Columbia Science Review

Volume 3 Issue 1
Spring 2006

Quantum Computers and the New Information Age

Hurricane Katrina: A Man-Made Phenomenon?

The Songbird and the City

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Misfolded Protein of Doom

Centennial Prof. Koji Nakanishi

Proceedings of Summer Undergraduate Research Fellowship 2005

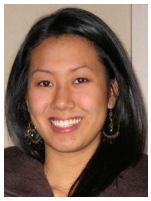
The Columbia Science Review

The Columbia Science Review strives to increase knowledge and awareness of science and technology in Columbia community, by presenting engaging and informative approaches to contemporary science and technology that include, but are not limited to:

- Exploration into contemporary issues of science, including research, policy, and opinion.
- Features on current faculty research.
- Opportunity for students to publish their scientific research.

Contributors to This Issue

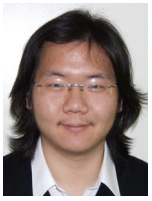
Andrea Appleton is a student in Graduate School of Journalism, in magazine concentration. Her article on birds monitoring is on page 16.



Melody Chou is a sophomore in Fu Foundation School of Engineering and Applied Sciences, majoring in Chemical Engineering with minor in Materials Science/Engineering and Psychology. Her faculty profile on Dean Jack McGourty is on page 24. - "It was my pleasure to write for CSR!"

Robert Heller is a junior in Fu Foundation School of Engineering and Applied Sciences, majoring Earth and Environmental Engineering. His article on Hurricane Katrina is on page 26.

Adam Kaufman is a Rabi Scholar in Columbia College where he is a junior majoring in Biochemistry. He is interested in immunology and public health issues and is presently conducting research at Memorial Sloan Kettering Hospital and Columbia Presbyterian Hospital. His article on Prion is on page 8.



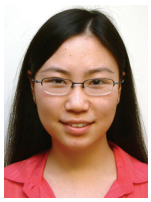
Donghun Lee is a Rabi Scholar in Columbia College. As a junior double majoring in Biochemistry and Economics-Mathematics, he is interested in computational biology as well. His SURF abstract on crossover effects of testosterone and LH in *X. laevis* is on page 30.

Jean Li is a senior in Columbia College, majoring in Chemistry. Her faculty profile on Centennial Professor Koji Nakanishi, Department of Chemistry, is on page 19.
- "We got more bounce in California."

Jonathan Mo is a first-year student in Columbia College, pursuing majors in Biology, Astronomy, and concentration in Computer Science. His article on Quantum Computing is on page 12.
- "I support popularization of science, and I think CSR is an excellent example!"

Jakob von Moltke is a student in Graduate School of Arts and Science, pursuing Masters of Biotechnology degree. His article on Heat Shock Protein 90 is on page 20.

Christopher O'Conor is a sophomore in Fu Foundation School of Engineering and Applied Sciences, majoring in Biomedical Engineering. His faculty profile on Dean Jack McGourty is on page 24.



Jing (Meghan) Shan is a junior in Fu Foundation School of Engineering and Applied Sciences, majoring in Biomedical Engineering. Her SURF abstract on paracrine regulation of human BMSC growth is on page 30.

Julien Dumoulin-Smith is a junior in Fu Foundation School of Engineering and Applied Sciences, majoring Applied Mathematics. His article on Poverty Mapping in CIESIN is on page 6.
- "Internship at CIESIN was great."

Calvin Sun is currently a sophomore in Columbia College at Columbia University in the City of New York. He works in Dr. Richard Axel's laboratory at the Columbia University Medical Campus. His SURF abstract on olfactory receptor dimerization is on page 29.

Devorah Abberbock is a junior in Fu Foundation School of Engineering and Applied Sciences, majoring in Biomedical Engineering. Her SURF abstract on automated myocyte imaging is on page 29.

Aylin Gezgin is a junior in Barnard College, majoring in Neuroscience & Behavior. Her SURF abstract on leptin injection and lipolysis in rats is on page 29.

Sarah J. McNally is a senior in Barnard College, majoring in Psychology. Her SURF abstract on effects of three dieting types on eating regulation is on page 30.

Questions? Comments? Article Submissions?

Please visit us at

www.columbiasciencereview.org

Dear readers,

Welcome to the fourth issue of *Columbia Science Review*. This semester marks the third anniversary of Columbia's first student science publication. In recognition of the past and hope for the future, it is worthwhile to reflect upon why we are here, what we are doing, and where we are going.

We are here to present science to the public — a daunting task. It is hard for scientists to recognize and limit jargon in their writing. It is even harder, if not impossible, for a non-science person to read and understand scholarly journal articles.

Columbia Science Review strives to end this stalemate by featuring articles on scientific topics written in a more accessible manner meant for the general public — that is the Columbia community. This approach benefits not only the artists and historians who need to understand the track of modern society, but also the mathematicians and mechanical engineers who might enhance their art by using concepts from molecular biology. When it comes to scientific topics outside their specialties, both groups are equally matched in their ability, or lack thereof, to understand the specialized esoteric terms of a remote discipline. But in our age of collaboration and multidisciplinary projects, it is often very helpful, if not imperative, for all of us to understand emerging new fields of science. *Columbia Science Review* is in itself a multidisciplinary project. Every word reflects the hours our writers spent to compose and revise their manuscripts; every reference shows the fidelity our reviewers have toward the original scientific content; every sentence demonstrates a careful balance between scientific rigor and ease of reading made possible by the editors; and every image is a visual aid precisely positioned by the layout designers to best illuminate the article. We know first hand the inherent difficulties in a collaboration, so we hope to make that process a little easier for you, our reader.

I would now like to highlight a new addition to *Columbia Science Review*. Starting with this issue, *Columbia Science Review* will be the official venue for the publication of "Proceedings of Summer Undergraduate Research Fellowship (SURF)." The Columbia SURF program is offered by the Department of Biological Sciences to a small group of undergraduate student interested in biological research. This competitive program offers hands-on research experience, enhanced by weekly seminars and research discussions. Participants present their work by lecture or poster in a conference setting in early February. Selected abstracts will then appear in *Columbia Science Review*.

Due to an overwhelming number of submissions to this issue, we were forced to postpone several very appealing articles to a future issue. I apologize for this arrangement, and please allow me to re-emphasize that all contributions are greatly appreciated. We encourage you to submit your work to the Columbia community. Instructions for authors can be found through our web page: http://www.columbiasciencereview.org

Now without further ado, it is my pleasure to present to you *Columbia Science Review*, Spring 2006. We owe much of our rapid expansion to our contributors, staff members, faculty advisors, sponsors and especially to you, our readers. Thank you all.

Cordially,

Jing (Meghan) Shan
Editor-In-Chief
Columbia Science Review

The mission of the student organization Columbia Science Review is to increase knowledge and awareness of science and technology in Columbia community, where two huge hurdles lie along the way. Written by students, printed in full color, the publication *Columbia Science Review* since its first issue has represented the student-driven effort to lower the hurdle between the science students and the general public. Congratulating its second anniversary, I daresay that Columbia Science Review has potentials to address the other hurdle without neglecting the first.

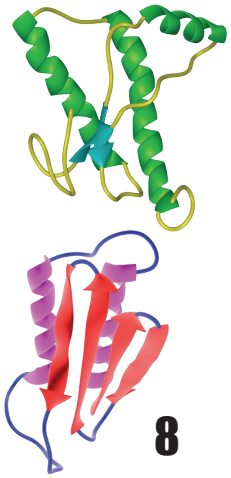
We are at a time where students pursuing career paths in science and technology are endowed with greater opportunity to conduct independent research. A substantial portion of their time and effort is devoted to reading professional journal articles, performing experiments, reflecting on the progress, and contemplating the future direction of their research. However, not every idea from students turn into experiments, and not all student research projects mature into scholarly publication. Why are most student perspectives not publicized? Why are most student researches not published? Among many reasons, there is one reason that is irrelevant to students' effort – the publication cost.

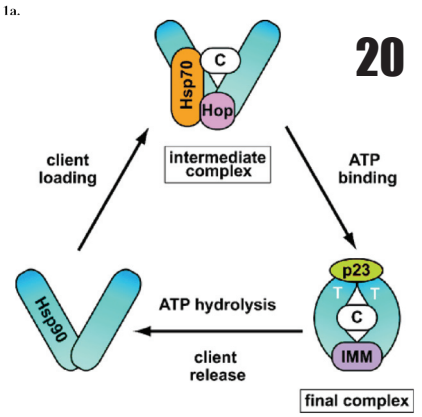
Columbia Science Review will introduce a scholarly journal that combines the merits of online publication and the impact of print publication. The *Journal of Columbia Science Review* will publish articles in electronic formats, so that no financial burden hinders students from publishing their scholarly works. Meanwhile, select articles of the highest qualities from the *Journal* will be featured in the publication *Columbia Science Review*. Through this unique cooperation, the *Journal* will become a scholarly platform with maximum accessibility for students to present scientific perspective and research to fellow students and faculty members.

It has been my greatest fortune to be involved in Columbia Science Review, whose aim and potentials far exceed other projects with ostentatiously similar activities. On behalf of Columbia Science Review, I appreciate generous supports from the Activities Board at Columbia and the Office of Undergraduate Admissions, invaluable advices and helping hands from fellow students, faculty advisers, and most of all, Lauri Straney in Student Developments & Activities, whose help made Columbia Science Review a notable reality.

Warmest regards,

Donghun Lee
President
Columbia Science Review





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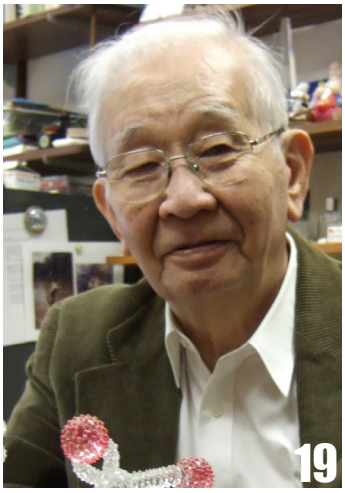
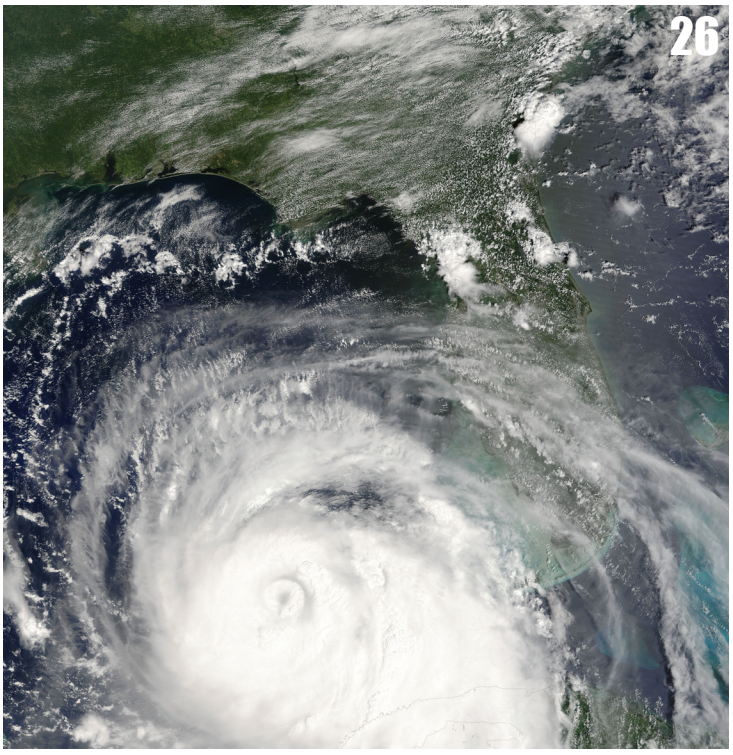
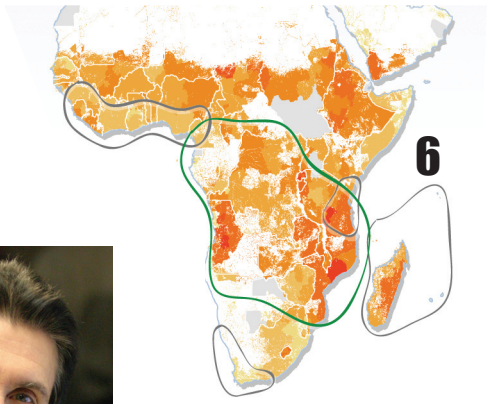
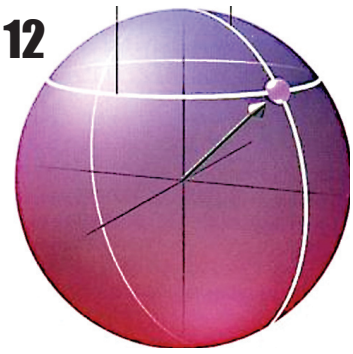


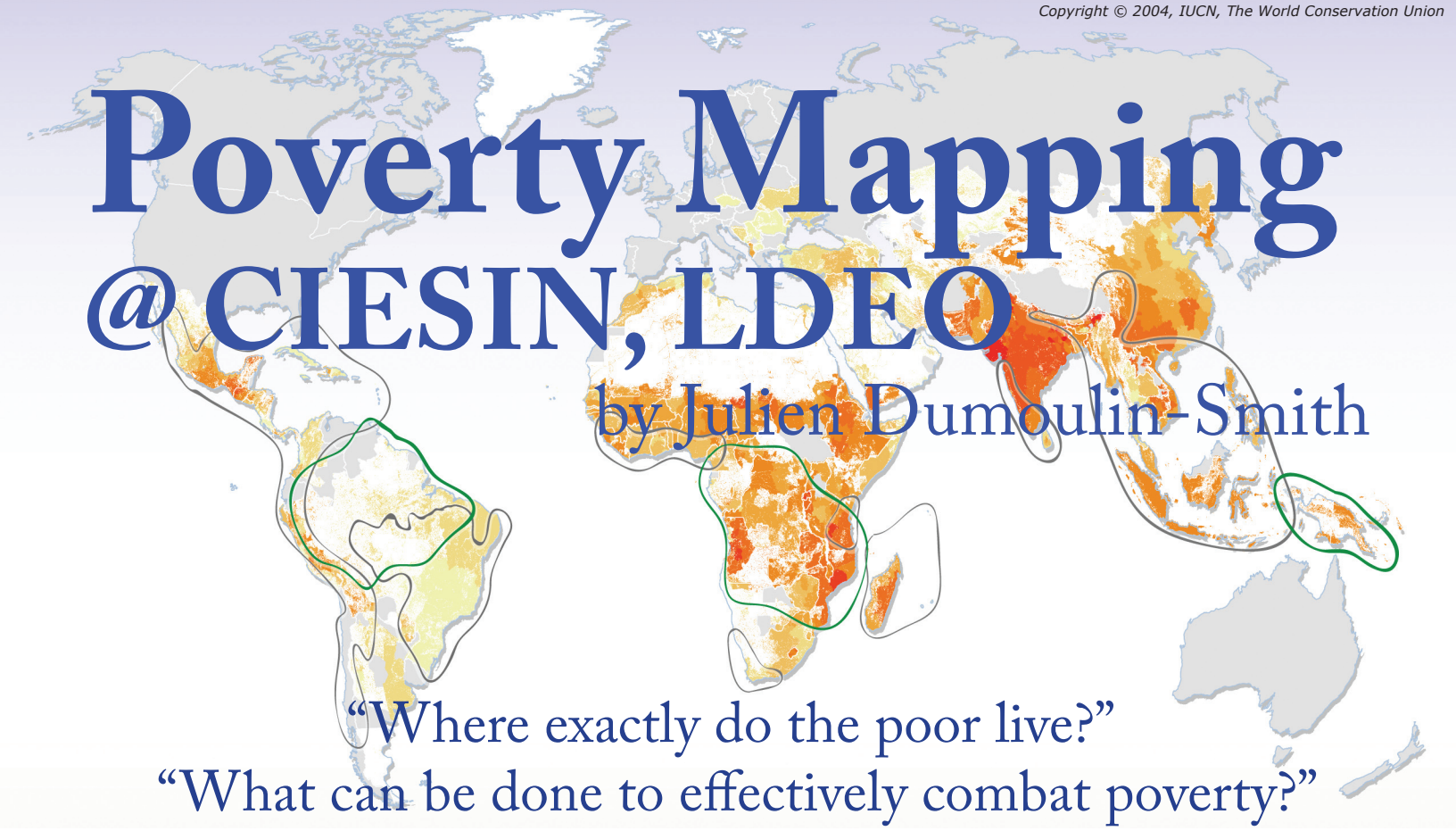






Poverty Mapping @CIESIN, LDEO

by Julien Dumoulin-Smith



"Where exactly do the poor live?"
"What can be done to effectively combat poverty?"

In the worldwide battle against poverty, understanding precisely where the problems exist is a central element in ensuring effective and efficient policy making. Floating in an abundance of information and statistics, are two interconnected questions that policy makers must ask themselves: "Where exactly do the poor live?" and "What can be done to effectively combat poverty?"

Researchers at the Center for International Earth Science Information Network (CIESIN), part of the Lamont Doherty Earth Observatory, have been working to develop a detailed map of world poverty under a grant from the World Bank. The ultimate goal of the project is to assemble a detailed world atlas of poverty data with precise information available down to the district level. The data is being drawn from all kinds of sources, from NGOs to national statistical centers and compiled into one vast poverty database.

However, with this new plethora of data comes the task of synthesizing and processing this immense dataset to reveal poverty trends that could prove useful to policy makers. Over the last couple of months, CIESIN has been experimenting with different indices to develop what will hopefully become a measure of the spatial distribution of poverty within a country.

The use of indices to describe and compare data patterns is a cornerstone of political science. The application of indices describing poverty trends for entire countries could prove useful for comparisons to other social statistics, such as population inequality or income inequality. They could also be compared against classic political science indicators, such as political freedom or even the World Bank's own World Development Indicators.

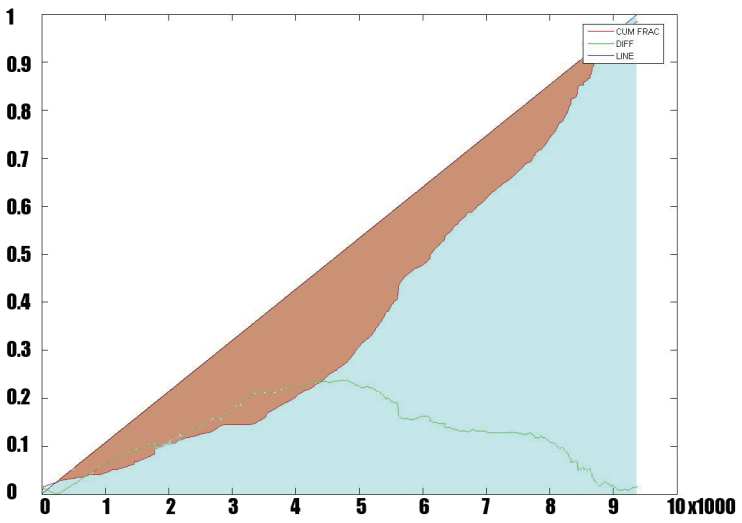
Indices used in order to quantify and compare trends in countries illustrate the key role that the clever deployment of statistical ingenuity could play in bringing forth quality indicators to the spatial poverty community. The goal of our specific indicator was to balance the robustness of the data available in the spatial distributions of poverty with the flexibility to accurately compare the degree to which the poverty is spread across countries.

Our team took a two pronged approach to developing this indicator. The first was to analyze literature on the only subject that has really investigated spatial distributions: biodiversity. There is a long tradition of ecologists who have developed mathematical methods to measure the relative density of animal and plant life. Numerous papers and books have been written on the subject; however all seemed to rely on measuring population inequalities by examining how empirical data deviated from an even spread or evenly dense population. The two indicators we settled on were

$$E_D = D / D_{MAX} = \left(\frac{1}{\sum_{i=1}^{S}(P_i)^2}\right) * \left(\frac{1}{S}\right)$$

$$E_H = H / H_{MAX} = \left(-\sum_{i=1}^{S} P_i * \ln(P_i)\right) / \ln(S)$$

The E_D is the value for the Simpson's Evenness Index and the E_H is the value for the Shannon's H index. P_i in both cases is the proportion of total poverty that exists in region i. In later versions, P_i was weighted with a variety of different techniques.



Above is a visual explanation of how the Lorenz curve works. The example above is the area-weighted case for Malawi plotted in MatLab.

the Simpson's Evenness Indicator and the Shannon's H Indicator. Both work in almost identical fashions, but produce different results.

Our second approach to determining our poverty distribution indicator was to implement a Lorenz curve. A Lorenz curve approach is fundamentally the same as those implemented in the biodiversity literature, in that they both examine the degree to which a distribution deviates from an even distribution. The Lorenz curve can typically be found in the GINI index, an indicator measuring income inequality for countries. This measure uses basic integrals to calculate the percent deviation from a perfect deviation.

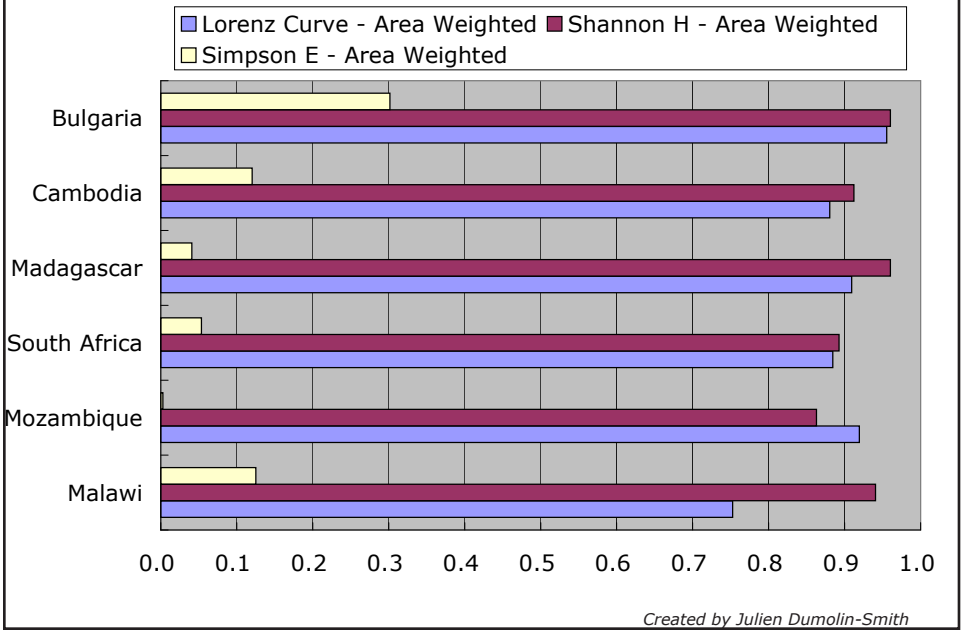
Finally, we found that it would be appropriate to apply different weighting schemes in order to highlight different aspects of the data. Since spatial distributions rely on the relative area of the districts, we found it reasonable to assign a weight to the indicator that was proportional to the relative area of each district. Districts in all of the pilot countries analyzed were considerably smaller in urban areas, yet had larger populations than those of extremely large rural districts. Therefore, the area weights we assigned had a substantial impact on the indicator result.

In a further attempt to remove bias from our indicator, we developed a population weighting scheme, which weighted districts according to their population instead of their area.

From our research we were able to distill three solid indicator approaches for calculating the spatial distribution. For each of these, we created three different weighting schemes: unweighted, area-weighted, and population weighted. In developing and analyzing the indicator, we realized the importance that large poverty-dense urban centers had on a country's overall spatial distribution of poverty. While the highest rates of poverty were found in many of the rural districts, the bulk of the poor lived in and around urban areas. However, due to a lack of readily compiled spatial poverty data, it would be statistically difficult to determine the consequences of poverty distributions.

As a result, our work at CIESIN recently has been to focus on applying these same poverty indicators to population distributions, for which there is ample data already available. Here, we used a dataset created by CIESIN entitled the "Gridded Population of the World" (GPW). Using this dataset, we hope to test our indicators and hopefully find the consequences of population distributions. Eventually, we hope to return to the poverty spatial distributions to compare poverty distribution trends with population distributions.

The indicator values given in the following charts are preliminary poverty distribution indicator values for our pilot countries.



If anyone is interested in following up on the datasets or would like more information on the indicator development project, please don't hesitate to contact the author at jpd2109@columbia.edu or visit CIESIN's website at www.ciesin.org

The Misfolded Protein of Doom

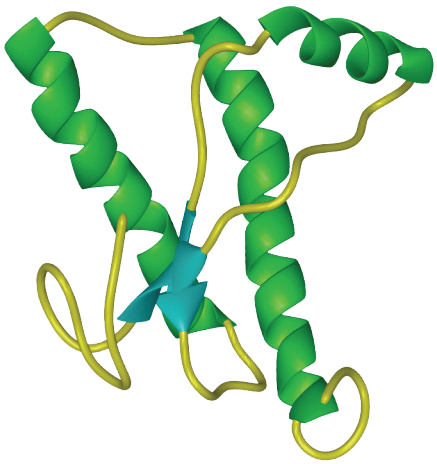
We have long known that infectious diseases are caused by viruses, bacterium, fungi or parasites. In the past twenty years, however, scientists have identified a new infectious agent quite unlike the others. Coined prions, a meld of the two words proteinaceous and infectious, the newest member of the club is a misfolded protein and has been deemed responsible for a host of contemporary brain diseases in both animals and humans. These diseases are called transmissible spongiform encephalopathies (TSEs). Characterized by tiny holes, which give infected brain tissue the appearance of being spongy, TSEs are rapidly progressive after a long incubation period and are always fatal. While the incidence of prion diseases in humans remains relatively rare, progressive neurodegenerative disorders caused by these encephalitic agents could potentially be at the heart of the next epidemic. The incubation period of misfolded prions is thought to span ten to twenty years in humans. This fact coupled with currently inadequate detection measures highlights the potential for an outbreak of TSE that could result in the death of thousands.

The United States Department of Agriculture has, to date, reported three cases of Bovine Spongiform Encephalopathy (BSE), a prion disease of cattle more commonly referred to as "mad cow" disease. The most recent case was confirmed on March 13, 2006 in a cow raised on an Alabama farm. The U.S.D.A. is now attempting to locate the subject cow's birth cohort and any of its offspring. They are also conducting an epidemiological investigation to determine the cow's exact age - vital information that would indicate whether the cow was born before the Food and Drug Administration implemented a ban on ruminant-to-ruminant feeding practices. A preliminary diagnosis made by the veterinarian who euthanized the animal suggests that the cow was more than 10 years old, promising news to the feed ban that was instituted in 1997.

Since no parts of the infected animal have entered the human and animal food supply, no risk seems to be posed to public health in this instance. Even so, this recent announcement underscores the need for surveillance and effective controls of BSE to avoid an outbreak similar to the one that occurred in the United Kingdom and other European nations in the mid 1980s, which did get passed on to humans. Other prion diseases must be monitored as well. Chronic Wasting Disease (CWD), a prion disease of elk and deer, may prove to have human relevance, particularly here in the United States where hunters kill a large number of deer and elk for game each year. Direct contact with infected cervids and consumption of their meat could pose a risk. Moreover, environmental factors such as contaminated feed and water stations may be implicated in the indirect transmission of CWD. The issue of transmissibility of prions within and among different species warrants further investigation.

The Pathology of Prions

Prions are anomalies in the world of infectious disease. Typically, a pathogen requires its own genetic material to establish an infection, but prions are made solely of proteins and do not need the otherwise necessary nucleic acid, DNA or RNA. Nobel laureate Dr. Stanley Prusiner identified the prion protein (PrP) in the early 1980s and proposed that it exists in two forms, normal and infectious. He labeled the benign prions cellular prion proteins (PrP^{C}), and the harmful prion proteins scrapie prion proteins (PrP^{Sc}) to represent the prions that cause transmissible spongiform encephalopathies in humans and animals. While benign and pathogenic prions have virtually identical amino building blocks, the harmful prion protein has a different folded shape. "In its benign state, the backbone of the prion twists into multiple helices. PrP becomes the infectious, scrapie prion, when much of the backbone stretches out, forming so-called beta strands"[1]. When these beta sheets aggregate, they form amyloids, which are associated with a multitude of other misfolded protein disorders. Accompanying the structural change of the prion protein are various biochemical property changes as well. The PrP^{C} prion is soluble in nondenaturing detergents and PrP^{Sc} is not; PrP^{C} is readily digested by proteases, whereas PrP^{Sc} is partially resistant [2].



Two folding styles of Prion protein. Left is normal (PrP^{C}) shape, whereas

Although the exact means of proliferation of the PrP^{Sc} protein are still unclear, scientists hypothesize that pathogenic prions enter the brain cells and convert benign prion cells into scrapie prions. The PrP^{Sc} molecules continue to propagate; transforming PrP^{C} molecules into PrP^{Sc} molecules until the brain is laden with these infected brain cells. Recently, molecular geneticists have isolated a PrP gene. In inherited cases of TSE, in contrast to acquired or sporadic cases, there is always a mutation in this PrP gene, which increases the propensity of the PrP^{C} protein to spontaneously convert the PrP^{Sc} protein.

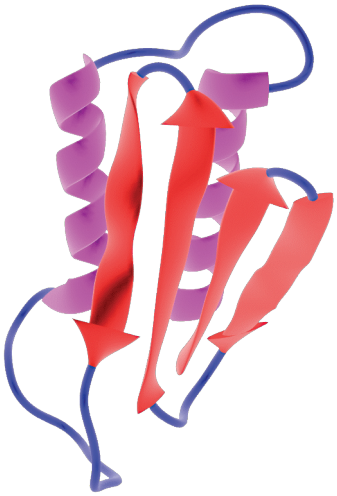
Animal Prion Diseases

Scrapie, the first prion disease, was discovered in the 1700s. It affects the central nervous system of sheep and causes infected animals to scrape off their wool, giving rise to the name of the disease. Locomotive and behavioral changes ensue, and eventually the sheep die. Sheep can infect each other by direct contact, but currently Scrapie has not jumped the species barrier to humans. Other animal prion diseases include Transmissible Mink Encephalopathy, Feline Spongiform Encephalopathy and Ungulate Spongiform Encephalopathy, but, as noted, it is Bovine Spongiform Encephalopathy (BSE) and Chronic Wasting Disease

(CWD) that pose the greatest health risk to humans.

In 1986, BSE surfaced in the United Kingdom wreaking havoc on the British beef industry through the early 1990s. Indeed, by 1993 more than 1,000 cases per week were being reported. The source of the outbreak was traced back to livestock feed that contained infected cow and sheep parts. Although rendering guidelines and feeding bans were established in 1988, they were not strictly enforced until 1991. It took more than two years after the enforcement for the number of reported cases of BSE to decline, but it did not stop there. The mad cow epidemic took on new and frightening proportions in 1996 when eleven British young adults were diagnosed with a TSE that appeared to be linked to Bovine Spongiform Encephalopathy. Scientists identified the cause as consumption of tainted beef.

Similar cases of encephalitis have appeared in other hoofed animals. Termed mad deer disease because of similar symptoms to BSE, Chronic Wasting Disease (CWD) likewise has a long incubation period and is feared to become the BSE of North America. To date, CWD has been found in deer and/or elk in thirteen states and two Canadian provinces. CWD has been seen in both wild and captive cervids. Transmission seems to occur by direct contact with saliva, urine, or feces of infected animals. Indirect contact through crowding, artificial feeding, and contaminated pastures on deer farms is also believed to facilitate transmission, though at the moment there is no certainty. The persistent infectivity of the prion in the environment and the elusive nature of transmission have raised concerns about the risk to humans. Thus, although CWD does not appear to be a food borne disease, protocols for the handling and processing of these animals have been recommended by federal and state wildlife management agencies.



Picture Courtesy of Ingeborg M.M. van Leeuwen

right is Prion (PrP^{Sc}) shape.

Human Prion Diseases

Human prion diseases can be spontaneous, genetic, or acquired. The most common of all human prion diseases is Creutzfeldt-Jakob Disease (CJD), which can occur in any of one of the three designated modes of transmission. The classic form of CJD, which occurs spontaneously and has an annual incidence of approximately one case per one million people, was first recognized in the 1920s. Typically striking patients in their sixties, the clinical manifestations include dementia with early onset of neurological deficits leading to death within one year. The median duration of the illness is four to five months. Familial CJD (fCJD), a hereditary form of the disease, is the result of a genetic mutation in the normal prion gene rendering it analogous in formation to that of the Scrapie prion. The acquired forms of Creutzfeldt-Jakob Disease are Iatrogenic CJD (iCJD) and Variant CJD (vCJD). Iatrogenic CJD is transmitted among humans as a result of infected tissue implants, use of contaminated neurosurgical instruments, or the administration of human hormones extracted from the organs of human cadavers. Relatively rare, with an occurrence of less than 1% of the cases of prion disease, iCJD highlights the need for proper protocols and testing within hospital settings.

Variant CJD (vCJD), the other acquired form of Creutzfeldt-Jakob Disease, came to the fore as a result of the Bovine Spongiform Encephalopathy outbreak in the United Kingdom. Acquired through ingestion of beef contaminated with the BSE agent, vCJD has been reported in approximately 160 cases with the initial and the majority of cases occurring in Britain. Subsequent cases have appeared in France, Italy, Ireland, Canada and the United States, however, the long incubation period renders it impossible to know how many people presently have the disease. Clinical features of vCJD are distinct from CDJ. These differences make the two diagnoses distinguishable. Variant CJD presents in younger individuals, typically in their twenties. The median duration of the disease is 13-14 months, a longer period than that of classic CJD. Psychiatric and behavioral changes occur as with classic CJD; however, with vCJD there are delayed neurological signs as well as painful dyesthesiasis. Moreover, the presence of the pathogenic prion is readily detected in the lymphoid tissue, which is not the case with classic CJD.

Recently, blood transfusions have recently been proposed as a means of transmission of vCJD among humans. The deaths of two individuals in Britain from vCJD, both of whom received transfusions from persons who suffered from vCJD but were as yet undiagnosed, suggests the need for strict blood donation rules. Indeed, the FDA, the agency responsible for setting national blood safety guidelines here in the United States, has established guidelines on geographic donor deferrals which, *inter alia*, preclude donations of blood from those who have visited or lived in the United Kingdom for a total of 3 months or more between 1980 and 1996 or who have received a blood transfusion in the United Kingdom between 1980 and the present. Donor deferrals are also in place for those who lived in France for 5 years or more between 1980 and the present, and for military personnel and their families who resided for a period of 6 months or more on military bases in Northern Europe between 1980 and 1990 and in Southern Europe between 1980 and 1996.

Kuru, another acquired human prion disease, once existed among the Fore tribe of New Guinea because of their funerary practice of eating the brains of their dead. When this cannibalistic ritual ceased the disease disappeared. Other human prion diseases are Fatal Insomnia, which can occur spontaneously, Sporadic Fatal Insomnia (sFI), or genetically, Fatal Familial Insomnia (FFI). They are clinically indistinguishable. Additionally, Gerstmann-Sträussler-Sheinker disease is a familial prion disease.

Hope on the Horizon: PMCA Technology

In view of the fact that BSE has crossed the species barrier, the need for development of early detection devices to minimize the transmission of TSEs is paramount. The sole means for detecting these diseases is to identify the presence of PrP^{Sc} in brain and lymphoid tissue, which up until this time could only be detected when there were significant concentrations in these tissues. A new technique developed by Castilla et al. and reported in *Nature Medicine*, proposes the biochemical detection of PrP^{Sc} in the blood by amplifying PrP^{Sc} in a test tube. The method employed

is known as PMCA, protein misfolding cyclic amplification. In PMCA, PrP^{Sc} is incubated-with excess Prp^{C} to enlarge the PrP^{Sc} aggregates, which are then sonicated to generate multiple smaller units of PrP^{Sc} that have the same biochemical and structural properties as brain derived PrP^{Sc} [3]. This PMCA method detected PrP^{Sc} in the blood of hamsters suffering from Scrapie with 89% sensitivity and 100% specificity, thereby providing the possibility of a noninvasive means of testing for TSEs [3].

The science of prions runs counter to basic biological principles, specifically, that despite their lack of DNA or RNA, pathogenic prions nevertheless propagate through contact with benign prions. It is a nascent field of science where much is still unknown. Genuine public health issues exist, particularly with Variant CJD and Bovine Spongiform Encephalopathy because of the potentially far-reaching negative effects of these two types of TSEs. Moreover, the long incubation period suggests that there may be more people harboring TSEs. Accordingly, noninvasive means for the testing of blood and/or urine must continue to be explored. Likewise, research must investigate ways to prevent the misfolding of the normal prion protein into an abnormal prion protein. A cure may not be in the immediate offing, but prevention is surely a viable pursuit.

Information for this article and sources that provide specific information regarding the subjects discussed herein was provided by:

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Quantum Computers and the New Information Age

By Jonathan L. Mo

What is a Quantum Computer?

We cannot escape the growing influence that computers will have on our lives. As the technology behind computers becomes more affordable and more powerful, these machines, once thought of as experimental hardware, have gained a role in nearly every aspect of human endeavor. Genetics, cryptology, intelligence, astrophysics, entertainment, and of course computer science, are only a few of the realms that quantum computing could change forever. As we know, faster computers are always "better." They improve the speed at which vast and complex calculations can be solved, and they enable us to solve ever more difficult issues in social and physical science. But never before have we been on the brink of such a profound change in the way computers operate, and ultimately, will shape the world even more than they already have.

Imagine if computers could be exponentially more powerful. Based on Moore's Law, the data density of integrated circuit chips doubles every 18 months. This is a measure of technological advancement, and has more or less been observed. But even with cramming more and more transistors, logic gates, and bits onto a silicon wafer, there are finite limits to the processing power inherent in the basic design of the modern computer – scarcely anything more than an algorithm machine following programmed linear instructions.

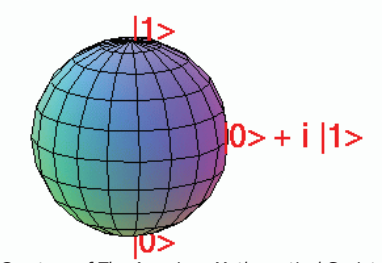
The factorization of large numbers (used in encryption coding) is one of the current problems that simply defy resolution using current technology, unless tremendous computing power is used. What if we could have a computer that was capable of simulating the parallel processing power of an impossible 10^{150} computer processors?

Enter the quantum computer. Today's classically based computer processing takes the form of interpreting binary, where data can be stored as either a one or a zero. Quantum computers, so named because they utilize the atomic reality of quantum physics, are able to manipulate data values that take the form of ones and zeroes, as well as having the unique capability of existing as both numbers at the same time. This seemingly illogical phenomenon arises from a quantum mechanical observation known as *superpositioning*.

Whereas our current computers utilize the classical "laws" of physics, quantum computers obey the laws of quantum physics, ushering in an entire new realm of computer science. This, along with greater speed, and vastly greater amount of data storage, provide for some unique possibilities for data manipulation and computer solutions to problems that cannot be solved with current technology.

The Qubit and Fundamentals of Quantum Computing

At the heart of the quantum computer lays the qubit. The qubit, which is short for "quantum bit," is the quantum computer's unit of information, just as the bit (binary value) is for our classical computers. The qubit has the ability to represent a one and a zero, just as a regular bit, but also of being able to exist as both a zero and a one at the same instant in time. This emerges out of quantum physics as a result of superpositioning, where a particle can essentially occupy two locations at the same instant in time. Before one analyzes the physical implications of the qubit, it is important to understand exactly what a qubit is, and how it would function in a quantum computer.



Courtesy of The American Mathematical Society

A topological representation of a qubit in 3-dimensional space. Note the ability of the qubit to exist in both the zero and one state simultaneously.

In a register (group of data values) containing 3 classical bits, 8 (2^3) possible values in binary can be stored, such as 000, 001, 010, etc. But the register can only store 1 value in a single instance of time. Now, a register of 3 qubits would have the capability of storing all 8 values possible at a single instance in time, in what is known as a "quantum superposition." Additional qubits added to this register would increase the capacity exponentially, with N qubits able to store 2^N values at once. If this register was then set in a quantum superposition of different numbers (eight values in

this case), then mathematical operations could be performed on all eight values at once. With a basic understanding of quantum mechanics, one could think of qubits as atoms (which is in fact a current method for testing quantum computer theory). Technically, a qubit can be implemented using any particle that has two distinct "spin states," that are observable and measurable. These are the characteristics of atoms.

While this oversimplifies what is ultimately a complex science, a qubit's exact state can never actually be determined. This is a result of the quantum reality that it is impossible to accurately measure the amplitude (of the wave function) of any one state. What must be done instead is that a sampling of several measurements must be taken in order to create a "density" expression for the amplitude, or state, of the wave function. This density is then computed in reference to the density apparent in the rest of the system (qubit), and a value for the qubit is obtained. In the previous example, if all 8 of the values stored on the qubit were actually the same value, one might think a problem exists, since the data is actually being "mapped" to a single point in the wave function, which represents the qubit. What actually occurs is simply an increase in density for that particular value, and thus, adding more values does not complicate a qubit. Rather the opposite in fact, because the density of that particular value would be significantly higher than the others. Even though the qubit is only storing that one value, the density function provides probabilities for values that are technically not being "stored on the qubit." Thus, many fewer measurements are required to accurately compute the value (remember it's a binary value!) of that qubit. See the figure below.

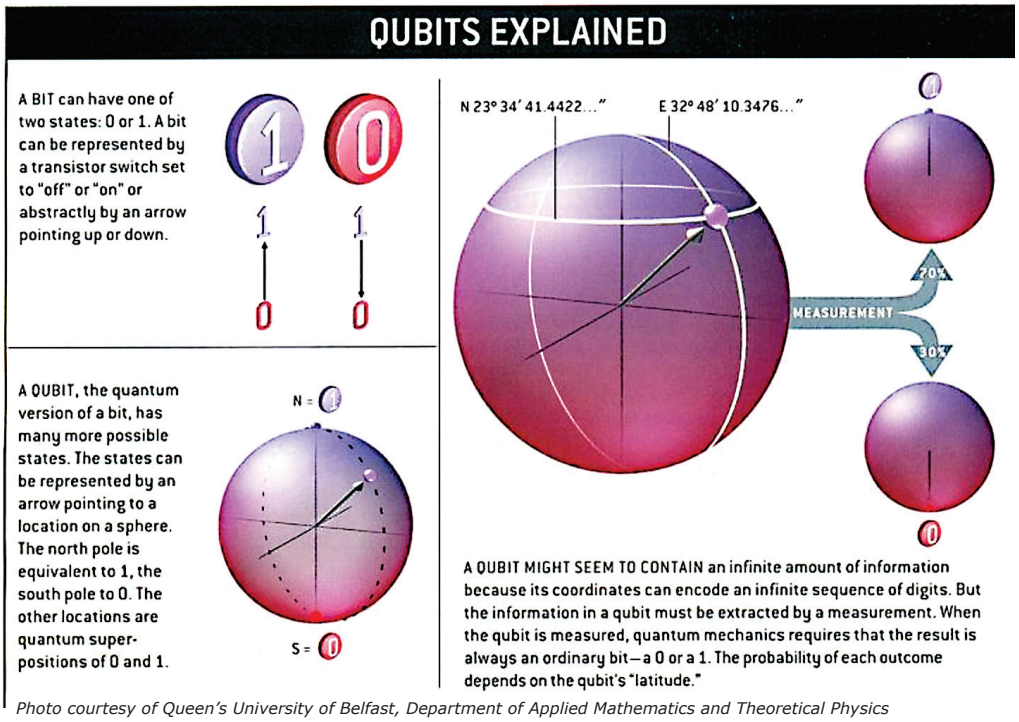


Photo courtesy of Queen's University of Belfast, Department of Applied Mathematics and Theoretical Physics

If we consider qubits as atoms, then all the quantum rules also apply to the data encoded as qubits. For instance, atoms all have quantized energy states, which are discrete and easily definable. If all three qubits/atoms in this example were in an initial, or ground state, then as energy were added to the system to excite the atoms to elevated quantum states, the overall system superposition would be modified. Varying the amount of energy would produce varying permutations of quantized energy states for the atoms. During this so-called "evolution" of quantum states, each number in the superposition is affected. This creates a situation simulating a tremendous, parallel computation, but in a single register, and thus, in a single element of hardware. For a classical computer, this is analogous to performing a computation in one clock cycle of a computer processing unit that usually take many, many cycles. Essentially, all eight values stored inside a 3 qubit register all exist at the same time, encoded in that register as the quantized energy states of atoms. As mathematical operations are performed on the set, they resonate through all the values which have been encoded within it, like the energy states of the atom, and thus the operations are performed on all the values at once. In order to perform the equivalent calculation, a classical computer would have to execute the same computation 2^N times, or alternatively have 2^N processors operating in parallel. When referenced to quantum computing, this phenomenon is called *quantum parallelism*.

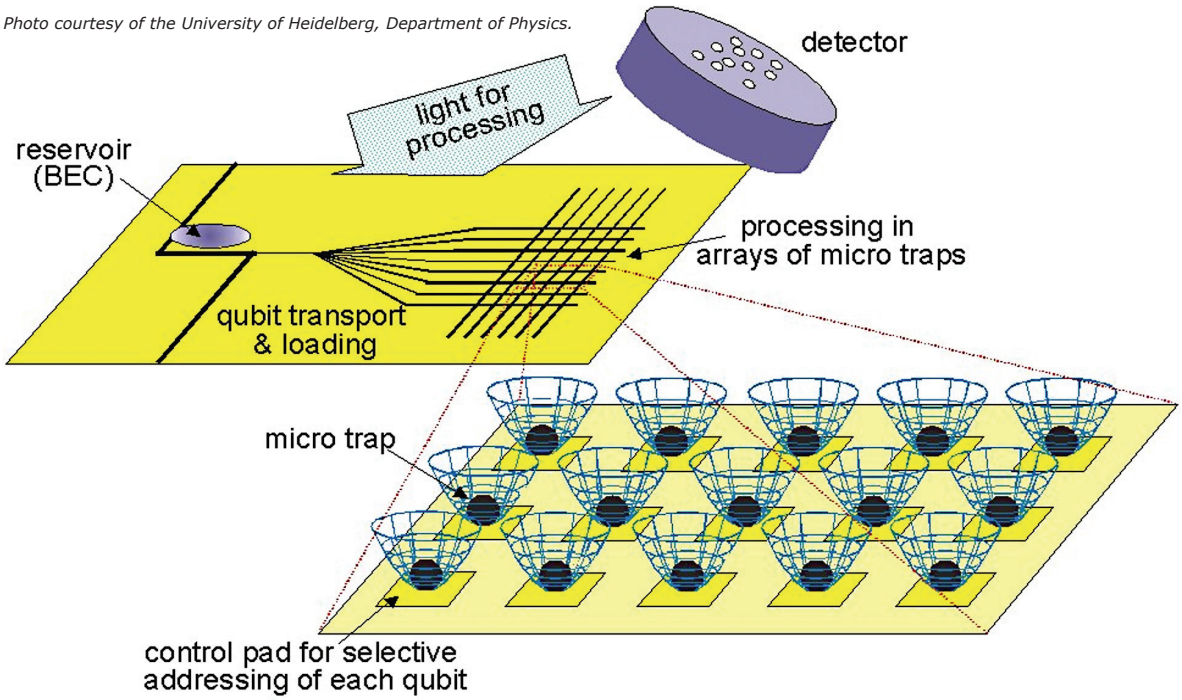
Consider the case of 500 qubits versus 500 bits. 500 bits couldn't even encode a single JPEG image. A quantum system this size, though, would compute on 2^{500} states at once, through superpositioning. This is roughly $3.3*10^{150}$ bits! The cool earth JPEG image at the title of this article is about a 623,000-bit image, or 76 kilobytes. A quantum system of 500 qubits could store $5.3*10^{144}$ of those images, while 500 classical bits cannot even store one!

Besides superpositioning, quantum computational theory also involves a key interpretation of quantum mechanics. Without providing the necessary mathematics, *The Copenhagen Interpretation* is meant to solve the problem of phenomena (like light) that can behave like both particles and waves, more generally described as statistical and non-statistical behaviors. This interpretation states that the act of measuring the atom, electron, particle, or other material, instantaneously causes the wave-function of that object to collapse, becoming a single value. In terms of the qubit then, this is exactly what occurs. The superposition of values could be thought of as a continuous body of data. After the computational operations are carried out on the superposition, the final actual measurement of the result collapses the entire superposition of data into a single value. The qubit, upon measurement, returns a single value. This concept is the driving force behind quantum computing theory, and is one of the most exciting possibilities in computer science today.

In a nutshell, to answer the often-posited question, "How

does a quantum computer work?" one could simply say that it involves the manipulation of an atom's quantum spin state, which models the ever-important binary system required for a stable computer. The spin up state represents a 1, the spin down state, a 0. The special nature of quantum mechanics however, finds that "unobserved" particles are capable of executing both spins simultaneously, this is the *superposition* concept mentioned earlier, and the binary 1 or 0 emerges *only* when the system is measured.†

Photo courtesy of the University of Heidelberg, Department of Physics.



Possible structure of a true quantum computer. The qubits sit on a panel of control mechanisms, arranged in an array that allows photons to perform "operations" on the qubits, either individually, or in combination.

While this requisite increase in data storage and simultaneous parallel calculation is obviously revolutionary, as well as being of tremendous interest to both hardware and software developers, it is ultimately not the aspect of quantum computers that could alter the fundamentals of computational science.

Quantum Algorithms and Possible Applications of the Quantum Computer

Quantum computers, operating tremendously differently from classical computers, will require their own algorithms. Quantum algorithms are perhaps the most powerful new aspect of quantum computing in general. Taking advantage of quantum superpositioning, where many terms can be contained in a single value, quantum computers introduce whole new methodologies to programming.

One key motivation for creating a quantum computer involves the subset of computer science known as cryptography, or the encryption and security of data. Many high security data encryption methods, such as computerized bank accounts, use what is known as factorization algorithms as part of their encryption method. These codes essentially require a machine to factor extremely large numbers, a mathematically daunting task, and in many cases, simply "impossible" on classical machines. The factorization of large numbers, such as say, 486,452 already takes classical computers a very long time to compute. Trying to factor a number with 40 digits would reach into the time-scale of centuries! Therein, of course, lays the security of the encoding method.

However, if a computer could be developed that is able to factor large numbers in a meaningful timeframe, then much of the highest security algorithms in use would be rendered vulnerable. This, compounded with the concept of the dramatically improved security of quantum algorithm encryption methods, is one of the driving forces behind quantum computer research.

Perhaps the most famous quantum algorithm to date is *Shor's Algorithm*. While somewhat complex in its actual formulation, Shor's Algorithm is capable of factoring large numbers N in polynomial time, as opposed to classical algorithms, which factor the same numbers in exponential time.

Another well-known algorithm is Grover's algorithm, which was developed in 1994. This quantum algorithm is essentially the quantum computer version of the basic sequential sort algorithm in classical computers. While classical machines can only guarantee finding a value via the sequential search method in a list after N operations, with N being the list length, Grover's quantum algorithm allows the target to be found in the list in $.758\sqrt{(N)}$ operations.

Even more interesting are the myriad of different coding methods and new programming languages that would undoubtedly be born were quantum computers to become a physical reality. For instance, quantum computers can be coded with somewhat more ambiguous statements than classical coding, where code can actually refer to values that technically don't exist in the code, but are buried in a qubit superposition somewhere in the program. The quantum computer could then, for instance, be told to "take the superposition of all previous values, and perform such and such operation on all that data" while causing only a single value to emerge and be reported. Code that is technically in superposition

† *technically this is not true. Via the use of what is known as a "quantum information processor" a small number of atoms can be controlled in such a way that quantum decoherence does not occur (the wave-function does not collapse), and thus the actual state of the system can be measured explicitly.*

while still available to be referenced and operated upon makes for extremely complex and diverse algorithmic possibilities for the quantum computer.

When can I buy a Quantum Computer?

It is important to realize that despite all of the theory and moderate amount of research being conducted on quantum computing, no quantum computer has ever been constructed. Estimates of time frame on the construction of a quantum computer range from very soon to never. There are some computer scientists who believe that there is simply no way to overcome the complex interactions that tend to disrupt the quantum parallelism phenomenon at the atomic level. As the number of qubits increases from the few that have been used in testing, the quantum interference will become very difficult to contain. In other words, as more and more qubits become involved, the computation invariably loses qubits (read: information) to the outside environment. This results in data loss, which is known as *decoherence*.

The current short-term objective of many researchers, in reference to the eventual construction of a quantum computer, focuses mainly on attempting to control atomic behavior at the level of atoms themselves, and photons.

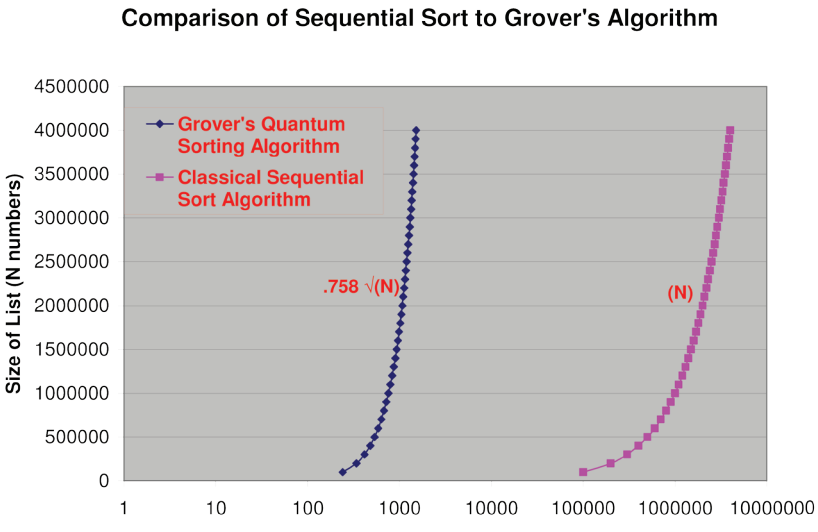
In any case, whether a quantum computer is ever built or not, the fundamental differences between quantum and classical computing must be understood and reconciled, such that quantum computers, if possible, can become integrated with classical machines.

The New Information Age

From the social and pure sciences to the government, military, and corporate regimes for which they were originally intended, the computer processor remains humanity's loyal assistant in our quest to both understand nature and improve our quality of life.

Given that quantum computing could change the entire way in which both software and hardware are produced, it is vital to first understand all the intricacies of both the theory and the proposed methods for constructing a quantum computer. While the interdisciplinary field of quantum information has received a deeply theoretical and conceptual treatment, relatively few experiments have been conducted, both due to the difficulty of such experiments, as well as the lack of private sector funding.

While it may yet be many decades before this computer becomes a physical reality, the use of quantum mechanics to solve problems at the macroscopic level could usher in an age where parcels of information as small as atoms are the reality. Computing will be based not only on our understanding of the atomic world, but our manipulation of it.



Graph created by Jonathan Mo.

This graph depicts the extreme difference in speed and efficiency between the classical sequential sorting algorithm, and the quantum-sorting algorithm. Note the extreme shift to the left (which means less operations are required to sort a given number of values) of the quantum algorithm.

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The Songbird and The City

by Andrea Appleton

A Blackpoll Warbler

Eric Slayton and Chad Seewagen arrive at the field site separately, each in his own car. They gather binders and cardboard boxes from their trunks and carry them to the laboratory at the bend in the road. Neither of them says good morning. The sound of voices would be jarring in the murky morning half-light and civility is for strangers.

They seem an unlikely pair. Eric has a watchful intensity and a narrow aquiline nose, like a hawk, his favorite bird. At 40 years old he wears his clothes with a casual slouch, a baseball cap hooding his eyes, the legs of his pants pooling a bit around the ankles. His straight brown hair is thick, sticking out from under his hat in unruly chunks. There is a small tattoo of a feather on his upper left arm.

Chad is 26, tall and clean-cut. He carries a cell phone to the field, and wears jeans and tennis shoes. He seems wholesome, with his broad shoulders and large hands, like he might be good at basketball. His short hair is a brilliant red, loud in the muted gray-green woods.

They are half-brothers, born of different fathers and almost a generation apart. Both are graduate students studying conservation biology and both have an abiding love for birds. Chad attends Columbia University and Eric Antioch College, and together they run the New York Bird Monitoring Program, sponsored by the Wildlife Conservation Society. I have asked to spend a few days with them at their field site on the grounds of the Bronx Zoo. Eric and Chad hope to determine if passing migratory songbirds are finding enough food in these woods - berries in fall and insects in spring - to fuel their journeys. *I* want to know how on earth they intend to find out.

We have driven down a crumbling asphalt road to get to this forgotten corner of Bronx Park. We are in a short stretch of forest where migratory songbirds descend to rest after a long night's flight. Many migratory birds travel hundreds of miles before stopping to rest, so they often arrive here depleted of energy.

Neotropical migrants, like those quietly settling in the trees around us, are in trouble. The North American Breeding Bird Survey, one of most respected studies of population changes in songbirds, lists almost a third of the Neotropical species they track as having declined in population since 1966. Concerned ornithologists have blamed habitat destruction in northern breeding grounds, and also in Central America, where many spend the winter. But along urban stretches of the East Coast, orphaned patches of metropolitan woodland are also vital to their survival, since they provide a place for birds to replenish their energy. Because forests are relatively rare in this stretch of their flight path, a kaleidoscopic variety of exhausted birds funnel into New York City parks during spring and fall migration. Yet Eric and Chad's is the only urban stopover ecology project to date along the entire Atlantic Flyway, the wide migratory highway that roughly follows the coast.

The laboratory consists of a folding table and two green camp chairs in the middle of the road. A scale in a cardboard box, a collection of aluminum identification leg bands sorted by size in film canisters, a binder, a toolbox, "The Sibley Guide to Birds," and

several short lengths of PVC pipe lie scattered on the table.

It is a gray dawn in early fall and the temperature is fickle, with currents of warm and cool air blowing like a lake turning over. We keep putting our jackets on and taking them off. An iron railing, listing and bent where the hillside has eroded away, separates the lab from the woods. The land drops off into thick woodland that descends to the banks of the Bronx River, visible in glints through the canopy. Behind us is a hillside bulging with boulders, spindly oak and maple gripping the soil where they can. In the surrounding woods twelve mist nets hang unfurled, not visible from the road and hardly so up close. They are delicate, gossamer things, about eight feet high by thirty-five feet long, with the bottom edges brushing the ground. One can see how a bird concentrating on foraging might fly right into one.

The field station. Eric holding bird and Chad sitting.

Much of the time in the field we spend waiting. The sense of expectation, the camp chairs, the radio, all evoke the tranquility of a fishing trip. Every once in a while we fan out to check the nets. Spiny sweetgum balls, acorn caps, and the first browned oak leaves crunch underfoot. Most of the mist nets, some now with the still dark lump of an entangled bird, are down near the river. From a distance, the trapped birds seem to be levitating in mid-air.

On one of these recon expeditions, Eric halts abruptly, swiveling his head to the right. "Pissh pissh." He forces air through his teeth, as if imitating the sound of someone peeing. We wait for something to happen. He tries again. "Pissh pissh."

Suddenly a soft chipping floats up from a nearby bush. "Butter butt," says Eric, nodding. He sees my blank expression. "It's what they call the yellow-rumped warbler." And he strides away; scuffed brown boots crunching off down the road.

We gather at the table to examine our catch. Four bulging, wriggling white cotton bags hang from a row of coat hooks on the railing. Eric loosens the drawstring on one. He reaches in the bag and removes a small brownish bird with a black-striped head and a brilliant yellow smudge in front of its eye. It is a white-throated sparrow, known for its song - "Old Sam Peabody" or "Oh Sweet Canada," depending on the translation. Unfortunately for us, this bird is not a long-distance migrant, but the brothers put it through their usual battery of tests. All the information they gather is entered into a national bird banding database, and may help in another project.

It is quiet here, by urban standards. The crickets are still chirping peacefully but the waking Cross-Bronx Expressway is a dim rising hum. Canadian geese honk as they fly past and a rooster does his roosterly duty at a house across the river. An aging radio on the table emits a tinny buzz just loud enough for us to make out "Hey Jude." An hour of Beatles classics is a Sunday morning ritual at the lab.

Eric holds the sparrow like a cigarette, head between middle finger and forefinger, wings restrained. The sparrow is docile as Eric chooses a band of the right size and clamps it on a leg with a pair of pliers. He gently fans out one of its rich brown wings. The feathers are edged in beige, forming two pale parallel bars. He hooks a small ruler over the shoulder and measures the wing, and then the tail. The bird blinks, for the first time since emerging from the bag.

"Wing seventy. Seventy-one."

Chad writes down the measurements in centimeters for wing and tail.

Eric sprays the sparrow's head with a water bottle, pushing the wet feathers up into a mohawk with one finger. He peers at the tiny scalp, blows on it to get a better look at the skull.

"AHY. Eye. Sex unknown."

AHY means After Hatch Year, an adult. The brown eyes of this sparrow have a subtle red tinge that a younger bird's wouldn't. After years of intimate study, Eric has something of an avian sixth sense. Depending on the bird, he may check the color of the inner beak, the amount of wear on the feathers, the pattern of the plumage, and the arrangement of the skull bones, since birds develop a second layer of cranial bone as they age.

A female Black-throated Blue Warbler

But white-throated sparrows are a motley crew, tough to categorize even by gender. And if you aren't sure, as in the sex of this specimen, you don't guess.

"Oh! It's missing a toe. Look. It's missing the hallux." Eric touches the pink nub where the hind toe used to be.

"Oh. Yeah." Chad raises his head briefly and returns to recording.

Dawn's arrival is subtle on this day, a gray washing off into white. The birds that have been wise enough to remain in the trees make only tentative chipping sounds. Despite their caution, as many as half of them won't make it back next year. To survive

migration, a bird must stay on course, dodge predators, avoid urban hazards like windows and cars, and ride out bad weather. Chad calls it "running the gauntlet."

Eric turns the sparrow over and blows on the furcular hollow, an area just above the wishbone and just below the throat where birds store fat. He exposes raw flesh, pink and dimpled. He puffs on the soft plumage under the wing, looking for the bristles of new feathers.

"Five fat. Zero. Two." Chad records the amount of fat stored and the degree of molting. Growing new feathers takes energy, energy otherwise needed for migration, so the molt score is an important variable. But the fat score, from zero to five, is crucial. With a "full tank" of fat, a bird has a much higher chance of living to see another stopover site. A human would have to gain nearly eight pounds a day to equal the percentage of fat put on by some of the long-distance migrants, like the vibrant Magnolia Warbler, bound for Central America.

For the brothers, the onset of winter means it is time to crunch numbers, of which there will be plenty. In the fall of 2004 they caught 400 birds of 45 different species, 25 species of Neotropical migrant. Their data from past field seasons so far suggests that visiting birds are indeed eating their fill, but another year's worth of data is still to come. Using an equation that compares average songbird flight speed (24 miles per hour), fat reserves, and rates of energy use, they found that most songbirds could probably fly some 370 miles on their Bronx fuel, or as far south as North Carolina, a warmer and wilder place.

But Neotropical songbirds are a diverse bunch. Different species migrate at different times during the season, as, sometimes, do males and females of the same species. Older, wiser birds also tend to crowd younger birds out of prime stopover habitat. And the current Bronx Park site is comparatively wild. Other city parks tend to be more landscaped, with plant species chosen to please the human eye rather than the songbird belly. Given such variables, it is too early to celebrate the brothers' preliminary results.

Eric and Chad have another year of fieldwork at Bronx Park left, for a total of three springs and three falls. Following their research here, they would like to cast their nets in other parks in the New York City area. They hope their research will help convince the Parks Department to manage parks as habitat for migratory birds, increasing the likelihood of migrant survival. They also seek volunteer participation by birders, who could help them by reporting sightings of banded birds in their study area. Such reports help the scientists determine how long the birds tend to linger in the site.

Eric suddenly turns the sparrow upside-down and pops it into a short length of PVC pipe that sits on the scale. The scale is inside a cardboard box, so a gust of wind will not destabilize the reading on the sensitive machine.

The tail feathers fan out the top of the pipe like a dried flower arrangement. We wait for the numbers on the scale to settle.

Weather and time have left their mark all around us, buckling the asphalt, warping the hard iron railings. Still, it's only a short walk to nature at her most impeccably groomed, the Bronx Zoo. The nearest exhibit is The World of Birds. Visitors pay to see the exotic toucans and birds of paradise, sunbitterns and carmine bee-eaters. And yet in the unkempt forest beyond the cages, dozens of songbird species routinely stream through on their flight to the tropics. American redstarts, wood thrushes and ovenbirds all pause here, as do less far-flung visitors like our sparrow.

Chad doing breath sampling.

Chad records the bird's weight and then slides it out of the pipe headfirst into his hand. Its final test looks something like dollhouse CPR. Chad places the bird's beak into a small tube attached to a party balloon. The tube is connected to a tank of pure oxygen. The sparrow's round eyes blink. The balloon barely moves, in and out with tiny inhalations and exhalations.

The bird breath samples are stored in vacuum-sealed vials and sent to a lab for carbon isotope analysis. This new technique should confirm if the bird is burning precious fat reserves when it should be burning berries. The test may even reveal its diet, distinguishing between the fruits of the Virginia creeper, the northern arrowwood, and the black cherry. Some birds leave more tangible evidence: pokeberry-purple poop on the cotton bags.

"The oxygen must give them a little rush, which is probably good," says Chad. He opens his hand and the sparrow darts off towards the river through the understory. "Sends them on their way refreshed."

Eric holding a black-throated blue warbler

Centennial Professor Koji Nakanishi

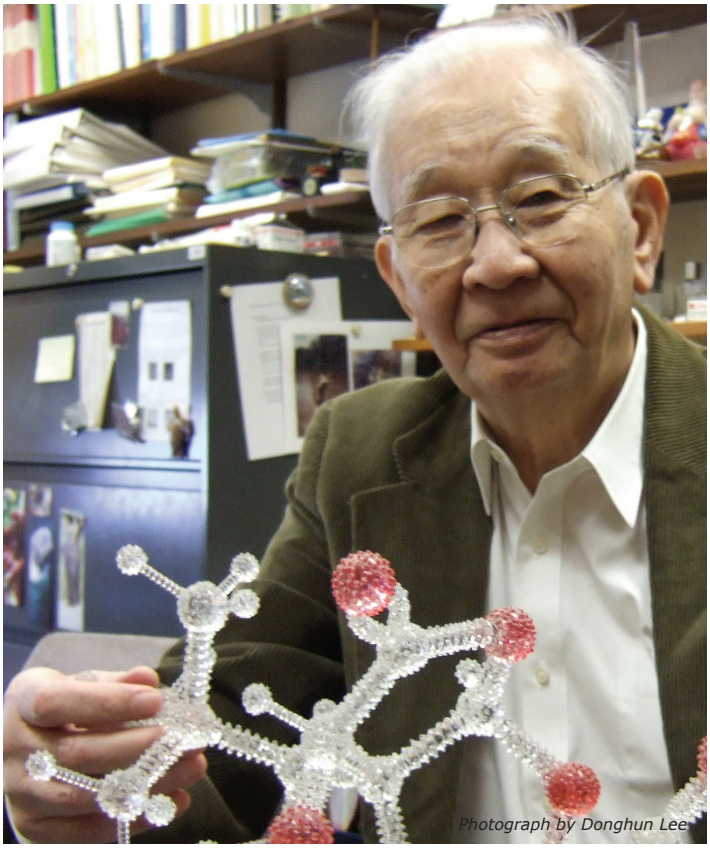
Faculty Profile

by Jean Li

Though it may seem as though natural products chemistry has little impact on your daily life, with the wave of a magician's wand, you can surely conjure up a mental image of the copious bottles of *Ginkgo biloba* often passed by at grocery and nutrition stores across Manhattan. What you may not know is that the isolation and characterization of the extracts from the ginkgo biloba tree spawned a world of unique and elegant chemistry, aimed at understanding and using the potential latent in nature. Central to this investigation is an amateur magician and young at heart Columbia professor, Koji Nakanishi.

Born on May 11, 1925 in Hong Kong, Nakanishi is truly a man of the world. He was raised in Lyon, London and Alexandria, before his parents returned to Osaka, Japan. Following the achievement of his bachelor's degree in Chemistry, he was chosen as one of the first Japanese students to do post-graduate work in the United States at Harvard. At that time, Harvard was a well-spring of organic chemistry, housing such greats as Robert B. Woodward and Columbia's own Gilbert Stork. Professor Nakanishi's time spent in the US was seminal to his 1969 decision to move his lab from Tohoku University. Fate had a hand in his move; fate and a misunderstanding on the part of a Columbia administrative assistant. Manchester University in England, upon the retirement of Arthur Birch, made him his first job offer, and Columbia followed suit. Amidst repeated telephone calls from Professors Breslow and Stork, Professor Nakanishi told Columbia administration that he would make a decision after paying one more visit. This was accidentally interpreted as an acceptance, and as Breslow and Stork telephoned, delighted, Professor Nakanishi decided to go with a decision that, in part, had already been made for him!

Any foray into the complex world of natural products chemistry begins with the isolation of a compound, which Nakanishi calls "the most challenging step." Then, a natural products chemist attempts to determine the structure of the compound as well as its role in physiological and pathological cascades. As one of the foremost natural products chemists in the world, it should come as no surprise that Professor Nakanishi has become quite proficient at both steps in this process. In fact, during the course of his career, Professor Nakanishi has isolated and investigated over 200 biologically active natural products. Also, to aid in his structural determination studies of newly discovered compounds, Professor Nakanishi has had a hand in developing widely applicable spectroscopic tools such as the Nuclear Overhauser Effect (NOE) in Nuclear Magnetic Resonance (NMR), first observed and applied during Nakanishi's ginkgolide studies in 1967. Professor Nakanishi also deserves credit for his significant contributions to the chemical understanding of chirality; in the late 1960s with graduate student Nobuyuki Harada, he developed the exciton-coupled circular dichroic method, a most versatile and nonempirical micromethod for determining the absolute configuration of complex molecules. The studies along this line is actively being continued at Columbia University under Dr. Nina Berova, a leading expert in chiroptical spectroscopy.



Professor Koji Nakanishi with a Ginkgolide model.

In his quest to find novel compounds of physiological interest, Nakanishi has traveled the globe and back again. Professor Nakanishi has served as both the director of the chemistry unit at Biosphere 2 in Arizona as well as one of the six directors at the International Centre of Insect Physiology and Ecology in Kenya. In the end, no matter how far he travels in his quest for science, Nakanishi is proud to call Columbia his home.

At any given moment, Professor Nakanishi can be seen striding with determination down the halls of Havemeyer, an ever-present figure at the departmental colloquia and a rigorous advisor to his group. With a dozen postdoctoral students spread over three major platforms, the Nakanishi lab can only be seen as a sheer force of chemistry, driven by Nakanishi himself. When asked to describe his motivation, he ascribes it to "a broad overall interest in science," citing also a fascination for "biology and life-related issues that can be solved by imaginative chemistry."

As for his advice to young, up and coming researchers, Nakanishi has two pearls of wisdom. The first is to be multidisciplinary and interdisciplinary but also "nondisciplinary." It is perhaps, a paradigm set by Nakanishi himself, as his research has wandered across all of bioorganic chemistry, from the seminal work on ginkgolides to research in the mechanism of vision. In true Nakanishi-fashion, his second piece of advice is to "work as hard as possible when you are young and have the energy because if you work hard when young, it helps in maintaining your momentum when you get older." One must then wonder if Professor Nakanishi accidentally stumbled upon a secret youth serum amidst his studies of shark repellants and crustacean molt inhibitors because at 80, his momentum has yet to slow.

Drugging the Chaperone

Scientists Investigate a New Approach to Treating Cancer

by Jakob von Moltke

In December of 1971, congress passed the National Cancer Act, ushering in America's 'war' on cancer amid great optimism that science would soon conquer this horrible disease. Thirty-four years later, despite enormous strides in our understanding of cancer, the exponential growth of research in molecular biology, and the development of high-tech diagnostics and treatments, few cures exist, especially for malignant tumors. Current therapies either target fundamental cellular processes, in an attempt to eliminate cancer cells before endangering the patient's life, or target mutations associated with specific cancers.

Recently, a novel and exciting therapeutic approach representing a hybrid of traditional chemotherapies and target-based therapies has entered the clinical pipeline. Inhibitors designed to disrupt the protective role of heat shock protein 90 (HSP90) target the molecular guardian of numerous mutated proteins associated with cancer. By disrupting just this one protein, scientists hope to inhibit the lifecycles of many cancerous cell types. The natural affinity of HSP90 inhibitors for cancer cells suggests that this approach may represent a viable human therapy.

Cellular Chaperones & Cancer

Inside every cell of the body there is a special set of proteins that serves as a cellular guardian, protecting and guiding the other proteins of the cell. Such proteins are aptly named chaperones, and the proteins that they guide are known as their clients. Chaperone proteins protect the cell from both intra- and extracellular stressors by helping their client proteins to fold correctly, travel through the cell, bind other proteins, and turn on or off. Within the cell, chaperones stabilize mutations that give rise to proteins with altered amino acid sequences. These mutated proteins would likely be dysfunctional without chaperones, which have a tolerance for slight alterations and assure that proper folding, translocation, and binding continue to occur. The function of the cell therefore remains stable despite underlying mutations, defining chaperones as a kind of mutational buffer[1].

Chaperones protect the cell from external stressors, particularly environmental extremes such as heat, the presence of toxins, or low nutrient levels. In order to function properly, proteins must maintain a precise three-dimensional shape. Environmental stressors frequently alter the shape of proteins, rendering them inactive, while at the same time new proteins are produced to deal with the changing environment. Cells experiencing environmental stress express higher levels of chaperone proteins, which in turn maintain stability by refolding inactive proteins and ushering new proteins through development.

The protective role of chaperone proteins makes them particularly critical for the stability and survival of cancer cells. The extracellular environment of cancer cells is often unusually harsh as the body mounts an immune attack; additionally, their rapid growth outpaces nutrient and oxygen supplies. Cancer cells also carry a wide range of genetic mutations and must survive despite altered protein function. In fact, these underlying genetic mutations and the unique abilities they confer distinguish cancer cells from normal cells in the body. Scientists have identified eight such distinct abilities.

In a landmark paper, biochemists Hanahan and Weinberg defined six characteristics that a normal cell must acquire to become an invasive cancer cell:

(1) The ability to grow without signals from other cells,
(2) Ignore anti-growth signals from other cells,
(3) Avoid the normal cellular self-destruct mechanism known as apoptosis,
(4) Divide and replicate without limit
(5) Promote growth of nearby blood vessels that supply nutrients, and
(6) Move around the body and invade other tissues[2].

Cancer cells are additionally characterized by an abnormally high rate of genetic mutation and usually gain the ability to evade the body's natural immune attack.

Clearly, any cells carrying these characteristics are incredibly difficult to destroy, grow rapidly, spread throughout the body, and pose great danger to a patient.

These features all originate from mutations in the cellular DNA and, although cancer cells are almost never genetically identical, the mutations tend to occur in a specific set of genes defined as oncogenes and tumor suppressor genes. Scientists are constantly identifying new oncogenes or tumor suppressor genes associated with cancer and a list of cancer markers is rapidly emerging. Remarkably, an enormous number of those genes identified as cancer-causing oncogenes or tumor suppressor genes are also among the clients of a single chaperone protein known as heat shock protein 90 (HSP90)[3]. Table 1 demonstrates how HSP90 chaperones oncogenes and tumor-supressors are associated with every one of the eight characteristics described for invasive cancer cells. While novel cancer therapies inhibit just one mutated protein, HSP90, being the chaperone for so many cancer genes, represents a single target with broad-acting potential. Regardless of which particular subset of HSP90 clients carry mutations, nearly all cancer cells rely partly on HSP90 to maintain cellular stability; disrupting HSP90 can kill or at least weaken these cells.

Drugging the Chaperone

Scientists actually discovered the dependence of cancer cells on HSP90 unknowingly long before the interaction between

HSP90 and cancer genes was revealed. In 1980 Japanese researcher Kazuya Sasaki discovered that he could block growth in tumor cell cultures with 90% efficiency by bathing the cells in geldanamycin, a naturally occurring compound previously known for its anti-fungal properties[4]. Since Sasaki's early experiments, scientists have discovered that geldanamycin does, in fact, bind HSP90 and prevent its normal chaperoning function.

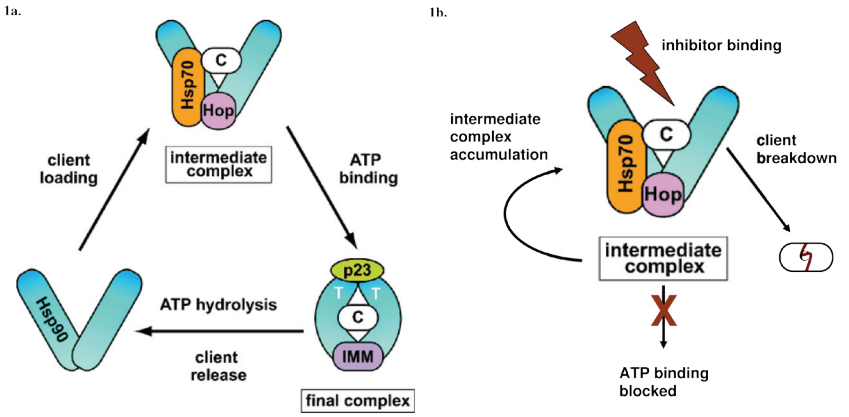
HSP90 chaperoning occurs in a cyclic pattern, binding and releasing client proteins as chaperoning becomes necessary (Figure 1a). The cycle begins when HSP90 binds various accessory proteins and the client protein to form an intermediate complex. In the next step, adenosine tri-phosphate (ATP) binds to the intermediate complex and recruits an additional protein, forming a molecular clamp around the client protein to facilitate chaperoning. After chaperoning, the clamp releases the client, and the multi-protein complex dissociates[5]. This ATP-dependent cycle is typical of chaperone proteins, and is disrupted by blocking ATP binding. Geldanamycin, its molecular derivatives, and another naturally occurring compound called radicicol all bind to the ATP binding site in HSP90 with much higher affinity than ATP itself[1]. With ATP binding blocked, the intermediate HSP90/client complex cannot form the molecular clamp around its client proteins to complete normal chaperoning (Figure 1b.). The intermediate HSP90/client complex accumulates in the cell, where it either disrupts normal cellular functions or is degraded[6]. As in Sasaki's early experiments, HSP90 inhibition has been shown to stop cellular growth and even to promote cellular self-destruction, particularly in cancer cells[7, 8].

Life Without Chaperones

Although the anti-cancer effects of HSP90 inhibitors in the laboratory are remarkable, their use as human cancer therapies raises significant concerns. HSP90 is present and active in all cells of the body and is crucial for survival. Mouse embryos without the HSP90 gene never survive[1]. Blocking HSP90 chaperoning therefore presents the risk of undesirable side effects in healthy cells. Remarkably, however, research has shown that HSP90 inhibitors naturally have a far greater affinity for tumor cells than healthy cells, clustering around the cancerous cells both in tissue cultures and live mice. Scientists believe that this affinity derives from the accumulation of HSP90/client protein complexes in cancer cells. The mutated HSP90 client proteins expressed abundantly in cancer cells place an increased demand on the chaperone cycle, increasing cellular levels of the multi-protein chaperone/client complexes compared to healthy cells. HSP90 inhibitors have a 100 times greater binding affinity for the HSP90/client protein complex than for uncomplexed HSP90 protein, driving the observed accumulation around tumor cells[9].

Also of concern, is the risk of disrupting other ATP binding interactions. ATP is the primary energy source of the body and ATP/protein binding interactions are crucial and abundant. Careful analysis of the ATP binding site in HSP90 has revealed, however, that it has an unusual shape known as a Bergerat fold. Few known proteins use a Bergerat fold to bind ATP, suggesting that HSP90 inhibitors that bind this site will enter into equally few side reactions[10].

Lastly, an emerging theory about the role of HSP90 and other chaperone proteins in evolution may also have implications for the use of HSP90 as an anti-cancer therapy. Scientists have suggested that the capacity of chaperone proteins to stabilize genetic mutations may allow small changes in the cellular DNA to accumulate over time with little or no change in the cell's function. Under particularly extreme environmental stress, however, the chaperones cannot keep pace with the number of client proteins requiring chaperoning. In effect, the mutational buffer of chaperone proteins is overwhelmed, allowing previously "dormant" mutations to give rise to new cellular functions. Scientists hypothesize that this expression could result either from altered chaperone/client interactions or by bypassing the chaperone entirely. In most cells, expression of these mutations will lead to weakening or even death, but in some cells a mutation may arise that confers an advantage for cellular survival in the changing environmental conditions, leading to evolution through processes of natural selection. This theory has exciting implications for the study of evolution, as it may explain the rapid evolutionary leaps observed in fossil records, but in the clinic it could promote undesirable side effects. If the HSP90 inhibitors mimic extreme environmental stress they may allow the cancer cells to express previously dormant mutations, of which cancer cells have many, that may yield drug resistant or more invasive cancer strains[1].



Figures adapted and modified from Teresawa et al. by permission of Oxford University Press.

Figure 1: HSP90 Chaperone Cycle & Its Inhibition
a. Normal client chaperoning by HSP90 proceeds in a cyclic manner. HSP90 and accessory proteins form a multi-protein complex that binds the client protein. ATP binding recruits an additional protein to form a molecular clamp around the client and facilitate chaperoning. ATP release opens the clamp and the proteins dissociate.
b. HSP90 inhibitors, such as geldanamycin, 17AAG, and DMAG, bind the multi-protein complex and block ATP binding. The chaperoning cycle stalls, leading to accumulation of the multi-protein complex and eventual breakdown and removal of client proteins.

	Sources: [1-3, 13, 14]	Cancer Characteristic							
		Growing without other cell signals	Evading cell death	Ignoring anti-growth signals	Invading other tissues	Replicating without limit	Promoting blood vessel growth	Rapid DNA mutation	Evading immune attack
HSP90 Client Protein	Akt		X	X					
	CDK2			X		X			
	CDK4			X		X			
	HIF1a						X		
	MEK	X							
	MMP2				X				
	p53							X	
	RTK		X	X					
	SRC tyrosine kinases	X		X					
	Steroid horm. recept.	X		X					
	Survivin		X						X
	Telomerase					X			
	VEGFR2						X		

Table 1: HSP90 & Cancer. The current list of known HSP90 clients includes proteins associated with each of eight characteristics commonly found in lethal cancer cell populations. Continuing research of HSP90 clients and the cancer genome will likely illuminate more linkages, as well as provide insight into the underlying mechanisms of these interactions.

Clinical Trials and Beyond

Clinical trials of HSP90 inhibitors are now underway to test the theoretical promise of this novel therapeutic approach. Pre-clinical studies revealed that when naturally occurring geldanamycin is metabolized in the human liver it yields potentially toxic molecules, so scientists designed two chemical geldanamycin derivates with improved toxicology and higher HSP90 binding affinity. The two derivatives, 17-allylamino-1-demethoxygeldanamycin (17AAG) and 17-(demthoxy),17-dimethylaminoethylamino geldanamycin (DMAG), are both in clinical trials.

In order to gain FDA approval, novel drugs must pass through four general stages to prove efficacy and safety as a human therapy. The first testing phase is pre-clinical trials, followed by phase I-III trials. The entire process takes many years to complete. DMAG currently remains in pre-clinical and phase I trials, but 17AAG has advanced to numerous phase II trials[11].

Because it remains unclear whether HSP90 inhibition kills cancer cells or simply weakens them, 17AAG is being tested both as a standalone therapy and in combination with traditional chemotherapies. The trials span more than ten kinds of cancer, including breast, prostate, and skin cancers, as well as non-specific solid tumors. This range of trials highlights the potentially broad applicability of HSP90 in the treatment of cancer[11]. To date, the results from clinical trials are promising and in line with expectations, however it remains far too early to make meaningful predictions[12].

While clinical trials continue, additional scientific research into and development of HSP90 and its inhibitors remain equally important. Scientists must clarify the effect of HSP90 inhibition on the cancer cell cycle to determine if treatment kills the cancer cells or simply keeps them from growing. Inducing complete cancer cell death may require clinically toxic doses of HSP90 inhibitor, in which case HSP90 inhibitors should be developed as combination therapies, weakening the cancer cells before other treatments induce cell death.

Research should also continue to pursue better HSP90 inhibitors. Chemists and biologists can use both predictive modeling techniques and high-throughput screens to identify molecules that inhibit HSP90 at lower doses and have fewer toxicological side effects in humans.

Parallel to the HSP90 inhibitor research, scientists also continue to identify additional HSP90 client proteins and to further illuminate the mutations associated with various cancer types. As these two lists grow, it will be important to look for synergies to identify cancer types associated with the most HSP90 clients, suggesting a greater reliance on HSP90 chaperoning. Improved genetic sequencing and analysis techniques may one day allow doctors to identify cancer cell mutations in HSP90 client proteins on a patient by patient basis, so the most effective treatment plan with the fewest side effects can be selected.

If the dependence of cancer cells on HSP90 demonstrated in the laboratory bears out in the clinic, the potential for novel cancer therapies is tremendous. HSP90 inhibitors represent an exciting alternative to current cancer therapies, combining the selective inhibition of targeted therapies with the potential to treat many different cancers.

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Dr. Jack McGourty

Faculty Profile

by Melody Chou & Christopher O'Conor


Photo Courtesy of Dr. Jack McGourty

SEAS freshmen remember him from his early morning Gateway lectures. Many students in the College, Barnard and General Studies have experienced the engaging yet relaxed style of one of his required science courses. The administration at Columbia has undoubtedly witnessed his contributions to the University's academic landscape. Whether you know him as Professor, Doctor, Dean, or just Jack, he is the same man that so many have come to know and admire: Dr. Jack McGourty.

Dr. McGourty plays many simultaneous roles here at Columbia University. His contributions in the classroom are paralleled by his influences on campus, which are duly matched by his dedication to the entire New York community and beyond. Today, he has become a household name of sorts, renowned among students, faculty, and New York City residents alike.

Eight years ago, Dr. McGourty came to Columbia with a vision – a vision to change the face of Columbia's approach to science, integrating other disciplines and ideals into the engineering curriculum. He strived to establish an innovative approach to the field of engineering and science, and he achieved such an ideal almost immediately. Through the addition of a service component to the Gateway course, students are required to not only engage in, but also to contribute to the surrounding community outside of the 116th street gates. From the very start of their careers as Columbia University students, SEAS freshmen are able to acquire a sense for the world of engineering, but most importantly, the applications of their talents to the world at large. One group of students, in the spring semester of 2005, was given the task of designing and modifying playground equipment for disabled children at a local city school, PS 79. With this project, students worked with the New York Parks and Recreation Department and were able to engage with the community through their engineering efforts. It is clear that Gateway both enriches the community in which Columbia resides as well as the students that have traveled here to learn, which proves to be the crux of its innovation. Dr. McGourty valiantly defends his goal to develop students' sense of responsibility to their community:" [I initially tried] to figure out the best way to teach design and to develop this sense for 'service learning' in students." His method was to "teach by doing," marrying technology and community awareness with his radical efforts. This course alone has revolutionized the stance on engineering curriculum, but Dr. McGourty did not end his vision there.

In recent semesters, Dr. McGourty expanded his impact and introduced new courses not only geared towards engineers, but also towards the rest of the University. Science, Technology, and Society (STS), a course actively endorsed by the SEAS Dean Zvi Galil, was designed by Dr. McGourty to heighten the awareness of this intricate interplay that technology and science have with culture, ethics, economics, and many other topics. Combining students from General Studies, Columbia College, and SEAS, the class of around 300 students is teeming with knowledge and points of view from every imaginable perspective, an attribute of which Dr. Gourty takes full advantage. In this way, the entire class is able to see the complete contextual landscape of the issue at hand. When David Packman, the CEO of eMusic.com, was brought in as a guest speaker to discuss digital rights management and media distribution in the fall of 2005, the class was alive and engaged with viewpoints from musicians, engineers, psychologists, and historians, making for a controversial discussion typical of STS lectures – a type of discussion unprecedented by any other course at Columbia.

Most recently, Dr. McGourty advocated for and founded a Center for Technology, Innovation, and Community Engagement, representing "one way to institutionalize the philosophy." It is a research, development, and training organization devoted to promoting and expanding technology-based community service learning initiatives here at Columbia. It is an institutional center for service learning programs, which, thanks to Dr. McGourty, encourages students and teachers out of the classroom and into the local community. This program is geared not only towards the Columbia community, but also toward the surrounding residents of

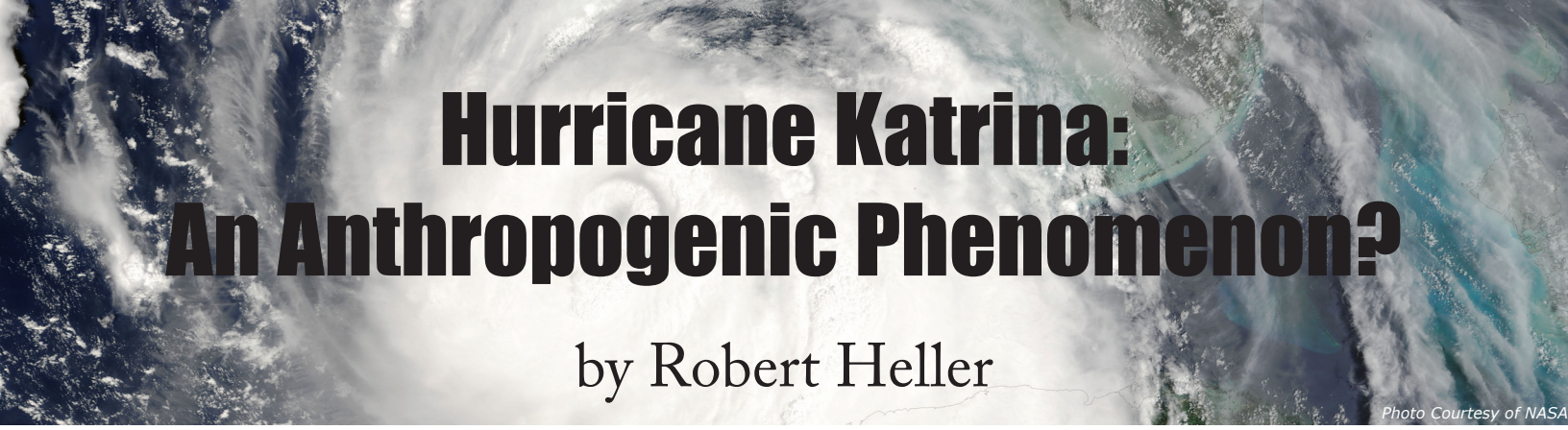
New York City. This particular initiative brings in residents from the city to work in the University's state-of-the-art Botwinick Gateway Laboratory, learning advanced computer skills and actively participating in the improvement of their community. This program has proven extremely successful, uniting the residential community with the academic community.

His contributions do not stop there. Dr. McGourty also hopes to eventually create a concentration or minor in the area of "Science, Technology, and Society" in both Columbia College and SEAS. He hopes that by taking faculty from various departments such as sociology, psychology, economics, history, and engineering, and forming a separate interdisciplinary department that focuses on service learning and the applications of technology in society, more focus and success can be derived from the socially-conscious scientist. Envision a department that can both harness the leading research and knowledge of the distinguished scientists and engineers and apply it to urban environments, developing countries, and other underserved communities. To date, there is an Interschool Advisory Committee that was solidified in the past year, which marries the various disciplines under the "STS" category.

Gateway served a purpose that was interestingly related to its name: catalyzing the growth of service learning in science. It was the general successes in Gateway Lab that laid a solid foundation for Dr. McGourty's vision of integrating service learning into other areas. What began as an idea to "set the tone for technological education " has certainly bloomed into a growing success that is changing the face of engineering today. While Dr. McGourty's endeavor of developing "contextually-sensitive technology leaders" in the SEAS education has been acknowledged, his reach will be felt beyond the walls of the engineering centers more and more in the years to come.

In the words of Dr. McGourty, "Our education would be remiss if we didn't focus on the process of scientific discovery as well as its social consequences." The University's noble mission will certainly be well-served as his influence and infectious passion spread to all regions of academia.

In-Class Photograph from Science, Technology, and Society



Hurricane Katrina: An Anthropogenic Phenomenon?

by Robert Heller

Photo Courtesy of NASA

On Monday August 29, Hurricane Katrina ravaged New Orleans, Louisiana and Mississippi, leaving a trail of destruction in her wake. It will be some time until the full toll of this hurricane can be assessed, but the devastating human and environmental impacts are already obvious.

Katrina was the most feared of all meteorological events, a major hurricane making landfall in a highly populated, low-lying region. In the wake of this devastation and the unprecedented ferocity of the 2005 hurricane season, many are questioning their previous notions regarding global warming. Could New Orleans be the first major U.S. city ravaged by human-caused climate change?

During the 2005 Atlantic hurricane season, a record twenty-seven tropical storms formed, of which a record fifteen became hurricanes. Of these, seven strengthened into major hurricanes, while a record-tying five became Category 4 hurricanes and a record three reached Category 5 strength, the highest categorization for hurricanes. Among these Category 5 storms was Hurricane Wilma, the most intense hurricane ever recorded in the Atlantic.[a]

Compare this to an average Atlantic hurricane season of ten tropical storms, six becoming hurricanes, and only about 2.5 reaching Category 3 or higher.[b] But could global warming in truth have had anything to do with this?

It is perhaps first most important to describe the phenomena of anthropogenic global warming. Fossil fuels such as gasoline, methane and propane contain mostly carbon. When these fuels are burned, they react with oxygen and produce carbon dioxide, along with energy in the form of heat for us to utilize.

Because of our heavy use of fossil fuels, the amount of carbon dioxide in the atmosphere has been increasing since the Industrial Revolution (see figure 1). The destruction of forests, which convert CO_2 to oxygen, also contributes to the overall increase in carbon dioxide.

How can increasing concentrations of carbon dioxide cause global warming, one might ask? The answer is fairly straightforward. Most solar radiation is emitted from the sun to the earth in wavelengths shorter than 3,000 nanometers, corresponding to the ultraviolet, visible, and reflected infrared bands of the electromagnetic spectrum. The heat energy radiated from the earth, however, is released in thermal infrared wavelengths longer than 3,000 nanometers.[c] Carbon dioxide doesn't absorb incoming radiation from the sun, but it does absorb some of the radiation released from the earth at longer wavelengths. When a molecule of carbon dioxide absorbs heat energy, it goes into an excited unstable state. It can become stable again by releasing the energy it absorbed. Some of the released energy will go back to the earth and some will go out into space. So in effect, carbon dioxide lets the light energy in, but doesn't let all of the heat energy out, similar to how greenhouses work.

It is important to note that carbon dioxide is not the only greenhouse gas. There are numerous others that work by the same mechanism, such as water vapor, methane, nitrous oxide, sulfur hexafluoride, and chlorofluorocarbons. One quickly notices that with the exception of water vapor, these are all gases which would not occur naturally in the atmosphere except in very small concentrations (or in some cases, such as CFCs, not at all) relative to what they are now. Carbon dioxide is the most significant greenhouse gas (although methane is quite considerable as well) in the context of global warming because its atmospheric concentration is increasing to a much higher magnitude than most of the others.

Currently, the amount of carbon dioxide in the atmosphere is increasing at the rate of about one part per million per year.[d] Carbon dioxide has a variable atmospheric lifetime, defined as the amount of time a molecule resides in the atmosphere before returning to the earth, of about 200-450 years.[e] We are disrupting the equilibrium between atmospheric and terrestrial carbon dioxide by emitting it into the atmosphere faster than the earth's cycle can handle. The result is a near exponential increase in the atmospheric carbon dioxide concentration, as shown in figure 1.

Skeptics pause here and say, "OK, so the concentration of carbon dioxide is increasing, and in theory that could cause a greenhouse effect and warm the atmosphere. But we are not observing drastic temperature changes, and isn't it also true that the earth has naturally varying temperature cycles?"

And thus the debate begins. It is true that the earth undergoes natural warming and cooling cycles. This is well understood, as is the fact that small-scale cycles of about 40 years exist within larger-scale cycles of 400 years, which in turn exist inside still larger scale cycles of 20,000 years, and so on.[f] But it is becoming increasingly more agreed upon within the scientific community that the warming trends we are currently witnessing seem to fall outside the realm of what is natural.

The opinion expressed by the UN Intergovernmental Panel on Climate Change (IPCC) and explicitly endorsed by the national science academies of the G8 nations, is that the average global temperature has risen 0.6 ± 0.2 °C since the late 19th century, and that it is likely that "most of the warming observed over the last 50 years is attributable to human activities."[g]

Skeptics find here yet another place to pause and ask, "What's with all the fuss over a slightly warmer environment?" The possible retributions are severe and abundant. A few examples include sea level rise, impacts on agriculture, reductions in the ozone

layer, spread of disease, and increased intensity and frequency of extreme weather events. The latter is regarded as many as being already well underway.

Kerry Emanuel is a leading professor in meteorology currently working at MIT in Boston. His work in atmospheric dynamics is well regarded among the meteorological community. In particular, he has specialized in atmospheric convection and the mechanisms acting to intensify hurricanes. Emanuel published his first paper on "The dependence of hurricane intensity on climate" in 1987, and he has continued to pursue the topic since. His latest paper, "Increasing destructiveness of tropical cyclones over the past 30 years," was published in the August 2005 edition of *Nature*. The article discusses his theory on how elevations in SST (Sea Surface Temperature) can, and have caused an increase in hurricane intensities.

Emanuel begins the article by explaining a mathematical expression one can use to evaluate the destructiveness of a hurricane. He proposed in a 1998 publication a means for measuring the power dissipated of a storm as:

$$PD = 2\pi \int\int C_D \rho |V|^3 \, r dr dt$$

where C_D is the surface drag coefficient, ρ is the surface air density, $|V|$ is the magnitude of the surface wind, and the integral is evaluated over the radius of the storm and the lifetime of the storm. The PD has units of energy, coinciding with intuition. As one might presume, this is a difficult equation to evaluate even with modern storm data, and impossible to evaluate from historical data which rarely contain records of storm dimensions.[h]

Emanuel contends that one can easily simplify this expression by employing two techniques. First, one can approximate the surface air density and the surface drag coefficient as constants. Then, by recognizing the detailed studies which show that peak wind speeds exhibit little if any correlation with measures of storm dimensions, one can ignore storm dimensions by looking at peak wind speed. He defines a power dissipation index (PDI) as:

$$PDI \equiv \int V^3_{max} \, dt$$

Where V_{max} is the maximum sustained wind speed at the conventional measurement altitude of 10m, and the integral is evaluated with respect to time.[8]

Emanuel employed his expression for PDI to storm data from the past 75 years to obtain a value for total power dissipated annually. He then contrasted the curve describing variations in PDI to the curve describing changes in annually averaged SST over the same period (separated into defined hurricane regions). The results he obtained are very convincing. For example, in the North Atlantic (figure 2) there seems to be clear relationship between the two time series ($r^2 = 0.65$), suggesting that SST exerts a strong control on PDI in this region. One sees that over the last 30 years, the total hurricane power dissipation has more than doubled. This result was not confined to the North Atlantic region, but rather followed suit in several of the regions Emanuel investigated.[8]

Emanuel's findings have caused quite a stir within the scientific community. Emanuel attributes this to the "signal [he] found being unexpectedly strong, and the paper being published in the midst of a devastating hurricane season." He also comments that "meteorology has long been susceptible to received wisdom, and my paper went against that."[i]

As is often the case in science, his findings were stumbled upon while he was in pursuit of something else. He was researching a pet theory of his regarding the role of hurricanes in thermohaline circulation. It was during his research for this that he developed his PDI expression, and noticed the remarkable upward trend over the last 30 years. While Emanuel inadvertently noticed this groundbreaking trend in hurricane intensities, two other researchers had already suspected and were in direct pursuit of it.

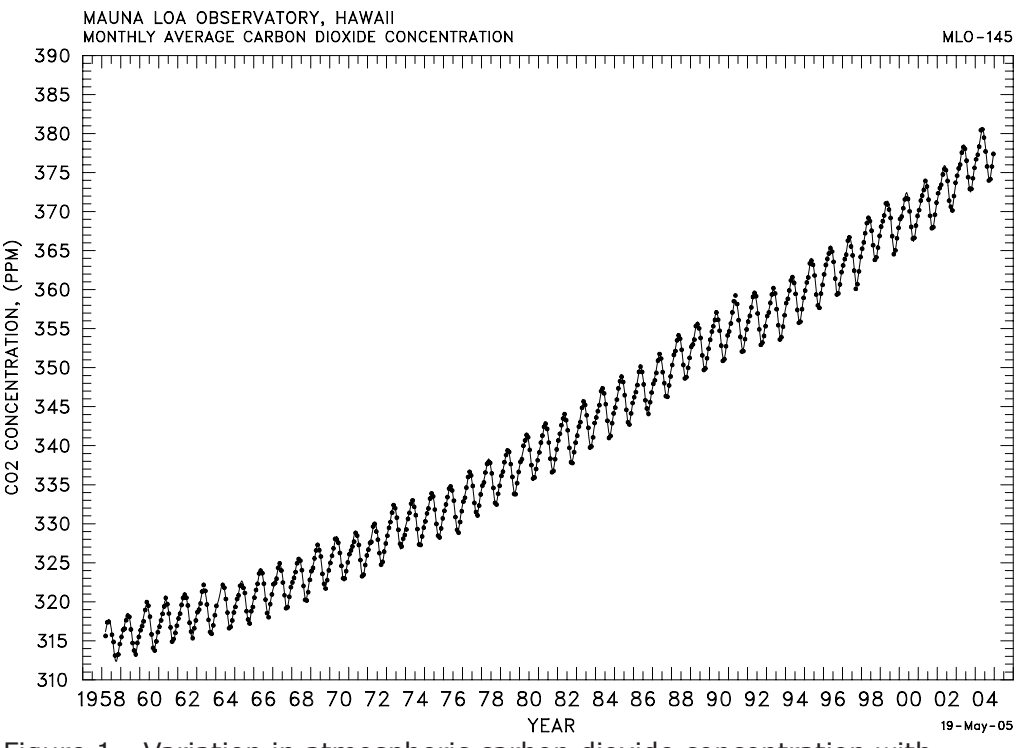


Figure 1 - Variation in atmospheric carbon dioxide concentration with time. (Courtesy of Carbon Dioxide Information Analysis Center, Oak Ridge National Laboratory, U.S. Department of Energy)

Peter Webster at the Georgia Institute of Technology and Greg Holland of the National Center for Atmospheric Research have both devoted a great amount of research toward investigating the same phenomena as Emanuel. The two took a more direct approach, gathering data from tropical cyclones all over the world since 1970, when reliable satellite weather data first became available. They found that the frequency of intense category 4 or 5 storms has nearly doubled. Their research was published in the journal *Science* just two weeks after Katrina hit. "The end result is basically the same" as Emanuel's, says Holland. The two separate studies yielding essentially the same conclusion reinforce one other. "Our analysis indicates global warming has already increased the likelihood of storms like Katrina happening," says Holland, "although

we can't say it caused Katrina itself."[j]

Based on estimates by NASA's Goddard Institute for Space Studies located at Columbia University, 2005 was the warmest year since reliable wide-spread instrumental measurements became available in the late 1800s.[k] The dangers poised by such warmth are very nearly unanimously agreed upon within the scientific community. Emanuel himself notes that it is his opinion, and most other experts in the field, that "the evidence is quite strong that the upward trend over the last 25 years is largely anthropogenic."[9]

With so many experts from all over the world agreeing upon the reality of anthropogenic global warming, one might ask why the topic is portrayed in the media as a matter of a two-sided debate. As it turns out, global warming is indeed the center of a fierce debate, essentially between science and politics. George W. Bush has taken the stance that the cost of mitigating global warming is too large to take action, and that has indeed been the position of the US when it comes to any policy action regarding global warming.

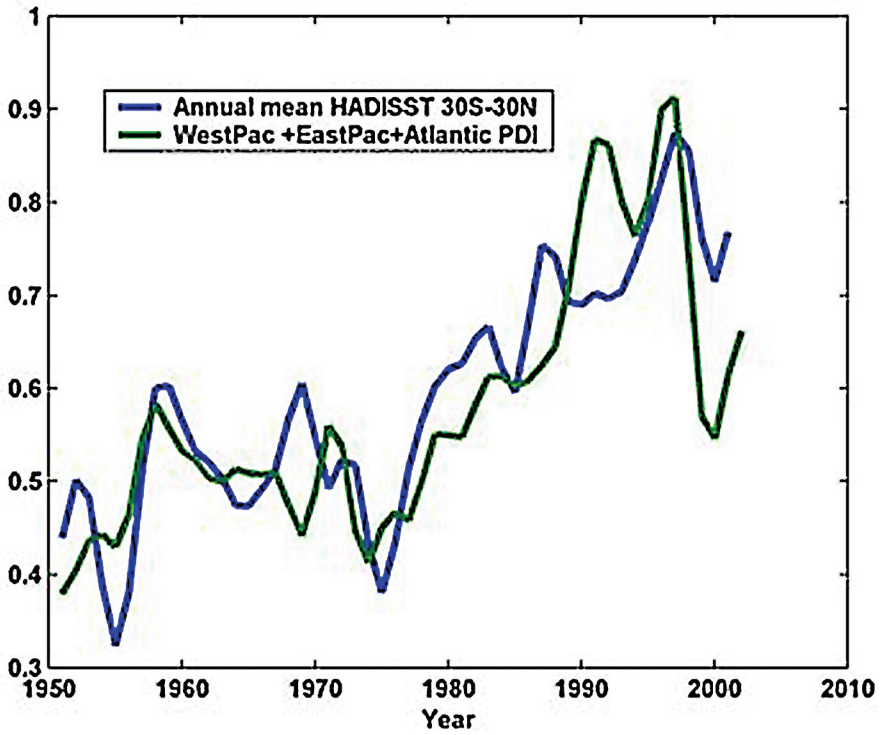


Figure 2. A measure of the total power dissipated annually by tropical cyclones in the North Atlantic (the power dissipation index, PDI) compared to sea surface temperature (SST). (Graph Courtesy of Kerry Emanuel)

The Intergovernmental Panel on Climate Change (IPCC) has predicted an average global rise in temperature of 1.4°C (2.5°F) to 5.8°C (10.4°F) between 1990 and 2100. Based on that, the United Nations proposed in 1997 the Kyoto Protocol, an amendment to the United Nations Framework Convention on Climate Change (UNFCCC). Countries that ratify the protocol commit to the objective of a "stabilization of greenhouse gas concentrations in the atmosphere at a level that would prevent dangerous anthropogenic interference with the climate system."[l] As of February 2006, a total of 161 countries have ratified the agreement, with the most notable exception being the United States. Bush dismissed the protocol as too costly, describing it as "an unrealistic and ever-tightening straitjacket."[m]

Many contend that the United States should worry less about the economic ramifications, and more about the expense to the environment. It's true that the Kyoto Protocol has several shortcomings and is in many ways a band-aid for a bullet wound. Nevertheless, it sets the precedent for a globally cooperative effort regarding the environment, and for bigger and more effective actions involving greenhouse gases and global warming in the future.

We are amidst an unprecedented period in the history of the earth. Never before has there been a species present with the capability of altering the earth to the same extent as humans. There is no valid debate on the issue of whether or not we are altering the atmosphere; we clearly are. There can also be no debate over whether or not this can cause global warming; it is scientifically proven that it can. Nobody would argue that global warming caused hurricane Katrina. But it is definitely possible that the phenomenon factored into the ferocious 2005 hurricane season. The Unites States needs to overcome its reluctance to take action and take on a leading role in the worldwide effort to prevent global warming and its dangerous effects.

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The Proceedings of SURF 2005

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Intracerebroventricular Injection of Leptin Induces Peripheral Lipolysis in the Rat

Aylin Gezgin[1], Joseph Vasselli[2], and Paul J. Currie[3]

Leptin is a peptide hormone that is produced by adipose cells and has been shown to decrease food intake and increase resting metabolism. Leptin also stimulates lipolysis, the breakdown of fat, when directly incubated with adipose cells. Lipolysis is regulated by both peripheral mechanisms and by the central nervous system. Past studies have demonstrated that centrally administered norepinephrine induces peripheral lipolysis, which causes an increase in plasma glycerol and free fatty acids, the breakdown components of triglycerides. In this study, we attempted to demonstrate the effect of centrally administered leptin on peripheral lipolysis. We first attempted to replicate the previous findings that norepinephrine (NE) stimulates lipolysis, as demonstrated by an increase in plasma free fatty acids and glycerol, in order to confirm the efficacy of our experimental method. However, we were unsuccessful in replicating these findings, potentially due to long sampling intervals. We plan to replicate the NE test with shorter intervals. Furthermore, due to time constraints, we were unable to test the effects of leptin on peripheral lipolysis. Testing with leptin and its agonist MT-II is currently underway.

1. Barnard College; 2. Obesity Research Center, St. Luke's Hospital; 3. Department of Psychology, Barnard College

Dimerization of Olfactory Receptors

Calvin Sun[1], Filippo Mancia[2], and Richard Axel[2]

G-protein-coupled receptors (GPCRs) are integral membrane proteins directly involved in physiological responses to a varied collection of stimuli. Although GPCRs were traditionally thought to act as monomers, there has been increasing evidence that they may form dimers. Hypothesizing that the mode of dimerization of olfactory receptors is similar to that observed for other GPCRs, we used the technique of cysteine-scanning to investigate the 4th and 5th transmembrane helices of a mouse olfactory receptor (mOR28). Twenty single amino acid mutants were designed to introduce cysteines along these transmembrane helices. A series of experiments were undertaken to transfect these mutants individually as well as to co-transfect combinations of mutants from the 4th transmembrane with mutants from the 5th transmembrane. Through immunoprecipitation followed by Western Blot analysis under non-reducing conditions the objective was to detect disulfide bond formation, and hence the presence of a dimer, in the mammalian olfactory receptor.

1. Columbia College; 2. Department of Biochemistry and Molecular Biophysics, Columbia University Medical Center

Creation of a microchannel for automated myocyte imaging

Devorah H. Abberbock[1], Charles R. Haggart[2], and Jeffrey W. Holmes[2]

To provide a more efficient way to image myocytes for a hypertrophy experiment a poly(dimethylsiloxane) microchannel was designed using soft lithography. Initially myocytes adhered to the surface of the poly(dimethylsiloxane). The microchannel was subsequently made functional through treatment with bovine serum albumin(BSA); however, myocyte flow was too fast to be of practical use. After undergoing some further trials and modifications, the microchannel should speed up myocyte image collection significantly.

1. Fu Foundation School of Engineering and Applied Sciences; 2. Department of Biomedical Engineering, Columbia University

Effects of Three Types of Dieting on Eating Regulation

Sarah J. McNally,[1] Harry R. Kissileff[2], and Michael R. Lowe[3]

Women can be classified into three groups according to past and present dieting: current restrained dieters (RD: currently dieting, score >15 on Herman & Polivy revised restraint scale (1980)), restrained nondieters (RND: not currently dieting, restraint score >14), and weight suppressors (WS: 12 lb difference between highest and current weight, maintained for 6 months). Among these groups, eating behavior differs in response to various manipulations, e.g. providing subjects with a small preload meal followed by ad libitum access to another meal. These three types of dieters have yet to be studied using the same methodology at the same time in a controlled laboratory setting. In the present study, mean intake by RD, RND, and WS groups of a single item yogurt shake breakfast with and without a preload was compared with mean intake of a nondieting, nonrestrained control (C) group. RDs (N = 6), whose intake was low without, ate less ($p<0.05$) with, than without, the preload (37.23 g + 46.59 SED) than Cs (N = 15, 179.03 g + 29.47 SED) and WSs (N = 7, 169.46 g + 43.13 SED). RNDs were intermediate in their response to the preload (N = 7, 83.73 g + 43.13 SED, $p<0.06$). These results indicate that dieters may be using cognitive cues, rather than physiological signals, to maintain low food intakes, i.e. RDs may be insensitive to, or ignoring, hunger signals.

1. Barnard College; 2. Obesity Research Center, St. Luke's Hospital; 3. Department of Psychology, Drexel University

Investigating Crossover Effects of Testosterone and Luteinizing Hormone in *Xenopus laevis*

Donghun Lee[1], Eun-Jin Yang[2], and Darcy B. Kelley[2]

Conventionally, luteinizing hormone (LH) is considered to trigger masculine behavior indirectly by stimulating the testis to secrete testosterone. However, in *Xenopus laevis*, behavioral evidence from male calling suggests that human chorionic gonadotropin (hCG), an LH homolog, can increase masculine behavior in castrated males when co-administered with testosterone. The question is: how do hCG and testosterone cooperate synergistically without testes? It is hypothesized that this cooperation is achieved through increased LH receptor and/or testosterone receptor mRNA expression levels at dorsal tegmental area of medulla (DTAM), and cranial nucleus IX-X in *X. laevis*, which can be artificially induced by administering exogenous hCG in vitro and/or testosterone in vivo. To examine the hypothesis, 32 sexually mature *X. laevis* frogs are tested with gonadal hormonal (testosterone propionate) treatment in different length in time (1, 3, 5, 12 week), combined with in vitro hCG (LH homolog treatment) or saline for 16 hrs. Quantitative PCR will be performed to observe responses in receptor mRNA expression levels.

1. Columbia College; 2. Department of Biological Sciences, Columbia University.

Paracrine Regulation of Human BMSC Growth

Jing Shan[1], I-Ning E. Wang[2], and Helen H. Lu[2]

The anterior cruciate ligament (ACL) is the major articular ligament of the knee and it connects to bone through a fibrocartilage interface. The lack of a functional interface between bone and soft tissue-based ACL reconstruction grafts compromises long term graft stability and clinical outcome. The mechanism of fibrocartilage regeneration is not known. Our hypothesis is that bone marrow mesenchymal stem cells (BMSC), when exposed to soluble factors secreted by osteoblasts and fibroblasts, are recruited to the graft site and may facilitate interface regeneration. To test this hypothesis, media from both co-cultured and individually cultured groups of human fibroblasts and osteoblasts were added to single cultures of BMSCs. The effects of conditioning media on BMSC proliferation, alkaline phosphatase (ALP) activity, type I and II collagen and proteoglycan deposition, and gene expressions of types II, X collagen were examined over a 28-day period. It was observed that fibroblast conditioned media induced cell proliferation, while osteoblast and co-culture conditioned media suppressed BMSC growth. In addition, fibroblast conditioned media decreased ALP activity while osteoblast conditioned media increased proteoglycan production in BMSC cultures. The results of this study suggest that soluble factors secreted by osteoblasts and fibroblasts have an effect on the growth and chondrogenic potential of BMSCs. These paracrine interactions may be important in the regeneration of a fibrocartilage interface between soft tissue and bone.

1. Fu Foundation School of Engineering and Applied Sciences; 2. Department of Biomedical Engineering, Columbia University

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If you have any questions on the Proceedings of SURF or the Columbia Science Review, please contact sciencereview@columbia.edu. Inquiries on the SURF program should be sent to Dr. Alice Heicklen (ah2289@columbia.edu).

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