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The Columbia Science Review

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The Columbia Science Review is a publication of Columbia University students who aim to provide an engaging and informative approach to contemporary scientific and university research. CSR brings together students of the sciences and the humanities to examine the process and elegance of scientific discovery and problem solving.

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In This Issue

Editor's Note

The challenges faced by society today are of no greater magnitude than those faced throughout history. Our avian flu is history's small pox. Our terrorism is history's Crusades. Our poverty is history's poverty. The severe difference between our challenges and those of the past is that we now have the money and technology to overcome a vast many of them. Whether or not we choose to do this, however, is a function of our collective literacy in science and technology.

Science and technology exist in two forms. The first is literal; in order to beat the avian flu, we need virologists. In order to build structures capable of withstanding the blast from a terrorist's bomb, we need engineers. The second is consequential; science both affects and is affected by political atmosphere, public opinion, and trends in spending. In order for great ideas in science and technology to be implemented, we need great scientists, as well as politicians and citizens who understand the pros and cons of their new ideas. This is what I mean by our "collective literacy in science and technology."

Unfortunately, we are verging on collective illiteracy. The American public increasingly views science as esoteric, and enrollment by students in many science or technology majors is precipitously declining. Indeed, less than 2% of high school students today will go on to earn a degree in engineering. As a result of this, our ability to implement great ideas, like the ones described on the pages of this journal, is tenuous.

As Americans' aptitude in science and technology declines, two problems will arise. First, the literal: research and development will stagnate. This will create a downward spiral because talent to fill technical jobs will be lacking and those jobs will be outsourced. But as this work moves overseas, students will have less and less an incentive to study science because no jobs will be waiting for them. Second, the consequential: the legislature and public will be incapable of making intelligent decisions on science policy and education. Convincing American taxpayers to fund science initiatives will become more difficult because the public will not be educated to the extent that it can appreciate the technical justification. Research and development, as well as science education, will become under funded and will not be able to compete with other powerhouse countries.

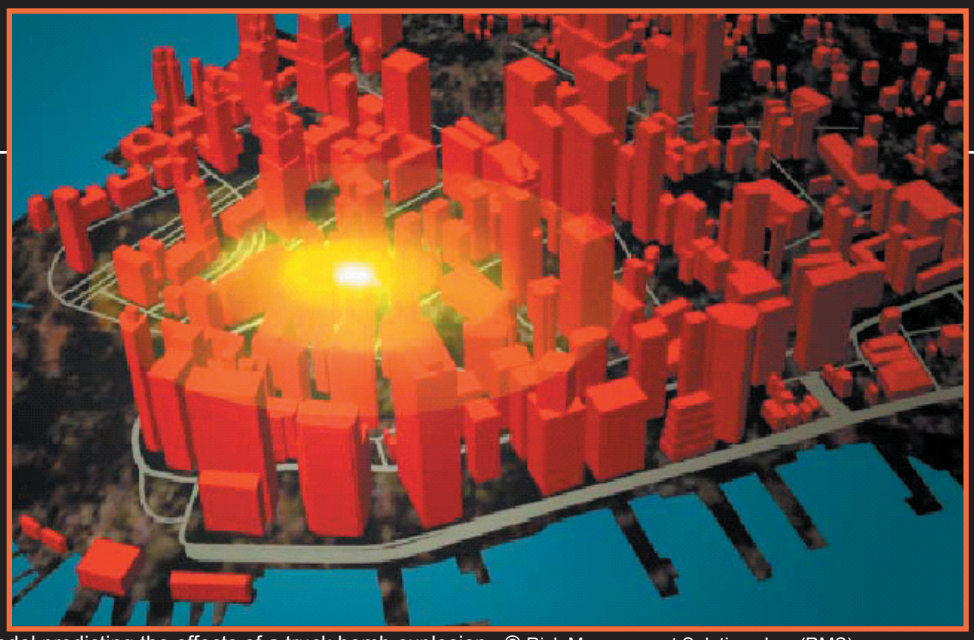
If one is able to grasp the level to which science and technology pervades our social and economic progress, as well as our physical health, one is able to appreciate the severity of this problem.

In the recent past, America's scientific prowess had been bolstered by students and professionals from other countries, such as India and China. But as economies in these countries continue to develop, this stream of scientific talent will dry. Indeed, this past December, the New York Times reported that many of the technology wizards who came from India to attend university in the U.S. and who in the 1990's would have stayed to secure lucrative jobs are now returning home to do the same thing in India.

The solution to this problem is complicated and tangled. One could say that better education is the key. This is legitimate, but naïve. Even if we improve public education in America, we still need to provide students with an incentive to pursue degrees in science that are very, very hard. Money is certainly an incentive to work hard, but careers in business or law are often more lucrative.

Should we more generously pay our scientists and science educators? Should citizens be willing to forego fat paychecks for the "honor" of being a discoverer? The answers to these questions are grounded in social values and are beyond the scope of this journal. What is clear is that if Americans do not soon reinstate science and technology as the drivers of social, economic, and medical progress, we will be faced with a paradox: it takes acumen in science to understand the justification for pursuing, funding, and teaching it. But it takes a strong education in science to develop that acumen. Unless we address our deepening illiteracy, we will not only become incapable of advancement in the field; we will be unable to recognize our deficiency in the first place.

Matthew S. Berry
Editor-in-Chief



A model predicting the effects of a truck bomb explosion. © Risk Management Solutions Inc. (RMS)

Our Last Line of Defense

Facing the Threat of Terrorism with New Technology

By Henry Thompson

A new wave of funding is allowing researchers to develop innovative methods for confronting terrorism. But are they raising more questions than answers?

Amongst the crowds of the morning commute, mesmerized by our daily routines, few details stand out. Every day millions of commuters drone to the rhythm of the train schedule: in and out of subway doors; through turnstiles. With reports of increased "chatter" and steady adjustments of the color-coded threat level, many commuters have at one time or another been snapped out of their morning daze, however briefly, by bomb-sniffing dogs on the subway or an increased police presence at turnstiles. These dogs and the keen eye of the police officer epitomize the low-tech response to the western world's new found terrorist threat; a response that is proving inadequate at best. This fact was clearly illustrated when four terrorists carrying backpacks filled with explosives casually boarded the London transit system. Thirty nine people were killed in synchronized explosions aboard three subway trains. An additional thirteen were killed an hour later from a blast atop a double-decker bus. But we do not have to look at these examples to know how vulnerable we are. We realize it everyday as we pack ourselves anonymously into mass transit. It is almost derisory that such low-tech countermeasures are our last line of defense against the threat of terrorism.

Today we find a global situation that requires truly ingenious solutions that will affect not only the police officers, federal agents, and military personnel that are used to dealing with threats, but nearly everyone that lives and works in places vulnerable to attack. NYC officials have already implemented random searches at subway entrances using a new hi-tech bomb detector. But are these measures enough? How much more personal freedom are we willing to commit to this effort? Are we willing to accept the costs of fighting terrorism? What other solutions are within reach? Scientists and researchers around the globe are trying to answer these questions, and what they are finding is truly intriguing. The attempt to defend ourselves against terrorism encompasses many different fields and scientific disciplines. This attempt has both technological and social components and is challenging researchers to find solutions in new, exciting, and sometimes controversial ways.

Dealing with another attack

Imagine another day like September 11th. New York City's morning commuters are greeted with another shocking attack, but this time it is a radiological dirty bomb set off in lower Manhattan. Tens, possibly hundreds of thousands of people are affected. An event of comparable magnitude actually happened in Goiânia, Brazil, where a container of cesium-137, used for radiation treatment, accidentally opened. In the days following, over 100,000 people sought radiation screening to determine whether they had been exposed to dangerous levels. Of these, only about 250 were found to be contaminated.[1] Could disaster teams in New York City deal with this overwhelming number of potential victims? How would they be able to determine which needed immediate treatment?

Columbia University researchers are currently working on new technologies to tackle this exact problem. Equipped with a $25 million grant from the National Institutes of Health (NIH), researchers plan to alleviate this potential problem in three phases. First, Columbia researchers will develop a new device to test bodily tissues for indications of exposure, using robotics and rapid image analysis. Second, they will develop an easily transportable device, small enough to fit in a large truck, that will conduct rapid molecular screening. Finally, they will develop a completely non-invasive method of screening. This tool will be able to test sweat, urine, or saliva to pick out those exposed to radiation.[2]

These three tasks are being carried out by a team of researchers from The Mailman School of Public Health, The Department of Mechanical Engineering, The Center for Radiological Research, and The Center for New Media Teaching and Learning. Lead by principle investigator David J. Brenner, Ph.D., D.Sc., professor of radiation oncology and public health, Columbia has amassed a truly multi-disciplinary team to conquer a problem that is both highly technical and necessarily socially applicable.

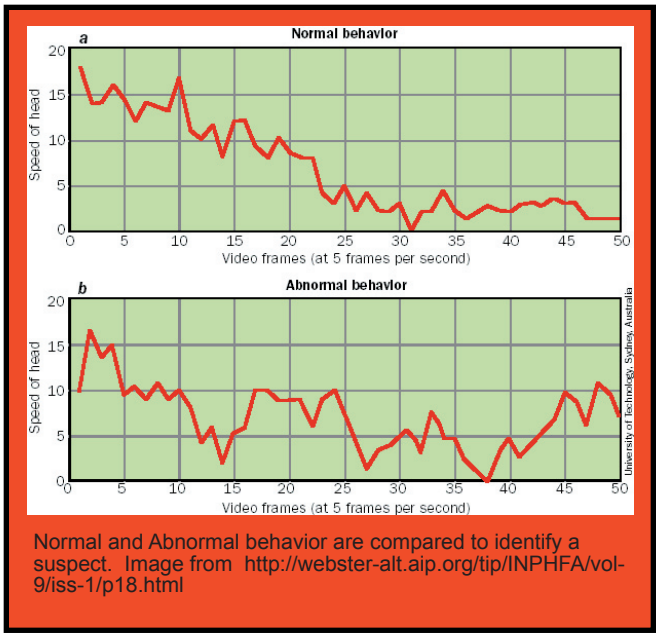
Dr. Nabil Simaan, Ph.D of Columbia's Mechanical Engineering Department, gets to experience this multidisciplinary effort first hand. As a participant in the project, he will design a robotic system to process blood samples. In effect, he brings the humanity of the patient and the science of the testing devices together. He believes that quick processing is key to maximum throughput. "The most challenging and important part of my project will be integration. The [robotics] engineering has to mesh with the testing devices in a highly efficient way," he said. Dr. Simaan also mentioned other projects that are being made possible through government funding, including many new and promising technologies in the areas of search and rescue robotics. It is a very exciting time for researchers working in these areas because new interest and funding are advancing inquiry into many important and complex topics.

Although other institutions are participating in the research, development, and the eventual implementation of this device, Columbia leads the effort mainly because of its world renowned radiation research and its prime location in the city. Currently this project is only in the startup phase, but researchers plan on achieving full success of all three components within five years. In the meantime, researchers elsewhere are working on ways to protect our citizens from terrorist acts before they occur.

Smart Surveillance

In 1998, the New York Civil Liberty Union counted over 2,400 public surveillance cameras in Manhattan. According to the NYCLU's "NYC Surveillance Camera Project", the number today is likely more than three times this figure.[3] It is rare to find a spot in the city where a camera is not recording your behavior. In London, another hotspot for public surveillance, cameras were instrumental in identifying the July 7th attackers, and even helped observe their methods. However, it is evident that mere observation will not make a suicide bomber think twice, nor is it likely to alert someone in time to do something. So when we talk about preventing an attack, we need to talk about smart cameras: a camera (or system of cameras) that has the ability to recognize objects, such as people and weapons, analyze behavior, and alert the proper authorities.

The first stage of smart camera development is already completed, with companies boasting the capability to detect unattended packages, perimeter breaches, and suspicious vehicles. New Jersey Transit has begun using a camera system that analyzes rider behavior through comparison to an algorithm, alerting personnel to certain abnormal behaviors.[4] Such algorithms can presumably be trained to pick out a person wearing excessively warm clothing in an effort to conceal explosives. However, this technology is still primitive compared to what is needed to accurately detect a terrorist. More sophisticated devices are being developed and are not far from reaching a usable form.



Normal and Abnormal behavior are compared to identify a suspect. Image from http://webster-alt.aip.org/tip/INPHFA/vol-9/iss-1/p18.html

A study at the University of Technology in Sydney has produced initial data on using smart cameras to detect suspicious behavior. This study is based on the simple fact that there is a correlation between suspicious behavior and erratic body movement. [5] Researchers have developed surveillance software to distinguish between humans, packages, and other images captured by a camera. In this study, the software is able to track the movements of a subject's head, process these movements, and assess a risk rating. In one particular experiment, a store's parking lot was monitored. The camera system was able isolate a subject's head, measure head speed, and compare it to a standard model of a shopper moving between the store and their parked vehicle.

Head speed and suspicious behavior correlate in this case because a subject looking to steal from a parked car slows down to look into many different cars before committing the crime. However, while these cameras can certainly pick out abnormal behavior and alert security personnel accordingly, they only represent a small step towards the ultimate goal of detecting terror before it happens. The main idea is that certain observable behaviors are correlated to deviant intent.

Cameras looking to detect a would-be-terrorist are going to have to be able to pick out slightly more specific behaviors and combine many different types of data. For example, systems built to analyze eye movement and perspiration could be used to detect signs of uneasiness. Cameras that examine body geometry interfaced with a method to detect weight distribution may provide clues to the weight of a persons' bag or backpack. Both systems could be used to pick out suspects and could be networked with each other to provide a more accurate risk assessment. And of course, such systems do not have to stay confined to the visual spectrum of light. It is quite a simple task to have cameras analyze other parts of the electromagnetic spectrum as well, giving hints to the contents of a bag or even checking for the presence of certain chemicals. Numerous companies have already developed camera systems for detecting humans and objects through walls using UWB (ultra-wide band), a frequency that can easily pass through most non-conducting materials.[6] Could experts in these different areas combine their efforts and produce a system that could detect a terrorist more efficiently than dogs and police? It seems likely. The real question may be not be whether it is possible, but whether it is possible without disregarding personal freedoms. New interest and funding will make extremely powerful surveillance systems possible, but will the public accept this new electronic scrutiny?

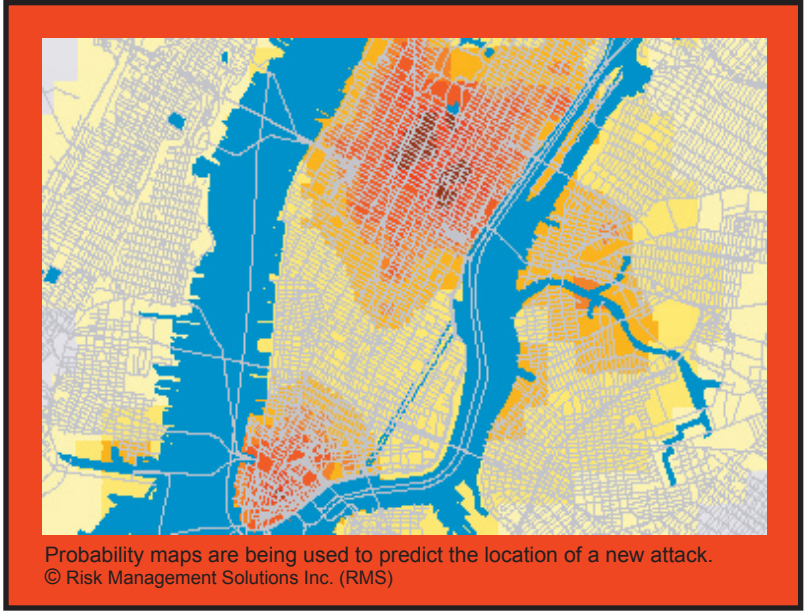
Apparently, the very freedoms that we are trying to protect in this war on terror are a limiting factor on potential solutions. That is, there is much work left to be done in the area of surveillance, not just in the development of the technology, but also in the fields of morality and ethics concerning use of cameras and other types of surveillance in public. And with current smart cameras costing up to $10,000 each, these technologies cannot be implemented everywhere. To make these high tech systems work efficiently, they must be placed in a strategic and noninvasive way. As researchers around the world continue to work on these systems, they hope to find a niche where terrorists are efficiently outsmarted, while a certain amount of privacy is maintained.

Cataloging the Digital Human

An emerging technology that has already drawn opposition on the basis of privacy is biometric identity methods; in particular, plans to introduce in Europe ID cards containing biometric information, such as fingerprints, have drawn huge protests from citizens abroad. Nevertheless, we continue to see advancement in this field. A few examples include digital face and voice recognition, hand geometry, iris and retina scans, typing style recognition, and even analysis of a person's style of walking to determine identity. Many of these biometric techniques can and are being used to assure identity, but for the most part, they are used within companies or military facilities and are only used to identify a small number of people. However, when the databases containing such personal information start to grow, these types of technologies may arouse unease.

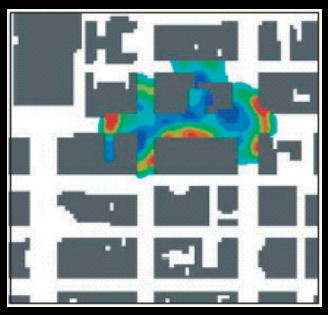
The digitalization of a person's signature will soon be a part of everyday life because it has a huge advantage over other biometric identification technologies: public acceptance. People are already accustomed to signing as a means of identifying themselves. We will likely see credit card companies verifying signatures to reduce fraud, but an application for preventing terrorism also lies within a relatively new technology termed *dynamic signature recognition*. Old signature recognition techniques rely exclusively on analysis of a two dimensional image of the signature, while

dynamic signature recognition measures movement in three dimensions and elapsed time, making it much more reliable. This new method helps recognize "signing behavior." This is crucial because while replicating the appearance of a signature is simple, replicating the way someone signs their name is much more difficult. This means that natural rhythm - pauses between strokes, and even the amount of pressure applied at different parts of the signature - can be measured and analyzed. One hurdle that biometric identity is currently climbing is false acceptance and false rejection. Because there is some variation to the way people sign their names each time, these devices need to be carefully calibrated in order to allow for personal variation while still rejecting forgeries. With the added scrutiny of *dynamic signature recognition*, false accept and reject rates can be drastically lowered.



Probability maps are being used to predict the location of a new attack.

One obvious application for dynamic signature technology comes at securing international borders. The airline industry already plans to allow frequent flyers, who choose to give biometric info (and pay extra), to move to the front of security lines. It is reasonable to envision a day when you are expected to identify yourself by signing your name before entering a country. After all, you are expected to sign all kinds of other forms when passing through customs. The basic procedure would probably work something like this: you hand the customs agent your passport, which contains a smart-chip containing basic information like height, weight, and eye and hair color. But more importantly, this chip also contains information about the way you sign your name. The smart-chip is scanned and you are asked to sign a form that has been placed on an electronic pad similar to the one already used at the bank or grocery store. However, this one is not only sensitive to movement in the horizontal and vertical axes; it is also sensitive to the amount of pressure applied to the page. So, by signing to affirm that you have not smuggled too many garbanzo beans back, you can also prove your identity. Sounds simple enough, right? It is the hope of many companies that have worked to develop this technology that this simplicity will allow dynamic signature recognition to become publicly accepted, and thereafter, widespread.



An example of blastwave propagation.

Probability and Materials Science

Despite advancements in identification technology, it is likely that some terrorists will again find their way onto American soil. On September 11th, the terrorist's weapons of choice were jumbo-jets carrying tons of jet fuel. As we all remember, the initial impact and explosion of the airliners caused only a small fraction of the total fatalities and final damage. The majority of the destruction came after the crash; the extreme heat of burning jet fuel and other flammables caused steel trusses in the World Trade Center towers to weaken. The end result was nearly 3000 fatalities, families ripped apart, and billions of dollars in cleanup and rebuilding costs. Some researchers have found another counter terrorism niche between the moment of explosion and the aftermath: studies in blast propagation, structural design, and materials science may make buildings less likely to collapse.

One way of offering protection from terrorist attacks may be to use new, safer building materials. For example, glass is one of the most dangerous building materials in use, not because it lacks structural strength, but because it shatters into high velocity fragments, essentially turning a targeted building into millions of projectile weapons. Glass shrapnel from bomb blasts alone causes a staggering number injuries and deaths. Of course, we do not want our workspaces to feel like bomb shelters. Thus, many companies have developed laminated and treated glass products that are indistinguishable from normal glass, except that they have the ability to withstand blasts or break in to smaller, lower velocity pieces.

Additionally, there is a new wave of composites and polymers that offer strength advantages over traditional reinforced concrete. For example, one cement-based material utilizes high strength steel fibers, among other additives, and magnificently outperforms concrete in heat tested tension and compression tests, as well as in blast strength tests.[7] This new amalgam and many other materials also promise to outperform concrete in tests involving fracture. Just like glass, fragmented pieces of concrete intensify the damage and injury caused by a blast. This phenomenon can be reduced by making materials resistant to such fracture.

The terrorists that carried out the London attacks used conventional explosives. And despite the large amount of attention given to chemical, nuclear, and biological threats, conventional explosives remain the most likely weapons because they are relatively inexpensive, easy to produce, and hard to track. There is a whole field devoted to analyzing bomb blasts and developing new materials to minimize the resulting damage. Although this science is not exact and we cannot make our structures completely resistant to damage, we can do a lot to lessen injury and the magnitude of casualties.

But the application of this new material needs to be focused on high risk areas, for a number of reasons, not the least of which is cost. Insurance companies are already on to this idea: how do you predict the likelihood and magnitude of an attack and aftermath in a certain geographical area. This is risk modeling, and the idea is to simulate the decision making process used by terrorist groups in choosing targets and to use probability to determine a threat level. This usually includes picking certain likely attack spots and applying already established computational models, like those used in fluid dynamics, to determine likely effects. The truth is, however, this is easier said than done. With different geography, architecture, and building layout, and with weather varying from day to day, only rough probability estimates are feasible. Nonetheless, this modeling assists in helping pinpoint places that need the most protection.[8]

End of an Era

Until recently, most city dwellers sought tirelessly to make the morning commute less boring; now an atypical journey is more than one could ask for. Today we live in a new era; an era of new threats and new challenges, an era in which America is forced to guard against foreign threats on its own soil. Amid recent color coded warnings, false alarms, and natural disasters, the failings of our response seems painfully evident; we are not adequately prepared to deal with monumental threats.

Luckily, this era is also one of constant technological advancement. On the horizon, we can see the fields of blast wave propagation and materials science applied to current and future architecture to protect our structures, the old surveillance

camera is undergoing a serious revolution, technology can allow law enforcement officials to see through walls, and new ways to deal with the aftermath of an attack are being developed right here at Columbia. As researchers, companies, and governments around the world continue to struggle to deal with terrorism, many previously unexplored solutions are being considered. With each newly developed tool comes new problems and limitations. These limitations can be technological challenges or can come from the struggle to make new technologies publicly acceptable. By combining resources, researchers hope to overcome these obstacles. What we are seeing is a new multidisciplinary approach that hopes to find the delicate balance between effectiveness, efficiency, and the protection of personal freedoms.

After September 11th, modeling techniques must be used to assess terror risk. These technologies promise to help protect a highly valuable resource; this resource is routinely transported in airplanes, on buses, aboard subway trains, and is packaged most densely in our cities, among office buildings, museums, schools, and train stations. This highly valuable resource is the people of America. Our citizens. They are our workers, researchers, our families and friends. As time passes, it seems more and more likely that we will see another act of terror on American soil. As time passes, we also see the hope of new solutions, new strategies, and new tools. It is this promise of new technology that provides the hope of protecting our people and preserving our delicate future.

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Life in the Cosmos

A Journey into the Unknown

By Sandeep Soman

Now several years into the new millennium, we are still faced with the same questions that have dogged us seemingly since the dawn of humanity. Are we alone in the universe? Are there other intelligent beings in the vast reaches of space? Will alien visitors be friendly or hostile? While we have no definite answers, new information is pouring in at an astonishing rate. Ever-advancing technology allows us to discover stars and potential planets, while new theories continue to change our assumptions about the resiliency and potential of life.

Image: Courtesy of NASA

Image: Courtesy of NASA

So is there life in the cosmos? "Yes," says Caleb Scharf, a Columbia professor whose research interests include astrobiology. "I believe that somewhere, there is intelligent life." He echos a public majority. A recent National Geographic poll revealed that 60% of respondants believe that there is life outside of planet Earth. For many, it seems highly improbable that in the midst of such an expansive universe, the planet Earth should be the only place that higher beings call home. However, it is precisely this line of reasoning that leads to the famous Fermi paradox: If there are so many alien races out there in the cosmos, why have we not found any sign of them?

To find planets suitable for extraterrestrial life, we must first discover suitable stars, and that is an enormous challenge. There are over 100 billion stars in the Milky Way alone, which is merely one of an incalculable number of galaxies in the universe. Of the stars that have been documented, many have grown too large, exhausting their energy too quickly to allow life forms to develop. Meanwhile, stars that remain too small are unable to develop many of the heavy elements required for life. It is those moderately-sized stars like our sun that, in their cores, convert hydrogen to helium that are the most promising candidates.

While research on, and the resulting discovery of, stars has been formalized in spectroscopic analysis, finding planets has been more of a problem. The first confirmed planets outside of our solar system were discovered only a little over a decade ago. While currently over 150 planets have been found, most of them are approximately Jupiter-sized, gaseous, and lacking in the solid composition that characterizes Earth. Programs such as NASA's Kepler mission, which will launch in 2008, have been fashioned with the goal of finding those rare Earth-sized planets that are far more likely to contain life.

Any discussion about aliens has to include the father of modern extraterrestrial hunting, Frank Drake, who designed the famous Drake Equation over 40 years ago to deduce the number of intelligent and communicating civilizations in the galaxy. In the 1960s, the prevailing notion was that any intelligent civilization would be sophisticated enough to communicate via radio waves. Drake's equation combined this and a number of other factors in an attempt to quantify exactly how many intelligent civilizations inhabit the universe.

Unfortunately, the Drake Equation is at best an imprecise measure because of the uncertainty of the many variables involved. For example, how are we to accurately gauge exactly what the expected lifespan of intelligent civilizations in the galaxy is, when we have only one instance from which to draw data? "The whole philosophy of writing down all the factors, while it is useful in early work, is also very limiting," says David John Helfand, a Columbia professor in the astronomy department. "It is stimulating though, for calculating the frequency of conditions for life, because it is so wide open. It is useful as a thought experiment, but not for practical purposes."

Even with models like the Drake Equation, we still do not have an accurate measure of how many other intelligent life forms share the cosmos. "The Drake Equation is a little bit arbitrary. It can be used as a springboard, a convenient way of listing things that should be considered. But I don't think it's ever likely to be very accurate on a quantitative basis," Dr. Scharf says.

However, Drake's legacy lives on in programs such as SETI, the Search for Extra-Terrestrial Intelligence, a private organization founded in 1984. SETI tries to detect alien radio signals and has spent money on recent initiatives such as Project Phoenix, which uses some of the world's largest telescopes and most sophisticated spectroscopy. Based on the profusion of radio waves due to human activity in our own solar system, it would seem obvious to curious extraterrestrials that life does exist here. However, no conclusive evidence of abnormal radio wave activity has yet been discovered in over 40 years. "It is an enormously long shot. The payoff would be spectacular, of course, but still, using private money is vastly preferable," Dr. Scharf says.

The possibility of alien life brings up the importance of clarifying the enormous difference between life on other planets and *intelligent* life on other planets. Dr. Helfand defines an "intelligent" civilization as one with "the means to communicate across interstellar distances. Radio waves are the cheapest way to do this. So an 18th century person on Earth would not be intelligent in a cosmic sense. This would be 'technological intelligence,'" Dr. Helfand says. Will discovering microscopic bacteria in the depths of Europa resonate with us, on an intrinsic level, as much as finding actual little green men in flying saucers?

Yet, it is probable that we will discover tiny and simple organisms first. Life is present almost everywhere on Earth, from the most inhospitable reaches underwater, where a single ray of sunshine has never penetrated, to boiling hot springs, to the frigid plains of the Antarctic. These conditions, which were thought to be too hot, cold, salty, acidic, or dark to sustain life, are proving to be just the opposite. Sunlight only extends a few hundred feet below the water's surface, but organisms have been discovered miles below. If life exists in these areas, why can't the same be true on other planets?

As more and more research is done on the life found in Earth's most remote habitats, scientists gain a better understanding of just how durable life is and where it can originate and thrive. This has led to a reassessment of our views on a star system's habitable zone: the area surrounding a star where liquid water can exist on a planet's surface. This zone encompasses only a small band of our solar system, including Earth, and having boundaries near Venus and Mars. However, it is important not to restrict any possibility of life only to this area. For instance, distance from the Sun need no longer be a limiting factor since we now know that planets with atmospheres can regulate heat through the Greenhouse effect and that locales as far away as Saturn may support water.

Despite the fact that scientists are increasingly looking at planets further and further from the sun as possible life-supporting habitats, our neighbor Mars continues its long history of providing fodder for alien-seeking enthusiasts. Just this past September, a NASA group using the *Spirit* rover found the first compelling evidence of water on the Red Planet, hidden in the Gusev crater. Recent evidence also shows that glaciers exist outside of the Martian poles and influence its climate even today. Research in recent years has also proven that the planet once had a powerful magnetic field and underwent plate tectonics similar to those on Earth, but that the field has not been active for around three billion years. In 1996, tiny fossils that were found in ice from Allan Hills, Antarctica, were presumed by many to have been blasted here from Mars. This led to a flurry of media attention, but no conclusive proof.

However, even if water exists on Mars, many other factors seem to rule out the possibility of life on the planet. For example, the Martian atmosphere is too thin to trap

The Drake Equation, developed by Frank Drake in the 1960s, is an attempt to figure out of how many civilizations in the Milky Way exist that we can communicate with. A look at its components:

N= R x Fs x Fp x Ne x Fl x Fi x Fc x L

N- The number of civilizations in the galaxy that we can possibly communicate with
R- The rate of new star formation in the Milky Way
Fs- The fraction of stars that can have planets capable of supporting life
Fp- The fraction of these stars with planetary systems
Ne- The number of planets per star which can support life
Fl- The fraction of these planets that actually have life
Fi- The fraction of these planets that develop intelligent life
Fc- The fraction of these planets with species able to communicate across space
L- The expected lifetime of such a civilization

the sun's heat or protect the planet from the onslaught of unchecked ultraviolet rays. Also, a surface temperature that averages -75 degrees Fahrenheit, almost 140 degrees less than the average surface temperature of Earth, may prohibit life from developing. Mars shows how rare it is for all the right conditions to converge and produce a planet like Earth that can support life. As much as Mars fascinates us, it is probably not going to lead to a miraculous finding.

While advanced alien civilizations may not be coming to meet us soon, the discovery of even the simplest microorganism would be a huge breakthrough, as momentous a discovery as any in the history of science. "It would be profoundly important. We still only have one instance of life: ourselves. Two is infinitely better than one example, and it would provide evidence that life developed separately," Dr. Helfand says. "We have to be convinced that there is not a common relationship between the two; do we have the same or different DNA and replication structure? The answers to these questions will also tell us more about life on earth." Who can say whether alien life would follow the carbon-based model of every living organism on Earth? Could life develop without being carbon-based, forming around silicon, for example, or ammonia? Unfortunately, there is no way to know the answer to these questions without actual specimens.

The results of discovering extraterrestrial life would be staggering. A complete overhaul of biology would be required, not to mention the social and religious implications. "The first impact would be that it would require the revision of essentially all of the religions in the world, especially those that are earth-centered," Dr. Helfand says. "It would change peoples' attitudes towards life on this planet, and our social problems."

New developments and discoveries are being brought to light at incredible rates. One such event happened this past October when scientists discovered organic compounds containing nitrogen, using NASA's Spitzer Space Telescope. Polycyclic aromatic compounds, which previously were not considered very important to life, were found in space to contain nitrogen, an immensely important element for life. The compounds found have structures similar to Earth-bound molecules such as chlorophyll. If those compounds could exist deep in the reaches of space, then there is the possibility that they can develop on other planets as well.

Despite the promise of space research, the technical difficulties are considerable, and for many, not worth the time, cost, and effort. The logistical problems resulting from an interstellar search for life are staggering. With current technology, humans cannot simply hop on a spaceship and arrive at the nearest star system. Such a voyage would last millennia. Worthwhile space voyaging to other stars is currently as beyond our capabilities as traveling to the moon was for scientists in the Middle Ages.

This begs the question: is it really worth our time to search for intelligent life in the universe? Many of the same people who would have supported the boom in space interest in the 1960s now believe that money used for space travel could be put to better use solving any number of pressing domestic problems. Britain is in the midst of a ban on sending humans into outer space, and the United States seems to be in no hurry to get there either. A proposal by President Bush in January of 2004 to return to the Moon, to reach Mars, and to increase NASA's budget by $1 billion a year was immediately met with opposition from other politicians and even the general public. For every proponent of space travel, it seems there are just as many, if not more, dissenters.

Considering how splintered our own planet is, we may have little chance of presenting a unified front in our exploration of space. "The next generation of searching for life on other planets has to be an international effort here on Earth," Dr. Helfand says. Between the U.S., Russia, and other major players, a united worldwide program would be leagues ahead of everything done in the past.

Despite discordance on policy, spending, and even a belief in alien life, the human spirit continues to be saturated with curiosity. It is a fascination with the unknown that drives our search for life on other planets, just as it drove our search for the New World and our treks to the moon. That we currently face so many more questions than answers may be the best reason to presume that our search will continue. Will we make contact in our lifetimes, or will we carry on in our current state for centuries more, unaware of our position in the cosmos? At the rate that technology is advancing, it seems almost certain that new methods will be developed to let us expand past the traditional boundaries of the solar system, but will this lead to fruitful results, or only more questions?

And what about the aliens themselves? How will they interact with us? Popular opinion seems to be split between the friendliness of *E.T.* and the evil Martian conquerors of H.G. Wells' *War of the Worlds*. Will they want to improve our civilization, or subjugate it for their own purposes? Only time, and perhaps a little bit of luck, will reveal the answers.

The Jet Propulsion Laboratory at the California Institute of Technology defines the habitable region as "the region around the system's star where we can expect to find liquid water at the surface." As is obvious from the figure, only Earth falls in this zone. Image: Courtesy NASA/JPL-Caltech

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Is the World Perched for the Coming Avian Flu Pandemic?

By Adam Kaufmann

It is not a matter of if, but rather a matter of when. The H5N1 virus, more commonly known as the Avian flu, ominously looms on the horizon as the world's next pandemic. Since H5N1 has exhibited a resistance to anti-viral agents such as amantadine and rimantadine, and since we currently lack a vaccine to protect against human infection, an outbreak of Avian flu could result in deaths rivaling the pandemics of 1957 (Asian Flu) and 1968 (Hong Kong Flu). It could, in fact, result in worldwide deaths comparable to that of the Spanish Flu pandemic of 1918, which is estimated to have killed anywhere from 20 million to 100 million people. As a result, the World Health Organization, the United Nations Food and Agriculture Organization, the Centers for Disease Control and Prevention, and the U.S. National Institutes of Health are on high alert making avian influenza surveillance a top priority. Any hope of preventing catastrophic mortality rates rests in tracking genetic mutations in the H5N1 virus; however, some nations have not only been reluctant to share human samples of the virus with various health organizations, but have also contributed to the declining effectiveness of the available antivirals by tacitly granting permission to their farmers to use these drugs on poultry. This overuse could trigger the virus to genetically mutate and become resistant.

Avian influenza, which has killed tens of millions of birds, does not generally infect humans. Nonetheless, cross species transmission has occurred and resulted in approximately 67 human deaths since 1997. Thus far, Asia has been the epicenter of the H5N1 virus, but recent findings in Russia, Finland, Turkey, and Romania suggest that this highly pathogenic influenza is migrating westward. This new and unsettling development has many countries seeking to develop national response plans, but large amounts of unused vaccine coupled with the high risk of lawsuits by those who suffer negative reactions from the inoculation has, for years, hindered the involvement of pharmaceutical companies in the planning process. Government contracts are providing an incentive for the research and manufacture of much needed vaccines, but many public health experts believe the sudden push may be too late to meet the anticipated overwhelming demand. Moreover, the rapid evolution of the virus would, in all likelihood, render a stockpiled vaccine an ineffective weapon against any mutated form of the virus.

U.S. National Strategy

Feeling pressure from congressional lawmakers and health officials about the urgency of the situation, President Bush recently unveiled his administration's $7.1 billion plan to battle this brewing global epidemic, which could exact a devastating toll on the American populace. Entitled the *National Strategy for Pandemic Influenza*, a three pillared strategy has been set forth that emphasizes preparedness and communication, surveillance and detection, and response and containment. The plan attempts to utilize the full power of the federal government as part of its efforts, but notes that since an outbreak will most likely occur on many fronts within the United States, a highly coordinated approach between federal, state, and local governments is necessary for an effective infection control strategy.

A critical component of the plan involves government expenditures for the stockpiling of vaccines and antivirals. However, the particulars of the plan reveal that the purchase is limited to vaccine doses for 20 million people and 24 million treatment courses of antivirals; in essence, an amount necessary to meet the needs only of first responders and the exceptionally weak. Cognizant of the fact that present vaccines would probably prove inadequate in the face of a truly virulent bird flu pandemic and that the existing method of producing vaccines—using chicken eggs to develop antibodies—is antiquated, additional funds have been earmarked for engineering an accelerated means of vaccine production so that all Americans can be vaccinated in a timely manner. Further, the federal government will subsidize,

Image from: http://the.honoluluadvertiser.com/dailypix/2005/Jun/07/op07a_b.jpg

in part, the purchase of antivirals by individual states, though 75% of that cost is to be borne by the states. Whether the states, many of which are already saddled with budgetary concerns, will be able to allocate money to these preparedness funds remains uncertain.

Two issues detailed in the plan that are likely to raise red flags are the quarantine provisions and the attempt to limit the liability of vaccine manufacturers. Various trial lawyers' associations have begun to balk at capping liability, but the quarantine might prove to be an even thornier issue. In addition to alarming the general public, enforcement could be problematic. The President, by executive order, has the power to quarantine in instances where certain communicable diseases threaten the population at large. Pandemic influenza has been added to that list. Thus, authorizing the detainment of a contagious individual entering the nation is unambiguously within the confines of the law. Less obvious is the legality of home quarantine and, during an outbreak, restricting movement within the U.S. of those who are not contagious. President Bush has suggested that the military might be called upon to assist with implementation of quarantine, but Dr. Irwin Friedlander, director of the National Center for Disaster Preparedness at Columbia University's Mailman School of Public Health has stated that such action would be tantamount to creating martial law in the United States. Nonetheless, the degree of public support for government action would probably be dependent upon the gravity of the influenza outbreak.

It is important for the American public to keep in mind that government action, as enunciated in the *National Strategy,* is predicated solely upon the Avian influenza virus evolving into a new strain to which humans have no exposure. Thus, there need not be concern about a sweeping government response, which could include quarantine, to influenza outbreaks other than H5N1 virus. What then are the hallmarks of the various strains of influenza?

The ABCs of Influenza

Influenza is a respiratory infection caused by an RNA virus of the orthomyxoviridae family. Influenza viruses have been classified into types A, B, and C, with type A being the most common influenza and the one responsible for the most lethal epidemics. It can infect humans as well as avian and mammalian species, including but not limited to birds, pigs, horses, seals, and whales.

Influenza type A viruses are divided into distinct subtypes based on two glycoproteins on the surface called haemagglutinin (HA) and neuraminidase (NA). Scientists have identified 15 different HA protein subtypes (H1-15) and 9 different NA protein subtypes (N1-9). Multiple combinations of the two subtypes are possible and thus, there are different scientific names for influenza type A, such as H1N1, H3N2, H3N8, and H7N2. Wild birds are a natural reservoir for all subtypes of influenza A viruses, whereas only some influenza A subtypes are commonly found in people.

Haemagglutinin and neuraminidase continually mutate by mixing together their genetic material, eventually resulting in new strains of the virus. Thus, if the same cell was infected with the H3N5 virus and the H2N2 virus, a genetic re-assortment could yield the H3N5, H2N2, H3N2, or H2N5 viruses. This process, known as *antigenic drift*, is the reason individuals are vulnerable to the influenza virus throughout their lifetime. In contrast, *antigenic shift* refers to a new influenza A subtype that results from a sudden change in the hemagglutinin protein or the hemagglutinin and neuraminidase protein combination, which then becomes established in the human population. Currently, H1N1 and H1N2 are circulating generally among the human population while the H2N2 virus, which was present between 1957 and 1968, vanished upon the emergence of H3N2, which caused the 1968 pandemic. The H3N2 strain continues to circulate today.

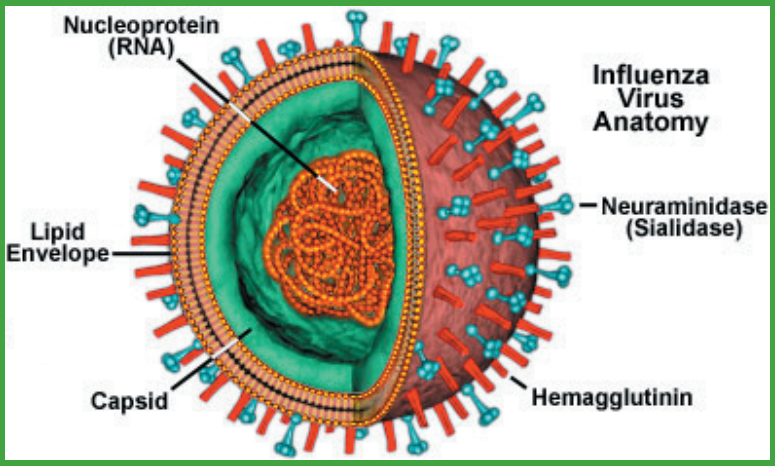
Influenza type B viruses are not categorized by subtypes. They can infect humans and are capable of causing human epidemics though not pandemics. Accordingly, influenza type B strains are included each year in the influenza vaccine. Unlike influenza A subtypes, influenza B strains are only capable of antigenic drift. Influenza type C, which is also not divided into subtypes, poses only a mild threat of illness to individuals and thus is not significant in terms of public health.

The Fowl Truth About Avian Influenza

Birds are infected solely by influenza A and are subject to all subtypes of influenza A, though the most prominent subtypes are H5, H7, and H9, with each potentially having 9 distinct N antigenic types. Although feral aquatic birds are natural hosts for influenza A viruses, they typically do not get sick themselves (there was, however, an outbreak of H5N1 among migratory and other wild birds in China in May 2005). Feral aquatic birds often spread the virus to other birds by shedding the virus in their saliva, fecal matter, and nasal secretions. Recent evidence collected by the World Health Organization indicates that the increased incidence of shedding among certain birds has heightened the risk of contamination to other birds and species.

Domesticated birds are particularly susceptible to viruses of H5 and H7 subtypes, both of which can be classified as low pathogenic and high pathogenic. The level of pathogenicity bears directly upon the mortality rate with high pathogenic avian influenza virus causing the death of 90-100% of infected poultry. Pathogenicity is determined in part by the presence of arginine and lysine at the cleavage site of the H molecule. The susceptibility of the H molecule to specific enzymes found within certain cells that break down protein determines how dangerous the virus is and what tissues it will infect.

Avian influenza outbreaks in poultry generally result in the slaughter of millions of birds. In 1997, when Hong Kong's



This spherical virus is responsible for causing influenza.

poultry population was stricken with the H5N1 strain of avian influenza, health officials there ordered the destruction of more than 1.5 million birds. In 2003, due to a devastating outbreak of avian influenza subtype H7N7, 30 million out of a total population of 100 million birds were killed in the Netherlands. In 2004, 19 million birds were culled in British Columbia because of the spread of the H7N3 strain of the virus. Indeed, the list of nations that have suffered major outbreaks of avian influenza goes on and on. The United States has not escaped the fowl plague. In 1983 and 1984 avian influenza resulted in the destruction of 17 million birds, costing the poultry industry, consumers, and taxpayers $65 million.

Avian to Human Transmission of H5N1

Considered to be intermediate hosts, domestic fowl serve as the conduit for avian influenza from wild aquatic birds to humans. Avian influenza transmission from domestic poultry to humans is similar to that of human influenza transmission among humans, occurring primarily through inhalation of infectious droplets or fomite contact, though other routes may exist. Clinical manifestations of avian influenza among infected patients depend on the subtype. In H7 infected patients, conjunctivitis appears to be a dominant characteristic with higher viral loads in the eye than in the pharynx. By contrast, in avian influenza viruses of the H5N1 subtypes, diarrhea is a frequent occurrence, suggesting that human feces are a possible source of transmission. In the latter subtype, there is no evidence of conjunctivitis and only minimal evidence of rhinorrhea.

Thus far, quarantine and depopulation of affected flocks has helped limit the potential for widespread avian influenza infection in human beings but has not totally eradicated the risk to human health. As of September 2005, there have been 116 documented human cases of H5N1 influenza. The catastrophic ramifications of this cross species contamination have spurred scientists to evaluate the imminence of a flu pandemic.

Serological Studies

A cohort study, conducted by Bridges et al. and reported in the *Journal of Infectious Diseases*, examined serum samples of Hong Kong poultry workers and government workers who were involved in culling operations after the 1997 outbreak of H5N1 that resulted in 18 human cases of highly pathogenic avian influenza. Seeking to detect H5-specific antibody, the researchers employed a microneutralization assay followed by a Western blot assay that was performed at the Centers for Disease Control and Prevention.

The study revealed that poultry workers and government workers who were involved in efforts to depopulate the poultry had higher H5 seroprevalence rates than those not exposed to infected human patients and those with low levels of poultry exposure. Government workers had H5 seroprevalence rates of 3%, which is almost equivalent to the rate of 3.7% among health care workers who cared for H5N1 stricken patients. Poultry workers had H5 seroprevalence rates of 10%, similar to the rate of 12% found among members of the same household as infected patients. Not surprisingly, the study noted an increased risk for viral amplification specifically among those working in live poultry markets where butchering occurred. Although none of the 18 reported human cases were part of the cohort, the numbers indicate that "a substantial number of mild or asymptomatic infections occurred in these occupationally exposed populations," thus making this group important in evaluating the risk of cross species transmission of avian influenza.

A similar serological study was conducted thereafter by Puzilli et al. that examined avian to human transmission of highly pathogenic avian influenza H7N1 and low pathogenic avian influenza H7N3 in Italian poultry workers during an outbreak of influenza in poultry from 1999 to 2003. The seropositivity rate in the collected samples from exposed workers was 3.8%, which confirmed the findings of the survey by Bridges et al.

How then does limited exposure in certain high-risk occupations translate into a pandemic disease that could threaten the entire human population?

Mixing Vessels

All influenza viruses have the ability to mutate. Accordingly, strains can emerge for which humans have no preexisting immunity (antigenic shift), thereby heightening the risk of person to person transmission and creating the very real possibility of a new pandemic virus. Moreover, swine and humans may serve as mixing vessels for mammalian and avian influenza viruses. The Indonesian government recently confirmed that a large percentage of their pig population, though asymptomatic, tested positive for avian influenza (H5N1) virus. Given that pigs can harbor both bird and human flu viruses, they can become a mixing vessel for a new strain of avian influenza that can readily infect humans. Consequently, pigs must be closely monitored - particularly because pigs and poultry are often raised within close proximity to each other. Likewise, with increased mobility among the human population coupled with the global growth of the poultry population, humans may assume the role of mixing vessel for the reassortment of genome units of avian and human influenza. Should that occur, widespread human to human transmission will be realized.

A human pandemic of avian influenza may be impossible to prevent, but understanding the dynamics of the virus and the modes of transmission are key to the establishment of a line of defense. Monitoring live bird markets to ensure that chickens are kept away from other birds and altering farming practices so that pigs and poultry are separated are important preventative measures. Instituting such agricultural protocols, however, will be a difficult task in the poor countries of Southeast Asia. Therefore, public education about poultry handling and food preparation in those nations is vital.

Richer nations must likewise do their part. They must invest the necessary money to aid pharmaceutical companies in the mass production of anti-viral agents that can be administered not only orally, as is presently the case, but intravenously as well, which will assist with the speed of absorption. Moreover, wealthier nations must insure that there are a sufficient number of well-funded laboratories ready, willing, and able to immediately pursue development of a new vaccine in the advent of the mutation of the avian influenza virus. The United States has recently taken the first step. Other nations must follow suit. Ultimately, these actions by the richer nations of the world must be taken not only for the benefit of their populations, but for the benefit of all persons in need.

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Math in the new Millennium

By Negar Dolatabadi

The Clay Mathematics Institute recently selected seven open problems in mathematics as the *Millennium Problems*. These classic problems, which have resisted solution for decades, were selected on the basis of their significance in mathematics and their application to a variety of fields. The Institute announced a one million dollar prize for the solution to each problem, with the goal of promoting interest in mathematics.

Resolution of these problems is important to mathematics not only in furthering interest, nor for the simple purpose of garnering a mathematical proof, but also to advance mathematics itself, for often the significance of the mathematics discovered *while* researching such problems surpasses that of the specific problem for which they were developed!

The descriptions below were written in close consultation with the Clay Mathematical Institute official problem descriptions and through interaction with experts in the field. The statements made are by no means this writer's "discovery", nor are they written solely based on the author's knowledge of the problems. We encourage those who are interested in further information on the problems to refer to the Clay Math website:
http://www.claymath.org/millennium

Riemann Hypothesis

The Riemann Hypothesis has been open for over a century and is one of the most famous unsolved problems in mathematics. First formulated by Bernhard Riemann in 1859, this problem involves the distribution of the zeros of the Riemann zeta function $\zeta(s)$, a complex-valued function defined for all $s \neq 1$. This function has certain so-called "trivial" zeros for negative even integers ($s=-2,-4,-6,...$); the Riemann Hypothesis makes a strong statement about the remaining (non-trivial) zeros of this function: every nontrivial zero of the Riemann zeta function has real part $\frac{1}{2}$.

The traditional formulation of the Riemann Hypothesis somewhat obscures its relevance to number theory, for the location of the zeros of the zeta function is deeply connected with the distribution of prime numbers. Thus, the simple question of where the zeros of the zeta function occur has profound applications to the field of number theory.

Hodge Conjecture

The following description of the Hodge Conjecture is the official problem description given by the Clay Mathematics Institute:

"In the twentieth century, mathematicians discovered powerful ways to investigate the shapes of complicated objects. The basic idea is to ask to what extent we can approximate the shape of a given object by gluing together simple geometric building blocks of increasing dimension. This technique turned out to be so useful that it has been generalized in a variety of ways, eventually leading to powerful tools that enabled mathematicians to make great progress in cataloging the objects encountered in their investigations.

"Unfortunately, the geometric origins of this procedure of gluing pieces together procedure became obscured during this process of this generalization, and it became necessary to add pieces that did not have any geometric interpretation. The Hodge conjecture asserts that for particularly nice types of spaces called projective algebraic varieties, the pieces called Hodge cycles are actually (rational linear) combinations of geometric pieces called algebraic cycles." A solution to the Hodge Conjecture would thus close a significant gap in our understanding of algebraic varieties, the central object of study in the field of algebraic geometry.

Poincaré conjecture

Formulated by Henri Poincaré in 1904, this conjecture deals with the characterization of the three-dimensional sphere among all closed 3-manifolds.

An n-manifold is a shape that, around each point, looks like the n-dimensional Euclidean space; for example, a circle is a 1-manifold, and the 2-sphere (the surface of a ball) and the 2-torus (the surface of a donut) are 2-manifolds. The 2-sphere has a distinguishing characteristic among the closed 2-manifolds: it is the only one for which every loop on it can be continuously collapsed to a point without pulling the loop off its surface on any other closed 2-manifold (it is possible for a loop to get wrapped around the surface in such a way that it can't be collapsed). The Poincaré Conjecture asks if this characterization holds for closed 3-manifolds as well: among all closed 3-manifolds, is the 3-sphere the only one with this property?

In late 2002, Grigori Perelman of the Steklov Institute of Mathematics in Saint Petersburg announced that he had shown the conjecture to be true, by proving a much more

"Conjecture de Poincaré" by Stéphane-Alexandre Dani
This and his other works can be found at: http://www.art-dani.com/

general conjecture known as Thurston's Geometrization Conjecture. According to the experts in the field, Perelman's proof is still being checked. One of the key people in this process is Richard Hamilton of Columbia University. Perelman's findings are considered to be the most significant work done on the Poincaré Conjecture thus far.

Navier-Stokes Equation

Perhaps you have considered the turbulence of a plane during a flight, or you have felt the breeze while on a sailboat. What you might not know is that in both cases, the movement of the air is believed by many mathematicians to be described by a set of equations called the Navier-Stokes Equations**.** Named after Claude-Louis Navier and George Gabriel Stokes, who formulated them in the 19th century, these equations describe the flow of fluids and air. Navier-Stokes equations establish how changes in pressure and dissipative viscous forces between the molecules of the medium result in a change in momentum of the particles of the fluid or gas. In other words, these equations embody the balance of different forces applied on an area of gas or fluid.

The Navier-Stokes Equations have tremendous applications in the description and modeling of a wide variety of physical phenomena; including ocean currents, blood flow, and the design of air crafts, yet no answer is known to the most basic mathematical question that one could pose about such a system: "Do smooth, infinitely differentiable initial conditions always lead to smooth solutions?" This Millenium Problem asks for a proof that smooth initial conditions *do* always lead to smooth Navier-Stokes solutions.

Yang-Mills existence and mass gap

Quantum Mechanics describes the world of atomic particles in much the same manner as Newton's laws of classical mechanics describe the macroscopic world. Almost half a century ago, Yang and Mills introduced a remarkable new framework for quantum mechanics: Quantum Yang Mills Theory, which attempts to explain the physics of subatomic particles and their interactions [1]. Arguments at the rigor level of theoretical physics show that Quantum Yang Mills Theory entails what is known as a "mass gap," in which certain quantum particles have positive masses, even though classical waves travel at the speed of light. This property was discovered by experimental physicists and confirmed by computer simulations; however, the mathematics of the situation are poorly understood [1]. This Millennium Problem asks for a mathematically rigorous treatment of Quantum Yang Mills Theory and the mass gap; that is, formal mathematical verification of what is believed, theorized, and observed to be the case.

P vs. NP

Stephen Cook of the University of Toronto and Leonid Levin of Boston University formulated this computation theory problem independently in 1971. Ever since its announcement, it has held the attention of both mathematicians and computer scientists.

The **P vs. NP** problem deals with the contrast between P, a problem that is solvable in polynomial time, and NP: being able to verify in polynomial time that a solution to the problem is correct. The ultimate question is whether P=NP. We know that every P problem is an NP problem; the P vs. NP question asks whether every NP problem is a P problem. In other words: given any question whose answer can be checked easily, is it always possible to find the solution easily? For example, given a large whole number X, we might be asked to factor X as a product of whole numbers greater than one. If the factors are known, this can easily be checked by multiplication (so it is an NP problem), but *finding* those factors seems to be a much more difficult task, perhaps not doable in polynomial time; thus it is not clear whether this is a P problem**.**

For such questions, no one has managed to prove (or disprove) that any NP problem is so hard as to be impossible to solve by a computer in an efficient manner. In the modern digital world, this problem has significance to a wide range of issues, from efficient algorithms to digital security.

Birch and Swinnerton-Dyer Conjecture

An *elliptic curve* is a specific type of curve that is of central importance in the field of algebraic geometry. Like the Pythagorean Theorem, the set of all rational points on a given elliptic curve is of particular interest. In particular, for each elliptic curve, we can consider how many rational points lie on the curve, which is measured by the "rank" r. If $r=0$, this means that there are only a finite number of rational points on the curve, while higher ranks indicate larger and larger infinities of such points.

To each elliptic curve, we can assign what is called an L-*function* "L(s)", which can be expanded in a Taylor series in (s–1). The Birch and Swinnerton-Dyer Conjecture states that the L-function can sense the rank of the curve's group of rational points. It asserts that the rank of the group of rational points over an elliptic curve E is reflected in the order of zeros of the associated L-function, L(E, s) at s=1. That is, if we expand L in powers of (s-1), then the first non-zero term of the resulting Taylor series will be $(s-1)^r$. In other words, the rank of the group determines the power of the dominant term in the Taylor series, and vice-versa.

The Birch and Swinnerton-Dyer conjecture has been proven only in special cases. However, there exists extensive numerical evidence for the truth of the conjecture.

In 1999 Andrew Wiles and Richard Taylor proved the Taniyama-Shimura theorem to prove Fermat's last theorem. Their results also apply more generally to all elliptic curves; however, no substantial advances have been made for curves with rank greater than 1.

Reference

1. The Clay Math institute official problem description website: www.claymath.org/millennium

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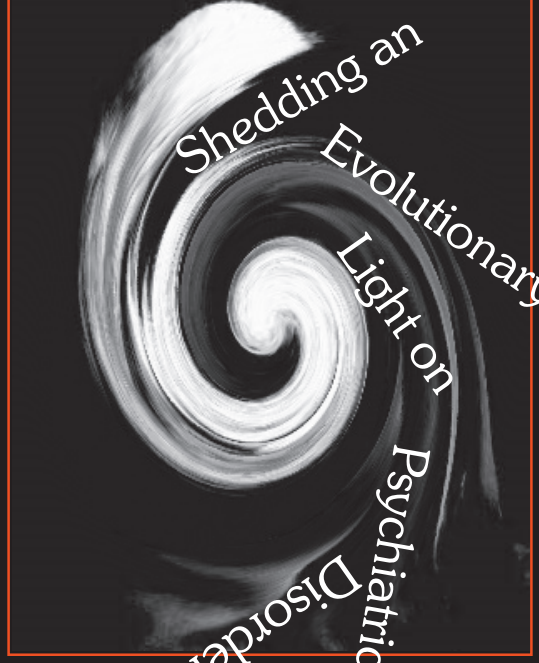
Negar Dolatabadi is a senior Applied Mathematics major at the Fu Foundation School of Engineering and Applied Sciences. She is very excited to have been a part of CSR this year!



By Robert Heller

Charles Darwin returned to England in 1836 from his five-year voyage on the *H.M.S. Beagle* at the age of 27. He was on the cusp of one of the most extraordinary careers in the history of science; however he was also quite a wreck. The globally known brilliant thinker became an infamous recluse upon his return to civilization. His ailments are cited as "constant attacks" that included heart palpitations, shortness of breath, trembling, chest pains, insomnia, bouts of nausea, and "swimming in the head." His hermit lifestyle left him confined to his home in Kent, which he would leave only when necessary, in a carriage with darkened windows. Darwin never learned the brand of the malady from which he suffered; however, he was quick to recognize the positive affects it had on his research. Before he died, he wrote that, "ill-health, although it has annihilated years of my life, has saved me from the distraction of society and its amusements." Today, it is generally agreed upon that Charles Darwin was afflicted with Panic Disorder with Agoraphobia.

Time magazine's Person of the Century, Albert Einstein, was born in Germany in 1879. He did not speak until he was 4 years old, and was unable to read until the age of 7. This genius among geniuses was described by one of his teachers as "mentally slow, unsociable, and adrift forever in foolish dreams." He was infamously distractible, unorganized and messy, socially awkward, and yet infinitely creative. Regarding his unorthodox ways, Einstein himself said, "He who joyfully marches in rank and file has already earned my contempt." Today it is believed that Einstein's unconventional nature can be attributed to what is known as ADHD, or Attention Deficit Hyperactive Disorder.

Both of these brilliant minds were profoundly affected by abnormalities that fall into the realm of psychiatric disorders. The term 'disorder,' however, might be somewhat of a misnomer. Emerging research is investigating not only the genetics behind these psychiatric conditions, but the beneficial aspects of them as well.

ADHD is a behavioral syndrome marked by inattention, distractibility, restlessness, inability to sit still, and difficulty concentrating on one thing for any period of time. It occurs in roughly 5% of all school children and can persist into adulthood.[1] Treatment usually entails counseling and/or prescription medication. There are more than 20 genetic studies providing evidence that ADHD is, at least in part, an inherited disorder. Family studies of ADHD have consistently supported a strong familial tie (see figure 1). They have identified a two- to eightfold increase in the risk for ADHD in parents and siblings of children with the condition.

Studies of twins have also been used in order to fully determine the extent of its heritability, or the degree to which ADHD can be attributed to genetic factors, as opposed to contrast to environmental ones. Heritability is given on a scale of 0 to 1; 0 meaning that the trait is not genetic at all and 1 meaning that it is entirely genetic. Based on these studies, displayed in figure 2, the mean heritability for ADHD was shown to be 0.77.[2] As a frame of reference, the habitability of height has been studied extensively and has a value of 0.75.[3]

Recent studies sponsored by the National Institute of Mental Health point to two parts of the brain that are abnormal in people with ADHD. One is the basal ganglia, a pair of nerve clusters in the middle of the brain involved in routine behaviors. The other is the right prefrontal cortex, involved in planning, organizing, attention span, impulse control, and control over responses to sensory stimulations. Studies have identified many of the cognitive abilities dependent on the prefrontal cortex to also be related to changes in the dopamine innervation in this area.[4] Single photon emission computed tomography (SPECT), a method of brain imaging using gamma rays, has shown that the dopamine transporter is elevated by approximately 70% in people with ADHD. This evidence is in concordance with genome scan data recognizing the 7-repeat allele of the human dopamine receptor D4 gene (DRD4) to be the gene most strongly implicated in ADHD.[5]

Panic Disorder is another psychiatric condition, characterized by repeated bouts of intense fear that seem to come out of nowhere. The body has a natural response to danger known as "fight or flight," in which the autonomic nervous system is stimulated in response to a person perceiving a threat or danger. For people with Panic Disorder (PD), this autonomic response is triggered for no apparent reason. The symptoms are similar to those of a heart attack, and include: shortness of breath, tachycardia, chest pain, nausea, vomiting, choking sensations, and thoughts of dying. This commonly leads to changes in behavior, such as the one seen in the life of Charles Darwin. This development associated with PD is called agoraphobia, in which people avoid social and other situations out of fear. The preferred means of treatment generally includes counseling and medication.

Clinicians have been aware of the disproportionate concurrence of PD with other medical conditions for quite a while. However, until recently, little progress had been made as to the cause of this phenomenon. Myrna M. Weissman of Columbia's College of Physicians and Surgeons is one of the leading researchers in the genetics of panic disorder. Weissman conducted two studies consisting of full genome scans of 19 families in her first study, followed by one with 41 families in a subsequent study. She found striking and consistent evidence for a susceptibility gene on chromosomes 13 and 22. Chromosome 13 showed particularly impressive evidence of linkage, with a maximal LOD (logarithm of odds) score of 4.6.[6] In other words, the probability of chromosome 13 being linked to PD is approximately certain, with a value of 1.

Numerous family and twin studies, which are of utmost utility in the field of genetics, have been conducted for PD as well. Six family studies using direct interviews of relatives and two family history studies have been independently conducted; all indicated that PD is highly familial. These studies found an eightfold median relative risk of PD in first-degree relatives of probands (first affected and diagnosed individuals in a family) with PD in comparison to relatives of controls. Five twin studies of PD have been conducted as well. These studies indicated a definite genetic contribution and a heritability score in the range of 0.46 to 0.62.[7]

ADHD and PD are just two of the many psychiatric conditions for which genetics is being found to play a major role. One of the primary implications of these findings is the possibility of an evolutionary process taking place, and the question of whether certain psychiatric conditions are favorable or disadvantageous.

The scientific community is beginning to examine ADHD from a novel perspective, shifting focus to the positive aspects as opposed to the renowned negative ones. These beneficial effects can include high energy, empathy, quick wittedness, creativity, a speedy grasp of the big picture, and a tremendous display of enthusiasm. This accounts for the simultaneously exasperating and endearing nature of people with ADHD.

While a mind flitting from one thought to another may not be advantageous when trying to master material for a biology test, nonlinear minds can excel at combining thoughts and ideas in innovative ways. "While students are learning the details of photosynthesis, the ADHD kids are staring out the window and wondering if it still works on a cloudy day," writes Honos-Webb, a psychologist at Santa-Clara University.[8] JetBlue Airways founder and CEO David Neelman is famously frank about his ADHD, crediting it with his creativity and "out of the box thinking" that allowed him to pioneer several discount airlines and the e-ticket. Thom Hartmann, an expert and author of numerous books on the disorder, writes that people with ADHD are "our most creative individuals, our most

extraordinary thinkers, our most brilliants inventers and pioneers."[9] In his book, Hartmann also posits that people with ADHD may also carry genetically coded aptitudes that were at one point, and may still be, essential for human survival and that contribute richness to the culture.

Randolph Nesse, an evolutionary psychiatrist at the University of Michigan, has been studying psychiatric conditions within an evolutionary context for over two decades. Nesse believes in the importance of a complete biological explanation incorporating both proximate and evolutionary explanations for psychiatric conditions. He argues that such studies are essential in order to better define the border between normal and pathological, to help to explain why certain disorders are so common, and to provide a basis for sensible decisions about when different pharmacological manipulations are likely to be helpful or harmful. Ideally, Nesse writes, "evolutionary considerations should provide a conceptual framework within which the [physiological] mechanisms can be better understood, and [these] findings should provide tests of evolutionary hypotheses."[10]

Nesse argues that the panic attacks associated with PD are less a problem of maladaptation than a case of too much of a good thing. A certain amount of anxiety is good for people, and as Nesse contends, is "part of a highly evolved and adaptive defense mechanism and protects us from getting too close to cliff edges or hungry lions, just as the immune system protects us from bacteria."[11]

PD and ADHD are not the only disorders that scientists are looking at in a new light. Nesse and his colleagues have been examining nearly all diagnosable psychiatric conditions in an evolutionary context. This includes depression, which may be beneficial in unpropitious situations in which effort toward a goal may be likely to result in danger, loss, bodily damage, or wasted effort. In such situations, pessimism and a lack of motivation may give a fitness advantage by inhibiting certain actions, such as: futile or dangerous challenges to dominant social figures, actions in the absence of a crucial resource or a viable plan, efforts that may cause bodily damage, and events that might agitate a "currently unsatisfactory major life enterprise when it might recover or the alternative is likely to be even worse."[12]

It is important to note that psychiatric disorders are complex disorders in which simple patterns of inheritance generally have not been found. It is likely that a host of genetic risk factors interact with each other and the environment to produce clinical psychopathology. However, this does not negate the proven genetic contribution, thus making these psychiatric disorders possible selectable traits subject to evolution.

What are the implications of the numerous positive aspects of these heritable psychiatric conditions? One certainly must reconsider their label as a 'disorder' whose symptoms should be treated and annihilated. Natural selection shapes predators, bacteria and viruses, and other humans, all of whom may benefit from harming us. To protect ourselves from these dangers, natural selection has shaped a wide variety of protective defenses such as pain, fever, nausea, and anxiety. These are not causes of disease, but the body's ways of preventing damage; yet because they are painful and associated with problems, we often confuse them with diseases themselves.[13]

This raises the issue of determining a point at which the negative aspects of a condition outweigh the positive ones, and thus require the condition to be treated. This task is obviously quite daunting due to the apparent uniqueness of not only each psychiatric condition, but each individual, as well. It seems the present rule of thumb amongst physicians and psychologists is to treat as soon as the negative symptoms of a condition are recognized, without analyzing the positive ones.

At this point in time, there is a great deal of research that still needs to be done regarding an evolutionary approach to medicine. This is perhaps more important than ever as we are amidst what appears to be an age of pharmaceuticals. Recognizing when it is appropriate to use these drugs seems to be as crucial as their creation, for few of us would, in retrospect, suggest medicating Einstein or Darwin, both of whom were obviously quite adept at reaping the benefits of their so called "disorders".

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Figure 1 Family studies in attention-deficit/hyperactivity disorder (ADHD).[14]

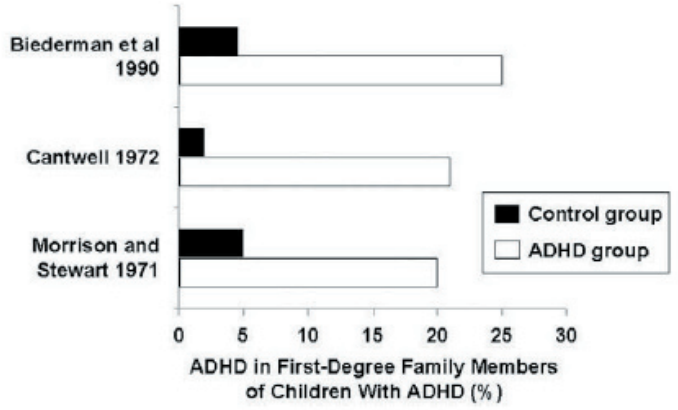
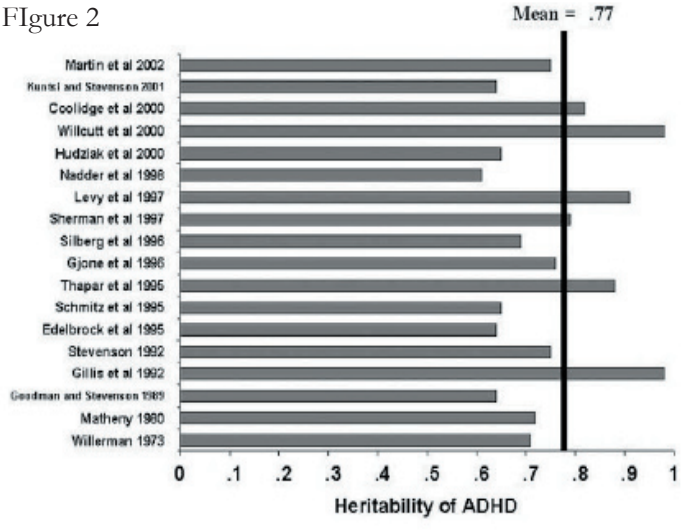


FIgure 2



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Neuropathic Pain

By Christopher Schell

Visualize a time when you were cooking or ironing your clothes. Since you were either not paying attention or just caught up in a Red Sox vs. Yankees' game, you burnt yourself. When you were burnt, your body sent a signal to your brain that told you to withdraw from the excruciating heat. Now imagine having that same throbbing, burning pain at a constant rate without ever having touched a stove or an iron in the first place. In this instance, the pain is no longer an immediate effect, but a chronic one known as neuropathic pain.

A Psychological Experience

Pain is a language that our bodies use to signal that something is either wrong or of an urgent matter[1]. It is not only physical, but also psychological in that it is closely tied to our minds and emotions; the way we interpret how we feel is in essence how pain is expressed. This relates to the fact that the brain holds such power over the body. If, in the process of receiving a burn, your brain did not interpret the burn as a hurtful feeling, you would not have pulled away and therefore, you would not have felt "pain." Pain is subjective and depends on both the situation and the individual (one person does not necessarily experience the same pain as another); that is, pain can not be completely articulated as a physiological experience. It must also be considered as a psychological phenomenon.

Psychology defines four major categories of pain: nociceptive pain, neuropathic pain, psychogenic pain, and visceral pain[2]. Neuropathic pain delivers a feeling of pain even though there is no immediate cause. This dysfunction of the nervous system is the rewiring of the initial system of nerves in the region of prior pain both anatomically and biochemically[4]. During an injury or trauma, there are three different types of pain that the body can experience: immediate, acute, and chronic. In the case of immediate pain, the body might not necessarily feel the pain or have any perception of it, but the brain signals the more instinctual notion of staying or retreating from the "danger" at hand. Acute pain immediately follows the rapid decision made by the influence of immediate pain. In this acute phase, healing mechanisms (biochemical, neuro-adaptational, and volitional) are set in place in order to return the body to its former state. Neuropathic pain is an example of chronic pain, the type of pain that persists after the resolution of acute pain[2].

During injury or trauma, the transducers within the nervous system convert mechanical signals into electrical ones. These signals are then intercepted by pain receptors known as nociceptors which are nerve cells that respond to noxious stimuli (i.e. abnormal tissue conditions and irregular temperatures). These nociceptors then release chemicals such as Bradykinin, Histamine, Prostaglandins, and Substance P, which decrease the amount of pain experienced while they convey the signal through their axons (the tail endings of which send and receive signals) via the neurological pathway of the spinal cord. Also, the nociceptors release endogenous analgesics that can cause pain relief and sedation. From the spinal cord, the electrical signal is then transmitted to the central nervous system (CNS) where the brain interprets the signal as pain. When this process is hampered by the breakdown of the nerves themselves (neuropathy), peripheral neuropathic pain (neuropathic pain of the peripheral nervous system), or central neuropathic pain (neuropathic pain of the central nervous system), the brain begins to interpret messages sent from these nociceptors as somewhat of a "pseudo-signal"[3]. This pseudo-signal mimics nociceptive pain, also known as somatic or acute pain, and the body believes that it has experienced damage[2].

Control vs. Cure

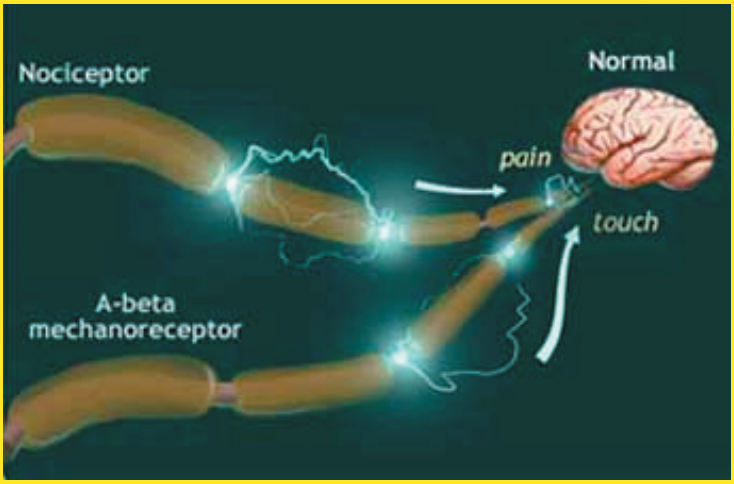
Interpreting the perception of pain is the most important part of solving the issues that relate to pain. Contemporary drugs that treat nociceptive and visceral pain are not necessarily able to "cure" neuropathic pain. For decades, scientists have been confronted with the problem of being able to sufficiently control neuropathic pain and its cause[8]. For example, the Society for Neuroscience reported in 1999 how morphine was normally used for patients with neuropathic pain as an answer to the immediate problem. However, the morphine only acted as an indirect treatment by initiating an opiate receptor on the nerve cells' surfaces that interrupted calcium deposits within the cell (these deposits are thought to influence pain). In short, the largest obstacle currently faced is the complete control of the pain itself.

Pain recognition is an intricate process to understand. As stated by Dr. Richard Blanck of the Neurological Associates of Long Island, neuropathic pain is one "that takes on a life of its own." As a result, both emotional and physical (genetic) characteristics come into play. The degree of pain felt by the patient can be increased or decreased by the person's specific state. For example, a person could have a horrible accident and never feel any pain beyond the acute phase, while another may have a minor headache that can become a major migraine due to that person's mood and current state of mind. This pain that results from mood and state of mind is known as psychogenic pain. Genetics are also important in that someone's genetic make-up might increase their susceptibility to a higher degree of neuropathic pain. Thus each person's case must be considered individually[8].

According to Gary Bennett, a Professor of Neurology and Director of Pain research at Allegheny University of the Health Sciences in Philadelphia, 1.5% of the US population suffers from neuropathic pain, and more than 1.6 million patients suffer from neuropathic conditions other than back pain. Some of these conditions include: diabetic neuropathy, post-herpetic neuralgia, cancer-related pain, spinal cord injury, causalagia or reflex sympathetic dystrophy, multiple sclerosis, phantom (post-amputation) pain, post-stroke pain, HIV-associated pain, and tic douloureux. Regarding these conditions, Bennett says, "typically, the patient experiences a more or less constant burning or dysesthetic pain…painful symptoms characteristically appear first in the toes, then in the rest of the feet, then in the hands, and then in the midline chest."[4]

Current Research: A Promising future

Scientists have developed various ways to alleviate neuropathic pain. One method involves the use of Omega Conopeptides, which act as calcium blockers that regulate the amount of calcium the nerve cell takes in[4]. A study done on an ocean snail of the genus *Conus* found that the venom this snail uses to kill fish can be used



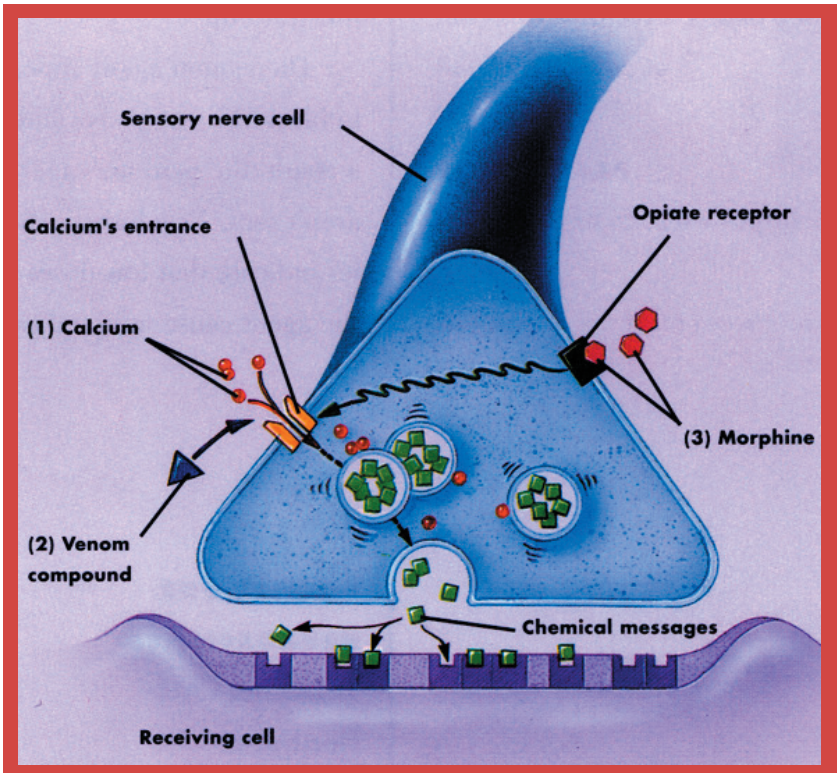
The electrical signal is intercepted by nociceptors and transmitted to the brain, which interprets the signal as pain.
Image from: http://history.nih.gov/exhibits/pain/docs/page_09a.html

to block the calcium entrance on the membrane of the nerve cell and therefore prevent the overabundance of calcium within the cell. Calcium regulates the release of chemicals that nerve cells use to communicate. Knowing this, scientists used a synthetic replica of the venom that works as an obstructing agent against the pathways that calcium follows, disrupting the communication of pain transmitted by the cells[3].

Another study on anticonvulsant medications showed promising results with the use of chronic constriction injury (CCI) rats. The medications were meant to block a type of glutamate receptor known as the N-methyl-D-aspartate (NMDA) receptor. These receptors are signaled to nerves by nociceptive fibers in order to articulate pain. By regulating the amount of receptor produced, the amount of pain is minimized. This animal study undertaken by Gary Bennett and Xie Yikuan took a closer look at demyelination (echoes that travel up and down the axons of the nerves and are caused by the bioelectric depolarization of an impulse) and how CCI rats responded when taking the anticonvulsant medications. The study involved tying a ligature around the sciatic nerves (nerves within the body that enable movement and feeling and that are located in the spine and hip bone) of the hind paws of the rats, thus aiding in demyelination. Two drugs, felbamate and gabapentin (neurontin), were used in this study and each drug was tested based on the amount of withdrawal the rat had from four different stimuli. The stimuli were: heat hyperalgesia (noxious heat to the hind paw), mechanical hyperalgesia (using the point of a safety pin), mechanical allodynia (von Frey hairs), and hind paw guarding. Hyperalgesia is an increased response to a stimulus that is normally painful and allodynia is pain due to a stimulus that does not normally provoke pain. Felbamate was found to be more beneficial than gabapentin, but since felbamate was later found to cause liver failure and aplastic anemia, the use of gabapentin has become more widely accepted. Bennett and Yikuan also attempted a study with specific NMDA blockers such as glycine. Unfortunately, these blockers had a significant side-effect: since NMDA occurs at a high density in the cerebral cortex, drugs that block its receptor can have a major psychological effect. Among NMDA blockers, none are yet ready for clinical use[4].

Gabapentin was also used in a 1998 study involving patients suffering from diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN) which is pain that follows shingles (herpes zoster). In the DPN study, 26% percent of the patients given gabapentin felt a relief of pain compared to the 15% of patients who received the placebo, and this is statistically significant. The PHN study was double blind (both the patient and the administrator of the drug did not know whether the drug was neurontin or the placebo) and involved 229 patients being studied for a period of eight weeks. The study concluded with a statistically significant reduction in neuropathic pain. Sixteen percent of patients were pain-free after taking neurontin compared to the 8.8% percent of patients that were treated with the placebo[5]. Though neurontin has found much success, its successor lyrica (pregabalin) has been found to be even more efficacious than gabapentin. In 2004, lyrica was determined to be more potent than its predecessor. A double-blind study was done on 529 patients who were provided with 150mg-450mg treatments per day. The patients with the lyrica and not the placebo reported a significant reduction in pain and maintained better sleep[7].

In 2005, scientists at the Ann Arbor Healthcare System and the University of Michigan Medical School were able to use gene transfer technology in order to block neuropathic pain. Using a virus known as herpes simplex or HSV (the virus that causes cold-sores and genital herpes), the researchers were able to take a disabled form of the virus and inject it into rats with nerve damage. The drug itself contains a chemical known as glutamic acid decarboxylase (GAD). The HSV acts as a carrier for this gene, which is delivered to the nucleus of the nerve cells near the spine. From there, the gene moves to nerve terminals and spurns the production of GABA, a neurotransmitter that acts as a controlling agent for the nervous system. Dr. David J. Fink, professor of Neurology at the University of Michigan Medical School said, "GABA is the main inhibitory neurotransmitter in the nervous system…it's like a hall monitor for the nervous system; it damps down neurotransmission between cells to keep things quiet." By producing more GABA neurotransmitters, the activity between nerves is controlled to a greater extent and neuropathic pain can therefore be greatly reduced. "If we can block transmission of the signal at the first neural synapse, it will never reach the brain and you won't feel the pain," says Fink[6].



How nerve cells transmit pain with the help of calcium
© 1999 Lydia Kibiuk

In the future, scientists plan to conduct the first phase of experiments on human patients. Current medications are promising, and the associated research has added significantly to our knowledge of pain perception.

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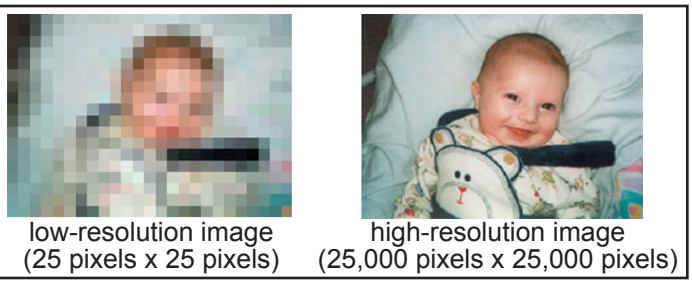
Understanding and Overview and

1. Overview

Imagine an average day in your life. You wake up and go about your daily activities, usually based on a routine you have made from examining things that have happened in your past. However we do not live on auto-pilot, and so this plan will inevitably change in many ways throughout the day due to sensory input that your eyes, ears, nose, mouth, and skin relay to your brain. Now, think about these senses, and especially, how they compare to each other. You can easily imagine a distinct smell or sound alerting you to a certain pleasure or danger you might want to act upon or avoid before you ever see it, but these smells and sounds would have to be quite specific for us to react to them. Most often, our nose, mouth, ears, and skin alert us to some form of stimuli, and then we probe the stimuli with our eyes to understand it. As the cliché goes, "a picture is worth a thousand words". Given the way the human brains work, visual information is much more efficient than our other forms of sensory input in guiding our brain's activities.

With a growing understanding of the properties of light and the advent of computers and monitors, we have standard ways of representing images on monitors through simple file formats that can be exchanged and viewed easily using computers and other forms of technology. These computer files are the "images" that we seek to understand and be able to process. Monitors display their output as separate values for a discrete number of *pixels*, or dots of various colors lined up horizontally and vertically that fill the rectangular space of the monitor's display.



low-resolution image (25 pixels x 25 pixels)

high-resolution image (25,000 pixels x 25,000 pixels)

This image of a baby, shown at a very low resolution (a small number of pixels per edge) and a very high resolution (a large number of pixels per edge), illustrates the way pixels come together to visually represent a scene. The high and low resolution images are each made of blocks of color, but the blocks are much smaller and blend in with each other in the high resolution picture to very accurately portray a visual scene - as if we are seeing it in reality.

Electrical engineering includes the study of mathematically manipulating images and image or movie files on computers; this field is called *image processing* or *computer vision*; it is closely tied to artificial intelligence because our intelligence processes and our brains are dependent on visual information. Currently, researchers are working on image representation techniques, image compression techniques, and various image processing techniques including systems of image classification for tasks such as computerized camera monitoring, automatic video retrieval, labeling, and classification, and image search engines (such as Google Images). Understanding the mathematical representation of images is crucial to success in these fields.

2 Mathematical Representation of Images

Mathematically, an image is defined as a two-dimensional matrix of pixels, each with an assigned value taken from a predefined range (for example, the set of primary colors).

2.1 Pixels

Each pixel has a coordinate (x,y). The set of pixel coordinates is then

$$\{(1,1), (1,2), (2,1), \ldots, (x_r, y_r)\}$$

…where x_r is the resolution of the image horizontally, and y_r is the resolution of the image vertically. An example is the common resolution of a computer monitor: 1280x800. This means that your monitor has $x_r = 1280$ pixels in each horizontal row and $y_r = 800$ rows from top to bottom.

The image file assigns a value (i.e. color) to every coordinate in the set of pixels. Essentially, then, an image is a discrete function f(x,y) defined at each (x,y) as one value out of the set of possible pixel values.

2.2. Color Spaces and Grayscale Intensities

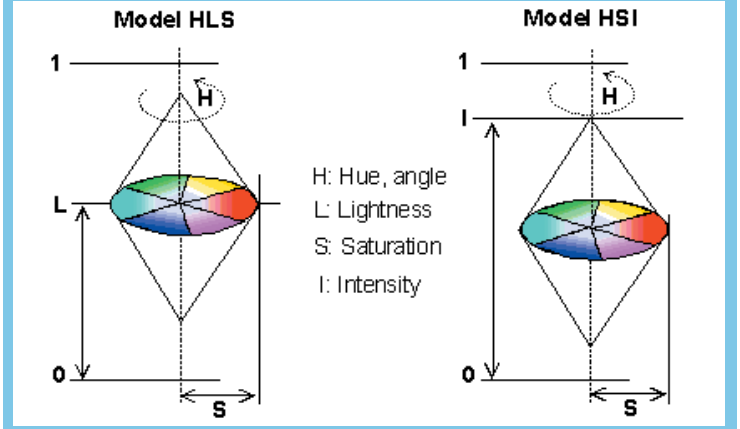
The value that each pixel is assigned by the image comes from a pre-determined range. This value range is called the *color space* if the image is a color image, or the *grayscale intensity range* if the image is black and white. By studying the human eye and the properties of light, we have developed accepted models for color formation, which make up our color spaces. One of the most common of these color spaces is the RGB space, short for red, green, and blue: the primary colors. This color space assumes all colors are made up of varying amounts of red, green, and blue, so each pixel can be assigned one of those colors. White, the absence of color, is also an allowable value, typically defined as 0. If the value for red, green, and blue is the maximum for the pixel, the pixel will be black, or all colors. The maximum value for the pixel determines the number of values in the pre-determined value range. For example, an RGB color space with 256 values will have 256 colors equally spaced between white and red (or green or blue); any of which can be the red (or green or blue) component of the pixel's color value. The grayscale intensity range operates under the same principle, but has only one component, which ranges from light to dark in grayscale, equally spaced from zero intensity up to the maximum in the intensity range.

There are many other color spaces that can be used to provide varying levels of accuracy. One particularly useful color space is the HSI space, which stands for hue, saturation, and intensity. Like the RGB space, the HSI space has 3 components, but these components are not strictly base colors, they are 3 measures of image perception that are actually more representative of the physical actions of the eye. In this color space, hue represents the color tone, and the saturation and intensity then move this tone around the spectrum. Another common color space is the CMY color space, which stands for Cyan, Magenta, and Yellow. These are related to the RGB values, but C = 1-R, M = 1-G, and B = 1-Y. This is useful for printers, as it allows the background to be white (i.e. the color of the paper) and only prints the markings that are distinct from the background, thus saving ink.

The pixel range and value range of any picture can be rescaled mathematically. The pixel range is commonly referred to as the resolution of the image, and shortening or enlarging this range requires averaging values over areas to delete pixels, cut down the pixel size, or enlarge the pixel size.

Previously, we discussed the representation of images as a function f(x,y) for pixels (x,y) in the pixel set. For a grayscale image, the intensity represents the value for the function, and is the

Variations of the HSI color space



(C) 2002 SEII EM-MI Image from http://semmix.pl/color/models/emo18.htm

Processing Images Techniques

By Rustam Salari

only component. However, a color image has multiple functions associated with it, one for each component of the color space. For example, in an RGB space, an image would have 3 functions associated with it, $f_r(x,y)$, $f_g(x,y)$, $f_b(x,y)$, representing the value at each pixel of red, green, and blue that would be mixed to create the final value f(x,y) for the pixel.

3. Getting Information from Image Pixels

There is a great body of literature written on the mathematical representation of images and the problems and concerns associated with that process; but equally important is the processing of the images once they have been appropriately represented. As we saw previously, the image's information is stored in pixels. The pixel values are thus what we need to focus on to understand the processing of the image.

3.1. Pixel Neighbors

Because the pixels of an image blur together to give realistic visual information to the human eye, a pixel is very closely tied to its neighbor pixels. For the pixel of an image at coordinates (x,y), there are a few commonly used sets of neighborhood pixels.

$N_4(p) = \{ (x+1, y), (x-1, y), (x, y+1), (x, y-1) \}$
(4-neighbors)
$N_D(p) = \{ (x+1, y+1), (x-1, y+1), (x+1, y-1), (x-1, y-1) \}$
(diagonal neighbors)
$N_8(p) = N_4(p) \cup N_D(p)$
(8-neighbors)

Rescaling the pixel value ranges or color space/grayscale intensity ranges often depends on these neighborhood sets, as do many image processing and compression techniques.

3.2. Color/Intensity Histograms

One of the simplest yet most important image processing techniques is a histogram of the color or grayscale intensities found in the image. A histogram function is a discrete function $h(r_k)$

$h(r_k) = n_k$

…where r_k is the kth level in the color space or grayscale intensity range and n_k is the number of pixels in the image that have value r_k.

As we can see from its definition, a histogram function is a measure of how many times each possible value occurs in a set of values (in this case, an image). If there are an infinite number of possible values, this function loses meaning, and so a histogram function requires a discrete, or finite, set of values, which images obviously have. Histograms are very useful for matching or identification purposes, especially on localized regions in images, as distinctive histogram values would have to be reproduced in similar images.

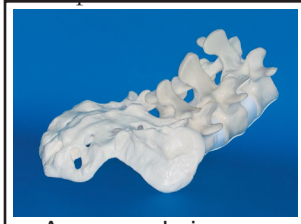
3.3. Distance Measures and Gradients

Distance is a concept that can easily be applied to visual information. Because of this, mathematical distance measures are very useful tools in image processing. A mathematical distance measure is a function on a set that obeys three properties:

I. $d(x,x) = 0$ and $d(x,y) \geq 0$ (distance is non-negative)
II. $d(x,y) = d(y,x)$ (distance is independent of direction)
III. $d(x,z) \leq d(x,y) + d(y,z)$ (distance obeys triangle inequality)

While the most common distance measure is Euclidean distance, which obeys arithmetic rules on the real number system, there are many other distance measures that can be very useful. For example, the *Mahalanobis* distance measure is a measure of "how many standard deviations away" two points are within a probability distribution. While visually, the *Mahalanobis* distance on a plot of a distribution is counter-intuitive to our notion of distance, it functions very effectively in problems involving distributions that require a distance measure.

To understand images, which represent visual information as spatial objects that we hope to mathematically define, we must have some method of finding objects in the images. Intuitively, objects can be found by their edges; this is an important first step in sorting visual information. The most common method to find the edges of an object is by taking a *gradient* or *difference function*, which measures the change in the pixel value from some set of neighboring pixels. For an appropriately defined gradient function, a large value will denote a pixel that could be the edge of some object. We know the pixels near it are very different colors, so there are probably multiple spatial objects near that pixel in the image.



An example image

Pixels of large value change (edges)

4. Image Segmentation and Pre-Processing

Images of the same general type can often be wildly different in structure. The similarities that cause the images to be of the same general type might only be noticeable in certain regions of the image, or on the basis of a few distinct features. If this is true for a particular image processing problem, a common strategy is to first segment the image, or separate the image into regions based on the edges of objects in the image. The regions that contain the valuable information for our particular processing problem can be identified and then processed, making the processing smaller in scale and more refined. This type of technique can be "learned" by the computer by taking a variety of sample images of a similar type and looking for values in corresponding regions that seem to be distinctively similar.

Other pre-processing techniques can help make image processing and comparison more effective. Some common pre-processing techniques, including the smoothing and sharpening of the image, are designed to help separate noise from the true image. For example, by enlarging the contrast between colors in the image, we can see a more noticeable separation between noise pixels and the original pixels of the image. If, instead, we wish to make the noise pixels in an image less noticeable, we can smooth the image by averaging the pixel value with its neighboring pixel values.

Histogram equalization is a sharpening technique that can provide contrast in an image with many pixels whose values fall within a small range (for example, a picture of the sun has most of its pixels

The RGB color space

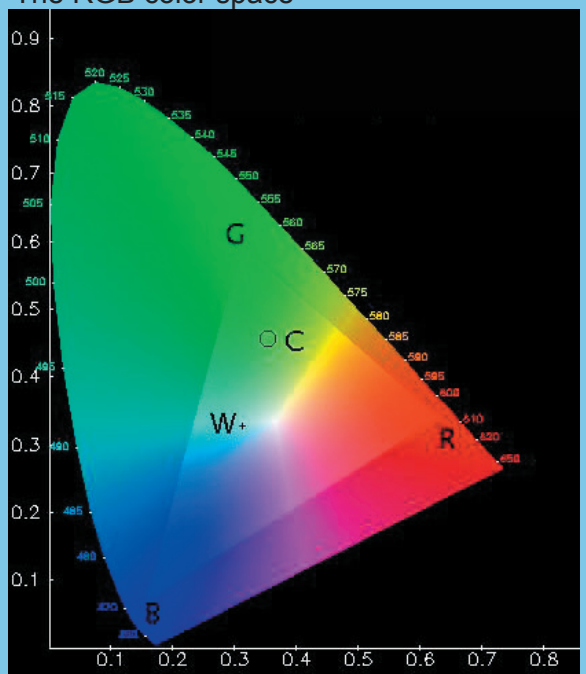


Image from http://dx.sheridan.com

valued shades of red). If an image is very dark in color, most of the pixels will have large values and will be within a proportionally small range of the entire color spectrum. If, then these large values were given a proportionally larger contrast, and the smaller values that are more spread out are given proportionally less contrast, the image will appear sharper. From these examples, we see that not only is image pre-processing an integral part of image processing in general, but is very specific to the task and is difficult to generalize.

5. Image Classification

One of the central problems of image processing is the classification of images and intelligence techniques that can be based on these classifications. To classify an image, we usually frame our decision in a probability distribution that is based on features that possess measurable quantities we wish to use to guide our classification.

For example, assume we want to create an image processing system to classify people as adults or kids, and we have shots from a fixed camera that are of people a fixed distance away. We could use the height of the person in their image as a feature, labeled x. The person's age state is denoted as n, where n_1 is an adult, and n_2 is a kid. The probability that the image is of state n_1 given a feature value x is denoted as $p(x \mid n_1)$, and can often be found by examining the feature values of a well-chosen set of sample images (both positive and negative examples). The probability that a random image is of an adult, denoted $p(n_1)$, is based on the likelihood that an adult or child was put in front of our camera. Given these two probabilities, we can find the probability that a person is of a particular state using Bayesian Decision Theory. This formula is as follows:

$$p(n_1 \mid x) = p(x \mid n_1) * p(n_1) / p(x)$$

…where $p(x) = [\, p(x \mid n_1) * p(n_1) \,] + [\, p(x \mid n_2) * p(n_2) \,]$

This framework provides the maximum likelihood decision for a classification problem, given all of the prior probability distributions. Much of the research done in the field of image classification lies in estimating these probability distributions when they are unknown, as they often are. From simple parametric techniques to more general statistical learning techniques, statistical pattern recognition is a very interesting and prominent field in applied mathematics today.

6. Conclusion

We have examined some simple and useful techniques in the field of image processing. These techniques are by no means comprehensive, and the variety of techniques illustrates their specificity and the complexity of the problems in general. The tools mentioned should provide fundamentals for an instinctual understanding of images as very simple mathematical tools that have very complex representations and procedures.

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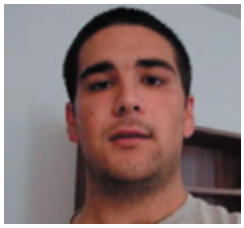

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Deconstructing the Mind: Columbia Scientists Investigate Perception and Memory

By Anthony DeCostanzo

"I remember coming to the realization at some point that every thought, and every perception, were physical changes in my brain." Kenneth Miller is explaining to me how he came to study the interface between mind and universe. His Einsteinian hair seems perpetually windblown, and his facial expressions rapidly shift between deep concern and amusement, while remaining an amalgam of simultaneous surprise and curiosity. "I see the mind as the last frontier scientifically. We seem to have a general understanding of matter, the creation of the universe, evolution of life…[but] we can't really say much about what the mind actually is." Ken studies how the external world enters our mind and becomes a physical reality in our brain that we can store for perhaps our entire lives. This miraculous process is divided into sensory transduction, wherein energy from our environment is converted into electrical impulses in the brain, and memory, wherein these impulses are stored. These two processes interact to produce a rich and seamless yet subjective representation of the external world within our minds. We often take this internal facsimile of reality for granted, unconcerned with the cellular and molecular events underlying it. But a group of researchers at Columbia, Ken Miller included, are immersed in the physical construction and deconstruction of the human mind.

Our memories define us. We can often recall experiences or feelings from infancy, before we could even speak. When we think of who we are, we search our memories, and we identify with what we find. If there is any doubt about how strongly our memories define us, we can simply try to imagine that suddenly they were all taken away from us….

What, then, are memories? We hear about memories that are short-term or long-term, or perhaps declarative or procedural. We may even be familiar with some of the brain structures that process memories, such as the hippocampus and neocortex. But how, on the level of the cell or molecule, do our experiences of external physical phenomena become psychological phenomena that we may store for our entire lives?

Our memories are the stored constructions of experiences that enter us through the five senses. In order to observe the world around us, we transduce energy from the physical world into electrical impulses in our nervous system. Light energy enters our eyes and strikes photoreceptors in our rods and cones, which then transduce it from photons into an electrical impulse that travels through neurons and into our brain (the visual cortex in the occipital lobe, Figure 1)[4]. So the physical world never ceases to be physical while it enters us and we perceive it. From this point of view, we are merely energy transducers, sampling the energy around us (e.g. light) and converting it into another form (nerve impulses in the visual cortex) that enters our brain and ultimately encodes our memories.

Perhaps no other sense impresses more upon our memories than vision—not surprising considering that it involves as much as 50% of the human brain. Vision is processed in a region of the occipital lobe (the back of the brain) known as the visual cortex.

Ken Miller came to Columbia last year to establish the Center for Theoretical Neuroscience with Larry Abbott, which so far includes six laboratories. Ken's work mostly concerns a part of the visual cortex called V1, the junction in which nerve signals originating in the eye are translated into meaningful representations in the brain (Figure 1)[4]. V1, also called the primary visual cortex, is noted for containing neurons that respond to edges of a specific orientation. There is a set of neurons in V1, for example, that only activate strongly when the eye is shown a vertical line. If you show the eye a horizontal line, those neurons will not activate nearly as strongly. Processing in V1 could be thought of as analogous to an artist making a drawing. The artist consciously breaks down a subject into a series of lines or edges with different orientations. Each neuron in V1 has a preferred orientation, such that it is most responsive when the retina of the eye sees an edge that is either vertical, horizontal, or anything in between. This is called "orientation selectivity," a property of most cells in V1. This phenomenon has been extensively documented since its discovery by Nobel laureates David Hubel and Torsten Wiesel in 1959, with recordings in the cat visual cortex.[3] Orientation selectivity combines with other selectivities (such as color selectivity and motion selectivity) in different regions of the visual cortex to form our brain's representation of images.

"I'm more of a cortex person," Ken says, to contrast his work with that of other theoretical neuroscientists who also study visual processing. "I see V1 as a piece of primary sensory cortex that is convenient to work with since it has a clearly defined set of inputs." The inputs Ken is referring to come from the thalamus, a central relay system for signals from all five senses. The part of the thalamus that relays visual information from the retina is called the Lateral Geniculate Nucleus (LGN, Figure 1)[4]. LGN activity during development is important for constructing the mature properties of V1. Ken has recently created a model that accurately predicts the patterns of LGN activity required to achieve the remarkable property of orientation selectivity in V1.[5]

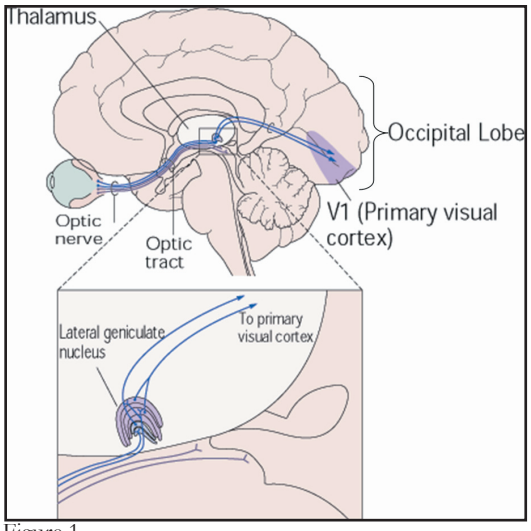

Figure 1
Image from Kandel, Eric, et al. *Principles of Neural Science,* Fourth Edition

The work of Ken and other researchers exemplifies how a network of cells can develop emergent properties such as selectivity for elementary feature characteristics such as orientation, color, motion and depth. These emergent properties are the first step in our subjective reconstruction of the physical world.

Aniruddha Das is determinedly rifling through a colossal filing cabinet that contains a fair sampling of all human knowledge about vision, discretely organized into thousands of folders. Aniruddha also studies the interface between mind and universe.[1] "Can you free-fuse?" he asks, as he darts back to the table while staring at the article he has just found. After realizing what free fusing is, I find myself staring at an imaginary point in distant space trying to get my brain to see two separate images as one. Aniruddha speaks quickly and precisely: "Vision was regarded as bottom–up, historically, while other forms of sensory experience seemed very interactive. Now it's recognized that low-level visual processing is influenced by our interpretation of surfaces."

Since completing a PhD in physics in the laboratory of Nobel laureate Charles Townes at the University of California, Berkeley, Aniruddha has turned his attention to studying vision, first as a post-doctoral fellow in the laboratory of Charles Gilbert at Rockefeller,

Figure 2

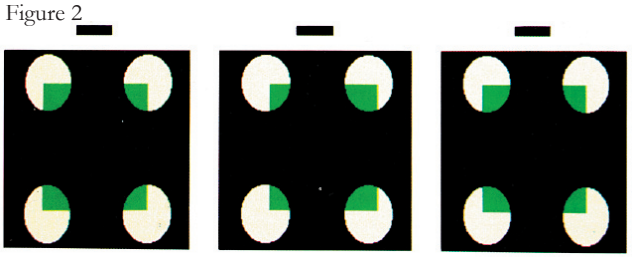

Image from Nakayama K, et al. "Transparency: relation to depth, subjective contours, luminance, and neon color spreading". *Perception.* 1990. Volume 19.4, pg 497-513

and now as an Assistant Professor at Columbia University's Center for Neurobiology and Behavior. He is standing in front of me explaining the kinds of questions he seeks to answer. He has handed me a page that contains two stereograms organized as three separate images (Figure 2)[6]. His smile indicates that he's sure I will understand what he's trying to show me. For the time being, he's wrong. I continue to strain my eyes and tilt my head, wondering what he's getting at.

What Aniruddha's not telling me is that there has recently been a revolution in our understanding of visual processing. For some time it was thought that orientation, color and motion are sensed as discrete features of the world that are subsequently assembled into a whole. For instance, when we are shown a drawing of a green square, different sets of neurons in our visual cortex that respond to horizontal lines, vertical lines and the color green all activate in a specific pattern that causes our brain to "see" a green square. However, in recent years it has become clear that this is not entirely accurate. Even intuitively, we've all experienced some form of optical illusion that makes us "see" things that are not really there. This notion seems to extend to the very basics of visual processing: as much as a series of lines and colors can form a surface to our brain, the surface we subjectively see can influence our perception of lines and colors.

After a few minutes of straining my eyes and moving the page forward and back, I finally see what he's been explaining. Fusing the image on the left with the one in the middle yields a three-dimensional stereo image of a black screen with four holes on top of a green square. If the middle image is fused with the one on the right, however, it appears that the green square is transparent and hovering *above* the black screen. This simple optical illusion, Aniruddha explains, is actually both optical and cortical. The optical illusion is in seeing the four green corners as closer to the viewer; this causes a cortical illusion wherein we "see" the green spill over into the black. Our brain falsely adds green to account for its own expectations. This demonstrates that our brain *interactively* constructs an image rather than simply building it from basic information such as lines and color; our brain adds these basic elements to our "vision" where it sees fit.

All of these processes happen simultaneously, without any conscious effort on our part, to give us a continuous visual representation of the external world. Our brain acquires information about lines, colors and depth and arranges this information into surfaces and forms in higher cortical areas, and still further into objects and scenes in yet higher areas. Once arranged, the higher areas that represent, for example, surfaces can then feed back into the lower areas to influence the perception of lines and colors, which then feed again into the higher areas in a rapid cycle of reconstruction, to ultimately give us a seemingly unadulterated image. But our perception is in fact interactive at the most basic levels of processing. What our brain sees is not necessarily what our eyes see. These illusions seem to be a normal part of the cortical representation of vision, implying that some of our most cherished possessions are something of a compromise between objective reality and practical biological constraints.

Although these curiously adjusted facsimiles are somewhat suspect, the fact that our sensory experience is tweaked by our brains is not going to stop us from treasuring our memories. This leads us to ask how sensory information gets stored. Indeed, our sensory experiences would simply enter and exit our brain without a trace if it weren't for our memory. This is the juncture wherein we become ourselves, and cease to be merely sensory processing machines. This is the principle that has motivated generations of neuroscientists to attempt to resolve the elemental question: How do we form memories?

In 1953 William Scoville, a surgeon at Hartford Hospital, removed the entire medial temporal lobe of one of his patients (Figure 4, original drawing from Scoville's report)[7]. The patient, referred to

by his initials HM, has himself become a chapter in the history of neuroscience. The surgery was a treatment for an epilepsy from which HM had suffered for more than ten years and which had continued to grow more acute. After this radical surgery, HM suffered profound anterograde amnesia; that is, although his short-term memory remained intact, he could no longer consolidate information into his long-term memory. This fact marked the beginning of a revolution in neuroscience wherein the *hippocampus*, which resides in the medial temporal lobe, came to be understood as the site for memory formation (Figures 3)[4,7].

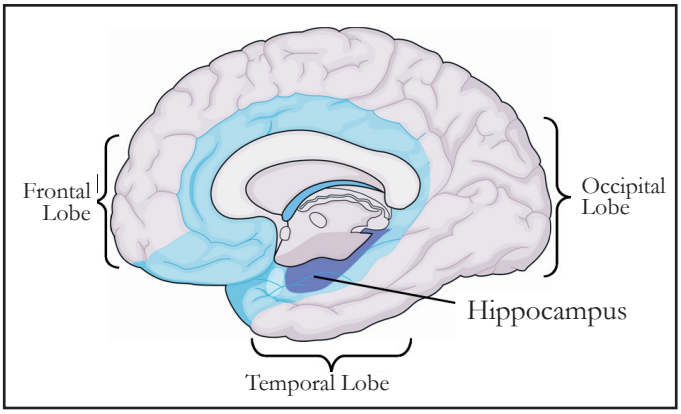

Figure 3
Image from Kandel, Eric, et al. *Principles of Neural Science,* Fourth Edition

This leads us to the work of Steven Siegelbaum in Columbia's Pharmacology Department and the Center for Neurobiology and Behavior, whose laboratory is among the few sponsored by the Howard Hughes Medical Institute. He places his research in context: "The mind is a complex circuit phenomenon, and by understanding circuits we can begin to gain insight into this higher order phenomenon." Steve studies hippocampal synaptic plasticity, the cellular and molecular circuit representation of learning and memory. When one looks at someone's face, for example, information throughout the visual cortex is processed to give an image of the face; then this information is passed along through other cortical regions into the hippocampus. Then, over a period of minutes to days or weeks, the hippocampus facilitates the storage of information about the face through an interactive process of communication with those areas of the visual cortex that were originally activated. This process often takes place without any conscious effort—we simply remember the face of someone we've just met. Without the hippocampus, information enters the visual cortex and is then passed along to the prefrontal cortex (within the frontal lobe, Figure 3)[4] for short-term storage for up to a few minutes, but it is then lost. Indeed, although HM's recollections of early childhood remained perfectly intact after the surgery, he never recognized the faces of his own doctors despite being visited by them several times a day. He had lost the ability to construct new long-term memories.

Steve Siegelbaum's work focuses on the cellular and molecular events in the hippocampus that allow it to perform the task of memory construction. When we think of a memory of someone's face, we are experiencing an emergent property of a network of cells. This memory does not reside in any single cell, so how can we conceive of the cellular component of memory? In the most abstract sense, a memory can be thought of as any trace; something that once formed will, by definition, remain for some period of time. So by this definition, even a letter drawn in the sand qualifies as a memory; the letter once drawn has left a trace—the sand "remembers" the letter. By extension, that same letter carved into a granite slab is also a memory, and we can accordingly contrast short and long–term memories: while our sand-drawn letter will soon disappear as a result of the elements, our granite-carved letter will likely survive for our entire lives. This most sparse definition is intended to emphasize the physicality of memory. This principle is no different when it comes to the human brain. Through modulation of neuronal activity, physical changes occur within our brain. These physical changes are our memories.

The brain is said to be *plastic* in its ability to change itself to store information. The physical changes associated with memory formation happen at synapses (Figure 4)[4] between neurons, and therefore fall under the rubric *long term synaptic plasticity*. This type of plasticity includes both long-term potentiation (LTP) and its physiological opposite, long-term depression (LTD), which are respectively a long-term strengthening and a long-term weakening of synaptic strength. Since the discovery of LTP in 1966 by Terje Lomo, this field of cellular neuroscience has rapidly expanded and was the focus of the research that recently garnered Eric Kandel, another professor in the Columbia Center for Neurobiology and Behavior, the 2000 Nobel Prize in Physiology or Medicine. It is now thought that these changes in synaptic strength (which occur at a cellular level) underlie the emergent, network-level formation of memories.

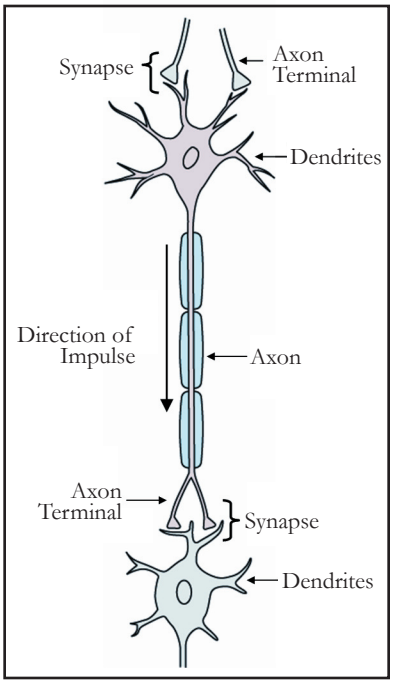

Figure 4
Image from Kandel, Eric, et al. *Principles of Neural Science,* Fourth Edition

It is impossible to discuss the activities of neurons without describing the *action potential*, the electrophysiological basis of neuronal signaling. An action potential is an impulse that propagates very rapidly down the length of an axon (Figure 4)[4]. It is sometimes referred to, as in the above discussion of vision, as neuronal activation, or sometimes nerve conduction, nerve signaling, or neuronal firing. Steve Siegelbaum tells of his early inspirations in neuroscience: "In high school I read a description of the action potential written by Isaac Asimov, which described the discoveries of Hodgkin and Huxley. I was fascinated by the fact that we could understand nerve signals in the brain as well-behaved physical phenomena." Indeed, the Hodgkin and Huxley equations, formulated from experiments done in the 1930s and '40s, are famous for the prescient exactness with which they model the action potential.[2] For their work, Sir Alan Hodgkin and Sir Andrew Huxley received the Nobel Prize in 1963.

Steve now focuses much of his energy on elucidating LTP and LTD in the hippocampus, the site of memory construction.[9] These changes in synaptic strength take place according to defined rules that are based on the firing rates of the neurons involved. Slow firing rates tend to result in LTD, and the synapse is therefore "weakened," while fast firing rates tend to cause LTP, resulting in a "strengthened" synapse. Since the discovery of LTP and LTD, it has become increasingly clear that there are in fact many ways to achieve the overall weakening or strengthening of a synapse. Each mechanism involves the activity of specific ion channels, receptors, enzymes, and other molecules. Furthermore, there is a *genetic basis* for the activity of each of these molecules. "I am now more concerned with assessing the role of ion channels and other molecules in plasticity using transgenic mice," Steve says, referring to his lab's recent use of transgenic and knockout mouse models, wherein certain genes are either artificially added to or deleted from the mouse genome. These genetically-altered mice differ from "wild-type" mice in their ability to form memories and, accordingly, have differences in their hippocampal synaptic plasticity. These are the kinds of experiments currently being done in Steve's lab and other labs in the Center for Neurobiology and Behavior to study the role of specific genes in memory construction.[9]

So, we have transduction of light energy into neuronal firing (action potentials) in the visual cortex, into coordinated firing in the hippocampus, into alterations of gene expression and…voila… a memory for life. Indeed when we are at a loss for the material comforts of this world, we often comfort ourselves with the notion that our experiences and memories are possessions that cannot be taken away from us. This, paradoxically, is grotesquely and brutally untrue.

When asked how he came to study Alzheimer's disease, Dr. Scott Small is likely to respond, "I got tired of lying to people." The people he is referring to are his patients. Scott Small is a neurologist at Columbia University Medical Center's Taub Institute for Research on Alzheimer's Disease and the Aging Brain. After completing a fellowship in neurobehavior at Columbia in 1998, Scott joined the faculty of Columbia as Herbert Irving Assistant Professor of Neurology. Before subspecializing in Alzheimer's disease, Scott intended to study the normal physiological function of the hippocampus using a brain-scanning technology called functional magnetic resonance imaging (fMRI). fMRI yields information about oxygen consumption in the brain, which in turn is correlated with neuronal activity. He is describing to me his reaction to treating Alzheimer's patients. "As a neurologist, most of your patients have Alzheimer's. Invariably you find yourself struggling to find the words to give them the bad news, and it is almost always bad news."

Scott was faced with a fundamental flaw in the human condition. His patients who may initially have only mild forgetfulness soon suffer a loss of that which they hold most dear. Along with not being able to perform routine tasks, the individual is stripped of the ability to recognize the faces of people who have accompanied him for his entire life. A lifetime of mental construction is deconstructed as this individual is plunged into confusion and disorientation.

"You find yourself wanting to give their family a glimmer of hope where there is none. I had to involve myself somehow in addressing this." Using his skills in fMRI, Scott has been studying the brain dysfunction that causes Alzheimer's. The early stages of the disease seem to affect the hippocampus and associated structures of the brain. Involvement of the hippocampus had been suspected for some time, since the early symptoms are essentially anterograde amnesia, similar to that experienced by HM. Although the hippocampus and entorhinal cortex (the input to the hippocampus) are now known to be affected, Scott's goal is to determine with *high resolution* fMRI the specific regions of the hippocampus and associated structures that are impaired in Alzheimer's disease. As he puts it, "The hippocampus is a circuit, so the best way to evaluate hippocampal function is to evaluate each node in the circuit." The nodes include the entorhinal cortex and each of the subregions of the hippocampus—Dentate Gyrus, CA1 and CA3 (Figure 5)[4]. By comparing the brains of Alzheimer's patients to those of healthy elderly patients, Scott has found that Alzheimer's patients seem to have altered patterns of activity in various subregions of the hippocampus.[8] Scott believes that "the spatial pattern of dysfunction among hippocampal subregions will be the unique signature of Alzheimer's dysfunction."

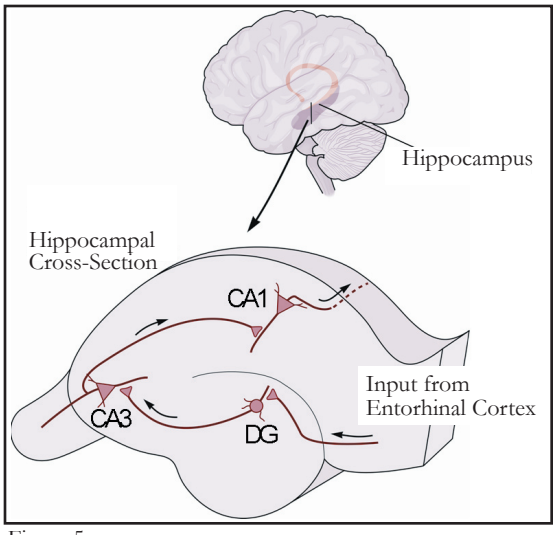

Figure 5
Image from Kandel, Eric, et al. *Principles of Neural Science,* Fourth Edition

"Alzheimer's disease appears to be a synaptic failure," Scott says, referring to a mounting body of literature that shows a profound effect on long-term synaptic plasticity in animal models of Alzheimer's.[10] The most probable cause of impaired synaptic plasticity appears to be the accumulation of a small peptide, amyloid-β. This peptide has been shown to impair LTP when it is artificially administered to the hippocampus. Furthermore, transgenic mice that overexpress the amyloid-β precursor have impaired LTP as well as memory impairments. The normal, nonpathological function of amyloid-β is not known, but its role in diminishing LTP suggests that it may modulate normal long-term synaptic plasticity. Whatever its role in normal physiology, pathologically high levels of amyloid-β seem to effectively deconstruct what normal hippocampal physiology is designed to construct: memories.

At every level of organization, the human mind is constructive, often representing our world with a paradoxically subjective, meticulous façade. Our senses transduce energy from our surroundings into nerve signals, which are assembled into increasingly more complex and "meaningful" representations in our cortex. As exemplified by the simple illusion presented earlier, these representations are interactively constructed in the cortex between lower areas that process basic features (such as lines or colors) and higher areas that assemble these basic features and modify them to best fit expectations. These representations remain temporary until they are processed in the hippocampus, wherein they are constructed into long-term memories by interactive firing between the hippocampus and the same high-level cortical areas in which they were processed earlier. Once so constructed, these memories are maintained in the areas of the cortex that originally participated in processing; images are stored the visual cortex and sounds in the auditory cortex. However, as with anything that can be constructed, memories can be deconstructed, through mechanisms that appear to abuse the cellular machinery for construction. This begs for an immense appreciation of the delicate balance between our mind's constructive and deconstructive tendencies.

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Think Nanotech, Think Big

By Carey Chen

Nanotechnology, the branch of engineering that develops technology sized at about one billionth of a meter, is the buzz word these days. Governments around the world have realized the potential and value of nanotechnology and have started investing in ambitious initiatives. This paper assesses the present state of research in major countries and considers future implications and possibilities resulting from global research in nanotechnology.

There are two categories used to analyze a country's position in nanotechnology research: activity and technology development strength[1]. Lux Research, one of the world's leading nanotech advisory firms, developed this method. "Activity" evaluates the current volume and quality of nanotech innovation and also provides a quantitative measurement of competitiveness. The criteria for this category include the number of initiatives and dedicated nanotech research centers per nation, as well as its volume of invested venture capital. "Technology development strength" measures a country's capability to commercialize its innovations.

Initiatives and Dedicated Nanotech Research Centers

The number of initiatives and dedicated research facilities is a measurement of a country's focus on nanotech R & D at the national, regional, and local levels. Measurement on all three levels is important because of the varying scope of many projects. For example, the U.S. National Nanotechnology Initiative (NNI) is broadly aimed at creating jobs and inward investment[2], while India's Nanomaterials Science and Technology Initiative (NSTI) has only a narrow academic focus.

Indeed, large nations boast a great number of centers that focus on myriad topics. The U.S. leads the way with 103 centers, followed by Germany with 57[1]. The number of dedicated centers also has a positive correlation with the number of nanotech academic publications by a specific country, as seen in Figure 1. Countries limited by their small physical sizes claim fewer centers, but have laser focus on specific applications. For instance, South Korea's National Nano-Fabrication Center targets electronics applications.

Venture capital and commercialization

Corporations have become important partners in the effort to commercialize nanotechnology. BASF, General Electric, and Samsung have dedicated research groups that focus on commercialization, giving rise to centers like the NanoTechnology Research Center in Taiwan and NanoFrontier in Singapore, which focus on marketable technology and materials.

Corporations are not the only for-profit institutions following nanotech's progress; venture capital (VC) firms are making sizable investments. High-risk ventures can be funded in many ways, from institutional VC to reduced-rate loans issued by state-owned banks. Of the 243 nanotech VC deals that Lux Research has tracked from 1999 to September 2005, 63% of those deals resulted in the distribution of funds to U.S.-based companies[1]. VC and corporate investment are particularly important when government funding proves insufficient. An example is the deal between Germany's Degussa and the state government of North Rhein-Westphalia to fund a Nanotronics Science to Business Center for $65 million, with $11 million in subsidies over five years[3].

Technology Development Strength

The final ranking category is technology development strength. Three criteria prevail here: spending and high-tech manufacturing as a percentage of GDP; specialized technology and science workforce and Ph.D. holders; and government infrastructure for effective technology commercialization.

Research & Development spending and high-tech manufacturing are the lifeblood of technological development. In measuring R & D spending as a percentage of GDP, smaller countries come out on top, led by Israel at 5.1%[4]. High-tech manufacturing measures job creation resulting from nanotech innovations. An agriculture-intensive economy like Australia generates as little as 2% of its GDP from manufacturing; whereas the tiny nation of Singapore derives 37.2% of its GDP from this source[5].

A skilled workforce along with education in science and engineering provide another benchmark. Russia leads in the number of Ph.D. degrees granted in science and engineering and in technical workforce. However, Russia has been slow to leverage this large group of educated workers. Germany and the U.K. also have numbers of technical workers. Germany retains many of its educated, but many of the U.K.'s great minds have become expatriates[6].

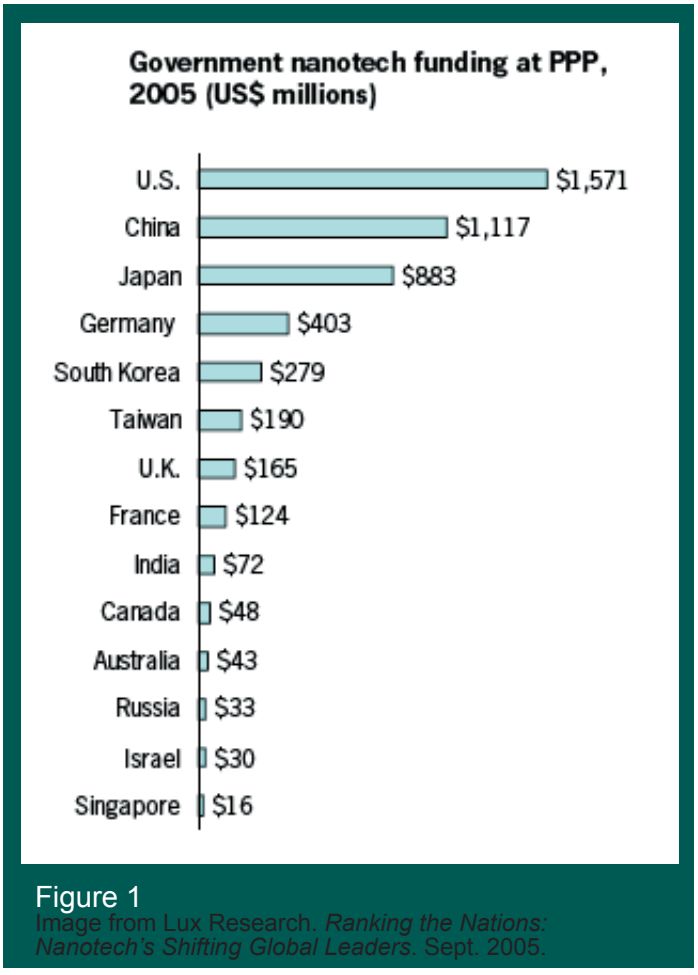

Figure 1
Image from Lux Research. *Ranking the Nations: Nanotech's Shifting Global Leaders*. Sept. 2005.

Based on the ranking methodology described above, four countries emerge as the dominant players of today: the U.S., Japan, Germany, and South Korea. The U.S. leads in nanotech activity, and has the strength necessary to commercialize its developments. Although the U.S. earns a smaller share of its GDP from high-tech manufacturing (given its relatively small science and technology workforce), it remains strong in R & D investment.

Japanese corporations provide substantial funding at home and to countries around the globe. Given their long term inclination toward product development, companies like Toshiba and NEC invest heavily in R & D.

Germany is the dominant force in Europe because of its 57 nanotech centers, which actively and regularly publish. While German start-ups typically focus on specific applications, corporate giants like Siemans and Bayer direct several large-scale nanotech initiatives.

South Korea's high rank is largely attributed to generous government and corporate spending. Samsung, for example, owns diverse nanotech activities ranging from antimicrobial nanosilver coatings for refrigerators to carbon nanotube field-emission displays[1].

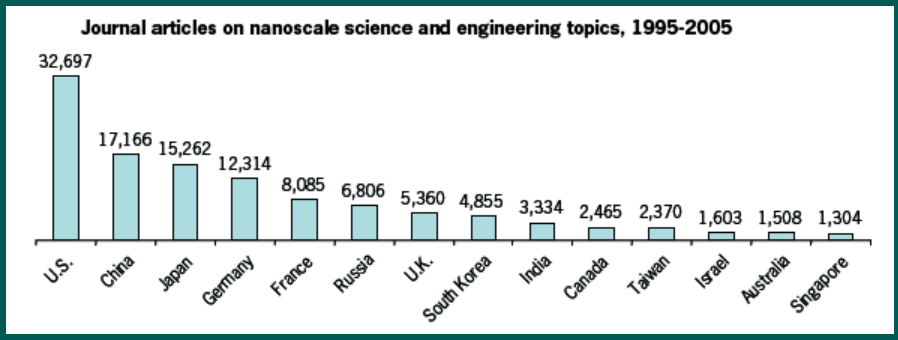

Figure 2
Image from Lux Research. *Ranking the Nations: Nanotech's Shifting Global Leaders*. Sept. 2005.

Niche Players

There are many countries that, while not dominant players, contribute meaningfully to the advancement of nanotechnology. Taiwan is distinguished by its nanotech commercialization and has a strong network of centers, funded both by the government and corporations. With its focus on nanoelectronics commercialization, it has also established an extensive set of international research collaborations. One example is the deal with the National Research Council (NRC) of Canada[7].

Israel draws more venture capital than Taiwan or Singapore. However, because of the lack of domestic corporate nanotech funding, Israeli start-ups have had to seek large foreign companies as strategic partners. For example, ApNano Materials collaborates with Volkswagen (Germany) and Hacto (U.S.) on its nanoparticle-based lubricants[8].

Currently, nanotech development is relatively localized due to the required specialized knowledge, as well as high costs and speculative returns. Many of the leading players are establishing partnerships, either from country to country or country to corporation. This trend will in turn "create linkages that exploit complementary ecosystem roles[1]." Global collaborations between innovators and manufacturers will soon proliferate. China remains well- suited for the role of manufacturer, while France has the potential to excel as an innovator.

Countries that are currently lagging in the nanotechnology race will most likely cooperate to pursue common goals; recent collaborations include India's agreement with Canada and the Asia Nano Forum, which will allow New Zealand to partner with established powerhouses like Japan.

Whether the advancement of nanotechnology by leading countries and partnerships among new players continues to succeed depends in large part upon media portrayal and public perception. The media in the U.S. and European Union have been hesitant to label nanotechnology as "the next best thing" due to the fact that they have labeled other emerging sciences with that same title, only to watch them fizzle. The Asian media, on the other hand, praises nanotechnology as *the* driving force for economic growth and technological dominance. The sharp contrast in perception has led to debate on the future of nanotechnology.

Public perception is notoriously unstable. Quite a few consumers already have prejudices about this emerging technology. Walking past a bus stop at Cornell University this summer, I saw graffiti that read "Stop nanotech now." The fact that Cornell is one of the magnets for academic nanotech research in the U.S. makes this juxtaposition all the more sobering. Investors and researchers in this emerging field will have to closely monitor the public's ever-evolving attitude about nanotechnology and invest in promotional and educational initiatives to ensure that citizens appreciate the many ways in which nanotechnology can improve our lives.

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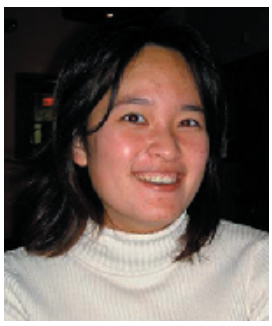

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FINDING LIFE'S STRUCTURE

An Introduction to Structural Genomics

By Nicholas Gulati

Proteins play an undeniably vital role in our lives. When people say that our genes define who we are, what they really mean is that the proteins encoded by our genes determine how we look, how we feel, and how we respond to stimuli. On April 14, 2003, the International Human Genome Sequencing Consortium announced the completion of the Human Genome Project; human DNA had been sequenced in its entirety. Now, following in the footsteps of this titanic scientific achievement, structural genomics has emerged as a fascinating new field of science with endless potential.

The goal of structural genomics is to determine the structures of all proteins in the genome. Unfortunately, finding the structure of proteins is much harder than discovering the sequence of DNA. Like genes, proteins consist of a linear chain of building blocks. These blocks are built from combinations of twenty different amino acids. Each amino acid chain folds into a complicated three-dimensional formation, and the shape of the formation has a dominant effect upon the protien's function. Some proteins involve several distinct amino acid chains linked together, which makes determining their structures even more difficult. Since protein structures can not be fully understood simply by knowing their amino acid sequences, they must be physically mapped. The two primary methods of mapping are bombarding crystals of a protein with powerful x-ray beams in a process called x-ray crystallography, and bouncing radio-frequency signals off a solution of proteins in a nuclear magnetic resonance machine.

X-ray crystallography involves placing proteins in a perfect crystal lattice, meaning the proteins must be lined up in a very structured way. Crystals are three-dimensional, solid groups of molecules arrayed in a geometric pattern. Examples of widely known crystals are sugar, sodium chloride, and diamond. After the proteins are placed in a crystal lattice, x-rays are reflected off of the lattice and, since there are so many planes that cut through the lattice, the reflections of the x-rays can be used, along with mathematical algorithms, to create a map of the protein's structure. Unfortunately, crystallization is very difficult to perform on proteins, especially those found in humans. This is because researchers must engineer *Escherichia coli* or other bacteria to produce the proteins that they want to characterize. These proteins then have to be purified and dissolved in water, which is an essential step for creating the crystals used in x-ray studies. The next step is to try to coax the proteins to form well-ordered crystals. This crystallization procedure is troublesome since proteins are relatively large molecules and they are dynamic; they do not easily stay still in a lattice. A fundamental problem of structural genomics that arises from this crystallization step is that human proteins are harder to crystallize than *Escherichia coli* proteins. According to Dr. John Hunt, manager of the Northeast Structural Genomics Consortium's crystallization group and a researcher on structural genomics at Columbia University who directs crystallography along with Dr. Liang Tong and Dr. Wayne Hendrickson, "fundamental improvements in structural genomics are necessary; and not just in optimization of the process." As of now, 10% of human proteins have been crystallized compared to 30% of bacterial proteins. Dr. Hunt hopes that both of these figures will be raised to 50% within the next several years. Many advances have been made to optimize the processes involved in structural genomics. One such optimization technique is the use of robotic gear to speed protein purification. There now exist several robots that assist crystallization and highly efficient methods for determining protein structures from good crystals.

Nuclear magnetic resonance (NMR) is a physical property associated with magnetic attributes of atomic nuclei. NMR studies a magnetic nucleus, like that of a hydrogen atom, by aligning it with an external magnetic field, and then disturbing its alignment using electromagnetism. Researchers then measure the response to this disturbance. Although the process of NMR spectroscopy is much more tedious than x-ray crystallography, it is able to find the structures of certain proteins that x-ray crystallography can not.

The Protein Structure Initiative (PSI) is a project sponsored by the US National Institutes of Health (NIH) whose goal is to advance structural genomics. Since proteins come in a relatively limited variety of shapes, PSI is targeting what it calls "unique" proteins, or proteins whose structures cannot be determined based on their sequences' similarities to other proteins with known structures. Therefore, there is an important distinction between "unique" protein structures and "new" protein structures, which are simply proteins whose exact configuration is not currently present in the Protein Data Bank. Not all new structures are equally useful to the PSI because if two proteins have at least 30% of their amino acid sequences identical, their structures can be assumed to be roughly equivalent. In September 2000, the NIH set a goal that within 10 years, structures would be determined for 10,000 unique protein homologs, corresponding to about a third of all proteins encoded by the human genome. Many of these were anticipated to be bacterial proteins that have 30% sequence identity to a human protein's sequence. However, based on the current status of the research, it is likely that the final tally will only be between 4,000 and 6,000 structures. Still, the PSI has come a long way. It is important to understand that structural genomics projects have been organized to evaluate large numbers of candidate targets, often of the same protein in various organisms, and at the same time, to work on them in parallel. In other words, the aim is to determine the structure of representatives of particular protein families; representatives whose structures are not found are often simply the result of success elsewhere. For instance, many of the proteins that have a unique position in sequence space have actually shed light on a further large amount of homologous proteins whose structures can now be modeled for the first time. The PSI has found that only a small percentage of its completed structures sport new folds (folds are the general shape of a protein once it assumes its three-dimensional form). This means that proteins may adopt similar three-dimensional shapes even if they have largely different patterns of amino acids.

In the United States, there are four primary consortia working on structural genomics. These include the Joint Center for Structural Genomics (JCSG), the Midwest Center for Structural Genomics (MCSG), the New York Structural GenomiX Research Consortium (NYSGXRC), and the Northeast Structural Genomics Consortium (NESGC), in which Columbia University is a participating institution. Since there are four major groups

competing to find as many protein structures as possible, certain public policy issues have been raised concerning the way in which this competition should be monitored. Despite the competition, two-thirds of the protein structures that the four groups have determined are unique structures. As of now, the NESGC has determined 89 protein structures using NMR spectroscopy and 127 protein structures using x-ray crystallography. There are also several large structural genomics research groups outside of the United States. In fact, the stampede into structural genomics began in Japan with the opening of the RIKEN Genomic Sciences Center in Yokohama in 1998.

Even though the field of structural genomics has met with many difficulties, it has made great progress and still has a great deal of potential. Of the 30,000 proteins in the human genome, 2% of them have thus far been determined that would not have been determined without the structural genomics project. Also, according to Dr. Hunt, "Conservatively, in the next five years, this project will find structures for 10 percent more of the human genome." This figure assumes no increase in productivity, which will most probably not be the case, since there have been several technological improvements to aid in the process of determining protein structures.

The potential biological insight that can be gained from structural genomics is invaluable. According to Dr. Hunt, the structural genomics project has the ability to provide a "grand amount of information that will be useful to a great deal of people." One specific application of this project is in understanding disease states. By studying the proteins that are involved in human genetic diseases, these illnesses can be better understood. Also, in some cases, determining a protein's structure can shed light on its previously unknown function. For instance, Barry Honig and his research group at the Columbia Medical School recently found that two proteins whose functions were previously unknown are actually RNA binding domains that are very important in biology. Also, the NESGC has solved the structure of a protein that adds a methyl group to ribosomal RNA and in the process confers antibiotic resistance to bacteria. This structure, according to NESGC director Guy Montelione of Rutgers University, has suggested inhibitory compounds that could revive current antibiotics, and it has spawned a separate research program on that topic. Yet another protein structure revealed details on the way plants bind a signaling molecule called salicyclic acid, and this discovery challenged the traditional understanding of the functioning of plants' immune systems. In Montelione's words, "Not only are we spinning out new science, but new science initiatives."[2] Clearly, the influence of structural genomics extends into many areas of biology, and this field is capable of leading to large amounts of scientific knowledge.

Thank you to Dr. John Hunt of the Deptartment of Biological Sciences at Columbia University for his invaluable input.

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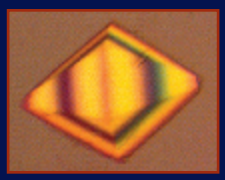
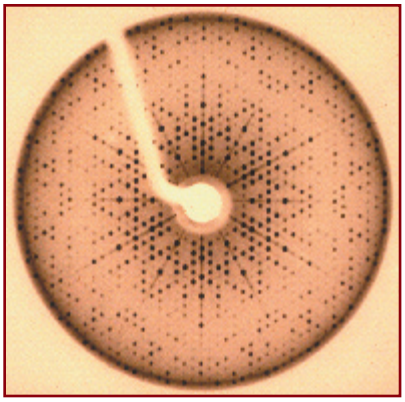
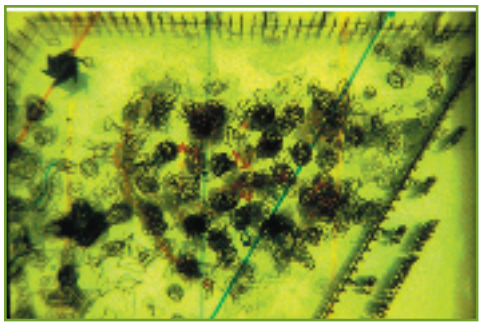
Visualizing Protein Structures: From Crystal to Schematic Drawings



A crystal of ras protein, a protein essential in many signal transduction pathways.



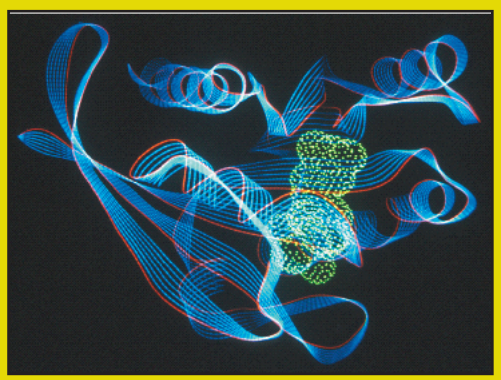
During x-ray crystallography, crystal diffracts radation.



An electron density map of the ras protein is constructed from the gathered data.

Images courtesy of Professor Liang Tong, Department of Biological Sciences

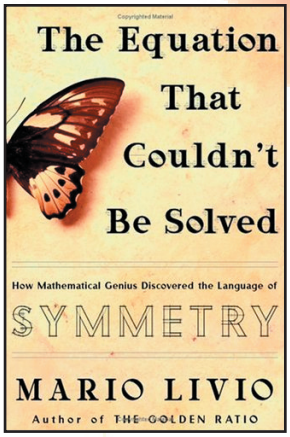
Schematic Drawings of Ras Protein



By Rachel Eisenberg

Although it often passes unnoticed, many of the operations in our everyday lives follow certain sets of permutations. Each morning, for example, there are a number of ways to put on a pair of pants. When choosing a mate, the Kariera tribe of Australian Aboriginals follows a specific set of rules to arrange an appropriate marriage into one of their four types of communities. At first glance, these two situations may seem entirely independent, but upon closer observation, even the non-mathematician can see that they possess a surprising symmetry. Each of these groups is actually a permutation of a fundamental set of rules.

The proposition that seemingly disparate operations can be seen as specific realizations of a single abstract entity is the basis for a revolutionary branch of mathematics known as group theory. An understanding that these groups are mathematically identical allows scientists and mathematicians to make generalizations and use them to predict the properties of group members and their transformations. Mathematicians call the different realizations of one group isomorphic, which means that they all have an identical basic structure that is the same as a group of permutations. The two examples in the opening paragraph are expressions of a group known as the Klein four-group. This group was named in honor of the German mathematician Felix Christian Klein, who first realized that geometry, symmetry and group theory are inextricably linked. [1]



The Equation That Couldn't Be Solved: How Mathematical Genius Discovered the Language of Symmetry by Mario Livio takes the reader on a journey through the history of group theory. The book begins with an overview of its origins and ends in a discussion of present day research that uses group theory and symmetry. Throughout the book, Livio includes entertaining biographies of the participating mathematicians that provide a fuller and more intimate account of the development of group theory.

A working knowledge of group theory and symmetry is particularly important because group theory allows for a more profound understanding of many concepts in mathematics and science; from physics to psychology. As Sir Michael Atiyah, winner of the 1966 Fields Medal and 2004 Abel Prize in Mathematics said in response to Livio's book, "Symmetry is one of the guiding principles of mathematics and its story deserves to be told in a way that reaches a large audience. Created by two young and tragic geniuses, Abel and Galois, it has a romantic appeal that transcends technicalities."

Livio is most successful in explaining the mathematical and historical struggle to solve the quintic equation. Here, he effectively combines a concise history of group theory's origins with biographical intrigue. Livio's work grasps the rich dynamic interplay between hard math and the characters that develop it, pushing forward the idea that science can be both personal and palpable.

Livio starts his story with the original development of group theory. Mathematicians had been working for millennia to develop formulaic solutions to series of equations. The most familiar example is the quadratic equation, a second order polynomial equation of the form of $ax^2 + bx + c = 0$. The roots can be found by completing the squares and then solving for x, resulting in the famous formula. However, when faced with the quintic equation, a fifth order polynomial in the form of $a_5x^5 + a_4x^4 + a_3x^3 + a_2x^2 + a_1x + a_0 = 0$, three centuries worth of exploration proved fruitless. A breakthrough finally came in the early nineteenth century when Evariste Galois and Neils Abel concurrently demonstrate the insolubility of the quintic equation.

The key to Galois's proof is the realization that an equation is best defined by its "symmetry profile", not its degree. An equation's symmetry profile, now known as its Galois group, is "a group of permutations that represents the symmetry properties of the equation." (1: 170)

Galois then went on to prove that an equation is solvable by a formula when its given Galois group is also solvable, because then the equation can be broken up into smaller steps with equations of lower degrees. He completed his proof by showing that the quintic equation did not have the appropriate type of Galois group, and was therefore not solvable by an equation.

Beyond resolving one of the most troubling questions in mathematics at the time, Galois revolutionized the way in which we approach equations and created an entirely new field of mathematics. Symmetry and group theory took hold as a central tenet of mathematics and gave mathematicians valuable new tools.

Group theory provided the perfect solution to the chaos that was taking hold of geometry in the mid- to late nineteenth century. To deal with different situations in nature, mathematicians had developed an incredible number of generalized, abstract non-Euclidian geometries. In order to bring order to an overwhelmed field, Klein suggested that geometry should not be defined by objects or shapes, but by the group of transformations that leaves an object invariant. To define a geometry, in other words, a mathematician must define the symmetry group that is its blueprint.

Group theory and symmetry are applied in similar fashion to a variety of fields. Quantum mechanical symmetry groups are used to predict the properties of previously unidentified elementary particles. Evolutionary biologists focus heavily on the prevalence of bilateral symmetry, or left-right symmetry, in many species. Many animals possess facial symmetry, which means that the left and right sides of their faces are roughly identical. Biologists believe that this is important to the predator-prey relationship because it explains how animals are able to recognize potential threats. Additionally, when mating, individuals are more attracted to symmetrical mates because this is an indication of good genes.

Livio's work is laudable for his extensive coverage of the applications of group theory, which has the potential to advance a variety of scientific fields. Although it effectively conveys the overall message of the importance of symmetry, however, some of the details of his examples are rather confusing.

Writing a book that is both academically significant yet understandable to the public can result in a work that is stuck in limbo. Although Livio manages to provide a readable introduction to group theory, his discussion of the mathematical inner workings of symmetry and group theory is not comprehensive. With only his book as a basis of knowledge in group theory, it would be hard to understand his later, more complicated application examples, such as the logistics of string theory, or how mathematicians predict the existence of elementary particles.

Despite these occasional difficult concepts, Livio's writing is exciting and consummates with curiosity and questioning. Livio also delivers resonating philosophical questions about both the phenomenon of symmetry and the nature of genius. And while his writing draws upon the latest research, it makes room for the potential breakthroughs that may follow. "Even if symmetry is not the final answer," says Livio, "it is surely a fruitful one."

Reference

1. Livio, Mario. *The Equation That Couldn't Be Solved: How Mathematical Genius Discovered the Language of Symmetry*. New York: Simon & Schuster, 2005.

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