Volume 9 Fall 2003

Massachusetts Institute of Technology Undergraduate Research Journal OODOTAA

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UNDERGRADUATE RESEARCH JOURNAL

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Advisor Les Perelman

Design/Production Lynn Horsky Jocelyn Humelsine Heidi Wormser

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Massachusetts Institute of Technology 77 Massachusetts Avenue Cambridge, MA 02139

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Pelcome to the Fall 2003 Issue of the *MIT Undergraduate Research Journal.* In this ninth issue of *MURJ*, we present a few research reviews in fields ranging from biological engineering to microlensing, in hopes that our readers will delve into the world of the scientific unknown. Within these pages, we also include features examining topics such as research funding and data overload.

Our reports and features, as always, are written in such a manner as to make them accessible to all members of the MIT community. We hope that this interdisciplinary journal will provide an opportunity for our readers to learn of research in disciplines other than their own. We also hope that this journal will serve as a forum for debate and discovery, through which our readers may access arguments relating to the intersection of scientific research and public policy.

We extend our profound gratitude to those who make this goal possible. We acknowledge the advice and assistance of our advisor, Dean Les Perelman, the professors who review our work, and the continued support of *The Tech*. We would also like to thank Dean Larry Benedict, as well as the UROP and RLSLP offices, for their financial support of *MURJ* this semester, which made this publication possible. Special thanks also go to the Departments of Materials Science and Engineering, Architecture, Chemical Engineering, Economics, Management, Aeronautics and Astronautics, Political Science, and Nuclear Engineering for their monetary contributions.

If what you read piques your interest, we invite your input for the Spring 2004 issue—to either join the *MURJ* team or submit reports on your own research. Submissions will be due by the middle of January 2003. Please email murj-submit @mit.edu or visit our website, http://web.mit.edu/murj/www, if you have any other questions or comments.

Sincerely,

The Editors of MURJ

MIT Science News In Review

[Architecture]

MIT Researchers Build Dream Village to Replace Earthquake Victims' Homes

Mear Adapazari, Turkey, MIT Professor Jan Wampler is building Berikoy, a dream community to replace a village destroyed by a 1999 earthquake that measured 7.4 on the Richter scale. The groundbreaking ceremony was on June 6.



The "groundbreaking" ceremony for Berikoy was actually a "concrete-shoveling" into the forms that had been laid for the foundations of the first houses.

Wampler, together with graduates Rukiye Devres Unver and Barbara Brady, as well as students from his international workshop course, designed the village according to the residents' desires. Before, concrete apartments on loose topsoil buckled under the quake's force. Now, galvanized steel frameworks atop underground rock will create stable homes and collectively owned community centers, a library, and a computer center. The cooperative microvillage will derive heat and power from solar panels and windmills, fertilizer from sewage, and rainwater from reservoirs. The residents, with average family incomes of less than \$400 a month, need to pay less than \$100 monthly for two- to three- bedroom homes measuring 700-900 square feet. After paying for materials, workers older than 18 must also donate 500 hours of labor, which can include carpentry, construction work, cooking, childcare, and other services.

The project, costing \$1.5 million, is supported by Habitat for Humanity and the Turkish foundation CEKUL. —I. Lim

[Astro Physics]

Birth of X-Ray Binaries

A team of scientists led by David Pooley of MIT recently found that double-star systems, or binary stars, are formed as a consequence of globular clusters colliding with each other. Using NASA's Chandra X-ray Observatory, Pooley and his team observed X-ray sources in 12 globular clusters in our galaxy. A globular cluster is a collection of millions of stars in a spherical formation and about a hundred lightyears in diameter. When globular clusters run into each other, the gravitation of one star may draw another star into its orbit. These two stars form a binary system and produce X-rays that can be detected. Pooley found that the number of X-ray binaries is closely correlated with the rate of encounters between stars in the clusters. This research solves the long-standing mystery of binary star formation and has profound implications to the understanding of globular cluster evolution. -H. Wang

[Biology]

A Grade-A B-Cell Study

The post 9/11 era has transformed the American people into a fearful collective paranoid of its personal health. The faceless phantom we anxiously await has the potential to invade our bodies without our knowledge and take control within seconds, or worse. Our defense rests in the hands of molecular biologists such as MIT graduate Todd H. Rider of the Biosensor and Molecular Technologies Group in Lexington, Massachusetts. His successes will provide integral steps toward diagnosing the presence of pathogenic bacteria, agricultural pathogens, anthrax, and other feared biowarfare agents.

Rider and his research group have created CANARY (Cellular Analysis and Notification of Antigen Risks and Yields), a sensor that causes cells to fluoresce when exposed to pathogens and other contaminants. B lymphocytes (commonly known as B cells) are white blood cells that secrete antibodies and are thus central to an organism's immune response. Rider and his team genetically engineered a strain of mouse B cells, spliced with the jellyfish gene that produces a protein that glows. The new cells were further engineered to respond to certain bacteria and viruses.

The implications of this achievement are endless: The functions of these modified B cells may be used to diagnose water quality, indoor air quality (for diseases such as Legionnaire's), and a growing list of pathogens that include smallpox, plague, and chlamydia. The cells will be kept viable in a luminometer, where the cells' responses may be monitored.

The work is supported by the Defense Advanced Research Projects Agency and the U.S. Army Soldier and Biological Chemical Command. —E. Slutsky

Phytoplankton Genes Sequenced

Scientists from MIT, the University of California at San Diego, and Sthe Centre National de la Recherche Scientifique's Station Biologique de Roscoff have recently announced the genetic sequences of four related types of phytoplankton. These phytoplankton, which live in the ocean, are extremely important for several reasons: They are the world's smallest photosynthetic organisms, at the bottom of nature's food web, and crucial to climate fluctuations due to their role in atmospheric carbon dioxide regulation. Investigating the functions of the 2,000 genes in the organisms will lead to a better understanding of ecological systems and the photosynthetic process. Once the key mechanisms and gene functions are identified, scientists hope to create a model of photosynthesis based on the phytoplankton. Understanding how these small organisms create biomass from sunlight could help generate better methods for energy production. Scientists will also have the capability to compare the different forms of the organism to study their different ecological niches. The four sequences being reported are Synechococcus and three strains of Prochlorococcus. Different strains of the same phytoplankton, for example, exist at different depths in the ocean. Analysis of the gene sequencing data can therefore be used to study the immense diversity of ocean life. —K. Rivoire

MIT Researchers Pinpoint Potential Genetic Basis of Schizophrenia

MIT Nobel Laureate Susumu Tonegawa discovered that genetically engineered mice missing calcineurin, a brain protein, display schizophrenic behavior. Calcineurin plays a vital role in the central nervous system as a part of the biochemical pathway linking the receptors for the brain chemicals (neurotransmitters) NMDA and dopamine.

Tonegawa, director of the Picower Center for Learning and Memory at MIT, first found that these mice, like schizophrenia patients, had an impairment in short-term memory, also known as "working memory". Picower scientist Tsuyoshi Miyakawa further determined that the mice exhibited other schizophrenic abnormalities, such as aberrant social behavior and attention deficits. Picower scientist David Gerber and Rockefellar's Maria Karayiorgou found a correlation between a calcineurin gene and schizophrenia. Tonegawa hopes to find the specific genes and proteins involved in the calcineurin pathway so that new drugs can be developed to cure various cases of schizophrenia.

The study on human genes responsible for susceptibility to schizophrenia was funded by the Picower Foundation, the National Institutes of Health, the Howard Hughes Medical Institute, the Otsuka Maryland Research Institute, the McKnight Endowment Fund for Neuroscience, the EJLB Foundation, and the New York City Council Speaker's Fund. —I. Lim

[EECS]

New Navigation Technology Will Reveal Archaeological Treasure

MIT Professor David Mindell and his colleagues at the Woods Hole Oceanographic Institute (WHOI) have developed "Exact," a navigation system, to probe ocean depths too deep for divers. The system uses a wireless sonar assembly of three acoustic beacons, called transponders, to locate and to explore archaeological sites thousands of meters below the ocean surface. *Exact* can achieve an accuracy of less than a cubic centimeter.

The host transponder on the remotely operated vehicle (ROV) pings the other two transponders placed at the edges of the archaeological site. The amount of time the ping takes to reach each transponder, along with measurements from sensors on board the ROV, are used to calculate the position of the vehicle.

Exact, combined with ultrasonic imaging technology developed by MIT's DeepArch research group to profile objects buried in sea mud,



EXACT transponders are placed around site and their positions precisely calibrated.
 EXACT transponders listen for coded "ping" from JASON, respond with coded ping.
 Travel times of acoustic signal are used to triangulate JASON position, accurate to ~1 cm3 three times per second.
 Position data is fed-back into control system; under automatic (closed-loop) control, JASON runs straight tracklines over wreck site at slow speed (0.1 meters/sec).
 Sonar beam on vehicle scans across wreck site and records precise altitude information. Data is then combined with vehicle positioning and attitude to produce microbathymetry plot of site.
 Digital still photos are taken simultaneously for mosaic.

will identify and map archaeological artifacts buried at the bottom of the deep seas.

"The thing that makes artifacts important is their spatial relationships to each other," said Brendan Foley, who earned a Ph.D. in the history and archaeology of technology from MIT in June 2003. "The minute you remove an artifact from a site and put it somewhere else, then you've lost information." -J. Wong

[Materials Science]

\$50 Million Army Grant Awarded for Nanobiotechnology Research

In order to develop technology to better equip soldiers of the 21st century, the Army is funding a three-university consortium, including MIT, University of California at Santa Barbara, and California Institute of Technology. Up to \$50 million over a period of five years will be given to try to understand and utilize biological synthesis of materials. This collaboration has been named the Institute for Collaborative Biotechnologies (ICB). MIT's Angela Belcher, the John Chipman Associate Professor of Materials Science and Engineering and Biological Engineering, will be directing MIT's component of the research. Belcher has used biological organisms to grow and assemble semiconductor and magnetic materials. These organisms can be further manipulated to make liquid crystals for display technology and components for self-assembling electronics. Her team hopes to understand and develop ways for biological organisms to produce enhanced materials that have various signaling and processing applications. ICB was inspired by the fact that biological systems use different mechanisms to produce materials and integrated circuits for sensing, computing, and information processing such as that found in humans.

-H. Wang

[Mechanical Engineering]

MIT Crew Team? Think Again.

The locomotion of life, for the most part, has been limited to swimming, flying, and traversing solid surfaces. To transcend the normal modes of mobility and to perform a graceful ballet atop a liquid surface (while hopefully remaining dry) is to be Jesus Christ, or more modestly, an almost supernatural insect known as the water strider.

The ability of the water striders (of the family Gerridae and others) to walk on the surfaces of ponds and lakes had once been explained as the effect of the waves that their movement generates. As the insects sat on the water surface, their gentle, subtle movements created waves strong enough to push them forward. In 1993, however,



Left: A water strider passes over a layer of water that has been dyed blue and lit from below, illuminating the stopping vortices shed during the deceleration phase of the strider's motion. Right: Graduate students David Hu, left, and Brian Chan with their creation, Robostrider.

young MIT graduate students and an associate professor fused mathematics and mechanical engineering with modern technology and the ancient art of observation.

Mathematics graduate student David L. Hu and mechanical engineering graduate student Brian Chan, along with the guidance of John W. M. Bush, associate professor of mathematics at MIT and author of the study, have determined how the insects perform this once-misunderstood phenomena: The six legs of the insects form dents in the water surface. They then use their middle pair of legs as oars to paddle forward and are lifted by the motion of the water "un-denting" itself. The waves that the rowing motion creates are actually insignificant.

After the threesome employed mathematics, the use of high-speed photography, and a range of visualizing techniques to solve the paradox, Chan was delegated the task of creating a mechanical model of the insect's movement. The mechanical strider that was developed, although representing the culmination of a decade long paradox, was simply composed of a 7-Up can, stainless steel wire legs, and an elastic band surrounding a pulley system.

Historically, the first scientists were those who observed even the most simplistic natural phenomena and sought reasoning, an analytical and systematic understanding of an event that seemed to defy logic. Bush, Hu, and Chan have demonstrated the very fundamentals of scientific thought as they looked toward an insect to explore hydrodynamic forces and mechanical propulsion. The genuine scientist must look toward the simple, ignored, and abandoned to find a playground on which scientific, engineering, and mathematical fields can learn together and discover together.

Hu is continuing his research on surface swimmers by observing the locomotion of Microvelia, Mesovelia, and Physidae.

-E. Slutsky

Lithium lons Directly Imaged for the First Time

A research team has achieved atomic resolution of lithium ions for the first time by using focal-series reconstruction of exit surface

Denny's Paradox emerged to question the accepted notion. Mark W. Denny, a marine biologist at Stanford University, claimed that young water striders were not able to swim because their legs were too weak to create waves. Yet somehow, even young striders were able to glide on water surfaces. And so the riddle remained until two waves (ESWs) of LiCoO₂ undergoing high-resolution transmission electron microscopy (HRTEM), according to the July 2003 issue of *Nature Materials*. The paper's lead author, Yang Shao-Horn, is an assistant professor of mechanical engineering at MIT. To create images of the LiCoO₂ lattice, HRTEM interprets the phase change between an initial electron beam that is passed through the LiCoO₂ lattice and the emerging electron wave, known as ESW, which has undergone interaction with the potential field created by cobalt, oxygen, and lithium atoms.

"Lighter" atoms such as lithium scatter electrons more readily than "heavier" atoms such as oxygen and cobalt, and hence require resolutions higher than those required for heavier atoms. The team used a computer simulation program developed by Michael O'Keefe, a collaborator on the project, to predict that cobalt would become visible at 2 angstroms, oxygen at 1.4 angstroms, and Li at 1 angstroms. Experimental data confirmed the hypothesis.

Additionally, visibility of lithium was found to improve with sam-

ple thickness as a result of "increasing proportion of dynamic scattering contributing to the electron wave at the specimen exit surface." The optimum thickness was found to be 17 unit cells. "Operation of lithium rechargeable batteries is dependent on reversible lithium inserand extraction tion processes into and from the host materials of lithium storage," according to the authors of the team's paper. It cites rechargeable batteries for laptop computers as a pervasive example of LiCoO2 application. -J. Wong



A computer simulation shows how columns of atoms in lithium cobalt oxide, seen end-on, ought to appear. The inset is the actual image taken with a transmission electron microscope. It shows the arrangement of lithium ions among cobalt and oxygen atoms in the compound lithium cobalt oxide. The oxygen atoms are bright and sharp-edged, the cobalt atoms are fuzzy, and the lithium atoms are small, weak, and look a little stretched.

[Neuroscience]

MIT Researcher Discovers LTD Mechanisms in Visual Cortex

In the August issue of *Nature Neuroscience*, researchers from MIT and Johns Hopkins University Medical School explained the mechanisms behind blindness caused by vision deprivation to one eye. The blindness, due to synaptic decay, has been attributed to long-term depression (LTD), a lasting decrease in neuron activity. Normally, LTD is a mechanism that helps shape synaptic pathways in early development. However, mechanisms behind LTD have not been well understood.

The researchers were led by Mark F. Bear, a professor of brain and cognitive sciences in the Picower Center for Learning and Memory at MIT and a Howard Hughes Medical Institute investigator, as well as Hee J. Chung and Richard L. Huganir of Johns Hopkins. Other researchers included Arnold J. Heynen, a Picower Center research scientist; Bong-June Yoon, a Picower research associate; and Cheng-Hang Liu, an MIT graduate student. They reported that LTD in the visual cortex could be induced in newborn rats by depriving one eye of visual input.

In addition, Bear and his fellow researchers discovered the molecular changes that result in LTD. In particular, they discovered that LTD in the visual cortex is caused by a loss of glutamate receptors. Glutamate is a neurotransmitter frequently found in visual areas of the brain, allowing signals to pass from one neuron to another. Without glutamate receptors, a neuron will not receive visual signals, leading to synaptic decay. —M. Burns

Prefrontal Cortex of Brain Contains a Checklist

MIT researchers reported in the August 29 issue of *Science* that the prefrontal cortex of the brain contains an area that acts as a "checklist," keeping track of movement sequences that have been performed. The study was conducted by Ann M. Graybiel, the Walter A. Rosenblith Professor of Neuroscience at the McGovern Institute at MIT, and Naotaka Fujii, a research scientist in the Department of Brain and Cognitive Sciences.

In the study, neural activity in the prefrontal cortex was recorded in monkeys that had been trained to make a sequence of movements. The recorded neurons responded with each movement. However, when the movement sequence was completed, an extra response was recorded in the same neurons. Graybiel and Fujii report that the extra response is the checklist, activity that allows the brain to note which behaviors have been performed.

The existence of a checklist could explain some of the symptoms associated with damage to frontal cortex regions. A lack of a checklist system could result in repetitive behavior, as the brain is not aware that the behavior has been performed. In fact, such repetitive behaviors are frequently observed when the frontal cortex has been damaged.

Graybiel and Fujii also recorded from basal ganglia regions in the brain. The recordings suggest that basal ganglia and prefrontal cortex regions bind the individual behaviors within a behavioral sequence into larger chunks.

The study also revealed that the prefrontal cortex neurons intensify their responses at the start of a movement sequence. This phenomenon may also explain the symptoms of Parkinson's disease, in which patients have tremendous difficulty initiating any sequence of movements. -M. Burns

[Physics]

Pulsar Speed Limited by Gravitational Radiation

 \mathbf{M}^{IT} physicists at the Center for Space Research in collaboration with colleagues at NASA and in Scotland and the Netherlands

recently reported that gravitational radiation may act as a regulator limiting the speed of pulsars. A gravitational wave is a ripple in space, first predicted by Albert Einstein. This finding confirms a previous theory by scientists at the University of California at Santa Barbara. A pulsar is born from an exploded star and is so dense that a sphere 10 miles in diameter is as massive as the sun. It can spin as quickly as one revolution per millisecond; as the pulsar draws in material from a companion star, its rate of speed can increase dramatically. The researchers hypothesize that a feedback mechanism exists in which as the speed of the pulsar increases, gravitational radiation is released, which deforms the star and reduces the rotation. This limit to the speed of rotation prevents pulsars from selfdestructing. Physicists hope that the Laser Interferometer Gravitationalwave Observatory now in operation will be able to detect directly these gravitational waves that limit the speed of a pulsar, and the pulsar can be studied in further detail.



Material accumulating on the pulsar surface can sometimes ignite, causing thermonuclear flashes that emit bursts of X-ray light. These thermonuclear flames spread across the surface of the pulsar in a few seconds. The team established that "burst oscillations", a kind of flickering, during these X-ray bursts provide a direct measure of the pulsar's spin rate.

-K. Rivoire

The Future of Nuclear Power

A committee of MIT researchers recently announced the results of a study investigating alternatives to carbon fuels such as nuclear power. Fossil fuels comprise more than 90 percent of carbon emissions in the United States. This is only about half of total power in the country, so reducing greenhouse gas emission necessitates a change in power type. Current problems with cleaner fuel choices such as nuclear power include high costs and concerns about safety, environmental effects, security, and nuclear waste management. The study offered a number of recommendations to further the use of nuclear power, including tax benefits for companies producing technology without carbon and increased investigation and research by the Department of Energy into the health and waste management issues associated with nuclear power. The researchers also suggested improving the efficiency of current fuels, for example by research into more efficient engines, as well as researching other renewable sources of power.

-K. Rivoire

World Science News In Review

[Archeology/Biology]

Recent Research Suggests Neanderthals Not Our Ancestors

 $\mathbf{B}_{(mtDNA)}$, the Neanderthals might not be our ancestors as many scholars had previously thought. For ages researchers have been trying to solve the mystery of early human origin. The Replacement Model suggests that the early modern humans (e.g., Cro-Magnon) left Africa and replaced the Neanderthals in the European regions, while the Multi-Regional Theory argues that the two populations not only coexisted, but also interbred. The latter theory suggests that our genes should reflect an ancestry of both species, a scenario not supported by the most recent research. Scientists recently found reasonable resemblance between modern humans and the Cro-Magnon. The study, however, only investigated the mitochondrial DNA (mtDNA), the one kind of DNA currently available. MtDNA is passed down to offspring by the mother; therefore it is not perfectly certain that Cro-Magnon did not interbreed with Neanderthals-an argument that Multi-Regional proponents support. The major qualm people have with the Replacement Model is that it suggests modern humans are more related to a species that lived 45,000 years ago than a species that lived 20,000 years ago. The solution to the mystery may not be elucidated in the near future because analysis of nuclear DNA from ancient samples is not currently feasible. Scientists, however, hope that the advance in human genome mapping will provide other pieces of the puzzle. -W. V. Lee

[Biology]

New Discovery in Early Prostate Cancer Detection

The diagnosis of prostate cancer has L always been tricky; its treatment is even more so. Over treatment can lead to unnecessary suffering from the side effects, while under treatment can pose mortal danger. Over the years, several predictive markers have been developed to aid in accurate diagnosis and therefore adequate and effective treatment. Among the first markers are prostate-specific antigen (PSA) concentration in blood, Gleason score (which measures the tumor's grade), and the tumor's stage, which is determined by its size. Kattan nomograms, a popular set of algorithms used to predict the probability that a given therapy will cure a patient's cancer, can combine the three markers. It was widely used in the 90s and could predict



Orange staining marks the presence of the protein EZH2 in prostate cancer cells on the left of this composite image. Red squares on the DNA microarray at right identify genes that are active in metastatic prostate cancer. Green squares indicate genes that are repressed.

up to 80 percent accuracy. Next came gene-expression profiling, a technique that utilizes DNA microarrays to determine a cell's potential to become cancerous. Although this marker has worked well with other cancer types, it has not been very helpful in prostate cancer diagnosis until now. Mark A. Rubin and his team at Harvard University have recently identified a gene for the protein EZH2, whose presence is a likely sign of prostate cancer metastasis. Another research team, led by William L. Gerald, has been able to design a new combination of markers that includes the old indicators as well as the newly discovered EZH2. This combined method was able to predict up to 90 percent accuracy of the metastasis potential within four years of prostate removal surgery. At the same time, other studies of non generelated diagnostic markers are also underway. Magnetic resonance imaging (MRI) is one. Ralph Weissleder of MGH and his colleagues found that micro-magnetic-particle injection can effectively increase MRI's precision and thus accurately and non-invasively show whether the cancer has metastasized or not. Scientists hope to collaborate and draw from all aspects of the existing markers to develop the best method for diagnosis.

–W. V. Lee

Scientists Recognized Gene Responsible for Dyslexia

yslexia, a learning disorder that causes difficulties in written and Doral expression, affects at least one in 25 people. Although the cause is unknown, scientists have recently identified a gene that might be responsible for the disease. Geneticist Juha Kere of the Karolinska Institute in Huddinge, Sweden, and his team have pinpointed a gene named DYXC1 on chromosome 15 as one of the culprits for the disorder. He explained that disruption of the gene would result in blocked or altered production of a certain protein that only specific brain cells can respond to. Furthermore, Kere has found that the molecular makeup of this protein is significantly different from its analog in apes. The discrepancies might be a key to the evolution of Homo sapiens. Meanwhile, another team led by geneticist Shelley D. Smith of the University of Nebraska Medical Center is investigating another gene on chromosome 6 that might play a role in causing dyslexia. Further research is required to find out if DYXC1 is linked to other developmental disorders. -W.V. Lee

Another Study Confirms Pregnant Women Must Use Common Sense

The stability of the period between conception and early embryonic development is integral for the healthy growth of a newborn. The smallest aberration during this period has the potential to cause a miscarriage. A new study reports that pain-killing medications such as aspirin, ibuprofen, and others, taken during this fragile period, may increase the likelihood of a miscarriage.

Performed by the Kaiser Foundation Research Institute in Oakland, California, the study sampled 1,055 women who had just received a positive pregnancy test result. Fifty-three of these women reported using NSAIDS (the heading under which nonsteroidal anti-inflammatory drugs are classified) other than aspirin. Of those 53, 13 women experienced a miscarriage. This represents an 80 percent increase in likelihood, as compared to the 762 women who had not used any NSAIDS at all. The 22 women who reported using aspirin were 60 percent more likely to experience a miscarriage. On the other hand, the 172 women who took acetaminophen (Tylenol,) a pain-killing medication not classified under NSAIDS, did not experience increased risk of miscarriage.

NSAIDS alleviate pain by interfering with cyclooxygenase, an enzyme that leads to the production of lipids known as prostaglandins. Prostaglandins are responsible for pain and inflammation, among other functions such as aiding in smooth-muscle contraction, and thus their suppression fulfills the intended purposes of NSAIDS. Postaglandins are synthesized by the uterine lining during implantation and emerge to play an integral role in monitoring and maintaining healthy embryonic functions. Their absence may provide the direct link between NSAIDS and miscarriage.

Criticism has been reported, notably from Nick Henderson, director general of the International Ibuprofen Foundation in Marborough, England. He has been quoted in labeling this study as "alarmist." Scientists do warn women that this study is, in fact, small and may not provide a definitive conclusion. Further studies must be investigated to draw a direct link between NSAIDS and miscarriages. Yet the fact remains that women must be careful and cautious during pregnancy, limiting the amount of medications and risk factors they expose themselves to. —E. Slutsky

[Chemistry]

Licorice Compound Might Swallow SARS Threat

Glycyrrhizin, an antiviral agent isolated from licorice root, could become the most effective defense against severe acute respiratory syndrome (SARS). SARS is a highly contagious disease that broke out in the Far East early this year, and then was inadvertently introduced to North America by several carriers.



The SARS coronavirus emerged in November 2002 and killed hundreds before being contained, but new drugs are needed in case it re-emerges.



Jindrich Cinatl and colleagues at the Frankfurt University Medical School, Germany, tested the antiviral properties of five drugs (ribavarin, 6-azauridine, pyrazofurin, mycophenolic acid, and glycyrrhizin) against the SARS coronavirus. Each compound has previously been used for its antiviral, antitumor, or immunosuppressive properties. Ribavirin is currently most often used to treat SARS infection. Effective against unrelated HIV-1 and hepatitis C infection, glycyrrhizin has been proved to be effective in inhibiting viral replication. It probably increases nitrous oxide synthesis, and it is known to affect cellular signaling pathways like protein kinase C, casein kinase II, and various transcription factors. —I. Lim

Liquid Crystals Improve

Researchers have created a new class of liquid crystals that selectively reflect light, a breakthrough that could improve the quality of future optical devices. The new crystals are stable at high temperatures and have a low melting point, a temperature versatility that materials developed earlier lack.

British chemists John Goodby and Isabel Saez had concentrated their research on dendrimers, large molecular structures with useful properties but incapable of functioning independently. However, when they modi-

fied the dendrimers



The texture of a liquid crystal chiral nematic phase

to generate a hybrid organic-inorganic system, Goodby and Saez were able to incorporate the dendrimers into huge fabricated crystals made of buckyballs. "We could put a chemical unit that had a functional property into a giant liquid crystal and have it self-organize," said Goodby. "This is effectively what proteins do, but we were doing it in an advanced materials sense!"

The similarity with proteins raises the possibility of synthesizing "materials with protein-like properties," akin to a "molecular machine," with implications as yet unknown. The new materials could more immediately be applied to improve optical filters, digital watches, and coatings for transparent surfaces, all current common uses of liquid crystals. —D. Barclay

[Earth, Atmospheric, and Planetary Sciences]

New Correlation Buttresses Dark Energy Theory

The correlation of galaxy locations and cosmic background radiation is a contribution to the growing body of evidence supporting the theory of dark energy, according to new work reported in the August 2, 2003 issue of *Science News*.

Advocates of the dark energy theory attribute the acceleration of the expansion of the universe to the mysterious substance heretofore called dark energy. Cosmic background radiation is remnant radiation from the Big Bang.

Four independent studies from the Wilkinson Microwave Anisotropy Probe (WMAP) correlated with maps of galaxy locations. All four studies show a relative blue-shift, indicating a higher energy, in cosmic background radiation emerging from regions of high-matter concentration, such as galaxy superclusters, when compared to cosmic background radiation emerging from regions of lower-matter concentration. Hence, the studies show a positive correlation between matter concentration and the apparent energy of cosmic background radiation.

The energy gained by photons entering a region of matter should equal the energy lost by photons leaving the region, resulting in zero increase in energy. However, the studies observed a slight increase in energy. According to the analysis in the studies, dark energy pushes matter apart during the period when photons traverse the matter so that the photons expend less energy as they leave the matter. The difference in energy is the observed energy increase, according to the studies.

The four studies were conducted by: R. Scranton et al. of the University of Pittsburgh; P. Fosalba et al. of the Institut d'Astrophysique de Paris; S. Boughn of Haverford College, and R. Crittenden of the Institute of Cosmology and Gravitation in Portsmouth, England; and M. Nolta of Princeton University. —J. Wong

[EECS]

Hopping for Bandwidth: Rooftop Networking

o you ever dream about surfing the Internet from anywhere in the \mathbf{D} world? Researchers from the MIT Roofnet project are trying to make that dream come true. With the help of a whole lot of rooftop antennas, computer science professor and project leader Robert Morris and his students are building a network of computers equipped with Wi-Fi cards to efficiently route data packets. At the expense of a fireplace, users of the Roofnet can get Internet access equivalent to broadband cable, with no monthly payments to an Internet provider. Antennas are mounted to the rooftops so that data packets can hop from one roof to the next until they finally reach a computer that is connected to the fixed Internet in the MIT computer science building. This multihop mesh network technology has drawn interest from research groups at Carnegie Mellon, Rice, and UCLA, and companies such as Nokia, Intel, and Microsoft. Community mesh networks like Roofnet are believed to be a promising way of bringing wireless networking to a majority of the population, especially people in rural areas where wired broadband access is not feasible. Roofnet is different from regular community-owned wireless networks because its nodes are not permanently connected to the network. Instead, the network constantly checks existing links and forms new ones, thus making the network more dynamic. This technology still has to overcome some practical issues. Unpredictable weather conditions and environmental disruptions can severely degrade the packet signals. MIT researchers are currently debugging and fine-tuning their routing schemes in hopes of utilizing them in more complicated systems such as using car antennas becoming mobile nodes. -H. Wang

[Materials Science]

Layered Assembly on the Rise

R apid advances in a materials construction technique have opened the door to its possible commercialization in the near future. The technique, which progressively adds nanoscale coatings to surfaces, allows for a greater degree of control over the material's properties than traditional methods.



Fruit Fuzz. Melons protected with Yasa-sheet (left) don't rot as quickly as those left to fend for themselves (right).

"This field is reaching the point where we're really starting to harvest some very interesting new technologies based on these materials," said Michael Rubner of MIT. "This is going to be a very exciting time in the next few years and beyond." Researchers are trying to use layered assembly techniques to improve everything from solar cells, aviation equipment, and body armor to artificial bone, biomedical devices, and fruit preservation.

Experimentation is facilitated by the procedure's technical accessibility. Dipping a negatively charged solid surface into a positively charged solution and letting it dry yields one layer of coating. That leaves only the need to repeat the process numerous times, which can be done by robots. Louisiana Tech University researcher Yuri Lvov characterized the method as "very simple, even primitive."

This simplicity appeals to numerous small start-ups such as Strala Materials, Capsulution, and Shiratori NanoTechnology, which believe that the layering technique can be mass-produced cheaply. Larger businesses such as CibaVision have also exhibited interest in building an industry around the emerging technology. Profits as yet remain elusive, but interest in the field is certainly not. —D. Barclay

[Math and Biology]

Cellular Circuits

Researchers are developing cellular computer programs, organic circuits dependent on genetic material. "We're basically hacking DNA instead of software," said Ron Weiss of Princeton University.

Certain genes instruct a cell to produce one type of protein if another type of protein is present. By organizing the cells into chains and altering their genetic instructions, digital logic gates can be created. For example, if protein A inhibits a cell from forming protein B, a primitive inverter results. Biological AND gates can also be built (by using the inverter on DNA, of course), so theoretically any type of circuit is possible. Weiss's group has designed a five-gene circuit in E. coli bacteria that generates fluorescent proteins whenever the concentration of a surrounding chemical falls within a certain level. This could assist environmental engineers in detecting toxins. If slight variations of the circuit were made to respond to different conditions, the resulting protein patterns could even form a topographical map of toxin concentration.

However, researchers are hindered by the time-consuming work of programming the cells in the first place. Each genetic modification requires a lengthy procedure using enzymes to cut out the relevant sections of DNA, reorder them, and insert them into the target organism. Linking two cells in a circuit requires that a number of factors be closely synchronized, so even a small amount of error can cause the procedure to fail.

To get around this problem, much genetic-circuit engineering work revolves around computer modeling to simulate conditions before they occur. Although those computers currently use inorganic circuits, in the future, it's anyone's guess. —D. Barclay

[Neuroscience]

Enzyme Disrupts Tau Tangles

 \mathbf{R} aging mice from developing protein knots in their neurons. These

knots, caused by the tau protein, are frequently found within the neurons of patients with Alzheimer's disease. It is believed that Pin1 could lead to new treatments for the disease.

The study was conducted by Kun Ping Lu of the Beth Israel Deaconess Medical Center in Boston, Tony Hunter of the Salk Institute for Biological Studies in La Jolla, California, as well as their colleagues, and was published in the July 31 issue of *Nature*. Lu and Hunter were the original discoverers of Pin1 in 1995, showing that the enzyme interacts with the tau protein, which is normally a critical component of the internal skeleton of a cell. However, in Alzheimer's disease, molecular tags known as phosphates bind with tau, forming protein tangles within neurons.

In 1995, Lu and Hunter discovered that Pin1 binds with the tagged tau proteins, causing the phosphates to be released. The recent study showed that mice with an inactive Pin1 gene experience neuron loss as they age. Examining the brains of the mice, Lu and Hunter discovered that within the areas affected by neurodegeneration, tau proteins are tagged with phosphates, forming tangles within the neurons.

The researchers also studied the preserved brain tissue of Alzheimer's patients, noting that the lowest percentage of neurons with tangles was found in regions with the highest concentration of the Pin1 enzyme. ■ —M. Burns



The Ethics of Research Funding

Katarzyna Puchala

"Scientific progress on a broad front results from the free play of free intellects, working on subjects of their own choice, in the manner dictated by their curiosity for exploration of the unknown."

- "Science the Endless Frontier," Vannevar Bush, 1945

Even question the value of research-diligent study of various phenomena performed by network of agencies, individuals and facilities interacting in order to generate knowledge and harness it in the form of inventions. Indeed, scientific investigation, the discovery of the unknown, drives the economy, improves our health and quality of life, and provides a safer environment. Given how valuable the research enterprise is, it requires equally sufficient funds in order to thrive. This issue influences many in society and must be further explored.

Since research results affect everyone in society, information or products emerging from a scientific discovery should have the characteristics of a public good that is available to all. This concept brings about the issue of democratization of science. Since science supports social needs like health care that involve everyone, its exercise and output should be available to anyone. Nevertheless, introducing a democracy into the scholars' world can prove catastrophic; some issues in science are not to be voted upon: A century ago, a democratically chosen gov-ernment of one of the states passed legislation establishing pi as a rational number! Moreover, some people still lobby for creationism to be taught along with Darwin's evolution in public education.¹ Thus, the pursuit of science should be left to highly specialized individuals and institutions. Still, since it concerns everyone by giving rise to commercialization, it must be responsive to society's needs while getting fair resources necessary for the pursuit of research that will benefit the members of society.

How should society determine the needs of science? Who should be responsible for that? Should it be one institution? Should the research be public or should anyone be free to pursue research? Other questions arise regarding economic efficiency, or in other words, the challenge of relevance. How can the researchers demonstrate to the donators that their research is worth all the money? This problem becomes harder to solve when it comes to public funding—spending taxpayer dollar would seem to require reaching a general consensus.

When looking for incentives for public funding in research, many often focus on externalities.² If an individual agent were to fund a research project expecting profits from the venture, very often there would be more benefits than he or she can capture since some will spill over to others. Even though all of the benefits may exceed the cost, the individual benefits to a particular agent may not be sufficient, rendering the enterprise too costly to exploit by this individual. Public funding is expected to fill this gap.³ Another solution to this problem is utilizing club goods, suggesting that if one donator is not able to secure enough benefits to make the enterprise worthwhile, several of them can possibly internalize the externalities to a sufficient extent.

Some consider this solution a highly successful approach when public funding may not be enough. Public funding is not sufficient to cover all possible research. Moreover, public governance of resource allocation is not as knowledgeable as a club of highly specialized agencies interested in a given topic. A consortium of agencies or people who are focused on a given branch of research and familiar with the technology or research route and its

potential costs and applications will make wiser decisions and be more effective. This allocation of money can thus provide secure investment; the greater knowledge of the specialized individuals increases the probability of success. Ownership of a given investment expedites the process of profit making rather than governing thousand projects across a country as in case of public funding, which hinders close attention to particular ones.

Nevertheless, the issue of accessibility of research results arises. If a research program is covered from private sources as opposed to public money then the investors have a justified right to own the results of work. On the other hand, science should provide us with public goods accessible to anyone to be utilized to the benefit of society as a whole. Second, there exits a risk of monopolization. Companies funding a particular research would not like its profit to spill over to those who did not contribute to its development.¹ Therefore, they will try to secure all the output knowledge. It may take time before society will be allowed to gain from such research. It is debatable whether this aspect does not defeat the purpose of a scientific enterprise. Some may argue that monopolized research is better than none. However, rather than some secret research being performed on a side and public research struggling to reach the same goal, maybe the two should be merged.

By the same argument, defense spending for research seems questionable. The controversy behind military engagement in scholarly research did not exist prior to World War II. But during the war, scientists proved the value of research in military projects and therefore received funding from presidential agencies.⁴ Afterwards, the Navy Department established the Office of Naval Research to facilitate scientific investigation. This example was followed by the Army as well the Air Force, which started supporting science by establishing the Office for Ordinance Research and Office of Scientific Research in 1951. ONR supported 40% of campus-based research of basic sciences by 1950 in the US. By 1957, 84% of federal research funds were earmarked for military purposes. In the mid-1960's, many academic scholars engaged in a protest against the US military involvement in the Vietnam War. It led to a distaste for the military establishment on campuses across the country; subsequently many universities, including MIT, Princeton, SUNY/SB and Stanford, adopted policies encouraging their faculty "not to seek research grants and contracts from the Department of Defense", which caused DoD to withdraw its support.4

However, with the change in management of DoD, the importance of basic research for modernization of the US military forces was recognized and the support of military agencies of the campus-based research started to grow again. It grew to such an extent that in 1995, *The Tech* claimed that the impact of a proposed cut in DoD research support would have been catastrophic for the Institute with the previous year's \$61.6 million from the

DoD accounting for nearly one-fifth of MIT's total federal research funding. DoD money still forms the backbone of the nation's academic research in science and engineering; the department funded 42 percent of all engineering research at universities in the 1990s according to National Science Foundation figures. With that figure, the DoD was, and still remains, the single largest supporter of research in engineering.⁵

The military establishment's influence raised an alarm in mid 1980s, when a need for redefining the relationship was called upon.⁶ MIT operates under the principle of free scientific pursuit of knowledge for its own sake, implying freedom to choose one's research direction. However, the availability of military money puts academic decisions into an economic framework of operation. The resulting bias causes MIT to allocate its resources in a disturbing manner, causing the technical fields that do not offer immediate military applications to stagnate.

The controversies arise mostly from the restraints military funding places on the academic world. The money could be devoted to other purposes concerning everyone like researching new therapies to dangerous diseases. As citizens of this country we all participate in its expenses no matter if we like their purposes or not. Still defense systems may prove as valuable as a new therapy. The controversy mostly stems from the fact that military related research often operates under auspicious of safety and state security, which threatens the economic and social purposes of research. As in the case of private funding, the military has a right to impose restrictions on release and accessibility of information resulting from research. Security issues are an excuse powerful enough to withhold the information brought by researchers. Again, this issue is not new; in 1981, MIT declined \$250,000 contract from the Air Force because of federal control over the research results (unpublished communication: Alice Ghast, Sept. 11, 2003).

In case of applied research this sanction seems plausible. If the military is looking to learn something highly specific relating to their operation it may not concern anyone else and could be kept confidential. However, the money from the Department of Defense goes to a variety of disciplines, many of which are devoted to basic research, where the release of findings is crucial for advancement.

Last but not least, many controversies arise from pharmaceutical companies supporting biotechnology research. This interest definitely does not follow from a selfless beneficiary interest. Instead, there exists a clear sense of purpose; a company needs to support specific work because the results will help develop better products, which in turn will let the company gather more market shares. An example of this kind of collaboration may be Genomics Institute of the Novartis Research Foundation, which openly states that they maintain "a close relationship with Novartis Pharma, engaging in collaborative projects with their research teams, as well as providing exciting opportunities to further expand technological innovation."⁷ Yet, the *relationship* with the institute seems a fair play since it was co-founded by the company itself. Many biotech or pharmaceutical companies usually enter the arena of campus-based or public research by luring scientists with immense funding. These opportunities have a profound impact very often changing the direction of research projects.⁸

In summary, a question arises whether there exist an ethical way of funding research. It seems that there is

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- always a party left unsatisfied; federal money cannot support everyone; private and military funding may harm society by monopolizing the outcomes of research. Society should create an environment for scientists where they can work for its benefit. A favorable policy may be an answer to this problem. If we could grant long patents to outstanding discoveries, introduce tax exempt benefits or help in reducing financial risk, research would be facilitated to a great extent, without spending, sharing or dividing even a cent of public money.
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Too Much Data

Kelley Rivoire

Imost everyone has seen the unending columns of numbers associated with the movie *The Matrix*. Today, that ceaseless stream of data is reality for researchers in nearly all disciplines. Every day, telemarketers and pollsters survey millions of people. Surely the results aren't analyzed one by one. What about a series of measurements from a device, one every second? How does the owner spot a malfunction? Researchers can't escape the volumes of data accumulating; instead, they must learn to handle and analyze them.

As technology, particularly instrumentation, improves, more and more data can be collected faster and faster, but the management of this data cannot always keep pace. New methods are needed for storage, searching, sort-



ing, and analyzing. As Caltech Professor of Astronomy George Djorgovski writes, "Raw data, no matter how expensively obtained, are of limited utility without the effective ability to process them quickly and thoroughly, and to refine the essence of scientific knowledge from them." The goal is to find "interesting scientific results" using "statistically sound and objective" techniques that are "automated as much as possible."¹

Usama Fayyad, author of *Advances in Knowledge Discovery and Data Mining*, defines the new field of data mining as "the nontrivial process of identifying valid, novel, potentially useful, and ultimately understandable patterns in data."² This problem of finding patterns in large amounts of data unites many scientific disciplines and requires all to face similar dilemmas.

In biology, the recent sequencing of genomes will allow researchers to map genes with their function—if they can cope with thousands of simultaneous measurements. Physicists might soon discover a new, important particle—if they can recognize small anomalies in petabytes of data. Web searchers can access information from people all over the world—if search engines can accurately index and rank Web pages. Examining and understand-ing data problems in this broad range of fields and the solutions proposed by scientists in each is important; because problems encountered by each technical area are similar, solutions used by one discipline can help researchers in a completely different field.

Web Crawling

Though relatively new, the Internet is inundated with links and is thought by many to be "too unstructured."³ To navigate the Web, a user must sift through vast amounts of data, much of which is irrelevant. In opposition to this hypothesis of an unstructured Web is the idea that, though complicated, the Web is a graph that can be traversed. The successful development of search engines indicates at least a modicum of structure present in the Web. In 1994, the most popular search engine recorded 1,500 queries per day. In 1997, Altavista reported about 20 million queries a day.⁴ Crawling the Web and ranking pages have been the basis of a number of recent computational and mathematical studies, the most prominent of which led to the 1998 creation of the Google search engine by graduate students Larry Page and Sergey Brin at Stanford University.⁵

Google

Prior to Google, many popular search engines such as Yahoo! were run using indices created and maintained by humans. Automated search engines, on the other hand, often led to results listing irrelevant matches. Google sought to use an automated search engine while still maintaining high-quality results. Google's goal was to place the most relevant links at the top of the results list, so that users could sift through fewer irrelevant links.



How does Google rank pages so accurately? The idea is that more relevant pages will have references from many other Web sites, whereas less relevant pages will not be mentioned. How does Google tell the importance of the referring page? It ranks these Web sites also. These ideas are the basis of the PageRank system created by Google to rate each Web page. PageRank counts the number of links pointing to a Web page, normalizing by the total number of links from a given page. The normalization prevents any single Web page's references from contributing too much to a ranking. PageRank is also special because the text that references a link is indexed with the page referred to rather than the referring page. This provides a better description of pages and allows indexing of pages containing images or other data types without text that cannot be otherwise indexed. PageRank also attaches increased weighting to larger, bold words, taking the visual factors of a Web page into account. When a user enters a query, Google counts the weighted hits to create a PageRank. For queries with multiple words, hits occurring near each other receive a greater weighting.

By using these techniques of crawling, indexing, and sorting the Web, Google achieves good precision in a small amount of time in its searches. As time progresses, it will continue to update its methodology to save time and storage space.⁴

Teoma

Though Google is the dominant search engine on the Web today, computer scientists are developing other search engines to improve Google's techniques. *Teoma*, meaning "expert" in Gaelic, was founded by Rutgers University Computer Science Professor Apostolos Gerasoulis in April 2000. One year later, Teoma.com was launched on the Internet, and in September 2001, Ask Jeeves, Inc., began to use the Teoma search engine, making it the third-most used today. Early this year, Teoma released an improved version of its engine, Teoma 2.0, with a set of advanced tools. Teoma hopes to compete with Google and provide an alternative search engine for Web browsers.⁶

How does Teoma work, and how is it different from Google? Teoma lauds its "community-based" approach to searching that uses only Web pages in the area of the query. Teoma defines communities as "groups of Web pages that are closely related to the same subject."⁷ In Google, a ranking is developed by counting links from other sites. In Teoma, on the other hand, only sites concerned with the subject of the search string are used in counting links. The idea, as journalist Kieren McCarthy writes, is that "Google asks about a certain expert in the field and then goes and takes a poll from people in the street over which one they think is best. Teoma would



ask all the experts in the field which one of themselves they think is best." By restricting the number of pages used to create the ranking to only pages dealing with the topic of the query, Teoma can often find obscure but relevant sites that Google might have missed.⁸ Teoma calls this idea of counting references only from relevant sites "Subject-Specific PopularitySM."⁷

Teoma also emphasizes a real-time, dynamic search method in contrast to Google's more static system. After the user submits a query, Teoma dynamically looks for communities, more specifically searching for "authorities" in the community. By searching real-time, Teoma can find a community even for new pages.⁹

Features to modify and improve searches also appear in Teoma. After a user enters a query, Teoma not only displays the results but also provides two options to the right of the screen, labeled "refine" and "resources." Refine allows a user to select a specific community of sites developed real-time by Teoma in which to continue the search. This allows a user to further focus his search. The resources option lists sites within a community that contain links to other sites related to the query. This gives the user access to references by authoritative sites on the subject.



So, should users stop using Google and start using Teoma? Maybe not yet. Google contains a much larger index than Teoma, even though Teoma's index has expanded by more than 500 percent to now include more than 500 million links.⁷ Teoma also lacks a cache and advanced searches such as the Boolean search.⁸ By understanding the differences between Teoma's searching techniques and Google's, however, users can decide which will better answer their query.

Biology

DNA Microarrays

A key recent development in biology is the sequencing of genomes of different species. A genome consists of all the DNA in an organism, including genes that contain information for making proteins that determine the appearance and functionality of an organism. Even a simple organism such as a bacterium has 1.8 million bases with one gene per thousand bases. The human genome consists of roughly 3 billion DNA base pairs with about 30,000 genes: one gene for every hundred thousand bases. This April, the International Human Genome Sequence Consortium announced the completion of the Human Genome Project, which sequenced each of the DNA base letters in humans with an estimated accuracy of less than one error out of every 10,000 genes sequenced. Now that biologists know the gene sequence of humans and other organisms, they can try to determine gene expressions and coexpressions, that is, traits to which the genes map. The implications of their results will be enormous: Understanding the genes linked with disease could lead to improved understanding and treatment of ailments such as heart disease, diabetes, cancer, and deafness.¹⁰ Already, more than 1,400 genes have been linked to specific diseases.¹¹

How do biologists search for genes linked with specific expressions out of the millions of base pairs in the genome, especially since many sections of the genome appear to have no function?¹² One of the most popular methods to map genes to their expressions is cDNA microarray analysis, which allows simultaneous measurements of several thousands of genes.¹³

To perform a microarray analysis, a biologist first extracts mRNA from a sample. Because mRNA in organisms is later transcribed into proteins, by measuring mRNA, the biologist can indirectly determine protein level. The mRNA is then changed into cDNA, a synthesized, single-strand form of DNA.¹⁴ This cDNA is labeled with fluorescent dyes that bind to a slide with DNA sequences from known genes. The activity level of each gene can be determined by looking at the fluorescence intensity and locations of fluorescence. By simultaneously examining mRNA levels in thousands of genes, scientists can find relationships between subsets of the genes, such as in feedback loops.¹⁵



The staggering number of concurrent measurements, however, causes problems.^{14, 16} As Sylvia Spengler, an expert in biotechnology databases with the Center for Bioinformatics and Computational Genomics at Lawrence National Laboratories writes, "Clearly, it is shortsighted to gather large amounts of data that cannot be analyzed in a timely manner."¹⁷ For experiments to be useful, they must be designed for analyses, and specific analytical methods should be determined before measurements are made.

Experimental Design

Many random variables enter into the measuring process. Noise, for instance, can occur at any stage in the process. Within a single slide, temperature and illumination changes, or even dust, can affect measurements. From slide to slide, other variables such as the use of different dyes can vary fluorescence readings. This alone can significantly affect data.^{16, 17} A recent simulation model of cDNA microarrays required more than 20 parameters, each with a probability distribution, to represent factors such as spot geometry and background noise.¹³

Even without noise, statistical difficulties are inherent in the design of a microarray experiment. A good statistical experiment tests several variables with many repetitions. Due to the high cost of gene chips, generally about \$1,000 each, and the scarcity of rare gene samples, repeated measurements typically do not occur. This means that although many conclusions seem significant, they actually occur only by random variation. Commonly, scientists assign the chance to be 5 percent that a variable will appear to be significant when it truly is not (i.e., a "false positive"). This factor practically vanishes in most datasets. When testing 10,000 genes at once, however, 5 percent suddenly becomes 500 "significant" results generated by chance alone. Typically, statisticians perform tests to reduce this kind of false positive; however, many of these "multiple comparison" tests are not designed for the extremely large number of comparisons that microarray analysis presents and are therefore not necessarily applicable.¹⁶ New methods for reducing the number of false positive results are being developed, such as that by Westfall and Young specifically formulated for microarray analysis but applicable to other fields of research as well.18

Data Analysis

Regardless of these false positives, how do scientists even begin to find significant results? Statisticians and





data analysts are being challenged by this problem. Data is first standardized by a process called normalization to try to reduce noise in the measurements. Then data analysts use pattern recognition methods to look for significant relationships in the data.

One method to find correlations is to use a permutation test. A permutation is a rearrangement of elements in a group, in this case, a random arrangement of the measured microarray data. The permutation test is used to compare the level of significance in the original data to the levels of significance in sets of randomly permuted data: data mixed up in a random order. This random data can then serve as a comparison to the original, nonpermuted data. If the permuted, random data shows a similar level of statistical significance to the original data, then the trends in the original data are reproducible by chance alone and are therefore insignificant. If the original data shows a much stronger statistical significance than the random data, then the statistician can conclude that a true significant pattern exists. To visualize these potential significance patterns in both the original and the permuted data, topological terrain maps can be employed using recently developed software.¹⁹ By using the permutation test, a statistician has a higher level of certainty that his results are truly "significant" than if he looked only at the original data.

Cluster analysis, another technique to study patterns in data, has also been used in analyzing microarray data. Cluster analysis compares data by creating a vector for each gene and each experiment, creating a data matrix. Genes are then "clustered" into groups, and the distances between their expression vectors are measured.¹⁷ Many variations of clustering exist. In hierarchical clustering, clusters are connected in a treelike progression. In kmeans clustering, a specific number of clusters is specified, and data is classified into clusters to minimize distances within a cluster as compared to the distances between clusters. So-called "supervised" methods such as support vector machines (SVM) use labeled data to train a machine to distinguish observational data as members or nonmembers of a group. Used in correlation with these methods are data reduction techniques, such as principal component analysis (PCA), which reduce the dimensionality of data and are useful to determine the number of groups necessary for a cluster analysis such as k-means.20

Future of Microarray Analysis

Microarray analysis clearly presents a number of difficulties in both experimental design and analysis stages. Analysis of the data is tricky because, as John Quackenbush with the Institute for Genomic Research writes, "The methods that are used to analyze the data can have a profound influence on the interpretation of the results."20 New guidelines stressing minimum information about a microarray experiment (MIAME) have been created by the Microarray Gene Expression Data Society. These guide researchers in the areas of repeated measurements and design. Journals are also mandating stricter statistical analyses of data, eliminating "sloppy statistics" that lead to "faulty conclusions" and mandating data to be submitted with papers.¹⁶ Members of the field recognize the difficulties and are working to minimize these problems so that microarray analysis can revolutionize biology, leading to a better understanding of genetic diseases.

Physics

Particle Physics

Particle physics, the study of basic atomic and subatomic elements of matter, uses high-energy particle accelerators to collide and detect particles at high speeds. This results in large volumes of recorded data. The problems associated with sharing these vast datasets resulted in the creation of the World Wide Web in 1990 by Tim





Berners-Lee, a scientist at CERN, the European Laboratory for Particle Physics, to allow physicists all over the world to share data. Even the World Wide Web, though, is not sufficient to handle the amounts of data physicists will soon collect.²¹

Researchers at CERN, located in Geneva, Switzerland, are currently building the Large Hadron Collider (LHC). The LHC will search for the Higgs particle, a currently undetected particle thought to give other particles their masses. In the LHC, collisions will occur at energies of up to 14 TeV, the highest ever; collision numbers could be as high as a billion; the annual volume of data collected will be five petabytes (10 to the 15th power). Though scientists predict 800 million collisions will occur every second in the LHC, Higgs particles are likely to be seen in only 100.22 This amounts to finding a needle in a haystack bigger than any before. Data storage, data accessibility, and data analysis are all problems. Several international initiatives have since been created to handle these problems. The Grid Physics Network addresses the IT problems present using Petascale Virtual Data Grids. The project works on creating systems of software to allow users in locations across the world to analyze data. The project aims to make a data toolkit to aid with this complicated analysis.²³ Another project dealing with similar problems is GIOD.

GIOD

A collaborative project between Caltech, CERN, and the Hewlett Packard Corporation, Globally Interconnected Object Databases (GIOD) deals with information technology and data issues of the LHC, creating an object database with reconstruction, analysis, and visualization tools. The database is complicated by a need to make it accessible to an international group of physicists. The systems created must be tested for scalability with simulated high-energy physics data to ensure correct handling of the many megabyte events.

Since the data in the GIOD project is so complex, an object-oriented system is used to describe them. Object-oriented programming languages such as C++ and Java are focused around creating a system in which data can be represented as "objects" according to their attributes and behavior. Examples of objects can be particle tracks, intersection points of tracks, and particle assignments.²⁴ Commercial object-oriented database management systems are used in GIOD to help sort and move through data quickly. These objects can keep track of the complicated relationships present in the data and help physicists extract data of interest in searches.²⁵

Analysis

Analysis of particle physics results involves significant data mining. One common method is the use of an artificial neural network (ANN).²⁶ A neural network, also called a neural net, is an algorithm that uses a computer to recognize patterns in a set of training data. This creates a set of criteria by which to predict the classification of other samples. ANNs and other statistical software modified for use by physicists have been created and made available.27 The Stanford Linear Accelerator Center (SLAC), for example, maintains a collection of software for everything from data acquisition to data analysis of high-energy physics experiments.28 By using ANNs and these other highly complicated tools, physicists can search for anomalies or patterns, giving them the possibility of finding a Higgs particle among millions of collisions.

Astronomy and Astrophysics

In order for astronomical experiments to be effective, they must draw data from locations as far as light years away with complicated instruments that make enormous numbers of measurements. Astronomical experiments such as the Laser Interferometer Gravitational-wave Observatory to observe gravitational waves of pulsars and supernovae as well as Sloan Digital Sky Galaxy to create a database of features in the sky, also face problems in data collection and analysis.²³

World-Wide Telescope

A project called the World-Wide Telescope or Virtual Observatory will collect astronomical data and allow access by Internet users. Vast quantities of astronomical data are collected annually from locations such as the Hubble Space Telescope, the Chandra X-Ray Observatory, and the Digitized Palomar Observatory Sky Survey. Because astronomical objects like galaxy clusters can behave differently in different wavebands, observations across the entire sky are necessary. Each year, with instrumentation improvements, more data can be collected. Even a single spectral band from the sky can hold



as much as a few terabytes of information. Each scientist cannot individually keep this data, so astronomers need a digital repository to allow access to the data from numerous locations. Astronomical data is further complicated by the need to calibrate data to the instrument on which it was measured, meaning that data must undergo corrections before it is useful, and the individual groups who measured the data must perform these calculations.

The World-Wide Telescope project will allow access to data from the entire sky for all historical experiments, so that international groups of scientists can analyze data. It is also hoped that this project will help regulate the way in which data is measured, as consistency in terminology, units, representations, technology, and data structures will be required of such a database.²⁹

Data-Mining in the Sky

Even with a digital repository of data, searching for specific objects such as quasars or galaxy clusters can be difficult in these terabytes of pixels. Statistically sound methods from machine learning and artificial intelligence must be utilized for these vast searches. Clustering techniques, similar to those in microarray analysis, are used to group objects that belong together. To do this, first the number of clusters must be estimated, usually assuming what statisticians call a normal, Gaussian distribution: the bell curve. One way to determine the number of clusters is to use a Bayesian technique that uses probabilities of previous events, called prior probabilities, to more accurately predict outcomes. To look for patterns and classify data, other methods using these Bayesian prior probabilities techniques can be used. Bayesian inference methods predict the most likely fit for data. Further refinement can be made by adding a penalty term to reflect the bias inherent in the model due to the reliance on prior probabilities.³⁰

Other Examples

Problems of large data sets and data mining occur in many other situations. Detecting anomalies is one general application. Companies can collect information to try to detect fraud, such as in credit card scams. Governments can collect information about millions of individuals to search for patterns that might identify a terrorist. Large databases can also be used to analyze consumer spending patterns, satellite and meteorological data, process control, and even the likelihood of risk for insurance and actuarial purposes.^{2, 17, 27, 31, 32, 33, 34}

Commonalities Across Disciplines

Across all of these disciplines, many of the same problems with these large datasets appear. First, data must be measured and investigated. Often this involves using dimensionality-reduction techniques such as principal component analysis, multidimensional scaling, and new methods such as independent component analysis used in functional magnetic resonance imaging. Data can then be explored using vector clustering techniques.



By assuming items in the same clusters share features, researchers can create and test hypotheses. Models are then derived using learning algorithms. Two kinds of models are typically employed: generative models that capture causal relationships and Bayesian networks that use previous outcomes to predict future results. A model of connected points, called a graph, can also be used, as in the case of the World Wide Web. Next, predictions made by the models can be tested. For this, large amounts of labeled data must be used. Finally, the model is revised, and data is again collected to test the corrected model.³⁵

These steps of collecting and analyzing large amounts of data allow scientists to examine gene expression, particles such as the Higgs boson, astronomical data, and the World Wide Web. Specific analytical techniques are applicable to all these data mining situations, such as dimensionality reduction methods, clustering techniques, and classification algorithms. The techniques used in microarray analysis to find significant trends among thousands of concurrent measurements can be used by other fields searching for significant patterns in their datasets. The databases and software being created by particle physics give others ideas about how to circulate their data among an international group. The ideas of modeling the World Wide Web as a graph can be used for other problems involving complicated graphs with nonobvious connections between elements. A solution in one field is often broadly applicable to many other problems.

Skills for Undergraduates to Handle Large Datasets

With the vast amounts of data aggregated today, what subjects should undergraduates study to prepare themselves for this influx? Data-mining itself represents the boundary of many fields, among them database management, artificial intelligence, machine learning, pattern recognition, and data visualization. These areas fall under the main subject lines of computer science, engineering, and statistics. Though statistics is generally concerned with analysis of data, statisticians tend to want proof in more rigorous ways than data-mining allows. As a result, statisticians have been left out of the process, and other disciplines have taken over.^{2, 35, 36} Truly, however, to best understand the data, members of all these fields should contribute. The general steps used to analyze large datasets of observation, data reduction, data clustering, hypothesis generation, modeling, and testing of predictions involve all of these subjects.³³ Statistics must be utilized for data reduction techniques like principle component analysis and hypothesis testing. Computer science disciplines such as artificial intelligence and machine learning are used for data clustering, hypothesis generation, and modeling. Engineering and statistical considerations are frequently taken into account in setting up an experiment prior to data collection. All these disciplines are important for complex datasets, and students would be well advised to be familiar with each. Furthermore, whether biologists or meteorologists, research groups should employ diverse team members such as statisticians and computer scientists to properly handle the data and correctly interpret results. In this way, a world growing increasingly complex every day can be analyzed reliably and accurately.

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The Search for Essential Drugs

Lakshmi Nambiar

Though developed nations have seen an explosion in the research and manufacture of essential drugs, these medicines do not reach the vast numbers of ailing people in those nations. Over one-third of the world population still lacks basic access to necessary drugs. Even where drugs are available, distribution and administration is so inefficient that afflicted persons never receive the benefits of the drugs. A recent study reports that up to 75 percent of antibiotics are prescribed inappropriately in teaching hospitals in developing countries. Worldwide, an average of only 50 percent of all patients receive medicine that is properly administered. Only 30 percent of the countries in the developing world have any kind of fully functional drug regulatory authorities, and many drugs or medicines invented are never tested for potency or efficacy. While a section of the population in developed countries enjoy the full benefits of research and development, all nations need access to essential drugs.

It is now the task of the World Health Organization (WHO) to evaluate the status of essential drugs and take immediate measures to improve the situation. Ensuring the availability and efficient distribution of essential drugs all over the globe has been a task of this international organization since its creation. This involves the full cooperation of various national governments, the private and public sectors in those countries, and health professionals and administrators. Every decision made and implemented has enormous consequences for the health of the world's masses.²

With the invention of aspirin in 1897, the last century has witnessed the creation of a number of drugs that have revolutionized the treatment of diseases ranging from the common cold to HIV. The first modern antibiotic was introduced in 1941, and three years later the first antitubercular drug was developed. In the fifties, the first oral contraceptive was tested, and in the following decades thousands of synthetically produced pharmaceuticals have been introduced. However, with this came the problem of a profligacy of essential and nonessential drugs saturating the market. With the extraordinary success of drug companies and their ability to increase research came another avalanche of drugs. Differentiating between the real-life saving drug and the purely commercial is still a serious problem.³

It became absolutely necessary to create some kind of coherent grouping of these drugs, terming them as essential and nonessential. In 1977, the WHO created the first Essential Drug List. This first list identified 208 individual drugs that together could provide safe and effective treatment for many widely spread communicable and noncommunicable diseases and proved to be an invaluable resource to local governments in evaluating their needs.¹ This document also formed the basis for state health policies and programs for many governments, who, along with other health departments, now universally follow this list. The updated list, prepared by a WHO expert committee, contains 306 individual drugs.⁴

Today, many national governments formulate their policies based on this Essential Drug List, and it serves as a valuable tool to determine which drugs are most needed for optimal health. However, the implementation of such policies is beset with problems owing to the various socio-economic conditions and individual needs of each country. Advanced industrial nations have sound health policies and resources to research and manufacture, but many in the developing world lack that potential. There are other problems in the areas of access, financing, prices and trade barriers, potency and quality testing, rational use and uniformity in national policies.²

The entire international community must cooperate in order to improve the spread and distribution of essential drugs. The drug policy of a country is usually formulated by taking full consideration of the various guidelines issued by WHO and other world bodies ensuring the availability and safe administration of essential drugs to the needy. Many illnesses suffered by the poorest people in various parts of the world could be prevented, treated, and even eradicated by simple pharmaceutical products such as vaccines and drugs. Many developed nations have identified the need for essential drugs reform and have supported UN efforts to implement the recommendations of essential drugs policy. For instance, the Netherlands currently has an advanced health care system and spends 8.2 billion guilders on prescription drugs. The Dutch regard health insurance coverage for drugs as a civil right. But even under this belief system, there are sects of people who are denied the benefits of health insurance, such as low-income workers and new immigrants who lack health insurance (Netherlands: Country Profile).

Poor access is a serious problem because many people cannot afford costly drugs. Many nations have identified the challenges involved with health care issues: a) poor people must have access to affordable essential drugs; 2) more research must go into diseases afflicting poorer populations; and 3) there must be more effective distribution of the medicine so that it may reach the people who need it the most.⁷ According to WHO estimates, the amount of money spent on research on medicines is \$56 billion. But less than 10 percent of this is spent on illnesses that afflict more than 90 percent of the world's population. The health care industry is thus geared to the needs of the wealthy.

Many poor nations cannot afford to buy essential drugs for their people, since the governments are already burdened with foreign debt and loans from the International Monetary Fund and World Bank. Since the drug companies invest heavily in research and would like to recover their cost with profit, many of the newly discovered formulations become prohibitively expensive for poorer countries. For instance AZT, the patented drug for the treatment of HIV, costs more than fifteen thousand dollars a year per patient. Many HIV patients in Asia and Africa die of AIDS without ever receiving the benefits of this drug because their governments or they themselves cannot afford it. This is where the roles of private sector and drug companies come into play.

There is a need for increased cooperation between private and public sectors. Drug companies should increase spending on research affecting economically deprived people. The private sector should also invest a share in their profits in the manufacture and free supply of most crucial drugs. The government would have to cooperate with private industrial corporations to help fund this research.⁶

Research projects such as the Global Alliance for Vaccines and Immunization (GAVI), a World Bank project created to address the health care problems of poorer nations, strive to address the needs of every person. It provides an essential vehicle for drug companies to market their already tested vaccines to developing countries. Initiatives such as Special Program for Research and Training in Tropical diseases (TDR) and Medicines for Malaria Venture (MMV) are also working toward these goals.⁷

Another area that needs some scrutiny is the implementation of intellectual property rights. With large companies holding on to their patent rights, poorer nations cannot manufacture these medicines more cheaply by themselves, even if they have the resources. Prices could be lowered if the current rules awarding the original patent holders were relaxed and many drug policies deregulated.

One solution is to encourage efficient strategies to promote affordability and access. The Third Regional Meeting on Reimbursement and Pricing of Medicines in the Countries of Central and Eastern Europe in Prague came up with several plans: Periodic meetings and forums are vital in order to allow an exchange of information. Also, country profiles on pharmaceutical policies for different countries should be made readily available to all nations. In addition, price comparisons would be helpful to national authorities trying to improve the distribution of prescription drugs.⁵

Many organizations and governments steadfastly believe in the importance of administering essential drugs to both developed and developing nations. Solutions must be implemented in order to ensure that every nation maintains the health and well-being of its citizens.

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Angiogenesis:

An Examination of both Tumorigenic and Rehabilitative Properties

Erik Makhni

The study of angiogenesis is making a profound impact on the biological and medical world. Angiogenesis has been found to play such a vital role in tumor progression that has long been the focus of study by microbiologists. Further, it has recently been gaining attention in clinical research as well, as a possible therapeutic agent in the assistance of cardiac deficiencies and recoveries. But what is angiogenesis, and, more importantly, how does it have the ability to both be a source of cancer sustenance and cardiac rehabilitation?

Angiogenesis is a term that refers to the "recruitment" of blood vessels. These blood vessels are recruited to masses of cells, as they provide the cells with a source of oxygen and a waste reservoir. Without a readily available, nearby source of blood, the proliferating cells would not have the chance to grow and survive. Angiogenesis is a natural phenomenon that allows for cell growth (both for numbers and size). However, angiogenesis is an extremely intricate process, regulated by several different pro- and anti-angiogenic factors. Further, it is triggered by different physiological conditions as well. In this review, the role of angiogenesis both in tumors and in cardiac rehabilitation, will be examined more closely.

History

Much of the foundation of angiogenesis research was laid down by Professor Judah Folkman. In 1971 Folkman published an article in the *New England Journal of Medicine* discussing this new theory of angiogenesis based on several years of work. In his research, Folkman noted that tumors would never grow past a certain critical size unless increased vasculature was introduced. In his paper, he also discussed the theory that tumors contain new blood vessels, which were somehow recruit a diffusible factor he referred to as TAF- tumor angiogenesis factor. Finally, he wrote that, in theory, if this angiogenesis could be turned off, the tumors would remain small in size, and ultimately not as harmful. Of course, as in many cases of theoretical innovation, he was met with *extreme* pessimism from the scientific community. It took almost 10 years for the academic public to acquiesce to the notion that there was, indeed, new vasculature in tumors. Finally, more than 30 years after his publication, tumor angiogenesis is a focal point in cancer research. In 1984, Folkman and his crew published another paper in *Science*, exposing the world to the first found angiogenic factor. This paper caused an impetus of research: There are over 15 known angiogenic factors.¹

Molecular Basis of Angiogenesis

The diffusion limit for oxygen in vivo is approximately 100-200 ?m. Beyond this distance, oxygen cannot reach cells, and they will suffer from hypoxia, or a lack of oxygen pressure. How the cells call on new vessel formation is of extreme interest to scientists, and much work has been dedicated to mapping the path taken. Small vessels are composed of endothelial cells (ECs), and it was thought that, while an embryo, vessels developed from endothelial progenitor cells, and as an adult, vessel formation stemmed from ECs. However, it is currently believed that endothelial progenitors contribute to vessel formation both in the embryo and in the ischemic tissues.² Many factors are responsible for this ultimate formation.

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Research has pointed to several angiogenic factors, both pro-angiogenic and anti-angiogenic. Angiogenesis is regulated by these two determinants, and errors in either of the two sets could cause an imbalance in the regulation of angiogenesis. One of the main pro-angiogenic factors is the vascular endothelial growth factor (VEGF). It is thought that VEGF is the "critical rate-limiting step in physiological angiogenesis."3 In vitro it has been shown to promote the survival of ECs from such blood vessels as arteries, veins, and lymph. Further, in vivo, VEGF stimulates angiogenesis as well, mainly targeting endothelial cells. Ferrara et. al. also refer to VEGF as a "survival factor," preventing apoptosis in ECs in tissue culture by upregulating anti-apoptotic proteins (i.e. Bcl-2). And so, VEGF remains the key focal point in the study of angiogenesis onset.3 Along with VEGF, several other factors have been found to promote angiogenesis, such as TGF-? and -? (transforming growth factor), and IGF (insulin growth factor).³

On the other hand, there are also prominent antiangiogenic factors. I am currently working on a project that deals with the major anti-angiogenic factor, Thrombospondin-1 (Tsp-1). There are several different factors that are involved in the Tsp-1 pathway, which seems to be overall regulated positively by p38. Like VEGF, the pathway is tied to the infamous oncogenic Ras pathway.

The "Angiogenic Switch"

The sheer complexity of cancer has been illustrated over and over again with each new experiment in the field. There are so many different pathways and factors that can be mutated or altered to bring about tumors that it is impossible to explicitly determine when angiogenesis kicks in and turns on itself. The "angiogenic switch" is a term that refers to the balance between pro- and anti- angiogenic factors. When the balance is in favor of the pro-angiogenic factors, angiogenesis results, and it is this "tipping of the balance" that is being studied to determine how tumorigenic cells are able to promote angiogenesis.

To more closely study the turning on of the switch, one may examine the physiological factors that trigger angiogenesis, such as hypoxia. As stated by Ferrara et. al., an increase in tissue mass will cause hypoxia, which will in turn cause an upregulation of gene expression of pro-angiogenic factors. Further, mutations can also stimulate angiogenesis. A mutation in the Ras pathway will cause an overstimulation of VEGF, which will ultimately promote angiogenesis as well. A mutation in tumor suppressor genes can additionally cause a similar effect.³

There are many ways that tumor angiogenesis occurs, physiologically. In a review in *Nature*, Carmeliet and Jain postulated several different ways in which tumor angiogenesis may be instigated. One possibility is that the host vessel system expands by either budding or sprouting. Another option is that vessels are formed by the insertion of interstitial tissue into preexisting vessel lumen. Finally, a third possibility is that EC precursors (angioblasts) aid in vasculogenesis. In other words, they contribute to the addition of endothelial lining in these vessels.⁴

Upon even closer study, one may observe that tumor angiogenesis brings about a very different vasculature then normal angiogenesis. In a review article by Bergers and Benjamin, it was stated that tumor blood vessels may be "irregularly shaped, dilated, tortuous and can have dead ends."⁵ They go on to state that some of the leakiness and hemorrhagic properties of these vessels may be due to the overproduction of VEGF, with cancer cells even "integrated into the vessel wall."⁵

All the studies, however, make clear that the angiogenic switch is turned on at different stages in tumor development. Hence, it is difficult to attempt to create a magic drug that could eliminate this extra angiogenesis (among other complications). However, experiments have shown that inhibiting VEGF does downregulate angiogenesis, and so research is being conducted to investigate this further.

Rehabilitating Effects

Just as angiogenesis may assist tumor growth and development, it also helps to repair normal vasculature, as in the aftermath of a heart attack, also known as a myocardial infarction (MI). The narrowing or blocking of blood vessels leads to blocks in the ischemic system which ultimately cause tissue damage. Without sufficient blood flow through these vessels, nutrients are not properly exchanged with the cells of the tissues; oxygen is not delivered, nor are wastes disposed of. Further, one of the leading causes of MIs is such a blocking in coronary arteries. One way of alleviating these blocks is to perform bypass surgeries, in which blood vessels from other parts of the body are used to provide an alternate route of blood around blocked regions; however this approach is not feasible for many patients. Angiogenesis is being studied as a possible means of increased vasculature and vessel rehabilitation for these patients.⁶

Several experiments have been performed investigating the therapeutic effects of angiogenesis. Many experiments have yielded promising results, lending even more credence to the possibility of therapy via angiogenesis. One way to induce therapy is via gene therapy.

Gene therapy is ideal for a patient suffering from an MI or even a peripheral infarction, and who cannot receive traditional "revascularization therapies."⁷ As defined by Herttuala and Alitalo, gene therapy is a transfer of nucleic acids to somatic cells, conferring a therapeutic effect. There are several benefits to gene therapy, such as the ability to act locally within a patient. Further, gene therapy offers the possibility for prolonged recovery, along with possibly avoiding a procedure that could cause harmful side effects.⁷

Gene therapy was used as a method of cardiac repair in an experiment by Li, Takemura, and Kosai et. al. Adenovirus was used as a genetic carrier, and was



injected into the muscles of the hind limb of mice following an MI. This adenoviral vector expressed hepatocyte growth factor (HGF), a pro-angiogenic molecule. As

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expected, HGF levels rose in these mice, compared to HGF levels in control mice (in which LacZ was used). Further, in these experimental, HGF-upregulated mice, there was improved left ventricular remodeling, and overall increased recovery efficiency. The researchers concluded this type of gene therapy to be effective in providing a possible approach against subsequent problems with heart failure.⁸

Research is also being directed toward approaches other than gene therapy. In a similar experiment by Nishida, Li, and Hirata et. al., bone marrow cell infusion was studied as a remedial factor in cardiac repair. Bone marrow cells (which normally help induce angiogenesis) were injected into the left ventricular anterior wall of damaged hearts in experimental rats. Following the injection, cardiac function was evaluated at regular intervals. It was found that the bone marrow cell injection caused an increase in levels of angiopoietin-1 (a proangiogenic factor) and in VEGF in the anterior wall, which induced angiogenesis. These influences helped retrieve increased cardiac functioning in the heart.⁹

Conclusion

Angiogenesis is a potent phenomenon in natural physiology. Beginning with Folkman's visions back in the late 1960s, modern science has come a long way in its evaluation of the biology of angiogenesis. Even though it has proven to be a sustaining element for tumors, insight into the several known anti-angiogenic factors may provide clues for controlling tumor angiogenesis. And, insight into pro-angiogenic factors is being used for angiogenesis' possible remedying effects on vasculature damage.

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Extra-Solar Planetary Microlensing

Michael David Sekora

I. Introduction

Throughout history, people have debated the existence of life elsewhere in the universe, prompting researchers to seek out planets in other systems that could give rise to life. The current search for extra-solar planets has scientists asking whether the structure of our solar system is unique or different from other systems. By investigating the dynamics of various planetary systems, researchers can theorize how our solar system and other systems formed, what conditions gave rise to our solar system being similar to or different than other systems, and what the evolution of various planetary systems will be.

Before 1990, investigation of planetary systems was limited to looking at our own. Researchers have since developed many methods for detecting extra-solar planets and have discovered dozens of them.¹ Each method is sensitive to certain types of planets based on the planet's size and orbital motion. However, because distant planets are very faint, these methods are indirect and planets are detected mainly by their influence on nearby stars.

II. Extra-solar Planet Detection

The classical methods for detecting planets include radial velocity measurements, astrometry, and photometric detection of transits. Radial velocity measurements can be gained by fitting the Doppler shift of a large number of features within a star's spectrum and removing the motion of the observer relative to the barycenter of the star system and other known motions. Astrometry detects planets by observing the wobble they induce in the motion of their stars projected onto the plane of the sky. Photometric detection of transits can spot a planet passing in front of the disk of the star once per orbit when viewed from Earth.1 Although the classical methods are sensitive to certain types of planets, they complement one another because they measure a similar range of semi major axes and parameters.

However, there are some drawbacks to using classical methods. First, they are limited to nearby systems because they rely on light from either the parent star or the planet itself. Second, they are not sensitive to low-mass planets: Essentially, they can only detect giant planets, brown dwarfs, and low-mass stars. As Guadi (2002) showed, the systematic floor of radial velocity surveys implies that extra-solar planet Earth, Uranus, and Neptune analogs are probably inaccessible to radial velocity measurements. Third, these methods require that a system be observed for at least one full period of its companion.2

Microlensing is a new and alternative way for detecting extra-solar-planets and was first proposed in 1991 by Mao and Pacynski. Their work was expanded upon in 1992 by Gould and Loeb.2 Microlensing is a general relativistic effect that occurs when light from a distant star is bent by a massive object (i.e., the lens) as the light passes near the object on its way from a source to an observer. Microlensing seeks to overcome some of the drawbacks associated with the classical methods.

III. Gravitational Lensing

A. Deflection of Light

Here are some of the basic equations and ideas in gravitational lensing. One of the most famous results of general relativity is a ray of light deflected as it passes by a massive object. In Newtonian mechanics this deflection angle (a) can be calculated as follows. A ray of light passes by a massive object at a distance b (i.e., the impact parameter). Here, we shall assume the massive object is a point mass that exerts an acceleration perpendicular to the direction of the motion of the light ray:³

$$g = \frac{GMb}{\left(b^2 + z^2\right)^{3/2}} , \qquad (1)$$

where *G* is the gravitational constant, *M* is the mass of the point object, and *z* is distance. The deflection angle equals the total integrated velocity (v) divided by the speed of light (c):

$$v = \int g \cdot dt = \int g \cdot \frac{dz}{c} = \frac{2GM}{bc} , \qquad (2)$$

so:

$$\alpha_{Newtonian} = \frac{v}{c} = \frac{2GM}{bc^2} . \tag{3}$$

In general relativity (GR), this deflection angle is multiplied by a factor of 2, which results from the Schwartzchild metric:⁴

$$\alpha_{GR} = \frac{4GM}{bc^2} \, \cdot \tag{4}$$

From this result, one can calculate the Einstein ring, which is one of the most important equations in gravitational lensing, as we shall see later. $\theta_{observer}$ is the angle made by a ray of light coming from the source that has been bent and is currently incident on the observer's line of sight with the line connecting the observer and the source. Also, D_{OL} is the distance from the observer to the lens (i.e., the point mass in this case); D_{LS} is the distance from the lens to the source; and D_{OS} is the distance from the observer to the source to the source. Therefore:

$$\theta_{observer} = \frac{b}{D_{OL}} \tag{5}$$

and

$$c = \frac{b}{D_{LS}} + \theta_{observer} \,. \tag{6}$$

If one solves for $\theta_{observer}$ and eliminates the impact parameter, then:

0

$$\theta_{observer} = \theta_{Einstein} = \left(\frac{4GMD_{SL}}{D_{OL}(D_{OL} + D_{LS})c^2}\right)^{\frac{1}{2}}.$$
 (7)

This can be rewritten as:

$$\theta_{Einstein} = \left(\frac{4GM}{Dc^2}\right)^{\frac{1}{2}} = \left(\frac{2R_{Schwartzchild}}{D}\right)^{\frac{1}{2}},$$
 (8)

where $D \equiv \frac{D_{OS}D_{OL}}{D_{LS}}$; $R = \frac{2GM}{c^2}$ is the Schwartzchild

radius of the lens. ${}^{\scriptscriptstyle 5}$

For a microlensing event, this equation can be approximated as: $^{\scriptscriptstyle 2}$

$$\theta_{Microlen \sin g} \cong 3 \times 10^{-7} \left(\frac{M}{0.3M_{Sun}} \right)^{\frac{1}{2}} arc \sec onds \cong$$

$$4 \times 10^{-22} (M)^{1/2} arc \sec onds$$
(9)

M (kilograms) is the mass of the extra-solar object and M_{Sun} is the mass of the Sun (1.99×10³⁰ kg). As one can see, $\theta_{Microlen \sin g}$ produces a very small result, especially when Earth, Uranus, or Neptune extra-solar analogs have a mass between 1×10²⁴ kg-1×10²⁶ kg. Despite the small separation in the images (i.e., the small Einstein ring), an extra-solar microlensing event is detectable and will be discussed shortly.

B. Time Delays

Because the trajectory for which a deflected light traverses is curved, the amount of time it takes a light ray to propagate from a source to an observer increases. This increase in time is known as the time delay. To calculate the time delay and other lensing effects, one must work in two dimensions. The source is described by an angular position \bar{u} . The source emits a ray of light that passes by a massive object (i.e., the lens) in the foreground. The massive object has an impact parameter with the angular position \bar{x} . Here the ray of light is deflected by the gravitational field of the lens. Similar to how we assumed in the Einstein ring calculation that the massive object was point like, we must now assume that the lens occupies only a small fraction of the total path length (i.e., the thin lens approximation). The time delay can be viewed as equaling a geometric delay plus a gravitational delay, where the gravitational potential roughly corresponds to a lens's mass distribution:

$$\tau(\vec{x}) = \frac{1 + z_L}{c} \frac{D_{OL} D_{OS}}{D_{LS}} \left[\frac{1}{2} |\vec{x} - \vec{u}|^2 - \varphi(\vec{x}) \right]^{\frac{1}{2}}, \quad (10)$$

where z_L is the red shift of the lens and $\theta(\bar{x})$ is the twodimensional gravitational potential.⁶ The time delay equation is important when modeling an observed gravitational lens and hypothesizing how, why, and where images will appear.

C. Lens Equation and Magnification Tensor

The geometry of lensing (i.e., the positions where images will be observed after light is deflected by a lens) can be described by Fermat's Principle: Rays of light follow paths that form images, which represent stationary points in arrival time.^{3,6} This principle also corresponds to coherent phases that result in positive interference. The stationary points where images form represent solutions to the lens equation:

$$\vec{u} = \vec{x} - \nabla \varphi(\vec{x}) . \tag{11}$$

This equation relates the source position (\bar{u}) to the image positions (\bar{x}) via the deflection angle:⁶

$$\alpha = \nabla \varphi . \tag{12}$$

Solutions to the lens equation can be related to the time delay equation, such that:

$$\nabla \tau = 0 \Longrightarrow \bar{x} - \bar{u} - \nabla \varphi(\bar{x}) = 0.$$
 (13)

In addition to the lens deflecting light from a distant source to create multiple images, the lens magnifies each image differently. The magnification (μ) is described by the determinant of the Jacobian of the lens mapping:^{3, 6}

$$\mu = \det(\mathbf{M}) = \det\left[\left(\frac{\partial \vec{u}}{\partial x}\right)^{-1}\right] = \det\left[\begin{bmatrix}1 - \varphi_{xx} & -\varphi_{xy}\\ -\varphi_{xy} & 1 - \varphi_{yy}\end{bmatrix}^{-1}\right]. \quad (14)$$

The subscripts following the gravitational potential denote partial derivatives with respect to x and y. As shown earlier, typically the separation in the images of an extra-solar microlensing event is small. In such a case, it is important to observe image magnification rather than image separation. Moreover, when individual images are indistinguishable, one must observe the combined differential image magnification as a function of time. This idea will be further investigated in following sections.

D. Caustic and Critical Curves

In some cases, a gravitationally lensed image may become very intensely magnified. This occurs because the source has a unique position with respect to a caustic curve and subsequently a critical curve. Critical curves exist in the image plane and are locations where images become infinitely magnified (theoretically). However, no gravitationally lensed image is ever really infinitely magnified because no source is point like. Critical curves are defined as:⁶

$$\det(\mathbf{M}^{-1}) = 0. \tag{15}$$

These critical curves are where one would observe very bright images (i.e., highly magnified sources). By mapping the critical curves back to the source plane, one forms caustic curves—locations in the source plane where multiple light rays collect. Any source lying near a caustic is highly magnified. If a source crosses a caustic, the number of images changes by two (i.e., two images are created or annihilated).^{3, 6}

IV. Extra-Solar Microlensing

Reports

Extra-solar microlensing is one form of gravitational lensing that occurs when compact objects such as lowmass stars and planets pass close to an observer's line of sight of a distant star. Because microlensing occurs with compact objects, microlenses are modeled as point like masses. This point like structure dictates the formalism of the lens's gravitational potential and causes the lens to split the source into two images separated by $\sim 2\theta_{Einstein}$.²

Because the observer, source, and lens undergo independent motion, the angular separation of the images and the image magnification are functions of time. Usually, the images produced by a microlens are difficult to resolve. Therefore, the only observable element is the sum of the magnified flux of the two images. Due to the low resolution, microlensing can only be detected when the source-lens-observer alignment changes, which alters the flux of the images.³ Therefore, in order to detect a microlensing event one needs to monitor sources for variation in brightness. (See Appendix for diagrams illustrating a microlensing event).

In a microlensing event, three parameters define observables. These parameters include the time of maximum magnification, the impact parameter, and the characteristic time scale for the event. As we saw earlier, a microlensing event is a function of time, so the characteristic time scale for this event follows:

$$t_{event} = \frac{\theta_{Einstein}}{\delta}$$
, (16)

where δ is the proper motion of the lens-source.² For a microlensing case, this equation can be approximated as:²

$$t_{Microlensing} \cong 20 \left(\frac{M}{0.3M_{Sun}} \right)^{\frac{1}{2}} days \cong 3 \times 10^{-14} (M)^{1/2} days$$
, (17)

where the values for the mass of the extra-solar object and the mass of the Sun are consistent with earlier calculations.

The primary observables that are defined by the above parameters are the mass ratio (*q*) and the instantaneous projected separation (*d*) between the planet and star.² The mass ratio is the most important observable because it gives direct information about the planet-star system. The instantaneous projected separation only gives statistical information about the semi major axis (*a*). As Guadi (2002) illustrated, the planet must be near one or both of the images in order to be detected. Moreover, the images are near the Einstein ring radius while the source is significantly magnified. Therefore, microlensing is sensitive to planets with $d \sim 1$. This corresponds to:

$$a \sim D_{OL} \theta_{Einstein}$$
, (18)

and for the microlensing case:²

$$a_{Microlensing} \sim 2AU \left(\frac{M}{M_{Sun}} \right)^{\frac{1}{2}} \approx 1 \times 10^{-15} (M)^{1/2} AU$$
. (19)

V. Microlensing Advantages and Disadvantages

Microlensing has several advantages over classical extra-solar planetary detection methods. First, microlensing enables detection of planets at distances up to several tens of kiloparsecs, because no flux is needed from either the lens or the source.^{2.5} Second, the strength of the planet's signal weakly depends on the planet/primary mass ratio, where the signal drops as \sqrt{q} . This advantage makes microlensing the only method capable of detecting Earth-mass planets.⁷ Third, microlensing is sensitive to planets at separations of d = 1 - 10 AU without having to monitor the entire orbital period.²

However, there are some disadvantages in using microlensing to detect extra-solar planets. First,

microlensing events are essentially non repeatable and occur for only a short time, which makes follow-up observations very difficult.^{2, 5} Second, in gravitational lensing, it is nearly impossible to completely deduce the lensing potential from observational data because the lens cannot be removed to observe an undisturbed source plane. As a result, one is unable to completely model the system due to degeneracies. However, degeneracies can be broken if there is independent knowledge of the scale of the source plane.³

VI. Conclusion

Gravitational lensing has become an important observational method in astrophysics and planetary physics. It has allowed researchers to probe cosmology and discover the structure of nearby planetary systems. Monitoring many microlensing events would provide information on the distribution of planets within our galaxy. Although the many parameters involved in monitoring microlensing events results in mainly statistical data, microlensing remains the only method for detecting extra-solar planetary Earth analogs, which could harbor life.

Appendix

Figure 1 is a diagram taken from Kuijken (2003) that illustrates a microlensing event as a function of time. In the lower diagram, the lens (i.e., possibly a low-mass star or planet) is designated by an x. The Einstein ring, which is the critical curve in this case, is shown by a dotted circle. The upper graph demonstrates how the combined flux of the two images (the darkened objects) changes as the source (the small, complete circle) moves with respect to the planet.

Figure 2 is a computer simulation taken from the March 6, 2002, Astronomy Picture of the Day (http:// antwrp.gsfc.nasa.gov/apod/ap020306.html). The computer simulation is credited to Rychard Bouwens at the University of California Observatories/Lick Observatory, the Advanced Camera for Surveys Team, and NASA. The diagram illustrates what one would observe if light from a distant non point like source or sources (e.g., a luminous galaxy or galaxies) passed through and was

Figure 1. A microlensing event as a function of time.



Figure 2. what one would observe if light from a distant non point like source or sources passed through and was deflected by another galaxy.

deflected by another galaxy. The concentric patterns are known as archlets and are another manifestation of gravitational lensing.

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Three Gorges Dam:

Fortune or Folly?

Aadel Chaudhuri

The Yangtze River in China, the third largest river in the world, has long awed painters, writers, and poets. For centuries it drew people to its banks for trade, transport, and spiritual purposes, as evidenced by archaeological studies.³ Like the Nile and Indus rivers, the Yangtze's fertile banks gave rise to one of the earliest human civilizations. Perhaps the ancient people came to settle on the Yangtze's welcoming banks because the land was ideal for growing crops; or maybe they were stopped in their tracks, awestruck by the breathtaking site of the Yangtze cascading through a set of chasms known as the Three Gorges. According to Chinese legend, "The scenic channel was carved in stone by the goddess Yao Ji as a way of diverting the river around the petrified remains of a dozen dragons she had slain for harassing the peasants." It makes one wonder whether these people would still choose to settle there if the majestic gorges were replaced by a sheer concrete wall and 360 miles of the free-flowing Yangtze were replaced by a still water reservoir.

While a debate over the gorge's charm versus the dam's charm could provide some insight into the controversy surrounding China's Three Gorges dam project, this paper will instead discuss a more central aspect of the controversy—China's energy needs and the dam's environmental consequences. Environmentalists stress that the dam project, which would make the Three Gorges dam the largest in the world, will have severe environmental consequences including disruption of the river ecology and the extinction of endangered species.¹ Chinese government officials, however, counter that the dam is necessary to propel China into the 21st century.¹ They say that without it, China will continue to have difficulty in providing energy to its immense population.¹ Additionally, they stress that energy obtained from the dam is more environmentally friendly than alternative sources, which in China's case would be the burning of coal.¹ Both sides have their supporters, although it seems that the government's opinion, assuming sufficient financial support, will stand regardless of the environmentalists' position.¹

The government's reason for building dams seems valid and fair. The building of small dams along the Yangtze River seems justified because they will provide energy without causing too much irreparable harm to the river ecology.¹ The Three Gorges dam, however, due to its enormity, is projected to have severe ecological consequences. Although it will help China reduce the burning of coal, a terrible air pollutant with global ramifications, the benefits may be undercut by its estimated effects—the predicted extinction of endangered river animals, the loss of countless archaeological sites, and the displacement of millions of people.³

Sandra Burton, the former *Time* magazine bureau chief in Hong Kong and Beijing, agrees with the environmentalists' point of view. Her article, "Taming the river wild," which was published in 1994, explains why the Three Gorges dam will not provide enough energy to justify its negative environmental consequences. Despite being published over eight years ago, the article discusses issues that are very relevant, as the Three Gorges dam is still under construction. Just as in 1994, we can only guess what the eventual economic and environmental aftermath of this immense project will be.

"Taming the river wild," begins by outlining the negative environmental, societal, and historical consequences of the Three Gorges dam. Burton states that the dam "will not only displace people but also devastate wildlife and

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alter the landscape forever".¹ In this way, the article's introductory paragraphs clearly state the author's point of view. In what follows, however, we find that Burton's views are not as black and white as her article's introduction suggests. While she doesn't support the Three Gorges dam, she also recognizes the problems in China's current energy system. Thus, she acknowledges the Chinese government's point of view but, in the end, still believes that there is a better and more environmentally friendly energy alternative to both dams and China's status quo coal-based power plants.

Burton explains that "Chinese leaders argue vehemently that Three Gorges is vital to their country's future—and actually good for the environment as a whole".¹ She says that the Chinese government's rationale for building the Three Gorges dam is to prevent the periodic flooding of the Yangtze and to provide a

clean, renewable source of energy.¹ Coal supplies 75 percent of China's energy needs.¹ Its widespread use has heavily polluted the air and has made respiratory diseases a major problem in China.¹

Burton goes on to argue that "how China meets its energy needs has an impact far beyond its boundaries."¹ She explains that emissions from Chinese power plants cause acid rain in Japan and Korea.¹ Moreover, because China is the world's second largest producer of greenhouse gases, it is a major contributor to global warming.¹ Burton explains that additionally, China's 11 percent annual economic growth rate is driving energy requirements even higher.¹ She argues that if coal burning continues to supply the majority of China's energy, the environmental consequences will be catastrophic.¹

While she is against China's reliance on coal for energy, Burton does not feel that building dams such as the Three Gorges is a good solution. Her argument is an economic one in which she quotes experts and displays several statistics. In her article, Burton states, "Experts say hydropower will account for no more than 20% of China's electricity generation by 2010."1 Additionally, she states that China's "potential dam sites are in the less populated southwestern part of the country, making it expensive to transmit electricity to the industrial north and east."1 Thus, Burton argues that dams are a poor solution to China's energy problem because they provide a relatively low percentage of the country's total energy requirement and due to the logistical expenses of transporting the energy to areas that need it most.

Following this, Burton proposes alternative methods for China to reduce its heavy dependence on the burning of coal. She toys with the idea of nuclear energy, and she mentions that Jiang Xinxiong, president of the China Nuclear Indusry Corp., predicts that an additional 20 nuclear power plants will be online by 2020.¹ However, she quickly

dismisses the notion that nuclear energy will solve China's problems, given the controversy surrounding it and China's "failure to adopt international nuclear safety standards," which has "discouraged foreign investors from helping China build commercial reactors."¹

After this analysis, Burton concludes that China in fact has no alternative to coal. According to experts, "The best China can hope for ... is to find cleaner, more efficient ways to burn the plentiful fossil fuel."¹ Doing so will reduce the amount of pollutants and soot released when burning coal.¹

Burton continues by discussing factory devices that wash coal fuel, decreasing the amount of soot produced.¹ Following this, she states that despite such technologies, "Even if coal is burned cleanly, it produces large amounts of carbon dioxide, the most common green-



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house gas."¹ She reasons that the burning of coal should be avoided if possible. At this point in the article, Burton is left in an interesting position. It seems that she is choosing among several suboptimal energy choices, all of which require billions of dollars to develop on a large scale. Thus, she concludes by stating that China needs \$300 billion to develop clean energy projects.¹ She suggests that if these projects are not as controversial as dams, it may be possible to raise the money with help from foreign investors.¹

Burton's analysis has many points of agreement-it appears necessary for China to explore alternative energy sources that will help reduce her dependence on coal. However, unlike Burton's view, many believe that utilizing dams, despite their negative ecological consequences, is a necessary step in this process. An editorial published in Asiaweek in 1996 titled "Asia Needs Dams: And yesthere are ways to minimize ecological damage" supports this viewpoint to a great degree. Like "Taming the river wild," this article is quite old. Nonetheless, many of its arguments are still valid today since it discusses issues that are still pertinent, and supports a position that continues to be defended by dam-backers in Asia. It is interesting to note that a more recent issue of Asiaweek, published in 2000, contains an article that argues a viewpoint opposite the 1996 article.

The editorial "Asia Needs Dams..." argues that dams are necessary in developing Asian nations for energy

production. It essentially supports the Chinese government's point of view with regard to dams. The editorial begins by acknowledging the environmentalists' point of view by stating several negative aspects of dams. It states that among other things, "The structures ... displace legions of people and devastate wildlife."²

The editorial continues by explaining why Asia in particular is an ecologist's nightmare. It states that Asia's dam projects such as the Three Gorges dam and India's Narmada dams are so large that they require World Bank involvement.² It is interesting to note, however, that in the wake of intense controversy the World Bank recently withdrew its support for the Narmada dam. The editorial argues that the Western media enjoys portraying Asian dams as "evil monoliths built on the premise that modernization is more important than the people and wildlife they affect."² Thus, it says "many [dam projects] are stalled for years in the crossfire of environmental study and counterstudy."²

The article's author feels that this is tragic because "[dam] projects stand to improve immeasurably the lives of the surrounding populations by providing power to spur the local economy and to create jobs."² He states that the Arun dam in Nepal, for example, would have brought electricity to the 90 percent of Nepal's population who still rely on firewood for cooking.² The project, however, was shelved when Germany withdrew its support due to vigorous lobbying by its Green party.²

The remainder of the editorial is a powerful yet concise argument for why Asia needs dams, regardless of Western pressure suggesting otherwise. It states that "the World Bank predicts that the region [Asia] will spend \$600 billion over the coming decade to meet its energy requirements."² The editorial further argues that if Asia acquires this energy from fossil fuels, it will only worsen the region's already serious pollution problem.² Although the editorial mentions clean and less controversial alternatives such as wind and solar power, its author dismisses them as being difficult to fund and develop quickly.²

Thus by rationalizing that other energy options are either environmentally or economically less feasible than dams, the *Asiaweek* editorial concludes that dams are necessary for Asia. It states that "dams provide a cheap, renewable and non-polluting source of energy."² Furthermore, the author reasons that dam utilization in underdeveloped Asian nations such as Nepal can in fact improve the environmental situation. In Nepal, a country with a wellspring of rivers, energy from dams can help stop the deforestation that occurs when people who are currently deprived of electricity burn wood for their energy needs.² He goes on to argue that deforestation can in turn cause flooding and propagate detrimental siltin effects.² He feels that these environmental and energy concerns make dams a necessity for Asia.

Like "Taming the river wild," the *Asiaweek* editorial concludes by suggesting environmentally amicable solu-

tions to improve Asia's energy systems. Its author reminds us that the World Bank already has stringent ecological impact and displacement of people guidelines that must be met before it lends money toward a dam project.² He also suggests possible technological techniques of making dams ecologically friendlier by mimicking seasonal river patterns as is being done in the Glen Canyon dam in Arizona.² In addition, he urges donors to exercise their rationale when funding a dam project. As an example, the author asks, "Does Malaysia need a dam with a reservoir the size of Singapore?"² He does, however, mention that if such a project is economically vital, it should be seriously considered.²

As a closing point, the article condones clandestine dam projects that are not disclosed to the public until the last minute. It quotes Mr. A. Kadir Jasin, a group editor of *Malaysia's New Strait Times*, as having said, "Public fear and scepticism cannot be avoided when things are done in secret and agencies involved are at loggerheads with one another."² The editorial's author believes that open discussion between a nation's government and people over dam projects, even if heated at times, will help build national support for such projects.²

The analysis performed in the *Asiaweek* editorial is very thorough. It provides a compelling economic and environmental reason for building dams, arguing that although not ecologically perfect, dams are cheap and environmentally safer than the common alternatives (fossil fuels). It is troubling, however, that a piece of evidence sited in the article is no longer valid. In contradiction to the article, the World Bank is no longer funding the construction of India's flagship Narmada dams. This notwithstanding, the article makes a logical argument about dams in Asia that holds even with this inconsistency.

The two articles, when taken together, present an interesting mixture of viewpoints on Asian dams, particularly the Three Gorges dam. "Taming the river wild" by Sandra Burton argues that dams are ecologically harmful and economically not viable enough to be worth pursuing. She suggests improving current fossil fuel—[one N]based systems in China to provide cleaner energy. "Asia Needs Dams: And yes-there are ways to minimize the ecological damage" argues an opposite viewpoint—that dams are economically viable and necessary for Asia's future, and that they are environmentally safer than the alternative fossil fuel based systems.

Like both authors, I believe that it is necessary for China to explore alternative energy sources that will help it reduce its dependence on coal. However, unlike Burton and like the *Asiaweek* author, I believe that utilizing dams are a necessary step in this process. According to Burton, the Three Gorges and associated dams will provide "no more than 20%" of China's energy source by 2010."¹ Burton also quotes experts who say, "The best that China can hope for ... is to cut coal's portion of the energy mix from 75% to 60% by 2010."¹ These statistics



show that hydroelectric power from dams will provide 15 to 20 percent of China's energy by 2010. This is a very substantial amount, given that it will largely be the result of damming only one river, the Yangtze. While dams such as the Three Gorges may not be a complete solution to China's energy problem, Burton's own evidence shows that their use in China can substantially decrease the country's dependence on coal. The *Asiaweek* article reinforces this notion by describing how other Asian dams such as the Nepal's Arun dam have promised to improve the country's dire energy situation.

Despite dams seeming necessary for China to improve its energy situation and decrease its reliance on coal, other energy options should also be looked into seriously. The Three Gorges dam, given its enormous proportions, may be too drastic a measure. It will flood surrounding cities, forcing millions to move elsewhere, bury historical artifacts, and drive to extinction endangered species such as the baiji dolphin.³ For these reasons, work on the Three Gorges, in spite of its energy promises, should be discontinued. The smaller dams downriver on the Yangtze, however, because they promise to provide China with energy without such drastic consequences, can be utilized effectively. Although these dams may not be able to provide the bulk of China's energy needs, perhaps supplementing them with ecologically friendly energy sources such as wind and solar power could help China realize its environmental and economic goals.

The *Asiaweek* editorial dismisses such clean renewable energy sources as being too high-priced and difficult to develop. But it may be that these may hold the key to China's and Asia's future. The European Union uses 70 percent of today's utilized wind energy, with Denmark harvesting 18 percent of its total energy from wind.⁴ Given Asia's rapid rate of development, it seems very reasonable for China and the rest of Asia to follow suit. It is unfortunate that both the *Asiaweek* editorial and "Taming the rivers wild" had to choose an energy system by process of elimination—the best of many environmentally bad choices. I look forward to seeing Asian governments in the future, after doing such an analysis, choose a clean, ecologically safe, renewable energy source such as wind or solar power to depend on. Although the continent would not have the world's largest dam, Asia would be a model for the rest of the world to follow.

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Breaktbrough:	A company that VALUES: integrity, teamwork, quality, community, family, THE INDIVIDUAL
Breaktbrougb:	A company on the threshold of COMMERCIAL SUCCESS
Breaktbrougb:	A company that is INNOVATION
Breaktbrougb:	A company that MAKES A DIFFERENCE
Breaktbrough:	ImClone Systems Incorporated

ImClone Systems is a dynamic organization dedicated to developing novel therapeutic products in the field of oncology. Our efforts have resulted in a broad spectrum of innovative targeted cancer treatments. Our employees are committed to provide quality products to cancer patients. In efforts to fulfill this commitment, ImClone Systems fosters the integration of the principles of teamwork and scientific integrity into all facets of the Company's activities. We believe that these principles will benefit patients, physicians, and our employees while creating value for our community.

At ImClone Systems you will enjoy a competitive salary and benefits package which includes: stock options, 401K plan, and tuition reimbursement.

MANUFACTURING	CLINICAL AFFAIRS
ENGINEERING	INFORMATION SERVICES
FACILITIES	RESEARCH AND DEVELOPMENT
CHEMISTRY	QUALITY ASSURANCE/QUALITY CONTROL

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Targeted *S*ncology^{*}

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