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# ACADEMIC SCIENCE NEWS&REVIEW™

New York Edition

November◆1996

## Meave Leakey: Shedding Light on Earliest Human Origins

by Peter S. Bernstein

Meave Leakey of the Museums of Kenya is interested in the base of the hominid tree. The human family was created when an arboreal, ape-like ancestor split from the family of African apes. Molecular biologists, extrapolating from structural differences between ape and human proteins and the assumption of a relatively constant rate of mutation, estimate that the hominid split occurred some 5-6 million years ago. Leakey's recent finds near Lake Turkana in Kenya, East Africa, are dated about 4 million years ago, pushing the hominid fossil record back towards this shrouded occurrence.

In a talk at the State University of New York at Stony Brook, Leakey described the fossil fragments of a new species of early hominid, *Australopithecus anamensis* (or "southern ape from the lake"). The area around Lake Turkana (which is actually a sizeable inland sea) has yielded many hominid fossils over the last few decades. Currently, Leakey's team has been searching an area southwest of the lake known as Kanapoi, which has exposed sediments deposited by the fluctuating lake levels between 4-5 million years ago. Over the last two excavation seasons, they have discovered several fossils, including hand and arm bone fragments, a complete upper and lower jaw, a piece of the ear region of a skull, and upper and lower sections of tibia.

Many of the fragments resemble those of another species, *Australopithecus afarensis* ( or "southern ape from the afar region of Ethiopia"), whose best-known representative is "Lucy," a partial female skeleton discovered by Donald Johanson of the Institute of Human Origins in 1974 at Hadar, Ethiopia. Lucy was small in stature, had long ape-like arms, and lived 3.2 million years ago; other fossils of this species indicate it already lived several hundred-thousand years before that. Lucy also walked on two legs, as indicated by structural differences between her hip and leg bones and those of apes. Bipeds have adaptations such as concave, socket-like condyles at the knee, and a buttress of flared bone at the bottom of the tibia, in order to support the greater weight that their legs must carry.

Leakey's newly-discovered tibia closely resembled that of *afarensis*, suggesting not only a close relation to that species, but also that this

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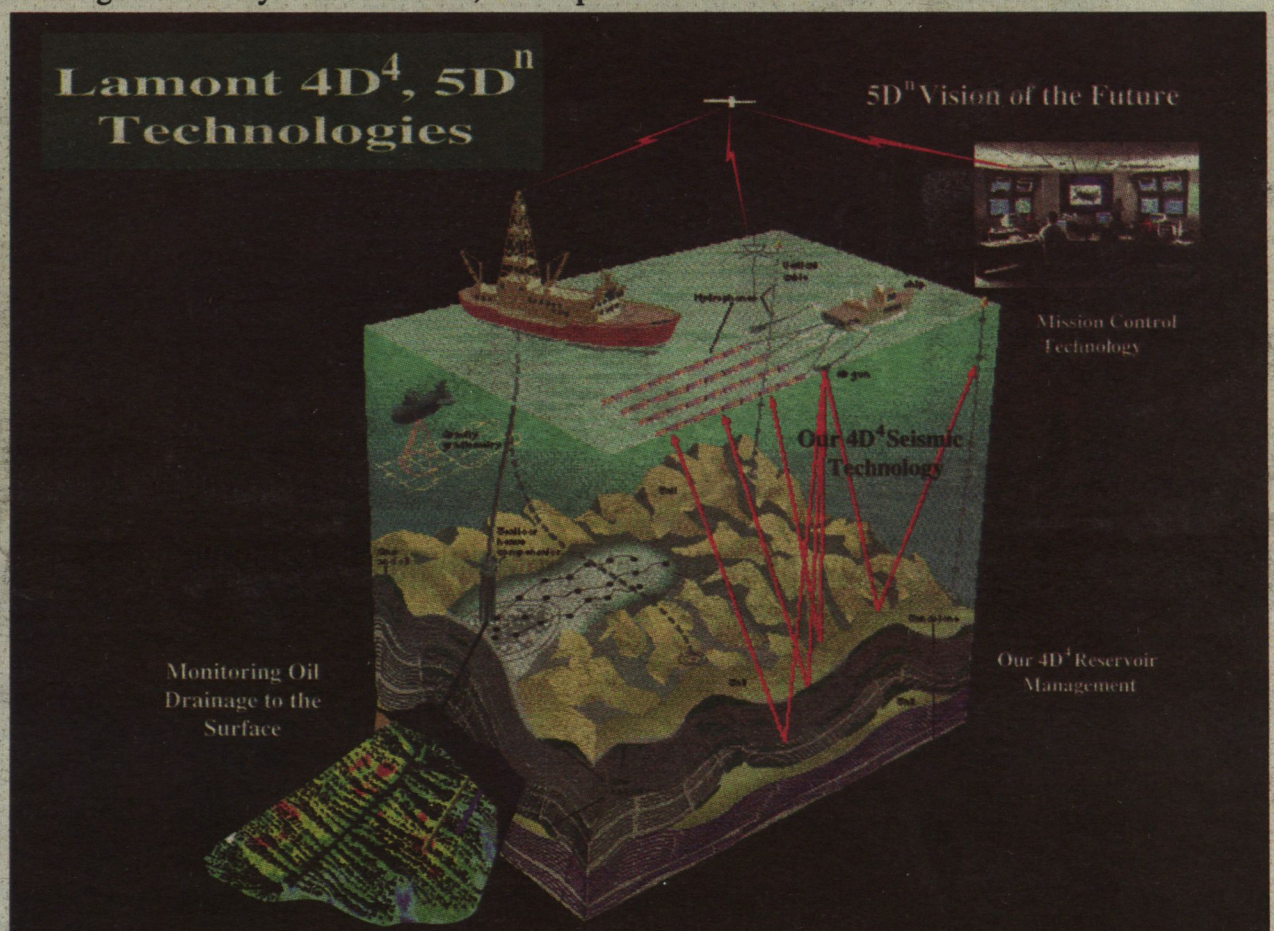
## New Software Allows Geophysicists Virtual Access to Oil Fields

### 4D Analysis Increases Yields from Existing Oil Supply

by Elizabeth Belton, *ASN&R* Staff Writer

Searching for new sources of oil in an increasingly fragile environment may be no longer necessary. New software, developed at the Lamont-Doherty Earth Observatory at Columbia University, transforms seismic wave information into an animated film of an oil pool's journey through rock formations. With the help of this software, oil companies can extract up to 30% more oil from oil fields, allowing for greater exploitation of current oil fields, and reducing the need to search for new ones.




Overview of Lamont-Doherty's Geophysical Software Concept

The software, called "Lamont 4-D Software," was developed by a research team of computer scientists and geophysicists at the Observatory. Funded partly by major American oil companies such as Amoco and Chevron, the research project to develop the software was also funded by a million-dollar grant from the University and a 9 million dollar grant from the US Department of Energy.

Lamont 4-D Software, which can run on an IBM or Sun Microsystems workstation, is some of the most advanced technology available to oil companies. Called four-dimensional because it is an advance over current 3-D software, it includes a "time" factor; interpreting data collected over a period of time and allowing engineers to see what has transpired in the oil field as well as to predict how future oil will course through rock formations.

Oil fields exist in porous layers of sandstone and carbonate. Drilling into an oil field is much like sticking your hand down into a hole and feeling around blindly. Most of the oil in a

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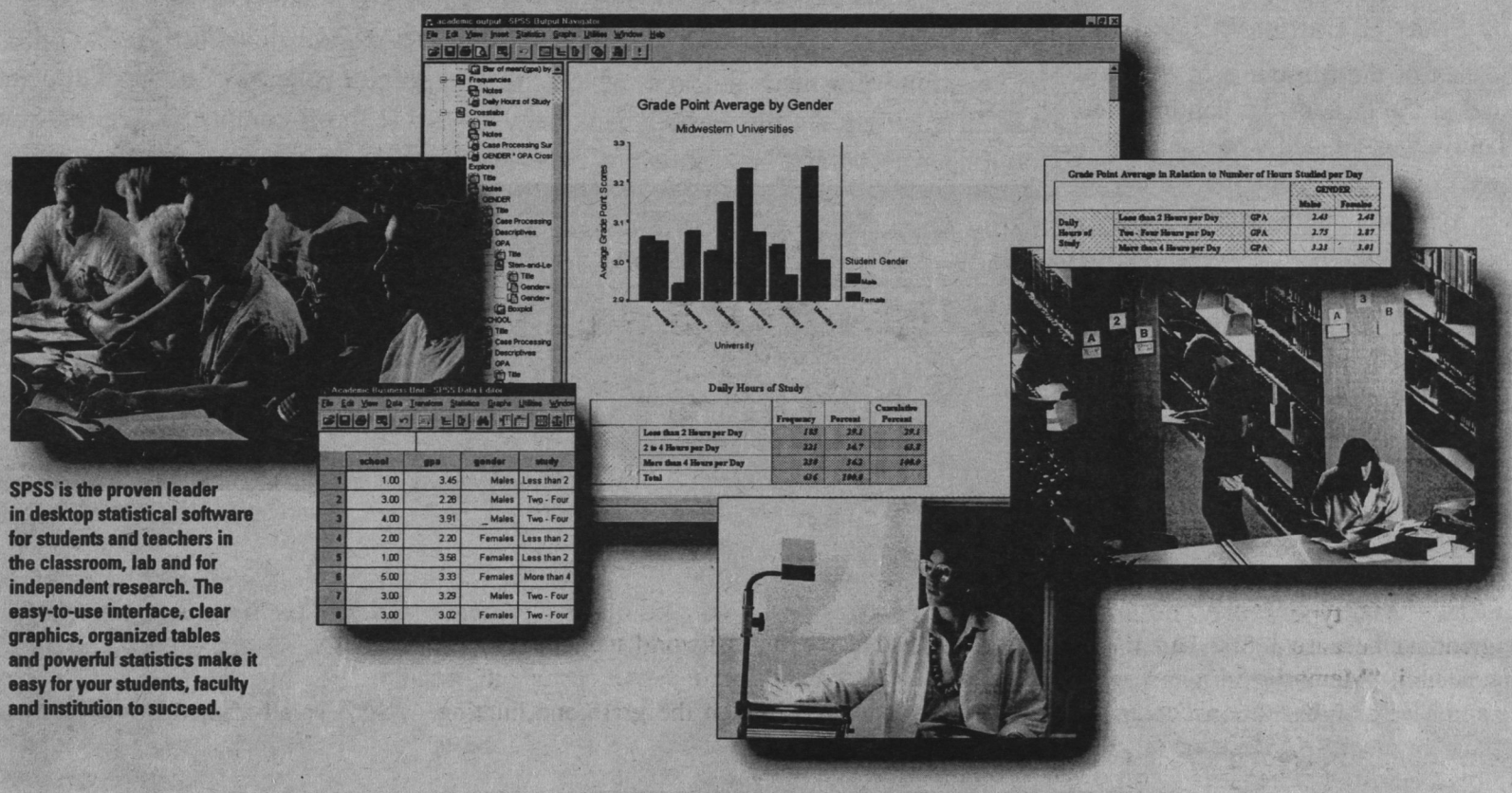


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# NYU Professor Studies Powerful Effects of Olfaction on Memory

## Ursula Stäubli of the NYU Center for Neural Science

by Gretel Schueller

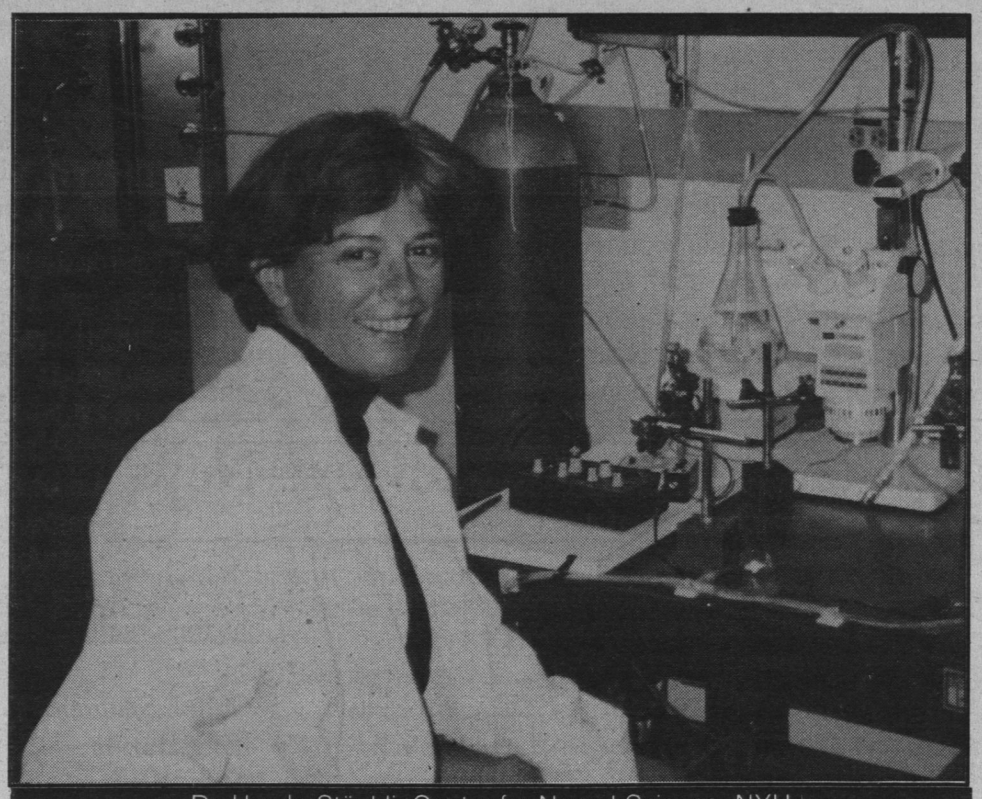
In three pounds of delicate tissue, billions of cells learn from a lifetime of experiences and contain memories unique to each of us. The smell of fresh yogurt is imprinted in Ursula Stäubli's memory. "When I smell a certain type of yogurt, it reminds me of my grandma because I first had it at her house," says Stäubli. "Memories of odors are very long lasting and have a high emotional content."

Smell spurs our memory. Unlike the other senses, smell needs no interpreter—its effect is immediate and undiluted, triggering powerful images and emotions. Smell is associated with so many memories because the nose links them directly to the hippocampus, in the limbic system of the brain, which helps form memories and interprets odors.

Dr. Ursula Stäubli is an associate professor of neural science at New York University's Center for Neural Science. She is the only one in her department, and one of few researchers anywhere, who study olfactory memory to understand how the brain learns. Stäubli studies the memory of smell in rats as a model for learning in higher animals. In general, most memory researchers study visual memory. "This center should be called the Center for Visual Science," she jokes. "It's sexy to be visual because we are such visual animals."

Seventy percent of our body's sense receptors cluster in the eyes. But life on this planet was not always dominated by ocular humans. Smell was the first of the senses. In the primordial seas, odor molecules dissolved into a watery solution absorbed by membranes containing millions of cilia-covered receptor cells in the upper part of the nasal cavity. The receptor cells respond quickly to even subtle whiffs of a scent, firing chemical impulses, which travel by olfactory nerves to the olfactory bulb, or smell center. Over time the sense of smell was so successful that the small lump of olfactory tissue atop the nerve cord evolved into a brain.

As creatures slowly crawled out of the oceans and evolved to see the vast world spread out before them, vision gradually became more important than smell for slinking through the grass and hunting. "The olfactory memory is really a privileged anatomy because it's simple and evolutionarily very old, older than sight," explains Stäubli.



Dr. Ursula Stäubli, Center for Neural Science, NYU

Because the basic design of olfactory memory is simple compared to that of sight, studying it can provide a lot of information about the biology of memory, she says. She compares olfactory memory and the brain with an engine in a tractor. If you start fiddling with a Ferrari, it's going to be hard to understand because of all the details and specializations. You don't know what's important and what is not. If you look at a simple tractor, it's basic, no frills. You can understand more easily what the important thing is that makes it work," explains Stäubli. In the same way, understanding the brain is easier when starting with the simpler olfactory system.

A small-framed woman dressed in jeans and a sweatshirt with a perpetual tan, a shining smile and a sing-song Swiss accent, Ursula Stäubli could be mistaken for a student or a downhill slalom racer (a trophy is hidden in the corner of her office). But she is serious about her work—even if it was the thought of Paris in the spring that ignited the spark to study behavioral neuroscience.

As a teenager in Switzerland she wanted to be a veterinarian, but soon decided that she didn't just want to take care of the "birds and cats of old women." An interest in biochemistry followed. "I wanted to learn what was inside a cell. That fascinated me—all the little parts, the organelles, the mitochondria" she says. At the University of Zurich she began her studies in biochemistry, but switched to biology—I almost went into entomology," she remarks with a touch of horror at the thought now. Luckily, that spring, one of her professors had a friend in Paris who was looking for a student to work in his behavioral neuroscience lab. Stäubli jumped at the chance. Her research has since taken her to McGill University in Canada for two years and the University of California at Irvine for eight. For the past three years she's been busy at NYU.

The human brain, with its billions of neurons, is one of the most complex objects in the known universe. We carry it around in a box on our shoul-

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# The Medical Trainee: Still Awake After All These Years?

by Douglas G. Adler, M.D.

Young physicians, like myself, fresh out of medical school and in residency training programs, are known as house officers. A typical house officer works, on average, eighty to one-hundred hours per week. For most, the work day begins before seven in the morning, and it is only the quick and efficient doctor who can sign out to the on-call team of doctors before seven that evening. As for weekends, well, the patients are still in the hospital on weekends, and thus still need looking after. Usually, house officers come in to work on one or both weekend days and stay until the middle of the afternoon. Also, depending on the rotation, a typical house officer spends every third or fourth night in the hospital as a member of the on-call team, admitting patients and handling problems that arise with patients already in the hospital. Some surgical training programs have the house officers take call every other night.

Needless to say, this sort of schedule can wear down even the most eager of young physicians. Fatigue becomes a constant companion, six hours of uninterrupted sleep starts to feel like manna from heaven, and a candy bar from a vending machine often functions as lunch.

It didn't take me very long to start to question the system and wonder if there wasn't a better way. The paradoxes of the system were readily apparent. Why, I wondered, are the doctors with the least amount of training left with the maximum amount of minute-to-minute responsibility? If hospital inpatients are so sick that their private physicians couldn't manage their cases at home, why are mere trainees left in charge once these extremely ill people arrive at the hospital? Why do house officers have to go so long without sleep? Wouldn't it make more sense, I have thought many an evening as I am awakened from sleep by my beeper, to have the front line of doctors in the hospital well rested so that they could make decisions with a clear head?

While books such as *Intern, Doctor X,* and, most famously, *The House of God* have sought to highlight the plight of the house officer, the truth behind residency training is somewhat less dramatic. What I feel to be the truth only became apparent to me when I could put some emotional distance between my feelings about the work and what the work really means and is for.

While junior house officers do have a tremendous amount of responsibility, they are, in fact, subject to quite a lot of supervision (whether they realize it or not.) Senior house officers review their decisions and both are in turn supervised by senior staff physicians known as "attendings." All documented notes in patient charts, medication orders, and instructions to nurses are checked over, even if in a cursory fashion, at least once a day. But, by being the first person called as problems arise, junior house officers learn, of necessity, to take charge and make vital from-the-hip decisions.

**At 3 a.m. as the young doctor runs to an emergency with a stethoscope in one hand and a chocolate bar in the other, is there a "take-home message" that he or she must come to learn?**

Patients are often hospitalized not because the outpatient M.D. "fouled up" or "got in over his head," but rather because the hospital offers care around the clock, which even the most dedicated physician in private practice cannot provide. For most patients, being under the care of a doctor who might only be weeks out of medical school is far superior to trying to manage a difficult illness, which might suddenly worsen, at home. Plus, hospitals also offer 24-hour nursing care, which is often critically important to the recovery of the patient.

As for the long hours house officers must work, there are two schools of thought. The cynical view (and one that I once held) is that, since house officers are paid a flat salary, financially it is in the hospital's best interest to work them the maximum number of hours, thus milking the house staff for all they are worth. They could, after all, hire more residents to cover the necessary work. Many a young doctor has felt no less than swindled when a good look at any paycheck stub prompts a recalculation of their wages on an hourly basis. Most discover that they earn less than five dollars an hour, comparable to what one might make flipping burgers at the local fast food emporium. Not a pleasant realization to someone who has most likely gone deeply into debt just to attend medical school in the first place.

A more philosophical view of things leads some to ponder whether there is some deeper meaning to the hundred-hour weeks and thirty-six hour shifts. At three a.m. as the young doctor runs to an emergency with a stethoscope in one hand and a chocolate bar in the other, is there a "take-home message" that he or she must come to learn, in addition to all the required facts and formulas, before residency ends?

Eventually, I came to understand and accept that medicine is a 24-hour a day job, and that academic hospitals, especially in the current downsized climate, will not hire more residents. When five p.m. arrives the sick do not simply get better and go home to watch the evening news while they eat their supper. I realized that we, the house officers, are there to watch over the patients no matter what the hour. A patient's situation can turn for the worse at any time, and someone has to be there to take care of it. I realized that I was that person. The buck stopped with me. If I had not internalized that one lesson at some point in my training, all my years of study would have been for naught.

Medical training is designed to be neither fun nor easy, and I'm the last person in this world that I would have expected to defend some of its most unpleasant facets. It is meant to convert recent medical students into capable physicians in a small number of years. To do so, tradeoffs have to be made. A thirty-six hour shift is eminently worth the hassle if it prompts realizations that will affect the way I practice for a lifetime. I still hate being up all night, skipping meals, and being paid minimum wage, but I understand why I'm doing it and what it's doing for me.■

*The author is a house officer training in internal medicine in Boston, Massachusetts.*


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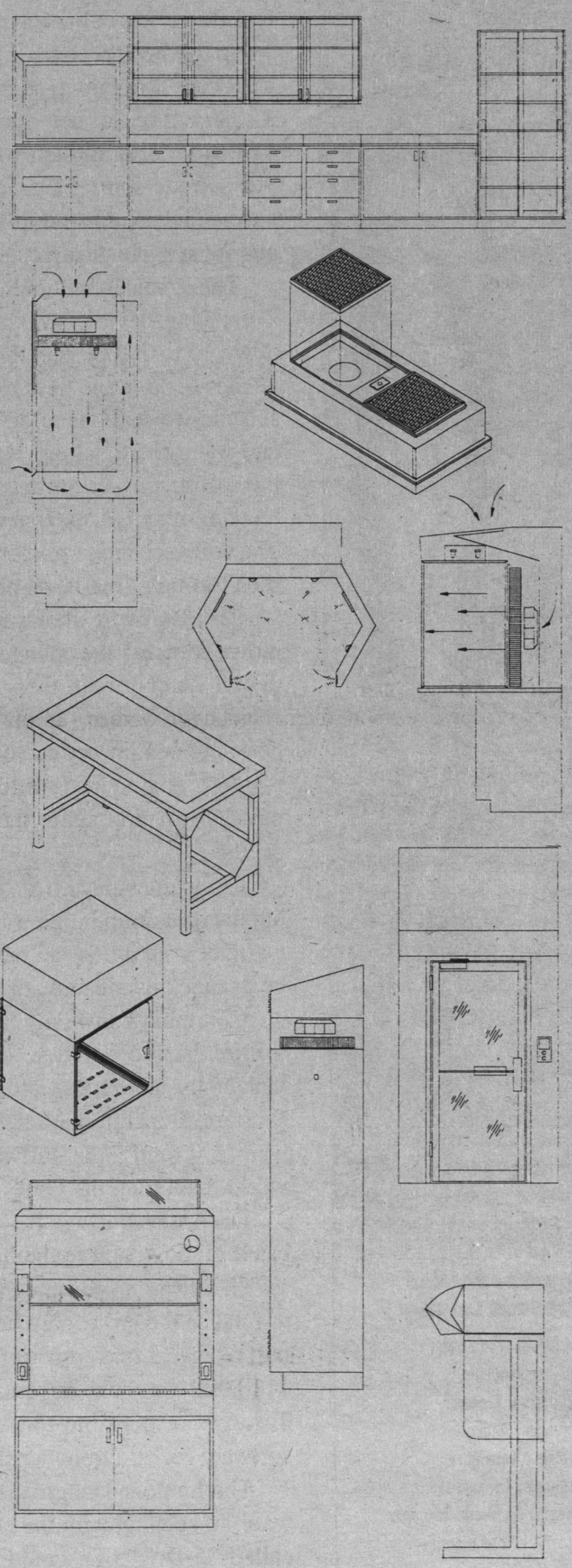

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field is left behind after drilling ceases, because it is impossible to see or predict blockages, or to see what is happening down in the field while the oil is being drained. Although engineers have been conducting seismic testing for years, the new 4-D software promotes greater depth in understanding the life of an oil field.

"We always had an idea that gravity was controlling oil and gas," says Dr. Roger N. Anderson, a geophysicist who is Director of Petroleum Technology Research at the Observatory, and the head of the research team that developed the software. "Instead, it turns out it's all embedded in porous rock, and the path that the oil takes to get to the well is tortuous because there's more of a gravity drive... There's much more oil in fields, but since oil fields in Alaska and places are environmentally difficult to get to, you can get more of what you have already."

In 1993, The Department of Energy started the Dynamic Enhanced Recovery Program to study ways to cut energy costs. "The Program held a competition for new ideas, and we applied for it," Dr. Anderson says. "We won, even though we had the highest-costing project." Over three years, Anderson's team worked to use imaging techniques to incorporate a time factor into studying oil fields. The resulting software is the latest and most sophisticated step in seismic testing.

The first step in looking at an oil field is to create sound there. Using a listening device, similar to Navy sonar equipment, engineers reach down 15 to 20,000 feet through rock layers, to reach the oil fields. They create sound in the field by banging a hammer or using an airgun. These seismic waves bounce off the rock layers and record data about the oil and water there, taking "seismic snapshots" over a period of time. After the seismic waves are recorded, the profile is transferred, either by sattelite or other means, to a workstation running the Lamont 4-D software. The software then transforms the data, recreating the oil field as though seen through time-lapse photography.

"The software shows a cube of earth. It makes an animated film or movie showing the changes in acoustic properties, so you can see where the oil was between then and now," Anderson says. The seismic waves cause hydrocarbons in oil to appear as "bright spots" on the animation; petroleum engineers can also study the animation to determine the temperature and acoustic information from currently producing oil wells, past information about the well, and any potential changes which may occur.

Companies have been using 3-D technology for the past ten years, but the turnaround time was slow to interpret the data. With the new software, depending on the method of transference, the turnaround time can be as quick as a couple of days.

Columbia University has been granted two patents for the software; a third is under review at the US Patent Office. On October 4, the University announced the new software and stated that it had granted Western Atlas International, Inc. a world-wide license to market the software. Currently, the software is being used in 35 oil fields around the world, including the Gulf of Mexico and the North Sea.

Dr. Anderson says that Western Atlas will target the more sophisticated oil companies which have 3-D software, and thus have the necessary hardware to run the technology. Oil companies which gave money to finance the project are being issued free beta tests of the software, and will receive a free copy of the final product. The software alone will cost $120,000 for new buyers. 4-D Technology, a company in Houston, Texas, is responsible for sales, and providing software training on the software for additional cost.

The Lamont-Doherty Observatory is currently envisioning new software. In keeping with the rapidly advancing field, the software would be called "5-D." "5-D would exist in a command-and-control format, so you could run an oil field like you run a battlefield," says Dr. Anderson. Engineers or scientists could view the seismic "snapshots" at workstations as the information is being recorded, in real-time. "You could see it as it actually happens."■

# IN THE Spotlight

## Robert Pollack
Biological Sciences, Columbia

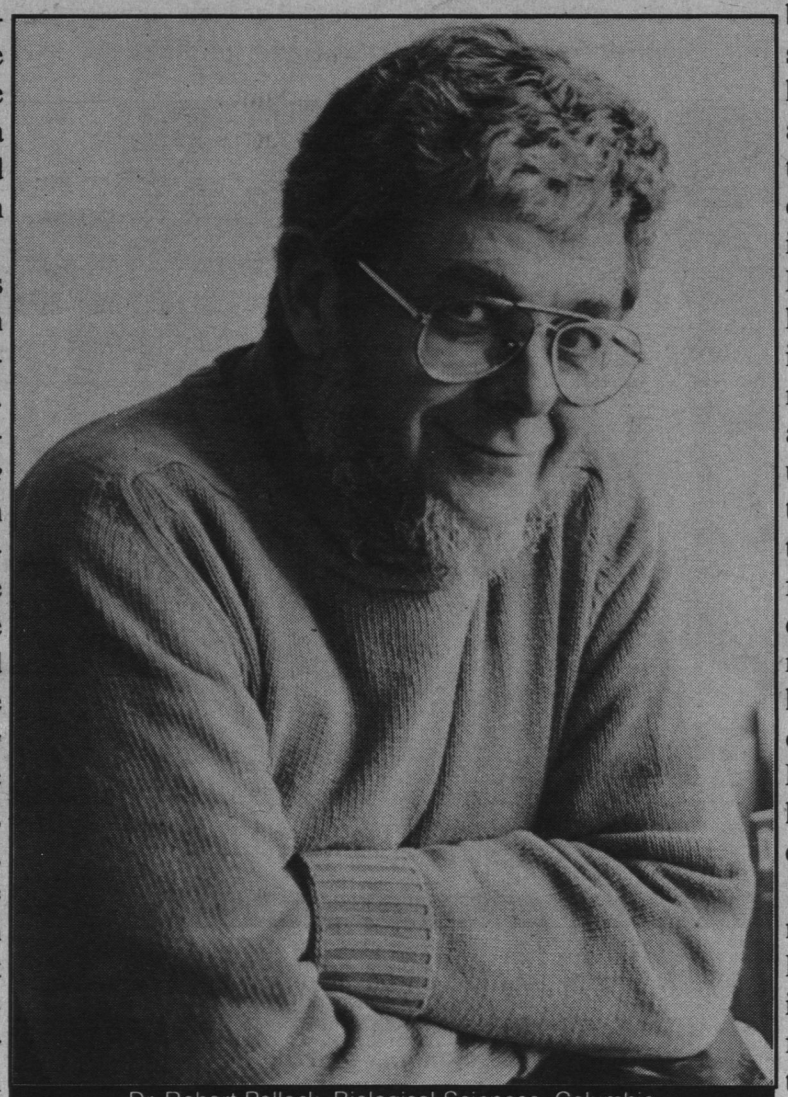
# Meditations on Molecular Biology: Reading the Human Genome as a "Text"

by Alan Packer

Robert Pollack, Professor of Biological Sciences at Columbia University and former dean of Columbia College, describes himself as being in "the third stage of a scientific career—life after the grant." At a time when each week brings hundreds of new journal articles in the fields of molecular, cellular, and developmental biology, and each year brings the establishment of new journals that fill the libraries and the databases, it is rare to find a scientist who is willing to step back and reassess the state of his field and his own place in it.

Dr. Pollack's unease with certain aspects of contemporary biology has its origin in some of the driving forces behind the fast-paced molecular era of life science research. One such aspect he refers to as "triumphalism," or—as described in *Signs of Life: The Language and Meanings of DNA* (Houghton Mifflin), his eloquent meditation on molecular biology and the broad implications of the Human Genome Project—the view of the living world's DNA as "a vastly complicated set of molecules from which laws may be derived, personality traits decoded, or new ways found to 'measure the precise genetic makeup of children.'" The second aspect, which is related to the practice of science, was addressed recently at a George Washington University symposium on "Science in Crisis at the Millennium," at which he remarked that "low morale (in science) is not a matter of too little money, nor of too few ideas, but of too little kindness and decency; it is a failure of custom and manners, a loss of special purpose, a diminution in the ability or the will to distinguish right from wrong and then to act rightly."

Although these concerns are not new to his thinking, his career path until recently has been a fairly conventional one. He was a Columbia College physics major who turned to biology as the molecular biology of the gene was beginning to be elucidated, eventually earning his Ph.D. for work on bacterial genetics at Brandeis University. At New York University, Cold Spring Harbor, and later at Columbia, he has worked at the interface of virology and cancer biology, specifically on the mechanisms of SV40-mediated transformation. His loss of enthusiasm for the life of the "funded scientist in mid-career" was due largely to the subordination of science to the process of grant writing, and the consequent loss of morale, trust, and most of all, the sense of community that he feels was more apparent a generation ago. Such scientists, Pollack writes, "become—not by design, but by default—people whose morale cannot be anything else but a linear output of funding input. When such a person's lab funding stops for any reason, morale has no back-stop; intellectual rigor, good character, broad knowledge base, sense of place in society, and sense of historical irony, are all absent, completely without power or utility to help."



Dr. Robert Pollack, Biological Sciences, Columbia

And so, a few years ago, after closing his lab, he began to carve out a new career as a scientist, one that he says has been a "morale-booster." This career involves continuing to teach both undergraduate and graduate students in courses on evolutionary and environmental biology, the molecular biology of disease, and an introduction to science for non-scientists. He also advises Applied Microbiology, Inc., a small biotechnology company working to develop new antibiotics and dietary supplements, counsels students on career choices, and, finally, writes about the potential consequences of research in human genetics for society at large.

*Signs of Life,* the writing of which was supported by the Guggenheim and Sloan Foundations, among others, has been called "the most distinguished book about science I have seen so far this decade," by Horace Freeland Judson, author of the classic history of molecular biology, *The Eighth Day of Creation.* In a recent conversation in his office on the Columbia campus, I had the opportunity to ask Pollack about some of the issues raised in *Signs of Life* and about his current work on a new book.

The central theme of *Signs of Life* is that the human genome is a text. This implies not only the obvious point that DNA is an information carrying molecule, but that its meaning, for both basic biology and for medicine, is neither simple nor entirely predictable. This view, he says, owes something to the work of literary theorists. "If one thinks of DNA as a text, not just metaphorically, but actually, one can ask the question about its knowability in the same way my colleagues in the English department were asking about the knowability of texts," he says. "Their answer in literature became my answer in science, medicine, and ethics; that is, it's knowable to an extent, but not perfectly." The ultimate unknowability of the genome is due in part to the basic biological fact that the readout of the genome via gene expression and protein function is context-dependent. "When sets of genes combine to become the bodies and minds of intrinsically unpredictable people," he writes, "the complete and final meanings of these sets cannot be fully captured." For Pollack, the indeterminacy of the genome has implications for many areas of biology, ethics, and public policy.

First among these is a new emphasis on molecular biology as an historical science. Pollack notes that "most colleagues of mine in molecular biology have not absorbed the fact that the genome is an historical text written by natural selection from common origins, and that therefore the loss of a species is the loss of information for molecular biologists." He agrees with Princeton molecular biologist Shirley Tilghman, who commented recently that the Human Genome Project has lately garnered overwhelming support from biologists due to the ongoing sequencing of the the genomes of model organisms, thereby energizing the fields of comparative genomics and molecular evolution. Pollack is particularly enthusiastic about the recent sequencing of the genome of a methanogen, Methanococcus jannaschi, which has led to the discovery of striking and unexpected similarities between the Archaea and eukaryotes. Rather than sequencing only one, supposedly canonical genome, this approach looks for "recurring patterns in the histories of genes," in the words of University of Illinois microbiologists Gary Olsen and Carl Woese. Developmental and evolutionary biologists are already taking advantage of sequence comparisons to identify genes that have been conserved over hundreds of millions of years of evolution,

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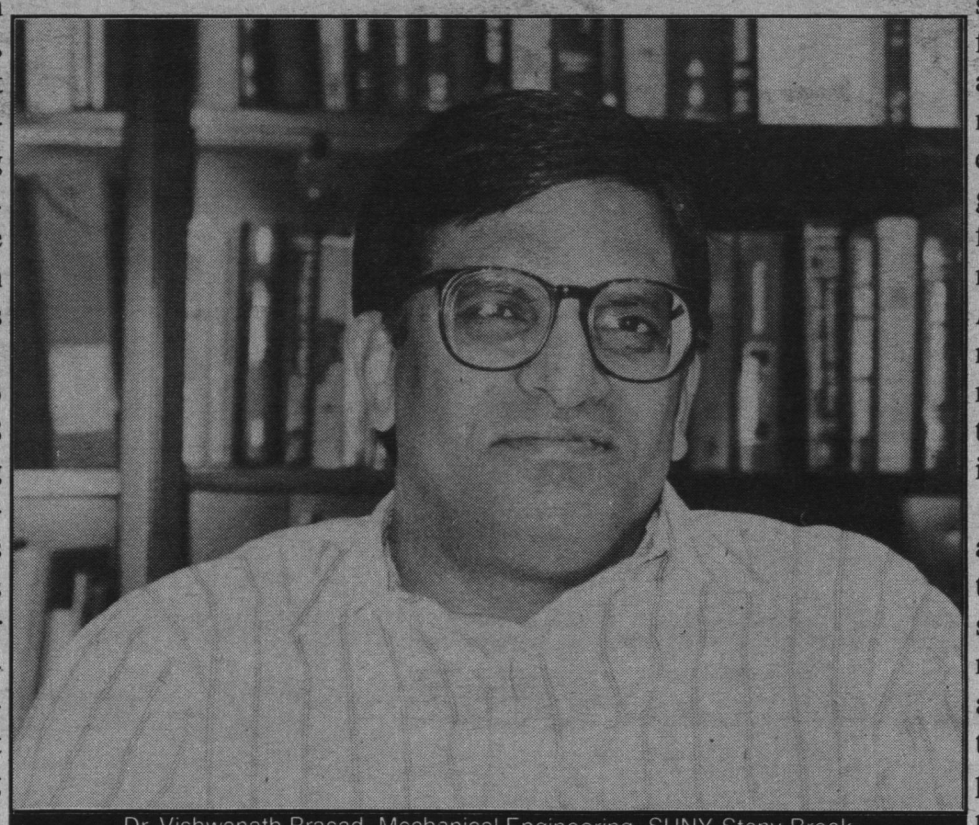
# Building a Bigger, Better Crystal

## New Understanding and Methods in the Quest for Improved Integrated Circuits

by Gretel Schueller

Nanotechnology may be the wave of the future, but Vishwanath Prasad is working on how to grow one of the electronics industry's integral components bigger. "All electronic devices are built on crystalline wafers," says Prasad, professor of mechanical engineering at Stony Brook University. Like studs in a wall, these minuscule chips are the building blocks of pretty much any electronic tool nowadays from computers and CD players to lasers and optical sensors. As these machines grow smaller, faster, and more powerful, so do the chips. Computer chips can be as thin as 500 nanometers—one billionth of a meter—and are cut from single silicon crystals. "At that scale, you want the wafer to be the best quality," he says. "The growth of single crystals is the critical beginning step for building electronic devices. So you want to have the crystal in the purest form. And high yield and high performance manufacturing requires large diameter crystals."



Dr. Vishwanath Prasad. Mechanical Engineering. SUNY Stony Brook

Thirty years ago, crystals were 3 inches in diameter. Now they're 8 inches—and engineers are pushing for 12 inches. "The bigger the substrate, the better the chip," explains Prasad. More substrate and thus less wire means a faster machine. So far there's been no success at the commercial level to create 12-inch crystals, but crystal growth research at Stony Brook is certainly becoming bigger.

Last year, the Crystal Growth Research Consortium, directed by Prasad, was awarded a Multidisciplinary University Research Initiative from the Department of Defense. The five-million-dollar grant will support the consortium of six academic institutions to research "Integrated Intelligent Modeling, Design, and Control of Crystal Growth Processes" together with the USAF Rome laboratory and several industries. The group's ultimate goal: to grow a bigger and better quality crystal, more quickly and more economically.

Professor Prasad came to Stony Brook in January 1993, after serving as a faculty member at Columbia University for nine years. A fan of math since highschool, he soon discovered that engineering allowed for more creativity, and "mechanical engineering was the most diverse field." His crystal growth odyssey began while researching aspects of thermal science at Columbia, and it hasn't stopped since.

The same principles are used in understanding crystal growth as the rules that govern the heating system in a home. Predicting water temperature and water flow through a heating system's pipes requires knowing such mathematical and physical concepts as tensile strength and surface tension of liquids, heat transfer, dynamics of fluid flow, turbulence, and stress—all factors which are also needed to determine crystal growth. The meat of Prasad's research centers around the Czochralski Crystal Growth process, one of the most widely used methods of growing crystals. The most common material for growing crystals is the semi-conductor silicon. At scorching temperatures of more than 1,400 degrees Celsius, a silicon crystal is created. A "seed" (a single, small crystal) is lowered into a heated crucible of melted silicon. As the melt flows upward away from the heat source, the fluid cools. Layer by layer, the melt slowly deposits onto the seed crystal and solidifies. As the crystal grows, it is pulled out of the fluid.

Because of the numerous variables such as temperature differences, surface tension, and buoyancy, the actual flow of melt is very complicated to predict. In fact, most of the concepts of physics are at play in this system. Increasing the size of the melting crucible only makes the process even more difficult to predict. The movement of melt, however, effects the ultimate crystal quality. If the parameters are not precisely correct, oscillations in the crystalline structure form. These defects cause the crystal wafers to have non-uniform conductivity. For example, explains Prasad, "convection currents because of heat and capillary reaction are bad for crystal growth." To suppress these detrimental currents, both the seed and the crucible are rotated opposite to each other, imposing a circular flow which cancels out the convection currents.

Growing a bigger crystal requires knowing which parameters to change and by how much. Prasad's work is two-fold: simulated growth and virtual growth. First, the actual growth process is simulated with chemicals and objects whose properties are similar. For example, a water-glycerin mixture replaces the silicon melt, and the seed becomes plastic. (The temperature is drastically lowered.) The experiment takes place at various rotation speeds and crystal-to-crucible radius ratios. Sometimes thermochromatic liquid crystals are added to see the temperature field and flow structure. A videocamera records all the details.

Since the variables constantly change and simulated experiments have room for error, Prasad and his team then do the simulations numerically, investigating effects of different parameters. The hum of computers greets you when you enter what Prasad calls the "process animation" lab. A display of red, green, blue, and yellow swirls moves across the computer screen— streamlines that show the flow of crystal melt. "It's a process animation of many simultaneous mathematical and physical processes," he says. "A virtual crystal growth." Other computer screens are filled with complicated-looking formulas, running from top to bottom. After checking if the virtual growth models fit the simulated experiments, the information is directly transferred to industries. "So the industry benefits right away."

New challenges are constantly arising. As technology moves towards opti-electronics, optical sensors, laser lights, and solar cells, new materials whose optical properties are better than silicon are growing the next generation of crystals. "The push is to go to a narrower and narrower wavelength," says Prasad. Chemicals like gallium arsenide can absorb and transfer light in a thin band of narrow wavelength. Because it's made up of two elements with very different properties, gallium arsenide can grow crystals only under extremely high pressure, typically 10 to 20 atm. Arsenide is highly volatile, while gallium is not. Syrupy-thick, boric oxide is used as an encapsulant to keep volatile gases from escaping the melt. So the effects of gas flow and high pressure are yet two more factors to consider in the total melt flow structure and melt-crystal interface.

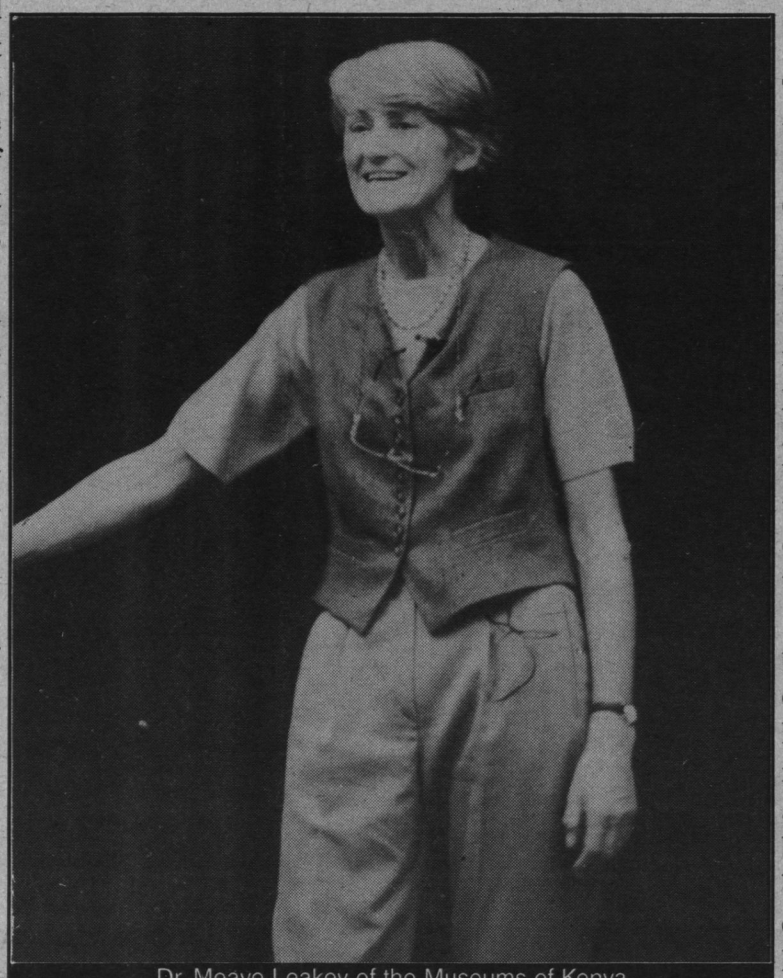
The consortium is, however, working on a process which may just make growing large crystals easier: Continuous Czochralski Growth of silicon single crystals. "Our idea was, why not drop small pellets of silicon in the melt continuously," says Prasad. "Then it can continuously grow, and you dont need large melts. Maybe it will be the answer to the big diameter crystal."

Hard work and a little luck ensure that Prasad and his colleagues will soon be successful in creating the perfect crystal. "I come from India," he says. "We believe in Karma—the essence is that you do your duties. If you keep on doing your duties, the results will come." He adds, "Luck is a big factor too. I have been lucky that I've had a super-bright group of people to work with."■

Continued from Page 1

4.1 million-year-old hominid was bipedal. Prior to this discovery, the oldest evidence of bipedality came not from direct anatomical evidence, but instead from a remarkable trail of fossilized footprints uncovered by Mary Leakey in 1978. The trail was pressed into volcanic ash 3.6 million years ago by three individuals who were clearly bipedal, and are presumed to be *afarensis*.

Although the leg bones resembled *afarensis*', the jaws were quite different, and more apelike, than in previous fossils. The canines of the new find were large, and the teeth were set into parallel rows, forming a 'U' shape much like those of apes. Most hominid fossils show more similarity to modern humans, who have teeth set in the form of an arch, or 'U', with the open end spread wider than the closed end. Both *afarensis* and the new specimens have molars larger and stronger than those of living apes, suggesting a tough grain- or seed-based diet. The cranial section was different as well, possessing a small ear hole. Modern humans and *afarensis* were able to insert a finger into their ears, but this hominid could not have done so. These marked differences from other species in the fossil record persuaded Leakey to classify her find as a new species of early hominid. "Traditionally, *afarensis* has been the base of the hominid line, and this is a step back," said Leakey.



Dr. Meave Leakey of the Museums of Kenya

Researchers studying early hominid fossils have made progress in understanding and classifying these early ancestors, but as in any discipline, questions remain. Early hominids were clearly bipedal, for example, but some controversy exists as to the nature and efficiency of their two legged movement. Some anthropologists, such as Owen Lovejoy of Kent State University, have argued that bipedalism evolved essentially in one step, so that early hominid bipedal locomotion would be nearly indistinguishable from the gait of modern humans. Others, such as Jack Stern and Randall Susman at SUNY Stony Brook, argue that the evidence points towards a more gradual appearance of bipedality. "Many at Stony Brook have argued that there is no question these animals are bipedal, but it's also clear that they retain a lot of features that are consistent with living in trees, possibly sleeping and eating in trees. These include comparatively long curved fingers and toes, and arms built for climbing," said John Fleagle, an anthropologist in the Department of Anatomical Sciences at Stony Brook.

Another issue in contention has been sexual dimorphism. The collection of *afarensis* fossils contains individuals which vary tremendously in size, the smallest estimated to have weighed no more than 30 kg, and the largest about 60 kg. This led several researchers, including Richard Leakey, to conclude that these fossils actually represent two separate species rather than males and females of the same species. Recent probabilistic studies performed at Stony Brook by William Jungers and students Brian Richmond and Charles Lockwood examined the chances that small sample sizes of bones could produce a large size-spread such as that seen in *afarensis*. These studies show that the range of sizes existing in early hominid fossils could come from an animal which displayed as much sexual dimorphism as a modern gorilla. "So it's not unreasonable that it was a very sexually dimorphic creature," said Fleagle.

Evidence suggests that the initial emergence of the hominid lineage is marked by the appearance of bipedality, but not by other traits once considered to be hallmarks of the human lineage, such as tool use and large-sized brains. The brains of the early hominids are not significantly larger than a chimpanzee's, and no tools are found until almost two million years later in the fossil record. Hominid evolution did not occur as a simple progressive lineage, where the traits of modern humans steadily developed in unison. This idea is often depicted by familiar cartoons showing a chimpanzee on the left, a modern human being on the right, and a linear progression of several "intermediate" stages in between. "The fossil record of australopithecines provides direct evidence that the cluster of features characterizing living humans are not inseparably linked, but rather evolved one by one," said Fleagle.

With determination and no small amount of luck, Leakey and her fossil-hunters hope to dig up the evidence needed to complete more branches of the family picture of early hominids, and to understand far more solidly the emergence of modern humans.

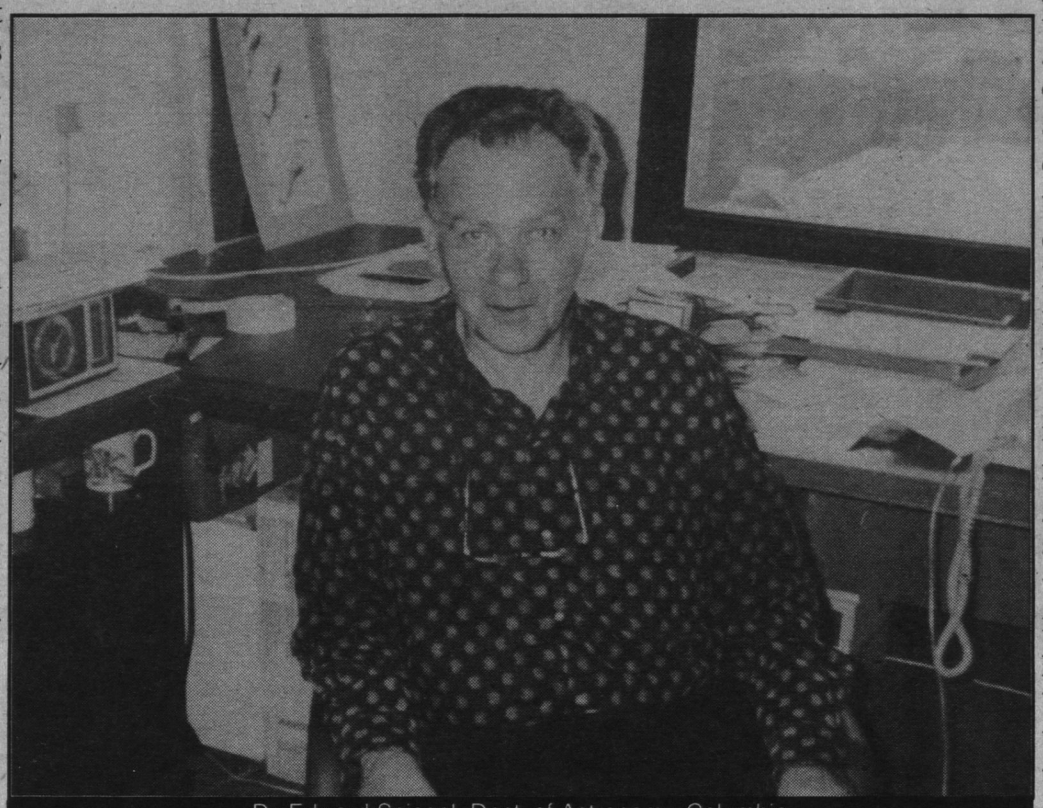
*Meave Leakey is head of the division of Paleontology of the National Museums of Kenya, in Nairobi. She is married to Richard Leakey, son of fossil-hunters Louis and Mary Leakey, whom she met upon joining Leakey's team in 1969. Dr. Leakey's lecture was sponsored by the SUNY at Stony Brook Graduate School and the Paleobiology Study Group.* ■

# Chaos Lives

## Columbia's Dr. Edward Spiegel Explains Why Chaos Theory Still Occupies Scientists

by James L. Ulrich

Whatever happened to Chaos theory? It was once a hot topic of science, and in the late 80's it enjoyed a certain notoriety among the general public, which was introduced to the theory through such popular expositions such as James Gleick' "Chaos" and Ian Stewart's "Does God Play Dice?" Chaos even made the best-seller list, romanticized by Michael Crichton's novel "Jurassic Park," which wove into its plot the exploits of dinosaur-battling chaotician Ian Malcolm. Yet just as the general public began to embrace chaos theory, mathematicians apparently lost interest in the subject. Some mathematicians claim that the popularization of chaos quickened the theory's demise. Yet not every scientist considers chaos to be a fad that has passed. According to Dr. Edward Spiegel, Rutherfurd Professor of Astronomy at Columbia University, it is actually quite alive and well.



Dr. Edward Spiegel, Dept. of Astronomy, Columbia

While Spiegel, commenting on the history of chaos theory, acknowledges that "it is true that a lot of easy and superficial stuff has been done," he views this as a blessing in disguise. A decline in general interest in the theory has left "only the really serious people carrying on. For many of them, the subject is now just getting under way."

And what exactly is chaos theory?

"The word [chaos] is in my view a misnomer, " Spiegel observes. "It's the Greek word for 'gap.' 'In the beginning was chaos,' meaning the void, nothing. Then around the seventeenth century, the word 'gas' was invented, which is a derivative of the word 'chaos,' because gas is a thing without much to it. Then of course, the motions of particles in a gas are very confused. So the modern use of 'chaos' grew out of that. And people latch on to these words."

Yet in mathematical terms, chaos is just another term for dynamical systems theory. Edward Lorenz loosely defines a dynamical system as "a system with a slight amount of randomness." Such systems have been studied in mathematics for centuries. Spiegel notes that "everybody knows the science fiction idea that if you go back in time, step on an ant, and then return to your own time, the world has been totally changed. That's what chaos is about. A slight change can make all the difference in the world, and everybody's known this forever, going back to Jacob Bernoulli (a seventeenth-century mathematician.)

"What's been discovered, though, in recent decades, is that this behavior can be found in very simple equations. It used to be thought that you needed highly complicated systems to get such complicated behavior- the equations of fluid dynamics, turbulent motion. But you don't. All you really need are certain kinds of conditions. Non-linearity is essential. [A non-linear system of equations is one in which the sum of two solutions of the system is not necessarily itself a solution.] That's the main event in chaos. The other thing is that, if you have a solution of a system of equations unfolding in time, and you make a slight change at some point in that solution, you get a new solution. The idea is that in dynamics, you separate the equations from the statement of the starting conditions. So now you have the equations, and you start a solution off at some starting condition. If you take a slightly different starting condition, you get a different solution.

"The question is whether those solutions remain close to each other, or diverge rapidly. If they diverge exponentially, then any slight misstatement of the initial conditions gets magnified by that exponential. Then you quickly fail to be able to predict anything. Our whole idea, going back two or three centuries, starting from Newton basically, was that the only thing that stands between us and predicting anything, leaving quantum mechanics out, was just our inability to solve the equations [of the system whose behavior was to be predicted.] But that's an inability that's intrinsic in the system. If you can't state with infinite accuracy the initial conditions, then your error will be amplified exponentially. That means prediction becomes impossible, even in classical physics. You have a classical analog of the Uncertainty Principle."

Yet it's not just a waste of time to attempt to forecast the behavior of a chaotic system. Spiegel suggests that "you have to change your notion of what forecasting is. You can predict probabilities. You can say where a system is likely to be in its possible range of states, how it's likely to behave. What you can do in the case of things like weather prediction is that if you continually update your input, you probably could predict a day or two. But long range weather prediction is now difficult to do." The difficulty arises from the sensitivity of weather systems to initial conditions.

"This property of sensitivity to initial conditions is shared by many many systems. But the interest is in systems with very few degrees of freedom, simple equations, because then you can begin to understand why it behaves that way [chaotically]. Take the tossing of a coin. People say that's random. But it's not random. Put the coin in a vacuum, and toss it there. We know the equations completely. But if you toss it in a fair way and it's a fair coin, you're going to have a hell of a time predicting what it's going to do. Because the slightest change in the initial toss makes all the difference. Now that's not chaotic, only because the coin toss ends. But if you have a way of reactivating the toss continually, that's a chaotic system. And it's not a random system, but a fully deterministic system."

Chaoticians are developing new approaches for mathematically determining whether a given system is chaotic or not, and for describing those systems which are. One approach involves the study of a system's periodic orbits. An orbit of a system is the path which it traces through its phase space, which in turn is an n-dimensional plot, against time, of the variables of the system. For example, the plot of a system of three variables would be given in three dimensional space. A periodic orbit is an orbit which repeats itself after a fixed period of time. Chaotic systems, it turns out, are replete with such orbits, which however are unstable. "If you put a thing on that orbit, and make a slight error in where you put it, it leaves," explains Spiegel. "When you're on top of a hill, and you push yourself slightly to the side, you roll down. Now these [unstable] orbits are there. They can be calculated. They approximate the true [overall] orbit [of the system.] You can describe [systemic] orbits in terms of these unstable periodic orbits. In fact these objects that you read about called 'strange attractors' can be described as these unstable periodic orbits. We have then a nice formalism for describing what goes on in a chaotic system. It's a whole new mathematical tack being launched on chaotic systems."

This new attack on chaotic systems is already reaping benefits. Indeed, one particularly well-known system turns out to be chaotic -- the solar system. "Nevertheless," Spiegel assures, "it appears to have long term stability. That's the mystery. The chaos is sort of a mild chaos. But that you kind of expect, because we're here."■

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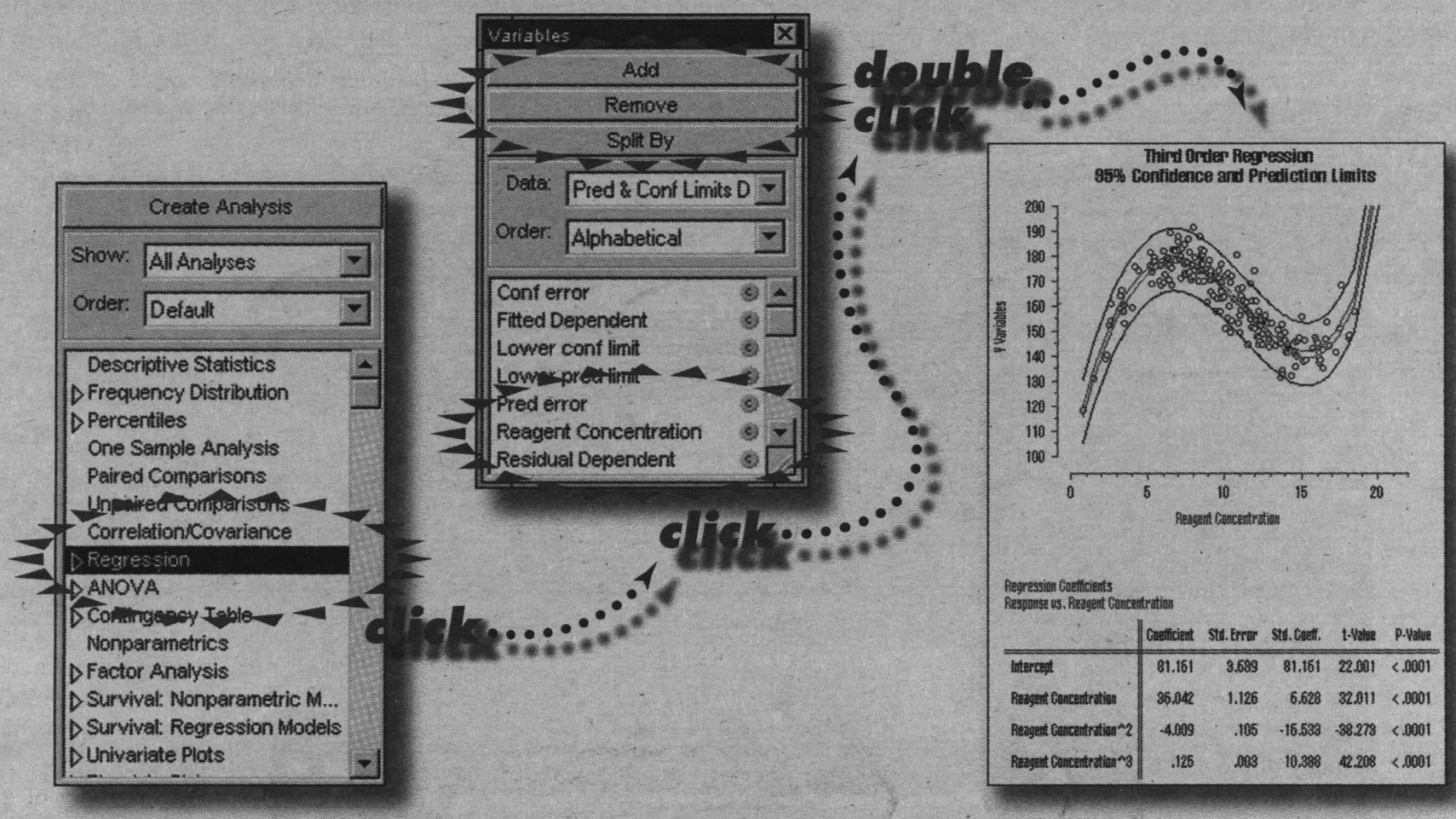


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# An Accessible Cosmic Voyage: Right at the Theater

## The IMAX film "Cosmic Voyage" Shows the Universe in Scale

by Ilana Harrus

"Les deux infinis", or "the two infinities," as the French philosopher Pascal called them, are the infinitely small and the infinitely large. Both fascinate us, for they are the limits of our own imagination. An IMAX movie entitled "Cosmic Voyage," now showing at the American Museum of Natural History, promises nothing less than a visit to these two seemingly unreachable boundaries.

The movie first ponders our subjective perception of scales and sizes and invites us on a journey toward the edge of the known universe. We start our exploration in Venice, Italy, peering at a group of dancers. The camera pulls back to 10 meters above the ground, then 100 meters, then 1000 meters, each time moving one logarithmic step farther than the previous frame. Venice becomes a point on the map of Italy, and Italy a small part of Europe. We soon see the Earth in its totality, and glimpse at the Moon. We pass the solar system, our galaxy, our neighboring galaxies, other galaxies, quasars and finish this outward journey, at the Big Bang, after having gone 26 steps, a total of 15 billion light years, away from Earth. The film zooms back to Earth and starts the exploration of the small scales, ending, after 16 steps, by looking at quarks inside a nucleus.

Aftermath of the Collision of two Spiral Galaxies, from the IMAX Film "Cosmic Voyage" photo credit IMAX Corp & NCSA

If this sounds familiar, it is probably because, according to Bayley Silleck, the writer, director and co-producer of the movie, it is his own remake of the 18 year old movie "Powers of Ten." In this new version special attention has been paid to the computer generated sequences; the stars positions have been derived from actual star maps provided by the Smithsonian Astrophysical Observatory, galaxy formation has been simulated by scientists from Princeton University and the University of Illinois at Urbana-Champaign, and more than 950 hours of computing time on a Cray C-90 were needed to determine the exact location of stars and gas in a spectacular scene showing the collision of two spiral galaxies.

This attention to detail is, however, somehow irrelevant. We are presented with pretty images, and the text accompanying them, although beautifully read by Morgan Freeman, glosses over a large number of open questions thus giving a too-simplified summary of the present knowledge. Some have reduced Shakespeare's work to a 2 hour show; likewise it can be a compelling desire to tell the history of the universe, describe infinitely small scales, the life and death of massive stars, the creation of the solar system, the appearance of life on Earth and evolution (not forgetting the extinction of the dinosaurs), in only 35 minutes. In this case, however, to claim a passion for detail is a little far-fetched. Cutting short of trying to cover the complete range of human knowledge, a true "Cosmic Voyage" would have been more relevant. For example, explaining in which ways the new insights given by the simulations included in the movie were important (they are, after all, genuine scientific results), or on a simpler level, why the journey had to stop at the end of 15 billion light years. Explaining such details would be more enlightening than trying to cover entire sweep of the ever-growing "Big Picture." Unfortunately, this reductionism seems to be the common trend in scientific movies geared towards the general public.

Still, "Cosmic Voyage" will please everyone who enjoys seeing impressive computer simulations, hearing good (although scientifically unjustified) sound effects while wondering over the beauty of the universe. There is, by the way, something not to be missed at the American Museum of Natural History. It is a spectacular exhibition on dinosaurs, located in the newly renovated Fossil Halls. It is a well thought-out, well organized and clearly explained exhibition. Discoveries on display range from the incredible dinosaur eggs, embryos and skeletons found in the Gobi desert in the early 90's by the Mongolian-American Museum Expeditions to the always impressive T-rex skeletons. At each step of the exhibition, a plaster model shows how evolution shaped the species shown, and in which way the change was an improvement over the existing design. This visit will also have you marvel at the beauties of the world.

And there is a movie too.■

*The American Museum of Natural History is located at Central Park West at 79th Street, New York, N.Y. Museum Hours: Sunday-Thursday: 10:00 a.m. to 5:45 p.m; Friday and Saturday: 10:00 a.m to 8:45 p.m. (Closed on Thanksgiving and Christmas Day). Admission: Suggested Museum admission is $8.00 adults, $6.00 students and senior citizens, and $4.50 children. Combined Museum and Imax theater admission is $12.00 adults, $8.50 students and senior citizens, and $6.50 children. Free Tours begin at 10:15 and 11:15 a.m., and 1:15, 2:15, and 3:15 p.m. Meet at Hall of African Mammals, 2nd Floor. Ask at the information desk for specialized tours and schedule for sign-language tours.*

*"Cosmic Voyage" is shown daily in the IMAX theater at 10:30 a.m. and 12:30, 2:30, and 4:30 p.m. On Friday and Saturday evenings, it is shown as a double feature at 6:00 and 7:00 p.m. with the IMAX film ``Stormchasers", a movie about meteorology.*

*For general information, call (212)-769-5100. Information at that number is also available in Spanish. On the internet: http://www.amnh.org*

Continued from Page 3

ders—inconvenient for research. But thanks to new technologies to see inside living brains and examine brain functions at the subcellular level, more has been discovered about the brain and the storage of memory in the past ten years than in all previous history. Recent developments in imaging, for example, have opened a window to the brain's architecture and functions. The body receives information at the "periphery"—the neuroscientists' word for everything that is not the brain—and encodes it as nerve impulses. Neurons, the network communicators of the brain, send and receive electrochemical signals in mere thousandths of a second across synaptic connections. The synapse between sending and receiving neurons is so small that it can be seen only with an electron microscope. Electrical impulses are sent by squirting neurotransmitter chemicals across the synapse, causing receptors to open. Brain fluid and its sodium ions flow through the channel. When enough ions swim in, the receiving neuron fires its electrical impulse to another neuron down the network. This electrochemical process is the basis of brain communication.

"The brain is closest to a supercomputer, but way better than anything existing now," says Stäubli. It is a jumble of electrical circuits—one square millimeter of cortex, the crinkly surfaced dome of the brain, contains 80,000 brain cells, making it the most complex electronic circuit board on Earth. What is amazing about this super computer is its plasticity—the brain's unexpected ability to increase its memory capacities without adding an extra hard drive. For Stäubli, the most promising model describing how memory is stored in the brain is Long Term Potentiation. LTP is an increase in the strength of connections between neurons (across synapses) that occurs when brain circuits generate and repeat certain rhythmic patterns of activity. Stronger connections among the brain's billions of neurons mean a better-functioning brain. Using LTP, the brain can essentially rewire itself to create memory.

Stäubli calls LTP the "substrate of memory." The more you learn, the more you repeat a particular electrochemical rhythm, the stronger the synaptic connections become and the easier it is for you to remember something. Before you smell a rose, an electrical "learning code" is sent telling each cell to "remember" whatever immediately follows.

The scent of your first prom date, the comforting smell of your childhood blanket are both biochemical phenomena stored as ethereal electrochemical codes in the synapses of different parts of the brain. "Memory is stored in many different places. Memory is not just a video that you replay, its stored in different places because they're different aspects to a whole memory, says Stäubli. When you talk about memory, people have this strange idea about what memory is, as if it were some monolithic sort of thing. But it's not."

Stäubli's lab is one big study of memory at different levels. The rooms are filled with oscillometers, amplifiers, dangling wires and electrodes, computer screens and printouts with patterns resembling the rhythm of a heartbeat, all to measure the waves of electrical activity in specific areas of a rat's brain. There are also microscopes to examine brain slices and video cameras to study behavior. Black and white patched rats wearing electrode grid caps scurry around in cages.

At the multicellular level, Stäubli and her team of doctoral and undergraduate students look at the neuronal activity in the hippocampus of rats as they process smell information. "Rats are very skilled at learning olfactory cues. They can learn many smells very quickly and they can remember them for a long time," explains Stäubli. If you want an animal model to help understand learning, it should be a model with properties similar to human memory. Rapid acquisition, high capacity and persistent memory traits are three important properties for memory that humans also have.

The rats' electrode hats connect to their hippocampus, measuring the neuronal activity. In "nose poke" tests, the rats learn apple versus woody aromas. The smells squirt out from holes in varying sequences and positions that the rats must learn to recognize and remember in a classical conditioning paradigm. Each time the water-deprived rat's nose pokes the right hole, he's given a water reward. As the rat learns to remember the sequence of sprays, the pattern of neuronal activity in the brain is altered in specific ways.

The electrodes going into the rats brain record 30-60 neurons at one time. That in itself is a big technological step. Until recently, researchers could only record from one neuron at a time. "One cell by itself is meaningless," says Stäubli. "Memory is stored in a whole ensemble of cells that interact in a meaningful way. If you have one electrode looking at one of these hundred cells you're not going to get the picture. It's like going to the museum and you have this big picture, but you only see this little part—everything else is covered. How are you going to get the whole picture by looking at one thing at a time?"

Stäubli's work is dependent on technological developments, especially with computers. "We could have never done what we do now five years ago, but with the present storage capacity we can analyze and record on-line," she says. "We have made many advances—at least in techniques—I don't know whether we've made any advances in what we know about the brain." She laughs, "Technically, we can do a lot more."

But Stäubli has made real advances. "She has had a remarkable string of successes," says Dr. Gary Lynch, with whom Stäubli worked in California and with whom she still continues to collaborate. Her work is very unusual in the field of behavioral neuroscience in that it holds its interest over time. The half-life of hot items in the field is measured in weeks—but Ursula's findings from ten years ago are still avidly discussed, repeated, and extended, says Lynch.

In fact, Stäubli and Lynch have managed to synthesize a class of drugs called Ampakines that greatly increase learning speed and memory retention in rats. The drugs work by causing the channel door of synapses to stay open longer so more current enters a neuron. The more current that travels into a neuron, the more likely it will be that the neuron will fire at the next neuron in line. Stäubli hopes the drug will work to reduce memory loss in mild cases of dementia, such as early Alzheimer's disease. Three human trials conducted in Europe have been successful so far.

More immediate and direct concerns are the never-ending problems of funding, tenure and the necessity to publish constantly. "There is a lot of pressure to publish, a lot of pressure to get grant proposals, to get tenure. I have to have a lot of publications," she says anxiously. "In general it's very hard to get money—we get squeezed from every side." In light of the recent government shutdowns and budget cuts her worries about funding are real.

Sometimes the politics of academia can be frustrating and the never-ending research disappointing. "Sometimes it's hard to keep myself motivated," says Stäubli. But she has ways. "I hope, for example, that the memory drug that we have been working on for many years will actually turn out to be a big thing that will be useful." Stäubli expresses a hope that many scientists share: that their work has some deeper meaning and lasting effect, that it won't become forgotten in some dusty journal. "It's fun to do basic research that is appreciated by your scientific community, but the ideal is to do some sort of earthshaking thing that stays around forever. Everybody wants to do something that makes a difference. I've had a few successes, little ones, not earthshaking, so that keeps me going—intermediate reinforcement I guess."

"My goal is to enhance memory in humans, then I would feel like I had really done something—my time in science has at least led to something useful," she says wishfully. "A lot of people do science and they're lucky if ten years later people still think this was a big deal. So I will be really happy if the drug could work in humans and be used. That would be really nice."■

## A ROLE FOR UROKINASE-TYPE PLASMINOGEN ACTIVATOR IN HUMAN IMMUNODEFICIENCY

Mark A. Handley, Roy. T. Steigbigel, Sidonie A. Morrison

*July 1996 issue of the Journal of Virology, Vol. 70, 4451-4456*

Abstract

Urokinase-type plasminogen activator, uPA, a proteinase which activates plasminogen by cleaving at -CPGRV-, was shown to cleave the V3 loop in recombinant gp120 of HIV-1 IIIB and MN strains, as well as a synthetic, cyclized peptide representing the clade B consensus sequence of V3. Proteolysis occurred at the homologous -GPGRA-, an important neutralizing determinant of HIV-1. It required sCD4, and was prevented by inhibitors of uPA, but not by inhibitors of likely contaminating plasma proteinases. It was accelerated by heparin, a known cofactor for plasminogen activation. In immune capture experiments, tight binding of uPA to viral particles, which did not depend on CD4, was also demonstrated. Active site-directed inhibitors of uPA diminished this binding, as did a neutralizing antibody to V3. Addition of exogenous uPA to the laboratory adapted IIIB strain of HIV-1, the macrophage-tropic field strains JR-CSF and SF-162, or a fresh patient isolate of indeterminate tropism, followed by infection of macrophages with the various treated viruses, resulted in several-fold increases in subsequent viral replication, as judged by yields of reverse transcriptase activity and p24 antigen, as well as incorporation, as judged by PCR in situ. These responses were reversible by inhibitors or antibodies targeting the proteinase active site or the V3 loop. We propose that uPA, a transcriptionally-regulated proteinase which is upregulated when macrophages are HIV-infected, can be bound and utilized by the virus to aid in fusion, and may be an endogenous component that is critical to the infection of macrophages by HIV-1.

## MUTATIONS IN THE C-TERMINAL FRAGMENT OF DNAK AFFECTING PEPTIDE BINDING

Burkholder WF. Zhao X. Zhu XT. Hendrickson WA. Gragerov A. Gottesman ME.

*Proceedings of the National Academy of Sciences of the United States of America. 93(20):10632-10637, 1996 Oct 1.*

Abstract

Escherichia coli DnaK acts as a molecular chaperone through its ATP-regulated binding and release of polypeptide substrates. Overexpressing a C-terminal fragment (CTF) of DnaK (Gly-384 to Lys-638) containing the polypeptide substrate binding domain is lethal in wild-type E. coli, This dominant-negative phenotype may result from the nonproductive binding of CTF to cellular polypeptide targets of DnaK, Mutations affecting DnaK substrate binding were identified by selecting noncytotoxic CTF mutants followed by in vitro screening, The clustering of such mutations in the three-dimensional structure of CTF suggests the model that loops L(1,2) and L(4,5) form a rigid core structure critical for interactions with substrate.

## CHROMOSOME END-TO-END ASSOCIATIONS AND TELOMERASE ACTIVITY DURING CANCER PROGRESSION IN HUMAN CELLS AFTER TREATMENT WITH ALPHA-PARTICLES SIMULATING RADON PROGENY

Pandita TK. Hall EJ. Hei TK. Piatyszek MA. Wright WE. Piao CQ. Pandita RK. Willey JC. Geard CR. Kastan MB. Shay JW.

*Oncogene. 13(7):1423-1430, 1996 Oct 3.*

Abstract

Chromosome end-to-end associations seen at metaphase involve telomeres and are commonly observed in cells derived from individuals with ataxia telangiectasia and most types of human tumors, The associations may arise because of short telomeres and/or alterations of chromatin structure, There is a growing consensus that telomere length is stabilized by the activity of telomerase in immortal cells; however, it is not clear why some immortal cells display chromosome end-to-end associations. In the present study we evaluated chromosome end-to-end associations, telomere length and telomerase activity with the tumorigenic status of human bronchial epithelial cells immortalized with human papillomavirus. Oncogenic transformation was initiated using radon simulated alpha-particles and cells evaluated as primary, secondary and metastatic transformants, The fewest chromosome end associations and lowest telomerase activity were observed in the parental immortalized cells, However, increased levels of telomerase activity were detected in alpha-particle survivors while robust telomerase activity was seen in the tumorigenic cell lines, The tumorigenic cells that mere telomerase positive and had the highest frequency of cells with chromosome end-to-end associations mere also metastatic, No correlation was found between telomere length and the different stages of carcinogenicity.

## MOLECULAR PHYLOGENY ANALYSIS OF FIDDLER CRABS - TEST OF THE HYPOTHESIS OF INCREASING BEHAVIORAL COMPLEXITY IN EVOLUTION

Sturmbauer C. Levinton JS. Christy J.

*Proceedings of the National Academy of Sciences of the United States of America. 93(20):10855-10857, 1996 Oct 1.*

Abstract

The current phylogenetic hypothesis for the evolution and biogeography of fiddler crabs relies on the assumption that complex behavioral traits are assumed to also be evolutionary derived, Indo-west Pacific fiddler crabs have simpler reproductive social behavior and are more marine and were thought to be ancestral to the more behaviorally complex and more terrestrial American species, It was also hypothesized that the evolution of more complex social and reproductive behavior was associated with the colonization of the higher intertidal zones, Our phylogenetic analysis, based upon a set of independent molecular characters, however, demonstrates how widely entrenched ideas about evolution and biogeography led to a reasonable, but apparently incorrect, conclusion about the evolutionary trends within this pantropical group of crustaceans, Species bearing the set of "derived traits" are phylogenetically ancestral, suggesting an alternative evolutionary scenario: the evolution of reproductive behavioral complexity in fiddler crabs may have arisen multiple times during their evolution, The evolution of behavioral complexity may have arisen by coopting of a series of other adaptations for high intertidal living and antipredator escape. A calibration of rates of molecular evolution from populations on either side of the Isthmus of Panama suggest a sequence divergence rate for 16S rRNA of 0.9% per million years, The divergence between the ancestral clade and derived forms is estimated to be approximate to 22 million years ago, whereas the divergence between the American and Indo-west Pacific is estimated to be approximate to 17 million years ago.

## USE OF FOUR MIRRORS TO ROTATE LINEAR POLARIZATION BUT PRESERVE INPUT-OUTPUT COLLINEARITY

Smith LL. Koch PM.

*Journal of the Optical Society of America A-Optics & Image Science. 13(10):2102-2105, 1996 Oct.*

Abstract

A geometric phase analysis is used to show that a minimum of four reflections is required to rotate the linear polarization of a laser beam by an angle 0 < phi < pi, subject to the constraint that the final beam path be collinear with the incident one. Elementary spherical geometry is used to compute a series of beam propagation vectors that give an arbitrary phi rotation and to determine the necessary mirror orientations. The method is applied to the case of phi = pi/2, which is useful for the design of a device needed in our laboratory. The properties of this device and the need for it are discussed in the light of operating experience with halfwave retardation plates used for polarization rotation of CO2 laser beams. (C) 1996 Optical Society of America.

## INFORMATION MEASURES QUANTIFYING APERIODIC STOCHASTIC RESONANCE

Heneghan C. Chow CC. Collins JJ. Imhoff TT. Lowen SB. Teich MC.

*Physical Review A. 54(3):R2228-R2231, 1996 Sep.*

Abstract

Aperiodic stochastic resonance (ASR) is a phenomenon in which the response of a nonlinear system to a subthreshold information-bearing signal is optimized by the presence of noise. We have previously characterized this effect by the use of cross-correlation-based measures. Here we apply a measure (transinformation) that directly quantifies the rate or information transfer from stimulus to response and show that the presence of noise optimizes the information-transfer rate. By considering a nonlinear system (the FitzHugh-Nagumo model) that captures the functional dynamics of neuronal firing, we demonstrate that sensory neurons could, in principle, harness ASR to optimize the detection and transmission of weak stimuli.

## NOVEL MUTATION IN THE MITOCHONDRIAL DNA TRNA GLYCINE GENE ASSOCIATED WITH SUDDEN UNEXPECTED DEATH

Santorelli FM. Schlessel JS. Slonim AE. Dimauro S.

*Pediatric Neurology. 15(2):145-149, 1996 Sep.*

Abstract

We describe an A-to-G transition at nucleotide 10044 in the tRNA(Gly) gene of mitochondrial DNA in a sibship in which the proband died at age 8 years after a severe encephalopathy, a brother died of sudden an unexpected death, and the other six siblings had a combination of symptoms, including apparent life-threatening events and gastroesophageal reflux. This novel mutation was very abundant (>90%) in liver and muscle of the proband and in several tissues, including blood, from his affected siblings (range 91-99%) but was less abundant in blood from the asymptomatic mother (88%) and maternal grandmother (85%). Our findings further enlarge the spectrum of clinical presentations associated with mitochondrial DNA mutations.

## PROLINE-RICH SEQUENCES MEDIATE THE INTERACTION OF THE ARG PROTEIN TYROSINE KINASE WITH CRK

Wang BL. Mysliwiec T. Feller SM. Knudsen B. Hanafusa H. Kruh GD.

*Oncogene. 13(7):1379-1385, 1996 Oct 3.*

Abstract

Arg is a ubiquitously expressed member of the Abelson family of nonreceptor protein-tyrosine kinases, Defining the Arg sequences that mediate its interaction with other proteins is essential to elucidating its role in cellular signaling, In this report we demonstrate that Arg associates with c-Crk, an adaptor protein composed of an SH2 domain and two SH3 domains, and examine the molecular mechanism of the interaction, In vitro experiments revealed that three proline-rich sequences with distinct specificities for SH3 domains are located in the Arg C-terminal domain, just C-terminal to the kinase domain, and that two of these sequences bind to the Crk N-terminal SH3 domain, These two sequences conform to the PsLPxK/R motif that has been observed in other proteins that bind the Crk N-terminal SH3 domain, The interaction of Arg with c-Crk in living cells was confirmed by the detection of coimmunoprecipitation in coinfected Sf9 cells, In addition, increased phosphorylation of c-Crk was observed in cotransfected COS cells, indicating that Crk is an Arg substrate, The site of c-Crk phosphorylation by Arg was identified as tyrosine 221, a residue whose modification has been shown to result in an intramolecular SH2 interaction and a folded conformation, These experiments extend the known Arg protein interacting motifs to include SH3 binding sites and suggest that Arg may function as an effector as well as a regulator of Crk activity.

## EXPRESSION OF MUC2 AND MUC3 MRNA IN HUMAN NORMAL, MALIGNANT, AND INFLAMMATORY INTESTINAL TISSUES

Weiss AA. Babyatsky MW. Ogata S. Chen A. Itzkowitz SH.

*Journal of Histochemistry & Cytochemistry. 44(10):1161-1166, 1996 Oct.*

Abstract

MUC2 and MUC3 are prominent mucin genes expressed in the human intestine. Using in situ hybridization with RNA probes, we examined the cellular distribution of MUC2 and MUC3 mRNA in normal, malignant, and inflammatory human intestinal tissues. In normal small intestine and colon. MUC2 mRNA was expressed exclusively in goblet cells and occurred throughout the entire height of the mucosa. MUC3 mRNA was expressed by goblet and columnar cells but was restricted to the villous compartment of the small intestine and the surface epithelium of the colon. Expression of MUC2 and MUC3 mRNA were both markedly decreased in poorly, moderately, and well-differentiated colon cancers but were preserved in mucinous colon cancers. In ulcerative colitis and Crohn's colitis tissues, MUC2 and MUC3 mRNA expression displayed a normal pattern regardless of whether the mucosa manifested active or quiescent inflammation. These findings indicate that MUC2 is goblet cell-specific, whereas MUC3 is related to maturation of intestinal epithelial cells. In colon cancers, the genetic regulation of MUC2 and MUC3 is different depending on the histological type of tumor. The constitutive expression of MC2 and MUC3 mRNA in inflammatory bowel diseases suggests that these genes may be necessary for maintenance of normal epithelial cell function during inflammation.

## CD40L IS IMPORTANT FOR INDUCTION OF, BUT NOT RESPONSE TO, COSTIMULATORY ACTIVITY - ICAM-1 AS THE SECOND COSTIMULATORY MOLECULE RAPIDLY UP-REGULATED BY CD40L

Shinde S. Wu Y. Guo Y. Niu QT. Xu JC. Grewal IS. Flavell R. Liu Y.

*Journal of Immunology. 157(7):2764-2768, 1996 Oct 1.*

Abstract

The CD40 ligand (CD40L):CD40 interaction plays an important role in the activation of both T and B cells, However, the mechanisms by which this interaction is involved in activation of T cells is still unclear, Here we show that CD40L is not essential for T cell response to TCR engagement if the APC have costimulatory activity, although it is essential for T cell mediated induction of such costimulatory activity, To determine the molecular basis of this activity, we have produced three mAbs that appear to recognize the costimulatory molecules rapidly induced by CD40L. Two of them recognize CD44H, which we showed to have CD28-independent costimulatory activity for T cells, The molecule recognized by the remaining mAb is hereby identified as ICAM-1, Furthermore, ICAM-1-mediated costimulation is likely to serve for a function similar to that mediated by the B7:CD28 interaction, as targeted mutation of CD28 renders T cell responses to Con A more dependent on ICAM-1.

## PRIMING EVENTS AND RETROGRADE INJURY SIGNALS - A NEW PERSPECTIVE ON THE CELLULAR AND MOLECULAR BIOLOGY OF NERVE REGENERATION

Ambron RT. Walters ET.

*Molecular Neurobiology. 13(1):61-79, 1996 Aug.*

Abstract

Successful axon regeneration requires that signals from the site of injury reach the nucleus to elicit changes in transcription. In spite of their obvious importance, relatively few of these signals have been identified. Recent work on regeneration in the marine mollusk Aplysia californica has provided several insights into the molecular events that occur in neurons after axon injury. Based on these findings, we propose a model in which axon regeneration is viewed as the culmination of a series of temporally distinct but overlapping phases. Within each phase, specific signals enter the nucleus to prime the cell for the arrival of subsequent signals. The first phase begins with the arrival of injury-induced action potentials, which act via calcium and cAMP to turn on genes used in the early stages of repair. In the next phase, MAP-kinases and other intrinsic constituents activated at the injury site are retrogradely transported through the axon to the nucleus, informing the nucleus of the severity of the axonal injury, reinforcing the earlier events, and triggering additional changes. The third phase is characterized by the arrival of signals that originate from extrinsic growth factors and cytokines released by cells at the site of injury. in the last phase, signals from target-derived growth factors arrive in the cell soma to stop growth. Because many of these events appear to be universal, this framework may be useful in studies of nerve repair in both invertebrates and vertebrates.

## STOCK STRUCTURE AND HOMING FIDELITY IN GULF OF MEXICO STURGEON (ACIPENSER OXYRINCHUS DESOTOI) BASED ON RESTRICTION FRAGMENT LENGTH POLYMORPHISM AND SEQUENCE ANALYSES OF MITOCHONDRIAL DNA

Stabile J. Waldman JR. Parauka F. Wirgin I.

*Genetics. 144(2):767-775, 1996 Oct.*

Abstract

Efforts have been proposed worldwide to restore sturgeon populations through the use of hatcheries to supplement natural reproduction and to reintroduce sturgeon where they have become extinct. We examined the population structure and inferred the extent of homing in the anadromous Gulf of Mexico (Gulf) sturgeon (Acipenser oxyrinchus desotoi). Restriction fragment length polymorphism and control region sequence analyses of mitochondrial DNA (mtDNA) were used to identify haplotypes of Gulf sturgeon specimens obtained from eight drainages spanning the subspecies' entire distribution from Louisiana to Florida. Significant differences in haplotype frequencies indicated substantial geographic structuring of populations. A minimum of four regional or river-specific populations were identified (from west to east): (1) Pearl River, LA and Pascagoula River, MS, (2) Escambia and Yellow rivers, FL, (3) Choctawhatchee River, FL, and (4) Apalachicola, Ochlockonee, and Suwannee rivers, FL. Estimates of maternally mediated gene flow between any pair of the four regional or river-specific stocks ranged between 0.15 to 1.2. Tandem repeats in the mtDNA control region of Gulf sturgeon were not perfectly conserved. This result, together with an absence of heteroplasmy and length variation in Gulf sturgeon mtDNA, indicates that the molecular mechanisms of mtDNA control region sequence evolution differ among acipenserids.

## SELF-ADJOINT ELLIPTIC OPERATORS AND MANIFOLD DECOMPOSITIONS .2. SPECTRAL FLOW AND MASLOV INDEX

Cappell SE. Lee R. Miller EY.

*Communications on Pure & Applied Mathematics. 49(9):869-909, 1996 Sep.*

Abstract

This the second part of a three-part investigation of the behavior of certain analytical invariants of manifolds that can be split into the union of two submanifolds. In Part I we studied a splicing construction for low eigenvalues of self-adjoint elliptic operators over such a manifold. Here we go on to study parameter families of such operators and use the previous "static" results in obtaining results on the decomposition of spectral flows. Some of these "dynamic" results are expressed in terms of Maslov indices of Lagrangians. The present treatment is sufficiently general to encompass the difficulties of zero-modes at the ends of the parameter families as well as that of "jumping Lagrangians." In Part III, we will compare infinite- and finite-dimensional Lagrangians and determinant line bundles and then introduce "canonical perturbations" of Lagrangian subvarieties of symplectic varieties. We shall then use this information to study invariants of 3-manifolds, including Casson's invariant.

## REPRESENTATION OF CORE DYNAMICS IN SLENDER VORTEX FILAMENT SIMULATIONS

Klein R. Knio OM. Ting L.

*Physics of Fluids. 8(9):2415-2425, 1996 Sep.*

Abstract

The numerical description of slender vortex motion faces several major obstacles: (i) The stiffness induced by the rapid rotatory motion in the vortex core, where peak velocities are an order of magnitude larger than the filament velocity. In a vorticity-velocity formulation, this stiffness is reflected by the singular behavior of the line-Biot-Savart integral as one approaches the vortex geometry. Regularization occurs physically by viscous smoothing of the vorticity. (ii) The vortex core vorticity distribution has a crucial influence on the vortex filament motion. Thus, an accurate description of the core structure evolution due to vortex stretching and vorticity diffusion is necessary. We propose a numerical scheme that allows an accurate description of the effects of axial flow in the core, viscosity and vortex stretching on slender vortex filament motion. The approach is based on incorporating the detailed asymptotic analyses of the vortex core structure evolution by Callegari and Ting [SIAM J. Appl. Math. 15, 148 (1978)] and Klein and Ting [Appl. Math. Lett. 8, 45 (1995)] for stretched viscous slender vortices into the improved thin-tube vortex element schemes of Klein and Knio (1995). The resulting schemes overcome the difficulties mentioned above except for the issue of temporal stiffness, which we leave for future work. (C) 1996 American Institute of Physics.

## THE PRODUCT-MOMENT CORRELATION COEFFICIENT AND LINEAR REGRESSION FOR TRUNCATED DATA

Chen CH. Tsai WY. Chao WH.

*Journal of the American Statistical Association. 91(435):1181-1186, 1996 Sep.*

Abstract

The random truncation model has been considered extensively in the literature. Tsai has noted that many previous results hold under the weaker assumption of quasi-independence between the failure time and the truncation time in the observable region of truncated data. We generalize the Pearson product-moment correlation coefficient to measure the association between both time variables in the observable region. We show that if the failure time and the truncation time follow a truncated bivariate normal distribution, then a zero value of the generalized correlation coefficient is equivalent to the quasi-independence. We propose a corresponding sample correlation coefficient and consider its asymptotic behavior. We also study an application of quasi-independence to truncated linear regression with its asymptotic results. The proposed estimator, stemming directly from the least-squares approach, is computationally much simpler and has a natural extension to multiple linear regression. A simulation study shows that the proposed estimator for regression slope competes well with available nonparametric estimators.

## CIRCUMSTELLAR PHOTOCHEMISTRY [REVIEW]

Glassgold AE.

*Annual Review of Astronomy & Astrophysics. 34:241-277, 1996.*

Abstract

The cooling flows or winds from evolved stars are ideal for the formation of molecules and dust. The main location of molecular synthesis is the outer circumstellar envelope, where UV radiation from the interstellar medium penetrates the envelope and, by photodissociating parent molecules, produces the high-energy radicals and ions that activate gas-phase neutral and ion-molecule chemistry. After introducing relevant observational results and theoretical ideas, the salient aspects of the photochemical model are described. The primary application is to the nearby C star, IRC + 10216, where 50 or more circumstellar molecules have been detected. Recent interferometer maps, with resolution approaching 1", provide the means to verify the main ideas of the model and to indicate directions for its improvement.

## IN SITU DETECTION OF PCR-AMPLIFIED HIV-1 AND EBV NUCLEIC ACIDS IN HYPERPLASTIC LYMPH NODES AND IN AIDS-RELATED LYMPHOMA

Becker JL. Steigbigel RT. Nuovo GJ.

*Journal of Histochemistry & Cytochemistry. 44(10):1085-1089, 1996 Oct.*

Abstract

The purpose of this study was to determine the in situ distribution of PCR-amplified HIV-1 and EBV DNA in hyperplastic lymph nodes and in AIDS-related lymphomas. PCR-amplified HIV-1 DNA was detected, on average, in about 30% and 20% of the CD4 and CD21 dendritic cells, respectively, in and around the expanded germinal centers of hyperplastic lymph nodes in seropositive, asymptomatic people. PCR-amplified EBV DNA was noted, on average, in about 20% of L26 B-cells. The amplified HIV-1 DNA was noted in race non-neoplastic cells in five AIDS-related lymphomas; the other three cases were negative for the viral DNA. Amplified EBV DNA was detected in five of eight lymphomas but in only three of these tissues did the viral DNA localize to the malignant cells. We conclude that although many cells in hyperplastic lymph nodes from people with early HIV-1 infection contain HIV-1 and EBV DNA, these viruses are often absent in the malignant cells of AIDS-related lymphoma. This suggests that although infection by these viruses and the concomitant lymphoid hyperplasia may predispose to lymphoma, the viruses are not required for maintenance of the malignant phenotype.

## CORRELATED MILLIMETER WAVE MEASUREMENTS OF CLO, N2O, AND HNO3 FROM MCMURDO, ANTARCTICA, DURING POLAR SPRING 1994

Klein U. Crewell S. Dezafra RL.

*Journal of Geophysical Research-Atmospheres. 101(D15):20925-20932, 1996*

Abstract

Ground-based observations of stratospheric ClO, N2O, and HNO3 were made almost continuously at McMurdo Station, Antarctica (77.9 degrees S, 166.6 degrees E), during the austral spring of 1994, using two separate microwave receivers. Vertical profiles of these trace gases have been retrieved from the pressure broadened emission spectra between September 4 and October 8, 1994. In early September, McMurdo was located well inside the polar vortex, and high mixing ratios of chlorine monoxide (up to 1.8 ppbv) were measured in the lower stratosphere. Because of vortex movement, later measurements were taken in edge regions, where ClO was found to be quite variable. This vortex movement also provided an opportunity to study relative changes between all three species. Almost no HNO3 was seen below 20 km during the measurement period, indicating that stratospheric air had been efficiently denitrified by polar stratospheric cloud formation. A significant increase of the nitric acid column was observed only around September 20, when McMurdo was closer to the outer edge of the vortex. At the beginning of the measurements, the vertical profiles of the inert tracer N2O had already descended so far that very little N2O was present above 20 km. During the observation period, the N2O distribution did not show strong changes except for a slight downward trend which increased with altitude. This indicates, as noted in previous years, that subsidence continued in the stratosphere over McMurdo Station until at least early October, when measurements were stopped. The temporal correlations between the behavior of ClO, N2O, HNO3, altitude, and temperature at the 50-hPa level, and of ozone measured by local ozonesondes show that changes in the atmospheric composition were partly due to dynamic effects. A backward trajectory analysis

## CLONING AND CHARACTERIZATION OF THE GENE FOR THE SOMATIC FORM OF DNA TOPOISOMERASE I FROM XENOPUS LAEVIS

Pandit SD. Richard RE. Sternglanz R. Bogenhagen DF.

*Nucleic Acids Research. 24(18):3593-3600, 1996 Sep 15.*

Abstract

Two distinct tissue-specific forms of DNA topoisomerase I with M(r) of 165 and 110 kDa have been purified from oocytes and somatic cells respectively of the African frog Xenopus laevis. In this paper, cDNAs encoding a Xenopus topoisomerase I were cloned using PCR primers derived from sequences of yeast and human topoisomerase I. A polypeptide expressed from a portion of the coding sequence was recognized by an antiserum directed against the somatic topoisomerase I that had previously been shown to be unable to cross-react with the oocyte enzyme. Thus, the clone encodes the somatic cell topoisomerase I. An antiserum raised against a synthetic peptide containing the sequence surrounding the active site tyrosine of the somatic topoisomerase I reacts with the enzymes purified from both oocytes and somatic cells, indicating that the two enzymes share some limited sequence homology. RNA blot hybridization showed that oocytes contain an abundant store of somatic topoisomerase I mRNA that is not efficiently polyadenylated in oocytes. This stored RNA contains a consensus cytoplasmic polyadenylation element that is found in a variety of mRNAs that are translationally repressed in oocytes. Microinjection into oocytes of in vitro transcribed mRNA prepared from a Myc-tagged construct of the somatic topoisomerase I sequence is translated to yield a 110 kDa product. This suggests that the oocyte-specific 165 kDa topoisomerase I is not produced by tissue-specific post-translational modification of the somatic topoisomerase I. The oocyte enzyme appears to be produced from a minor mRNA species in oocytes that has not yet been identified.

## COMPARISON OF IODONIUM-PRODUCING REAGENTS IN THE SHIFT REACTION OF A BROMOPROPYNYL ALCOHOL

Djuardi E. Mcnelis E.

*Synthetic Communications. 26(21):4091-4096, 1996.*

Abstract

A variety of iodonium-producing reagents have been compared for synthetic utility in the shift reaction of bromopropynyl alcohol 1 to dihaloenone 2. The combinations of I-2/HTIB, I-2/I2O5 and NIS/TsOH were found to afford excellent yields.

# CALENDAR OF SEMINARS,

## NOV 1-4

Nov 1: "About Some Algorithms in Braid and Knot Theories," Hanna Nencka, Univ. of Madeira, 1:00, Math Dept., Room 507, Columia University

Nov 1: "Curves Under Deformations of Strictly Pseudoconvex Surfaces," Bruno de Oliveira, Columbia Univ.,1:00, Math Dept., Room 417, Columbia University

Nov 1: "Discovery of a Nearby Neutron Star," Prof. Fred Walter, USB, 7:30 PM, ESS Building, Room 001, SUNY at Stony Brook

Nov 1: "Geometric Algorithms for Massively-parallel Distributed Manipulation," Bruce R. Donald, Dept. of Computer Science, Cornell University, 11:30, Warren Weaver Hall, Room 1302, New York University

Nov 1: "NMR Methods for the Observation of Interactions Between Biomolecules and Water," Anja Böckmann, Columbia Univ., 12:00, Black Building, Room 523, Columbia University

Nov 1: "Biochemical and Biophysical Characterization of HIV-1 Integrases: The Path to Three-Dimensional Structures," Dr. Alison B. Hickman, National Institutes of Health, 4:00, Meyer Building, Room 122, New York University

Nov 1: "Variational Construction of Aubry-Mather sets and Connection Orbits for Positive Tilt Maps," Sen Hu, Princeton University, 3:45 Math Tower, Rm 5-127, SUNY at Stony Brook

Nov 4: "New Microstimulation Studies of the Primate Superiao Colliculus," Dr. David Sparks, University of Pennsylvania, 12:00, Meyer Building, Washington Square, Room 122, New York University

Nov 4:"Arithmetic Betti Numbers," Number Theory, Henri A. Gillet, Univ. of Illinois at Chicago, 5:30 p.m., 507 Math., Columbia University

Nov 4:"The Exciting Lives of Young Stars: Origin of Winds and Studies of Protoplanetary Disks," J. Najita, Harvard-Smithsonian CfA, Cambridge, 1:15, Rm P-137 Harriman Hall, SUNY at Stony Brook

Nov 4:"Results of D. Ginzburg on Loop Groups and Langlands Duality - Part 2, "Representation Theory and L-functions, Paul Gunnells, Columbia Univ, 4:00 p.m., 507 Math., Columbia University

Nov 4: "Neural Induction in Vertebrate Embryos," Dr. Ali Hemmati-Brivanlou, Head, Laboratory of Molecular Vertebrate Embryology, The Rockefeller University, 4:00, Dept. of Biology, Main Building, Room 101-A, New York University

Nov 4: "First Results from the ARM (Atmospheric Radiation Measurements) Enhanced Shortwave Experiments," Robert Cess and Minghua Zhong, USB, 12:00-1:30, Endeavor Hall, Room 120, SUNY at Stony Brook

## NOV 5-7

Nov 5 "Good Real Algebraic Spatial Singular Surfaces for the First Part of Hilbert's Sixteenth Problem," Benoit Chevallier, Toulouse University, 6:00, Warren Weaver Hall, Room 613, New York University

Nov 5: "The Spatial-toTemporal Transform: An Intractable Problem in Oculomotor Research. Why?," Dr. David Sparks, Dept. of Psychology, University of Pennsylvania, 4:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 6: "The Geometry of Diffusion and the Diffusion of Geometry," Lecture VIII, "Change of Variables," Richard Hamilton, University of California, San Diego and Visiting Professor, Columia University, 4:30, Mathematics Building, Room 312, Columbia University

Nov 6: "The Effects of Deleterious Mutations on Molecular Evolution and Variation," Brian Charlesworth, University Chicago, 3:30, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 6: "Characterization of ATP-Dependent Nucleosome Rearrangement Factors," Dr. Toshio Tsukiyama, National Institutes of Health, 4:00, NYU Medical Center, School of Medicine, Room MSB 393, New York University

Nov 6: "M," New York Seminar on Geometry and Physics: Tom Banks, Rutgers University, 2:00 p.m., 613 Meyer Hall, New York University

Nov 6: "Parallel Algorithms for Simulation of Crystal Growth Processes," Wing K. Chu, Dept. of Applied Math and Statistics, USB, 10:00, Math Tower, Rm 1-122,, SUNY at Stony Brook

Nov 6: "Mechanisms of Coherent Structure, Creation and Destruction in Stratified-rotating Flow," Richard Peltier, Dept. of Physics, University of Toronto, 3:30-4:30, Warren Weaver Hall, Room 1302, New York University

Nov 6: "The Geometry of Diffusion and the Diffusion of Geometry,"Richard Hamilton, Univ. of Calif., San Diego and Visiting Prof., Columbia Univ., 4:30 p.m., 312 Math, Columbia University

Nov 7: "Genetic Control of Blood Cell Development," Stuart Orkin, Harvard Medical School, 4:00, HHSC, Room 301, Columbia University

Nov 7: "Stable Ergodicity," Michael Shub, I.B.M., 3:15 p.m., 507 Math., Columbia University

Nov 7: "Mutations in the Mouse Sodium Channel Scn8a Produce Cerebellar Ataxia and Muscle Atrophy," Dr. Miriam Meisler, University of Michigan, 4:00-5:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 7: "Recent Progress on Super-Diffusion Non-Linear Parabolic Equations," Geometry and Analysis:T. Daskalopoulos, Univ. of Calif., Irvine, 2:00 p.m., 507 Math, Columbia University

## NOV 7-11

Nov 7: "Futurism and the Auditory Unconscious," Prof. Orna Panfil, New York University, 6:00PM, 465 Sch. Ext., Murphy/Fried Lounge, New York University

Nov 7: "The Unusual Stereochemistry of Polymers: From Chiral Amplification to Motion Under Constraint," Prof. Mark Green, Polytechnic University, Brooklyn, 4:30, 309 Havenmeyer Hall, Columbia University

Nov 7: "Selected Topics in Hamiltonian Dynamics," Michael R. Herman, CNRS and Visiting Prof., Columbia Univ., 4:30 p.m., 507 Math., Columbia University

Nov 8: "The Infrared Spectroscopy of Hydrogen-Bonded Clusters: Cycles, Chains, Cubes, and Three-Dimensional Networks," Prof. Timothy Zwier, Purdue University, 4:00, Meyer Building, Room 122, New York University

Nov 8: "The Mitochondrial Protein Import Machine," Gottfried Schatz, Biocenter University of Basel, Switzerland, 12:00-1:00, Black Building, Room 1222, Columbia University

Nov 8: "The Polyhedral Resolution for Toric Varieties," Dave Bayer, Barnard College, 1:00 p.m., 417 Math., Columbia University

Nov 8: "A Viscoelastic Model for Turbulent Flow Over Undulating Topography, Progressive Waves and its Implications for Air-Sea Interaction and Sediment Transport," Qingpig Zou, Johns Hopkins University, 11:30, Endeavour Hall, Room 120, SUNY at Stony Brook

Nov 8: "Algorithms in the Mapping Class Group," Hessam Hamidi-Tehrani, Columbia Univ., 1:00 p.m., 507 Math., Columbia University

Nov 8: "Differential Rotation of the Earth's Inner Core," Prof. Paul Richards, Columbia, Lamont-Doherty Observatory, 2:10, Pupin Hall, Room 428, Columbia University

Nov 8: "Determinants of Laplacians, Liouville's Action, and a Version of Dedekind's eta Function of Teichmuller space," Peter Zograf, St. Petersburg Univ., Russia and Visiting Prof., SUNY, Stony Brook, 3:00 p.m., 520, Math at Columbia University. Followed by up to two hours of informal discussion and dinner at a local restaurant at 6:00 p.m.

Nov 11: "Luminosity Function Evolution of Young Star Clusters," W.P. Chen National Central University, Taiwan, CfA 1:15, Rm P-137 Harriman Hall, SUNY at Stony Brook

Nov 11: "Rates of Molecular Evolution in Plant Genes," Dr. Brandon Gaut, Department of Plant Sciences, Rutgers University, 4:00, Dept. of Biology, Main Building, Room 101-A, New York University

# COLLOQUIA, & SYMPOSIA

## NOV 12-14

Nov 12: "Supernova Explosions, Black Holes, and Nucleon Stars," Gerry Brown, USB Physics/ITP, 4:15, Harriman Hall, Room P-137, SUNY at Stony Brook

Nov 12: " Crystallographic Studies of Cyclin-Dependent Kinase Function and Regulation," Dr. Nikola P. Pavletich, Cellular Biochemistry and Biophysics Program, Sloan-Kettering Institute, 4:00, HHSC, Room 312, Columbia University

Nov 13: "Holding Chromatids Together to Ensure They Go Their Separate Ways: Analysis of Sister Chromatid Cohesion in Drosophila," Dr. Sharon Bickel, Whitehead Institute for Biomedical Research, 4:00, School of Medicine, Room MSB 393, New York University

Nov 13: "Mechanism of Cytokinesis Dictyostelium," Arturo deLozanne, Duke University Medical Center, 12:00-1:00, Black Building, Room 1222, Columbia University

Nov 13: "The Mother of Mass Extinctions: Life and Death in the Permian," Douglas Erwin, National Museum of Natural History, 10:00, Math Tower, Rm 1-122, Seminar Room, SUNY at Stony Brook

Nov 13: "Remote Sensing Tags: How They Work and the Materials Issues," Robert J . Von Gutfeld, IBM Research, 1:30-2:30, Mudd Building, Room 1024, Columbia University

Nov 13: "The Geometry of Diffusion and the Diffusion of Geometry," Lecture IX, "Partial Regularity," Richard Hamilton, University of California, San Diego and Visiting Professor, Columia University, 4:30, Mathematics Building, Room 312, Columbia University

Nov 14: "Large Scale Functional Analysis of the Yeast Cell Surface," Dr. Howard Bussey, McGill University, 4:00-5:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 14: "Laser Spectrsocopy in Crystals and Glasses, One Molecule at a Time," Prof. James Skinner, University of Wisconsin, 4:30, 309 Havenmeyer Hall, Columbia University

Nov 14: "B-50/GAP-43: A Calmodulin-Binding PKC Substrate Protein Involved in Neurotransmitter Release and Neurite Outgrowth," Dr. Loes Schrama, Rudolf Magnus Institute for Neuroscience, Utrecht University, Netherland, 12:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 14: "Combinatorial Signaling in Mesodermal Pattern Formation," Alan M. Michelson, Howard Hughes Medical Institute, Brigham and Women's Hospital, 4:00, HHSC, Room 301, Columbia University

## NOV 15-20

Nov 15: "Photochemistry in the Adsorbed State: Using Light as a Scalpel, and a Crystal as Operating Table," Professor J.C. Polanyi, University of Toronto, 4:00, Meyer Building, Room 122, New York University

Nov 15: "Studies in Organic Synthesis: Ginkgolides to Carbocyclic Nucleosides, Photocycloadditions to Asymmetric Aldols" Frontiers in Organic Chemistry Series, Sponsored by Ciba-Geigy, Professor Michael T. Crimmins, University of North Carolina at Chapel Hill, 4:00, Graduate Chemistry Building, Room 412, SUNY at Stony Brook

Nov 18: "Regulation of Salmonella Invasion: How and Why?," Dr. Catherine A. Lee, Harvard Medical School, 12:00-1:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 18: "Evolution of Blind Cave Fishes," Dr. Richard Borowsky, Department of Biology, 4:00, Dept. of Biology, Main Building, Room 101-A, New York University

Nov 18: "The Importance of Habitat Protection in NOAA Fisheries Management: Conserving Our Nation's Living Oceans," Dr. Nance Foster, Deputy Assistant Administrator for Fisheries, NMFS, 6:30, RSVP-Su Sponaugle at (516) 632-8693 or Nance Steinberg at (212) 924-8290, The Long Island Chapter of the Women's Aquatic Network, Marine Sciences Research Center, SUNY at Stony Brook,

Nov 19: "How Do We Find the Neural Correlate of Consciousness?," Dr. Ned Block, NYU, Dept of Psychology, 3:00-4:30, Main Building, Room 101A, New York University

Nov 19: "Magnetism in the Low Dimensional Limit," Roy Willis, Pennsylvania State University, 4:15, Harriman Hall, Room P-137, SUNY at Stony Brook

Nov 20: "The Geometry of Diffusion and the Diffusion of Geometry," Lecture X, "Isoperimetric Estimates," Richard Hamilton, University of California, San Diego and Visiting Professor, Columia University, 4:30, Mathematics Building, Room 312, Columbia University

Nov 20: "Two-phase Modeling of a Fluid Mixing Layer," David Saltz, Dept. of Applied Math and Statistics, USB, 10:00
Math Tower, Rm 1-122, Seminar Room, SUNY at Stony Brook

Nov 20: "The Effect of Relaxed Functional Constraints - the Photosynthetic Gene rbcL in Nonphotosynthetic Plants," Andrea Wolfe, Ohio State University, 3:30, Life Sciences Building, Room 038, SUNY at Stony Brook

## NOV 20-30

Nov 20: "Pressure and Stress Effects on Atomic and Interfacial Mobility, Michael J. Aziz, Harvard University, 1:30-2:30, Mudd Building, Room 1024, Columia University

Nov 21: "New Insights Into Regulated Pre-mRNA Splicing in Animals," Prof. Paul Bingham, USB, 4:00-5:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 21: "Reactivities of Metal-Ligand Multiple Bonds," Prof. Keith Woo, Iowa State University, 4:30, 309 Havenmeyer Hall, Columbia University

Nov 21: "Catalytic Enantioselective Aldehyde Addition Reactions," The Pfizer Lecture, Professor Erick Carreira, California Institute of Technology, 4:00, Graduate Chemistry Building, Room 412, SUNY at Stony Brook

Nov 22: "The GADS Experiment: Effects of Additional Aircraft Data on Jet Stream Analysis Errors," Joel Tenebaum, SUNY Purchase, 11:30, Endeavor Rm 120, SUNY at Stony Brook

Nov 25: "Cytoskeletal-Extracellular Matrix Interactions During the Establishment of Cell Polarity," Dr. Ralph Quatrano, Chair, Department of Biology, The University of North Carolina, Chapel Hill, 4:00, Dept. of Biology, Main Building, Room 101-A, New York University

Nov 26: "Open Problems in Plasma Fusion," Ron Davidson, Princeton Plasma Physics Lab, 4:15, Harriman Hall, Room P-137, SUNY at Stony Brook

Nov 26: "How Do We Find the Neural Correlate of Consciousness?," Dr. Ned Block, NYU, 3:00-4:00, Dept. of Psychology, Main Building, Room 101A, New York University

Nov 26: "What Can Miniatures Tell Us About Synaptic Transmission in the Brain?," Dr. John Bekkers, Division of Neuroscience, John Cartin School of Medicine Research, Canberra, 4:00, Life Sciences Building, Room 038, SUNY at Stony Brook

Nov 27: "Flaubert's Parrot: Passion and the Practice of Anthropology, " Prof. Di Losch, Univ. of New South Wales, Sydney, 4:00, 465 Sch. Ext., Murphy/Fried Lounge, New York University

Nov 30: "Role of Surfaces in Blood Coagulation," Dr. Yale Nemerson, Mt. Sinai School of Medicine, 4:00, HS Tower Level 3, Rm 6, School of Medicine, SUNY at Stony Brook

## DNA AND RNA STRAND SCISSION BY COPPER, ZINC AND MANGANESE SUPEROXIDE DISMUTASES

Dowjat WK. Kharatishvili M. Costa M.

*Biometals. 9(4):327-335, 1996 Oct.*

Abstract

Copper/zinc (Cu/ZnSOD) and manganese (MnSOD) superoxide dismutases which catalyze the dismutation of toxic superoxide anion, O-2(-), to O-2 and H2O2, play a major role in protecting cells from toxicity of oxidative stress, However, cells overexpressing either form of the enzyme show signs of toxicity, suggesting that too much SOD may be injurious to the cell. To elucidate the possible mechanism of this cytotoxicity, the effect of SOD on DNA and RNA strand scission was studied, High purity preparations of Cu/ZnSOD and MnSOD were tested in an in vitro assay in which DNA cleavage was measured by conversion of phage phi X174 supercoiled double-stranded DNA to open circular and linear forms, Both types of SOD were able to induce DNA strand scission generating single- and double-strand breaks in a process that required oxygen and the presence of fully active enzyme. The DNA strand scission could be prevented by specific anti-SOD antibodies added directly or used for immunodepletion of SOD. Requirement for oxygen and the effect of Fe(II) and Fe(III) ions suggest that cleavage of DNA may be in part mediated by hydroxyl radicals formed in Fenton-type reactions where enzyme-bound transition metals serve as a catalyst by first being reduced by superoxide and then oxidized by H2O2. Another mechanism was probably operative in this system, since in the presence of magnesium DNA cleavage by SOD was oxygen independent and not affected by sodium cyanide, It is postulated that SOD, by having a similar structure to the active center of zinc-containing nucleases, is capable of exhibiting non-specific nuclease activity causing hydrolysis of the phosphodiester bonds of DNA and RNA, Both types of SOD were shown to effectively cleave RNA, These findings may help explain the origin of pathology of certain hereditary diseases genetically linked to Cu/ZnSOD gene.

## MAIN-CHAIN COMPLEMENTARITY IN PROTEIN-PROTEIN RECOGNITION

Vakser IA.

*Protein Engineering. 9(9):741-744, 1996 Sep.*

Abstract

The existing theoretical approaches to protein-protein recognition concentrate on the details of the molecular surface at atomic resolution, while a possible role of the main chain in complex formation has been largely unexplored. To address this problem, we represented the molecules by C alpha atoms and applied the step-function potentials for intermolecular energy calculations. Since our goal was not to predict, as accurately as possible, the structure of a protein-ligand complex, but to reveal the role of the backbone in the formation of such a complex, all the potentials were identical and C alpha centered. Thus, for the specific purposes of our study, we do not simulate the difference in the side chains at the molecular surface. The structures were taken from known co-crystallized complexes. The intermolecular energy calculation was performed by a systematic 6-D search on a grid. The results revealed that in all cases tested (except antigen-antibody) the positions of the ligand at the binding site on the receptor corresponded to the lowest-energy configurations of the complex. The complementarity between the backbones, in general, may facilitate the initial placement of the ligand at the binding site of the receptor. At the same time, the identity and the specific conformation of the surface side chains play a crucial role in the next stage of the complex formation.

## SPIN-ORBITAL ANGULAR MOMENTUM COUPLING EFFECTS ON THE ELECTRONIC STRUCTURE OF NANOCRYSTALLINE SEMICONDUCTOR CLUSTERS

Tomasulo A. Ramakrishna MV.

*Chemical Physics. 210(1-2):55-70, 1996 Oct 1.*

Abstract

The effects of crystal structure and spin-orbital angular momentum coupling on spectroscopic transitions in CdS, CdSe, and CdTe semiconductor clusters are investigated using accurate pseudopotentials. These calculations reveal that spin-orbit coupling splits the exciton peak into A, B, and C transitions. The C transitions exhibit much greater blueshift with cluster size than the A and B transitions. Furthermore, the C transitions exhibit stronger quantum confinement effect in zinc-blende than in wurtzite clusters of the same size. The calculated transition energies are in good agreement with the experimental data and spin-orbit coupling is able to reveal many of the trends in the experimental spectral shifts.

## EQUAL ABUNDANCE OF POSITIVE-AND NEGATIVE-RESIDUE FIXED POINTS FOR RESONANTLY KICKED HARMONIC OSCILLATORS

Lowenstein JH.

*Nonlinearity. 9(5):1071-1088, 1996 Sep.*

Abstract

Consider a one-dimensional harmonic oscillator subjected to instantaneous kicks in resonance with its natural period, with the amplitude of the kick a real-analytic, periodic function of position. Viewed stroboscopically in phase space once every n natural periods, the system has an infinite periodic or quasiperiodic array of fixed points. Generically, the latter can be classified (away from bifurcations) as having positive residue (stable centres and reversing saddle points) or negative residue (nonreversing saddle points). It is demonstrated that the average phase-space densities of the positive- and negative-residue fixed points are equal.

## MATTER-MICROWAVE CORRELATIONS IN AN OPEN UNIVERSE

Kamionkowski M.

*Physical Review D. 54(6):4169-4170, 1996 Sep 15.*

Abstract

In an intriguing recent paper, Crittenden and Turok proposed cross-correlating the cosmic microwave background with tracers of the matter density to probe the existence of a cosmological constant. Here I emphasize that a similar cross correlation arises in an open universe and, depending on the redshift distribution of the tracer population and the matter density, may be comparable to or stronger than that in a flat cosmological-constant universe with the same matter density. The two cases can be distinguished through cross correlation with tracer populations with different redshift distributions.

## SELF-CONSISTENT, FREE ENERGY BASED APPROXIMATION TO CALCULATE PH DEPENDENT ELECTROSTATIC EFFECTS IN PROTEINS

Mehler EL.

*Journal of Physical Chemistry. 100(39):16006-16018, 1996 Sep 26.*

Abstract

A constrained variational approach is used to derive self-consistent equations for determining the optimal, pH dependent charge state of all the protonatable groups in a protein. The approach uses a screened Coulomb potential (SCP) with a sigmoidal, distance dependent dielectric screening function for calculating the interaction energies between the charges in a protein. In addition, a formula is derived from the integral Born equation, using radially dependent permittivities, for calculating the electrostatic free energy of transferring a charged group from pure solvent to a protein in a dilute solution. The relationship between the approach and the Lorentz-Debye-Sack theory of polar solvation is outlined, and the method has been applied to calculate the pK's of the titratable groups in bovine pancreatic trypsin inhibitor, hen egg white lysozyme, ribonuclease A, and ribonuclease T-1. The results are compared to recent calculations of pH dependent properties of these proteins that used the finite difference method for solving the Poisson-Boltzmann equation (FDPB). The comparison shows that the overall reliability of the present method is similar to that achieved by the FDPB approach but that the approach derived here is about 10(2)-10(3) times faster. The origin of this increase in computational speed is the calculational simplicity inherent in the use of a SCP and the fact that the method bypasses the need for numerically solving a second order differential equation for complex, many-body systems. The pH dependence of the pK is analyzed by comparing the pK(1/2) and the effective pK at pH 7. While the pK of most residues change only slightly, in some cases shifts up to 1.4 units were calculated, The SCP approximation is compared to the generalized Born (GB) treatment, and it is shown that the latter can be expressed in terms of an interaction that is damped by a sigmoidal screening function and a self-energy term. Comparison of interaction energies calculated from the two methods shows excellent agreement. In spite of this agreement and the reasonable overall root mean square deviation between calculated and measured pK, errors of more than one unit were found in several cases. The possible sources of these errors are analyzed and traced to the various approximations made in calculating the interaction and solvation energy contributions to the final pK. From this analysis several steps are outlined for improving these approximations that may help decrease the discrepancies between calculated and experimental results.

## HOST IMMUNE RESPONSE TO VESICULAR STOMATITIS VIRUS INFECTION OF THE CENTRAL NERVOUS SYSTEM IN C57BL/6 MICE

Christian AY. Barna M. Bi ZB. Reiss CS.

*Viral Immunology. 9(3):195-205, 1996.*

Abstract

In this report, the kinetics of cellular inflammatory changes in the brains of vesicular stomatitis virus (VSV)-infected C57BL/6 (B6) mice was determined. The behavior and survival rate of infected B6 were carefully monitored each day, Infectious viral titers and VSV antigen distribution were determined at several time points during the course of infection, Strong activation of both astrocytes and microglia was observed after VSV infection, Induction of type II nitric oxide synthase (iNOS) was detected in activated microglia in the olfactory bulb (OB) starting at day 4 postinfection, Induced expression of major histocompatibility complex (MHC) molecules and rapid infiltration of both T cells and natural killer (NK) cells were detected in the VSV-infected CNS, Collectively, these data indicate that the response to CNS infection in B6 mice, which is often primarily Th1 in characteristics, is comparable to BALB/c mice, a strain that often shows a Th2-dominated immune response.

## THE B-CELL-SPECIFIC TRANSCRIPTION COACTIVATOR OCA-B/OBF-1/BOB-1 IS ESSENTIAL FOR NORMAL PRODUCTION OF IMMUNOGLOBULIN ISOTYPES

Kim U. Qin XF. Gong SC. Stevens S. Luo Y. Nussenzweig M. Roeder RG.

*Nature. 383(6600):542-547, 1996 Oct 10.*

Abstract

OCA-B was initially identified as a B-cell-restricted coactivator that functions with octamer binding transcription factors (Oct-1 and Oct-2) to mediate efficient cell type-specific transcription of immunoglobulin promoters in vitro(1-3). Subsequent cloning studies led to identification of the coactivator as a single polypeptide, designated either as OCA-B (ref. 3), OBF-1 (ref. 4) or Bob-1 (ref. 5). OCA-B itself does not bind to DNA directly, but interacts with either Oct-1 or Oct-2 to potentiate transcriptional activation(1-5). To determine the biological role of OCA-B, we generated OCA-B-deficient mice by gene targeting. Mice lacking OCA-B undergo normal antigen-independent, B-cell differentiation, including appropriate expression of both immunoglobulin genes and other early B-cell-restricted genes. However, antigen-dependent maturation of B cells is greatly affected. The proliferative response to surface IgM crosslinking is impaired, and there is a severe deficiency in the production of secondary immunoglobulin isotypes including IgG1, IgG2a, IgG2b, IgG3, IgA and IgE in BCA-B-deficient B cells. This defect is not due to a failure of the isotype switching process, but rather to reduced levels of transcription from normally switched immunoglobulin heavy-chain loci. In accord dth the defective isotype production, germinal centre formation is absent in these mutant mice.

## PHARMACOLOGY OF A CAPACITATIVE CA2+ ENTRY IN XENOPUS OOCYTES

Gillo B. Sealfon SC. Minke B.

*Journal of Photochemistry & Photobiology. B - Biology. 35(1-2):77-82, 1996 Aug.*

Abstract

We have characterized pharmacological properties of inositol trisphosphate (InsP(3))-mediated calcium entry pathway in Xenopus oocytes via activation of Ca2+-dependent Cl- channels (I-Cl,I-Ca) as a sensitive indicator for increase in cytosolic [Ca2+]. This type of Ca2+ entry mechanism is known as a capacitative Ca2+ entry (CCE). Voltage-clamped oocytes were maintained in Ca2+-free medium and injected with InsP(3) which depleted the InsP(3)-sensitive Ca2+ stores. 10-20 min later, the oocytes were exposed, at 2-3 min intervals, to 5 mM Ca2+-containing medium for 5-10 s which evoked repeated inward Cl- current. No effect of external Ca2+-was apparent before InsP(3) injection. To determine the pharmacological characteristics of CCE, oocytes were incubated with various chemical agents in Ca2+-free solution and exposed to Ca2+ again in presence of the chemical. It was found that organic Ca2+ channel blockers were relatively ineffective in blocking CCE while the inorganic Ca2+ channel blocker La3+ was most efficient in blocking the current. Attempts to measure conductance increase when the Cl- channels were blocked during activation of Ca2+ influx were unsuccessful. Therefore we tested the hypothesis that the Ca2+ influx is mediated via a Ca-H transporter. Lowering the external pH (to pH 6.5) or application of the protonophore carbonylcyanide p-trifluoromethoxyphenyl hydrazone (EC(50) = 2 x 10(-8) M) effectively blocked CCE, Since Ca-H countertransport in the plasma membrane is coupled to Ca2+ extrusion by Ca-ATPase in vascular smooth muscle we suggest that the capacitative Ca2+ entry in Xenopus occytes may possibly arise from slippage of plasma membrane Ca-ATPase coupled to proton countertransport, a mechanism reported in a variety of cells, Ca2+ slippage may arise from the large Ca2+ gradient produced by the Ca2+ depletion protocol.

## A ROLE FOR PYK2 AND SRC IN LINKING G-PROTEIN-COUPLED RECEPTORS WITH MAP KINASE ACTIVATION

Dikic I. Tokiwa G. Lev S. Courtneidge SA. Schlessinger J.

*Nature. 383(6600):547-550, 1996 Oct 10.*

Abstract

The mechanisms by which mitogenic G-protein-coupled receptors activate the MAP kinase signalling pathway are poorly understood. Candidate protein tyrosine kinases that link G-protein-coupled receptors with MAP kinase include Src family kinases(1), the epidermal growth factor receptor(2), Lyn and Syk(3). Here we show that lysophosphatidic acid (LPA) and bradykinin induce tyrosine phosphorylation of Pyk2 and complex formation between Pyk2 and activated Src. Moreover, tyrosine phosphorylation of Pyk2 Leads to binding of the SH2 domain of Src to tyrosine 402 of Pyk2 and activation of Src. Transient overexpression of a dominant interfering mutant of Pyk2 or the protein tyrosine kinase Csk reduces LPA- or bradykinin-induced activation of MAP kinase. LPA- or bradykinin-induced MAP kinase activation was also inhibited by overexpression of dominant interfering mutants of Grb2 and Sos. We propose that Pyk2 acts with Src to link G(i)- and G(q)-coupled receptors with Grb2 and Sos to activate the MAP kinase signalling pathway in PC12 cells.

## IDENTIFICATION OF AN IMMEDIATE-EARLY SALICYLIC ACID-INDUCIBLE TOBACCO GENE AND CHARACTERIZATION OF INDUCTION BY OTHER COMPOUNDS

Horvath DM. Chua NH.

*Plant Molecular Biology. 31(5):1061-1072, 1996 Aug.*

Abstract

Tobacco genes that are induced in response to salicylic acid (SA) treatment with immediate-early kinetics were identified by differential mRNA display. Detailed analysis of IS10a, one cDNA clone identified by this method, revealed induction within 30 min of treatment, with a peak of expression at 3 h, that decayed rapidly thereafter. Treatment with the protein synthesis inhibitor, cycloheximide (CHX), also caused induction of IS10a mRNA to comparable levels, but the IS10a mRNA continued to accumulate after 3 h of induction. In combination, CHX and SA led to a superinduction of IS10a mRNA levels that was also sustained. Half-maximal induction was evident at ca. 100-150 mu M SA. In addition to SA, induction of IS10a occurred to varying degrees upon treatment with acetylsalicylic acid, benzoic acid, 2,4-dichlorophenoxyacetic acid, methyl jasmonate, and hydrogen peroxide, whereas treatment with other compounds had no effect. The proteins encoded by IS10a and a second highly homologous cDNA show sequence similarity to UDP-glucose: flavonoid glucosyltransferases.

## FINITE TIME LYAPUNOV EXPONENT AND ADVECTION-DIFFUSION EQUATION

Tang XZ. Boozer AH.

*Physica D. 95(3-4):283-305, 1996 Sep 1.*

Abstract

The diffusive transport of a scalar in a flowing fluid is determined by the advection-diffusion equation. If the how is chaotic, the properties of the transport are determined by the spatial and temporal dependence of the finite time Lyapunov exponent lambda(xi, t). The rapid diffusive transport occurs only along the field line of the vector <(s)over cap(infinity)>, which defines the stable direction in which neighboring points asymptotically converge. The geometry of the (s) over cap line affects the diffusive transport through the finite time Lyapunov exponent lambda(xi, t), which varies smoothly along an (s) over cap line. For example, the finite time Lyapunov exponent lambda(xi, t) of a 2D conservative system can always be written as lambda(xi, t) = lambda(N)(xi)/t + f(xi, t)/t root t + lambda(infinity) with <(s)over cap(infinity)> . V(0)f(xi, t) = 0 and lambda(infinity) the infinite time Lyapunov exponent. The spatial dependence of the finite time Lyapunov exponent is related to the geometry of the (s) over cap line through lambda(N) by <(s)over cap(infinity)> . del(0) lambda(N)(xi) + del(0) . <(s)over cap infinity> = 0. Diffusion is impeded if the finite time Lyapunov exponent becomes small along the field line of the (s) over cap, vector. It is shown that the finite time Lyapunov exponent has a sharp dip where the L line encounters a sharp bend. Hence the barriers for diffusion are located at these sharp bends of the (s) over cap lines, which are generic for chaotic flows due to nonhyperbolicity. This new class of diffusive transport barrier persists even in systems that are far from integrable.

## CHEMICAL WAVE REFRACTION PHENOMENA

Hwang SC. Halpinhealy T.

*Physical Review A. 54(3):3009-3012, 1996 Sep.*

Abstract

Motivated by recent work of Steinbock, Toth, and Showalter [Science 267, 868 (1995)] examining chemical wave propagation within membrane labyrinths soaked with Beluosov-Zhabotinsky reagent, we have investigated refraction phenomena using similar tools, with an eye to verify the general applicability of Snell's law for such nonlinear waves, as well as to unearth the physiochemical origin of the drastically reduced trigger wave velocities we find within quasi-two-dimensional porous media. Altered reaction-diffusion kinetics appear to play no role. Rather, our results indicate intramembrane wave-front curvature, induced perhaps by differential wetting properties, to be the mechanism responsible for these refraction effects.

## 5-HT3-LIKE RECEPTORS IN THE RAT MEDIAL PREFRONTAL CORTEX - FURTHER PHARMACOLOGICAL CHARACTERIZATION

Edwards E. Hampton E. Ashby CR. Zhang JY. Wang RY.

*Brain Research. 733(1):21-30, 1996 Sep 9.Brain Research. 733(1):21-30, 1996 Sep 9.*

Abstract

The aim of the study was to further characterize the pharmacological properties of 5-hydroxytryptamine (5-HT)(3)-like receptors in the rat medial prefrontal cortex (mPFC) using combinations of biochemical and electrophysiological approaches.

Phenylbiguanide (PEG) and three chlorinated derivatives, ortho-chloro-PBG (oCPBG), meta-chloro-PBG (mCPBG) and para-chloro-PBG (pCPBG), dose-dependently stimulated phosphoionositide (PI) turnover in fronto-cingulate cortical slices. All three chloro-isomers of PBG were equipotent in stimulating PI turnover. SR 57227A ((4-amino)-(6-chloro-2-pyridyl) L-piperidine hydrochloride, a novel compound with high affinity and selectivity for peripheral and central 5-HT3 receptors) dose-dependently stimulated PI turnover in fronto-cingulate cortical slices. The rank order of potency of all the 5-HT3 receptor agonists tested in the PI assay as compared to 5-HT was: 5-HT > 2-Me-5-HT > SR57227A > PBG = mCPBG = oCPBG = mCPBG. 5-HT and 5-HT receptor agonists depressed the firing rate of both spontaneously active and glutamate-activated quiescent mPFC cells in a current (dose)-dependent fashion. The rank order of effectiveness of these compounds was: 5-HT > SR57227A = 2-Me-5-HT = mCPBG = oCPBG = pCPBG = PBG. Unlike its action on the 5-HT3 receptors in the periphery or cultured cell Lines, D-tubocurarine chloride appears to be non-specific in blocking the depressant action of 2-Me-5-HT, gamma-aminobutyric acid and dopamine. Our results combined support the view that the pharmacological properties of 5-HT3-like receptors in the mPFC are not identical to those located in peripheral tissues and in cultured cell lines.

## SOLUTION CONFORMATION OF THE N-(DEOXYGUANOSIN-8-Y1)-1-AMINOPYRENE ([AP]DG) ADDUCT OPPOSITE DC IN A DNA DUPLEX

Mao B. Vyas RR. Hingerty BE. Broyde S. Basu AK. Patel DJ.

*Biochemistry. 35(39):12659-12670, 1996 Oct 1.*

Abstract

Combined NMR-molecular mechanics computational studies were undertaken on the C-8-deoxyguanosine adduct formed by the carcinogen 1-nitropyrene embedded in the d(C5-[AP]G6-C7). d(G16-C17-G18) sequence context in a 11-mer duplex, with dC opposite the modified deoxyguanosine, The exchangeable and nonexchangeable protons of the aminopyrene moiety and the nucleic acid were assigned following analysis of two-dimensional NMR data sets in H2O and D2O solution. There was a general broadening of several proton resonances for the three nucleotide d(G16-C17-G18) segment positioned opposite the [AP]dG6 lesion site resulting in weaker NOEs involving these protons in the adduct duplex. The solution conformation of the [AP]dG . dC 11-mer duplex has been determined by incorporating intramolecular and intermolecular proton-proton distances defined by upper and lower bounds deduced from NOESY spectra as restraints in molecular mechanics computations in torsion angle space. The aminopyrene ring of [AP]dG6 is intercalated into the DNA helix between intact Watson-rick dC5 . dG18 and dC7 . dG16 base pairs. The modified deoxyguanosine ring of [AP]dG6 is displaced into the major groove and stacks with the major groove edge of dC5 in the adduct duplex. Both carbon and proton chemical shift data for the sugar resonances of the modified deoxyguanosine residue are consistent with a syn glycosidic torsion angle for the [AP]dG6 residue. The dC17 base on the partner strand is displaced from the center of the helix toward the major groove as a consequence of the aminopyrene ring intercalation into the helix. This base-displaced intercalative structure of the [AP]dG . dC 11-mer duplex exhibits several unusually shifted proton resonances which can be accounted for by the ring current contributions of the deoxyguanosinyl and pyrenyl rings of the [AP]dG6 adduct. In summary, intercalation of the aminopyrene moiety is accompanied by displacement of both [AP]dG6 and the partner dC17 into the major groove in the [AP]dG . dC 11-mer duplex.

## THE ADSORPTION AND THERMAL REACTION OF DIMETHYLCADMIUM, DIMETHYLZINC AND TRIMETHYLGALLIUM ON GAAS(110)

Lasky PJ. Lu PH. Luo Y. Slater DA. Osgood RM.

*Surface Science. 364(3):312-324, 1996 Sep 1.*

Abstract

The adsorption of dimethylcadmium (DMCd), dimethylzinc (DMZn) and trimethylgallium (TMGa) on GaAs(110) has been studied using TPD and XPS spectroscopies. In the first monolayer, the dimethyl species adsorb molecularly at 80 K, but, upon heating, undergo dissociation. Thermal elimination of the hydrocarbon fraction of these precursors is found to proceed mainly via the formation and desorption of TMGa despite the fact that the only available gallium is strongly bound in the GaAs lattice. For the cases of 1 ML DMCd and DMZn adsorption, TMGa desorption is seen as two distinct peaks at 435 and 380 K, while Cd or Zn deposited in this manner subsequently desorbs in a single broad feature between similar to 400 and 700 K. The desorption of TMGa, obtained by TMGa molecular adsorption at 80 K, is found to be strongly coverage dependent with the sequential population of two states giving rise to peak desorption temperatures of 435 and 340 K as a function of increasing coverage. For all these adsorbates, it is suggested that this effect is due to reaction-limited TMGa desorption, resulting from distinct kinetic pathways to the formation of TMGa at low and high coverages. For all species, the results provide a useful comparison with similar earlier studies on GaAs(100).

## DEVELOPMENT OF SEDIMENT OVERPRESSURE AND ITS EFFECT ON THERMAL MATURATION - APPLICATION TO THE GULF OF MEXICO BASIN

Mello UT. Karner GD.

*AAPG Bulletin-American Association of Petroleum Geologists. 80(9):1367-1396, 1996 Sep.*

Abstract

High sedimentation rates can potentially lead to overpressuring and sediment undercompaction within basins. Sediments with anomalously high porosity, in turn, induce low thermal conductivities and so tend to act as a thermal insulator to the flow of heat, In the Gulf of Mexico basin (Gulf basin), the generation of overpressure is caused mainly by the inability of pore pressure fluids to escape at a rate commensurate with sedimentation. We modeled the generation and dissipation of abnormal sediment pore pressure due to variations in sedimentation rate, facies, formation porosity, and permeability within the Gulf basin using finite-element techniques to solve the differential equations of both heat and fluid transport within compacting sediments. We assume that the porosity-effective stress relationship within the sediment follows a negative exponential steady-state form when the pore pressure is hydrostatic. An important feature of our modeling approach is the assumption that sediments are incapable of significant expansion in response to increasing pore pressure, Sediments are assumed to hydrofracture when the pore pressure approaches the lithostatic pressure, rather than a common assumption of porosity expansion even in lithified sediments. From our modeling, we conclude that significant overpressures have been created (and dissipated) at various times within the Gulf basin and track, in general, the west to east migration of sediment loads deposited since the Cretaceous. Although predicted overpressures of more than 0.75 kpsi (i.e., an equivalent excess hydraulic head of 500 m) of Campanian-Maastrichtian age remain to the present day, the main phase of overpressure development in the Gulf basin is predicted to have occured during the Miocene-Holocene, Maximum overpressures (similar to 13.6 kpsi; excess hydraulic head of 9.4 km) are predicted for the present day, Overpressure development during the Miocene-Quaternary, a consequence of rapid sediment deposition associated with the Mississippi delta system, is also predicted to be associated with undercompaction, This undercompaction led to increased temperature gradients during the Miocene and Quaternary despite the fact that the anomalous basal heat flow engendered by extension had practically dissipated, We further predict that by the end of the Neogene, temperatures would have been approaching steady state over broad regions of the Gulf basin implying that the highest temperatures occur in the deepest parts of the basin. In contrast, during the Quaternary, the rapid progradation of-overpressured and undercompacted sediments resulted in a thick section that has yet to reach thermal equilibrium and thus is anomalously cold with respect to its present depth. The predicted vitrinite reflectance indicates that for most of the Gulf basin history, the depth to the top of the oil window remained at approximately 2.5+/-0.5 km below sea floor (bsf). Similarly, the depth to the base of the oil window ranged from 3.5 to 6.5 km bsf This relatively constant position of the top of the oil window defines a maturation "front" that propagated from the offshore into the onshore regions of the northern Gulf basin as a function of time. As such, hydrocarbon generation is predicted to have occurred continuously within the Jurassic and Cretaceous sections of the onshore region during the entire Cenozoic.

Prior to this, maturation fronts within each of the onshore basins resulted in maturation of Upper Jurassic source rocks during the Early Cretaceous. In the offshore Gulf Coast area, pre-Tertiary source rocks are predicted to be overmature for liquid hydrocarbons at present.

In the offshore regions affected by Quaternary sedimentation, the depth to the top of the oil window has been significantly depressed in response to sediment loading and subsidence.

# Selected Funding Updates

Compiled by Peter M. Saal
OFFICE OF THE VICE-PRESIDENT FOR RESEARCH—SUNY STONY BROOK

**NSF/INT: Cooperative Activities with Africa, the Near East, and South Asia**

The semi-annual deadline is February 1, 1997. Cooperative research, dissertation enhancement, and joint workshops involving partners in countries in these regions. Planning visit proposals may be submitted at any time. U.S. faculty advisers may apply for dissertation enhancement awards to support graduate students who are enrolled at U.S. universities and wish to conduct research in most of these countries. Contact: Division of International Programs, 703-306-1707; e-mail, rmondesi@nsf.gov.

**NSF/INT: Cooperative Science Programs with Argentina, Brazil, Chile, Mexico, and Venezuela**

Supports cooperative research, joint workshops, dissertation improvement grants, and program planning visits. For collaborative research projects and workshops, the foreign counterpart(s) must submit a parallel proposal to a counterpart agency in the host country. Semi-annual deadline is May 1. Contact the Division of International Programs, 703-306-1706.

**EPA: 1997 Research Grants Announcement**

The U.S. Environmental Protection Agency (EPA), Office of Research and Development (ORD), invites research grant applications in the following areas of special interest to its mission:

| | ***Deadline:*** |
|---|---|
| **Exploratory Research** | |
| • environmental biology | January 15, 1997 |
| • environmental chemistry | January 15, 1997 |
| • physics | January 15, 1997 |
| • human health | January 15, 1997 |
| • social science | January 15, 1997 |
| • environmental engineering | January 15, 1997 |
| **Ecosystem Indicators** | January 22, 1997 |
| **Issues in Human Health Risk Assessment** | |
| • The Human Health Effects of Complex Exposure Patterns | February 15, 1997 |
| • Variability in Human Responses to Environmental Agents | February 15, 1997 |
| • Consumer Right-to-Know | February 15, 1997 |
| **Endocrine Disruptors** | February 15, 1997 |
| **Ambient Air Quality** | |
| • Tropospheric Ozone and Fine Particulates | February 15, 1997 |
| • Special Opportunity Pre-proposals | January 15, 1997 |
| • Urban Air Toxics | February 15, 1997 |
| **Health Effects of Particulate Matter** | February 15, 1997 |
| **Drinking Water** | |
| • Microbial Pathogens | February 15, 1997 |
| • Disinfection Byproducts | February 15, 1997 |
| **Contaminated Sediments** | February 15, 1997 |

Copies of the 1997 EPA Research Grants Announcement may be found on the World-Wide Web at: **http://www.epa.gov/ncerqa**.

**NSF/CISE: Interactive Systems**

The program supports research that is fundamental to the design of technology and systems for human/computer communication, with a particular emphasis placed on interactive dialogue in several modalities. Proposals should be submitted as close to the target date as possible. Immediately following the deadline date, the panel will meet to review proposals. Contact: Dr. Gary Strong, Division of Information, Robotics, and Intelligent Systems, 306-1929, or by e-mail, gstrong@nsf.gov. Deadline: 02/15/1997

**NSF/CISE: Numeric, Symbolic, and Geometric Computation**

Proposals will be accepted in the areas of symbolic and geometric computing and automated deduction (Optimization, numeric computing, and computer graphics). Contact: Dr. Kamal Abdali, Div. of Computer and Computation Research, 703-306-1912. Deadline: February 28.

**NSF/CISE: Computer Systems, Architecture, and Software**

Proposals will be accepted in the areas of computer architecture and compiling techniques (Operating systems and distributed and parallel computing). Contact: Dr. Anand Tripathi, Div. of Computer and Computation Research, 703-306-1912; e-mail, atripath@nsf.gov. Deadline: February 14.

**NSF: Environmental Geochemistry and Biogeochemistry**

The goal of the Environmental Geochemistry and Biogeochemistry activity is to enhance fundamental, interdisciplinary research on chemical processes that determine the behavior and distribution of inorganic and organic materials in environments near the Earth's surface. Of particular importance are projects that characterize chemical parameters in both perturbed and unperturbed natural systems, clarify the chemical processes or behavior observed, or combine observations and interpretations into predictive models.

The Environmental Geochemistry and Biogeochemistry research activity supports studies on the physical-chemical-biotic behavior of chemical substances within one environment or by emphasizing research that focuses on a common chemical theme throughout a variety of environments. Environments of interest are soils, ground waters, surface waters, coastal marine and estuarine areas, and portions of the troposphere in contact with these environments.

This research activity encourages integration of critical inquiry from the disciplines of inorganic, organic, bioinorganic, and bioorganic chemistry (reactions in complex environments), geochemistry (characterization and distribution of chemical compounds in natural systems), hydrology (flow and transport), biology (dynamic influences of microbes and other communities), colloid, interfacial, and transport engineering (including generic mechanisms in porous media), and mathematics (analytical, statistical, and computational modeling of complex systems) to address environmental problems. Research projects combining approaches from other chemically-based science or engineering fields of study with these disciplines are also appropriate.

Research supported through this activity will facilitate development of a multi-faceted perspective and predictive understanding of the complex interactions of the geosphere, hydrosphere, biosphere, and atmosphere as they relate to chemical transport. The results will contribute to the knowledge base used by management and policy decision-makers in planning, development, pollution avoidance, remediation, and restoration activities.

Award durations of two to three years will be considered. Average annual award levels are anticipated to be approximately $50,000 to $100,000 per senior investigator. The total funding requested for each project, for all investigators, must not exceed $500,000. In FY 1997, NSF expects to make awards totaling approximately $ 5.1 million for this activity, depending on availability of funds. Award lists and abstracts for the FY95 and FY96 competitions are available on-line at http://www.nsf.gov/stratare/egch/envresop.htm

Proposals submitted in response to this solicitation must be received no later than 5:00 pm EST on **January 7, 1997.** Review and processing of proposals require approximately six months.

**NSF/CISE: Robotics and Machine Intelligence**

This program supports research in robotics and robotic perception, including computer vision and image understanding. Emphasis is on autonomous intelligent behavior of machines. Annual target dates are **February 15** and **September 15.** Panel review is in late spring and late fall. When submitting a proposal, please send a total of 15 copies. Proposals should be submitted as close to the target date as possible. Contact: Dr. Howard Moraff, Div. of Information, Robotics, and Intelligent Systems, 703-306-1928, or by e-mail, hmoraff@nsf.gov.

**PA-96-076: Anabolic Hormones in Bone - Basic Research and Therapeutic Potential**

The objective of this initiative is to elicit grant submissions which focus on the role(s) of systemic hormones, local growth factors, and bone-active cytokines which have specific or generalized anabolic effects on bone. While the primary focus is on basic research, the long-term emphasis is on identifying mechanisms or processes related to hormone action with potential applicability as targets for therapeutic agents for the treatment of diseases that adversely affect bone, including osteoporosis and primary hyperparathyroidism. Support mechanisms for this PA will be research project grants (R01) and First Independent Research Support and Transition (FIRST) (R29) awards.

**NIAID: Development of New Gene Therapy Vectors and Delivery Systems**

The purpose of this notice is to emphasizes the importance of this research topic to the National Heart, Lung, and Blood Institute, National Institutes of Health. Collaboration between small business concerns and research institutions, including colleges and universities, is encouraged to design and develop gene therapy vectors and delivery systems for cardiovascular, pulmonary and hematologic gene therapy. Such collaboration is essential in order to qualify for support under the Small Business Technology Transfer (STTR) program and is permissible under the Small Business Innovation Research (SBIR) program.

This program is open to all approaches for effective gene therapy vector designs and delivery methods. Research needs include, but are not limited to, the following: Gene Expression; Gene Delivery and Transfer; Target Cells; Cellular and

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Humoral Immunity; and Model Systems. Annual Receipt Dates: April 1, August 1, and December 1 for STTR; April 15, August 15, and December 15 for SBIR.

**PA-96-078: Novel HIV Vaccine Design**

The National Institute of Allergy and Infectious Diseases gives special consideration for funding to scientifically meritorious applications in response to Program Announcements. Our Program Announcements identify areas of ongoing research emphasis for the NIAID. The purpose of this Program Announcement (PA) is to solicit investigator-initiated research to study novel "high risk - high impact" HIV vaccine concepts in early stages of development.

The mechanisms of support will be the individual research project grant (R01), Interactive Research Project Grants (IRPG), the First Independent Research Support Transition (FIRST; R29) award, and the Small Research Grant (R03). Research support may also be obtained through applications for a competitive supplement to ongoing NIH-funded grants. Multidisciplinary approaches that involve collaborative efforts among investigators in the fields of basic immunology, molecular biology, cell biology, biochemistry, and infectious diseases are strongly encouraged. Examples of novel vaccine strategies responsive to this PA would include live virus vectors, bacterial vector-based vaccines, nucleic acid-based immunogens, adjuvants, and conformational (nonlinear) synthetic peptide vaccine approaches.

Vaccine concepts that are presently being tested in primate models or in clinical trials would not be responsive to this PA.

**PA-97-001: Steroid Receptor Structure - Functional Considerations**

The objective of this initiative is to elicit grant submissions which focus on integrating structural with functional information about the receptors in the steroid/thyroid/retinoid superfamily, including the orphan receptors for which no known ligands have been identified. Also referred to as nuclear receptors, the identification and characterization of the receptors for many of these hormones has revealed several examples of mutations in key domains or alterations in function which have been linked to human diseases, including vitamin D-dependent rickets, thyroid hormone resistance, and androgen resistance syndrome. In addition, hormones and their receptors in this large superfamily have been linked to breast, prostate (and other) cancers, osteoporosis, obesity, diabetes, and other diseases or disorders. Finally, agonists and/or antagonists of steroid/thyroid/retinoid hormones may have clinical utility for the prevention or treatment of diseases with significant health relevance to women, including breast cancer and osteoporosis. Application Receipt Dates: February 1, June 1, and October 1.

**PA-96-079: Ontogeny and Differentiation of the Liver and Biliary Tree**

The Division of Digestive Diseases and Nutrition of the National Institute of Diabetes and Digestive and Kidney Diseases wishes to encourage research applications in the identification and characterization of the cellular lineages of the liver and biliary tree. Support for this program announcement will be through the NIH research project grant (R01) award, the First Independent Research Support and Transition (FIRST) (R29) award, and the small grants (R03) award.

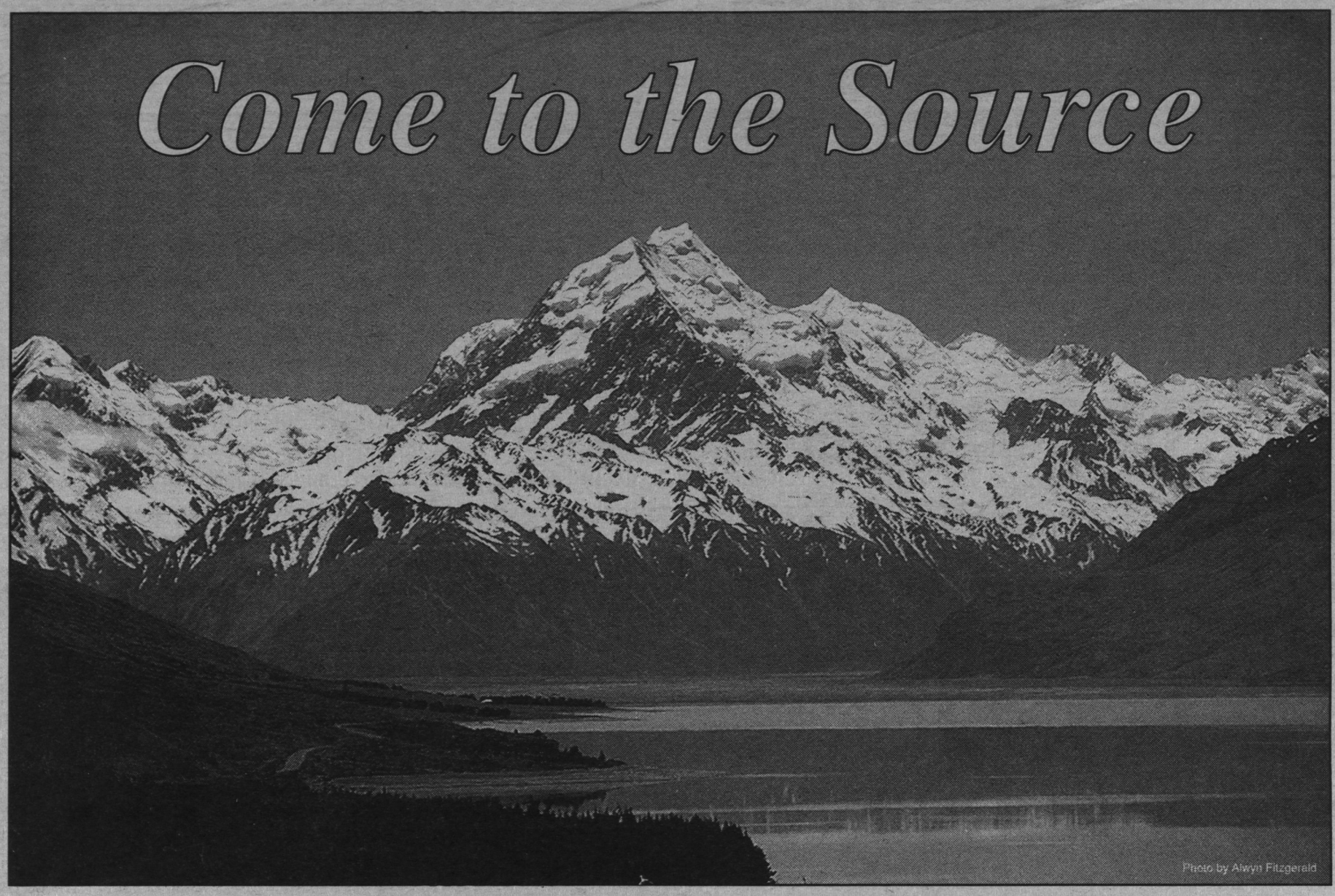
**PAR-97-002: Pilot Studies on Gene Therapy Vectors for Metabolic Diseases**

The National Institute of Diabetes and Digestive and Kidney Diseases invites applications for pilot and feasibility studies proposing innovative strategies for gene therapy vector development. These grants will allow investigators to obtain preliminary data on novel approaches to gene therapy relevant to the treatment of genetic metabolic diseases. Topics will be limited to pre-clinical vector development designed to increase the level and the duration of gene expression in vivo. Research designed to elucidate the basic mechanisms and cellular factors involved in the processes of vector entry and transgene expression will also be responsive to this PA.

This program will be supported through the exploratory/developmental grants (R21) mechanism. These awards are to demonstrate feasibility and obtain preliminary data. Thus, these grants will not be renewable; continuation of projects developed under this program will be through the research grant program. Projects will be limited to $100,000 direct costs per year and are limited to two years duration.

**PA-97-003: Immunobiological Consequences of Aging**

The NIAID and the NIA invite research project grant (R01), First Independent Research Support and Transition (FIRST) (R29) award, program project grant (P01), and small grant (R03) applications for basic immunological research that will clarify the effects of senescence on immune function. It has been well established that overall immune function declines with advancing age. However, because the immune system is highly complex, it is essential to understand the multifaceted nature of the age-related loss of immune function and to identify the primary changes in immune mechanisms that lead to the decline in immune competence. It is assumed that retardation, or reversal, of senescent changes in the immune system would benefit aging individuals, but the validity of that assumption, and approaches to perpetuating immunological vigor, are unclear. Although some important changes that occur as the immune system ages have been identified, much more work is required to address adequately the gaps in knowledge and promising scientific opportunities. The purpose of this Program Announcement (PA) is to stimulate research that will provide fundamental, conceptual insight into the rational design of prophylactic and therapeutic measures for improving the immunobiological health of aging humans.■

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# Nobel Laureate Leon Lederman Speaks About "Anti-Science" and his Great Passion: Education

by Gregory Gabriel

In 1988 Dr. Leon Lederman won the Nobel Prize in physics for his 1961 discovery of the existance of more than one type of neutrino. In accomplishing this goal he collected physical, hard evidence proving the existence of the smallest particles in the universe. These days, he has an equally ambitious and difficult goal- also requiring hard evidence, but not taken from particle accelerators or mathematical formulas. He is developing and implementing educational reforms addressing the decline of critical thinking.

On October 18th, Lederman spoke about this issue at the New York Area Skeptics (NYASk) third annual Isaac Asimov Memorial Lecture held at The United Engineering Center in Manhattan. In introducing Lederman, Dr. Larry Lesyna, president of NYASk, said, "I'd like to call neutrinos ghostlike," jokingly adding, "but you know how we skeptics feel about ghosts." Indeed this night's talk entertained the audience but also touched upon a wide range of issues.

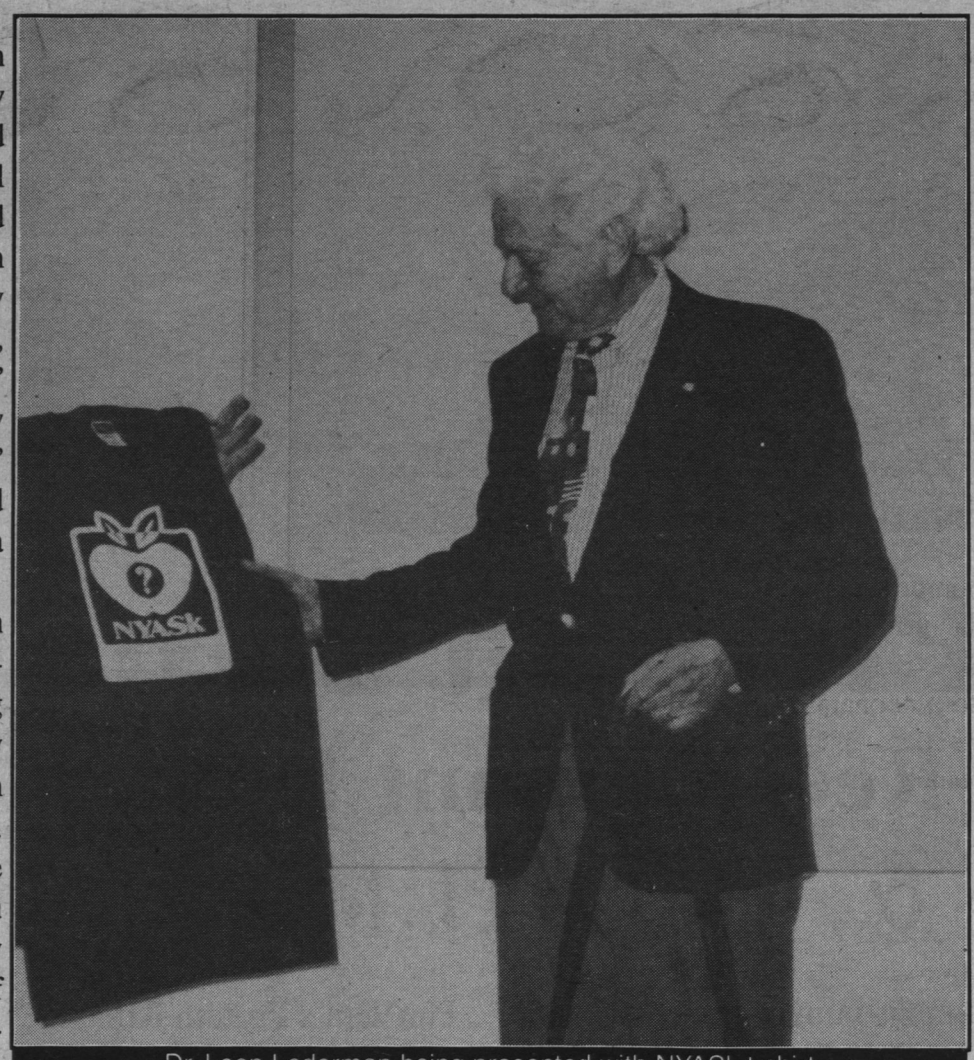
Having studied and taught in New York City, Lederman appreciated the warm reception welcoming him back home. He immediately jumped into a nostalgic story from his days at Columbia University. Quoting a linguist that he heard give a talk, Lederman said, "Did you know there are 1857 independently structured languages, in 67% of which two negatives imply a positive?" The linguist then asked, almost as an afterthought, "And did you know in not a single one of these languages do two affirmatives make a negative?" Continuing, Dr. Lederman said, "At that point a CU professor of philosophy, sitting in the front row, drolly said, 'Yeah, yeah.'"

Lederman, a very colorful speaker, brought up many topics, most of which he did not delve into deeply during his one hour talk. For the most part, this informal lecture catered to the audience of mostly NYASk members, their guests, and others curious about the changing role of science. He talked about the history of anti-science for the first half and his experiences with the educational system particularly in Illinois for the second half of the evening.

He introduced problems faced by the scientific community, namely, "the retreat of institutions that generally support scientific research, including industries, universities and national laboratories." Admittedly this problem requires a different approach than proving the existence of neutrinos. These problems contain social, and economical aspects. He identified two questions that these institutions are asking: first, can the advancements that come from critical thinking translate into dollars; and second, are these results immediate?

As background he described the anti-science movement and its prevalence in the past and present, a topic that NYASk is very familiar with. Quite simply, he defined anti-science as a method that deteriorates a person's ability to think skeptically. He was especially critical of the congressional pseudo- investigators in the past. These include Rep. John Dingle of Michigan who "brought up the spectre of McCarthyism in a very dramatic way," and Senator William Proxmeyer of Wisconsin who sought publicity through his shameless Golden Fleece awards.

In academics he cited certain individuals that, "seem to be proud of their ignorance of science, or mortified by a certain disconnection." Lederman recalled a hotbed of anti-science at Columbia University in the 1950's. He identified, at times by name, two types of professors in the humanities: those who he claimed either enjoyed understanding the processes of science and methods of thinking, and those self-confessed anti-science professors, who he speculated, were "too lazy intellectually to make the effort other humanists made."



Dr. Leon Lederman being presented with NYASk t-shirt

He also cited television commercials which are anti-science in nature since they try to force beliefs and unfounded claims onto unquestioning consumers. The rejection of "anti-science" sentiment is a continuing pursuit carried out by NYASk and many scientists such as Lederman.

Lederman concluded this issue stating, "Physicists have a genetic defect in that they need to solve problems." Thus, he moved from this ubiquitous problem of anti-science a more localized and solvable problem: the dated science curriculum in high schools today. Working closely with Illinois school officials, he is slowly renewing the educational system there.

As director of the Fermi National Accelerator at Illinois from 1979 to 1989, Lederman missed teaching, so he established a Saturday morning physics program for high school students. Through this successful program he had a chance, in cooperation with the governor of Illinois, to develop the Illinois Mathematics and Science Academy, a public high school for gifted students. This institution was inspired by the schools for gifted kids in New York and describes the academy as the "Bronx High School of Science of the prairie."

One of his main criticisms of high schools is the order in which the three sciences are taught. (He cited only the state of Pennsylvania, New York City, Chicago and a few other cities as the places where three years of high school science and math are even required at all to graduate) With few exceptions the traditional order is biology, chemistry and "for those who survived," Lederman quipped, "then physics."

"Biology," he summarized, "is the most complex discipline. DNA is a molecule which you learn about in chemistry . . . and molecules consist of atoms; something you learned in physics. More than a hundred years ago, in 1893, a committee of ten, chaired by the president of Harvard decided this order. The logic was impeccably- alphabetical!"

A year ago he started a formal program called American Renaissance in Science Education (ARISE) to eliminate this standard, which he views as illogical. It intends to make the curriculum more coherent by at least renaming the subjects Science I, II, and III. They also hope to integrate the curriculum so

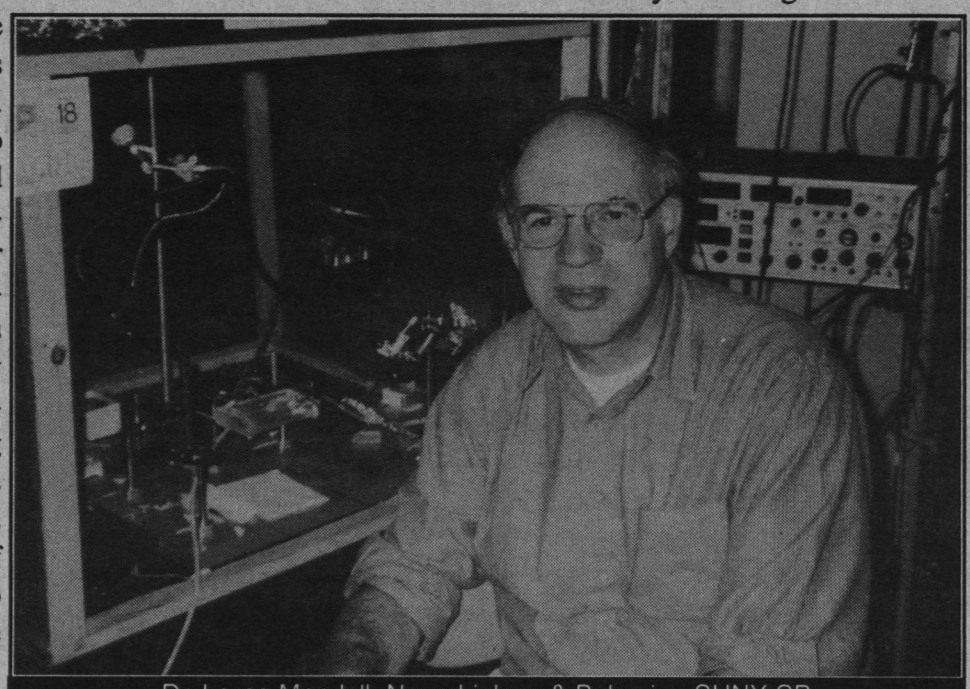
Continued on Page 31

# Stony Brook Scientist Elected to Presidency of Society for Neuroscience

## Known for Work on Nerve Growth Factor

by Matthew S. Seidner

Dr. Lorne M. Mendell was elected to be The Society for Neuroscience's President for 1998. Mendell currently serves as the Chair of the Department of Neurobiology and Behavior at SUNY Stony Brook, where he maintains his research endeavors as well as a commitment to teaching. His current research is related to nerve growth factor, and has turned up some potentially important applications for reducing hyperalgesia, or pain. His work expands on the traditional view that nerve growth factors (NGF) play their primary role only during development of the organism. He has shown that injecting NGF into the organism causes hyperalgesia, and that pain receptors can be blocked, in certain kinds of inflammations, by the antibody to NGF. Biotechnology companies are highly interested in potential applications of this research and have provided support in the form of relatively large supplies of NGF for Mendell's research.



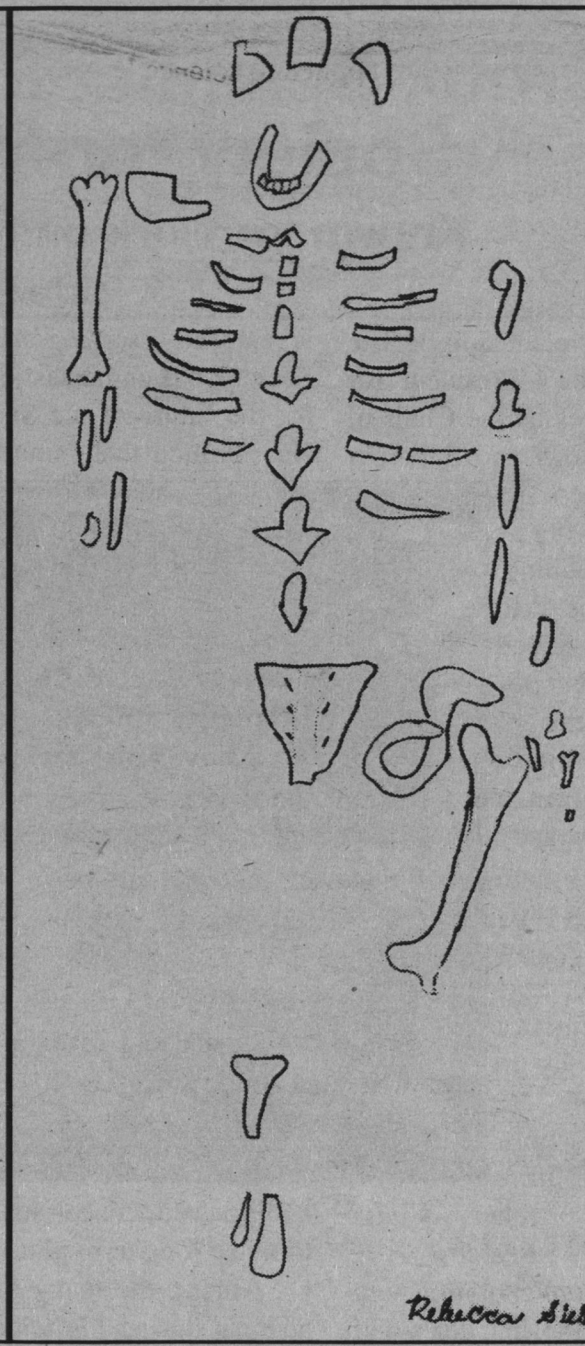
Dr. Lorne Mendell, Neurobiology & Behavior, SUNY SB

Other research, some in collaboration with scientists at the University of Florida, deals with another growth factor called NT-3. NT-3 is a molecule that, when introduced into a neonatal rat or cat, helps increase reflex function. It is unknown whether NT-3 is a substance that is normally supplied to nerve cells by muscle cells. One question, however, is if NT-3 is supplied to an injured nerve through a pump, will the nerve begin to function again, or at least cease its deterioration? The ultimate question being researched though the experiments with NT-3 and NGF is to learn the degree of plasticity of the nervous system, or how functionality can be regained by an injured nervous system. Mendell is also currently editing a book which will be titled "Presynaptic Inhibition and Neural Control Mechanisms" (co-edited with P. Rudomin and R. Romo), and is about presynaptic control mechanisms described at the physiological level.

The Society for Neuroscience is one of the largest academic societies, with over 25,000 members, and is based in Washington DC. Although primarily a tri-national organization, comprised of scientists in the US, Canada, and Mexico, the organization has been steadily growing to include members from all over the world. The Society's primary feature is its yearly convention, where scientists report their latest findings in basic neurosciences and clinical frontiers. (The conference is so large that it can only be held in select cities which can accommodate the roughly 20,000 attendees.) In addition, the society publishes the Journal of Neuroscience, which is the peer-review journal of choice for research publications in that field. Mendell, a leader in neuroscience research who is currently serving as the Treasurer of the Society, has enthusiastically discussed his ideas for the future of the Society for Neuroscience. He admitted that "since The Society is so big and you're there for such a short time, it's hard to make long term plans."

Among the many things that he intends to address during his tenure are education (from high schools to graduate and postgraduate levels), improving communication among neuroscientists via the World Wide Web, and to address issues that will ensure a long future in a field that is only beginning to recognize its potential for research applications.In addition, he is keenly aware of the need for scientists to explain, in layman's terms, the research that they do. The Society for Neuroscience sends out "Brain Briefings" to members of the media, Congress, and others, with the hopes of updating them on the progress in neuroscience. He feels that the study of the brain and nervous system, as well the rest of science, needs to be understood on some basic level by many more people than currently have any indication of what actually is done in the laboratory. "The public is very interested in health and preserving it, and they are also very interested in their brains and behavior because that's what makes us human. It distinguishes us from other members of the animal kingdom. There is a fascination that people have with the brain," said Mendell.

Mendell began his career at Duke University, where he spent twelve years. Sixteen years ago he came to SUNY Stony Brook. He teaches primarily in the Medical School, and occasionally in departments in Arts and Sciences. (Neurobiology is one of USB's two departments that have standing in both the medical and undergraduate sides of campus.) Being President of the Society for Neuroscience, Chairman of the Department of Neurobiology and Behavior, Principal Investigator on cutting edge research projects, and Editor of a neuroscience book should be enough, Mendell expects "to keep at least a little busy in the coming year!"■




"Lucy," best-known fossil specimen of early hominid *Australopithecus Afarensis.* (Drawn by Rebecca Sieburth)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that the mathematical lessons of one day are applied to science lessons the next.

ARISE also has an intervention program where they spend more than 100 hours a year per teacher for three years, training them in new instructional techniques and introducing them to current research in their respective fields. Revitalizing a whole school at a time, ARISE forms contracts with the local school council, the teachers and parents, and local social groups like the Urban League so that everyone is involved. Test scores are now being compiled for the schools that have been involved for the past five years. It was apparent in Lederman's voice how close he holds these issues to his heart. He shared his passion for children and science with the audience, and spoke with fondness about the students he sees using the labs at the Saturday morning research programs.

Lederman has taught and researched at Columbia University, and the University of Chicago, and is currently at the Illinois Institute of Technology. He continues to work on focussing education towards critical thinking. In addition to his academic and educational work, he has also written The God Particle, an anecdotal book that serves as a great introduction to physics.

NYASk is a group intersted in education as well, offering membership discounts to students, and sponsoring an annual essay contest for area High Schoolers. They have established a mentor program to discuss these essays with students and to suggest places to find critical resources. Members include educators, scientists in industry and academia, and journalists willing to volunteer their time and expertise.■

*The next lecture sponsored by NYASk will be held on November 13, and is titled "Are power lines dangerous to your health?" by NYASk president Dr. Larry Lesyna, also of Northrop Grumman Corporation. More information about NYASk and this event can be found on their web page at http://www.liii.com/~nyask.*

Continued from Page 7

and Pollack is hopeful that such an approach will also uncover evolutionary newcomers that have contributed to the emergence of language and consciousness.

Such a view of the human genome may also serve as an antidote to the urge to find laws that govern behavior and to improve certain human attributes by "perfecting" the genome. *Signs of Life* outlines the various attempts, in this, the century of genetics, to justify a program of eugenics by appealing to the supposedly scientific notion that genes are destiny. He comments, "I think any reasonable person I know would say that all interesting aspects of people are a mixture of what's inherited and what's learned. What's inherited is the information for the laying down of something which becomes a functioning brain by experience. And so, early experience must be formative for how the brain works." The attempt to select for complex polygenic traits such as intelligence is therefore not only suspect on moral and ethical grounds, but rests on the unsupportable belief that the connection between genotype and phenotype for such traits is straightforward. Pollack emphasizes that it is not, "and our freedom lies in the fact that it's not fully understandable."

Another aspect of contemporary biomedical science that is addressed in *Signs of Life,* and is a major focus of his new book, is the disregard for the unintended consequences of genome research and its application to problems of human health. Since the temporary self-imposed moratorium on recombinant DNA research two decades ago, he argues that "there hasn't been a second incident of publicly acknowledged introspective doubt. It's been pure triumphalism ever since. I think that is a problem. It's extremely unlikely that nothing of equal potential risk has occurred. It's more likely that the field has learned that the consequence of introspection is mockery, and it's just pulled in the wagons and become very defensive." He hastens to add that a few scientific leaders have addressed the economic, social, and ethical implications of the Human Genome Project, singling out Director Francis Collins for praise. Collins, he says, "is one of the guys who is not simply on the horse wherever the horse takes him."

One issue that already confronts physicians and their patients is that of genetic testing. Pollack describes the difficulties that accompany testing for mutant alleles of the BRCA1 gene. Carriers are at very high risk for breast cancer, but for those who test negative "there's no knowledge of their chances, and since BRCA1 accounts for only 10-15% of breast cancers, you have no idea what is the proper medical, ethical, scientifically accurate thing to say." He argues that women who test negative for BRCA1 mutations may be less vigilant in self-examination if they are under the impression that the test result means that they are at no risk for developing breast cancer. Collins, in a recent talk at Columbia's College of Physicians and Surgeons, identified other areas of concern, pointing out that for a woman who tests positive it is not at all clear what recommendations her doctor can make to reduce her risk. Another important issue is that of privacy. According to Collins, women who decide not to get tested for BRCA1 mutations at the NIH Breast Cancer Genetics Clinic cite fear of losing health insurance coverage as the most important reason. Although the recently passed Kassebaum-Kennedy bill prevents an insurance provider from denying someone access to coverage on the basis of such information, there is no limit placed on the cost of such a policy. An equally troubling situation confronts men being tested for prostate specific antigen, a marker for prostate cancer. Since false positives are possible, and since biopsy carries some risk, Pollack suggests that "if you gave it (the test) to everybody, it's statistically certain that you would do more harm than good." These kinds of unintended consequences are discussed in his next book, which he expects to appear in 1997.

In this book he will address another underappreciated aspect of genome research. He points out that the human genome contains, buried within it, "a large number of questions too frightening to ask. The full understanding of this sequence is going to tell us whether death is allelic, whether it's built into the genome, or whether it's not, and if it's not, then it's the consequence of uncontrollable, unknowable, stochastic, non-informational events, in which case there is a boundary to what we can do about it." Ironically, the information that is driving the era of molecular medicine may confirm (if it needed any confirmation) the one thing that we least want to have confirmed: that, as Pollack stated at the "Science in Crisis" symposium, "the eventual loss of self is inevitable." He suggests that such a realization should prod us to reconsider the wisdom of spending larger and larger amounts on health care at the very end of life, while neglecting the health care of the nation's children.

If the late Lewis Thomas helped to inspire a generation of scientists and interested non-scientists with brief essays on the wonder to be found in an appreciation of life at the cellular and molecular level, then Robert Pollack, while acknowledging the beauty of the picture of life that we are uncovering, may have a slightly different role to play. His current and future work may help to define the challenges that we face, not only in the laboratories, but in the clinics, courthouses and state houses as well. He writes in the belief that scientists must be forthright about the implications of their work and that an informed public must participate in the decision making process if we are to benefit from this research while avoiding its more troubling applications.■

*The author is a postdoctoral fellow in the Department of Genetics and Development and Center for Reproductive Sciences at Columbia University College of Physicians & Surgeons.*

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## BIOTECHNOLOGY TEACHING LABORATORY EDUCATES STUDENTS AND TEACHERS

The Biotechnology Teaching Laboratory (BTL), located on the SUNY-Stony Brook campus, provides a hands-on, insiders view of biotechnology research to students, educators, and industry employees. Through laboratory-based classes, on-site seminars, summer camps, and customized workshops, the BTL familiarizes participants with the concepts, techniques, and real- life applications of molecular biology and biotechnology.

"There is a growing interest and awareness in the importance of biotechnology in our lives," says R. David Bynum, Ph.D., Principal Investigator of the BTL. "The goals it [the BTL] seeks to meet are to make both the student and adult populations increasingly aware of biotechnology and the importance of it in the economic, health, and social aspects of our lives," he says.

The biotechnology industry now comprises more than 1300 firms nationwide, with nearly $13 billion in annual revenues. More than 40 approved biotechnology drugs and 21 food products are now on the market. "This is going to touch their lives at some point, whether they are a lawyer, a doctor, or a mechanic, so they need to have some basic understanding of what's going on," says Judith A. Scheppler, Ph.D., director of the BTL.

The BTL addresses this need through its varied programs. High school students conduct hands-on laboratory experiments to learn the basic techniques used in molecular biology research. Restriction enzyme analysis, agarose gel electrophoresis, bacterial cell transformation, polymerase chain reaction (PCR), and DNA fingerprinting, are just a few of the Laboratory's offerings. By exposing students to biotechnology early in their education, the BTL is opening the door to a potential career in the sciences.

With funding from the National Science Foundation, the Biotechnology Teaching Laboratory has launched the Long Island Group About Science Education (LIGASE), a consortium consisting of SUNY Stony Brook, Nassau Community College, Suffolk Community College, Brentwood High School, Uniondale High School, and several biotechnology companies. The goal is to educate a highly skilled work force to meet the needs of the expanding industry on Long Island.

A first step toward improving the quality of biotechnology education is the establishment of the Teacher Enhancement Institute, located in the School of Professional Development at SUNY Stony Brook. The program will educate high school and community college faculty in current concepts and laboratory techniques in biotechnology. Teachers and faculty will be encouraged to incorporate the experiments into their teaching plans. The LIGASE program will also outfit several "satellite" teaching labs at local colleges and high schools, to further the reach of the program.

The Biotechnology Teaching Laboratory has also taken an active role in providing biotechnology education to a broad range of adult interest groups. Customized workshops are designed to meet the specific training needs of industry sales, marketing and support personnel. Company employees can learn first-hand, how the products they sell are used in a variety of research environments. Introductory workshops for the general public are also available.

Funding for BTL programs comes from the National Science Foundation (grant # DUE 9602450), Center for Biotechnology, the Office of the Dean of the College of Arts and Sciences, and the Office of the Provost.

-Vicki Glaser-

## INNOVATIVE TECHNOLOGY GRANT (ITG) PROGRAM (DEADLINE FEBRUARY 10, 1997)

The Innovative Technology Grant (ITG) program, sponsored by the Center for Biotechnology, will support research in all areas of medical biotechnology, including drug design and development, immunodiagnostics, medical devices, biomaterials, and bioengineering. The Center will suppot research projects that involve new technologies, or novel applications of existing technologies, and that also have a strong potential for commercialization in the near term. The Center will support only new areas of research for a faculty principal investigator (PI). Research that already is supported by other sources is not eligible. Applications will be judged by the following criteria: 1) The quality of the science; 2) The potential for near-term (two-to-five year) commercialization;
3) Relevance to a New York State biotechnology or pharmaceutical company. Applicants are strongly encouraged to contact potential commercial partners as soon as possible to allow sufficient time to establish collaborations. The Center for Biotechnology will provide up to $25,000 to support ITG projects in partnership with New York State companies. The company is required to match these funds on at least a $1:1 basis for a total project budget of up to $50,000. ITG projects that do not have a prearranged New York State corporate partner may be budgeted for a maximum of $35,000.

## BIOTECHNOLOGY SEMINAR SERIES

The Center for Biotechnology is establishing a forum to increase interactions between research scientists in New York biotechnology companies and research scientists at SUNY Stony Brook. We are initiating a series of seminars in which industry scientists can present their research to members of academic departments at SUNY Stony Brook. The seminar will be followed by an informal gathering where individuals can discuss mutual interests in greater detail.

December 2, 1996, 4:00 p.m.: Richard Powell, Ph.D., Research Chemist, Technical Services, Nanoprobes Inc., "Molecular Microscopy: Metal Clusters as Better Biological Probes", Room 038, Life Sciences Bldg., SUNY Stony Brook.

December 9, 1996, 4:00 p.m.: James Maioriello, Ph.D., Manager, Chemical Services, Collaborative Laboratories, "Conjugation of Enzymes to Polymers for Use in Personal Care Products", Room 412, Chemistry Bldg., SUNY Stony Brook.

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