sleep paralysis

by Hila Katz

Imagine waking up and not being able to move. Someone or something is in the room, just out of sight. You cannot see what it is, only that it's creeping closer to the bed; helpless terror floods your mind. As it nears, you discern a dark, indistinct shape, human-like in form. Suddenly an enormous weight presses on your chest, crushing you to the mattress. Barely able to breathe, you gasp for air, convinced that death is near.

The experience, however, is not a confrontation with the supernatural or one's own imminent demise. It is an episode of sleep paralysis, a condition that can make one feel like a hapless victim in a horror movie. Sleep paralysis is a parasomnia, a deviance in the ordinary behavioral and physiological activity involved in sleeping and the states of conscious wakefulness that immediately precede or follow sleep. Researchers have linked sleep paralysis to the boundary between wakefulness and one particular phase in the sleep cycle – REM (Rapid Eye Movement) sleep, which is marked by several distinguishing characteristics. During REM, blood pressure, heart rate and breathing are elevated and more irregular than in non-REM stages of sleep. We dream more frequently and with marked vividness. And although the eyes dart back and forth in quick, involuntary movements, the body's skeletal muscles experience atonia, or muscle paralysis. What some researchers are interested in finding out is how the parasomnia sleep paralysis blends elements of REM sleep, such as the atonia, with the conscious awareness that we experience during wakeful states. Though it is still unclear how the brain might attain wakefulness during REM, uncovering the neuronal interactions and populations of neurons behind the sleep paralysis phenomenon could help us understand the similarities and distinctions between a brain in true REM – active but without conscious awareness – and a wakeful brain, which is both active and aware. Sleep paralysis episodes are brief, lasting from a few seconds to a couple of minutes, but they are rich with mystery and potential insight into the nature of consciousness.

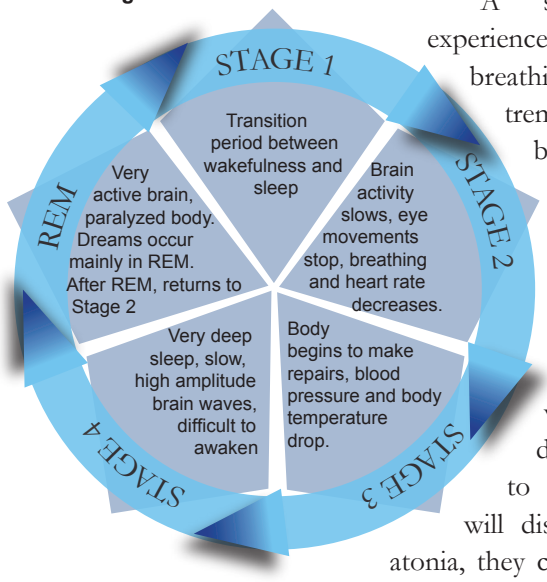
Studying sleep paralysis is a fairly recent endeavor, and the bulk of the findings consist of firsthand reports by people who have experienced its different manifestations. Sleep paralysis can be either hypnagogic or hypnopompic. Hypnagogic episodes occur at the onset of sleep and are made possible if a person slides from wakefulness into REM, which

in ordinary sleep cycles is not the first sleep stage to follow wakefulness; hypnopompic, or postdormital, episodes transpire when the sleeper awakens from REM and does not complete the transition to a wakeful conscious state. Though individual episodes of sleep paralysis differ in detail and length across person, place, and time, there are commonalities observed among sleep paralysis incidents. One of the lead researchers on sleep paralysis, J. Allan Cheyne of the University of Waterloo, has sketched out three general categories of experiences.

Researchers estimate that about thirty to fifty percent of people have gone through at least a couple of episodes of sleep paralysis in their lives

One category is a miscellaneous assortment of the most rarely reported experiences. These include sensations of floating and weightlessness or, stranger yet, an out-of-body feeling, described in a handful of reports as casting off one's body, moving independently of it, and having the rather jarring ability to look down at the body as it remains in bed. The cause of these sensations is poorly understood, though it is most likely related to certain activation patterns of vestibular neurons. Because the sleeper's body is paralyzed, the vestibular neurons are not getting feedback from the skeletal muscles and may only be taking their cues from internally generated dream imagery; a feeling of separateness or independence from the body might then arise.

THE SLEEP CYCLE
Each cycle lasts around 90 minutes and repeats 4-6 times in a night.



A second category of experiences involves constricted breathing and a feeling of tremendous pressure on the body, focused on the chest or head. The suffocating pressure is thought to stem from normal REM respiration, which is often rapid and shallow. Sleepers who gain consciousness during REM and attempt to draw deeper breaths will discover that, because of atonia, they cannot control the depth and regularity of their breathing; their bodies' resistance to their efforts could result in pressure and respiratory problems, compounded by a feeling of panic that makes breathing even more of a struggle. Scientific explanations aside, suffocation and breathing difficulties often figure in cultural scripts and supernatural accounts that are most likely rooted in episodes of sleep paralysis. From medieval times there are legends of incubi, demons that pounce on sleepers and choke them. A Canadian variation is the "old hag" attack, involving a crone who takes delight in sitting on people when they sleep and slowly crushing the breath from their bodies. Other cultures have terms for the heavy pressure and respiratory problems as well; in Mexico, for example, it is called 'subida del muerto' – the dead getting on top.

Supernatural stories are also linked to another category of sleep paralysis experiences – what Cheyne calls 'The Intruder'. This category deals largely with visual and auditory hallucinations, as well as the experience of the 'sensed presence', a feeling that someone else is in the room, some human or non-human figure lurking out of sight, peering at the sleeper from the shadows. Though there may be no sensory evidence pointing to the presence of another person or creature, the feeling is nevertheless accompanied by an unnerving certainty. Hallucinations may arise independently of the 'sensed presence', but the two are often intertwined, with the hallucination fleshing out the feeling of an intruder and lending it shape – as ghost, devil, rapist, perhaps a disembodied hand; if these perceptions are accompanied by the choking, bodily pressures from the second category, an entire of intrusion and physical may play out in a person's mind.

Auditory hallucinations during sleep paralysis include footsteps, voices, and shrieking wind, among many others. Unlike the sounds heard in an ordinary dream, these hallucinations are lifelike and clear, as if they are arising in the external world and are not the product of one's mind. Visual hallucinations tend to be less concrete and convincingly real than actual objects, but also seem to appear in external space and not in the mind. Both auditory and visual hallucinations take on an air of reality because during an episode of sleep paralysis, the eyes stop their characteristic REM movements, and sensory input from the world flows in; the sleeper is conscious of external surroundings and stimuli, while at the same time subjected to dream-related brain activity.

Top-down processing enables the brain to connect and assemble the scattered blots and splotches into a picture of a Dalmatian. The blots comprise sensory information (bottom-up data) brought to the brain through the eyes; the brain makes sense of them through stored mental representations and conceptions.

During REM, bursts of neuronal activity from the pons and neighboring brain stem regions travel to the thalamus, often called "the gateway to the cortex" because it constantly channels neural signals to parts of the brain responsible for higher sensory processing and mental functioning. Via the thalamus, the brain stem's REM-related discharges spread to numerous brain regions, including areas of the cortex that process visual information. This internally generated activity is thought to produce the intense, uniquely vivid REM dreams. In sleep paralysis, these vivid dream sensations can combine with the input from the external environment, leading to hallucinations and sensed presences that seem a part of the outside world.

But why does the distinction between products of the mind and exogenous stimuli break down during sleep paralysis? What mechanisms in our brain usually prevent us from confusing internally generated images with objects and people in our external environments? Sensory experience is not merely "bottom up"; that is, what we see is not just a product of the information pouring into our retinas and traveling to our visual cortex. Not only can our brains generate representations of the world, but when processing an external image or a scene, it can also fill in sensory details that may be missing, particularly when an environment is short on fine detail (as a sleeper's dark bedroom is). In our day-to-day lives we regularly fill in incomplete images and patterns (see figure above). Input from the external world interacts with the representations in our brain to generate a final picture of what we see, and most of the time the picture appears seamless.

At this point it is unclear to researchers how the brain manages to impose its own representations in an unsubtle, jarring way during sleep paralysis, and why these internally generated representations are treated as real. The fact that the sleeper is disoriented, in a dark room, and has stored cultural information about predators, ghosts, alien abductors and the like contributes to the reality and sense of narrative in an episode. The lack of external visual stimuli and the general silence of a dark bedroom may also make the visual and auditory hallucinations more realistic in contrast. For example, there is a condition called Charles Bonnet Syndrome (CBS), in which people with failing eyesight begin to see things in their external environments that they know are hallucinations; sometimes a hallucination takes on the form of a simple shape, while at other times it can be a cartoon monkey or even an image of a friend or relative. These hallucinations are thought to crop up in part because the people with CBS are not taking in as much input through their weakening eyes; internal visual representations – which, like exogenous stimuli, activate the visual cortices and pathways – then have an edge in the competition with what the eyes bring in from outside. People with CBS tend to experience hallucinations when they're in a quiet, familiar environment lacking in distractions or when they lie awake in bed at night. Similarly, the hallucinations of sleep paralysis assert themselves in places with minimal distractions and details. Studying the hallucinations of sleep paralysis could help us better understand how our mental representations might become perceivable in external space, and what ordinarily occurs at the neural level to inhibit our internally generated images from getting plastered onto the outside world.

What also befuddles the mind and might contribute to the hallucinations' reality is that during sleep paralysis the brain attains conscious awareness while not completely emerging from the REM stage of sleep. Sleep paralysis is poised between waking consciousness and a sleep stage, a boundary that is not as distinct as one might think. Though during REM

sleep sensory input from the outside world is largely shut out – making it difficult to awaken someone in REM – the amount of activity in the REM brain is comparable to and can even exceed the levels of activity in a wakeful brain. Electroencephalogram (EEG) recordings measuring the electrical activity on the brain's surface show that a brain in REM sleep has a pattern similar to a wakeful brain – high frequency, low amplitude, jagged brain waves. What REM exactly does for the brain remains unknown. It is thought that in infants and young children, who spend more time in REM than adults do, REM sleep assists in brain development by activating various areas of the cortex; recent research has also shown that fetuses experience REM sleep, and that the REM brain activity stimulates, among other regions, the visual cortex, furthering its development in a dark womb environment that offers no visual stimuli. The dreams that both children and adults experience during REM might be the brain's way of piecing together the random images and signals elicited by the great amount of brain activity; the same mechanisms that attempt to put together a narrative from the unrelated signals might also be involved in the way our conscious, wakeful brains construct coherent narratives from the events that we witness in our day-to-day lives. In studying sleep paralysis, we can explore the subtle distinctions between REM and the phenomenon of wakeful consciousness, which are poorly understood.

There has also been speculation about the more primal roots of sleep paralysis; an episode of sleep paralysis that contains an experience of 'sensed presence' along with constricted breathing resembles tonic immobility (TI). When certain animals are attacked and cannot flee or fight back effectively, they will sometimes use TI as a last resort escape strategy. During TI, the animal takes on the immobility and unresponsiveness of a corpse, a feint that can trick predators into momentarily letting their guard down or losing interest in the unresisting prey. In sleep paralysis, the sensed presence is usually perceived as watching and closing in on the prone sleeper the way a predator tracks its victim; if there is also strained breathing and pressure on the body, the sleeper interprets the experience as an attack, akin to how predators crush and suffocate their prey. Sleep paralysis episodes are almost always permeated by all-consuming fear, which might at first arise independently of the sensed presence but soon become exacerbated

Henry Fuseli's *The Nightmare* (1781) is a depiction of a demonic visitation during sleep paralysis.

by the sleeper's hallucinations or bodily sensations.

Given how unusual, and often terrifying, sleep paralysis is, one wonders how often people experience it. Researchers estimate that about thirty to fifty percent of people have gone through at least a couple of episodes of sleep paralysis in their lives; it's hard to generate precise figures, because not everyone who experiences an episode might be comfortable talking about it. A minority go through it as a more common occurrence – a couple of times a month or even once a week. The frequency of sleep paralysis has been correlated to another sleep disorder, narcolepsy. Though in a normal sleep pattern, the waking brain first enters a stage of light, non-REM sleep, narcoleptics go straight to REM and have reported frequent hypnagogic episodes of sleep paralysis.

Sleep paralysis – including its link to narcolepsy – remains difficult to study, however. Even if one did monitor a sleeper in a lab and take an EEG recording or fMRI scan, sleep paralysis episodes usually crop up irregularly, and might not appear just when the researcher wishes to record it; also, the occurrence of an episode could depend upon the sleeper's environment, making it more likely to occur in a familiar location such as a dark bedroom rather than a sleep lab. Even if episodes could be recorded more regularly, it would be difficult to sift through individual variations to find underlying neural commonalities. Some sleepers, for example, experience sleep paralysis only as an inability to move their bodies and do not report a sensed presence, hallucinations, or chest pressure; of those who are gripped by visions and alarming noises, the perceptions have great variety. For now, there is a heavy reliance on self-reports, and while these reports are altogether too widespread across gender, culture and race to suggest that there is a conspiracy of lies regarding the phenomenon, sleep paralysis research must be bolstered by the application of other experimental and observational paradigms.

In spite of the obstacles inherent in sleep paralysis study, the parasomnia can potentially lend insight to the human brain. Poised as it is between states of wakeful consciousness and the important REM sleep stage, sleep paralysis might illuminate the fine distinctions between different brain states and how the brain processes perceptual information; perhaps it might also help us gain an understanding of what consciousness is and how the REM sleep stage impacts the brain and its development and maintenance. Though often resembling an encounter with the supernatural, or an episode of madness, sleep paralysis could offer us a look into the mysteries of the human mind.

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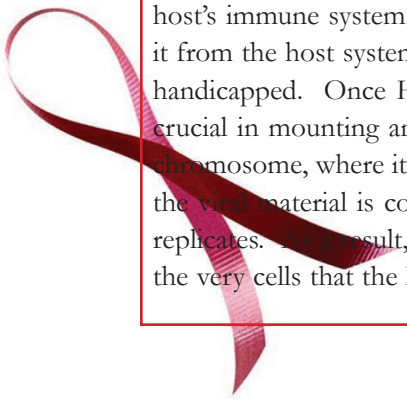
Hila Katz is a senior at Columbia College studying psychology.

HIV Evolution Resurrects Past Fears

by Vivian Ng

Early this February, doctors detected an evolutionary event that shook the health community: a man with a new virulent strain of HIV (Human Immunodeficiency Virus), the virus that causes AIDS (Acquired Immunodeficiency Syndrome). Granted, a new strain of HIV is not normally a great shock since this RNA-based virus has a high mutation rate. However, this strain is resistant to 3 out of the 4 types of drugs given in the highly publicized Triple Cocktail Treatment, currently the most effective method of suppressing the effects of HIV in HIV-positive patients.

HIV has a particularly devious way of attacking its host. Many viruses attack cells outside of the host's immune system, which leaves the immune system largely intact to fight off the virus and eliminate it from the host system. However, HIV infects the immune system directly, rendering the immune system handicapped. Once HIV enters the blood stream, it targets T-helper cells, a specific type of cell that is crucial in mounting an immune response against a foreign invader. HIV hides its genome in the human chromosome, where it can wait for an opportune moment before actually leaving the cell. While incognito, the viral material is copied and passed on to future generations of T-helper cells as the original host cell replicates. As a result, one virus can efficiently infect multiple cells. As viruses leave the cell, they destroy the very cells that the host needs to fight against these foreign invaders. HIV has evolved into an efficient



False Memories and Memory Distortion

by Yang Liu

Memory is easily manipulated. A mere suggestion can become a remembered fact. Take the example of two witnesses asked to give an account of a car accident. If before the questioning begins, one witness hears a misleading remark about a supposed yield sign that stood at the intersection, that witness will most likely tweak his memory to include the presence of the sign and report that it was there; the second witness, on the other hand, would make no such alteration to the memory of the scene. Even a testimony given in good faith is susceptible to the power of outside cues and suggestions; either an existing memory is reshaped, or an entirely new memory is created and planted in the mind as if it actually did occur.

The brain can't commit every little detail of our lives and our surrounding world to memory; there is too much out there for us process everything in depth and commit it all to memory. Our recollections tend to center on prominent, salient stimuli, events that depart from routine or that we think are unusual. When we try to recollect a certain scene, there are usually gaps and missing details. Either the mind can draw a blank, or it can attempt to fill in the gaps in our memories and the personal narratives of our lives. Outside cues and suggestions could prompt the mind – with its representations and conceptions – to invent a plausible memory or modify one.

Researchers are interested in the mental factors affecting memory manipulation. The imagination, or internal image generation, seems to be one powerful force in reshaping memory. A study conducted by Lyn Giff and Henry L. Roediger III of Washington University illustrates this point. In the first session of the study, subjects received instructions to perform an action, imagine performing an action, or simply do nothing but listen to the instructions. The actions were simple, one-movement steps, easy to recall – knocking on a table, crossing one's fingers, snapping a toothpick in two. In the second session, the subjects were instructed to imagine a fraction of the actions that they did not perform in the first session. Later on, they were asked which actions they did or did not initially perform in that first session. As it turns out, the more times subjects had imagined carrying out an action, the more likely they were to say that they had actually done it, even if this was not true.

An object of the imagination can take root in the mind as firmly as an actual object in the external world. Which parts of the brain might be central to the generation and influence of internal images? A study

by Ken Paller and Brian Gonsalves found that areas of the brain linked to internal image generation are highly activated when people initially imagine something that they will later recollect as an actual event. Study participants were scanned by an fMRI (functional magnetic resonance imaging) machine while looking at a screen that flashed a series of words placed alongside pictures. The words were all concrete nouns – nouns easily imaginable, such as tooth or cactus or mirror. Half the time these nouns were paired with their representative pictures, while the rest of the time the nouns were placed next to a blank rectangle. Whenever participants saw a blank rectangle, they were asked to imagine the picture of the noun next to it, and fill in the rectangle with their own imagination.

Twenty minutes after the study phase, participants listened to a random sequence of spoken words. A third of these words had appeared during the fMRI scan with a corresponding picture, another third had paired with a blank rectangle, and the final third had not appeared at all. For each word, participants had to recall whether they had seen it paired with a picture or not. Whenever participants falsely remembered a word – saying that the word had been paired with a picture, when it had not – researchers studied the fMRI scans to see which brain areas were uniquely activated in those moments when subjects had seen the word and imagined its corresponding picture in place of a blank rectangle. The precuneus, right inferior parietal cortex, and anterior cingulate in particular showed intense activation; these areas have been linked in past studies to visual imagery tasks and short-term visual memory of the spatial relationships between objects. A mental image might engage the hippocampus – a brain area key in memory encoding – much as a visual image produced by an actual object. Not only is visual imagination linked to brain regions uniquely its own; it also overlaps with visual perceptual pathways channeling information from the outside world.

Mental images that do take root in our mind are often strengthened by our expectations, emotions and general view of the world. Cultural norms, societal perceptions and popular opinion can modify our memories or fill in the blanks within our recollections. A bystander at a crime, for example, might falsely remember the gender or race of a criminal based on stereotype. A person discovering old childhood photos might make up a narrative to account for what was captured on film; these narratives could then take hold as actual memories. During survey studies, in which researchers pose questions about past events to participants, there is a potential for misleading responses. For instance, in a SIDS (sudden infant death syndrome) causal study, parents might be asked to recall the hours leading up to their infant's death. Along with questions about parental smoking and alcohol consumption, there might be a question on what sleeping position the infant was placed in. If conscientious parents had read in a book or newspaper about certain sleeping positions associated with more frequent episodes of SIDS, their grief, guilt, and ideas about SIDS could lead them to answer the survey by saying that they had placed their child in a position commonly thought of as dangerous, while in fact they might have no clear recollection at all. The survey question has served as a suggestion or prompt that leads them to think certain thoughts or create mental images, which they then latch on as truth. The published survey might then contain misleading information about the factors correlated with SIDS and further perpetuate widely held opinions.

MENTAL IMAGES AND PRECONCEPTIONS ARE COMPELLING IN PART BECAUSE WE ARE SO QUICK TO TAKE OUR MEMORIES FOR ACTUAL FACT, WHEN MEMORY IS FALLIBLE AND READILY SWAYED BY SUGGESTION.

Mental images and preconceptions are compelling in part because we are so quick to take our memories for actual fact, when memory is fallible

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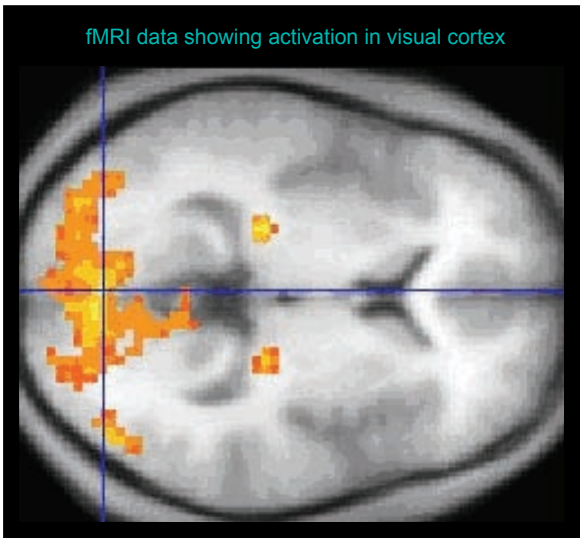

fMRI data showing activation in visual cortex

turning back the phages of time

by Adam Kaufman

A pressing world problem is the prospect that antibiotics, used dependably over the past sixty years against a host of bacterial infections, will lose their efficacy as pathogens become increasingly resistant. Faulty prescription of antibiotics for viral infections and industrial dosages to livestock for production purposes attest to the overuse and misuse of antibiotics, which have resulted in genetic selection of antibiotic resistant bacterial strains. “Superbugs” have evolved; initially resilient against one antibiotic, these microbes mutate, ultimately developing resistance to a variety of drugs including penicillin, methicillin, and vancomycin.

Antimicrobial resistance, more commonly referred to as drug resistance, has already emerged with regard to certain bacteria, such as Pseudomonas, which causes respiratory tract infections in cystic fibrosis and cancer patients, Staphylococcus aureus, which is the primary cause of hospital-borne infections, Enterococcus faecium and faecalis, which causes infections in the bloodstream, heart valves, skin and wounds, and Streptococcus pneumoniae, which causes bronchial and lobar pneumonia as well as strains of gonorrhea and typhoid.

Microbiologists and epidemiologists have acknowledged this problem for years. In fact, the Center for Disease Control and Prevention, the Food and Drug Administration, the National Institute of Health, and the World Health Organization, to name a few, have all initiated countermeasures. Three years ago, the WHO initiated the Global Strategy for Containment of Antimicrobial Resistance, which recommended intervention strategies that governments could undertake to halt, or at least stem growing drug resistance. Likewise, the CDC has a task force reviewing the problem, which has conducted active campaigns geared toward preventing antimicrobial resistance in hospital settings and promoting proper antibiotic use within communities.

While efforts of educating clinicians and the populace about the dangers of antimicrobial resistance are underway and pharmaceutical companies continue to develop new antibiotics, scientists are exploring the utilization of bacteriophages—tiny viruses that infect and destroy bacteria—as a viable option in the treatment and prevention of bacterial infections. Phage therapy originated in communist Russia and Eastern Europe. For a time in the 1930s, it was used in the West, but was abandoned due to inconsistent therapeutic results and the advent of antibiotics. New research, however, suggests that scientists may be able to engineer specific and effective bacteriophages, enabling them to operate as "smart" antimicrobial substitutes for antibiotics.

The Origins of Phage Therapy

Flourishing in diverse environments ranging from our bodies to the oceans, phages are one of the most abundant living organisms and have existed since life on Earth began. However, it was only in the early twentieth century that researchers demonstrated phage therapy to be a potential therapeutic to control

"Antibiotics Save Lives" from "Celebrate the Century Collection: 1940's" Antibiotics still save many lives today. However, their overuse and misuse have created the problem of antibiotics resistance.

Image from http://www.usps.com/images/stamps/99/antibiotics.htm

microbial infections. Bacteriophages were discovered in 1915 by the English bacteriologist Frederick Twort, while working with the bacterium Staphylococcus aureus. He observed that the bacterium was being destroyed by what he believed to be a virus, but he did not pursue those findings any further. In 1917, French-Canadian microbiologist and physician, Felix d'Herelle, was investigating an outbreak of dysentery among soldiers at the Institut Pasteur in Paris, when he contended that there existed a "virus parasite of bacteria" that served as a natural weapon against germs.

Seven years prior in 1910, d'Herelle was in the Yucatan during a plague of locusts. D'Herelle investigated an unusually high concentration of sick and dead locusts in a certain region. Noting the runny consistency of their stool, he concluded that the locusts had been infected by coccobacilli bacteria. He ran follow-up experiments, during which he noted that something was eating at the bacteria in the stool. Years later in Paris, d'Herelle repeated the same set of experiments on the feces of French soldiers suffering from dysentery. Upon culturing the Shigella bacteria that caused the dysentery, d'Herelle observed, just as he had in the Yucatan, that there were clear areas on the agar plates devoid of bacteria. Intrigued by the cause of these clear spots, he removed bacteria from the fecal matter through filtration, and then cultured fresh bacterial cells with the filtrate on agar plates. He then mixed portions of the plate devoid of bacterial growth with a culture of Shigella bacteria and found that the resulting solution was clear. Had there been Shigella in the resulting solution, it would have been opaque, leading him to conclude that through filtration, he had isolated microorganisms that devoured bacteria. He labeled them bacteriophages.

Believing that phages were a promising means to fighting diseases, d'Herelle continued to

experiment and publicize his results. In subsequent years, d'Herelle traveled to Soviet Georgia, where he and scientist Giorgi Eliava established the Eliava Institute. There they produced commercial phage products to treat a variety of ailments ranging from infected wounds to respiratory infections. To this day, the Eliava Institute continues to conduct therapeutic phage research.

In the United States in the 1930s, the pharmaceutical company, Eli Lilly, also manufactured therapeutic phages, but the use of bacteriophages was short-lived. A new class of drugs—penicillin and other antibiotics—took center stage. Doctors favored antibiotics because they were easy to use and could successfully kill a broad range of bacterial infections. Phage therapy was relegated to a secondary position in the fight against microbial infections.

The Facts on Phages

The process by which phages kill bacteria requires precision. Phage-bacterial interaction begins with the phage attaching itself to a bacterium and injecting its DNA into the host. It utilizes the genetic apparatus of the bacterium to replicate phage components. As the phage grows exponentially within the bacterium, the walls of the bacterium burst, a process known as lysis. These daughter phages then infect the nearby bacteria, eventually decimating the bacterial colony. Each phage can produce as many as a hundred daughter phages per half hour lytic cycle. This efficient self-replication greatly reduces the need to re-administer the phage, an ideal property for antibacterial therapy; however, there are limitations and problems with phage therapy.

One of the primary limitations of phage therapy is a narrow host range. Whereas antibiotics can be used without knowing the identity of the disease-causing bacteria, phages are very specific. The bacterium needs to be identified and targeted before phage therapy can begin, which can pose problems when time is of the essence. Proposed solutions include utilizing phage cocktails, a grouping of phages with broad host range, or developing of quick protocols for identifying bacteria.

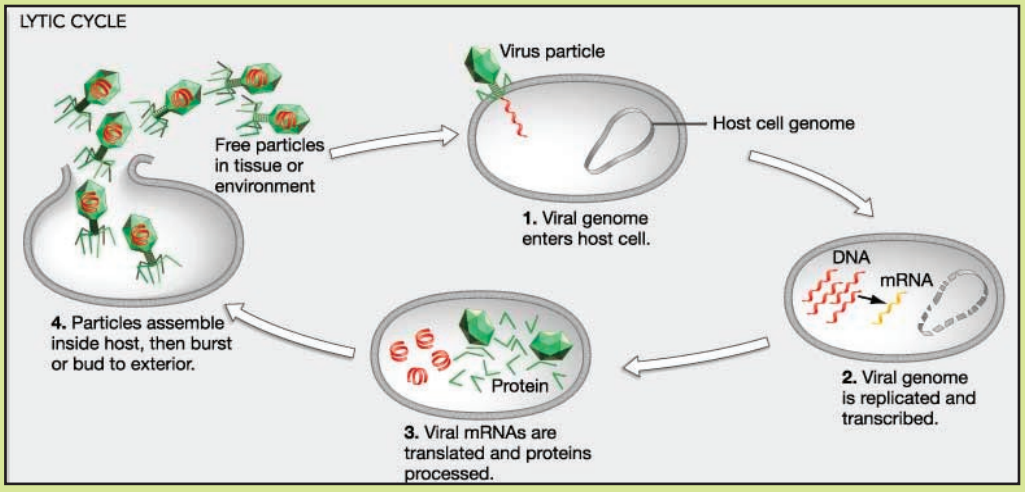
Another potential obstacle is that bacteriophages are rapidly removed from the body by the filtering organs of the reticuloendothelial system, whose cells engulf and destroy phage particles. In an effort to slow down the clearance rate, Dr. Richard Carlton together with researchers from the National Institutes of Health has developed a technique to identify phages that have a greater half-life. Known as serial passage, this patented technique involves injecting a phage into an organism, isolating the phages that survive for longer periods of time, and then reinjecting them into organisms until "long-circulating" phages have been isolated within an organism.

There is also the issue of phage resistant bacteria. Statistically, phage resistant bacteria should exist within a population of at least 10^6 bacteria, thereby rendering phages useless in those instances. However, a study was conducted using 1,000 times more bacterial cells than would normally be found in an infected environment, and yet the phage still successfully killed the bacteria.

As with antibiotics, resistance can develop through exposure to treatment. The mutation of a single gene might result in the loss of the receptor on the bacteria to which the phage binds, causing resistance. Partially resistant bacteria also present a problem. In

How a Phage Infects Bacteria

A T4 bacteriophage ("virus" on the illustration) injects its own DNA into bacteria ("host cell"). The viral DNA is replicated and proteins needed to construct the virus are made using resources in the host cell. Virus are assmebled inside the host, and when it is time, they burst out of the host cell, killing it in the process.



this case, phages are capable of binding and injecting genetic material into bacteria, but binding rates are low, rendering the phage virtually ineffective in curing a bacterial infection. Phages, in response to resistance, can likewise evolve to adapt to bacterial mutations, setting into motion a domino-like effect. Although phages can mutate to combat bacterial resistance, bacteria can in turn mutate to become refractory to the original phage as well as the mutant phages, perpetuating an evolutionary cycle in an arms race of sorts.

"With the rise of antibiotic resistant bacteria, new tactics for treating bacterial infections are necessary... Thus the scientific community is under pressure to delve further into understanding and developing phage therapy so that it might be used either independently in the treatment of disease-causing microbes or in conjunction with vaccines and antibiotics."

The Bordetella Bacteriophage Study

The issue of phage resistance was addressed in a recent study conducted by Dr. Jeffery Miller and his team of researchers. They studied the genome of the Bordetella bacteriophage, which is the phage that infects Bordetella bronchiseptica—the bacterium responsible for causing respiratory infections in mammals, and closely related to the bacterium that causes whooping cough. The Bordetella bacterium has a dynamic surface structure that Dr. Miller noted is "highly variable as result of a complex programme of gene expression mediated by the BvgAS phosphorelay, which regulates the infectious cycle." One would therefore expect that the ability to regulate surface receptor cells renders the Bordetella bacterium impervious to bacteriophage therapeutics. However, the researchers discovered that the Bordetella bacteriophage possess "microevolutionary adaptation" abilities that allow the phage to generate "new variants that may have become resistant to the previous phage." Simply stated, the genetic material of the Bordetella bacteriophage contains genes that mutate the part of the virus that attaches to the bacterial receptors, thereby circumventing the resistance that would otherwise occur because of the changing surface of the bacteria. Dr. Miller and his team believe that the phage's ability to diversify results from the existence of a "variability generating cassette encoded in the phage genome." The team is presently trying to determine how widespread this evolutionary adaptation is in nature. The hope is to eventually develop means of genetically engineering phages to treat phage-resistant bacterial infections.

With the rise of antibiotic resistant bacteria, new tactics for treating bacterial infections are necessary. For a variety of reasons, ranging from costs to the difficulty of obtaining FDA approval for new antibiotics, many pharmaceutical companies have little interest in developing new antibiotics. Thus the scientific community is under pressure to delve further into understanding and developing phage therapy so that it might be used either independently in the treatment of disease-causing microbes or in conjunction with vaccines and antibiotics. Clearly, phage therapy is not a panacea, but it is a promising option in the battle against antibiotic resistance.

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and readily swayed by suggestion. That memory does not provide a perfectly accurate record is a humbling realization. So much depends on memory – eyewitness accounts, media reports, historical primary source documents, as well as our own sense of who we are and what has happened to us. Some skepticism and questioning of our personal thoughts might partly safeguard our minds from readily assimilating an imagined object or event into our recollections. But because our original memories are, for the most part, incomplete, the mind will continue being vulnerable to inaccuracy, distortion, and memory modification.

Tweety the canary and Sylvester the cat always were both methodical and creative. Sworn enemies, they spent most episodes plotting and pursuing each other's doom, be it through culinary experiments like Tweety Pie or more complex endeavors involving drainpipes and bowling balls. But perhaps the most original and unexpected scenario in which the cartoon nemeses appeared has been at the center of a Barnard Professor's research with the deaf in Nicaragua. The cat and the canary are helping elicit evidence that children contribute greatly to the creation of language.

In her recent experiments with Nicaraguan Sign Language – built upon episodes of Tweety and Sylvester – Barnard Professor of Psychology Ann Senghas has released some of the most compelling evidence to date that children enter the world with an instinctive capacity for language. When exposed to formalized language, they have the ability to internalize vast amounts of linguistic information, from words to grammatical rules. But even when they cannot hear surrounding conversations and linguistic production, as was the case with deaf children in Nicaragua during the 1980s, Senghas proposes that children can generate this linguistic foundation all by themselves. In other words, they can create a new language.

"I was drawn to the youngest members of the deaf community in Nicaragua because they offered an opportunity to see how languages emerge and how they are shaped over time," Senghas said. "Each generation supplies a rich new complexity to Nicaraguan Sign Language."

As one of the youngest formal languages on the globe, Nicaraguan Sign Language (NSL) is fertile ground for research. It surfaced in the late 1970s when a group of 250 deaf Nicaraguans were united at two special education schools in Managua. The schools' objective was to teach them how to read lips in Spanish, efforts that met with little success in the years that followed. However, while the children's education failed, their ability to communicate with one another expanded. They had arrived in Managua with no linguistic platform beyond the "home gestures" they had used with their families. Within months of social interaction, the deaf students were combining these rudimentary signs into a type of pidgin language, lacking in grammar and other linguistic complexities but sufficient to express basic ideas and events. As new generations of children entered the school, they learned the gestures and added to them. By the mid-1980s, the system had become a recognizable, complex language.

What intrigued Senghas was the rapid transformation of NSL. Over a period of ten years (1980s), it moved from a simplified, gestural system to a formulized language, one eventually exhibiting universal linguistic hallmarks like noun-verb agreement, clauses, and complicated grammar (just like American Sign Language or spoken English). This was the type of evolution a linguist might expect to see unfold over 300 years, not within one generation. With no exposure to external influences, the question of where the fundamental structure for the language had originated, and how it got there so quickly, needed to be addressed.

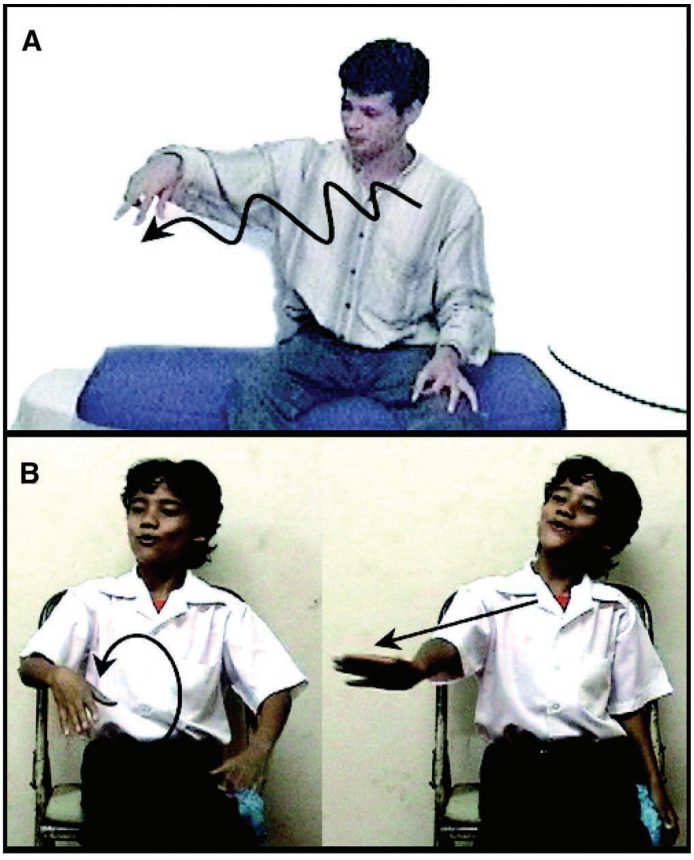
In 1999, Senghas and two other scientists[1] devised an experiment that would test for the inception of one of the universal hallmarks of language – the breaking down of holistic events into discrete pieces with smaller meaning. By their very nature, languages dissever the continuous motion of the world into highly specified matters of representation. If one wants to describe the fluid action of a snowflake spiraling down through the air in English, for example, one does so by describing the noun, the manner of travel, and the path in different fragments of speech: "snowflake," "spiral," and "down." Such separation not only enables speakers to describe an event more accurately, but also allows them to produce a nearly endless number of expressions from a limited set of words. Every language from Swahili to Japanese exhibits this characteristic of discreteness. Senghas wanted to know when it emerged in NSL.

She recruited 30 deaf Nicaraguans of various ages and split them into three cohorts: those who had learned NSL before 1984 (the originators), those who had acquired the language between 1984 and 1993 (1st generation), and those who had learned it after 1993 (2nd generation). All the deaf participating in the experiment had been using NSL since the age of six. Senghas showed the individuals in each of the cohorts an episode of *Tweety and Sylvester* titled "Canary Row" in which Sylvester climbs up a drainage pipe in pursuit of Tweety. Tweety throws a bowling ball down the pipe, Sylvester swallows it, and the ill-fated cat comes tumbling down the shoot, rolling into a bowling rink across the street. When the video was finished, each of the individuals was asked to describe the event to a peer.

The results were conclusive. 73 percent of individuals in the first cohort described both the manner and the path of Sylvester's fall down the drainage pipe in one gesture – they simultaneously twirled their hand and moved it down their bodies. The gesture, though communicative, was non-linguistic. It took a holistic event and described it holistically. On the other hand, 78 percent of second-cohort signers and 73 percent of third-cohort signers marked the manner and path of Sylvester's action in separate gestures. They made a twirling sign to indicate manner of travel first and then gestured down their bodies to indicate direction. Just as someone speaking English would have said "tumble" and "down," so too the majority of second- and third-cohorters had taken a holistic event and signed it sequentially through a series of elemental gestures.

"We saw evolution in action," said Senghas of her results. "The [Nicaraguan Sign] language is like an organism that's being shaped and refined by human minds."

Not just any minds, she added. It was the children in particular who generated the evolution of NSL from a non-language to a language. Senghas's results suggest that when young Nicaraguans came



into contact with a roughly assembled set of gestures (those created by the first cohort), they had an innate ability to add a linguistic foundation. They instinctively added grammar, clauses, and other complexities to the system they found around them, and they began dividing holistic events into fragmented signs. Thus, their ingrained understanding of language, prompted by the early gestures, was the creative force behind NSL. Equally apparent from Senghas's research is the fact that the older generation of signers (the first cohort) was incapable of adopting this added complexity. Just as your grandfather might still say "icebox" instead of "refrigerator," so too the first generation of Nicaraguan gesturers never learned the formalized NSL being created by their younger peers, despite extended exposure.

Judy Kegl, a Professor of Linguistics at the University of Southern Maine and the first sign-language expert who studied NSL, is encouraged by Senghas's work.

"It is now apparent that children come into the world with a language-ready brain," she said. "They look for certain types of linguistic complexity in the world around them…It's also clear that humans lose this faculty as they age."

Senghas's findings, released in the September 17, 2004 edition of *Science,* now raise a host of new questions. If children continue to tinker with language after universal linguistic hallmarks have emerged, do the modifications constitute refinement or merely change? If the former, when do children cease refining a language? Perhaps more interestingly, if children are in fact the progenitors of NSL, does this offer insight into how human language emerged in prehistoric times? In response to the last question, Senghas speculates that the "intergenerational force" that is presently driving NSL forward is likely what created the unbridgeable gap between humans and their ancestors years ago. One can imagine a scenario where adults developed a set of grunts and gestures that children who were predisposed to language could naturally pick up on. Those children demonstrating this basic language-learning capability would have been selected over time, and the cognitive capacity for language would have gradually emerged.

With two years left on a grant from the National Institute on Deafness and Other Communication Disorders, Senghas plans to delve into these issues more fully in the years to come. Whether she continues her research in Nicaragua with Tweety and Sylvester on board, however, remains to be seen.

Getting Older?

Mitochondrial Mutations May Be to Blame

by Patricia Peter

Though discovering the elixir of life is still a very remote possibility, new research into the phenomenon of aging is beginning to shed some light on the biological processes that occur in our bodies as we get older. A Swedish study, published in Nature magazine, has established a definitive link between mutations in the mitochondria and aging. A correlation between aging and the mitochondria has been hypothesized for some time, but this study implies that mitochondrial mutations trigger the aging process instead of merely serving as indicators of a process already begun.

The Energetic Organelle

One of the most important organelles in the cell, mitochondria are present in the thousands, found in all the cells of the human body except for red blood cells. Part of the reason for their ubiquity is their vital role in providing energy to the cells, converting the energy stored in food into adenosine triphosphate, or ATP, which can be used to power cellular processes. The two pathways in the cell responsible for approximately 90% or more of ATP production – the Krebs cycle and the oxidative phosphorylation electron transport chain (ETC) – both take place in the mitochondria. In addition to producing much needed ATP, the mitochondria are also responsible for regulating cellular response to stress and apoptosis.

Mitochondrial Missteps and Aging

Unique among the cellular organelles, mitochondria possess their own DNA, known as mitochondrial DNA (mtDNA), which produces the proteins necessary for ATP production. However, unlike nuclear DNA (nDNA) with its histones and other enzymes responsible for maintaining nDNA integrity, mtDNA is much more susceptible to damage, especially by free radical oxygen molecules, with which it comes into close contact when attached to the inner mitochondrial membrane. The irony is that the mitochondria's ETC and oxidative metabolism pathways are the primary sources of these harmful free radicals, such as the superoxide radical, hydrogen peroxide, and the hydroxyl radical, which ultimately contribute to mtDNA mutation and degeneration. As proposed by the free radical and the mitochondrial theories of aging (MTA), as mtDNA accumulates more and more mutations due to this free radical damage, mitochondrial ATP production is hampered and no longer able to satisfy the energy needs of the cell. The cells and tissues that experience this energy loss then gradually lose their functionality and die. Unfortunately, such mitochondrial damage primarily occurs in post-mitotic cells such as those of the brain, heart, and skeletal muscle, which no longer replicate

after childhood and are therefore irreplaceable. Because the multicellular organism cannot replace these cells, aging progresses as more cells die as a result of irreparable mtDNA damage.

Ever since Denham Harman of UC Berkeley initially postulated the link between mitochondrial function and aging, much research has been conducted to test the theory. One of the most telling studies in this field was conducted by Australian researcher Anthony Linnane who examined skeletal muscle tissue samples from both a 5-year old and a 90-year old human. Analyzing the mtDNA content in each of the samples, he found that less than 5% of the mtDNA sample from the 90-year old was in the form of full-length mtDNA; the rest was highly mutated. The 5-year old's mtDNA, on the other hand, was almost entirely normal. Another study discovered an inverse relationship between the rate of hydrogen peroxide production by the mitochondria and the maximum life span of a species, lending credence to the theory's emphasis on the link between radical oxygen species (ROS), mitochondrial damage, and organism longevity.

Although scientists knew of a correlation between mitochondrial degeneration and the aging of an organism, they still had to grapple with a new version of the chicken/egg debate: Which came first – decline in mitochondrial function or the biological process of aging? In other words, it was unclear whether the decreased functionality of the mitochondria was merely a manifestation of an aging process already begun or whether it in fact contributed to the onset of aging. Some research has, in fact, weighed in on the issue, asserting that the mitochondria have important roles in commencing the process of cellular aging. For example, scientists discovered that young rat cells degenerate rapidly when injected with the mitochondria from fibroblasts of old rats, that stimulating the production of free radicals in human fibroblasts results in senescence characteristic of old age, and that antioxidants, such as vitamin C, alleviate the oxidative stress experienced by the mitochondria, increasing mean and maximum life span in rats. The study conducted by Aleksandra Trifunovic and her associates last year has done much to support these previous efforts in establishing a causal link between mitochondrial damage and the onset of old age.

Of Mice and Mitochondria

In the study, Trifunovic at the Karolinska Institute in Sweden and her colleagues genetically engineered mice to contain a defective DNA polymerase-γ gene, which is involved in copying, proofreading, and repairing mtDNA. The mutation eliminated the enzyme of its proofreading capability, but did not affect its role in mtDNA replication. As a result, the normal amount of mtDNA was produced, but the mtDNA was more susceptible to mutations arising from errors in replication, and these mutations would accumulate as mtDNA continues to replicate. As expected, enzymes important for mitochondrial-mediated ATP production exhibited decreased functionality, leading to a decrease in total ATP production in the mutated mice.

The more unusual and interesting findings were the other physical effects the mutant mice exhibited as a result of their mutated mtDNA, which seemed to substantiate the mitochondrial theory of aging. At about 25 weeks of age, young adulthood in mouse terms, the mice showed symptoms indicative of accelerated aging, such as hair loss, osteoporosis, anemia, and reductions in fertility (see figure below). These results suggest that mtDNA mutations are the cause, not effect, of many features of aging in an

Phenotypes of premature aging are manifested in mutant mice (mut) with defective DNA polymerase-γ. Wild type mouse is shown below.

organism.

Although the findings of this study strongly support the theory that mitochondrial degeneration leads to the development of the aging phenotype, they do not exclude the possibility of contributions by other pathways such as those mediated by telomerase or p53. Nonetheless, any future models of the aging organism will surely include mitochondrial considerations.

Live Long(er) and Prosper?

What sort of implications does this study and the related Mitochondrial Theory of Aging have for all those eternal life seekers out there? Well, even though youthful rejuvenation may not soon be available in convenient chewable tablet form, there are several promising avenues of MTA research aimed at increasing longevity.

In addition to exploring possible methods of inhibiting mtDNA mutations via genetic manipulations, some dietary regulations may decrease the mtDNA-damaging effects of radical oxygen species in the cells. Caloric restriction has long been shown to be an effective anti-aging solution, extending the life span of rodents, worms, and possibly even primates by decreasing mtDNA damage by radical oxygen species. Though true caloric restriction would be too severe to be used as a common anti-aging therapy in humans, developing pharmacological agents that mimic caloric restriction could be utilized instead.

Supplementing our diets with more antioxidants could also reduce the damage caused to the mitochondria due to oxidative stress, though studies thus far have failed to substantiate this hypothesis. While mere vitamin supplements seem to have little effect on combating mitochondrial degeneration, injection of a naturally occurring class of antioxidants, nitrones, has yielded especially impressive results. The John Carney of the National Academy of Sciences conducted a study in which gerbils were treated with phenyl butyl nitrone (PBN), which binds with and traps free radicals to make them less reactive. Before PBN treatment, two age groups of these gerbils, young and old, were made to go through a maze. Initially, as would be expected, the older gerbils made more than twice as many mistakes as the younger animals. However, when injected with PBN, the older animals began learning at a more similar pace as the younger animals after only two weeks.

Another potentially useful antioxidant is coenzyme Q10 (CoQ10), which plays an important role in the mitochondrial ETC. In another study done by Linnane, he treated mice with a drug that mimics aging via mitochondrial impairment. The treated mice had less muscular endurance than untreated mice, reflecting a decrease in ATP production by the drugged organisms. Upon treatment with CoQ10, this damage was reversed and treated rats performed as well as normal rats in tests of strength. In addition,

> "...Although youthful rejuvenation may not soon be available in convenient chewable tablet form, there are several promising avenues of mitochondrial theories of aging research aimed at increasing longevity."

Rajindar Sohal at Southern Methodist University found that levels of CoQ10 have been linked to species life span – the highest proportions of CoQ10 correspond to the lowest production of ROS and the longest life spans – leading to the formulation of the hypothesis that the longer lifespan of mammals may be connected with the evolution of higher proportions of CoQ10 in mammalian species.

Despite the promise of longevity research focusing on the mitochondria as a key player in the aging pathway, possible real world applications are purely speculative at this stage. Though we do not yet know and probably will never discover a "cure" for old age, each new study in this field aids us in our understanding of that inevitable, often dreaded process of aging.

Patricia Peter is a sophomore student at Columbia College studying Biology.

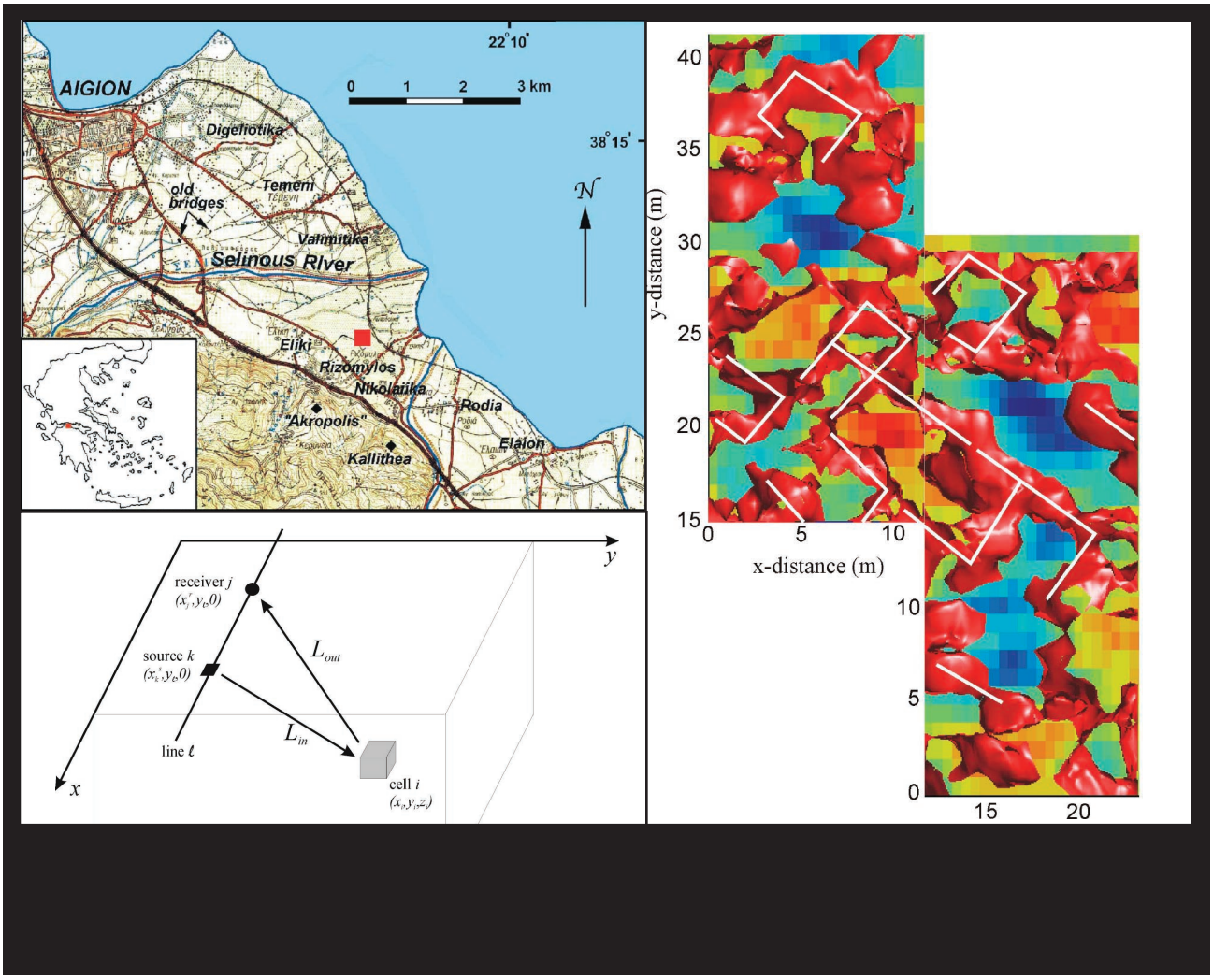
THE LOST CITY OF HELIKE

by Benjamin Witten

In the winter of 373 BC, a catastrophic earthquake and tsunami destroyed the classical Greek city of Helike. The city was submerged, leading some to speculate that it inspired Plato's epic story of Atlantis, written thirteen years after the city's demise. But contrary to Plato's account, the ruins of Helike remained visible under the sea. A traveler in the second century AD, Pausanias, and others described the sunken walls and a large bronze statue of Poseidon, the city's chief deity. Over time though, the many rivers of the region buried the ruins in layers of silt, and Helike completely vanished for thousands of years. Only in recent years, under the auspices of the Helike Project, has there been a tangible progress in locating the city, which lies in a region marked by tectonic upheaval and continual historical change.

The Helike Project, a group dedicated in finding the city, is not unique in its goals; from 1950 to 1990, other parties conducted searches using scuba divers and sonar to try to find the city on or underneath the seafloor. The Helike Project distinguished itself by changing the focus of the search from the sea to the land, when in 1991 it began drilling over one hundred boreholes on the coastal plain. Data extracted from the boreholes presented evidence for multiple occupational periods on the coastal plain, ranging from the Neolithic to the Byzantine, which according to Steven Soter, Co-Director of the Helike Project and Scientist-in-Residence for the Center for Ancient Studies at NYU, "potentially one of the most important archaeological sites in Greece"; Helike, of the classical Greek period, represents only one era and population of people who have lived in that area. One factor underlying the historical changes has been the region's tectonic activities. Evidence of raised fossil shorelines near the delta point to both tectonic uplift and subsidence, indicating that while Helike may have once been buried beneath the seafloor, tectonic activity has since raised it, where it may now lie among ruins and relics from other periods of time.

One of the Helike Project's investigative approaches has been to open test trenches throughout the area where the city is thought to lie. Though in 2001 this approach yielded building foundations and potshards from the fourth century BC – the time of classical Helike – these findings cannot be attributed conclusively to the ancient city. The project unearthed other interesting discoveries, including an Early Bronze Age town that might have also been submerged by an earthquake and an unusual pot of a kind made only in the city of Troy; it is the furthest west any artifact



from Troy has been discovered. Another unexpected find was a Roman Road that cut through many of the trenches. But from among these shifting pieces of historical time, the main portion of Helike has yet to be found.

One difficulty is that most of the area of interest cannot be excavated. It lies beneath farmland owned by local villagers. Not only would excavating on these people's land disrupt their farming and endanger their livelihoods, the Helike Project does not have the funds to compensate the farmers for crop loss or to buy the land outright. An alternative to extensive digging and trench-formation had to be found, and it was in 2003 that a team from the University of Oklahoma was brought in to perform non-invasive geophysical imaging of the area's subsurface.

A number of different geophysical techniques were tested to determine which would be best suited to find Helike and cause a minimal disturbance to the local villagers. A process called seismic reflection produced the best results on the test area near the Early Bronze Age site. To collect the data, a string of geophones – highly sensitive microphones – are pressed to the ground along a straight line. A series of sound waves, produced with a simple mallet striking a metal plate, are sent into the ground in between each geophone. The sound waves travel through the soil, and when they encounter a change in density, some of the energy reflects back to the surface and to the recording geophones. By knowing the wave speed through the soil and the round trip time from the source to the geophones, a depth can be determined.

After researchers go through a line of geophones, they move the microphones a fixed distance away and place them along a line parallel to the original line. The process is repeated until an entire area is mapped out in a grid pattern. With the information from the rows of geophones, various depths and features of an area's subsurface can be mapped out in a three dimensional image. In the images, structures that are shallower will usually date to a later time; as more time passes, a greater amount of sediment piles on top of buried walls and artifacts. This is an unusual application for seismic imaging which is normally

Breath Through Your nanotubes

by Carey Chen

Anyone boarding a long flight cringes at the thought of bone-dry air that inevitably leads to irritated eyes, a stuffy nose, and a scratchy throat. The world of nanotechnology is about to rub off on jumbo jets, though, and when it does, you will be able to breathe easier, literally. When Boeing puts its 7E7 airliner into service in 2008, chapped travelers will breathe air that is significantly more humid and similar to the air we breathe everyday. Airline executives and engineers have lauded the new aircraft as groundbreaking not only because it is kinder to passengers, but also because of the state-of-the-art material from which it is created: this sleek aircraft features a fuselage made of carbon fiber-reinforced polymer nanocomposites that resist corrosion and allow for a level of interior humidity never before possible.

Nanocomposites are made from nanotubes in the same way that pavement is made from gravel stuck in tar: the tubes are embedded in and held together by polymer. The term "nano" references the size of the tubes, which are measured in nanometers. A nanometer is one billionth of a meter. To put this incredibly small size into perspective, researchers working on nanostructures have to be careful to cover their skin, because a single skin cell is large enough to crush a nanostructure!

Carbon nanotubes are one of the most common types of nanostructures; they come in two forms, single wall or multiwall. Single wall nanotubes (SWNT) are seamless cylinders composed of carbon atoms in a regular hexagonal arrangement, closed on both ends by hemispherical caps. CNTs exist as a macromolecule of carbon, similar to a rolled sheet of graphite. Multiwall nanotubes (MWNT) look like the coiled shavings of chocolate one might see on a cake.

MWNTs were discovered accidentally in 1991 by the Japanese electron microscopist Sumio Iijima, who was studying the material deposited on the cathode during the arc-evaporation synthesis of fullerenes (Harris, 2002). He found that the central core of the cathodic deposit contained a variety of closed graphitic structures including nanoparticles and nanotubes, of a type that had never previously been observed. When asked about his observation, Dr. Iijima summed it up with one word, albeit a powerful one: "Serendipity" (Iijima, n.d.). This discovery immediately sparked a new area of research, and carbon nanotubes have been a hot topic ever since.

A primary challenge in processing SWNT/polymer composites is distributing the

Delft University of Technology and IBM in 1998. It was found that "SWNTs exhibit a very low resistivity. Electrical transport in good-quality metallic nanotubes is ballistic, that is, the electrons do not suffer from any scattering event over a few micrometers, even at room temperature. Semiconducting SWNTs are also ballistic on a length of at least a few hundred nanometers; more than is needed to fabricate CNTFETs" (Appenzeller & Avouris, 2004). The energy dissipation in the body of SWNTs is minimal, and the dissipated power density in the transistor channel is therefore reduced.

Other advantages of carbon nanotubes include a dramatically increased ability to do work and generate forces, as well as the ability to operate at low voltages and extremely high temperatures. These attributes make them useful in biomedical applications, as low voltages impart less stress on the human body, while the ability to withstand a range of temperatures allows them to function in numerous different body parts. Carbon nanotube artificial muscles are composed of billions of submicroscopic carbon fibers formed into sheets. The carbon nanotubes are found to be much stronger and more durable than either natural muscles or existing artificial materials (Township, 1999). Although the research is in an embryonic stage, CNTs are sure to revolutionize the future of biomedical science.

SWNTs typically have a tensile strength greater than 65 Gigapascals (which is 100 times that of steel at only one-sixth the weight), a modulus of elasticity on the order of 1000GPa, and an ability to withstand 10-30% elongation before fracture (Shelley, 2003). These superb mechanical properties suggest applications in the aerospace industry. The National Aeronautic and Space Administration benefits from SWNT-polyimide composites in that they exhibit "ultra-light weight, chemical stability, high thermal and electrical conductivity, hydrolytic oxidation resistance, radiation resistance, low solar absorption, low coefficient of thermal expansion, and mechanical durability" (National Aeronautics and Space Administration, 2002, p. 1). These attributes are desirable because the space shuttles of the next generation need to be resistant to rapidly changing temperature, pressure, and humidity.

Space shuttles are insulated with tiles that help protect the shuttle from extremely high temperatures and pressure during re-entry into the atmosphere.

And of course, Boeing's Dreamliner is using nanotube technology to create a more comfortable travel experience; this process has the added advantage of quick final assembly. Dreamliner can be assembled in as little as three days, while it typically takes 13 to 25 days to assemble a current Boeing model. The manufacture of different components, e.g. the engine, fuselage, etc. can be done independently by the different companies involved, and therefore, the final assembly only requires the work of Boeing's latest addition: an eight-headed robot moving about, applying carbon fiber tape to bring everything together.

While SWNT/polymer composites research has advanced quickly and generated a lot of excitement, challenges in the manufacturing process have yet to be overcome. Currently, there is not a low-cost production technique; the difficulty in processing raw SWNT products and maintaining the tubes' properties during composite fabrication and processing limits the rapid success of nanotubes as polymer fillers. Current prices range from $500-$1000 per gram of purified SWNTs (Vaia, 2002). Market projections, however, are optimistic. Daniel Colbert of Carbon Nanotechnologies, Inc. estimates that the market for compounded plastics will be $5 billion per year by 2005, and that the market for SWNTs to impart conductivity to polymers, and give them improved anti-static, electrostatic dissipation, and electromagnetic interference shielding capabilities, could reach $1 billion per year by 2005.

Nanotechnology has held a special place in the hearts of science fiction writers for decades. Now with NASA and other researchers leading the way, imagination is finally becoming reality. Considering the superior material properties of nanotubes, their wide range of applications, and their strong position in the market, it seems as though this small-scale wonder is about to blossom into a full-scale success.

Carey Chen is a sophomore in SEAS studying Chemical Enginnering.

A UNIVERSE ONLY A MOTHER COULD LOVE

by David J. Epstein

In his office on the fourth floor of the Mathematics Building at Columbia University, Peter Woit is paddling his chair across the rug with his feet. He needs to get to the blackboard, where he can begin frantically drawing twisting turning toroids that want to tear free of their two-dimensional chalk bodies. Woit's white and blue gridded shirt curves and crunches as he draws, erases, and draws again. His curvilinear facial features furrow. He appears briefly frustrated with the inability of the blackboard to show more dimensions. "This is one possible way, they think, to curve up extra dimension, beyond the three spatial and one time that we exist in today," Woit says. The diagram he is referring to looks like a partially unfolded cow udder. The straight cascade of brown hair that starts halfway back on the hemisphere of Woit's head gives him the look of a medieval duke. "Brian believes that string theory is the way the world works. Brian will tell you there should be one unique way that the extra dimensions arrange. Many theorists now think that there are some huge number, or perhaps an infinite number of ways the dimensions can be configured. The more they look, the more hideous string theory becomes."

The "Brian" Woit speaks of is physicist and mathematician Brian Greene, and he is busy across the hall, embroiled in one of his favorite evangelistic pastimes: creating believers in extra dimensions. A person standing in the fourth floor hall can listen to Greene through one ear and Woit the other. Greene is showing his students why Einstein failed in his quest to unite the two sets of physics laws – one set, general relativity, governs big objects like galaxies, the other, quantum mechanics, governs small things like electrons – and why there is room still to succeed. "Einstein could not have succeeded," he says. "He simply did not know enough physics yet." Greene is meticulously clad in black, from socks to sport coat, like he just stepped off the photo shoot for the back cover of his bestselling book, *The Elegant Universe*. He is leaning back, his elbow resting on a podium. His feet are crossed and he is whirling in soft circles the chalk that dangles between his fingers like a cigarette. Greene languorously, almost indifferently examines his board full of equations, like a painter appraising his own work, trying to decide if his most recent piece is a work of genius or a sham. From the side, Greene's face is a series of backslashes: acute nose, steep forehead, perfectly culled salt and pepper hair shaved into neat

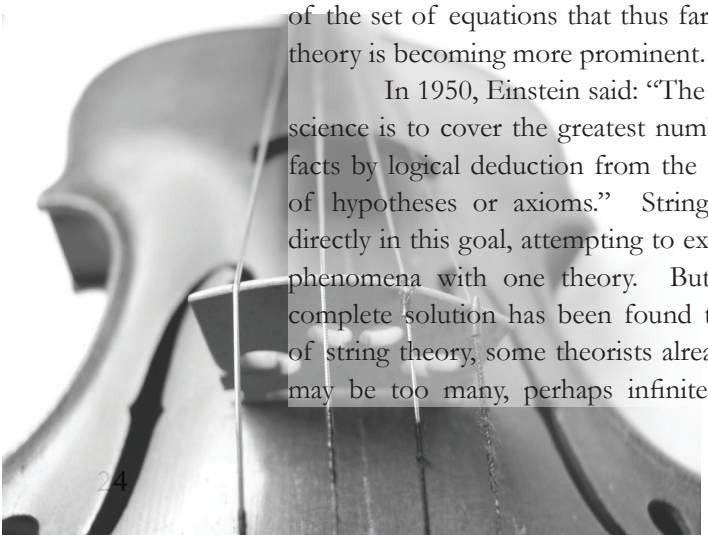
backslashy sideburns around his ears. "It is premature to say that there are too many solutions," Greene says. "I would prefer if there are few, or one. We don't understand string theory well enough yet to say there are many solutions. The theory is still elegant in its simplicity." Greene and Woit are part of the same department at Columbia. Woit often helps Greene fix his misbehaving computer. But the two men are worlds apart. Or six dimensions apart to be exact.

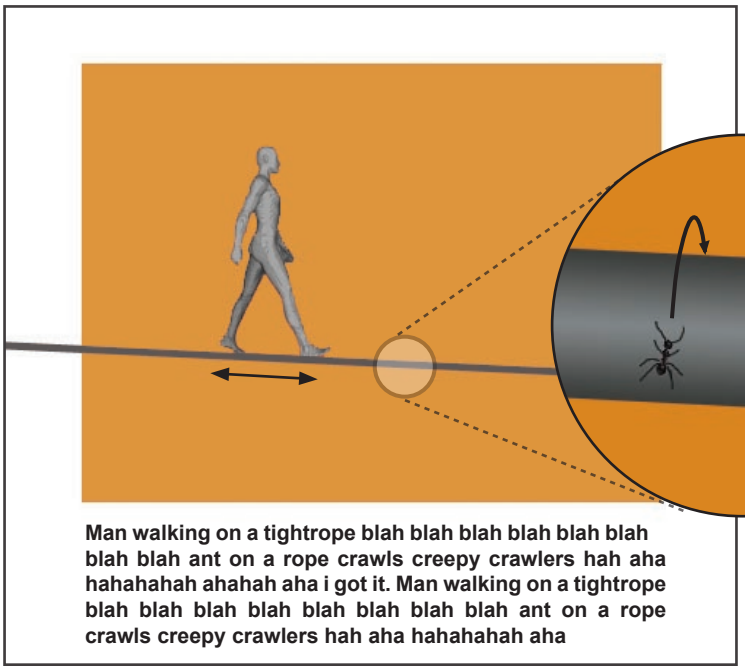
Greene is one of the most convincing proponents of string theory, a ten-dimensional conception of the universe that is currently the most popular candidate for describing the behavior of all objects, big and small, with a single theory. String theory suggests that one-dimensional "strings" are the most basic, indivisible building block of the universe. String theorists like to give the analogy of violin strings. When a violin string is stroked and plucked into various vibrational patterns, different musical notes rise from the instrument. Similarly, vibrating cosmic strings would create all the various particles and forces that exist in our universe, from those governed by general relativity, to those explained by quantum mechanics.

Woit is a string skeptic who prefers to operate in the world's four proven dimensions, the three spatial dimensions and time. His weblog, entitled "Not Even Wrong," is a crack at string theorists' inability thus far to produce anything that could potentially be falsified through experimentation. Both Greene and Woit are points along a spectrum of reactions to string theory. Greene is quick to concede that the theory has yet to come up with experimentally verified conjectures. But, like many of his colleagues, Greene's faith in strings is bolstered by their theoretical elegance. "Elegance," in this case, essentially means the ability of a single theory to explain many phenomena in our universe. But a potentially ugly blemish on the pristine face of the set of equations that thus far comprise string theory is becoming more prominent.

In 1950, Einstein said: "The grand aim of all science is to cover the greatest number of empirical facts by logical deduction from the smallest number of hypotheses or axioms." String theory follows directly in this goal, attempting to explain all physical phenomena with one theory. But even before a complete solution has been found to the equations of string theory, some theorists already believe there may be too many, perhaps infinite solutions, each one describing a different universe. If string theory turns out to give a large number of viable universes, then the power of a single theory to uniquely explain our own universe would, to scientists like Greene, be disappointingly diluted. Though string theory gained steam because scientists were attracted to its elegance, some are now wondering if the universe itself may be inelegant. Rather than a place that creates complex things from simple rules, the universe may be an extremely complex place that produces every outcome imaginable. As Stanford string theorist Leonard Susskind puts it: "It appears to me that our universe is one large Rube Goldberg machine."

String theory hopes to succeed in the task that stymied Einstein for the last 30 years of his life. He sought to find one theory that would unite general relativity with quantum mechanics, the two findings that revolutionized modern physics. General relativity is Einstein's theory that changed the way we think about space and gravity. According to general relativity, gravity, rather than a force, is the effect of a mass on the fabric of the universe. Like a bowling ball resting on a trampoline, a planet deforms the fabric of space, rerouting anything moving through the deformed area. General relativity allows scientists to predict precisely how most normal objects, from tennis balls to galaxies, will move through an area of space deformed by a mass. Where general relativity ends, at very small objects like atoms and electrons, quantum mechanics begins. Scientists can only predict the probability of how something as small as an electron will behave. Throw a baseball at the wall, and you can figure out exactly where it will hit and where it will fall. Shoot an electron at the wall, and it could end up somewhere along the wall, or it could turn up in China. This is known as "quantum uncertainty." Physicists can calculate the probability that the electron will appear on the wall as opposed to in China, but they cannot tell what will occur on any single test. The idea that the universe's laws for atoms and subatomic particles might resemble a slot machine did not sit comfortably with Einstein. "If general relativity and quantum mechanics do not fit together, you don't have your physics act in shape," says Samir Mathur, a string theorist at Ohio State





Man walking on a tightrope blah blah blah blah blah blah blah blah ant on a rope crawls creepy crawlers hah aha hahahahah ahahah aha i got it. Man walking on a tightrope blah blah blah blah blah blah blah blah ant on a rope crawls creepy crawlers hah aha hahahahah aha

University.

Today, the overwhelming majority of physicists still agree that nature should not be divided into separate laws for the large and small. "It's not like physics says, 'Okay, this thing's small so I'll do this, and this thing's big so I'll treat it this other way," says Mark Jackson, who is headed to Fermi Lab after recently receiving his Ph.D. in string theory under Greene's tutelage. By positing strings as the universe's smallest objects, string theory includes both gravity and quantum effects in a 10-dimensional universe in which everything arises only from strings. But this idyllic vision faces an ugly issue.

The 10-dimensional mathematics that allows string theory to merge gravity and quantum mechanics posits six dimensions that are so small as to be unobservable. String theorists contend that these dimensions are curved and coiled into a six-dimensional shape known as a Calabi-Yau shape. On a two-dimensional page, a Calabi-Yau shape looks something like a horde of snakes tangled together inside, around, and through a beach ball, (grad students have been known to use Twizzlers, three-dimensional flavor, of course, to visualize their homework). In the 1980s, when string theory was growing in popularity, relatively few Calabi-Yau shapes were mathematically described. String theorists were excited about searching through them to find the one that fit into string theory and described the phenomena of our universe. It was an optimistic time. "With some of the breakthroughs, we started seeing things in string theory that looked like real life," Susskind says. "Some people started announcing we'd have the final theory in six months." In those hopeful days, a particular property of string theory called "supersymmetry" helped strings to include general relativity.

Einstein's general relativity mandated that the universe could not be standing still. The mutual gravitational attraction of all matter should cause the universe to collapse back on itself, like a deflating balloon, in a final, fiery end: the Big Crunch. Einstein felt that the universe should not collapse, but should be eternal. So, he inserted into his theory a fudge factor, (yes, even Einstein fudged on his homework), that represented a repulsive force in the vacuum of space that would counteract gravity. Einstein's fudge factor is known as the "cosmological constant." The cosmological constant represents the energy in space, the "vacuum energy," that drives universal expansion, or, in Einstein's case, resists gravity just enough to keep the universe still. Edwin Hubble, however, subsequently proved that the universe was still expanding from the Big Bang like an inflating balloon; each galaxy or group of galaxies, like a point on the balloon, waving goodbye as its neighbors recede into the cosmic horizon. Faced with Hubble's discovery, Einstein discarded his fudge factor, and with it the vacuum energy, calling the cosmological constant the greatest mistake of his life.
n the absence of vacuum energy, supersymmetry helps strings provide an elegant theory of gravity, without violating quantum mechanics. Supersymmetry says that all particles – from light photons to the theoretical particle that causes gravity, the graviton – come into existence simultaneously with a partner particle. Theoretically, both particles in a pair arise from strings and have the same mass. "The idea is that they all come from the same single fabric," Greene says. In the equations of string theory, supersymmetric particle pairs cancel each other's energy out, leaving no room for vacuum energy. "But," says Woit, "no two types of particles having the same mass have ever been observed. So where are these superpartners hiding?" Thus far, nobody knows where they might be hiding, and nobody has proven that they do or do not exist. To make matters more complex, astronomers no longer prophesy the Big Crunch. Rather than gently

depressing the brake and then throwing it in reverse, the universe appears to be riding the gas. Universal expansion is actually accelerating. Einstein should not have discarded his cosmological constant. There appears to be a small vacuum energy in our universe that is acting as antigravity. Rather than ending crunched in a galactic sardine can, we will watch our neighbor galaxies disappear, never to return. Our galaxy will end not in a blazing crunch, but rather in a cold, lonely fizzle, like a candle burned to the bottom of its wick. But more pressing to string theorists than our pathetic finale is that supersymmetry, in the presence of vacuum energy, no longer holds. "Supersymmetry must be broken," Jackson says. "And we have no idea how badly." There still may be superpartners, but how wildly they differ from perfect supersymmetry is unknown. "If supersymmetry is barely broken, we may detect partner particles soon," Susskind says. "If supersymmetry is very badly broken, we may never detect them."

Without perfect supersymmetry, there are millions of Calabi-Yau shapes that could arrange the extra dimensions of string theory. Each individual Calabi-Yau has hundreds of variables that must be set to specify the six-dimensional "compactification," or balling up of the extra dimensions. These variables are of tremendous importance. "Changing these parameters," Woit says, "changes everything." One scheme of Calabi-Yau variables might give such a low vacuum energy that the universe would have stopped expanding and crunched long ago. Another scheme might dictate such high vacuum energy that universal expansion never would have slowed enough to allow planetary accretion in the first place. In that case, the Earth would have forever remained a pile of cosmic dust strewn about the widening expanse of space. To add to the heap of solutions, each distinct set of Calabi-Yau parameters itself dictates thousands, or tens of thousands of possible universes. In fact, the number of different possible universes is not only large, it is infinite. Fortunately, most of these infinite solutions can be thrown out, as they do not look anything like our universe. So what is the order of magnitude of the remaining solutions? "The question isn't 'What's the order of magnitude?'," Susskind says. "It's what order of magnitude is the order of magnitude." Susskind guesses that the number of relevant solutions is hundreds to thousands of digits long. "If this is elegant," Woit asks, "what shall we call messy?" But Greene maintains that this is no reason to give up on string theory. Even string theory's most avid proponents are quick to point out that much work remains. "Clearly we don't understand something basic about the whole thing," Mathur says. "But the hope is that when we find the silver bullet it will come clear."

Susskind envisions a mathematical screening process that can eliminate many of the Calabi-Yau configurations that do not produce realistic universes. "Brian Greene has the mathematical power to do something like that," he says. But even if Greene or somebody else does find a good mathematical filter, Susskind believes string theory will be left with an enormous amount of solutions that differ only in their vacuum energy. If this is true, then it is a pimple on string theory's elegant face that will not pass with puberty.

Susskind's idea can be appreciated by imagining an expanding soap bubble. As the soap bubble gets larger, the air inside the soap bubble changes slightly, and little soap bubbles begin to form inside the original bubble. The little bubbles expand also, each at a different rate dictated by the properties of its own private section of air inside the original bubble. Then even more bubbles form inside of the many bubbles within the big bubble. Pretty soon, there are lots of bubbles of different sizes, expanding at different rates. If Susskind is right, if there are many possible vacuum energies that satisfy string theory, it could mean that our universe is not the big bubble, but rather one of the inner, diminutive bubbles.

In the real world, of course, it is the vacuum of the universe that is expanding, not the membrane of a bubble. Physicists now believe that within a universe inflating according to a certain vacuum energy, interior sections of space with lower vacuum energy will expand at a separate rate, forming separate expanding sections – the small bubbles – each with a unique vacuum energy. So, Sussking says, if an enormous number of vacuum energies satisfy string theory, then somewhere in all the expanding pockets likely exists one pocket with the vacuum energy of our universe, in which planets form and life can exist. Susskind likens our vacuum energy to the water temperature in a particular region of the ocean. In that region, the temperature may allow a certain species of jellyfish to survive. We may simply live in

a bubble with a particular vacuum energy that allows for the evolution of life. Rather than shunning the idea of many possible bubble universes as the result of an incomplete theory, Susskind embraces it as the truth, ugly or not.

But many physicists do not accept this way of thinking. "When you resort to saying, 'Well, it is this way because if it weren't we wouldn't be here to observe it, then you have essentially given up the quest of explaining with physics," Jackson says. "You concede intellectual defeat." Jackson, Greene, and many other string theorists refuse to ride off into the cosmic sunset with the idea that our universe is one of a huge number of random possibilities. "A final theory should produce all the forces and particles we see from this simple idea of strings. It should have mathematics that cannot look any other way, and give a universe that can't exist any other way. Only then you cannot go any further," Jackson adds.

Susskind thinks this sort of intellectual valor stems from a philosophical longing for a beautiful, unique universe, and not from present evidence. "David Gross," Susskind begins, referring to his friend and prominent string theorist, "likes to quote that 1941 Winston Churchill speech." Susskind puts on his haughtiest British accent. "Never, never, never give up." He ditches the accent. "The problem with that is there are many people who spent their lives not giving up and not getting anywhere. It's not intellectual defeatism to look at the evidence. I'm sure people were disappointed when Darwin explained that people are the result of random variation, but their disappointment had no bearing on the truth." Within about five years, Susskind expects to see the community of string theorists leaning decisively either toward or away from his explanation.

One reason there has not already been a decisive explanation is because theoretical strings are much smaller than anything currently observable. The present method of smashing together particles in a collider to reveal smaller constituent parts comes nowhere near smashing the particles hard enough to reveal strings. Using current technology, a collider that might expose strings would have to be tens of millions of times the length of the distance between the Earth and the Sun. Even in a brilliant economy, the project seems unlikely. Rather, the best hope for proof of strings lies with astronomers, the pesky scientists who ruined perfect supersymmetry in the first place. By looking farther into space with telescopes, astronomers hope to see remnants of the universe from when it was so young and dense, that it could have provided the energies needed to act as a gigantic collider. Signatures of strings may exist in such observations. But nothing has turned up yet.

On the fourth floor of the Mathematics Building, Peter Woit is at his blackboard. He is moving chalk briskly through what he is quite sure are the three spatial and one time dimension of our universe. "The reason they look at string theory is because it has a quantum theory of gravity," Woit says. "But it doesn't have a four-dimensional theory of gravity. How that relates to our reality, I don't know. It isn't pretty."

A day later, Brian Greene is on the fourth floor. He just finished teaching his final class for the semester, and he is trying to get straggling students to finish the cookies that a girl brought to class. Greene is all black and white, from his hair to his shoes. Perhaps he is a man that prefers black and white. "If Susskind is right, it's very bold of him to give a positive outlook," Greene says. If Susskind is right, our universe is anything but elegant. If he is right, our universe is, in fact, random in the truest sense. Whatever the case, string theory remains the leading hope for a theory of everything. But with an undetermined order of magnitude of the order of magnitude of the number of solutions, we may have to learn that ugly universes need love too.

David Epstein is a reporter for the New York Daily News. He graduated from the Columbia School of Journalism in 2004.

Broken boats clog the harbor of Nagapattinam, a fishing village in the state of Tamil Nadu, India, after a magnitude 9.0 earthquake off the west coast of Sumatra, Indonesia generated a devastating tsunami in the Indian Ocean on Dec. 26, 2004. Almost 300,000 people--more than 16,000 in India alone--died as a result of these waves. Photo: Mohi Kumar

by Mohi Kumar

DR. DISASTER

At 00:58 Greenwich Mean Time on Dec. 26, 2004, the seismometer readings at earth science laboratories across the world tripped and danced, signaling that somewhere, disaster had struck. That somewhere was off the west coast of Sumatra, where the earth rumbled and ripped as the Indian Plate collided with the Burma Microplate, generating a tsunami that killed almost 300,000 people around the Indian Ocean.

"The seismic signal was so large that it circled the world, causing it be re-recorded by seismometers," said Arthur Lerner-Lam, a seismologist at Columbia University's Lamont-Doherty Earth Observatory (LDEO). "The earth rang like a bell—it resonated."

But to Lerner-Lam, the director of Columbia University's Center for Hazards and Risks Research, seismograms represent more than the science of wave motion. It represents the earth's violent power and its capacity to destroy human life. It is a thread connected to a web on which elements of natural disasters can be analyzed—its economics, psychological impacts, mitigation strategies, engineering implications, even its politics.

"I first experienced an earthquake during graduate school in California," Lerner-Lam said. "I was excited by it—it was like an amusement park ride. I thought, 'Neat! Let me get in line again!'" He smiled. "I was young and indestructible. To me, the earthquake was a symbol of the dynamic earth. I wasn't too concerned with its social consequences."

Only later, when working on mapping faults after a major earthquake in the mountains of Asia, did the chaos and destruction following disaster cause Lerner-Lam to wonder about how the science he studied impacted human life and how his profession carried an enormous responsibility to help mitigate suffering. "People faced death and sorrow; they were shocked

that this could happen to them," he explained. "But because American scientists were involved, the people equated scientific activities with hope."

To address these issues, Lerner-Lam helped to spearhead a re-evaluation of natural hazards across the world, focusing on how multiple hazards interrelate, how current urban planning methods in the Third World amplify disaster, and how the economic burdens of disaster force poorer countries to stay impoverished.

In light of the recent tsunami in the Indian Ocean, Lerner-Lam believes that now is the time to focus on the idea that disasters can become obstacles to sustainable development. "If we can, we need to use the tsunami to push the point that development must include preparation for environmental hazards," he said.

While Lerner-Lam agrees that the recent earthquake and tsunami were amazing displays of the earth's power, such phenomena in general are inevitable; what can be changed, he explained, is how people prepare for these inevitabilities. He remembered the 1999 earthquake in Izmit, Turkey, the 2003 earthquake in Bam, Iran, both killing more than 20,000 people each; he recalled his travels to disaster zones in Georgia and Armenia after devastating earthquakes leveled entire cities. "We keep having disasters when we know perfectly well what do to change this," he said, emphasizing that human suffering can be minimized during a geological event. "Unless we clarify and integrate between natural phenomena and the things that matter to people—such as their health and well-being—then we won't be able to convince them to do the right thing."

In this spirit, as countries surrounding the Indian Ocean are rebuilding themselves after the tsunami, Lerner-Lam is using his expertise and influence as a scientist to stress the importance of multiple hazard awareness to policy makers. "Data needs to be driven in a new way, to drive a much broader discussion of issues," he said. "We can do science and engineering, but what is interesting to me is what all this means to the people whose lives are affected by earth processes." Without this connection between science and policy, Lerner-Lam explained, people will continue to die.

Born in 1954 in Brooklyn, Lerner-Lam showed early promise for science and engineering.

He remembers playing for hours with his Erector construction set. "Tiny parts would be lost in the rug all the time," he chuckled. "I liked to take things apart, and put them back together."

"Once, at my grandfather's house, I took an alarm clock apart and put it back together and plugged it in to the wall," Lerner-Lam laughed openly, pushing his glasses further up his nose. "It blew a fuse. I'm lucky that I had a very tolerant grandfather."

His mother was a biology teacher in a public high school, and he can remember as an elementary school student helping her set up experiments for her class. But he got his first true taste of experimental science through helping his aunt and uncle, biology professors at the University of Kansas, with their research.

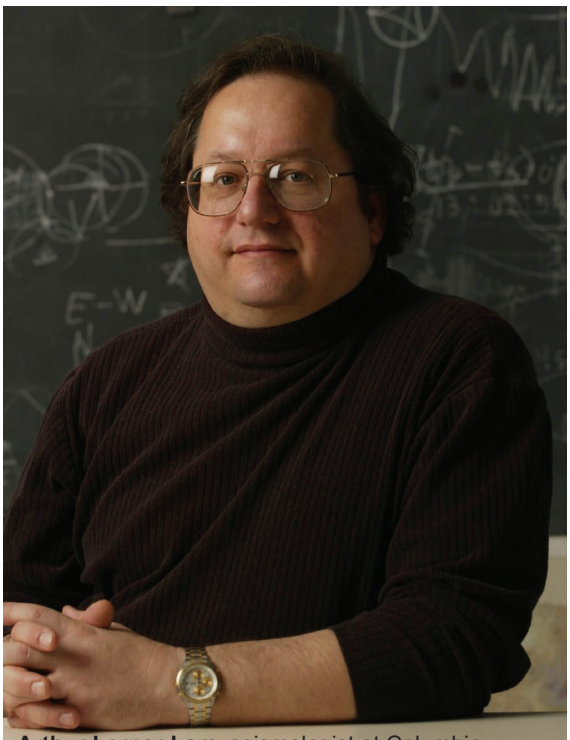
"My uncle was an embryonic biologist studying the consequences of generational manipulation of poultry," Lerner-Lam said, explaining that his uncle conducted breeding experiments with chickens. "I once had to hold a rooster while my uncle extracted its semen." His lips twitched, then he grinned. "Basically, I held the rooster while my uncle masturbated it to fertilize chickens. I think I was twelve at that point."

After that, Lerner-Lam explained, biology wasn't quite his thing. "It never stuck, unlike engineering

Photo: Mohi Kumar

and the mechanical aspects of making things work. But my aunt and uncle taught me the fun of doing experiments." They instilled in him a curiosity about the world and the creativity to discover for himself the answers to his questions, he said.

As a high school student, Lerner-Lam excelled in the qualitative aspects of science. However, only in college did his fascination for earth science emerge. As a freshman at Princeton University, he read a popular science book about plate tectonics, then an emerging theory. "It was called Heart of the Earth or something like that—I can't even remember now," he laughed at the recollection.



Arthur Lerner-Lam, seismologist at Columbia University's Lamont-Doherty Earth Observatory and director of the Center for Hazards and Risks Research

Intrigued, Lerner-Lam took an introductory earth science class. Though he described it as a 'rocks for jocks class,' he became hooked. As he took more classes, be began to be heavily involved in writing papers.

"They were about normal modes," Lerner-Lam said, explaining his research on the vibration of the earth after an earth after a major earthquake. "They were not published, but became touchstones for me to point to the importance of research for undergrads, and drove me to continue research as a career."

After earning a B.S. in 1974, he hopped from one top university to the next, earning his doctorate at Scripps Oceanographic Institute in 1982, and then researching as a post doctorate fellow at the Massachusetts Institute of Technology for the next two years. In 1984, he was hired as faculty at the Lamont Doherty Earth Observatory, where he served as a senior researcher and a professor.

David Simpson, the former director of the seismology lab where Lerner-Lam worked described Lerner-Lam as a first class scientist. "He helped revolutionize the computer network at Lamont—it was one of the first UNIX networks in the nation. He wasn't just a teacher, he worked with designing projects like these and carrying them out," Simpson said.

"Until I got to Lamont, I spent most of my career at a desk doing seismology, where the data comes to me," Lerner-Lam recalled. Dealing only with the mathematics of earthquakes sterilized the hazard by distancing science from the human suffering of natural disasters, he said.

Lerner-Lam's first taste of disaster response fieldwork came after the 1989 Loma Prieta earthquake in San Francisco, when Simpson sent him to California to assess its aftershock pattern by installing a dense array of temporary seismometers close to the earthquake's epicenter to determine a more accurate record of pattern of earthquakes.

Now, with current technology, we are able to mobilize aftershock pattern within a day," Lerner-Lam said. "No one had available industry to put that out before. This was an exciting piece of field work."

Lerner-Lam next studied the geology of Caucasus Mountains, establishing seismic networks in Georgia, Chechnya, Dagastan, and Ossetia as part of a program aimed to get Russian and American scientists to work together. The idea, Lerner-Lam explained, was to foster nuclear disarmament by establishing open monitoring for nuclear blasts in both countries. "Politics aside, this work opened up basic research lines about earthquakes and thrust faults in a previously unmonitored area," he said.

Lerner-Lam continued, "We traveled thousands and thousands of miles in Russian jeeps and trucks, even helicopters." Recalling an incident where his team sought to install a seismic unit at the foot of a glacier in the high reaches of the mountains, he remembered how a helicopter and its first-time pilot flew into a narrow canyon to drop them off. "The pilot got spooked, and refused to go further.

We told him to set us down high up on the canyon walls. We jumped off with 600 pounds of equipment, dodging propeller wash then headed down hill to a farm house." He laughed. "The look on the farmer's face when we told him we came from New York was priceless."

The team borrowed the farmer's donkeys to carry their equipment, and then set out to the main road with the farmer as a guide. "I have a picture of Art walking beside his donkey, with the seismic stations strapped on it, trying to get it up a hill," said Simpson, who was with Lerner-Lam at the time. "Those local people were absolutely unbelieving of where we came from."

When the team reached the road, the scientists hitchhiked south. "We waved a packet of cigarettes to flag down a truck." Lerner-Lam paused, then shrugged. "It's about Zen. You have to have the attitude that providence will get you where you want to go eventually."

The day after he returned to the United States from this fieldwork, the 6.8 Racha Earthquake devastated Georgia, killing 270 and leaving over 100,000 homeless. "A day later, I was back for aftershock work—there were a couple hundred," he said.

Yet without paperwork for Lerner-Lam get into Georgia, his team had to improvise. "The Russian scientists ended up dressing me up as a Russian laborer," he recalls. Wary of Georgian border police, they stuffed Lerner-Lam in an old army coat and put him in the back of their large truck, trying to pass him off as the peasant hired to move all the equipment.

"The Russian scientists told me, 'Shut up, we'll do the talking,'" Lerner-Lam continued. His team was stopped at the border. "When the military opened the back of the truck, I just smiled and waved. I was in my Zen mode. I had just seen Apocalypse Now, and was kind of in an 'up-the-river' mode too. It was fun. But I think after three or four days of smuggling me in, the guard figured us out. He kept waving us through though."

In Georgia, Lerner-Lam began to see how his work could have the potential to help people. In the Loma Prieta earthquake, "though there were deaths and damages, they were not heartbreaking," Lerner-Lam explained. Georgia, on the other hand, was a very poor and unprepared area. The flood plains where they built cities amplified the seismic waves and destroyed critical facilities like hospitals. There was no power or water, and damage to roads effectively cut them off from the world. "The buildings there, and in much of the developing world, are put together like tinker toys, with poor construction habits and poor material,"

Freshly cracked land after the magnitude 7.4 earthquake shook near Izmit, Turkey on Aug. 17, 1999
Photo by Mohi Kuma

Lerner-Lam said. "They are basically cemented rubble that's not re-enforced—floors collapse on each other like a stack of pancakes. What can be done if people are not prepared?"

In Georgia, Simpson remembers Lerner-Lam as being very sincere with the afflicted people he met. "Art serves well in foreign areas—this is an important part of making research work."

But beyond research, the scenes of destruction in Georgia caused Lerner-Lam to re-evaluate his role as a scientist. "There is something deeper going on than just analyzing earthquakes," Lerner Lam said. "With science there is hope. If you walk as a scientist into a country, you automatically have credibility—people believe science is automatically good. We have a responsibility to maintain that."

With this in mind, Lerner-Lam began to seriously look at hazard assessment as a science six years ago. In addition to teaching mathematical inverse theory, he developed an undergraduate seminar called "Science and Society" to explore the relationship between science and public policy. A year later, he collaborated with members of Columbia University's Urban Planning Department to discuss teaching a graduate seminar on environmental and natural hazard city planning.

In this class, which ran for three years, students of various disciplines examined natural hazards in Caracas, Venezuela; Istanbul, Turkey and Accra, and Ghana, looking to see what practices city officials could follow to prevent damage from earthquakes, landslides, and flooding before they happen.

"We all shared the ethic that we may not know enough about phenomenon, but we know enough to know when information can be used to help people. We can't be predictive in terms of time, but we certainly can be predictive in terms of where," he said.

The ability to research science while looking at the bigger picture earns him the admiration of his students. "His quantitative skills are stellar," said Kristina Czuchlewski, a seismologist who studied at Columbia University. "I remember talking to him about specific details like eigenvalue decomposition when he was my professor of Inverse Theory. He always took a step back though, to look at the bigger picture."

Czuchlewski worked on assessing the hazards of Caracas. "For that paper, Art should have been author—he was so instrumental in helping shape my ideas. But that wasn't really his goal. He just wanted the information out there," she said.

This dedication led Lerner-Lam to research how impoverished countries follow practices of rapid urbanization without considering how environmental hazards affect growth. In a series of maps and charts, earth scientists, geographers and economists at Columbia University, facilitated by Lerner-Lam, have highlighted the areas on the planet most prone to disaster, focusing on regions where multiple hazards generate multiple risks. The study, called the "Natural Disaster Hotspots: A Global Risk Analysis," was released this March by Columbia University, the World Bank, and other institutions.

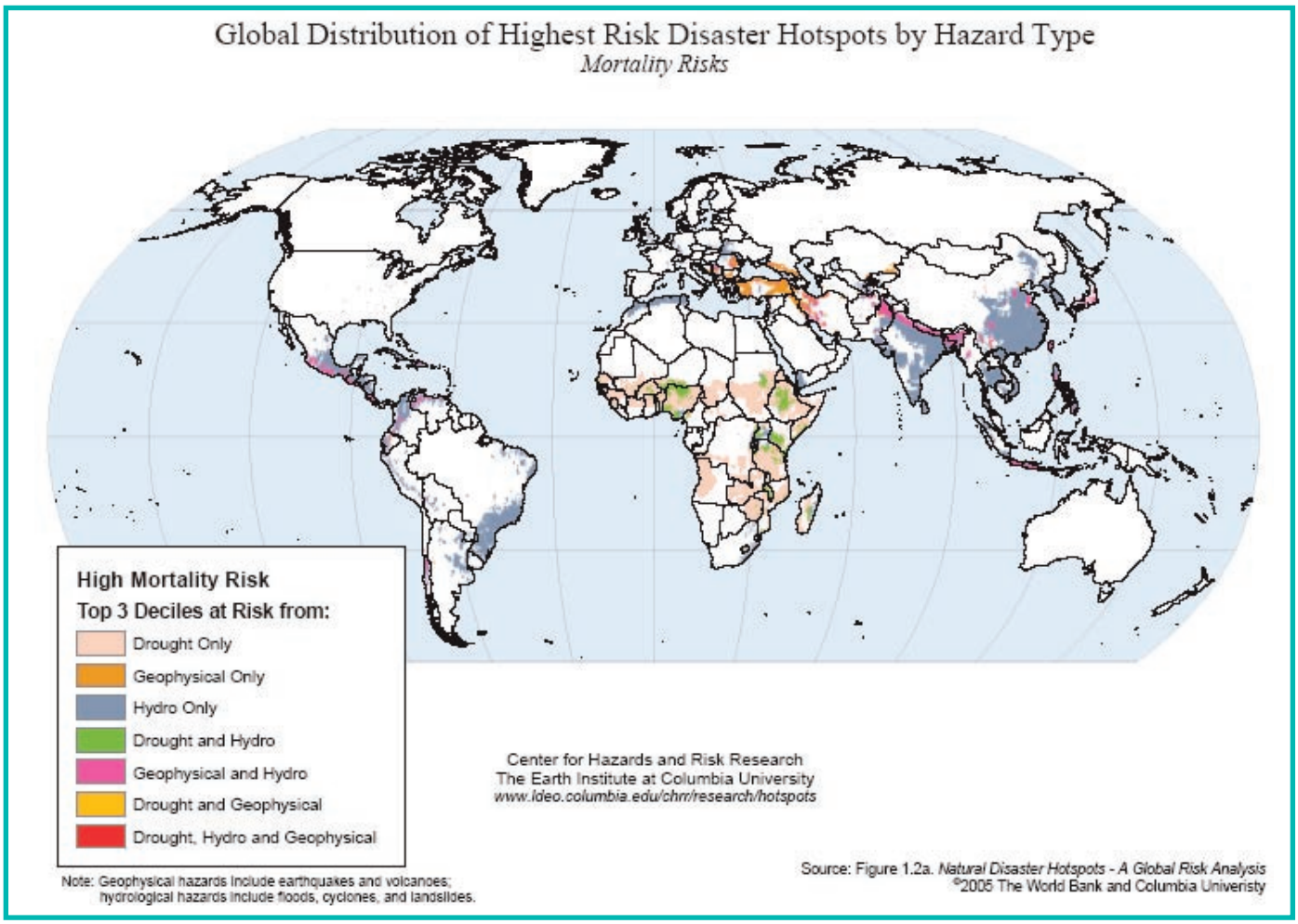
Integral to this study is how disaster relates to poverty, explained Lerner-Lam. "Persistent economic loss from natural disasters leads to a persistent and increased debt load for poor countries. Does this cause the country to be swamped out of investment in sustainable development? Does being poor cause disaster, or does disaster cause poverty?"

Research focused on answering these questions is a natural supplement to the U.N. Millenium Development Goals, said Chandrika Bahadur, a policy advisor for the United Nations. "Disasters are interrelated with poverty in a unique way," she said. "Countries in the developing world need to plan for this effectively" The Millenium Development Goals seek to address factors that cause extreme poverty in the hope that better practices can lead to economic sustainability.

But in order to achieve this sustainability, researchers need to understand how education about hazards translates into policy changes, Lerner-Lam argued. "I'm really interested in way scientific information is used by people," he said. "Science is very conservative—everything has error bars, caveats related to uncertainty of observation, sampling error and predictive error." But sometimes, Lerner-Lam asserts, these caveats are used to justify a conservative approach to handling problems.

"Uncertainty is not an excuse for inaction. Predictive elements to natural systems, when properly utilized ought to influence policy," he said. "We need to translate these geological inevitabilities into the episodic nature of natural disaster to motivate people to change their behavior,"

Bijan Khazai, a post-doctoral fellow studying earthquake engineering at the Earth Institute, is



impressed with Lerner-Lam's dedication to this issue. "I'm glad a group of people are looking at this through various fields—geology, geography, engineering, economy. Usually seismologists don't talk about these other issues. That in itself is a token that something exciting is going on here."

It is precisely Lerner-Lam's training as a seismologist that has given him the credibility to address how science should be used to influence policy after the Indian Ocean tsunami.

The Monday after the disaster, Lerner-Lam began to pull together scientists at Columbia University to respond to press inquiries. Through his coordination, demographers and geographers began to estimate the total population affected by the waves. But his interest in the implications of the tsunami went further. "A colleague of mine realized that the huge event struck poor countries, and we thought it was critical to put together our thoughts on the meaning of it all," he explained. He, along with other scientists, drafted a letter the U.N. Development Program stressing the importance of multiple hazard awareness in reconstruction, stressing scientific collaboration between countries. "We need smart recovery in these affected areas," he explained. "Not just to get communities back on the path they were on, but to do better, to translate this tragedy into a long term culture of hazard reduction and prevention."

Lerner-Lam is also actively helping countries plan for an Indian Ocean tsunami warning center. In early March, he attended a conference dedicated to Indian Ocean tsunami warning systems hosted by the U.N. Educational, Scientific and Cultural Organization as a science advisor for Thailand. His message to other nations stressed hazard preparedness. "We need to use this to catalyze added investment in other natural hazards—cyclones, earthquakes, floods" said Lerner-Lam, noting that cyclones kill thousands every year around the Bay of Bengal. "What you need is a Bay of Bengal hydro-meteorological disaster warning system. While warning for a tsunami, you also warn for typhoons and floods—it should not be a separate system."

>continued on **page 35**

illuminating
the Road to Development

by Matthew Berry

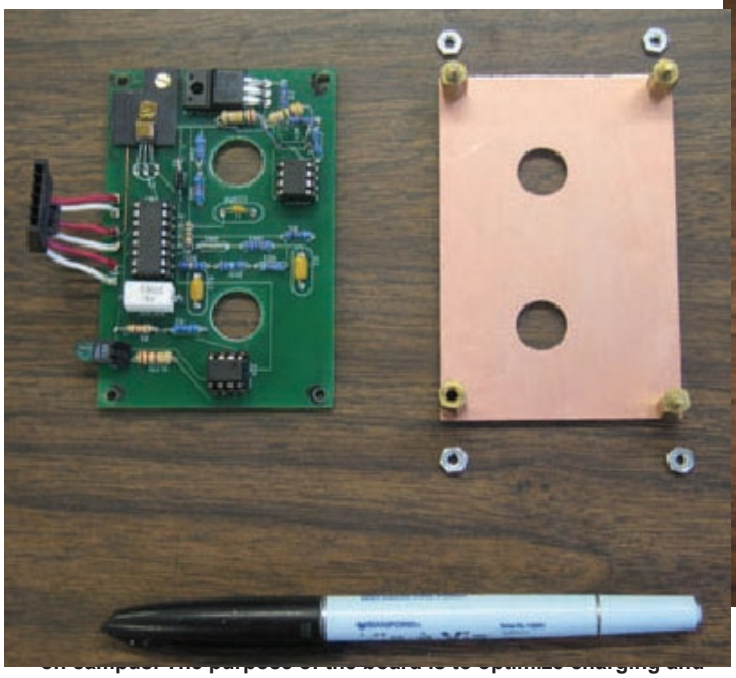
The United Nations Millennium Project represents one of the largest efforts to end poverty in the history of mankind. By the year 2015, all 191 United Nations Member States have pledged to meet eight goals (The Millennium Development Goals, or MDGs) that include eradicating extreme hunger and poverty, achieving universal primary education, ensuring environmental sustainability, and targeting AIDS. But while meeting the MDGs will require billions of dollars and cooperation between all nations, students at Columbia are working to make an immediate and positive impact on the lives of the world's poorest.

The MDGs work from the top down to implement a range of major poverty reduction initiatives. At the same time, The Earth Institute's Millennium Villages Project at Columbia University (a project complementary to, but distinct from, the Millennium Development Project) is working from the bottom up to provide villagers in selected locations in Africa with practical, economically viable solutions to their most immediate needs. An important objective of the Millennium Villages project is to test whether the multi-sectoral approach of the MDGs—which argues for the simultaneous implementation of development interventions in many areas at once—will reduce poverty and improve welfare on a relatively short time scale of years, rather than decades, and with currently available, proven technologies.

Imagine having to survive with little or no access to electricity. Most residents of wealthy, industrialized countries, if asked how we would cope, couldn't answer. But millions of people in Africa go a lifetime with only minimal access to electricity. While it may be common for African villagers to use disposable batteries to power appliances such as small radios, many have no consistent access to electric lighting, ovens, refrigerators, computers, or medical devices. And due to the high cost of connecting poor and remote villages to electricity grids, many of Africa's poor are likely will go without grid power for decades to come.

But what if African villages could have access to key energy services, such as electric lighting in the home, without installing power grids? This is one objective that the Millennium Villages energy interventions aim to achieve. Columbia students led by Professor Vijay Modi of the Mechanical Engineering department designed and created a portable battery system that young villagers can carry to school, charge during the day, carry home, and there use to power an electric light. The villagers benefit in that children are able to study at night using electric lights that are roughly 20 times brighter than the small kerosene wick lamps currently in use. This allows for improved educational opportunities and decreased reliance on wick lamps, thus reducing smoke and soot in the home.

Improving indoor air quality in village homes is another priority for Dr. Modi's team. Currently, over 80% of villagers cook and heat using biomass fuels (including firewood and charcoal, as well as stalks and other waste from farms) that generate smoke and pollution when burned indoors. Most villagers do not have chimneys in their homes, leaving them to breathe hundreds of times more particulate indoor air pollution in a day than deemed safe by the U.S. EPA. Estimates are that this results in respiratory disease responsible for approximately 1.6 million deaths annually. Because villagers may rely on biomass as a primary cooking fuel for years or decades to come, Dr. Modi's group is examining how to make the use of biomass as a fuel safer. To this end, the Millennium Villages project will



output capacity.

The final product designed by Columbia students: a battery with shoulder strap is attached to a lamp and reflector.

install simple smoke extraction tools (including smoke hoods and possibly chimneys) in selected households to examine how these can decrease exposure to pollution. If successful, this strategy may be used by the Millennium Development Project as a large-scale means of reducing respiratory disease.

By marrying engineering to development, the Millennium Villages project allows students at Columbia to participate in one of the world's great humanitarian efforts. Through innovation and teamwork, these students use research and technology to broaden the reach of applied science and make an immediate impact on the lives of the poor.

For more information on the energy-related interventions taking place within the Millennium Villages project, contact Vijay Modi, modi@columbia.edu or Edwin Adkins, Research Coordinator, at jea98@columbia.edu. Or visit http://www.earthinstitute.columbia.edu.

Matthew Berry is a junior student in SEAS, studying Civil Engineering

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Lerner-Lam's leadership has earned him the praise of his colleagues. "Art is a world-class expert on seismology and seismic hazards. He provided a lot of high caliber factual information on what happened and why" explained Maxx Dilley, a researcher in disaster and risk management at Columbia University's International Research Institute for Climate Prediction. "He knew the other scientists working on the seismicity of the region. But he also organized very efficiently Columbia University's overall response to the tsunami, and coordinated scientific perspective to disaster managers."

But to Lerner-Lam, praise for his efforts may be pre-mature. "On paper, we can fix anything," he said. "What matters is if we actually do fix anything."

Mohi Kumar is a student at the Columbia School of Journalism

FOR THE BIRDS

by David J. Epstein

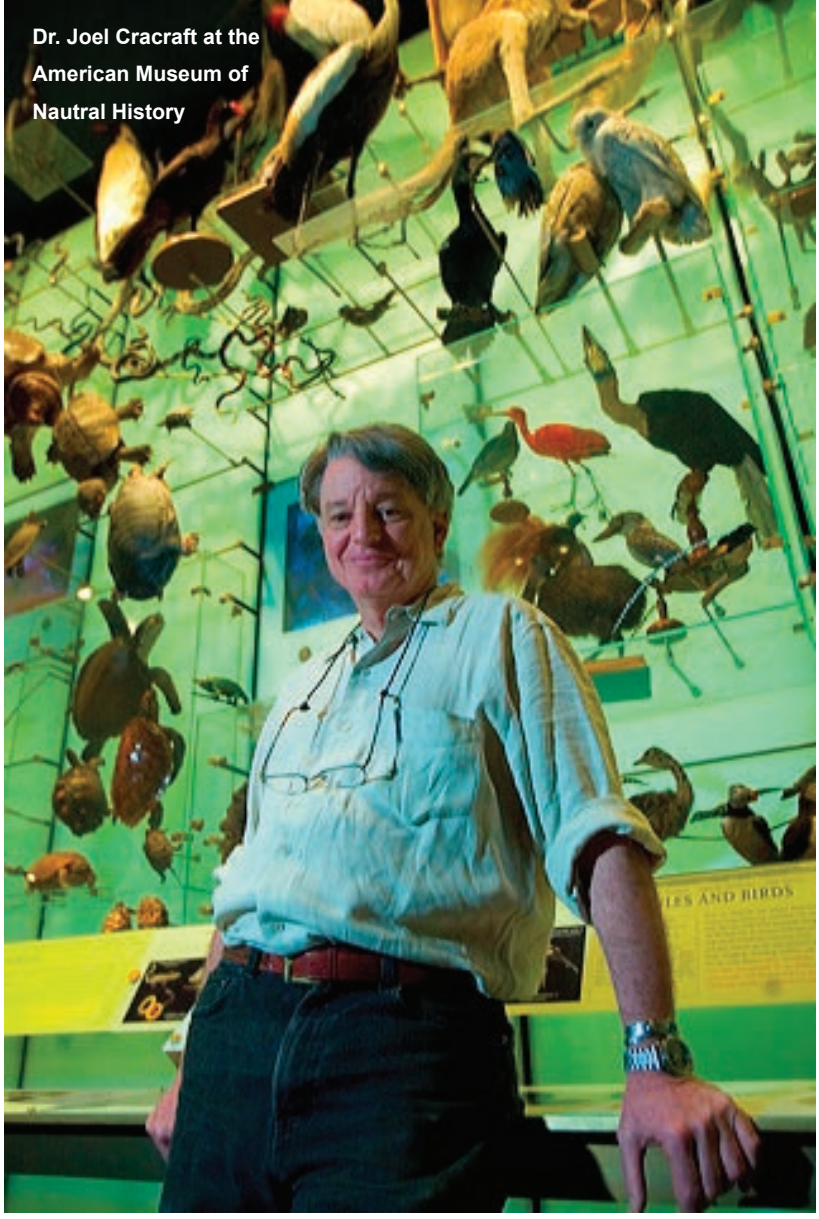
It's winter, and Dr. Joel Cracraft just flew back north. He had been in Antarctica, lecturing about birds, and putting forth his disputed theory about the ancestral lineages of modern birds. Now Cracraft is back in his fifth floor office atop the American Museum of Natural History. If Cracraft opened his windows, he could nearly step into the upper branches of the trees in Central Park. This is the nest from which he pushes his ideas about modern bird origins out into the scientific world.

In the past, paleontologists have found the vast majority of fossils of contemporary birds – which are called Neornithes, and include everything from puffins to pigeons and herons to hawks—in the Northern Hemisphere. These discoveries have led many to conclude that modern bird lineages arose in the Northern Hemisphere portion of the ancient supercontinent of Laurasia, the mass of land that later broke into North America, Europe and Asia. But Cracraft believes that the Neornithine fossil record suffers from sampling bias. "Historically there haven't been many paleontologists in the Southern Hemisphere," he argues. "Most of the work has been done by paleontologists based in the Northern Hemisphere, so most of the fossils have been found in the North."

Cracraft exudes a boyish exuberance, and the complementary boyish frustration with his opponents, as he spirals toward enthusiasm, his graying bowl-cut flopping about with each emphatic assertion. Cracraft is anything but exhausted. It does not show that he just returned from Antarctica, the heart of another ancient supercontinent – Gondwana, which became South American, Africa, Madagascar, Australia, India and Antarctica —where he *knows* bird lineages began. Not only does he know they began there, but that they did so before many paleontologists think they did: that is, before the extinction of the dinosaurs. Cracraft is determined to see his theory through to scientific victory. For him, the debate is about more than birds. "The lack of ability and desire to interpret evidence," he says, "is the greatest problem in our country today."

Cracraft's eyes drift as he begins to talk about his theory. It's like he's dragging up his own childhood memories. The biggest bone that Cracraft's scientific detractors employ in beating back his theory of Southern Hemisphere bird origins is the fossil record. Many paleontologists have said, simply, that the fossil record should be the guide by which bird lineages are determined. And that record has a paucity of Southern Hemisphere specimens that look like the early ancestors of modern birds. "My argument," Cracraft says, "was that there are other kinds of evidence that these lineages evolved in Gondwana, and that they are older than the K/T."

The "K/T" is the acronym for "Cretaceous/Tertiary." Sixty-five million years ago, a meteor about 10 kilometers in diameter slammed into the Yucatan Peninsula in what is now Mexico. It turned out to be a pretty wretched day for most life on Earth at the time.



Dr. Joel Cracraft at the American Museum of Nautral History

Photo by Lane Johnson

The force of the impact was roughly equivalent to 10,000 times the strength of the entire world's nuclear arsenal. The rock of the Earth flowed like lava at the impact site as dust and steam were hurled into the atmosphere, blackening the skies. Perhaps three-quarters of all species of animals disappeared forever as a result of the impact. That mass extinction marks the transition from a period of dinosaurs, to one without. Scientists know it as the border between the Cretaceous and Tertiary periods of Earth history, or the "K/T boundary" for short.

But Dr. Alan Feduccia of the University of North Carolina, Cracraft's archrival, cannot envision any way that Neornithes could have survived the K/T disaster. "These birds are the veritable miner's canary," Feduccia said. "To claim that they just sailed through the K/T boundary is just inconceivable."

Using fossils, scientists like Feduccia have come to the conclusion that modern birds originated following dinosaur extinction. They also believe that whether modern birds originated in the Northern or Southern Hemisphere is necessarily ambiguous, given the dispersal capabilities of birds. Few fossils exist that might be modern bird ancestors before the K/T boundary, and their relations to contemporary birds are unclear. But modern bird fossils abound in sediment that paleontologists date to be from about 5 to10 million years following the extinction. "The proof is in the pudding," Feduccia says. He points to over a dozen Cretaceous sites that have supplied researchers with hundreds of bird bones, but not a single one that is clearly related to contemporary birds. "There's just not a single [Neornithe] fossil before the K/T, and then there they are after it."

Feduccia believes that among the only birds that survived the meteor strike were "transitional shorebirds," the putative ancestors of modern rails, cranes and sanderlings. These birds can survive eating detritus that washes up on shorelines, possibly one of the only available food sources in the aftermath of the meteor. Feduccia subscribes to the theory that these shorebirds represent the link between the pre-meteor birds and the Neornithes that evolved in the aftermath. With many of the dominant life forms removed from the Earth, Feduccia says, a variety of bird lineages could easily have arisen to fill the suddenly emptied ecological niches.

His idea parallels a theory that some scientists, including Dr. Paul Olsen of Columbia University, hold, which posits that the apocalyptic clearing of dinosaurs allowed mammals, and eventually humans, to capitalize and become dominant on Earth. Most of the modern birds, Feduccia thinks, probably appeared within 10 million years. Other scientists doubt that such proliferation could have occurred so quickly, but Feduccia points to the finding by University of Michigan's Dr. Philip Gingrich that whales evolved from land-based ungulates in only eight million years. "It's hard to imagine any animal more specialized than a whale," Feduccia says. "If a whale can evolve that quickly, it is easy to believe birds could have."

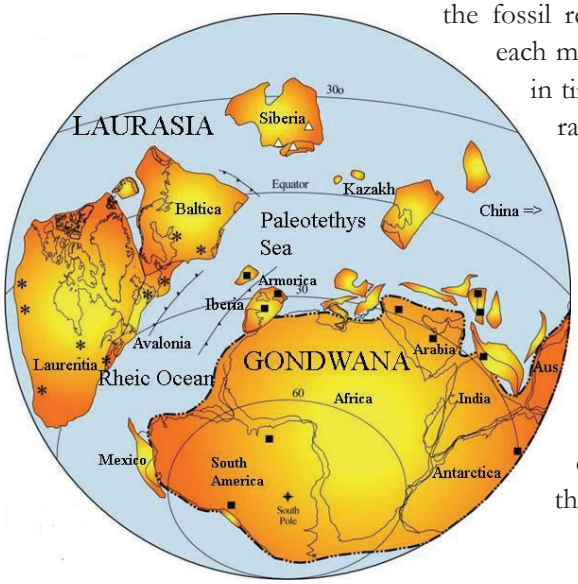
Fortunately, the debate has not stalled work on bird origins. Rather, if anything, the conflicting theories lend importance to the search for missing links in the fossil record. Feduccia is content to wait for to

"BOTH SCHOOLS OF THOUGHT SHOULD HAVE A MEETING OF THE MINDS," FEDUCCIA SUGGESTS. "BUT NOT ME AND CRACRAFT," HE SAYS CALMLY. "HE'S TOO BOISTEROUS, TOO RAUCOUS."

the record to fill out. Theories not aligned with his own do not seem to bother him much. "Both schools of thought should have a meeting of the minds," Feduccia suggests. "But not me and Cracraft," he says calmly. "He's too boisterous, too raucous."

Feduccia's ideas so enrage Cracraft that he flaps his arms wildly as he grasps for words with which to smash them. "Ridiculous! Feduccia doesn't even think that birds came from dinosaurs, and that's widely accepted," he says. "You see, people can see whatever they want. But what does the evidence say? People are not trained to look at evidence anymore. It's a huge problem."

Cracraft's research methods do not bank as heavily on the fossil record, as he finds it woefully incomplete. Rather, his approach is a combination of two techniques: biogeography and molecular clocks. Basically, Cracraft assembles family trees that depict the biological relationships of modern bird species. Then, he determines the rate at which DNA mutations, the assumed constant tick of the molecular clock, occur in the bird species. One way to do this is by examining the number of mutations in two living species that branched from a common ancestor at a point in history determined accurately through the fossil record and by assuming each mutation is evenly spaced in time. Once the mutation rate is known, Cracraft can examine the number of DNA mutations that differentiate the genome of bird species in his family tree. The number of mutations multiplied by the duration for each one to occur gives the time that has passed since the species separated genetically from a common ancestor. So, in a sort of reverse flipbook view of evolution, Cracraft and his colleagues use the rate at which DNA mutations occur to trace back modern species to the point at which they diverged from a common ancestor.



Some scientists insist that the calibration methods for molecular clocks are unreliable, and even the two researchers who first proposed the idea now believe that DNA mutations cannot be assumed to occur at a constant rate. Other methods have appeared, however, to account for [do you mean "account for" or "interpret" or "factor in" or something?] varying mutation rates, and Cracraft is confident in his calibrations. He insists that modern birds originated in the Southern Hemisphere perhaps 90 to95 million years ago, before Gondwana split into the continents we know now. The separated continents would have floated around like life rafts, dropping birds off at the various destinations in which they now appear.

As Cracraft explains this, he begins to segue into an issue he is also clearly passionate about: peoples' acceptance of intuition over evidence. "Feduccia says that species must have exploded into these abandoned ecological niches after the dinosaurs were gone. That's great for intuition, but where's the evidence? There's not one shred. Two-million people or dogs could fit in Central Park, but you don't seem them exploding into that ecological niche."

Cracraft is just getting started. "Let me ask you something, and I want you to think about this. If there was an ancestor fish didn't have eyes, and you find four species of fish that evolve eyes, isn't it *possible* to imagine that they all evolved eyes independently? But there's no evidence to support it. The bottom line is, it's *possible* to imagine anything, but what is the simpler explanation that has some evidence behind it. It's more likely that they evolved once from a common ancestor." He is talking at a frenzied pitch. Cracraft's pointy elbows wave so much he seems in danger of taking off. It is *possible* to imagine that an excavation of Cracraft would yield Archaeopteryx, or perhaps one of the missing link fossils from the Southern Hemisphere.

"The purple pill," he continues. He is making

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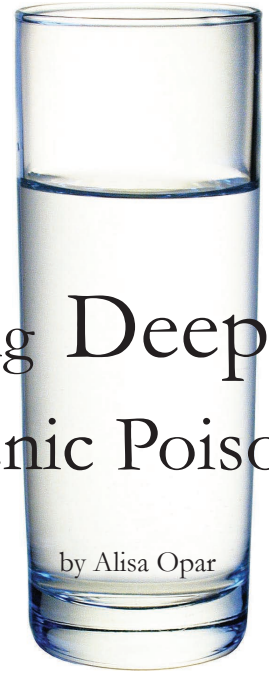


Digging Deeper into Arsenic Poisoning

by Alisa Opar

Sonali Hossain shyly lifted her sari to expose the lesions on her left thigh, her wrinkled hands shaking slightly as she grasped the bright orange and red material.

The sores on her legs and feet are common symptoms of chronic exposure to arsenic. As Sonali sat outside with her back resting against the mud foundation of her home, her husband stood nearby, shaking his head.

"Each day it gets worse," Jaber Hossain said. His bare legs and chest are free of any wounds. He is one of the lucky ones who somehow remain unaffected by the exposure. "We drink safe water now, and she tried the medicine from the clinic, but nothing helps."

For nearly two decades the Hossains drank from a well highly contaminated with arsenic. They did not know they were drinking arsenic; using the clear, refreshing water from a relative's well instead of murky surface water was an obvious choice for the couple, and they installed their own well in 1999. When Columbia University researchers tested wells for arsenic in 2000, the Hossains learned that while their new well was safe, the water from the relative's well they had used for years had an arsenic concentration nearly seven times the national standard for drinking water.

The Hossains are only two of the estimated 35 million of Bangladesh's 130 million inhabitants at risk of being poisoned by naturally-occurring arsenic in their drinking water. Given this mass poisoning, it has the potential to be one of the greatest human health catastrophes in the last century, comparable in scale to the estimated 30 million victims of the 1918 influenza epidemic. The crisis has brought scientists from around the world, including Columbia University researchers who have been working in Bangladesh since 2000. In March they returned to their project area in Araihazar to continue work on their 6-year project: Health Effects and Geochemistry of Arsenic and Lead.

In the 1970's international aid organizations and the Bangladesh government began installing tube wells, to permit pumping of ground water for drinking and cooking as an alternative to microbially-contaminated surface water. Well installation, rehydration programs and inoculations helped control the burden of diarrheal disease, which is the second leading cause of death in developing nations after infectious disease, and its incidence was halved. The convenience of safe water near their homes led people to install private wells, and by the 1980's international aid was no longer necessary to fund installation. Well installation continues today, and it is believed that approximately three quarters of the estimated 10 million wells in Bangladesh are privately owned.

In the 1990's an unintended consequence of this strategy—mass arsenic poisoning—became apparent. The scale of potential effects is staggering. Researchers estimate arsenic consumption has led to 100,000 cases of skin lesions and may cause as many as 270,000 deaths from various cancers. Other symptoms include skin discoloration, hardening of skin on hands and feet, cardiovascular disease, respiratory problems, and miscarriage.

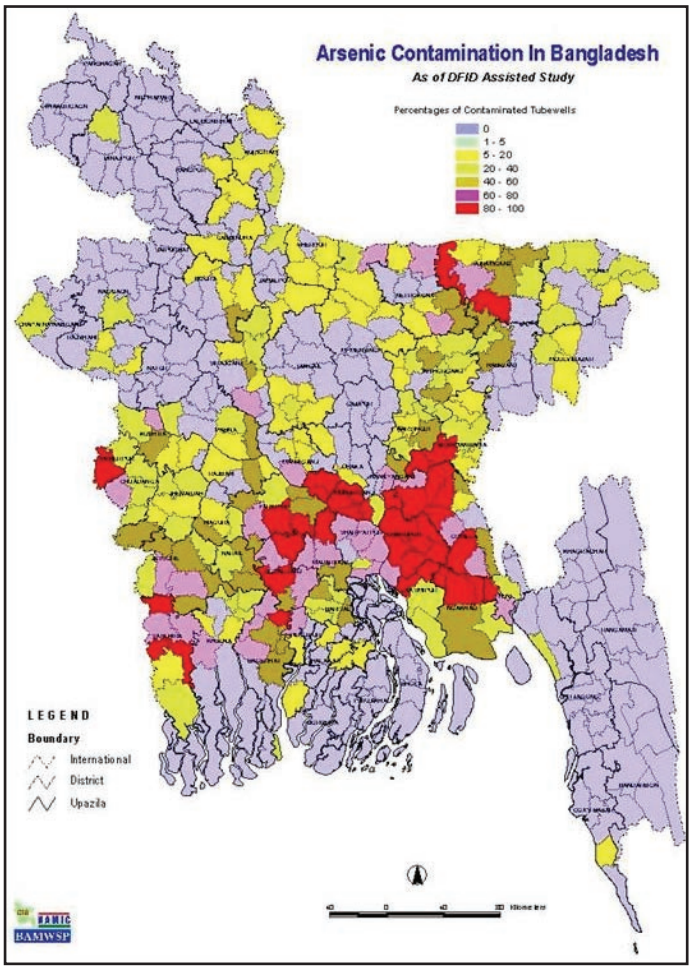
At the time the groundwater strategy was conceived, nobody realized that arsenic occurs naturally in ground water in various regions throughout Bangladesh, particularly in the south-central part of the country. The sediments that make up Bangladesh's sweeping delta contain arsenic, just like any sediment. Under most conditions, the arsenic is strongly bound to the surfaces of iron oxides contained in the sediment. Most scientists believe that the reason arsenic occurs in Bangladesh groundwater dates back 20,000 years, when sea level rose by 100 m, and led to the accumulation of sediment containing organic matter. Then, as the organic material decomposed and consumed all of the oxygen in the groundwater, the reducing conditions led to the dissolution of the iron oxides, consequently releasing arsenic as well. The result is higher arsenic concentrations in younger, typically shallower, aquifers; aquifers made of older sediments have much lower arsenic levels most probably because organic matter and mobilizable arsenic has been flushed out of these deposits over hundreds of thousands of years.

Cases of arsenic poisoning did not immediately follow well installation because arsenic poisoning is cumulative over time. The first reports of arsenic-induced skin lesions appeared in 1987, but the problem was not recognized by the government until 1993, when the Bangladesh Department of Public Health Engineering officially identified the first case of arsenic poisoning and, after testing, found wells with high arsenic concentrations. In 1997, at the urging of the World Health Organization, the World Bank sent a mission to Bangladesh to investigate the arsenic problem. As a result, the Bangladesh Arsenic Mitigation Water Supply Project was created and many private and government wells were tested to determine arsenic levels in ground water. Well spouts were painted green on safe wells and red on unsafe wells.

Today, thousands of wells remain untested, and in some instances people continue to drink from wells known to be unsafe.

"A lot of people are still drinking water they shouldn't be drinking, so I think what that reflects in part is that nobody has a really good idea of what to do," said Lex van Geen, geochemist at the Lamont-Doherty Earth Observatory. "The news we're getting from these big programs is essentially a menu of options and no real hard look at what works and what doesn't."

van Geen and the team of earth, health and social scientists from Columbia University collaborate with colleagues from the Department of Geology at the University of Dhaka and the National Institute of Preventative and Social Medicine. Together they assess the public health effects of arsenic and household responses to provision of arsenic information, investigate arsenic's origin and distribution in ground water, and establish safe drinking water sources. The Columbia University project encompasses a 25 km^2



region in Araihazar, located 20 km east of Dhaka. Of the 6,600 tested wells in the area, half contain arsenic levels exceeding the national standard for drinking water of 50 micrograms per liter—in some cases by as much as 10 times the standard, according to van Geen.

In addition to testing wells and attaching an identification tag to each well, the Columbia University team has conducted repeated surveys of well users. They've also installed 50 safe community wells in high-arsenic areas. Twelve thousand of the 70,000 people in the region are involved in the public health cohort project and give urine samples, allowing researchers to track the amount of arsenic in people's bodies; the urinary data shows a decrease in arsenic levels, with the biggest decreases in areas with high levels of arsenic. Last year, the team attached to the wells new plates with the arsenic level and a picture of a hand holding a glass; unsafe wells have an 'X' through the illustration. From questionnaires assessing residents' response to the arsenic mitigation one and two years after households learned whether their primary well was safe, the team determined that in one year sixty percent with unsafe wells switched to different source and after another year not only did people not return to their old wells, as some had predicted, but in fact the fraction at unsafe wells who switched to alternative wells rose to two thirds. This March, researchers are expanding their study area to the southeast.

"What we found in the last couple of years is that from our testing of the wells and trying to install community wells, and also comparing the impact of our activities on people's behavior and their urinary arsenic levels, is that [testing wells and drilling new safe community wells is] rather effective," said van Geen.

The interdisciplinary approach has been central to the team's effectiveness. For instance, they can gain an understanding of factors that might prevent someone from using another well, such as religious differences, social class, personal disputes and economics. "People have to decide that they care enough to change to a different source of water," said Malgosia Madajewicz, professor of economics and international and public affairs at Columbia University. Traditionally, Bangladeshi women collect water for their household, making multiple trips to the water source each day. "This costs, in terms of taking care of children, maybe having to pull children out of school to help with chores, or maybe a woman runs a small business for extra income, but she can't maintain it because getting water takes too much time," said Madajewicz.

The team's short-term solution to the arsenic crisis is encouraging people to switch to near-by safe private wells and testing new wells. In the latter category, deeper, safe community wells may offer by far the most cost-effective broad access. According to van Geen, arsenic is distributed such that a safe well is often less than 100 m from a contaminated well. Other options do exist for safe drinking water and will be used according to local conditions. But removal of arsenic from well water has generally not fared well to this point while rainwater collection is much harder in some parts of the country than in others and requires more maintenance than does a well. Surface water remains polluted with pathogens.

"It's ludicrous to think about going back to surface water," said Joe Graziano, Columbia University professor of public health. "The deep well strategy is really the consensus of the Columbia faculty" to achieve rapid, cost-effective access for everybody.

Not everyone agrees that deep wells are the answer. Charles Harvey, professor of civil and environmental engineering at MIT, is concerned that basic hydrologic engineering studies have not been done and warns that overdrawing deep wells in Vietnam has caused land subsidence, or sinkholes. "There are basic groundwater hydrologic issues that are usually checked out in the western world, such as: How much water can you get out of an aquifer? USGS is working on this in Bangladesh, but it will take years," he said.

Graziano admits that the precise recharge rates of the aquifers are unknown, but emphasizes that the drinking water which must be addressed first to reduce exposure to arsenic is a very small fraction of water use. Surface water could be used for irrigation, which represents 95% of Bangladesh's total freshwater consumption. This would remove a large strain on ground water.

Last year the Columbia University team drafted a national plan for providing rapid access to safe drinking water. The 5-year, $100 million strategy proposed using the techniques employed and knowledge gained in Araihazar and applying them gradually throughout Bangladesh. It acknowledges

that various options will be used for various reasons and calls for well testing and deeper safe community wells to assure that in the short run every household in Bangladesh gets access to safe drinking water. Community involvement in decision-making is an important aspect of the implementation of the plan. "We strongly believe that this is not a top-down solution," said Graziano. "Each village has its own decision-making process."

The World Bank and Bangladesh government have not adopted this backstop within the Bangladesh Water Safety Supply Program, which aims to provide safe water countrywide by 2015. The plan promotes piping water to all areas except villages of fewer than 200 households, where either surface water will be filtered or deep wells will be used. "Experience with BAMWSP has shown that a narrow arsenic-mitigation focus on rural water supply in Bangladesh is not sufficient to address the identified sector issues, which include both arsenic and bacteriological contamination of water supplies," according to a report by the World Bank, which funds BAMWSP. The stress on bacteriological contamination only heightens the value of groundwater, and the piped water in this national plan is ground water. However, the informed broad use of this valuable resource for drinking without piping has not yet been publicly embraced.

"There's still a strong lobby against the use of the aquifers," said van Geen. "It's still a red herring." Part of the problem may be communication. The Columbia team's findings are published in scientific journals not widely read by policymakers, van Geen said. The value of further communication to policy audiences has led the team to start drafting not only more policy oriented journal articles but also a short executive summary of the team's results and their policy interpretation. Though disappointed in the lack of impact of past outreach, the team remains committed to its study area—for which the team is currently in the process of renewing its funding—and the larger picture of national policy.

"The arsenic problem is enormous because tens of millions of people are drinking arsenic-laden water that we know to be devastating for their health, and probably killing millions of them gradually right now," said Jeffery Sachs, director of Columbia University's Earth Institute.

Alisa Opar is a student at the Columbia School of Journalism

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a point about Nexium, the heartburn pill that is advertised on television as a miracle drug. "People just want to take anything without knowing what the evidence is. They don't even bother to look at evidence, and that's a terrible problem in this country." What does he want to do about it? "More scientists in Congress," Cracraft says sternly. "Well," he hesitates. "But Frist," he says, referring to the lone doctor in Congress, "his agenda is so extremely conservative that he isn't doing any good."

Cracraft and Feduccia are icons at what for now is an apparent impasse in the scientific community. If any idea seems certain to spring from their dispute, it seems to be that looking at different evidence can lead to different solutions for the same question. Hopefully, the answer that has eluded consensus thus far will not always. "One of us is almost absolutely wrong," says Feduccia. "There's not much grey zone for one of us to seek refuge in. I like it like that, because we're likely to find out what the truth is."

Dave Epstein is a writer for the New York Daily News. He graduate from Columbia Journalism School in 2004.

Effects of Dopamine Agonists on the Working Memory and Locomotor Activity of AKT1-/- Mice

JAIMIE CHAN

Principal Investigator: Joseph Gogos

Post Doctorate Mentor: Wen-Sung Lai

ABSTRACT

AKT1 is a protein kinase involved in a number of neurological pathways and is believed to confer susceptibility to schizophrenia (SD). We used AKT1 knockout mice as a model for schizophrenia to study the function of AKT1 in working memory. A sample of 13 wild-type and 10 AKT1$^{-/-}$ mice was tested for working memory performance in a T-maze and their locomotor activity in an open field. While we could not detect a significant difference between the control group and the AKT1$^{-/-}$ mice in either working memory performance or locomotor activity, when challenged with dopamine (DA) agonists, they showed differences. A 0.25mg/kg quinpirole (DA D2 agonist) injection improved the working memory performance in wild-type mice, while a 5.0 mg/kg SKF 38393 (DA D1 agonist) injection impaired the working memory of AKT1$^{-/-}$ mice, suggesting a more complex role of the AKT1 gene in schizophrenia than is known today.

INTRODUCTION

Schizophrenia (SD) is a serious neurobiological disorder that has been the subject of much challenge and controversy. It is a prevalent disorder that affects 1% of the population worldwide. One of the challenges of schizophrenia research is to pinpoint causes for this complex disorder with symptoms such as hyperactivity, social withdrawal; perception deficits such as hallucinations and hearing impairment; and cognitive deficits affecting working memory. Because of the wide array of symptoms descriptive of SD, boundaries that distinguish SD from other neurobiological and behavioral disorders are controversial. Past research suggests that SD is familial, occurring at a higher frequency with affected individuals and relatives (Hallmayer 2004), suggesting a genetic causative agent. Evidence from neuropathology and magnetic resonance imaging (MRI) studies support the view that schizophrenia can be a consequence of disturbances in development of the brain starting as early as the intrauterine life, suggesting that the genetic causative agent acts very early (Karayiorgou and Gogos, 1997).

Recent studies by Emamian et al. have highlighted AKT1 (serine-threonine kinase 1) as a possible susceptibility gene for schizophrenia (Hallmayer 2004). AKT, also known as protein kinase B (PKB) plays an important role in the dopamine pathway of the central nervous system. Recent studies have shown that alterations in protein kinase and phosphatase activity in the brain may contribute to schizophrenia in humans (Emamian et al., 2004). An experiment that measured differences in protein levels of various protein kinases and phosphatases between SD patients and a control group of healthy individuals indicated significant differences in levels of AKT1. A follow-up comparison between post-mortem brains of schizophrenic with those of healthy individuals showed that levels of protein kinase AKT1 was 68% lower in the hippocampus and frontal cortex of schizophrenic individuals, while no differences were found in levels of the other two isoforms AKT2 and AKT3 *(see figure 1)* (Emamian et al., 2004). A decrease in AKT1 results in lower levels of phosphorylated glycogen synthase kinase-3β (GSK3β) (Emamian 2004).

Clinical research and basic experimental findings suggest abnormally high levels of dopamine receptors in schizophrenic patients (Emamian et al., 2004). Dopamine (DA) is a neurotransmitter involved in the control of locomotion, emotion, cognition, and reward, and can exert its behavioral effects by acting on a lithium-sensitive cascade involving AKT and GSK3 (Beaulieu et al., 2004). Separate findings indicate amphetamine, a non-selective dopamine agonist, as a stimulant that induces characteristic behaviors similar to SD. Experiments conducted on schizophrenic patients indicate that amphetamine psychosis is a drug state that exacerbates symptoms, such as auditory hallucinations similar to schizophrenia. Amphetamine is known to promote the release of catecholamines, in particular dopamine, and prolongs the action of the released transmitter by blocking reuptake. Rapid relief from amphetamine psychosis is often provided by injection of the dopamine antagonist chlorpromazine—a drug used in the treatment of schizophrenia. Typical antipsychotic drugs usually act in the brain by blocking postsynaptic receptor sites for dopamine, specifically those of the D2 type (Beaulieu et al., 2004). Such evidence leads to the hypothesis that schizophrenia may be caused either by excessive levels of free dopamine or by excessive postsynaptic sensitivity to dopamine, possibly due to an amplified population of postsynaptic dopamine receptors. These findings are formulated in the dopamine hypothesis of schizophrenia. Studies towards a working model of potential mechanisms of DA receptor signaling and sites of action suggest that dopamine may play a significant role in the regulation of AKT/GSK-3 pathway (*see figure 2*). However, the relationship between AKT and dopamine is still unclear.

In this study, we took advantage of AKT1 knockout mice

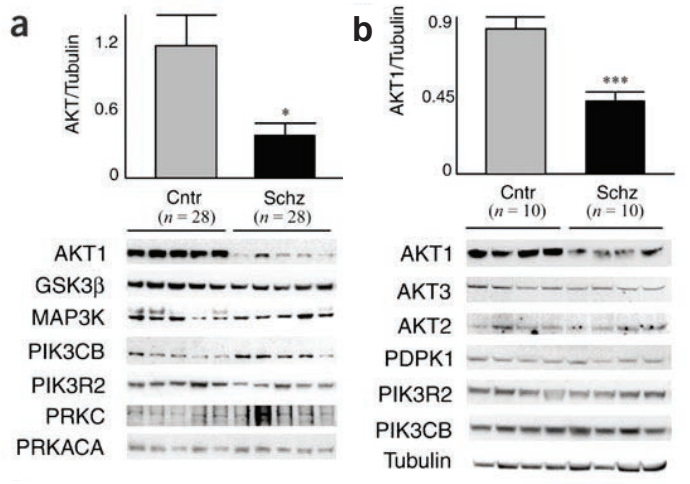

***Figure 1**: Levels of selected protein kinases and phosphatases in lymphocytes and frontal cortex neurons of schizophrenic and healthy individuals. AKT1 levels in lymphocytes (a) and frontal cortex neurons (b) were significantly lower in schizophrenic than in healthy individuals (from Emamian, 2004).*

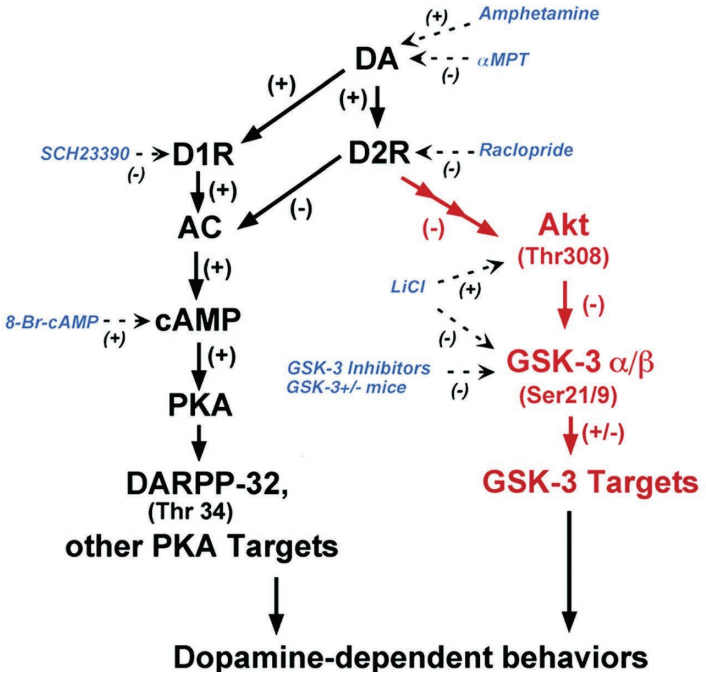

***Figure 2**: The dopamine hypothesis: a model of potential mechanisms of dopamine (DA) and dopamine receptor (D1R and D2R) signaling. In red, the AKT/GSK-3 pathway. (from Beaulieu, 2004).*

to study one important intermediate phenotype of schizophrenia, a defective working memory, the temporary storage of information that can be manipulated. Individuals suffering from schizophrenia have shown a breakdown of response in the memory pathway from sensory storage to short term working memory storage. We could not demonstrate an a priori working memory defect in AKT1$^{-/-}$ mice, but when we administered different dopamine (DA) agonists, we found significant differences in working memory between AKT1$^{-/-}$ and wild-type mice. Our findings suggest that the role of AKT in the dopamine pathway is more complex than previously thought and that a revision of the dopamine hypothesis is required.

RESULTS

AKT1$^{-/-}$ mice do not exhibit impaired working memory. Following a habituation phase, the mice were subjected to an 8-day learning phase, during which they were allowed to practice the T-maze task, which is to retrieve a reinforcer from alternating arms. This phase allowed us to examine each mouse's capability of performing the T-maze task. After eight days, all wild-type and AKT1$^{-/-}$ mice were equally capable of performing the T-maze task, with an accuracy ranging between 70% and 80% *(see figure 3a)*. It seemed, therefore, that the lack of AKT1 had by itself no measurable detrimental effect on learning or working memory of mice.

Dopamine-2 receptor agonists improve working memory in wild-type but not in AKT1$^{-/-}$ mice. According to the dopamine hypothesis, low AKT levels could stem from high DA receptor activity. The D2-specific DA agonist quinpirole (0.25mg/kg, "QPR0.25" or 0.85mg/kg, "QPR0.85" in *figure 3b,c*) was administered to both groups of mice, after which they were made to perform the T-maze task. Statistically significant deviations from saline controls were found in the performance of wild-type mice injected with 0.25mg/kg quinpirole. In these mice, the working memory had improved. In the 5-second delay analysis (i.e., mice had to wait for 5 sec in the start block before they could go on to retrieve the reinforcer from the T-maze, which increased the chance that they would 'forget' which arm they had entered previously), the average wild-type mouse committed 0-1 errors, compared to the 0-1.5 errors during the saline injection control test (P=0.01). Similarly, the average wild-type mouse committed fewer errors during the 20-second delay analysis of the 0.25mg/kg quinpirole test compared to the saline test, albeit the difference was not statistically significant. In AKT1$^{-/-}$ mice, the quinpirole injection did not show the same effect, suggesting that the improvement in performance should be attributed to the presence of the AKT1 gene. Another possibility is that the small dosage of D2 agonist was able to cause moderate hyperactivity (latency decrease) in the mice, resulting in an improvement in working memory skills.

Quinpirole (0.85mg/kg) elicited similar effects to quinpirole (0.25mg/kg). Again, the improvement in performance was much higher in the wild-type mice than in the AKT knockouts. According to the results from the 0.85 mg/kg injection, an improvement in the 5-second delay trials were greater than the 20-second delay trials, corresponding to similar data from the 0.25mg/kg injection.

Dopamine-1 receptor agonists depress working memory in AKT1$^{-/-}$ but not in wild-type mice. In order to examine effects due to the action of the D1 receptor, we injected the D1 agonist SKF 38393 (0.5 mg/kg, "SKF0.5" or 5.0 mg/kg, "SKF5" in *figure 3b,c*) into mice and let them perform the T-maze test afterwards. After a 0.5mg/kg injection, the average wild-type and AKT1$^{-/-}$ mouse performed about equally and similarly to the saline control. The injection of 0.5mg/kg SKF 38393 did not show significant effects in the trial. At a higher dosage (5.0mg/kg), however, AKT1$^{-/-}$ mice performed worse than wild-type mice. During the 5-second delay trials, this effect was visible, but only in the 20-second delay trials it became significant (P=0.36). Wild-type mice performed similarly in both saline and 5.0mg/kg injections during the 20-second delay trials. In summary, we found that D1 agonists impaired the working memory of AKT1$^{-/-}$ but not that of wild-type mice.

Simultaneous activation of D1 and D2 type dopamine receptors by amphetamine elicits identical effects on working memory of wild-type and AKT1$^{-/-}$ mice. Amphetamine causes amphetamine psychosis, a drug state similar to schizophrenia. It is known that amphetamine increases the dopamine response by binding to D1 and D2 DA receptors. Amphetamine (1.0 mg/kg, "AMP1" or 4.0mg/kg "AMP4") was injected into mice as above, after which they were subjected to the T-maze test. AKT1$^{-/-}$ mice injected with 1.0 mg/kg performed similarly to wild-type mice, committing an average of <2 errors in the 5 second delay and about 3 errors in the 20-

second delay trials (*see figure 3b,c*). An injection of 4.0 mg/kg of amphetamine resulted in a general increase in 5-second delay errors in both groups of mice. There was no significant deviation between wild-type and AKT1$^{-/-}$ mice in the AMP 4 test results. For the 20-second delay using AMP 4, both groups performed with similar accuracy levels, and the results from both groups were similar to the saline control.

AKT1$^{-/-}$ mice exhibit reduced locomotor activity. The open field apparatus was used to measure mouse locomotor activity for each drug after the T-maze test was performed. Significant differences between drug injections were found in the total distance traveled and total rest time in the D2 quinpirole injections. Both wild-type and AKT1$^{-/-}$ mice exhibited increased total rest time and decreased total distance traveled compared to the saline controls (*see figure 4*). Significant performance differences between wild-type and AKT1$^{-/-}$ mice were found in the saline, SKF5, and AMP1 injections. In these injections, AKT1$^{-/-}$ mice showed an increase in rest time and decrease in distance traveled when compared to wild-type mice. This divergence was found in dopamine agonist injections as well as saline injections, which indicates that AKT1 may play a significant role in the decrease of locomotor activity of mice.

DISCUSSION

Both AKT1$^{-/-}$ and wild-type mice were capable of learning the alternate-arm T-maze behavior equally well. The habituation period was important because it served to shape behavior. During this period, it was crucial to maintain each mouse's body weight at 10-20% lower than normal, as a restrictive diet motivates the mice to perform the task in order to retrieve the food reward. Both groups of mice performed consistently with an accuracy level greater than

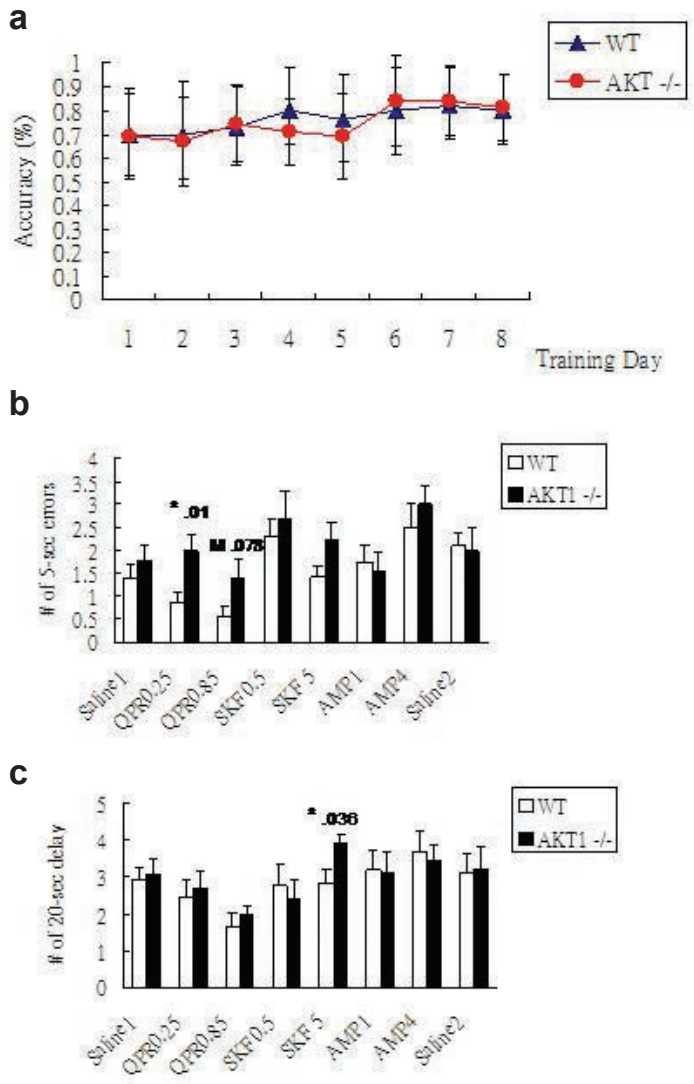

***Figure 3**: Performance of AKT1-/- and wild-type mice in the T-maze test. **(a)** Accuracy level (measured as the average percentage of times mice entered the correct arm to retrieve the reinforcer) during the 8-day learning phase. Both AKT1-/- and wild-type mice performed the T-maze task equally well with an accuracy greater than 70%. **(b), (c)** Performance of AKT1-/- and wild-type mice after drug injections (Saline1 and 2, vector controls; QPR0.25 and 0.85, quinpirole 0.25 or 0.85 mg/kg; SKF0.5 and 5, SKF 38393 0.5 or 5.0 mg/kg; AMP1 and 4, amphetamine 1.0 or 4.0 mg/kg). In each trial, mice were released from the start box after 5 seconds (b) or 20 seconds (c) and were then allowed to retrieve the reinforcer. The height of each bar indicates the average number of errors committed in each set of 10 trials.*

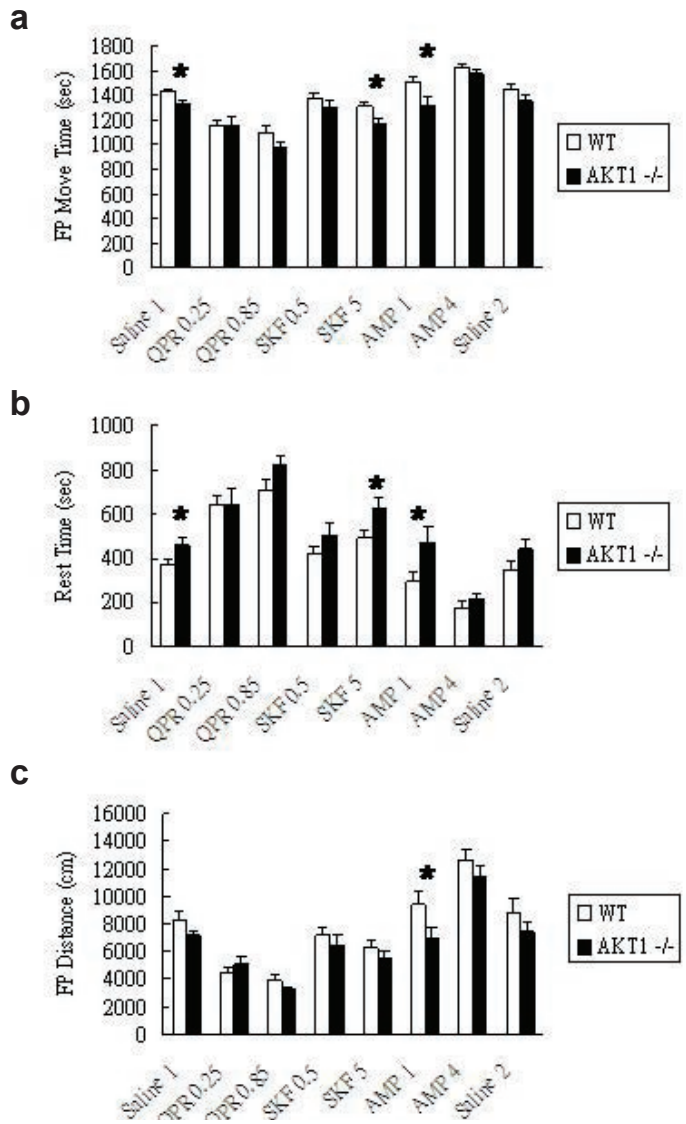

***Figure 4**: Locomotor activity of AKT1-/- and wild-type mice after performing the T-maze test under the influence of dopamine agonists. **(a)** Average total time the mice moved during a 30-minute session. An asterisk indicates significant decrease in move time in AKT1-/- mice compared to wild-type mice. **(b)** Average total time the mice were resting during the 30-minute session. An asterisk marks significant increases in rest time for AKT1-/- mice compared to wild-type mice. **(c)** Average total distance traveled.*

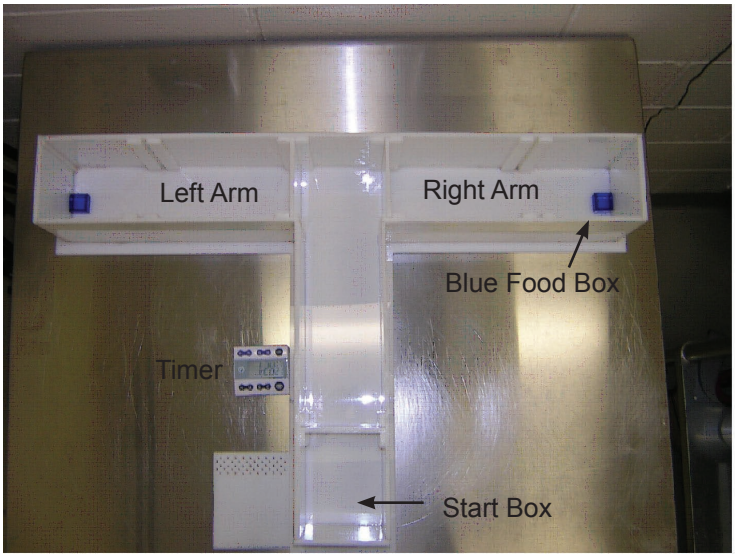

Figure 5*: The T-maze setup. Shown on the T-maze are the various compartments: the start box, the left and right arms, and the doors that block the entrance to each arm. At the end of each arm are identical blue boxes holding the reinforcer.*

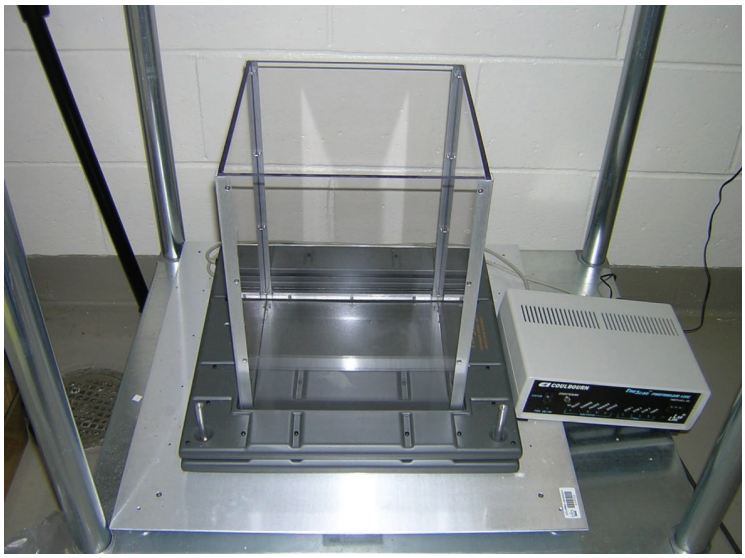

Figure 6: *The open field apparatus. The mouse was placed onto the platform after each T-maze drug test and its movement was recorded for 30 minutes.*

70% and were able to maintain this level of accuracy until the end of the learning phase. This suggests that there are no immediate differences in working memory between wild-type and AKT1$^{-/-}$ mice. However, it appears that AKT1 regulates the working memory of mice in a more complex and indirect way. Our experiments were not able to elucidate these mechanisms fully, and further studies are required.

All drugs were administered peripherally, and thus, the drug could take effect everywhere in the CNS. Some behavioral differences between the two groups were found with drug injections, which could be artifacts stemming from injections. Further, we introduced a 20-second delay to the T-maze test to challenge working memory to a greater extent. Also, more T-maze trials were performed in the drug testing phase, and could have led to these differences.

The saline control test was used at the beginning and end of each drug injection series as a negative control and in order to show that eventual changes were entirely dependent on the drug, and not due to the injection, which could have caused stress to the mouse.

Quinpirole administration improved the accuracy level of wild-type but not AKT1$^{-/-}$ mice, which performed similar to the saline control group. This increased accuracy due to quinpirole suggests an improved working memory of mice as a result of D2 stimulation by an as yet unknown pathway involving AKT1. Possibly, the presence of dopamine D2 agonist causes increased exhibition of dopamine-dependent behaviors, such as locomotor activity and cognition.

According to *figure 2*, D2 receptors play an important role in the regulation of AKT activity. An increase in D2 receptors will lead to a decrease in AKT activity. Thus, D2 agonists might be responsible for the decrease in AKT1 protein expression, which can affect the working memory of mice. D2 agonist drugs may have enhanced or triggered the effects of a missing AKT1 gene in knockout mice resulting in impaired working memory.

AKT1$^{-/-}$ mice performed worse than wild-type mice when injected with SKF 38393. This suggests that D1 agonists can play an indirect role in triggering working memory impairment in AKT1$^{-/-}$ mice. Drug-induced performance impairment was increased in the 20-second delay trials.

Amphetamine injections resulted in an overall accuracy decrease of both groups of mice during the 5 second and 20 second delays. This decrease was most pronounced in the AMP4 test, particularly in the 5-second delay tests of both wild-type and AKT1$^{-/-}$ mice. Amphetamine is a non-selective dopamine agonist. High levels of amphetamine cause amphetamine psychosis, a drug state that elicits symptoms similar to schizophrenia. Results from the amphetamine tests cannot be sufficiently linked to the AKT1 gene because both groups of mice showed an increase in memory impairment, and we found that amphetamine could disrupt a subject's performance both in the presence or the absence of the AKT1 gene. More research is required to link the mouse response to amphetamine to the AKT1 gene.

The open field test showed a consistent decrease of activity in AKT1$^{-/-}$ mice, as shown by a smaller average total distance traveled and an increased resting time. We are currently planning to broaden the parameters of the open field testing to include measures of vertical movements and the distance traveled in the center of the field, so that we can more accurately grasp the effect of dopamine agonists on the locomotor activity of AKT1$^{-/-}$ mice: The distance traveled at the center of the field is interesting, because most mice tend to stay along the sides of the field, possibly because of fear. The number of vertical movements could be an indication of hyperactivity.

The interaction between AKT1 and dopamine is complicated and much still remains unclear. Recently, Beaulieu et al. (2004) suggested a model in which the D1 and D2 receptors regulate dopamine-dependent behavior through different chemical cascades and pathways. However, our results show that the role of AKT1 is more complicated than this model suggests. More research on the role of AKT in the dopamine-induced cascade is likely to shed light on the mechanisms through which schizophrenia acts.

METHODS

Subject

A sample size of 23 mice was used in this experiment. Of the mice used, 10 were homozygous AKT1$^{-/-}$ mice, and 13 were wild-type littermates. The AKT1$^{-/-}$ mice were generated as described previously (Cho et al., 2001). Mouse genotyping was performed by PCR analysis of mouse-tail DNA. Both male and female mice were used, and each mouse varied in weight. All subjects were between 2 to 4 months of age.

Mice were housed individually in a temperature-controlled

room. All experimental behavior training and testing was performed between 10:00am and 5:00pm. Mice were kept in reverse day/light cycle with *ad libitum* access to water. Food restriction started at the beginning of behavioral training. Animal care was approved by the Institutional Animal Care and Use Committee at Columbia University and followed National Institutes of Health guidelines.

Apparatus

Two apparatuses were used in this experiment: a T-maze and an open field apparatus.

The T-maze was constructed of a white plastic material and was segmented into three parts: a start box and left and right arms (*see figure 5*). The dimensions of the maze were 18 inches from the base to the top of the T, 24 inches from the end of the left arm to the end of the right arm, 5 inches wide, and 6 inches in depth. There were four removable doors to the T-maze: two doors were used to form the start box, and one door to close either side of the arm. The T-maze was used to conduct the working memory tests.

The open field apparatus is a computer-powered instrument used to measure locomotor activity with the use of motion sensitive laser beams (Columbus Instruments, Columbus, OH). Its shape is that of an open square box with a 12-inch side length. A clear plastic material of approximately 15 inches in depth forms the four walls to the open field (*see figure 6*).

Experimental Procedure

Habituation Phase. The mice were kept in their individual cages for 7 days in order to become familiarized with their environment. They were given ample food in order to establish a consistent body weight. After 7 days, the diet was restricted deliberately to reduce each mouse's normal body weight by 10-20%, which was maintained throughout the course of all T-maze experiments. Each mouse was subjected to a 10-minute adaptation session, during which they were introduced to the T-maze with all doors opened for free exploration.

The adaptation session was followed by a behavior-shaping period. On four consecutive days, each mouse was guided from the start box to one arm of the T-maze by blocking the entrance to the previously visited arm. At the end of the concourse, the mouse could retrieve the reinforcer (a Kellogg's Chocolate Rice Krispy™). After an initial trial, in which both arms were baited with food, in each subsequent trial, the previously visited arm was blocked so that the mouse was forced to choose the previously non-visited arm. This forced alternation procedure (Seeger et al., 2004) was then repeated 9 more times (making a total of 10 trials each day), for four consecutive days, with each repeat separated by a 5-second delay in the start box.

8-Day Learning Phase. After the shaping period, the mice underwent an 8-day learning phase. Each mouse was subjected to daily training sessions in the T-maze. Each session consisted of 11 repeats. In the initial trial, both arms were baited. In the following 10 trials, the reinforcer was placed in the arm that had not been visited in the previous trial. A successful trial was recorded whenever the mouse entered the arm containing the food pellet. After an unsuccessful trial, the correct arm remained the same until visited by the mouse. Between trials, the T-maze was cleaned with 35% ethanol.

Testing phase. Mice that had reached an accuracy of at least 60% proceeded to the testing phase. Each session consisted of 16 trials (1 initiation trial followed by 15 trials), and the mice were treated in the same manner as in the 8-day learning phase. Mice that maintained an accuracy of 70% or greater (>11/15 correct) for two consecutive days proceeded to the drug testing phase.

Drug Testing Phase. The drug-testing phase consisted of 8 consecutive drug challenges to each mouse's performance in the T-maze. Briefly, each mouse was injected with saline, quinpirole, SKF 38393, or amphetamine and was then made to perform the T-maze test. Quinpirole (Sigma) was administered in dosages of 0.25 mg/kg and 0.85 mg/kg. SKF 38393 (Sigma) was administered in dosages of 0.5 mg/kg and 5.0 mg/kg. Amphetamine (Sigma) was administered in dosages of 1.0 mg/kg and 4.0 mg/kg. Saline, quinpirole, and amphetamine were delivered as intraperitoneal injections, and SKF 38393 was injected subcutaneously.

Thirty minutes after each injection, each mouse underwent the T-maze test as described above, with slight alterations: the delay time between each trial was varied between 5 and 20 seconds. In all, five 5-second delay and five 20-second delay repeats were performed for both left and right arms. In a concluding control trial, both arms were baited with a reinforcer, and the mouse had to choose the appropriate arm.

After each drug-challenged T-maze test, the mouse was placed into the open field apparatus to measure its locomotor activity. For 30 minutes, the apparatus measured the total distance traveled, total rest time, and total movement time. After the completion of the open field session, each mouse was returned to its cage.

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THE HYDROGEN ATOM IN $\mathbb{R}^4 \times S^1$

-ARTHUR LIPSTEIN, NARESH KUMAR, NADA PETROVIC

Abstract. Judging from our everyday experience, we might be led to conclude that we live in a universe consisting of one time and three space dimensions. It could be, however, that the world really has a higher space-time dimensionality, but that we are limited in our ability to experience all of its dimensions. In the early Twentieth century, Theodore Kaluza and Oscar Klein postulated the existence of an additional compactified space dimension in order to unify electromagnetism and general relativity under a single equation. Recent theories, in particular string theory, incorporate multiple compactified dimensions, which are too small to be measured by current experimental means and are only affected by gravity. In this paper, we consider the possibility that electromagnetic fields can propagate through extra spatial dimensions. Specifically, we first reformulate electrodynamics for a universe consisting of four space dimensions and one time dimension, with one space dimension compactified. Then, using the solution for the electromagnetic field produced by a point charge moving at non-relativistic speeds, we calculate the new hamiltonian for the hydrogen atom. We show that in the limit that the compactification radius of the extra dimension is much smaller than the Bohr radius, the traditional hamiltonian for the hydrogen atom is recovered with new first order corrections. These first order corrections break the degeneracy of the eigenstates of the unperturbed hamiltonian. The corrections to the energy levels of the hydrogen atom are calculated numerically using degenerate perturbation theory.

Figure 0.1. Klein (leftmost) is credited for interpreting Kaluza's theory of gravity and electromagnetism as a higher dimensional theory with a compact dimension.

1. Introduction

1.1. **Electrodynamics in $\mathbb{R}^4$.** To obtain the electromagnetic field for an arbitrary charge distribution, we go to Maxwell's equations:

$$\partial_\nu F^{\mu\nu} = \mu_0 J^\mu \tag{1.1}$$

$$\partial_\nu G^{\mu\nu} = 0 \tag{1.2}$$

If we define a vector potential A^μsuch that

$$F^{\mu\nu} = \partial^\mu A^\nu - \partial^\nu A^\mu \tag{1.3}$$

and apply the Lorentz gauge condition

$$\partial_\mu A^\mu = 0 \tag{1.4}$$

we find that Maxwell's equations can be written in the form

$$\partial_\nu \partial^\nu A^\mu = -\mu_0 J^\mu \tag{1.5}$$

Let's first consider Maxwell's equations in $\mathbb{R}^3$. If we have a static distribution, equation 5 reduces to

$$\nabla^2 V = -\frac{\rho}{\epsilon_0} \tag{1.6}$$

$$\nabla^2 \vec{A} = -\mu_0 \vec{J} \tag{1.7}$$

where $V = A^0$, $\vec{A} = A^1\hat{i} + A^2\hat{j} + A^3\hat{k}$, and $\hat{J} = J^1\hat{i} + J^2\hat{j} + J^3\hat{k}$.
In this case, $V$and $\vec{A}$ are given by

$$V(\vec{r}) = \frac{1}{4\pi\epsilon_0}\int \frac{\rho(\vec{r'})}{\left|\vec{r'} - \vec{r}\right|} d\tau' \tag{1.8}$$

$$\vec{A}(\vec{r}) = \frac{\mu_0}{4\pi}\int \frac{\vec{J}(\vec{r'})}{\left|\vec{r'} - \vec{r}\right|} d\tau' \tag{1.9}$$

If the distribution is not static, then we must take into account the time delay between the emission of electromagnetic signals from the moving distribution and their reception by the observer. The scalar and vector potential are therefore given by

$$V(\vec{r}, t) = \frac{1}{4\pi\epsilon_0}\int \frac{\rho(\vec{r'}, t_{ret})}{\left|\vec{r'} - \vec{r}\right|} d\tau' \tag{1.10}$$

$$\vec{A}(r,\vec{t}) = \frac{\mu_0}{4\pi}\int \frac{\vec{J}(\vec{r'},t_{ret})}{\left|\vec{r'}-\vec{r}\right|}d\tau' \tag{1.11}$$

where $t_{ret} = t - \left|\vec{r'}-\vec{r}\right|/c$. It can be shown that these potentials satisfy Maxwell's equations

$$\nabla^2 V - \frac{1}{c^2}\frac{\partial^2 V}{\partial t^2} = -\frac{\rho}{\epsilon_0} \tag{1.12}$$

$$\nabla^2 \vec{A} - \frac{1}{c^2}\frac{\partial^2}{\partial t^2}\vec{A} = -\mu_0 \vec{J} \tag{1.13}$$

subject to the Lorentz gauge condition

$$\nabla \cdot \vec{A} = -\frac{1}{c^2}\frac{\partial V}{\partial t} \tag{1.14}$$

If the charge distribution is a moving point charge q whose path is given by $\vec{r'}(t)$, then equations 1.10 and 1.11 reduce to the Leonard-Wiechert potentials

$$V(\vec{r},t) = \frac{1}{4\pi\epsilon_0}\frac{q}{\left|\vec{r'}(t_{ret})-\vec{r}\right| - \left(\vec{r'}(t_{ret})-\vec{r}\right)\cdot\frac{1}{c}\vec{v}_{ret}} \tag{1.15}$$

$$A(\vec{r},t) = \frac{\mu_0}{4\pi}\frac{q\vec{v}_{ret}}{\left|\vec{r'}(t_{ret})-\vec{r}\right| - \left(\vec{r'}(t_{ret})-\vec{r}\right)\cdot\frac{1}{c}\vec{v}_{ret}} \tag{1.16}$$

where $t_{ret}$is obtained from the equation

$$\left|\vec{r'}(t_{ret})-\vec{r}\right| = c\,(t-t_{ret}) \tag{1.17}$$

and $\vec{v}_{ret} = \frac{d\vec{r'}(t')}{dt'}\Big|_{t'=t_{ret}}$.

1.2. **The Hydrogen Atom in $\mathbb{R}^4$.** Let's apply the above ideas to calculate the potential energy of a Hydrogen atom in a universe with three infinite spatial dimensions, which we will model as an electron executing a circular orbit about a proton. Placing an observer at the coordinates of the electron, and taking all $\frac{v}{c}$ terms to be zero in the non-relativistic limit, we obtain the Coulomb potential:

$$V_{Coulomb} = \frac{1}{4\pi\epsilon_0}\frac{q}{R} \tag{1.18}$$

Calculating the magnetic field in the non-relativistic limit and dotting it into the magnetic moment of the electron, we obtain the spin-orbit coupling potential:

$$V_{SO} = -\vec{\mu}_e \cdot \vec{B} = \frac{e}{2m}\vec{S}\cdot\frac{\mu_0 e}{4\pi}\frac{\vec{v}\times\hat{r}}{R^2} = \frac{e^2}{8\pi\epsilon_0 m^2 c^2}\frac{\vec{S}\cdot\vec{L}}{R^3} \tag{1.19}$$

There is just one issue: our potentials are implicitly dependent on t_r. Recall that potentials that enter the Schrodinger equation must satisfy the classical assumption that information is transferred instantaneously, or equivalently that the particles are not significantly displaced during the time it takes for them to communicate. Since an electromagnetic signal sent from the electron must travel a distance of R to reach the proton, the electron will move a distance of $R\frac{v}{c}$ in the time it takes the signal to reach the proton. Hence in the non-relativistic limit, the electron will not have moved between the emission and reception of an electromagnetic signal, so our potentials are indeed usable for non-relativistic quantum mechanics.

The hamiltonian for the Hydrogen atom can subsequently be written as follows:

$$\hat{H} = -\frac{\hbar^2}{2m}\nabla^2 + V_{Coulomb} + \delta V_{SO} \tag{1.20}$$

where δV_{SO}, is a first-order perturbing term.

1.3. **Considerations for the Hydrogen Atom in $\mathbb{R}^4 \times S^1$.** Let us now consider what would happen to the Hydrogen atom hamiltonian if we add a compactified spatial dimension of length b. A coordinate system in a universe with an additional compact dimension is depicted in Figure 2.1. As will be shown in the following sections, this scenario presents two new complications that were not present in the previous case: firstly, there are an infinite number of paths that an electromagnetic signal can take between the proton and electron, and secondly, a the electron can interact with its own fields! In the limit that $R \gg b$, we expect the Hydrogen atom hamiltonian to reduce to equation 1.20 with additional first order correction terms:

$$\hat{H}' = -\frac{\hbar^2}{2m}\nabla^2 + (V_{Coulomb} + \delta V_{Coulomb}) + \delta V_{SO} + \delta V_{self} \tag{1.21}$$

where $\delta V_{Coulomb}$ is the first order correction to the Coulomb potential and δV_{self} is the potential due to the interaction of the electron with its own fields. Note that the correction term to the spin-orbit coupling potential is of second order, and is therefore neglected. Before embarking on the calculation of the new hamiltonian, we must first reformulate electrodynamics with one additional spatial dimension.

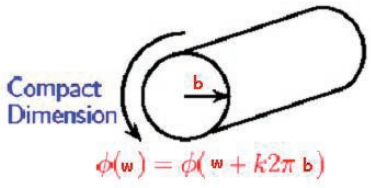

FIGURE 1.1. A universe with the geometry $\mathbb{R}^4 \times S^1$ can be represented as an infinitely long cylinder. In the above figure, a compact dimension of length $2\pi b$ is depicted as the circumference of the base of the cylinder, while the three infinite spatial dimensions lie along the surface of the cylinder perpendicular to the base.

2. Electrodynamics in $\mathbb{R}^4 \times S^1$

Equations 1.1 and 1.2 can be generalized to n spatial dimensions if we identify $F^{0\nu}$ with $\nu > 0$ to be the n components of the electric field, and $F^{\mu\nu}$with $\nu > \mu$ to be the $\begin{pmatrix} n \\ 2 \end{pmatrix}$ components of the magnetic field.

2.1. Static Solution.

In the static case, equations 13 and 14 then reduce to

$$\nabla^2 V = -\frac{\rho}{\epsilon_0} \tag{2.1}$$

$$\nabla^2 \vec{A} = -\mu_0 \vec{J} \tag{2.2}$$

where $\nabla^2 = \sum_{i=1}^{i=n} \partial_i^2$, and the constants ϵ_0 and μ_0 are not equal to their counterparts in three dimensions. If we restrict ourselves to $\mathbb{R}^4 \times S^1$, then $n = 4$ and we inherit the additional boundary conditions:

$$V(\vec{r}) = V(\vec{r} + b\hat{w}) \tag{2.3}$$

$$\vec{A}(\vec{r}) = \vec{A}(\vec{r} + b\hat{w}) \tag{2.4}$$

where $\hat{w}$ is the unit vector in the compact dimension. The general solutions to equations 2.1 and 2.2 are given by

$$V(\vec{r}) = \frac{1}{\epsilon_0} \int \rho(\vec{r}')G(\vec{r}, \vec{r}')dr'^4 \tag{2.5}$$

$$\vec{A}(\vec{r}) = \mu_0 \int \vec{J}(\vec{r}')G(\vec{r}, \vec{r}')dr'^4 \tag{2.6}$$

where integration takes place over the entire charge distribution (which is assumed to be confined to a region whose width in the compactified dimension is no greater than $2\pi b$) and G is the Green's function for $\mathbb{R}^4 \times S^1$, having the property

$$\nabla^2 G(\vec{r}, \vec{r}') = -\omega_4 \sum_{n=-\infty}^{n=\infty} \delta(\vec{r} - \vec{r}' - 2\pi n b\hat{w}) \tag{2.7}$$

where $\omega_4 = 2\pi^2$ is the surface area of the four-dimensional unit hypersphere, and b is the compactification radius.

It readily follows by linearity of Poisson's equation that the Green's function is given by

$$G(\vec{r}, \vec{r}') = \frac{1}{\omega_4} \sum_{n=-\infty}^{n=\infty} \frac{1}{|\vec{r}' + 2\pi n b\hat{w} - \vec{r}|^2} \tag{2.8}$$

Hence, the static solutions to Maxwell's equations in $\mathbb{R}^4 \times S^1$are given by

$$V(\vec{r}) = \frac{1}{2\pi^2 \epsilon_0} \sum_{n=-\infty}^{n=\infty} \int \frac{\rho(\vec{r}')}{|\vec{r}' + 2\pi n b\hat{w} - \vec{r}|^2} dr'^4 \tag{2.9}$$

$$\vec{A}(\vec{r}) = \frac{\mu_0}{2\pi^2} \sum_{n=-\infty}^{n=\infty} \int \frac{\vec{J}(\vec{r}')}{|\vec{r}' + 2\pi n b\hat{w} - \vec{r}|^2} dr'^4 \tag{2.10}$$

Note that the boundary conditions, equations 2.5 and 2.6, are automatically satisfied as a result of the summation.

2.2. **Physical Interpretation of the Electric Field of a Static Point Charge.** Suppose we place an electron at the origin. Then in Cartesian coordinates, the electric potential for an observer located at $(x, y, z, 0)$ is given by

$$V(x, y, z, 0) = \frac{e}{2\pi^2 \epsilon_0} \sum_{n=-\infty}^{n=\infty} \frac{1}{x^2 + y^2 + z^2 + (2\pi n b)^2} \tag{2.11}$$

We can understand the meaning of the summation by considering all the paths that an electric signal can take from the electron to the observer. If every dimension were infinite, than a signal could only travel along one path from the electron to the observer, notably the shortest possible line connecting them, whose distance would be $\sqrt{x^2 + y^2 + z^2}$. The potential in this case would be given by the $n = 0$ term of the summation, noting that in $\mathbb{R}^4$, the Coulomb potential goes as one over the distance squared. Since the fourth spatial dimension is compactified, a signal can also follow a path which wraps around the compactified dimension an arbitrary number of times (Fig 2.1).

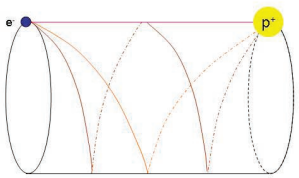

FIGURE 2.1. Since the fourth spatial dimension is compactified, a signal can follow a path which wraps around the compactified dimension an arbitrary number of times. Depicted above are three possible paths a signal can take between a proton and electron. In the pink path, the signal goes directly between the proton and electron without wrapping around the compact dimension. In the orange path, the signal wraps around the compact dimension once. In the brown path, the signal wraps around the compact dimension twice.

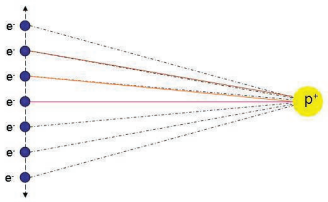

FIGURE 2.2. The potential between an electron and a proton in $\mathbb{R}^4 \times S^1$ can be thought of as the potential of a proton due to an electron at the origin plus an infinite number of image charges placed along an axis perpendicular to the line between the proton and electron at intervals of $2\pi b$. The pink, orange, and brown paths highlighted in this figure correspond to the three shortest paths a signal can follow in traveling between the proton and electron, depicted in Figure 2.1.

Noting that electric signals are constrained to follow the "straightest possible paths," the length of a path which wraps around the compactified dimension n times must be $x^2 + y^2 + z^2 + (2\pi nb)^2$. The potential due a field following this path is thus given by the nth term in the summation. Hence, equation 2.11 can be interpreted as the potential in $\mathbb{R}^4$ due to an electron at the origin plus an infinite number of image charges placed along the w axis at intervals of $2\pi b$ (Fig 2.2).

2.3. **Solution for a Moving Point Charge.** Going back to a general charge distribution $\rho(\vec{r}, t)$, if we no longer assume that the distribution is static, then Maxwell's equation and the Lorentz gauge condition reduce to equations 13-15, where ∇ is defined appropriately for four spatial dimensions. Noting that in the non-static case, we must take into account the transit time required for electric signals emitted from charges to reach the observer, let's make the following ansatz as to the time-dependent solutions of Maxwell's equations:

$$V(\vec{r}, t) = \frac{1}{2\pi^2 \epsilon_0} \sum_{n=-\infty}^{n=\infty} \int \frac{\rho(\vec{r}', t_{ret;n})}{\left|\vec{r}' + 2\pi nb\hat{w} - \vec{r}\right|^2} dr'^4 \tag{2.12}$$

$$\vec{A}(\vec{r}, t) = \frac{\mu_0}{2\pi^2} \sum_{n=-\infty}^{n=\infty} \int \frac{\vec{J}(\vec{r}', t_{ret;n})}{\left|\vec{r}' + 2\pi nb\hat{w} - \vec{r}\right|^2} dr'^4 \tag{2.13}$$

where $t_{ret;n} = t - \left|\vec{r'} + 2\pi nb\hat{w} - \vec{r}\right| / c$. It is a simple matter to show that these potentials in fact satisfy Maxwell's equations and the Lorentz gauge condition:

The potentials of a moving point charge can be obtained by taking $\rho(\vec{r},t) = e\delta(\vec{r}-\vec{r}'(t))$, where $\vec{r}'(t)$ is the path of the charge as a function of time, and multiplying each term in the summation by $\frac{1}{1-\frac{\hat{r}_n\cdot\vec{v}_n}{c}}$ in order to take into account the delay between receipt of electromagnetic signals from opposite ends of the charge (which holds even in the limit that the size of the charge goes to zero), where

$$\hat{r}_n = \frac{\vec{r}'(t_{ret;n}) + 2\pi nb\hat{w} - \vec{r}}{|\vec{r}'(t_{ret;n}) + 2\pi nb\hat{w} - \vec{r}|} \tag{2.14}$$

$$\vec{v}_n = \left.\frac{d\vec{r}'(t')}{dt'}\right|_{t'=t_{ret;n}} \tag{2.15}$$

and $t_{ret;n}$ is obtained from the equation

$$|\vec{r}'(t_{ret;n}) + 2\pi nb\hat{w} - \vec{r}| = c\,(t - t_{ret;n}) \tag{2.16}$$

The electric and vector potentials for a moving point charge are subsequently given by

$$V(\vec{r},t) = \frac{q}{2\pi^2\epsilon_0}\sum_{n=-\infty}^{n=\infty}\frac{1}{1-\frac{\hat{r}_n\cdot\vec{v}_n}{c}}\frac{1}{\left|\vec{r'}(t_{ret;n}) + 2\pi nb\hat{w} - \vec{r}\right|^2} \tag{2.17}$$

$$\vec{A}(\vec{r},t) = \frac{\mu_0}{2\pi^2}q\sum_{n=-\infty}^{n=\infty}\frac{1}{1-\frac{\hat{r}_n\cdot\vec{v}_n}{c}}\frac{\vec{v}_n}{\left|\vec{r'}(t_{ret;n}) + 2\pi nb\hat{w} - \vec{r}\right|^2} \tag{2.18}$$

3. Solution for the Hydrogen Atom in $\mathbb{R}^4 \times S^1$

3.1. Correction to the Coulomb Potential. Consider an electron orbiting a proton in four spacial dimensions with one compactified. It will presently be shown that in the limit that the compactification radius is much smaller than the Bohr radius, the electric potential reduces to the Coulomb potential along with a first order correction in the form of a Yukawa potential.

Placing the proton at the origin, and taking the electron to execute a circular orbit about the electron at radius R, it is readily seen that if the motion of the electron is non-relativistic, the potential of the configuration is given by the potential at the origin due to the electron:

$$V(\vec{0},t) = \frac{q}{2\pi^2\epsilon_0}\sum_{n=-\infty}^{n=\infty}\frac{1}{\left|\vec{r'}(t_{ret;n}) + 2\pi nb\hat{w}\right|^2} \tag{3.1}$$

From the symmetry of the problem, it is evident that the electric potential is independent of time, and is only dependent on R. Hence

$$V(R) = \frac{q}{2\pi^2\epsilon_0 R^2}\sum_{n=-\infty}^{n=\infty}\frac{1}{1+\left(\frac{2\pi nb}{R}\right)^2} \tag{3.2}$$

Applying the identity

$$\sum_{n=-\infty}^{n=\infty} \frac{1}{1+(\pi n x)^2} = \frac{1}{x}\cot\left(\frac{1}{x}\right) \tag{3.3}$$

the electric potential is given by

$$V(R) = \frac{q}{4\pi^2 b\epsilon_0 R}\coth\left(\frac{R}{2b}\right) \tag{3.4}$$

Recognizing $\pi b\epsilon_0$, where ϵ_0 is defined for four spatial dimensions, to be $\epsilon_0$defined for three spatial dimensions, and expanding coth $\left(\frac{R}{2b}\right)$ to first order in $\exp(-R/b)$ in the limit that $R \gg b$, we recover the Coulomb potential along with a Yukawa correction term:

$$V(R) = \frac{q}{4\pi\epsilon_0}\frac{1}{R}\left(1+2\exp(-R/b)\right) \tag{3.5}$$

In the limit that $b = 0$, we are left with the traditional Coulomb potential, as required.

3.2. **Spin-Orbit Coupling Correction.** In the canonical hydrogen atom hamiltonian, the spin-orbit coupling correction is applied only as a first order perturbation. Thus, it suffices to show that in the limit that $R \gg b$, the spin-orbit coupling term in $\mathbb{R}^4 \times S^1$ reduces to zeroth order to the spin-orbit coupling correction in $\mathbb{R}^4$, and to neglect all higher order terms. The spin-orbit coupling correction can in turn be obtained by investigating the interaction of the spin of the electron with the vector potential in the frame of the electron .

Let us therefore proceed by calculating the vector potential in the frame of the orbiting electron. In the electron's frame, the proton is executing a circular orbit with radius R. In the non-relativistic limit, the vector potential is given by:

$$\vec{A}(\vec{r},t) = \frac{\mu_0 q}{2\pi^2}\sum_{n=-\infty}^{n=\infty}\frac{\vec{v}_n}{\left|\vec{r'}(t_{ret;n}) + 2\pi n b\hat{w} - \vec{r}\right|^2} \tag{3.6}$$

$$= \frac{\mu_0 q}{2\pi^2}\sum_{n=-\infty}^{n=\infty}\frac{R\omega\hat{\phi}_n}{(R\cos(\phi_n)-x)^2 + (R\sin(\phi_n)-y)^2 + z^2 + (2\pi n b)^2} \tag{3.7}$$

where $\phi_n$is the retarded azimuthal coordinate of the nth image charge, and $R\omega\hat{\phi}_n$the corresponding retarded velocity. Furthermore it is evident from the symmetry of the problem that the vector potential is independent of time and that $\phi_0$can be taken to be zero without loss of generality.

Image charges that are close to the orbital plane are not displaced during the transit time of signals that are received by an observer located next to the electron. Although image charges located far away from the orbital plane are displaced during the transit time for their signals, their distances from the orbital plane are much larger than their displacements. Thus for both cases, the retarded time is given by the distance of the image charge from the orbital plane divided by the speed of light. More precisely,

$$t_{ret;n} = \frac{2\pi nb}{c} \tag{3.8}$$

It follows that $\phi_n$and $\hat{\phi}_n$are given by

$$\phi_n = \omega t_{ret;n} \tag{3.9}$$

$$\hat{\phi}_n = -\sin(\phi_n)\hat{x} + \cos(\phi_n)\hat{y} \tag{3.10}$$

In the limit that the vector potential is a slowly varying function of n, the infinite sum can be written as an integral over the variable $w = 2\pi nb$ with $dw = 2\pi b$ as follows:

$$\vec{A}(x,y) = \frac{\mu_0 q}{4\pi^3 b}\int_{-\infty}^{\infty} \frac{R\omega\hat{\phi}(w)dw}{\left[R\cos(\phi(w)) - x\right]^2 + \left[R\sin(\phi(w)) - y\right]^2 + z^2 + w^2} \tag{3.11}$$

$$= \frac{\mu_0 q}{4\pi^3 b}\int_{-\infty}^{\infty} \frac{R\omega\left[-\sin\left(\frac{\omega w}{c}\right)\hat{x} + \cos\left(\frac{\omega w}{c}\right)\hat{y}\right]dw}{\left[R\cos\left(\frac{\omega w}{c}\right) - x\right]^2 + \left[R\sin\left(\frac{\omega w}{c}\right) - y\right]^2 + z^2 + w^2} \tag{3.12}$$

With the vector potential in integral form, we shall now calculate $F^{\mu\nu}(x,y,z)$ according to equation 1.3, and evaluate it at the origin, where the electron is located. Since the vector potential is time-independent, we immediately find that $F^{\mu 0} = F^{0\mu} = 0$. The remaining components are given by

$$F^{12}(x,y,z) = -F^{21}(x,y,z) = \frac{\mu_0 q}{4\pi^3 b}\int_{-\infty}^{\infty} \frac{2R\omega\left[R - x\cos\left(\frac{\omega w}{c}\right) - y\sin\left(\frac{\omega w}{c}\right)\right]dw}{\left\{\left[R\cos\left(\frac{\omega w}{c}\right) - x\right]^2 + \left[R\sin\left(\frac{\omega w}{c}\right) - y\right]^2 + z^2 + w^2\right\}^2} \tag{3.13}$$

$$F^{13}(x,y,z) = -F^{31}(x,y,z) = \frac{\mu_0 q}{4\pi^3 b}\int_{-\infty}^{\infty} \frac{2R\omega z\sin\left(\frac{\omega w}{c}\right)dw}{\left\{\left[R\cos\left(\frac{\omega w}{c}\right) - x\right]^2 + \left[R\sin\left(\frac{\omega w}{c}\right) - y\right]^2 + z^2 + w^2\right\}^2} \tag{3.14}$$

$$F^{23}(x,y,z) = -F^{32}(x,y,z) = \frac{\mu_0 q}{4\pi^3 b}\int_{-\infty}^{\infty} \frac{-2R\omega z\cos\left(\frac{\omega w}{c}\right)dw}{\left\{\left[R\cos\left(\frac{\omega w}{c}\right) - x\right]^2 + \left[R\sin\left(\frac{\omega w}{c}\right) - y\right]^2 + z^2 + w^2\right\}^2} \tag{3.15}$$

At the origin, we immediately find that $F^{13} = F^{31} = F^{23} = F^{32} = 0$. The remaining two components are given by

$$F^{12}(0,0,0) = -F^{21}(0,0,0) = \frac{\mu_0 q}{4\pi^3 b}\int_{-\infty}^{\infty} \frac{2R^2\omega dw}{\left(R^2 + w^2\right)^2} = \frac{\mu_0}{4\pi^2 b}\frac{q\omega}{R} \tag{3.16}$$

Thus, at the origin there is an effective magnetic field $\vec{B} = \frac{\mu_0}{4\pi^2 b}\frac{q\omega}{R}\hat{z}$, which can be verified by calculating the Lorentz force on a particle instantaneously located at the origin moving with velocity v^ν:

$$F_\mu = F_{\mu\nu} v^\nu = \epsilon_{\mu\nu\lambda} v^\nu B^\lambda \tag{3.17}$$

The potential energy of the electron is subsequently given by

$$V_{SO} = -\vec{\mu}_e \cdot \vec{B} = \frac{e}{2m} \vec{S} \cdot \frac{\mu_0}{4\pi^2 b} \frac{e\omega}{R} \hat{z} = \frac{e^2}{8\pi\epsilon_0 m^2 c^2} \frac{\vec{S} \cdot \vec{L}}{R^3} \tag{3.18}$$

identifying $\frac{\mu_0}{\pi b}$, where μ_0 is defined for four spatial dimensions, to be $\mu_0$defined for three spatial dimensions. This is precisely the spin-orbit coupling correction obtained for the hydrogen atom in $\mathbb{R}^4$.

3.3. **Self-Interaction Correction.** With the presence of an additional compactified dimension, the field produced by an accelerating charge can interact with the charge itself. Presently, it will be shown that for the case of an orbiting electron, the self-interaction is negligible in the non-relativistic limit. In the case that the electron were not accelerating, the potential of the configuration consisting of the electron and its image charges, which will be referred to as the intrinsic self-interaction potential, is given as follows:

$$V_{intrinsic} = \frac{q}{\pi^2 \epsilon_0} \sum_{n=1}^{n=\infty} \frac{1}{(2\pi n b)^2} = \frac{q}{24\pi^2 \epsilon_0 b} \tag{3.19}$$

Note that in the limit b is zero, the intrinsic potential diverges. In the case that the electron is orbiting, the time delay for transfer signals between the electron and its image charges. Neglecting the transformation of the fields themselves that would have to be accounted for if the motion were relativistic, the potential of the new configuration of the electron and its image charges, which will be referred to as the total self-interaction potential of the electron, is given by

$$V_{total} = \frac{q}{\pi^2 \epsilon_0} \sum_{n=1}^{n=\infty} \frac{1}{2R^2 \left(1 - \cos(\omega t_{ret;n})\right) + (2\pi n b)^2} \tag{3.20}$$

where $t_{ret;n}$ is given by equation 3.8. It can be seen simply by looking at the first term of the series and noting that every term in the series is positive, that in the limit that b is zero, V_{orbit} diverges as well. The quantity of interest, however, is the discrepancy between the intrinsic self-interaction potential and the total self-interaction potential which will be referred to as V_{self}, and is given by:

$$V_{self} = V_{total} - V_{intrinsic} = -\frac{q}{\pi^2 \epsilon_0} \sum_{n=1}^{n=\infty} \frac{2R^2 \left(1 - \cos(\omega t_{ret;n})\right)}{(2\pi n b)^2 \left[2R^2 \left(1 - \cos(\omega t_{ret;n})\right) + (2\pi n b)^2\right]} \tag{3.21}$$

in the limit that V_{self} is a slowly varying function of n, the infinite sum can be written as an integral over the variable $w = 2\pi n b$ with $dw = 2\pi b$ as follows:

$$V_{self} = -\frac{q}{2\pi^3 b \epsilon_0} \int_{2\pi b}^{\infty} \frac{2R^2 \left[1 - \cos\left(\frac{\omega w}{c}\right)\right] dw}{2w^2 R^2 \left[1 - \cos\left(\frac{\omega w}{c}\right)\right] + w^4} \tag{3.22}$$

making the substitution $\omega = \beta c/R$ and the change of variables $u = w/R$, the integral can be re-written as follows,

$$V_{self} = -\frac{q}{2\pi^3 b\epsilon_0 R}\int_{\frac{2\pi b}{R}}^{\infty}\frac{2\left[1-\cos(\beta u)\right]du}{2u^2\left[1-\cos(\beta u)\right]+u^4} \tag{3.23}$$

Noting that the integrand is divergent at $u = 0$, the integral can be well approximated by expanding the integrand to second order about its pole,

$$V_{self} = -\frac{q}{2\pi^3 b\epsilon_0 R}\int_{\frac{2\pi b}{R}}^{\infty}\frac{2\left[1-\cos(\beta u)\right]}{2u^2\left[1-\cos(\beta u)\right]+u^4} \approx V_{self} = -\frac{q}{2\pi^3 b\epsilon_0 R}\int_{\frac{2\pi b}{R}}^{\infty}\left(\frac{\beta^2}{\beta^2+1}\right)\frac{du}{u^2} \tag{3.24}$$

Taking the limit that $\beta \ll 0$, and substituting ϵ_0 with its value in four dimensions, V_{self} is given by

$$V_{self} = -\frac{q\beta^2}{4\pi^3\epsilon_0 b} \tag{3.25}$$

The self-interaction correction is subsequently negligible in the non-relativistic limit, unless $b = 0$.

3.4. **Results.** Once the energy levels of the H-atom are obtained neglecting first-order corrections to the potential, the first-order correction to the energy due to the Yukawa and spin-orbit coupling corrections can be obtained using perturbation theory.

In calculating first order perturbations to the energy of the hydrogen atom we first obtain the matrix elements forV^{Yukawa} and V^{SO}as follows:

$$V^{Yukawa}_{nln'l'} = \langle R_{n,l}|\,\frac{-e^2}{2\pi\epsilon_0}\frac{e^{-r/b}}{r}\,|R_{n',l'}\rangle \tag{3.26}$$

$$V^{SO}_{nln'l'} = \langle R_{n,l}|\,\frac{e^2}{4\pi\epsilon_0}\frac{1}{m^2c^2r^3}\vec{S}\cdot\vec{L}\,|R_{n',l'}\rangle \tag{3.27}$$

where $R_{n,l}$is the n^{th}eigenstate with orbital angular momentum $\hbar^2 l(l+1)$ of the unperturbed radial Schrodinger equation.

The first order perturbations are then given by $V^{Yukawa}_{1010}$and V^{SO}_{1010} for the $n = 1$ state, and for higher energy states are obtained by diagonalizing the potentials in the subspace of degenerate states. The Yukawa and spin-orbit coupling corrections subsequently break the degeneracy of higher energy states. In particular for $n = 2$, the first order change in energy levels is given by the eigenvalues of the 2×2 matrix representations of the potentials. Thus the first order change in energy levels for $n = 2$ states due to the Yukawa correction is given by

$$\lambda_{\pm} = \frac{1}{2}\left(V^{Yukawa}_{2020}+V^{Yukawa}_{2121}\right)\pm\frac{1}{2}\sqrt{\left(V^{Yukawa}_{2020}+V^{Yukawa}_{2121}\right)^2+4\left(V^{Yukawa}_{2020}V^{Yukawa}_{2121}+\left(V^{Yukawa}_{2120}\right)^2\right)} \tag{3.28}$$

The first order corrections to the energy levels of the $n = 2$ states is plotted below as a function of the ratio of the compactification radius b to the Bohr radius a_0.

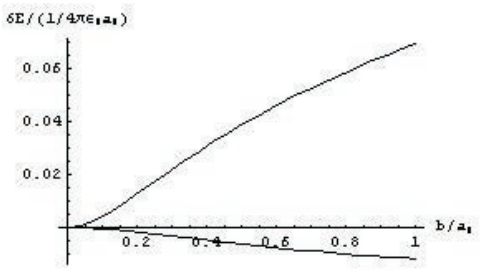

FIGURE 3.1. Plot of the first-order correction to the energy levels of the n=2 states of the hydrogen atom due to the Yukawa correction potential as a function of the ratio of the compact dimension to the Bohr radius. Range is 0<b/a<1, where b is the radius of the compact dimension and a is the Bohr radius.

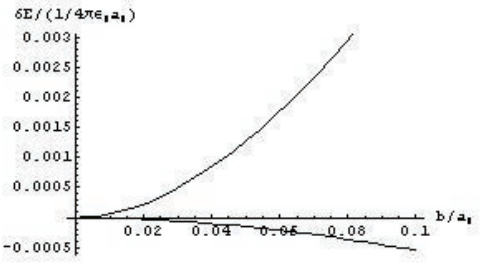

FIGURE 3.2. Same plot as above but with close-up in the range 0<b/a<0.1

Note that in the limit that $b \ll a_0$, the correction to the first order correction to the energy levels vanishes. The results of this numerical calculation have important physical significance, since breaking of the degeneracy of the energy levels of the hydrogen atom due to additional compactified dimensions can be measured in a laboratory. The results of this numerical calculation have important physical significance, since breaking of the degeneracy of the energy levels of the hydrogen atom due to additional compactified dimensions can be measured in a laboratory.

4. CONCLUSION

The study of additional spatial dimensions has fundamentally changed our perception of the structure of the universe. Furthermore, the study of additional spatial dimensions is of major importance since fully understanding the physics of additional spatial dimensions at the Planck-scale may one day lead to a theory that unifies gravity with all the other fundamental forces. Theodore Kaluza and Oscar

Klein were the first to realize the unifying power of theories with higher space-time dimensionality. They subsequently were able to write down an equation that unified gravity and electromagnetism simply by incorporating an additional compactified spatial dimension with the topology of a circle. Kaluza-Klein theory has recently been revived in an attempt to unify gravity with all the fundamental forces.

In this paper, we considered the possibility that electromagnetic fields can propagate through additional compactified dimensions. In particular, we have shown that in a universe with an additional compacitified spatial dimension with the topology of a circle, the solution of Maxwell's equation reduces to solving a set of five Poisson's equations with five periodic boundary conditions, have obtained explicit solutions for both the time independent and time dependent cases. After solving Maxwell's equations on the Kaluza-Klein model, we then use the solutions for the electromagnetic field of a non-relativistic point charge to calculate first order perturbations to the hamiltonian of the hydrogen atom in the Kaluza-Klein model. These first order corrections to the hamiltonian break the degeneracy of the of the energy levels of the hydrogen atom, which can in principle be measured in a laboratory. In this paper we provide plots of the first order corrections to the energy levels of the $n = 2$ states of the hydrogen atom which are obtained numerically using degenerate perturbation theory.

Note that in the above discussion, the Kaluza-Klein states of the hydrogen atom, i.e. the excited modes of the electron in the additional compactified dimension, were not discussed. It is straightforward to calculate the energy levels of the Kaluza-Klein states of the electron in the limit that the compactification radius is much smaller than the Bohr radius. In the aforementioned limit, the hamiltonian of the hydrogen atom is given by the following:

$$\hat{H} = -\frac{\hbar^2}{2m}\nabla^2 - \frac{e^2}{4\pi\epsilon_0}\frac{1}{|\vec{r}|}\left(1 + 2\exp\left(-|\vec{r}|/b\right)\right) - \frac{e^2}{8\pi\epsilon_0 m^2 c^2}\frac{\vec{S}.\vec{L}}{|\vec{r}|^3} - \frac{q\beta^2}{4\pi^3\epsilon_0 b} \tag{4.1}$$

where the coordinate of the compactified dimension is denoted as w and the kinetic energy terms is given by,

$$-\frac{\hbar^2}{2m}\nabla^2 = -\frac{\hbar^2}{2m}\left[\frac{1}{r^2}\partial_r\left(r^2\partial_r\right) + \frac{1}{r^2\sin\theta}\partial_\theta\left(\sin\theta\partial_\theta\right) + \frac{1}{r^2\sin^2\theta}\partial_\phi^2\right] - \frac{\hbar^2}{2m}\partial_w^2 \tag{4.2}$$

Since the potential energy of the hydrogen atom is independent of the w coordinate in the limit that the compactification radius is smaller than the Bohr radius, the electron is a free particle in the additional compactified dimension, and the energy levels of the hydrogen atom are subsequently given by $E = E_n + \delta E_{Yukawa} + \delta E_{SO} + \frac{\hbar^2 k^2}{2mb^2}$, where the first three terms correspond to the energy levels of unexcited Kaluza-Klein modes with first order corrections described in section 3.4, and the third term corresponds to the energies of Kaluza-Klein modes. Since the term corresponding to excited Kaluza-Klein states scales as $\frac{1}{b^2}$, in the limit that the radius of compactification is much smaller than the Bohr radius, the energies needed to excite Kaluza-Klein modes become much higher than the binding energy of the hydrogen atom, notably $-\frac{\hbar^2}{2ma_0^2}$, where a_0 is the Bohr radius. The Kaluza-Klein states of hydrogen are therefore not accessible in the laboratory since the hydrogen atom will ionize before one can even reach the energies needed to excite a Kaluza-Klein mode. What we have shown, however, is that the presence of an

additional compactified dimension can be detected without actually having to excite any Kaluza-Klein modes. In particular, an additional compactified dimension can be detected by measuring the degree to which it breaks the degeneracy of the energy levels of the hydrogen atom, which may be feasible in a laboratory.

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