

IN VIVO

Newsletter of the University of Tennessee Division of Biology

VOLUME 2, NUMBER 6

FEBRUARY - MARCH 2003

From the Director

Otto J. Schwarz, Ph.D.



The arrival of the New Year for the faculty, staff, and students of the Division of Biology was met with much anticipation and enthusiasm. For

the Interim Director, the first half of UTK's academic year veritably flew by, being filled on a daily basis with new challenges and opportunities. For me, the challenge was, and is, to understand the administrative bounds of the Director's position while simultaneously learning its responsibilities and opportunities.

I also suspect that the Division's staff was equally challenged by the idiosyncrasies and personality of their new Interim Director. What an interesting job this is. As you may be able to guess, I am having fun and am enjoying the challenge as well. We have many exciting events scheduled for this coming year. I look forward to telling you about their progress as they unfold in future issues of *In Vivo*.

However, we also faced some sadness with the loss of Refrigeration

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A study of proteins in complex

The Biochemistry, Cellular and Molecular Biology (BCMB) department has three new faculty members, all of whom will be introduced in this issue of *In Vivo*.

One is structural biologist **Dr. Nitin Jain**. Dr. Jain is a part of the Center of Excellence for Structural Biology (CESB) and the BCMB department. He studies the structure of protein complexes using Nuclear Magnetic Resonance (NMR) spectroscopy.

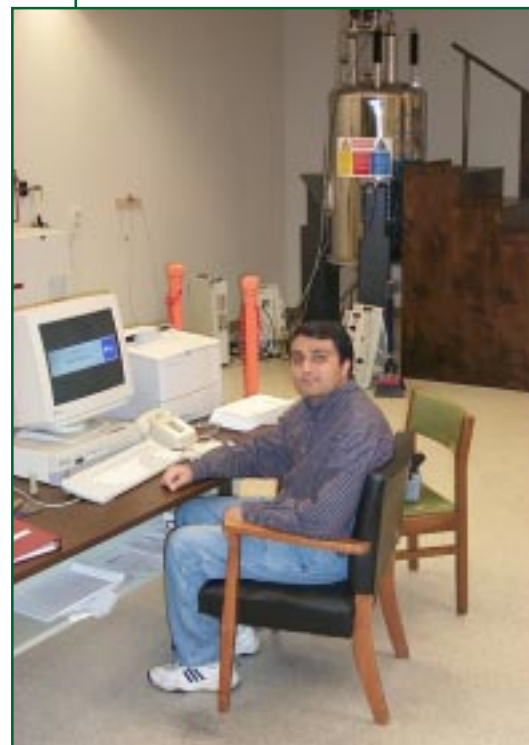
Like many other structural biologists, Dr. Jain studies the three-dimensional structures of certain proteins to determine their structure-function relationships. However, Dr. Jain is also interested in studying these proteins in complex with other proteins because he feels this approach will better answer questions on biological function.

He said, "Most proteins do not work alone, but as part of a complex network of several proteins and understanding the structural relationship between proteins in a protein to protein complex will better reveal the function of the individual proteins in context of their overall functional organization. We use NMR to look at protein complexes in solution and to study the structure and dynamics of the system in its physiological environment."

Using NMR as his main tool, Dr. Jain is able to look at large complex systems in a high through-put manner.

Dr. Jain has focused his research to studying two key protein complexes.

First, he studies the cell's immune response to bacterial infection by focusing on the role of the protein CD14 in the activation of the immune response. CD14 resides on the surface of the host cell and acts as a first line of defense. Dr. Jain said, "CD14 recognizes and binds endotox-



ins in the form of lipopolysaccharides present on the surface of the bacteria via interaction with another surface-spanning protein, the Toll-like Receptor (TLR)." This interaction signals certain pathways in a cell to activate immune response and resist infection. He wants to solve the structure of CD14 and then solve its structure in complex with TLR.

The implications of this work are

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"In Vivo" is printed on recycled paper

From the Head

Bruce McKee, Ph.D.

This has been a year of tragedy and renewal for the BCMB department. The loss of our friend and colleague **Dr. Pete Wicks** to cancer last summer was a terrible shock, one that is still fresh in our minds. Pete was one of our most respected faculty members, known especially for his dedication to teaching at both the graduate and undergraduate levels.

We have established a new annual award for graduate students to recognize excellence in teaching in Pete's honor. *The Pete Wicks Memorial Award for Excellence in Teaching* will be given to the graduate teaching assistant who most exemplifies Pete's dedication to teaching. It will be given out at the annual BCMB retreat in May. A memorial fund to establish this award is being set up and will be announced shortly. Donations from Pete's many friends and colleagues will be welcomed.

We have also been impacted by retirements this past year, both of faculty and staff. **Dr. Roland Bagby** retired at the end of May 2002 after 36 years on the UT faculty. Like Pete, Roland was best known for his dedication to teaching, especially in undergraduate physiology courses. **Dr. Ken Monty** retired in at the end of December 2002 after nearly 40 years of distinguished service. Ken was the first department head of the Biochemistry department and in recent years has been devoting his efforts to running several major outreach programs, including Governor's school and Science Olympiad. Both Roland and Ken will be greatly missed but both are expected to continue their scholarly and service activities on a part-time basis.

A staff retirement of special import



was that of **Anne Upchurch** in January 2003. Anne has been the BCMB administrative assistant since 1992. Her unflagging enthusiasm and good cheer, unflinching kindness to students and faculty with all manner of needs, and deep knowledge of UT procedures will be sorely missed. Fortunately, Anne has also agreed to return on a part-time basis as needed.

Renewal has come in the form of new department members. We added three new assistant professors this past fall, bringing the number of new faculty to six in three years. **Drs. Hong Guo**

and **Nitin Jain** were recruited jointly with the Center of Excellence in Structural Biology (CESB). Dr. Guo's expertise is in computer modeling of

enzymatic reaction mechanisms, and Dr. Jain's expertise is in determination of structures of protein complexes using NMR methods.

Dr. Sundaresan Venkatachalam (he goes by Sundar) is a mouse geneticist with interests in cancer and aging. All three are off to excellent starts, getting their laboratories set up, recruiting students to help with their research, and applying for external funding. We are delighted to have these outstanding young scientists join our staff, and are expecting great things from them. Each of them is featured elsewhere in this issue.

We also welcomed two talented new instructors to our staff this year. **Sharon Milewski** teaches our Human Physiology course and supervises the physiology laboratories, replacing Roland Bagby in that role. **Dr. Randy Brewton** is teaching our undergraduate molecular biology course, replac-

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Technician, **Lonald Daugherty**, of the Biology Service Facility (BSF). He suffered a sudden heart attack in December. He had been with BSF for three years and will be sorely missed by his colleagues.

So far this academic year, the Division has been able to obtain funding support from the College for the majority of its equipment requests targeted to maintain and enhance its laboratory offerings for the Core Biology courses for majors and non-majors. Some additional resources were found within the Division's budget to contribute toward departmental needs. Replacement of a piece of much-needed research infrastructural equipment was accomplished for Microbiology.

In addition, the Division was able to support the renovation of several structures being prepared for use as a field station on property bequeathed to

the Botany Department and located immediately adjacent to the Great Smoky Mountains National Park. The newly born research station is already being used by the All Taxa Biodiversity Inventory (ATBI) working in the National Park for sample sorting and data gathering.

Staffing of the Division continues to be a dynamic process. As was mentioned in the previous edition of this missal, the Departments are now running full stride in the UTK's employment process. With the combined help of the College office and our newest Center of Excellence in Structural Biology (CESB) we have managed to add a much needed staff member to the Division's Computer Support Group.

Laura Maples, the Division's Development person and Writer/Editor of *In Vivo*, has assured me that I will be able to describe in detail the plethora of services supplied by our talented support personnel and associated facilities in the next issue of this newsletter.

We are currently averaging better than two interview seminars per week in the Division at large. BCMB Head **Dr. Bruce McKee** is currently in the midst of engineering several of these staffing additions. This addition of *In Vivo* is focused on Professor McKee's primary responsibility, the guidance and nurturing of the Department of Biochemistry, Cellular and Molecular Biology (BCMB). His comments accurately reflect the dynamic level of activity present in not only BCMB, but in all sectors of the Division of Biology. I think that you will find the articles describing the research programs of several members of the BCMB faculty and staff of great interest.

To those of you who have kept a set of back issues of *In Vivo*, take a few minutes and page through the past 18 months of contributions. You have in your hands a brief window into the enormous diversity of interest and

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JAIN, from page 1

new insights into the mechanics of how CD14-mediated immune response is activated in a cell and if this activation can be controlled. Septic shock is an area where Dr. Jain feels his research could lead to therapeutic treatment. Another application could be the development of drug therapies to halt or prevent infection.

"Most proteins do not work alone, but as part of a complex network of several proteins and understanding the structural relationship between proteins in a protein to protein complex will better reveal the function of the individual proteins"

His second area of research involves the structural and dynamic characterization of two metalloproteins, Putidaredoxin and Cytochrome P450. These two proteins serve as a model system of biological electron transfer. The individual proteins have been studied, but P450 has yet to be researched structurally as a complex.

Dr. Jain said, "The P450 system is an important class of proteins that provides protection against toxins and foreign substances in the body because of their useful catalytic activity. This system could potentially function as an effective, environmentally safe biocatalyst." Model P450 compounds can be quite useful in detoxification of industrial wastes and aromatic pollutants in air. Dr. Jain is hoping to obtain funding for this part of the project from DOE's Genomes to Life program.

Originally from Bombay, India, Dr. Jain came to the States to pursue his Ph.D. at Brandeis University in Massachusetts. While there he met his wife. They are expecting their first child later this year. 

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Using mice to “knock out” cancer

Following better funding and resources with which to further his research, **Dr. Sundar Venkatachalam**, Assistant Professor, left his native India for Ohio State University in 1991. There he received his masters and his Ph.D. After graduation, he moved to Baylor College of Medicine in Houston for his post-doctoral work. He has now been with UT since August 2002 and has settled into his new life as a professor and scientist.

Although he has changed venues, he has not changed his focus. After losing a friend to cancer when he was 23, Dr. Venkatachalam began work in earnest studying the molecular basis of cancer formation and the functional analysis of tumor suppressor genes.

Dr. Venkatachalam studies the p53 tumor suppressor pathway in mice. He is currently using mouse models where the p53 gene has either been deleted or modified. Since the presence of p53 seems to be linked to the control of cell growth, Dr. Venkatachalam has found that deleting this gene increases significantly the rate of cancer in mice.

He has also found that deleting a part of the gene actually leads to cancer resistance. However, his studies also found that there was a price to pay for the enhanced tumor resistance. The cancer resistant mice were actually susceptible to premature aging and had a reduced life span by approximately 30 percent. These unexpected findings were published in the journal *Nature* last year.

Since he knows he doesn't need

the entire p53 gene to suppress cancer in mice, Dr. Venkatachalam believes that this will help researchers design novel p53 based vectors for gene therapy. The school of thought being, the smaller the gene, the easier it is to work with. He also hopes that this could yield gene therapies that can be used in concert with chemotherapy to help cancer patients

During the next few years, he plans to work on three

different genes. One gene is related to colon cancer and the other two are related to pre-mature aging. The tumor suppressor p53 is still the most notable part of his research because it provides a link between aging and cancer. He plans to apply for funding from the National Institute on Aging and the National Cancer Institute as well as other foundations that support research on aging and cancer.

“This research is coming at an important time as we have reached a milestone in biomedical research. The sequencing of the human and now the mouse genome combined with new strides in computational biology, make it easier for me to formulate the comparisons necessary. It is the best time to be a biologist”


In addition to establishing his research program in the BCMB department, he is establishing a relationship with the mouse genetics laboratory, or Mouse House at ORNL.

He hopes that his collaboration with ORNL will allow the identification of new genes that are involved in aging and cancer. Dr. Venkatachalam uses standard molecular methods for his research. He compares his findings in mutant mice with mutant mouse-derived cell-lines to study their cell cycle characteristics and responses to DNA damaging agents. He deletes or mutates one gene at a time at the genome level and then watches for the results in the full-grown mice.

He said, “This research is coming at an important time as we have reached a milestone in biomedical research. The sequencing of the human and now the mouse genome combined with new strides in computational biology, make it easier for me to formulate the comparisons necessary. It is the best time to be a biologist.”

He is aided by three undergraduate students **Amanda Gentry**, **John Michael Robertson** and **Warren Denning**. He plans to teach soon and will be involved with BCMB 512 - Fundamentals of Molecular Biology. In the future, he would like to teach an introductory course in cancer to undergraduates and graduates. He feels this would help to attract more students to this important field of research.

Dr. Venkatachalam moved to Tennessee with his wife and two children. He has an interest in writing poetry, but said that “graduate school has a way of changing your priorities.”

He enjoys his collaboration and comradelier within the BCMB department. Dr. Venkatachalam shares a common bond with the majority of the new faculty because of the tools and types of research in which they are engaged. He likes the new focus on functional genomics and feels this will bring UT to a new level of research quality. 

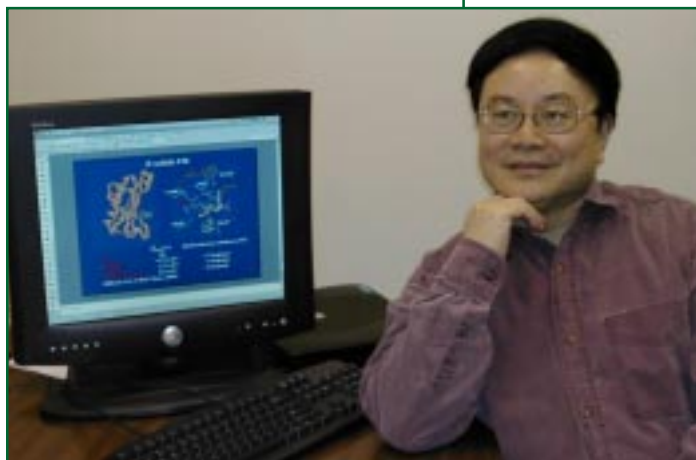
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Bringing proteins to “life”

Structural biologists determine three-dimensional views of proteins and protein complexes at the atomic level of detail using experimental techniques such as X-ray crystallography, NMR spectroscopy, and neutron scattering.

These techniques provide biologists with very useful structural information concerning the locations of individual atoms within proteins and protein complexes as well as the relationships between these atoms. A fundamental approach adopted by **Dr. Hong Guo**, a computational structural and molecular biologist, is to supplement such “geometrical” information with physical properties of the atoms, so that the atoms can “feel” each other physically.



He applies the laws of physics to provide biologists with interacting and dynamic pictures of proteins and protein complexes while functioning, along with important energetic information.

Dr. Guo is one of the newest Assistant Professors for BCMB. He has only been on campus since August, but already has established his computer laboratory and is able to aid his fellow biologists on and off campus. He takes the 3-D structures of proteins and protein complexes from structural biologists and treats the atoms with what he calls “a force field approach”.

In this approach, each atom is

assigned a charge and a size. The proteins and protein complexes are then described by “potential energy functions.” This treatment essentially changes the atoms from “geometrical objects” without physical “feelings” for their environments to physical objects.

As a result, the laws of physics can be applied to these atoms in proteins and protein complexes as well as to their mutual interactions. Dr. Guo then uses a computer to solve the Newtonian equations of motion for the atoms in proteins or protein complexes, which is a computational approach called molecular dynamics simulations that bring proteins to “life.”

For many biological processes, understanding proteins even at the atomic level of detail is not sufficient.

This is the case for enzymes, a large class of proteins that catalyze chemical reactions. Chemical reactions involve changes of electron distributions, and a key question is how an enzyme can make the change

of electron distribution from substrate to product much more efficient. The information at the atomic level of detail does not reveal much about changes of electron distributions.

To overcome this problem, Dr. Guo uses a combined quantum mechanical/molecular mechanical method for enzymes. By including quantum mechanics in the method, he is able to examine how electron distributions change during enzyme catalysis, to understand why enzymes can make chemical reactions much more efficient, and to predict the effects of mutations.


Dr. Guo said, “The analysis of the data generated from computer simula-

tions can help to stimulate the thinking of experimental biologists, giving them new interpretations on their data and new insight on what to do next.” This type of approach has been particularly successful for designing drugs and metabolic inhibitors.

Currently, Dr. Guo is working with BCMB faculty member **Dr. Dan Roberts**. Dr. Roberts said, “Dr. Guo will be collaborating with us on doing molecular dynamics simulations of ion and water movement through protein channels. This will aid us in understanding how structural differences in the pores of channel proteins results in differences in the rate and selectivity of water and solute flow, as well as in regulation of these properties.”

Unlike his peers, he does not use the typical wet laboratory for his work; he uses computers instead. He has the access to three supercomputers that help with the calculations. The supercomputers are at ORNL in Oak Ridge and the National Supercomputer Centers at University of Illinois and Boston University.

Dr. Guo did not start out in biology. He began his research in quantum chemistry at Jilin University in Changchun, China. Starting from quantum chemistry is, of course, not uncommon; both his former Ph.D advisor and postdoctoral supervisors at Harvard University, **Drs. Martin Karplus** and **Bill Lipscomb**, started with quantum chemistry first and so did their former Ph.D advisor, **Dr. Linus Pauling**, who got the Nobel Prize in quantum chemistry.

Dr. Guo said, “I found biological molecules much more interesting and challenging, and there are so many unanswered questions in biology.” 

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Just another day at the “Zoo”

Tina Tolley McConnell is an all-purpose staff member, who goes out of her way to get things done for the BCMB department and for the Center of Excellence in Structural Biology (CESB).

Her duties are split between the two entities and she is responsible for everything from accounting, web maintenance, grant preparation, payroll, faculty searches and seminar planning. Lately, she has been heavily involved with organizing the BCMB 615 seminars (see facing page).


Dr. Bruce McKee, department head of BCMB said, “Tina is a pleasure to work with, someone who goes out of her way to help get a problem solved. She is someone whose advice I value. We are lucky to have her.”

She has been with UT since 1984 and has worked in Records Management, the Bursar’s Office, Facilities Planning, and in Education for the Appalachian Rural Systemic Initiative.

Tina is a self proclaimed “Navy Brat”, who has lived on bases from California to Maine. When her father

retired to Tennessee, she began to settle as well. She started school at Bethany College in West Virginia, but after meeting her husband, **Tom**, she returned to East Tennessee to stay in 1982. She completed her bachelor’s degree in Anthropology in 1997 while working full time at UT.

In her spare time, Tina leaves the “zoo” of work at UT for another Zoo. She has been a volunteer at the Knoxville Zoo for 19 years. She has been involved with many programs such as “Boo at the Zoo”, community outreach, volunteer keeper in the primate department, coordinating Earth Day celebrations, Dogwood Arts Festival, taking animals to the Tennessee Smokies baseball games, and helping to hand-raise two tigers rescued from a circus. Recently, at the “Fantasy of Trees”, a local holiday event, she read a book about a hedgehog to children while holding a live hedgehog.

Her passion for animals doesn’t end when she leaves the Zoo. At home she has five dogs, two cats and two ferrets. 

tmconne@utk.edu



Tina at the Zoo with her niece Katana and nephew Braxton

The Seventh Annual “Friends of Biology” Golf Tournament

Sponsored by Fisher Scientific

Thursday, May 1, 2003
Centennial of Tennessee Golf Course
Oak Ridge, Tenn.
9:00 am Shotgun Start
Lunch Included

Four person best ball format
Entry fee \$60.00 per player
\$240.00 per team

Trophies awarded to 1ST
and 2ND Place teams
(Only foursomes will be eligible
for trophies)

Make checks payable to:
“Friends of Biology”
128 Neyland Biology Annex
Knoxville, TN 37996
Attention: Jan Hudson

For more information
call Jan at (865) 974-8761

Checks must be received by
March 28TH
Deadline for team changes
April 25TH

Centennial is a soft-spike facility and
proper dress is required.

This tournament has raised several
thousand dollars in the last six years
for the Support Fund of the Division of
Biology. Your participation continues
this successful effort.

Thank you!

Special Topics Seminar

A Structural Approach to Cell Biology BCMB 615

February

5th JoAnne Sweasy (Yale)
12th Steven Sprang
(Southwestern Med.)
19th Angela Gronenborn (NIH)
26th Elias Lolis (Yale)

March


5th Greg Petsko (Brandeis)
12th Bill Lipcomb (Harvard)
26th Holly Ingraham (UCSF)

April

2nd Sankar Ghosh (Yale)
9th Suzanne Scarlata (SUNY)
16th Rodney Rotstein (Columbia)
23rd Joanne Stubbe (MIT)

DIRECTOR, *from page 3*

scientific skill that is represented in the Division of Biology at UTK. Both you and I have had, and still have, the privilege of being part of UTK Biology and its traditions of teaching and research. In future editions of the newsletter, I hope to feature some of the successes of our alumni, both in and outside of academia.

One last gasp.... Our Botany edition of the newsletter (December 02) seemed to stir some interest in being part of the planned Conservatory-Greenhouse Complex. Although we have not yet begun our planned efforts at finding that single donor with very deep pockets, we have received several much appreciated donations that will be used to make the proposed facility a reality. We are in the process of creating a separate Conservatory-Greenhouse Complex development account should you find it necessary to obtain additional tax deductions for this and future years. Talk to you soon. 

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MCKEE, *from page 2*

ing Pete Wicks.

We are in the early stages of recruiting three additional assistant professors, two in molecular cell biology and one in eukaryotic genomics. We anticipate interviewing at least 12 individuals for these positions this semester and are looking forward to many stimulating seminars. The recruiting seminars will begin in February and will be open to all interested scientists.


The two new molecular cell biologists are expected to greatly strengthen the cell biology core area of BCMB, which has been depleted by retirements, and to bring new technology for studying sub-cellular structure and cellular dynamics. The candidates will bring expertise in a wide variety of areas of cell biology including nuclear substructure and gene expression, intracellular trafficking of macromolecules, cell-cell signaling and regulation of growth and development. They study a broad range of cell types and organisms, spanning the plant and animal kingdoms.

The eukaryotic genomics position is the fruit of a collaborative venture involving the Microbiology Department and the Graduate School of Genome Science and Technology (GST). It is the first new faculty position in BCMB since our inception, indeed the first since I came to UT in 1990, and is thus especially exciting. Genomics is the "new wave" in biology and an area in which BCMB is keen to establish expertise.

Genomicists take a global approach to studying gene function, making use of powerful new technologies that can monitor the expression levels of entire genomes simultaneously in single cells or determine the array of protein complexes present in cells of different types; they also make extensive use of computational methods to mine the vast arrays of data that result from genomic sequencing projects or other genomics experiments.

A major theme of the recent past has been building bridges with other

groups of biologists with related interests. We believe that the increased integration of the biological sciences requires a more collaborative approach to research and teaching than was needed in the past. Several of our faculty members have established productive collaborations with ORNL staff members and with biologists in the Nutrition and other departments, and at the UT hospital. Several are active in the Tennessee Mouse Genome Consortium, which unites biologists across the state in a joint effort to understand the mouse genome. Many of us are members and active contributors to the GST program. An ongoing partnership with the CESB led to the recruitment of two of our newest faculty, and a similar, though smaller collaboration with the Center of Excellence in Functional Genomics allowed us to successfully recruit Dr. Venkatachalam.

This spring BCMB and CESB are co-sponsoring a very exciting seminar series entitled "A Structural Approach to Cell Biology". Those seminars will be every Wednesday afternoon at 3:35 and should be of widespread interest to biologists across campus. I expect this theme of blurring lines between previously distinct departments and programs to accelerate as biology continues to become more integrated in the new millennium. 

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In Vivo

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FEBRUARY - MARCH 2003



Seventh Annual "Friends of Biology" Golf Tournament

Thursday, May 1, 2003
9:00 am

Centennial of Tennessee Golf Course
Oak Ridge, Tennessee

See page 6 for details

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