of Molecular

Biology, he studies Escherichia coli, a simple bacterium that gets around at much less than warp speed using just this kind of propulsion system. The tiny E. coli, one-tenth the diameter of a human hair, uses its engine to drive a propeller; a two-speed transmission gives the microbe forward and reverse capabilities.

<u>Dahlquist studies</u> the decision-making process that this simple organism uses to get where it wants to go. How does it remember where it's been? How does it compare its present and former positions? How does it decide which one it likes better? Researchers have discovered that the whole decision-making process relies on only six proteins--a remarkably economical design. Many other microbes use similarly simple control systems.



."Back in the sixties when I first got interested in this problem, I thought that we--the small group of scientists working on it--would figure it out in a few months or perhaps a few years. But it has turned out to be a great deal more complicated

and what we are finding is turning out to be a great deal more valuable to both science and society."

Researchers like Dahlquist have gathered thousands of bits of data, including the fact that humans do not use the specific proteins that bacteria rely on. Now, as strains of bacteria--some lethal--are developing resistance to traditional anti-biotics, pharmaceutical companies are taking notice. Building on the basic research developed in laboratories such as Dahlquist's, they are developing next-generation drugs that may be highly effective in eliminating certain sickness-causing bacteria.

."If a drug could disrupt the function of one of the control proteins within a microbe, it would essentially blind that microbe to biochemical changes in its environment. These changes can mean death to the microbe--and life to the person it has infected."

Dahlquist says that this kind of crossover from the university's basic research laboratories into practical applications is yielding ever-more-valuable results.

."The next decade should provide some outstanding advances in diagnosing and treating disease as well as potentially addressing some important sociological problems."

On this point, he cites work carried on at the UO in the <u>genetics of dogs</u>--what makes some breeds natural swimmers and others natural herding dogs. "As we come to fully understand the genetic control of these behaviors, it will shed important light on vital human behaviors that also seem to have a genetic component; aggression and alcoholism are just two examples", he says.

That is why the Brain, Biology, and Machine Initiative is essential, he explains. The initiative (see "<u>Taking the Initiative</u>") will give the UO the resources needed to take the next evolutionary step in science.

."We are on the threshold of a tremendously important era within many fields of science," he states. "This initiative is a bold assertion of the university's intention to contribute to these advances.

."It is important that we establish ourselves as a center of excellence while this new field is still forming. We did that with zebrafish research (see <u>Fishing for Answers</u>), and we are now a world leader in that area. This initiative represents a similar significant opportunity."

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# UNIVERSITY OF OREGON INSTITUTE OF MOLECULAR BIOLOGY

Frederick Dahlquist

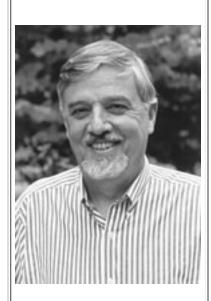
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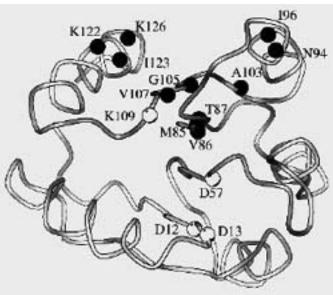
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#### Research Interests

My research group is involved with protein structure and function. One concern is macromolecular conformation and how conformational effects are related to the function of the macromolecule. While the investigation of this question is not restricted to any specific technique, nuclear magnetic resonance offers a particularly useful and powerful approach to this problem and is relied on heavily. Several molecular systems are under investigation. For instance, one problem is how the dynamics of a protein are related to its structure and thermodynamic stability.

The group studies the lysozyme of bacteriophage T4. This protein is under intensive investigation by researchers in several laboratories in the department and in the Institute of Molecular Biology. Nuclear magnetic resonance (NMR) offers an unusually powerful method to investigate the dynamics of this protein. Using two-and three-dimensional NMR techniques, all of the amide proton resonances can be selectively detected and assigned to particular amino acid residues. The amide proton resonances can be exploited in a number of ways to monitor the structure and dynamics of the protein. We are especially interested in defining the folding pathway of the protein in both an energetic and a kinetic sense.

The second area of interest is the phenomenon of chemotaxis in bacteria. When E. coli are placed in concentration gradients of certain chemicals, they either accumulate at the high concentration (for attractants) or low concentration (for repellents) regions of the gradient. The bacteria sense temporal changes in the concentration of attractant or repellent molecules and change their swimming behavior accordingly. This process requires sensing the concentrations of attractant or repellent, the behavioral response to rapid changes in these concentrations, and the relatively slow adaptation to new concentrations which returns the swimming behavior to the unstimulated condition. Adaptation is associated with the reversible methylation of four transmembrane receptors. These proteins receive environmental information from outside the membrane and transmit that information to the cytoplasm. We are interested in defining how environmental information is transmitted across the inner membrane and how that information is used to allow behavioral adaptation.



A Molscript drawing of the polypeptide backbone of CheY using coordinates derived from the solution structure as determined by NMR. The open circles represent the amide nitrogen atoms of the active site residues. The filled circles represent the nitrogen atoms of those amides resonances that are perturbed by interaction with the Chemotaxis-specific protien kinase, CheA.

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Updated: October 2003
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### Welcome to the Dog Genome Project!

The **Dog Genome Project** is a collaborative study involving scientists at the <u>University of California</u>, <u>Berkeley</u>, the University of Oregon, and the <u>Fred Hutchinson Cancer Research Center</u>. It is aimed at producing a map of all the chromosomes in dogs. Such a map can be used to locate the genes causing disease and those controlling morphology and behavior. <u>Continued here</u>.



#### **Our Collaboration Includes:**

- Cloning <u>Simple Sequence Repeats</u> which will act as signposts for the construction of the map. <u>Tetramer Repeats</u> at the FHCRC Dog Genome Group WWW server. These markers are available from Research Genetics.
- Localizing and ordering these markers on the dog chromosomes using linkage analysis and Fluorescent In Situ Hybridization (FISH).
- Generating Hybrid Cell Lines that have only one dog chromosome in them. For more information, see the FHCRC DGP page.
- Developing new techniques to aid in the faster identification of disease genes. One method currently being adapted for use in canines is the "Cleaved Amplified Polymorphic Sequences technique" (CAPS).
- Cloning very long stretches of dog DNA into manipulatable minichromosomes using Yeast Artificial Chromosomes (YACs).
- Using the <u>Dog Codon Frequency Table</u> to design PCR primers find the dog versions of already cloned human and mouse genes.
- There is a page available for you to get a quick look at how we map genes using DNA markers.
- For a more in depth description, check out the <u>Primer on Molecular Genetics</u> from the Department of Energy. (This is written about the Human Genome Project, but should help in understanding what the Dog Genome Project will be doing).



This site was originally created by Melissa DeMille with assistance from John Lovell. All questions relating to the Dog Genome Project should be directed to <a href="mailto:Jasper\_Rine@ls.berkeley.edu">Jasper\_Rine@ls.berkeley.edu</a>.



#### Wired to the Max

### Harnessing microchip muscle for a new and extremely powerful kind of science



.Working nonstop with hand calculators, it would take every man, woman, and child in the United States more than 125 years to equal what the Department of Energy (DOE) and Intel Corporation's new computer can do in just one second.

."Hardware is developing at a staggering rate," says Jan Cuny, a University of Oregon computer scientist.
"By the year 2002, there may be machines *hundreds of times this powerful*."

.What kinds of applications are researchers finding for all this new computing power?

The DOE's new ultrafast computer is being used to develop simulations that test the safety and reliability of the U.S. nuclear stockpile without underground testing-at great savings to both the treasury and the environment.

.Cuny and other UO researchers are playing a role

in this monumental effort. "Our work on the <u>DOE</u> project is focused on creating the layer of software that links scientists to the vast amounts of computational power their simulations require," she explains.

Cuny has a similar focus in other work with colleagues at the UO, where she is a member of the <u>Computational Science Institute</u>. This cross-disciplinary group of more than <u>20 researchers</u> applies computational power to problems in many academic disciplines.

."Researchers in <u>many fields</u> such as biology and geology are now collecting huge amounts of data," she says. "They want to sift through this information for subtle patterns. They want to integrate it

with other data using computationally intense methods. I work with these researchers to create a user-friendly package that gives them access to the computer technology they need."

For hundreds of years scientists have followed one of two approaches--experimental or theoretical-to do their work. But now Cuny and other researchers are helping computational science emerge as a third fundamental approach. The tool employs high-speed network technology, large-volume data servers, <a href="https://high-performance.graphics.org/">high-performance.graphics.org/</a> workstations and, at its core, <a href="https://powerful.gov/">powerful.gov/</a> parallel supercomputers such as those at the UO, which are capable of six to eight billion calculations per second.

"Computational science is an extremely powerful and rapidly evolving tool of increasing power and profound importance. It is changing the way scientists think about their work and redefining the arena of possibilities in which science is conducted."

Advanced computing will be a cornerstone of science as it will be practiced in the twenty-first century. That is why it is a cornerstone of the Brain, Biology, and Machine Initiative (see "<u>Taking the Initiative</u>"). As UO biologists, physicists, and neuroscientists expand the frontiers of knowledge, many will leverage their research with the power of advanced computational science.

."The Brain, Biology, and Machine Initiative will vastly expand our capabilities. It will provide us with much needed technical support such as programmers, operators and faculty members. It will enable us to broaden our use of computational science," Cuny explains.

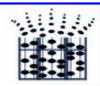
This advanced research environment will also create great opportunities for students. More and more science-related jobs will require training in computational science, she predicts. "And our students will be ready for those jobs. An important element of computational science is that it is collaborative—we teach our students how to work in multidisciplinary teams. This is a skill highly valued by employers."

As a discipline, computer science has been growing for decades, establishing a strong theoretical, experimental, and technological foundation. "Now," Cuny says, "we are ready for the next stage, applying the results of those efforts to multidisciplinary explorations. Investment in the Brain, Biology, and Machine Initiative is how we at the UO are building toward that remarkable future."

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### Computer and Information Science at the University of Oregon

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#### Bioinformatics Research Published in Nature

CIS graduate student, Bryan Kolaczkowski, and UO assistant professor of biology, Joe Thornton, used a small supercomputer to simulate the evolution of thousands of gene sequences on a hypothetical evolutionary tree. (cont.)

#### Colloquium Honors Work of Prof. Andrzej Proskurowski

The Department recently hosted a special Colloquium honoring CIS theory faculty Dr. Andrzej Proskurowski on the occasion of his birthday. (cont.)

#### Welcome to New Al Faculty Dejing Dou

The CIS department welcomes our newest faculty member, Assistant Professor Dejing Dou, whose research focuses on practical as well as theoretical aspects of Artificial Intelligence, Databases, Biomedical Informatics and the Semantic Web. (cont.)

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----- Under Construction -----

### Welcome to the DOE2000 Home Page!

DOE2000 is a new initiative to fundamentally change the way scientists work together and how they address the major challenges of scientific computation. To accomplish this change, DOE2000 will develop and explore new computational tools and libraries that advance the concept of "national collaboratories" and Advanced Computational Testing and Simulation (ACTS).

#### What's New?

- ACTS Toolkit Online Information Center Opens
- DOE2000 Retreat Announcement
- New Starts: ACTS Scientific Template Library

#### Overview of the DOE2000 Program

Launching DOE2000 involved careful definition of the objectives, goals, and mission. As a collaboratory effort, DOE2000 naturally involves the participation of numerous federal departments and programs, national laboratories, and universities.

- Vision and Goals
- Strategies
- Participants

#### **DOE2000 Program Components**

Currently, DOE2000 comprises three main components:

- Advanced Computational Testing and Simulation (ACTS) -- a program to provide an integrated set of software tools, algorithms, and environments that accelerate the adoption and use of advanced computing by DOE programs for mission-critical problems. The toolkit will include capabilities for representing complex geometries, solving diverse numerical equations, simplifying multi-language parallel execution, evaluating and enhancing code performance, and dynamically steering calculations during execution.
- National Collaboratories -- a research and development program to explore and develop laboratories without walls, which unite expertise, instruments, and computers, enabling scientists to carry out cooperative research independent of geography
- <u>Collaboratory Pilot Projects</u> -- early implementations of virtual laboratories that give scientists the technology to collectively observe and attack problems using combinations of ideas, methodologies, and instrumentation that do not exist at any single location

#### **DOE2000 Documents**

The DOE2000 initiative has developed over the course of several years, from a visionary white paper to a full-blown program.

- Executive summary -- initial white paper
- Overview document -- goals and benefits of the program components
- Program plan, March 1997 -- rationale, facilities, and activities

#### **Meetings and Workshops**

DOE2000 relies upon input and feedback from the scientific community. Workshops provide an important forum for DOE2000 discussions.

- DOE2000 Workshop, March 6-7, 1996 (report)
- 2th ACS Symposium on "Electronic Notebooks, Collaborative Computing, and

Internets/Intranets in Science," September 7-11, 1997 (announcement)

DOE2000 R&D Workshop, February 1997

#### **Related Material**

The Distributed, Collaboratory Experiment Environments (DCCE) program helped to identify aspects of the collaboratory environments (e.g., security architecture issues) that need further research and development.

- DCEE (Distributed Collaborative Experimental Environment)
- FY1997 DOE HPCC Implementation Plan -- including ACTS and national collaboratories
- Research articles citing results

#### For further information:

General: Mary Anne Scott, scott@er.doe.gov

Specific to National Collaboratories: Stu Loken, scloken@lbl.gov

Specific to ACTS: Jim McGraw, jmcgraw@llnl.gov



# Computational Science

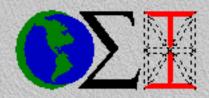
Univ of Oregon Computer Science Home

- Home
- Projects
- Publications
- People
- Conferences

Welcome to the University of Oregon Computer Science department's website for computational science. Computational science is a multidisciplinary field that combines research in the physical sciences with work in applied mathematics and computer science. There are several faculty and graduate students in the department involved in computational science-related projects such as bioinformatics, parallel computing, and software tools for computational science.

Follow the **projects** link to see what is currently going on in computational science or peruse selected publications in the **publications** page. The **people** link has information about some of the professors and students involved, as well as contact information. The **conferences** link is a list of computational science-related conferences.

University of Oregon Computer Science 2004 webmaster@csi.uoregon.edu



## **Computational Science Institute University of Oregon**

#### **Current Projects**

Here are links to some of the current projects by members of the institute:

- Tomographic Imaging Environment for Ridge Research and Analysis (TIERRA) [Toomey, Cuny, Malony, Harrop, Dunn]
- Distributed Array Query and Visualization (DAQV) [Hackstadt and Malony]
- ViNE [Cuny, Malony, Skidmore, Sottile]
- Virtual Research Vessel as an Educational Tool (VRV-ET) [Cuny, Sheehan, Rogers]
- Mutational Meltdown [Conery and Lynch]
- Genetic Simulation Library [Conery and Lynch]
- Parallel Recursion Project [Arnold and Haydock]
- NemaSys: A Neural Simulator for C. elegans [Ferree and Malony]

send feedback to: webmaster@csi.uoregon.edu



### **Taking the Initiative**

#### UO preparing to blaze trails in 21st-century science

The next century will see advances in science and technology that dwarf the remarkable accomplishments of the century now drawing to a close. Scientists will solve the mysteries of DNA and genetic coding, understand the development and organiza tion of the human brain, and push ever farther the speed, power, and usefulness of computer technologies. The University of Oregon is committed to making significant contributions to these advances. One important part of this commitment has taken form in the Brain, Biology, and Machine Initiative (BBMI). UO Vice Provost for Research Tom Dyke is directing the initiative.

.What is the Brain, Biology, and Machine Initiative?

.TD: The project draws together some of the UO's top scientists in the rapidly growing fields of <u>cognitive neuroscience</u>, <u>molecula r</u> and <u>evolutionary biology</u>, <u>materials science</u>, <u>optics</u>, and <u>computational science</u>. The common threads connecting their work to the initiative are information and information processing.

These areas are huge and vastly important. They address questions such as: How does the brain process information, and what are the analogies to modern computing machines and information science? How is information stored in the human genome and then expressed in the development of the human brain and body? How did this information evolve over time? What are the best ways to harness the power of new computers to analyze and visualize the massive amounts of data coming from new experiments? How can information

be encoded on laser beams to construct powerful new computers and networks?



Why at the UO and why now?

.TD: The UO has built a national reputation in each of the fields involved with the initiative. If this bold plan is funded, the university will be on the leading edge of the next "revolution" in science.

.That revolution will take place early in the 21st, century when we will see a remarkable integration of biological and mechanical information systems. Scientists in these fields will come together to explore some of the most important frontiers of science.

What is unique about the BBMI?

.TD: The BBMI builds on the university's long and unusual tradition of encouraging and supporting <u>interdisciplinary scientific research</u>—a tradition that man y of the top scientists on campus say attracted them here. This is the best approach for answering the complex, interrelated questions that the initiative addresses, and for asking new questions that are not even dreamed of now.



In this spirit, we will cluster many of our top researchers from different disciplines in a new 80,000-square-foot science building. It will house interdisciplinary laboratories and classrooms, faculty offices, and computing an d network facilities. At the technological heart of the BBMI are a pair of cutting-edge tools: two research-grade functional magnetic resonance imaging (fMRI) machines that allow researchers to study the brain as it functions.

How will the new facilities help the UO?

.TD: The initiative will allow the UO to attract new faculty members to teach and carry out research in newly emerging areas of technology and science. These top researchers will leverage millions of dollars in federal research funds for Oregon.

Will students benefit?

.TD: Students will have the valuable experience of studying and participating in research at a university that is at the forefront of both intellectual and practical developments. They will participate in and contribute to the next stage of the information revolution. UO undergraduates will be able to study under and work side by side with more of the most creative minds in the sciences. Graduate students will benefit from innovative programs such as that under development c urrently by biologists Mike Lynch and John Postlethwait. This program, where students will study how developmental p rocesses evolved over time, will provide an interdisciplinary education unavailable at other institutions.

.What practical benefits does this investment offer society?

.TD: The dramatic improvement in our understanding of the brain and body will contribute to new ways of treating and preventing disease. In addition, the advanced technologies will generate new companies for Oregon. One exam ple is the work of UO physicist <a href="Tom Mossberg">Tom Mossberg</a> in developing radical new ways of encoding information on laser beams is leading to optical switching and storage devices. A startup company, Templex Technology, Inc., is converting these advances into commercial applications.

Another faculty member, psychologist Don Tucker, has started his own company, <u>Electrical Geodesics</u>, to distribute brain-mapping technology coming from his <u>basic research</u>. This company has grown from eight employees in 1992 to more than twenty today--many of them UO graduates.

The initiative will accelerate the process of university know-how leading to advanced technology, jobs for our graduates, and wealth for our state. Educating highly skilled citizens and preparing them for high-paying high-t ech jobs is especially crucial as the state economy shifts from being resource-based to being high-tech oriented.

Are there other ways that investing in this kind of research benefits the state of Oregon?



.TD: The BBMI is a successor to the state-funded Centers of Excellence project in the 1980s. That project provided the financial framework that enabled us to recruit and equip many of the university's current younger scienti sts--including Tom Mossberg. It helped create the interdisciplinary research institutes that have generated more than \$130 million in federal funding from the state's original investment of \$4.8 million. This is money coming into Oregon. The Brain, Biolog y, and Machine Initiative is expected to have a similarly spectacular economic impact.

Where will funding for the BBMI come from?

.TD: The university plans to seek about \$15 million from the state, \$10 million from the federal government, and \$10 million in private gifts. This will pay for the building and equipment component of the initiative. The uni versity also needs about \$7 million in recurring state funds to hire 20 new science faculty members, ten technical staff members, and 40 graduate research fellows to implement the initiative.

.Will all the funding come at once?

.TD: We will fund the program step by step. The first phase will establish the fMRI facility. That will cost about \$6 million to purchase, install, and operate for five years. Success builds on itself. As we seek additional funding, we will let the research coming out of the remarkable fMRI facility demonstrate the extreme value of this endeavor.

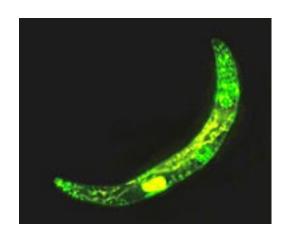
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**Purchasing** 

#### Center for Ecology and Evolutionary Biology University of Oregon



The Center for Ecology and Evolutionary Biology, established in 2002, promotes and facilitates research and graduate education in ecology and evolutionary biology. The center encourages scientific interactions among its members and between members and the wider academic community. It fosters a collegial and stimulating intellectual environment; supports the development of shared research facilities; and sponsors seminars, workshops, and colloquiums.

Because the varied expertise of its members is focused on related problems, researchers with specialties ranging from molecular evolution to the study of ecosystems directly benefit from interacting with one another. Active research programs use several approaches in the laboratory or in the field to investigate questions related to molecular evolution, evolutionary genetics, evolution of development, microbial ecology, pathogen-host interactions, global change, biogeochemistry, population biology, community dynamics, and ecosystem ecology.

Graduate students who are interested in working with one of the members of the center should apply through the Department of Biology. Students who want to work with an associate member from another department should apply to that department. Applicants should indicate an interest in the center on their application.

#### **Nature Bounces Back** on Sri Lanka's Coast

UO alums in Sri Lanka: Prithiviraj Fernando, Ph.D. (1998), Sanjayan Muttulingam, M.S. (1993).

2004 Retreat

#### **Research in the News**

Lab Reveals Surprising Finding in *Nature* 

Resurrecting Genes Helps Scientists Learn **About Extinct Species** 

Resurrecting the **Ancestral Steroid** Receptor: Ancient Origin of Estrogen Signaling

Thornton et al.

Genetic shift in photoperiodic response correlated with global warming

An exciting new website, "Evolution, Science and Society" giving the world an overview of the **Evolutionary Biology** discipline

Culture Collection of

Microorganisms From
Extreme Environments
(CCMEE)

The CCMEE is funded by a grant from the NASA-Ames Research Center and is a part of the NASA Astrobiology Institute.

National Academy of Sciences (PNAS online)

### <u>University of Oregon | Department of Biology | Eugene, OR | Life sciences at UO | Diversity at UO</u>

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