LABYrinth2013

The Science Journal of ManhattanHS for Girls

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BS"D

FOREWORD

BRENDA FROM—*Faculty Advisor*

Welcome back old friend, LAByrinth. It's been too long and I've missed you. Come here, turn around and let me look at you. You look wonderful—a new cover perhaps but essentially you have remained the same. Pull up a chair and share a cup of coffee with me. We have so much catching up to do.

How are the kids, you ask? They are great as you can see. They are working hard, growing, stretching to reach their potential. At their urging, we have initiated the creation of the first Science Club. They voluntarily met with me once a week giving of their lunch hour in anticipation of your visit. Each one scoured the science publications we have hanging outside the science lab to find a topic that beckoned to them. Look at the diversity of their interests, spanning the gamut from Microbiology (Englander, Greenberg), Neurobiology (Schuster, Miller, Gozland), Cell Biology (Jacobov), Anatomy (Bartfeld), Genetics (Grossman) to Computer Technol0gy (Salhanick), Theoretical Physics (Kopelowitz) and Synthetic Chemistry (Kurtz). They searched the literature to plumb the depths of the concepts, establish connections, and created a synthesis they truly own. Some of them even made predictions for the future. In the process, they have learned the value of process, and gained valuable research skills that will surely spill over to their other areas of academic endeavors. You should have seen them as they confidently presented their new knowledge in front of their peers and the entire student body. I was bursting at the seams with pride as I know you are too. As you read their words, hear the unique voice inffused in the writing. Enjoy the fruits of their labors.

But, we must not forget priorities and give thanks to all who made this possible. Foremost, my heartfelt gratitude goes to my students who fill my working hours with purpose and fulfillment. They inspire me with their curiosity and eagerness to learn. Their questions keep me on my toes, force me to hit the books and be a student once again. I am enriched through them. No less important, I am indebted to the administration at Manhattan High School for Girls, who have supported the standards of excellence in education in every discipline, dimension and endeavor. Appreciation goes to Ms. Chavi Stefansky for her valuable technical expertise and talents in preparing this issue of LAByrinth 2013 for publication. Most important, thanks to HKB"H for allowing us the briefest glimpse into the keyhole of his LABoratory, for giving us the faintest glimmer of understanding, and leaving us with an unquenchable thirst for more.

Time to go so soon? Well, don't be a stranger. Come back next year and we'll have so much to talk about again.

NOT JUST ANOTHER APPENDAGE

ARIELLA BARTFELD '13

Experience had taught me that most of my seven year old brother Joseph's tummy aches and boo boos were carefully choreographed ploys to get out of school that deserved none of my sympathy. Therefore, the morning of his appendicitis, I sleepily dismissed his moans as just another instance of his crying wolf. However, my ever empathetic parents, both practicing physicians, lay my wailing little brother on his bed and began prodding his general stomach area. When they were rewarded with an exceptionally ferocious howl after they poked the right lower quadrant of his abdomen, my parents looked up. Joseph had a genuine malady: appendicitis. This meant that his appendix was infected and needed to be removed before it burst and spread infection throughout his entire body.

Shocked that my brother's illness was legitimate, I agreed to babysit the rest of my

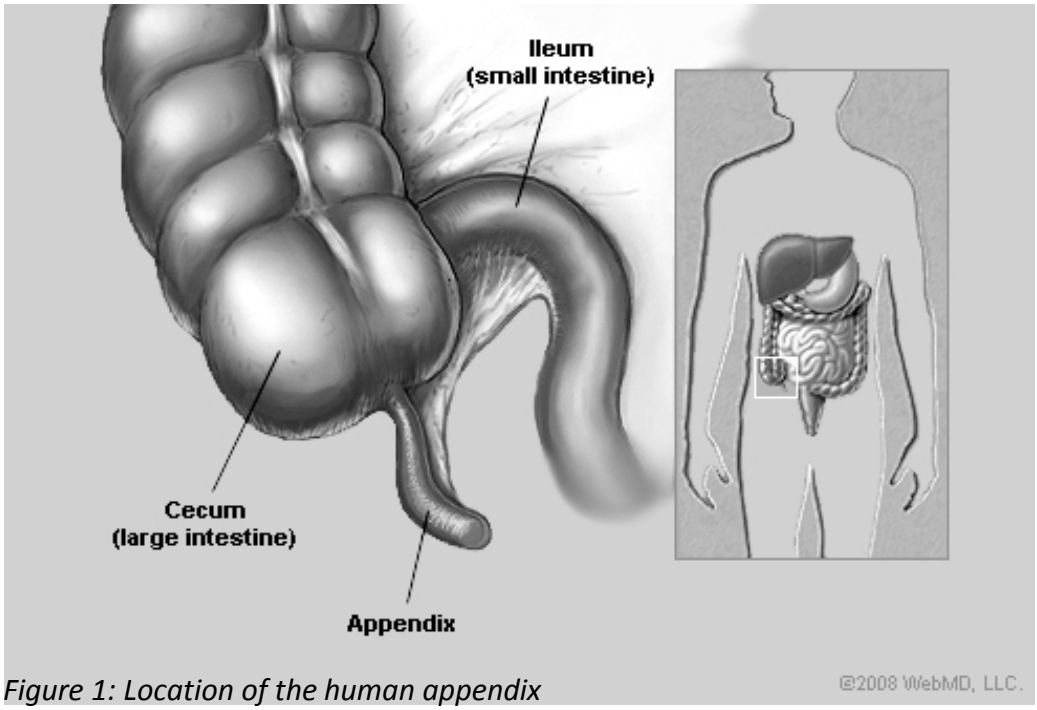

Figure 1: Location of the human appendix

brothers while Joseph was rushed to the hospital. There he was hooked up to an IV and put to sleep with the aid of anesthesia and a particularly boring *Charlie and the Chocolate Factory* video. Then, as he lay oblivious to the world, Joseph had his appendix removed through three tiny abdominal incisions, a laparoscopic appendectomy, that the surgeon assured would be quite painless. For a week Joseph basked in his new invalid status, groaning, limping, and reaping gifts. Once the novelty of his surgery wore off (and the stream of well wishers bearing gifts dried up), Joseph returned to school and normal

life. His quality of life was unaffected and his appendix deficit continues to seem inconsequential. However, research continues to uncover possible purposes of the supposedly useless appendix, and it appears that hasty removal of this wormlike tube may not have been the best option. Even though my brother cannot feel it, his appendectomy may have left him bereft of a crucial organ. Scientists are currently researching a slew of theories to explain what exactly made Joseph's appendix important.

The human appendix is a small dead-end tube connected to the cecum, or ascending colon, one section of the large intestine (figure 1). Nobody really knows its function, and no one is aware of it until it becomes inflamed, at which point it is surgically removed. At that point, no one is aware of its absence. It has been relegated to the heap of vestigial organs, one that might have had a long lost function in some far back ancestor. But that explanation does not really hold up to scrutiny. There is little evidence for an appendix in our evolutionary ancestors andrew mammals have any appendix at all. The appendices of those that do bears little resemblance to the human one.

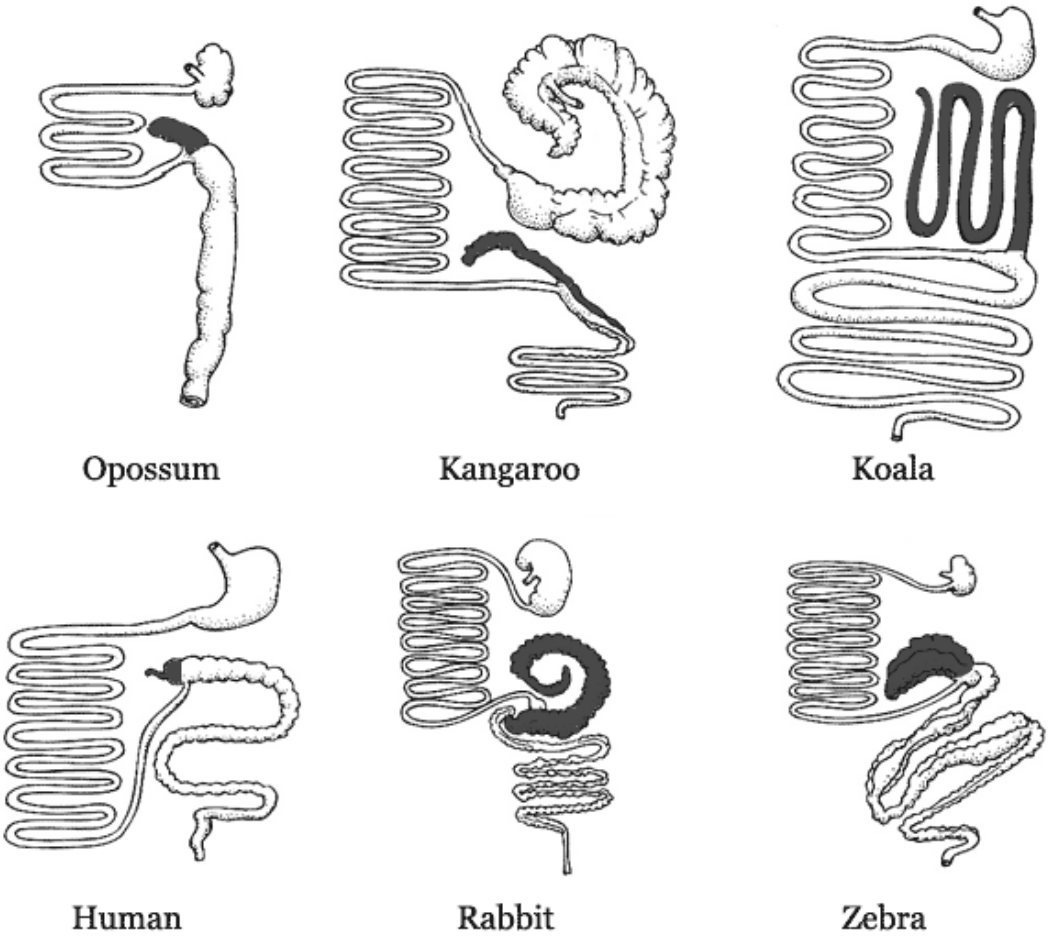

Figure 2: Comparative mammalian appendices

A separate team of researchers, with no specific interest in the appendix, was working to understand the interaction between the bowel's bacteria and the immune system. Coincidentally, the portion of the intestine they studied was an appendix sampling. Quite by accident, they discovered that the appendix hosts much more bacteria than the rest of the intestine (6). These bacteria form hardy biofilms, sticky colonies of microbial bacteria that populate the mucous lining of the appendix and the gut (2). The team neatly hypothesized that the human appendix stores a reserve of good bacteria, a "safe-house," that can be put to use when infection or disease incapacitates the intestine's circulating bacteria. However, this tidy justification of this vestigial organ's perseverance is rendered unnecessary by the hygiene hypothesis, which states that modern day societies keep human living conditions so ridiculously clean that our immune systems are left with nothing to fight. Therefore, when our bodies finally do encounter a germ, our immune systems get too excited and completely overreact. This overzealousness extends to the appendix, which can overwork itself into becoming inflamed, requiring surgical removal (6).

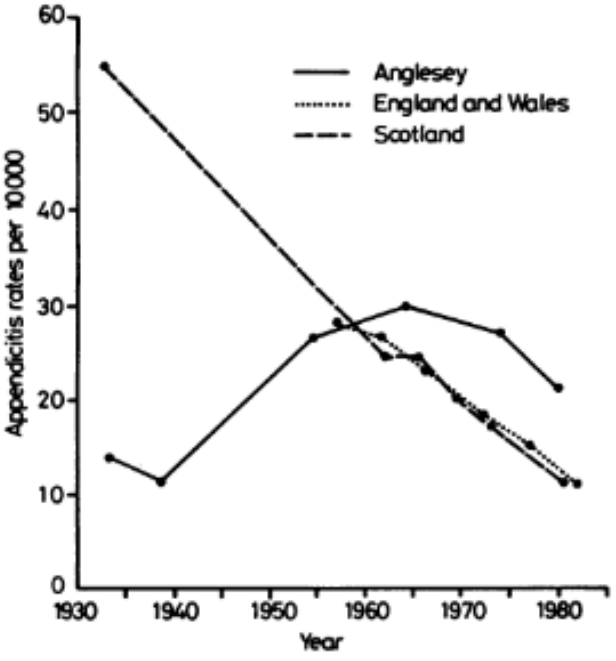

Figure 3: These findings show that the introduction of piped water into Anglesey, UK shortly after WWII is associated with a sharp rise in acute appendicitis rates. This occurred when the rates of appendicitis in Great Britain were falling.

An indirect epidemiological support of this hypothesis is the sudden, sharp increase of appendicitis cases observed in cities that have just installed running water, and thereby decreased the chances of contacting common germs (Figure 3) (1). Ironically, our own bodies' defense to something small can lead to a full blown appendicitis. Therefore, while hosting helpful bacteria may be a validation for the appendix's usefulness, this attribute may also be the reason why appendices routinely become infected and need to be taken out.

Even if, at the end of the day, the appendix does turn out to be a mere lump of useless tissue, it still has an irreplaceable role in

reconstructive surgery. Admittedly, this artificial use of the appendix fails to prove this little tube's intrinsic value but, reconstructing other organs with the appendix does show how our innovative species has endowed it with important utility. Surgeons can help patients who have lost their bladders to cancer or other disease to remain continent by refashioning the patients' appendix, along with a portion of the small intestine, into a replacement bladder and sphincter muscle. They can also repurpose the surprisingly versatile appendix into a replacement ureter, enabling urine to continue to flow from the kidneys to the bladder even after a patient has lost this vital organ (5). This is an alternative to the standard ureteric stent (Figure 4), a metal channel inserted in between the kidneys and bladder, which achieves an identical goal but also introduces discomfort, bloody urine, and some incontinence (4). While the normal appendix may turn out to be useless, the repurposed appendix can help preserve patients' comfort and quality of life.

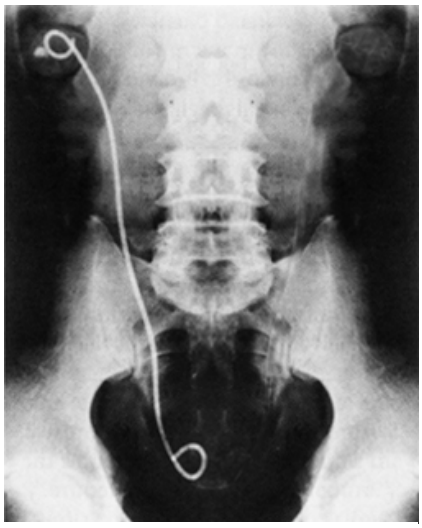

Figure 4: Uretic stent (in white) extending from kidney to bladder

In 1893 eighty-six human organs were dismissed as vestigial (3). But as science has progressed, almost all of these supposedly useless organs have steadily had their purposes revealed. Just like the pituitary gland and toe bones were docked from the vestigial list, I predict that the appendix will also eventually be proven to have a definite, vital role. One day appendectomies will be rare and future generations will shake their heads at our brutish disposal of an essential organ. However, we cannot get ahead of ourselves. We must remember that appendicitis left untreated is deadly and that, currently, the only solution is an appendectomy. All we can hope for is that the to-be-discovered role of the appendix will be able to be replicated for people, like my brother Joseph, who live sans this vermiform appendage.

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Fig. 1: http://img.webmd.com/dtmcms/live/webmd/consumer_assets/site_images/articles/image_article_collections/anatomy_pages/appendix3.jpg

Fig. 2: http://1.bp.blogspot.com/-BiDKFC4s2gQ/T0FNX2AB36I/AAAAAAAAAkE/hUOw1DtXf0k/s1600/guts.gif

Fig. 3: http://biology-forums.com/gallery/14755_26_10_12_5_22_58_96792213.jpeg

Fig. 4: http://www.bui.ac.uk/images/patientgfx/stentxray.gif

NEEDING AND NEEDLING THE MICROBIOME

GABRIELLA ENGLANDER ‘14

When most people look in the mirror, they think they perceive the image of a human being reflected back at them (Figure 1). That is only 10% true. In actuality, 90% of the human body is a thriving ecosystem of bacteria and micro-organisms called the microbiome, and the role it plays in health is just starting to be revealed. This aura of bacteria that makes up the microbiome performs numerous sustaining functions in exchange for raw food and shelter: Bacteria feed their hosts 10% of their daily calories, produce vitamins, keep hostile interlopers at bay, and produce molecules that help regulate the activities of human cells. These 10 trillion bacteria do not leave their human host alone for even a moment, from the messy process of birth to the mournful process of death (4). They are found in the gut, mouth, skin, scalp, and every other crevice and orifice that subtend from the body's surface (11). Study of the microbiome has revealed its utility in noninvasive diagnostics and restoration of health. If these microscopic co-tenants are respected, and treated kindly, with equal rights and liberties, humans and their bacterial counterparts can live peacefully and in harmony.

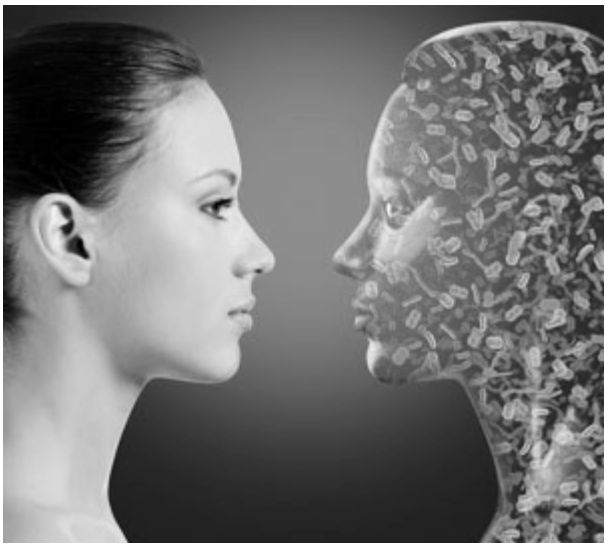

Figure 1: Your reflection

The recognition of the role the microbiome plays in human health has been steadily gaining momentum over the past five years, so much so that the National Institutes of Health has instituted the Human Microbiome Project, a new federal endeavor similar to the Human Genome Project, to characterize the microbial communities found at several different sites on the human body, including nasal passages, oral cavities, skin, gastrointestinal tract, and urogenital tract, and to analyze the role of these microbes in human health and disease (6).

Lest you think that humans and bacteria make strange bedfellows, the story gets stranger yet. All good ecosystems, like politics, require checks and balances to ensure that the population of symbionts do not get out of line and turn into parasitic freeloaders.

Layered onto this story of friendly collaboration between humans and their bacterial cohabitants lies an underbelly of suspicion. In a recent report, scientists discovered a behind-the-back treaty between humans and bacteriaphages—viruses that are specifically designed to attack bacteria. The mucous membranes that line the respiratory and digestive tracts make particularly good homes for bacteria, both good and pathogenic. These researchers found four times as many phage as bacteria in the mucus than in the surrounding tissue due to a mucosal protein that assists phage in their adhesion. If the bacteria grow beyond their carrying capacity, the phage will keep them in line, in effect acting as a backup immune system (3). Ingenious.

One of the particularly dangerous agents that can disturb the peace and harmony of the human/microbiome interaction is stress. The microbiome is particularly sensitive to stress and it can disrupt the ecological balance of the flora of gut dwellers (10). When an individual confronts a stressful situation, the hypothalamus, the command center of the brain, sends a distress signal to the pituitary gland at the base of the brain, which in turn stimulates the adrenal glands, atop the kidneys, via the sympathetic nerve system. The adrenal glands respond by pumping adrenaline, also known as the hormone epinephrine, into the bloodstream to activate certain physiological changes to combat the stressful situation. This is known as the HPA Axis (12) (Figure 2). One of the targets of the HPA axis response to stress is the epithelial lining of the intestines. The epithelial lining of the intestines must exercise exquisite sensitivity to allow selective passage of certain materials from the interior lumen to the blood capillaries, and to deny passage to others. The rise in hormone levels induces gut permeability, allowing bacteria and bacterial antigens to tiptoe across the epithelial barrier and activate a mucosal immune response, a response that provides protection to the gut's mucous membranes against invading pathogenic microbes (4). As a result, the microbiome's gut composition is altered, throwing the bacterial victims off balance.

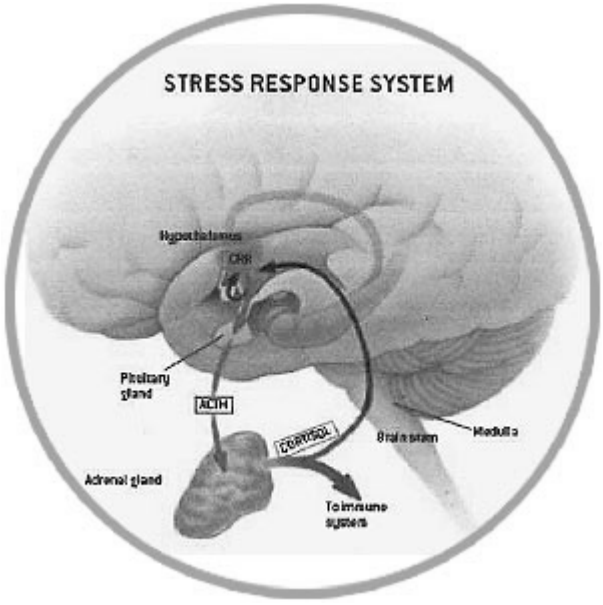

Figure 2: Hypothalamus-Pituitary-Adrenal (HPA) Axis

Many studies display evidence of the effects of stress on the microbiome balance. One study demonstrated that stress hormones, adrenaline and noradrenaline, promoted the growth of non-pathogenic isolates of E. coli and the growth of the pathogenic E. coli 0157:H7 strain in the microbiome (4). Other studies have demonstrated that early life stressors, such as maternal separation, have altered an adult rat's fecal microbiome compared to non-separated controlled rats (5). Additional studies have exhibited that psychological stressors can alter the composition and total biomass composition of the microbiome in infants (4).

Recently, the stage lights have focused on the idea of monitoring the change in the microbiome as an early warning diagnostic signal of disease and of manipulating these bacterial buddies to their host's advantage. One group of researchers was able to use the microbiome as a non invasive diagnostic tool to diagnose pediatric inflammatory bowel disease by inspecting the bacteria in stool samples (9). Manipulating the microbiome to restore health takes place through a transplant which introduces new bacteria or a transplant which removes harmful bacteria (8).

One such doctor treated his patients infected with *Clostridium difficile* (CDI), a bug that causes severe diarrhea, by transplanting feces from a healthy volunteer into the lower intestines. Yuck factor aside, the new heroic bugs in the feces multiplied rapidly and drove the culprit away. The transplant succeeded in 91% of the 77 patients with recurrent CDI who had undergone 2 or more failed courses of treatment; moreover, when the seven who did not respond were given a second course of treatment, six were cured (5). Despite having CDI for an average of 11 months, the patients responded to the stool transplant in just 6 days and none of the patients developed recurrent CDI without subsequently taking antibiotics during the follow-up (14).

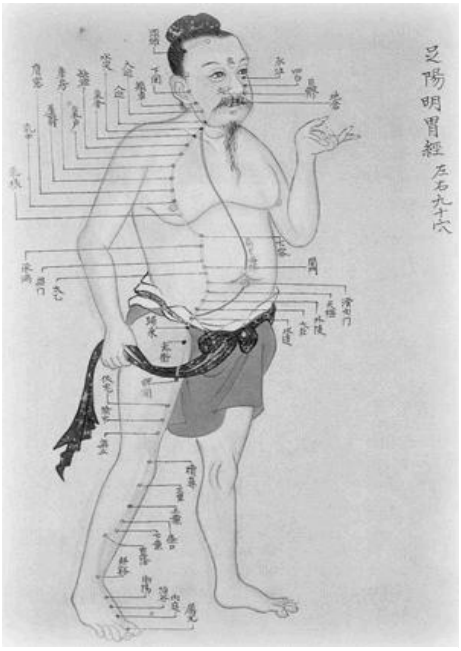

Figure 3: Qi meridians

Perhaps there are other therapeutic and less invasive thruways to affect and restore a disrupted microbiome. Acupuncture could potentially fit the bill. According to Eastern philosophy of medicine, the human body (and its newly discovered bacterial counterparts) is part of the total fabric of the universe, called the Tao, and is infused by a pervasive energy, referred to as Qi, that flows throughout the body in channels known as meridians. These energy-filled meridians can become clogged,

blocking the flow of energy that circulates the body (Figure 3, above). The cure for these obstructions is the treatment of acupuncture in which fine needles are inserted into the body to break up energy obstructions in the meridians and coax the Qi to flow again (13). Accupuncture was previously dismissed derisively by Western practitioners of medicine as Quacupunture, but double-blind studies (the gold standard in experimental design) have demonstrated that acupuncture provides quantifiable relief for a variety of ailments including diabetes (2). How does this seemingly ephemeral idea of Qi and Tao align with Western philosophy of medicine, which is grounded in tangible structures and actual molecules? Furthermore, how can acupuncture manipulate the microbiome and therapeutically restore health and balance?

One explanation speculates that the inserted needles cause physical responses in nerve cells, the pituitary gland, and other parts of the brain; these organs then release proteins, hormones, and brain chemicals that control a number of bodily functions. In this way, acupuncture has been shown to affect blood pressure, body temperature, boost the immune system, and cause the body's natural painkillers, hormones called endorphins, to be released (1). Several studies suggest that acupuncture reduces stress and improves the overall quality of life because it helps arteries and the nervous system to function better (7).

Here, two radically different ideas based on two radically different civilizations and philosophical orientations toward health converge, and the point of intersection is where stress, hormones and their affect on the microbiome connect. To put this idea more clearly, stress alters the microbiome and acupuncture activates hormones that relieve stress, ergo acupuncture restores human/microbial balance and health.

This hypothesis is based on a giant leap of faith, however this speculation should warrant further research. What if acupuncture does prove to be another valuable, therapeutic passageway towards curing a disrupted microbiome and restoring health without resorting to drugs with their ever-attendant harmful side effects? Perhaps, in the near future, this hypothesis will be supported and a gentler, less invasive avenue of maintaining human health and treating disease will become the norm. If more research was invested into the concept of using the microbiome as a diagnostic and curative tool, soon a doctor might only have to swipe a person's skin to deduce the patient's medical condition from the bacteria that appear on the swab: Perhaps that would become the only component of a yearly check up!

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CROSSING THE SAHARA

RACHEL GOZLAND '13

In 1963, Emil Frei and Emil Freireich, two cancer scientists, discovered failure (12;13). They had been testing VAMP—a controversial leukemia therapy consisting of an extremely high-dose and possibly lethal combination of four drugs—on several children. Despite being laughed at and called "insane, incompetent, and cruel" by their peers, they persisted in the program. The idea was certainly revolutionary, but strangely enough, it seemed to work. The patients appeared to recover from leukemia completely (Figure 1). The opponents of the project were forced to admit that yes, it was a phenomenon, but it was a success (12).

Figure 1: Emil Frei, nurse and patient

Their elation quickly turned to despair, however, as it was shortly proven to be no success. Eventually, a few children in remission began complaining about headaches, perhaps a seizure, maybe some tingling of a nerve in the face. Soon, the problems became more serious. They were all symptoms that pointed to a neurological ailment, and Frei and Freireich feared that leukemia might be colonizing the children's brains. They decided to look directly at the spinal fluid by means of a spinal tap—a procedure in which they withdrew some fluid from the spinal canal using a thin needle. Because spinal fluid has a direct connection to the brain via its circulation path, this would be the perfect way to observe what might be occurring within the patients' brains. They went cold at what they saw; leukemia cells were proliferating profusely in the spinal cord—by the millions—and they were, in fact, colonizing in the brain. Soon, the children would experience a quick devastation, as one by one, they fell into comas. The catch was this: There was no cancer anywhere in the rest of the children's bodies. All organs, with the exception of the brain, were freed from leukemia. The incredibly-afflicted nervous system was the one ugly stain on the otherwise successful project, but it would render that triumph a total defeat (12).

What Frei and Freireich had failed to take into account was one of the most important structural features of the brain: the blood-brain barrier (BBB)—the wall that separates the brain's neural tissue from the rest of the biological systems, protecting it from changes in blood composition, which could impair brain activity, as well as from toxins (4; 12). This filter, which consists of endothelial cells that form the lining of blood vessels, is highly-specialized, allowing only very specific molecules to enter the fluid that bathes the brain (Figure 2). The BBB thereby provides extremely protected conditions for the brain, allowing the nervous system to operate effectively (4; 5).

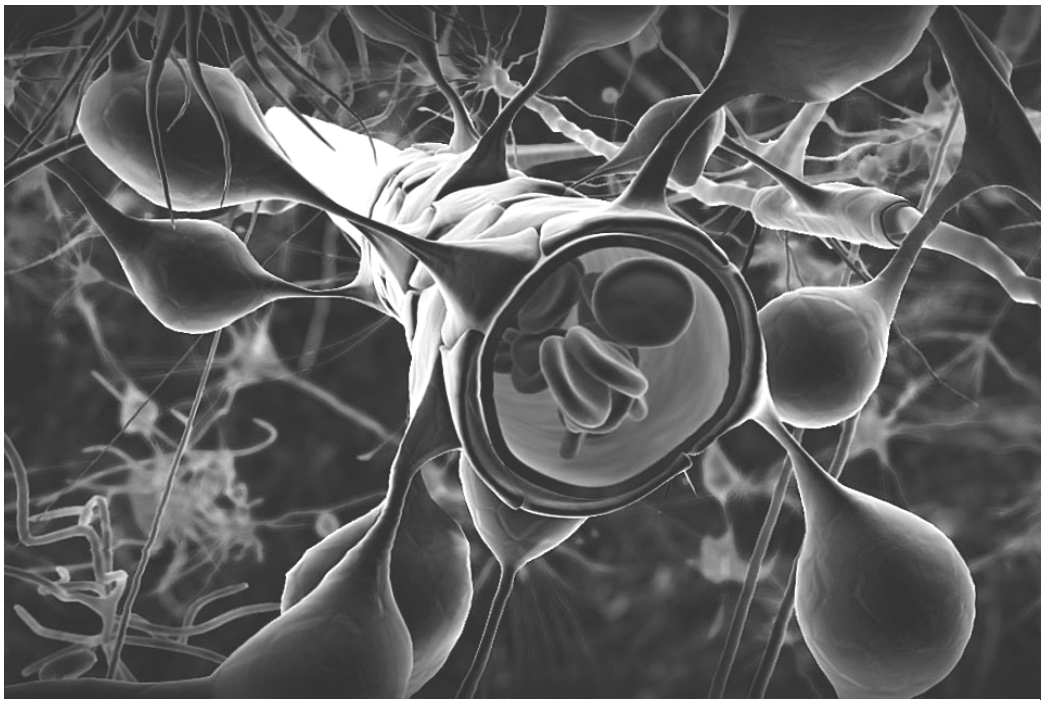

Figure 2: Blood Brain Barrier (BBB)-Astrocytes (cells in the brain that give biochemical support to the endothelial cells that make up the BBB) provide extra protective layer surrounding brain capillaries.

While the BBB provides safety for the brain, it has also proven to be a great obstacle for scientists searching for possible cures for many neurological diseases, such as brain tumors and Alzheimer's disease. Because the BBB is so selective, it is extremely difficult to find a drug that can cross it and reach a specific area of the brain to treat the disease (5). Frei and Freireich's project was unsuccessful because although the drugs eradicated leukemia throughout most of the body, the medication, despite its potency, could not cross the BBB. Consequently, the leukemia cancer cells grew unchecked and, for a while, unnoticed, within the safety of the untreated brain (12).

Almost fifty years after VAMP, scientists are still struggling to figure out exactly how to get past this BBB. This past year, however, a likely solution was discovered in what would seem the most unlikely of places—camelids. A newly-discovered class of antibody in camelids (including camels, dromedaries, llamas, and alpacas) can cross the BBB, diffuse into brain tissue, and reach specific targets within the brain (7). Antibodies are proteins manufactured by the B-lympocytes of the immune system, which target specific foreign invaders called antigens . The binding of an antibody to its antigen initiates the body's immune response (1; 2). There is much that renders this discovery quite extraordinary. To begin with, antibodies do not normally cross the BBB (11), let alone cross cell membranes and bind to antigens within brain cells (*11)*. How, then, does this particular antibody do both?

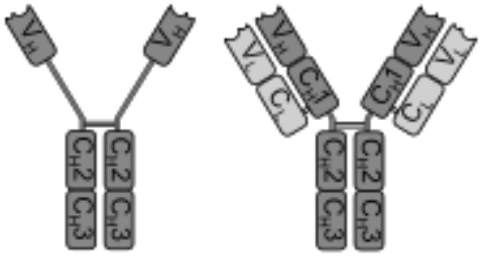

Figure 3: The diagram on the left is a model of camelid, 2 heavy chain only antibody. The diagram on the right is a model of a typical antibody, made up to two heavy chains and two light chains.

Typical antibodies consist of four protein sub units: two light chains and two heavy chains (*1*) (Figure 3). The heavy chains are attached to carbohydrates; the light chains bind to antigens (10). Almost all mammals only produce this type of antibody. Camelids are the one exception (8). Their antibodies consist only of—surprise!—heavy chains (11; 9). (Figure 3) However, they can still bind to antigens just as strongly as normal heavy/light-chain type antibodies, despite the lack of light chains. In fact, because these atypical antibodies consist of only two chains, they have lower molecular weights (6). Furthermore, VHH, the single-variable domain on the site of the antibody that recognizes and binds to the antigen (11), actually binds antigen with very strong affinity and is easily manufactured using E. Coli fermentation (9). All this makes camelid heavy-chain antibodies great potential candidates as carriers of therapeutics—they are so small, yet highly effective, allowing them to pass through tight intercellular space, while reaching a target and yielding significant effects (6).

Researchers created recombinant VHH using genetic material from two different sources (*14)* that would target human glial fibrillary acidic protein (GFAP), a specific marker of astrocytes (11), cells in the brain that give biochemical support to the endothelial cells that make up the BBB (3). This VHH was able to label the protein in the brains of live mice, proving it had crossed the BBB, without any treatment with chemicals of any sort to artificially increase its permeability (Figure 4) (11; 7). The hope that recombinant camelid

antibodies could offer a means to ferry drugs across the BBB offers tantalizing allure and is the subject of intense research.

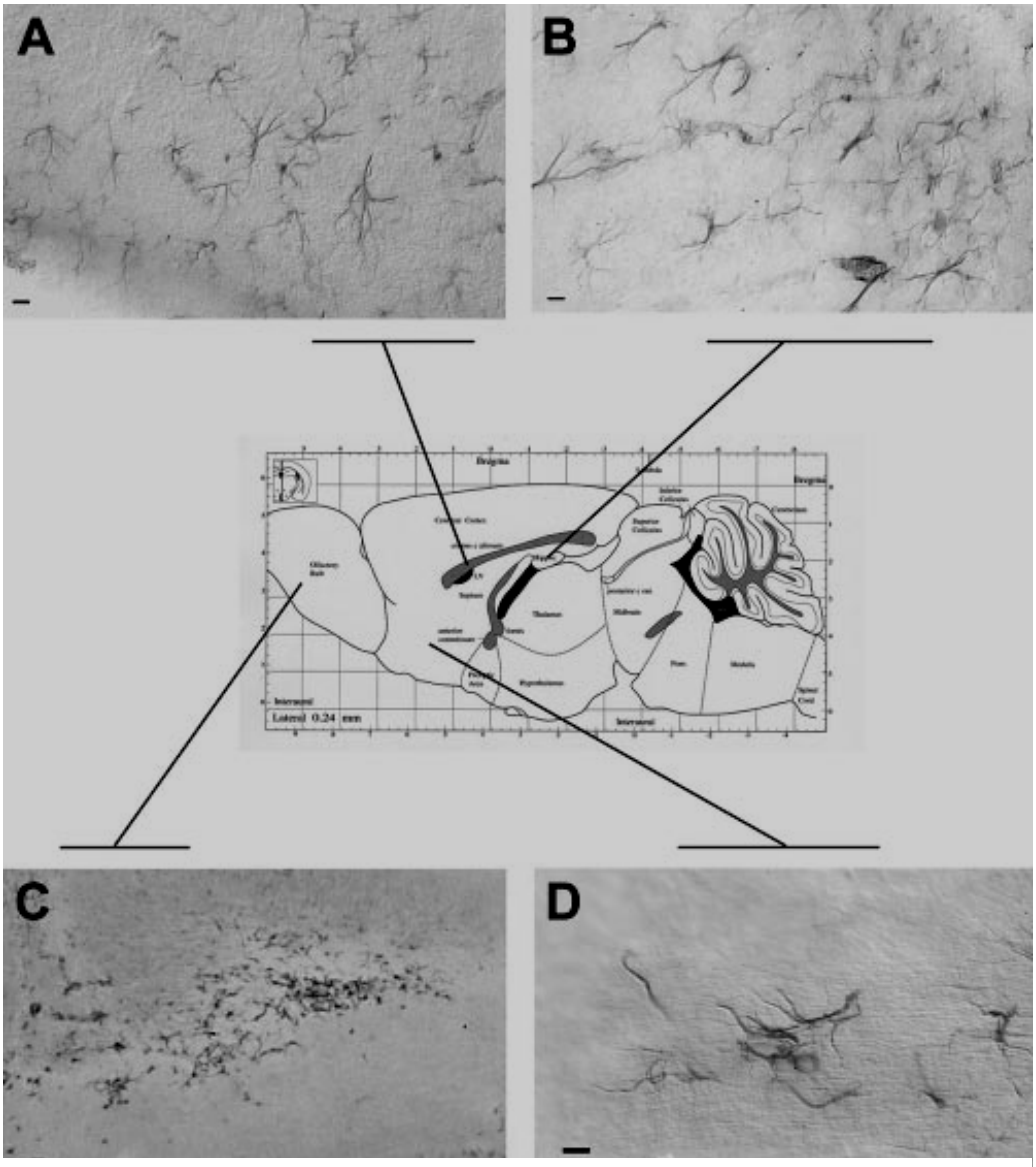

Figure 4: Evidence that mVHH E9 crosses the BBB in vivo and binds to GFAP in the cytoplasm of astrocytes of untreated C57BL/6 mouse brain sections. Mice were infused with 4 mg of mVHH via the left carotid artery for 60 minutes. They were then allowed 60 minutes before euthanization. Dark areas represent astrocytes from various parts of the mouse brain that incorporated mVHH that successfully crossed the BBB.

Camels do more than just traverse vast deserts; their antibodies can likewise cross the BBB (7). A feat like this means that neurological and neurodegenerative diseases, which

can cause their devastation by opening the BBB and allowing plasma, blood cells, drugs, proteins, and electrolytes into the cerebral tissue, will soon meet their match: a *natural* antibody that can penetrate the blood-brain barrier and also bind to specific intracellular targets within the brain (11). Such a finding means endless possibilities for sufferers of neurological diseases like Alzheimer's disease and brain tumors (7), because it means we can reach the human brain. It means we can touch what Frei and Freireich couldn't touch. It means we can help billions of people. It means we can change the landscape of medicine as we know it.

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BIOFILMS AND POPULATION DENSITY

AYELET GREENBERG '13

"High population density, especially in cities ... increases the number of causalities from natural disasters like the Haiti earthquake, which killed as many as 300,000. Cities located along major fault lines, like Istanbul, where the population has risen by more than nine million in the past fifty years, are major disasters waiting to happen (4)." More recently, Hurricane Sandy caused at least $65.6 billion of damage in the population dense regions of NY and NJ. Are we doomed by urbanization and Malthusian population sprawl, or are there untapped solutions just waiting on the horizon? Biomimicry is looking toward nature as a model to solve human problems. After 3.8 billion years of evolution, animals, plants, and microbes have honed solutions to their problems of life; they have retained what works and jettisoned what doesn't. Nature has found a way to turn population density into an advantage instead of a problem.

The inspiration came to me in the dentist chair, while the hygienist used a curette to vigorously scrape the plaque off my teeth to the point of blood-letting. My teeth were encased in bacterial biofilms (Figure 1). A biofilm is a well-organized community of bacteria that adheres to surfaces and is embedded in an extracellular slime layer with channels for nutrients to enter and waste products to exit. The human body is an excellent place for biofilms to thrive because it has a wide range of moist surfaces and mucosal tissue (3).

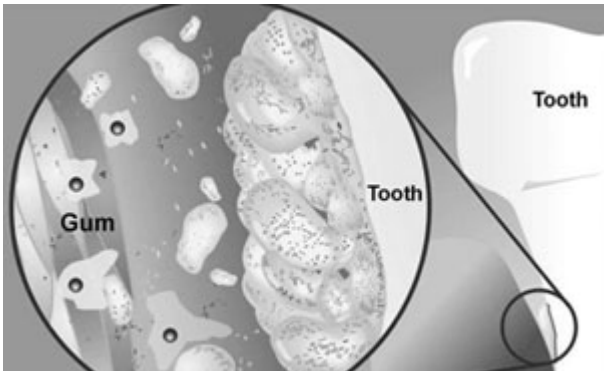

Figure 1: Hundreds of microbial biofilm colonize the human mouth, causing tooth decay and gum disease (2).

Bacteria are tiny organisms, that are hardly a threat when alone and free-floating. They can be simply washed away. However, in aggregate they can wreak havoc on human health. Bacteria communicate with members of their own species and even with bacteria of others species to coordinate their behavior in response to the density of the bacterial population. Through a process called Quorum Sensing, they produce and secrete signaling chemicals into their environment which bind to specialized receptors on the surface of neighboring bacteria. When these chemicals reach critical levels, a set of genes is turned on, group behavior is mounted in concert and by sheer virtue of their numbers,

bacteria become a formidable force. Quorum sensing is seen in group bacterial activities such as virulence, bioluminescence and biofilm formation (Figure 2)(1; 3).

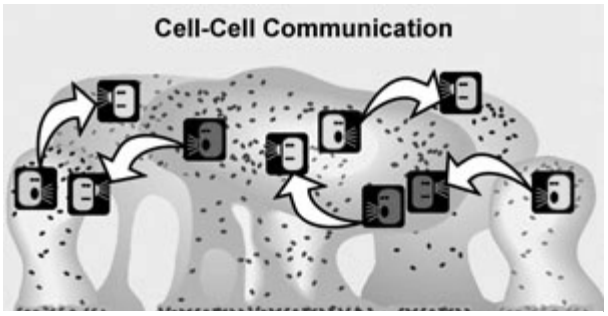

Figure 2: Sessile cells in a biofilm "talk" to each other via quorum sensing to build microcolonies and to keep water channels open (3).

When bacteria live together in a biofilm, a new set of genes is activated generating different characteristics from free floating bacteria. As the bacteria attach to a surface and each other they form communities with mutually compatible bacteria where emergent properties ensure survival. They form a "super organism" with specialized regions seen in higher order multicellular organisms. Bacteria living in the center of the biofilm may have anaerobic conditions, while bacteria at the edge of the biofilm may have an aerobic environment (Figure 3). The micro-colonies have different pHs and nutrients available so bacteria with different physiological needs can live together (2). Multispecies biofilms are ten times more resistant to compressive forces—hence the blood letting—than single species biofilms because the space is filled more efficiently, which makes them denser (5).

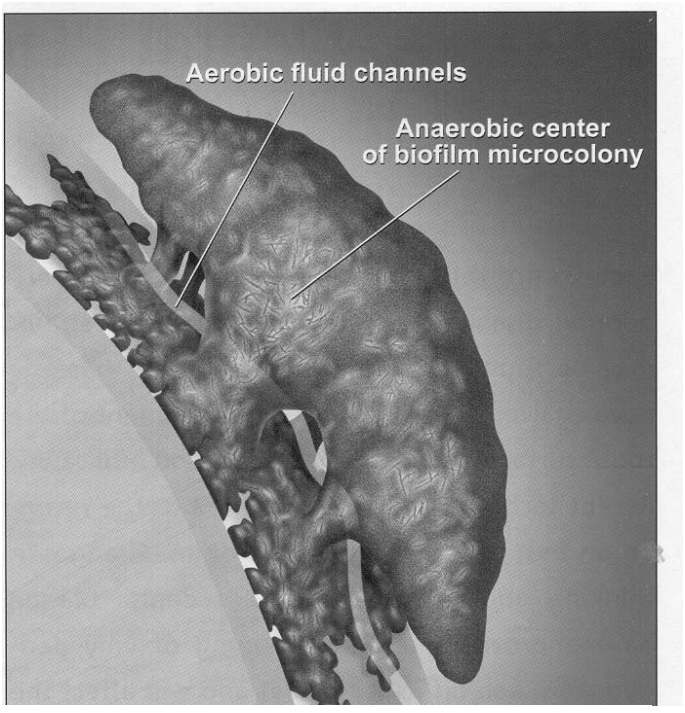

Figure 3: Illustration of aerobic environment at the edges and anaerobic environment towards the center of the biofilm (1).

Dental plaque biofilms begin developing when pellicles, thin coating of salivary proteins, attach to the tooth and provide a place for fimbriae, hair-like structures, to connect the bacteria to the pellicle and each other. Once the first bacteria stick, they produce substances that stimulate other free floating bacteria to join the community and

excrete an extracellular slime layer. The bacteria biofilm grows rapidly through cell division. The proliferating bacteria grows away from the bacteria that's already on the tooth, called coageration, which results in different bacteria linked to one another forming sessile mushroom-shaped micro colonies attached to the tooth surface at a narrow base. Following a few days of undisturbed plaque formation, the gingival margin becomes inflamed and swollen, resulting in the creation of a deepened gingival sulcus. The biofilm extends into this subgingival region and flourishes in this protected environment, forming a mature subgingival plaque biofilm, causing gingival inflammation. A subgingival bacterial micro-colony establishes in the gingival sulcus between three and twelve weeks after the beginning of supragingival plaque formation (Figure 4; 2).

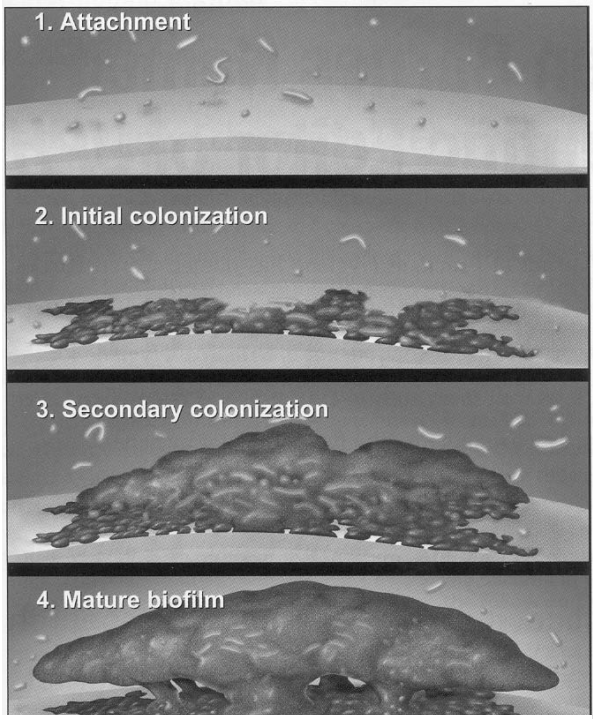

Figure 4: Stages of biofilm plaque development (2).

The production of extracellular polymeric substance(EPS), EPS chemistry and presence of divalent cations, hydrodynamic conditions during growth, quorum sensing, and fluids flowing around the biofilm (which transports nutrients, fluctuates pressures, and causes irregular architecture of the biofilm) influences biofilm strength (5).

The recent recognition of sub gingival plaque as a biofilm helps us understand its persistence and resistance. Antibiotics or medicine that kills free-floating bacteria needs to be strengthened 1,500 times to kill the biofilm and by that point it will kill the person before it kills the biofilm. Additionally, since biofilms live in a 'community' it is hard for the human immune system to kill them. Furthermore, the slime layer shields the biofilm against antibiotics, antimicrobial drugs, and leukocytes. So we need to physically remove plaque through frequent periodontal debridement of sub gingival root surfaces and visits to dental professionals such as dentists/hygienists, because sub gingival plaque within pockets cannot be reached by brushes, floss, or oral rinses alone. The professional must forcefully scrape off biofilms from between the gum and tooth (2).

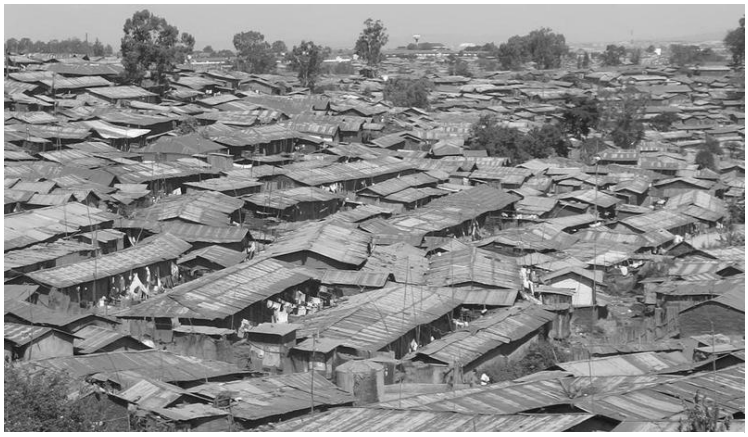

Figure 5: An aerial view of Kiberia, Kenya

Kiberia, in the Nairobi Area of Kenya, is Africa's biggest slum and second home to more than a million people (Figure 5, left). There are no governments, services, public schools, hospitals, paved roads, pumped water, and connected power lines. Every person is an opportunity and part of the workforce– vendors, barbers, carpenters, tailors, people selling soap, farmers milking cows and many other small jobs. The entrepreneurial spirit is pervasive and as a consequence, the economy is booming, incomes are rising, and Kiberia is becoming the world's most populated place (6). This type of synergy could never have occurred in the rural towns where these people come from. Kiberia is thriving because of population density and continues to be a magnet. Population density is not necessarily the problem; the challenge is how we use population density to our benefit.

Bacteria living in biofilms use population density to their advantage. The denser a biofilm is, the more resistant it is to antibodies/antibiotics. Looking to bacterial Quorum sensing, communication is the key to driving group behavior and changing the group dynamic. We have seen instances of this driving force in operation during the Arab Spring, when social media was the catalyst for group think change. Is social media biomimicry? An intriguing thought which deserves future exploration.

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THE PAISA GENE: The bravery of 5000 Antioquians

CHANI GROSSMAN '14

Patricia does not know if she has a future.

She has spent her whole life, as part of a 5,000-member Colombian family with a horrifying Alzheimer's gene (Figure 1), with the specter of future mental and physical breakdown looming over her. Her adult life has been spent caring first for her mother, who died of Alzheimer's a few years ago, and now for her forty year old brother, Johnhaider, who no longer knows her. Despite his relative youth, he is already in the late stages of the disease. Up until now, Patricia has escaped the disease, but she cannot know what the future will bring (2). Luckily for most of us, less than 5% of all Alzheimer's victims have genes that condemn them to Alzheimer's with 100% certainty (6). Those members of the unlucky 5% may be doomed, but they have an opportunity not granted to many—the possibility of saving the rest.

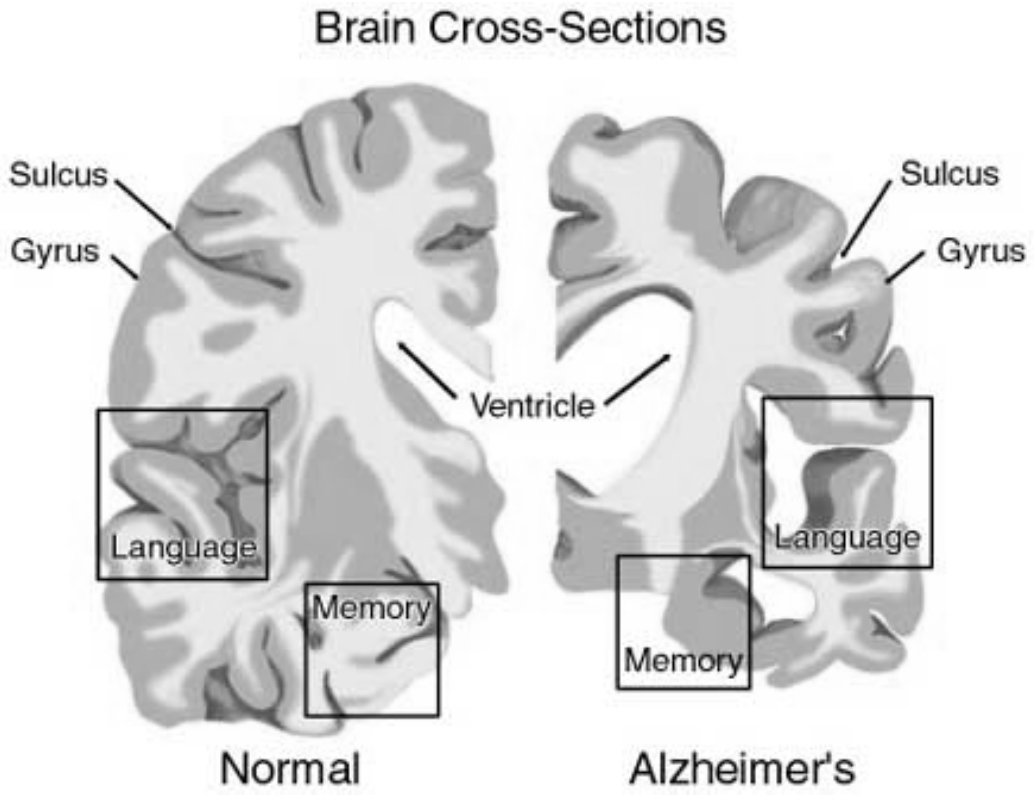

Figure 1: The marked difference between a normal health brain and a brain with Alzheimer's. Note the pockets of cell death in the diseased brain.

Most carriers of an Alzheimer's gene carry what are known as *risk genes*, genes which create a larger-than-normal chance of getting Alzheimer's. The most powerful Alzheimer's risk gene is apolipoprotein E-e4 (APOE-e4), which causes late-onset Alzheimer's and is the main genetic cause in about 25% of genetic Alzheimer's. APOE-e4 is a variation of apolipoprotein E, a gene on chromosome 19 that scientists believe may help mend connections between brain cells. A person carrying one copy of APOE-e4 is much more likely to get Alzheimer's than someone without an Alzheimer's gene or with a different Alzheimer's gene. Someone with two copies has an even greater risk (6).

Less than 5% of sufferers have the more elusive form of genetic determinant for Alzheimer's, the *deterministic genes* that guarantee, without a doubt, that the carrier will have Alzheimer's (6). The most common causes of deterministic genes are random mutations in the DNA coding for any of three proteins: amyloid precursor protein (APP), presenilin-1 (PSEN-1) and presenilin-2 (PSEN-2) (6). APP's normal function in the brain is unclear, but we know that there are 50 different mutations of APP which can cause Alzheimer's disease—the most common of which causes beta amyloid proteins in the brain to become longer, larger, and stickier. When these proteins accumulate, they cause plaques in the brain which are characteristic of Alzheimer's. These plaques clog the brain, cause pockets of cell death, and make it harder for it to perform vital processes (1) (Figure 1). Mutations in PSEN-1 and PSEN-2 can cause APP to produce more of this mutated, harmful beta amyloid (3; 4). Alzheimer's that is caused by these deterministic genes is called Autosomal Dominant Alzheimer's Disease (ADAD)- autosomal as it is not on a sex (X or Y) chromosome, but rather on one of the 22 autosomes, and dominant because even someone heterozygous, who only inherited the gene from one parent, will get the disease (6)

Only a few hundred families worldwide carry deterministic genes for Alzheimer's; the largest is the 5,000-member family in Antioquia, Colombia to which Patricia and Johnhaider belong (6). The disease entered the Antioquian gene pool through what's known in genetics as the *founder effect*—the small group of founders of the town, of whom probably only one originally carried the mutation, all intermarried, which spread the mutation throughout the area due to its dominant characteristics until there are now few who are unaffected (2) (Figure 2).

Figure 2: Map of Antioquia region of Columbia, SA.

The carriers of what the townspeople- and those who research them- call the “paisa” gene will eventually come down with Alzheimer’s. The child of one affected parent and one unaffected parent has a 50% chance of inheriting the gene- the likelihood of flipping a coin and landing heads; the likelihood grows to 75% if both parents are carriers (Figure 3). For the members of this family who are carriers of this deadly gene, symptoms will likely start in their early to mid forties. Full dementia will have set in by the time they are in their fifties. Patricia is in her forties now and hopes the disease has passed her by, but she still can’t be sure (2).

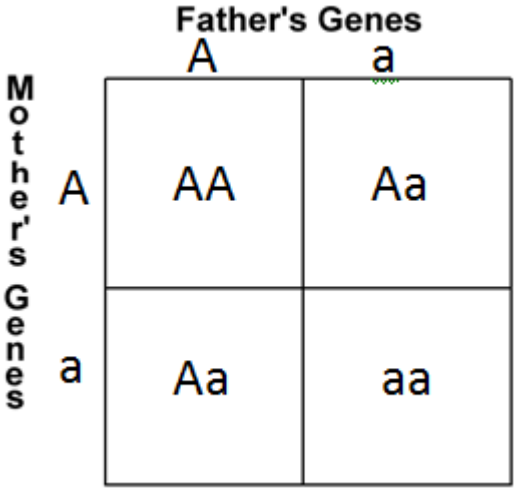

Figure 3: One possible scenario of inheritance of the Paisa gene—each parent carries one copy of the gene and each will end up with Alzheimers. The chances of their child coming down with Alzheimers is 75% and only 25% of escaping the disease (aa).

Many Colombian family members feel doomed by their genes. Many women refuse to have children in order to avoid the risk of passing on the genetic curse to another, innocent generation. However, Patricia and some of her family members feel that they have a unique purpose, a service to humanity that they alone can provide. Though they themselves may have no hope, they feel comforted in the knowledge that they can do something enormous for the rest of the world by volunteering to participate in studies to help find a cure for what may be the world’s “approaching pandemic,” as a scientist working with the Colombian family calls the ever-growing number of Alzheimer’s sufferers in a world with an ever-increasing life expectancy (2).

Scientists have already performed many groundbreaking experiments with the help of the people of Antioquia and hope to continue to do even more, including a test of a potential cure for Alzheimer’s set to begin in late 2012-early 2013, which aims to eliminate the plaque-causing beta amyloid. With the help of these studies, there have already been crucial breakthroughs. From one test, scientists have found the earliest point yet found at which Alzheimer’s-related brain structure alteration begins to occur. Researchers discovered that by the time that paisa carriers are as young as eighteen, biomarkers for Alzheimer’s have already begun to change and brain structure is already different than the structure of a healthy brain. This knowledge can be vital in the development of a drug that can, instead of removing the disease from the brain, actually prevent the disease

from occurring in the first place or catch the disease early, before it progresses to full malignancy and damage is irreversible (5).

Scientists and researchers expect rates of Alzheimer's to skyrocket with the ever-rising world life expectancy, a horrifying prospect in a world where the disease already runs rampant (2). Chances are everyone knows someone who has been stricken by this disease, left unresponsive, deaf to the world, weak and helpless. However, Patricia and other members of her family may very well hold the key to finally eradicate this disease from humankind, and even create knowledge that can flow over into our understanding of other diseases of the human brain, such as Jakob Creutzfeldt Disease, the human form of mad cow. A heartbreaking genetic curse for them—a blessing for us.

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Figure 2 http://www.richardmccoll.com/wp-content/uploads/2012/12/antioquia.jpg

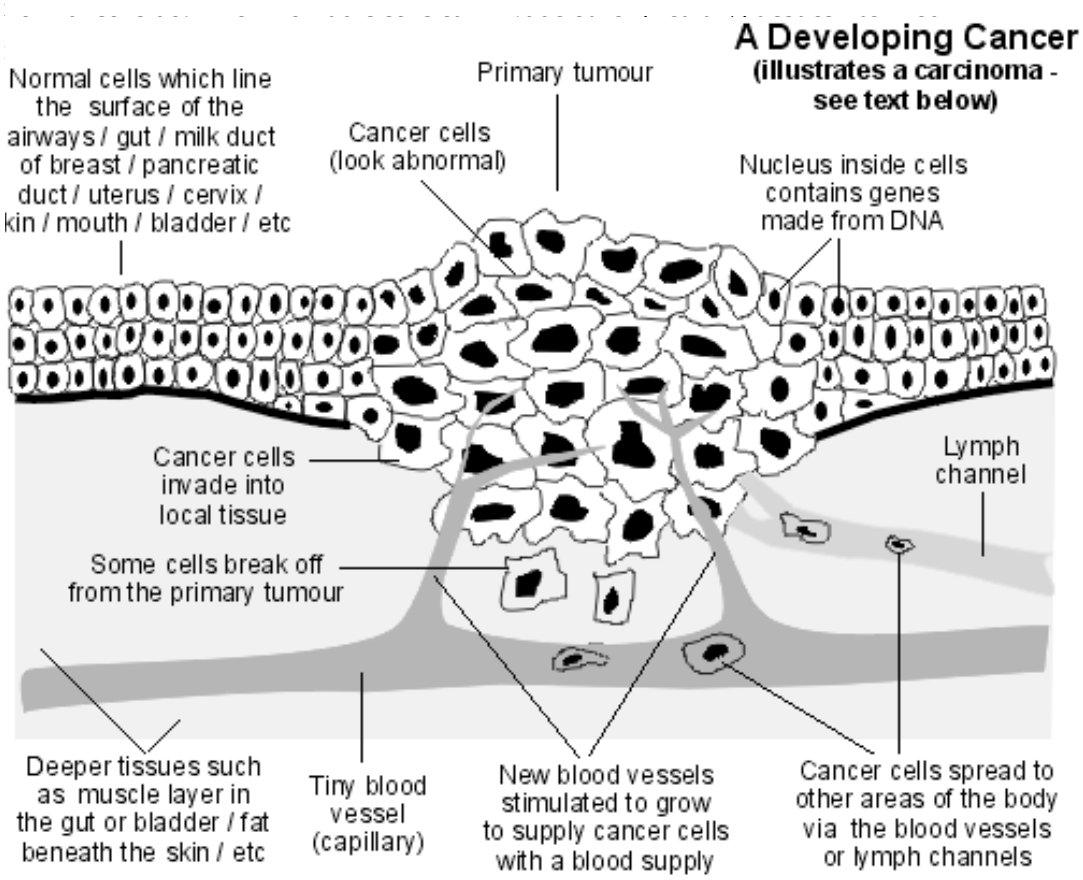
Figure 3, author.

LISTERIA AND CURCUMIN: A ONE-TWO PUNCH

YAEL JACOBOV ‘13

FarimRahank escorted his friend, John Smith, to an Indian restaurant, hoping to introduce him to the most delectable cuisine. While Farim was enjoying himself, John kept refilling his glass with water because of the overbearing taste of a certain spice that appeared in many of the dishes. It was the taste of curcumin; fiery orange in color, it comes from the root of the turmeric plant and has been used in ancient herbal remedies against various disorders, including Alzheimer’s, diabetes, acne, and cancer (5). Researchers at the Albert Einstein School of Biomedical Studies have been developing a vaccine by combining the bacterium *Listeria monocytagenes* (LM) and curcumin in the fight against cancer. An unlikely combination, it has never-the-less yielded promising results (1).

Figure 1: Cancer cells multiply uncontrollably, have irregular shapes, usurp growth of blood vessels carrying food and oxygen for themselves (angiogenesis), and lack cohesiveness which leads to metastasis.



Current treatments include targeting and destroying tumors through radiation therapy, surgery, and chemotherapy, but these cannot offer a total cure because they don't address the two main problems of cancer: metastases, and specificity. Metastasis causes 90% of mortality among cancer patients. Current treatments lack the specificity to attack cancer cells only, and not healthy cells (7).

The prospect of a vaccine against cancer offers a siren song that few cancer researchers can resist--it is their holy grail. Cancer vaccines exert an antitumor effect by prompting host immune responses, and they have the great potential for dodging the innate drug resistance of tumor cells, since the body's own immune cells are destroying the cancer, not drugs. Additionally, cancer vaccines that utilize the body's immune-defense system have extreme specificity for targeting tumor cells, low toxicity towards healthy cells, and the potential for a long-lasting treatment effect as the result of the genesis of immunologic memory responses.

How can the bacterium LM (Figure 2), which could contaminate food and result in infections in humans, be used in cancer vaccinations? Attenuated nonvirulent Listeria is genetically altered to carry cloned tumor associated antigens (TAA) in vivo to combat cancer. Once inside, the modified Listeria infects an antigen-presenting cell (APC) — a cell that induces a designed immune response tailored to the specific antigen—and delivers the TAA into the APC's cytoplasm. This triggers inherent and adaptive immune responses to the TAA, mediating tumor cell cytolysis (destruction). Other bacteria such as *salmonella*, *shigella*, *lactobacillus lactis*, and *E.coli*, have been tested in cancer vaccinations but are not as efficient at invading APC's as Listeria. So far, mouse trials have yielded promising results (4).

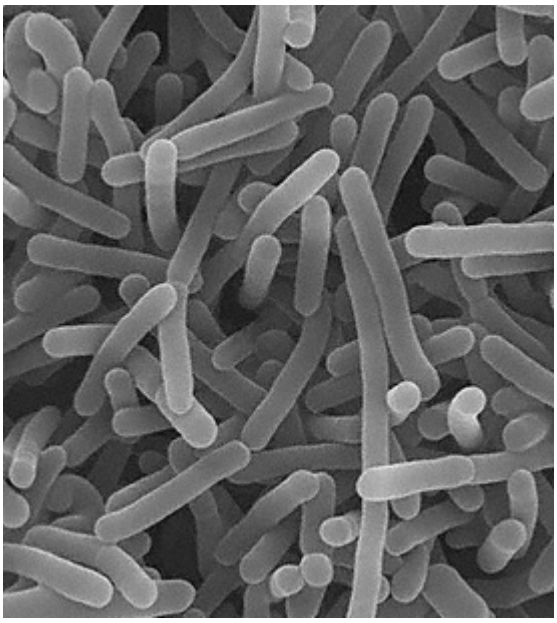
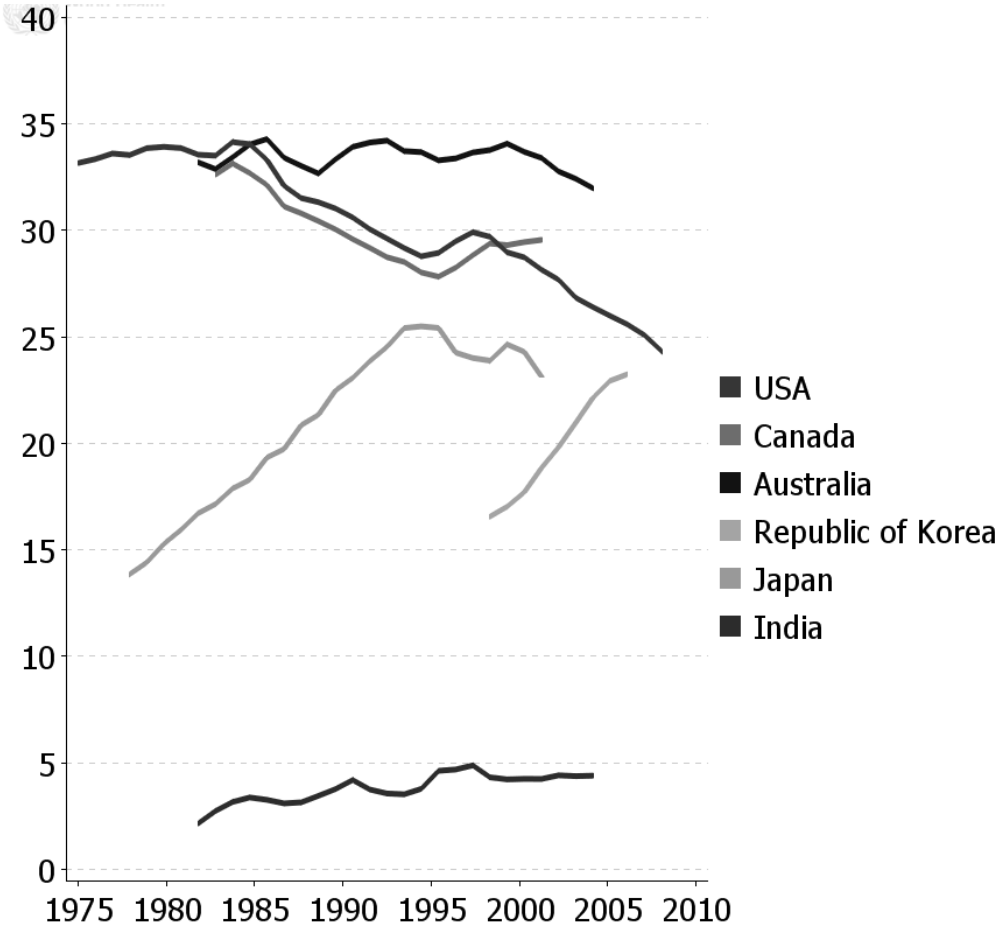


Figure 2: Electron micrograph of Listeria culture

Where does curcumin fit into this picture? Studies have shown that rates for colorectal, prostate and lung cancer are the lowest in India. Studies that compare various cancer rates between male and female populations in India and United States show that the rate for lung cancer in Indian males is 0.9%, compared to 5.86% in American males; 0.2% in

Indian females, and 3.4% in American females. This novelty can be explained by Indians' diet, which includes heightened consumption of fruits, vegetables, and spices, explicitly curcumin (6) (Figure 3).

Figure 3: Colorectal cancer rates in various countries. India is the curve at the very bottom.



Curcumin combats cancer through regulation of multiple cell signaling pathways that induce apoptosis—cell suicide. When initiated by the proper stimulus, apoptosis is triggered by the release of apoptosis-inducing factor (AIF), a mitochondrial protease (an enzyme). AIF moves from the mitochondria to cytosol and further to the nucleus, where it generates chromatin condensation and large-scale DNA fragmentation. It was shown that curcumin induces production of rapid reactive oxygen species (ROS), which have important roles in cell signaling, homeostatsis, and apoptosis. ROS is a stimulus that causes the release of AIF from the mitochondria to the cytosol and nucleus, initiating the apoptosis cascade.

The second major mode of cancer cell death is through the regulation of the cell cycle. The cell cycle is a set of events that result in cell growth and the division of the cell into two daughter cells. The stages of cell cycle are G1-S-G2-M. The G1 stage is "Gap 1." DNA replication occurs in the S (synthesis) stage. The G2 stage is "Gap 2." The M stage is the stage during which "mitosis" occurs, and when the nucleus and cytoplasm divide. Curcumin was found to induce G0/G1 and/or G2/M phase cell cycle arrest in mammary epithelial carcinoma cells, leaving its normal cells unaffected. Curcumin induced the expression of several cell cycle inhibitors in multiple human tumor cell lines. In human mantle cell lymphoma, curcumin causes cell cycle arrest at the G1/S phase of the cell cycle and induced apoptosis. Curcumin enhances the expression of tumor suppressor protein and also induced the accumulation of cells in G1 phase of the cell cycle in multiple human tumor cell lines by preventing them from proceeding to the next phase in the cycle. A recent report shows the curcumin induced activation of G2/M cell cycle arrest proteins and apoptosis in pancreatic cancer cells (2) (Figure 4).

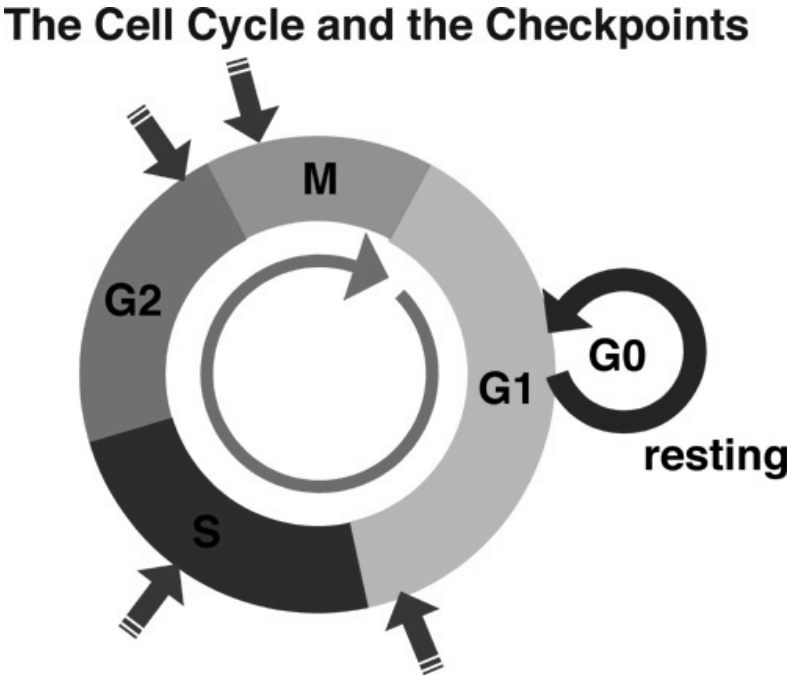


Figure 4: In the G1 phase, the cell is actively metabolizing, but not dividing. If it passes the G1 checkpoint, the cell proceeds onward toward mitosis (M) and cellular reproduction. Cells that proceed through the checkpoint unchecked can become cancerous.

Curcumin has a unique ability to discriminatorily kill tumor cells and not normal cells; however, the mechanism is speculative. Absorption and fluorescence spectroscopic methods revealed that there is higher uptake of curcumin in tumor cells than in normal cells. Glutathione levels in tumor cells are lower than in normal cells, increasing the sensitivity of tumor cells to curcumin (2). Glutathione, is an antioxidant, and is needed to relieve normal cells of oxidative stress caused by overproduction of ROS (8). Furthermore, curcumin's antioxidant property results from curcumin's control over the

glutathione levels. Thirdly, most tumor cells, but not normal cells, express active NF-κB and mediate their survival (2). NF-KappaB is an important regulator in cell fate decisions, like programmed cell death and cell proliferation (3). Curcumin can suppress the survival and proliferation of tumor cells by suppressing NF-κB-regulated gene products (2).

LM can contaminate food and cause infection (listeriosis), but on the other hand it can be modified to be used in cancer vaccinations. Furthermore, curcumin is an extremely fiery spice that can cause a burning sensation and may require a handful of TUMS, but it can also be used to kill cancer cells by means of mediating apoptosis and cell cycle pathways. Nature's immense biodiversity is our medicine cabinet, and therefore it behooves us to protect nature—our environment. When combining Listeria and curcumin we can create a vaccination that can deliver a lethal blow to an intractable enemy and most importantly, protect our people.

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Figure 1: http://medical.cdn.patient.co.uk/images/158.gif

Figure 2: http://microbewiki.kenyon.edu/images/5/51/20229A.jpg

Figure 3: http://globocan.iarc.fr/factsheets/cancers/Colorectal-tts-3i2.png

Figure 4: http://eishinoguchi.com/cellcyclecheck.jpg

QUANTUM TANGO

MICKY KOPELOWITZ

Scientists deal with facts much in the way that musicians deal with chords: it is their medium, and also their undoing. What I am about to tell you is fact, but it is fact so counterintuitive that physicist Richard Feynman could only describe it as "absurd." It is the fact that had Albert Einstein scribbling furiously on his deathbed, frantically trying to disprove what he felt was impossible. But science is not a sentimental field, and we cannot choose the theories we like and abandon the others. So this fact stands: *particles have no set velocity, spin, or position until they are measured.* They exist in a state of quantum fuzziness until they come into contact with the outside world, at which point they must assume one position out of infinite possibilities (3).

Quantum Mechanics began with the study of light. Light's nature had been a heated debate since the days of ancient Greece, but Isaac Newton seemingly put a cap on that when he published *Opticks* in 1704. In it, Newton emphasized that light is composed of distinct, minute particles. Some scientists contested this explanation and proposed that light is a wave, but Newton's impressive reputation ensured that his idea prevailed. In 1802, all that changed when the results of a simple experiment launched a projectile at the foundations of modern physics. These findings shattered former perceptions about the nature of light and led to the crystallization of wave-matter duality. This, in turn, spurred the development of quantum mechanics, a field unparalleled in awe and absurdity (5).

Thomas Young was already an accomplished Egyptologist and Physician when he sent the world of physics spinning. In his famous double-slit experiments, Young aimed a beam of light at a photographic plate by passing it through two pinholes. Newton's model predicted that light particles would act as paintballs, and at the end of the procedure, the plate would show two bright spots. However, when Young analyzed his data, he found that the photographic plate was marked by light bands of varying widths. Young recognized these stripes as an interference pattern—the basic indicator of a wave. Young published his results, establishing the wave nature of light, and in doing so he set physics on its most romantic adventure in recorded history (5) (Figure 1).

Young's experiments sparked a revolution. In 1905, Einstein observed a phenomenon called the photoelectric effect, in which light is absorbed and emitted only in specific units (3). This observation couldn't be explained by waves alone. Instead, Einstein introduced the idea of photons: packets of light energy that have particle-like characteristics (4).

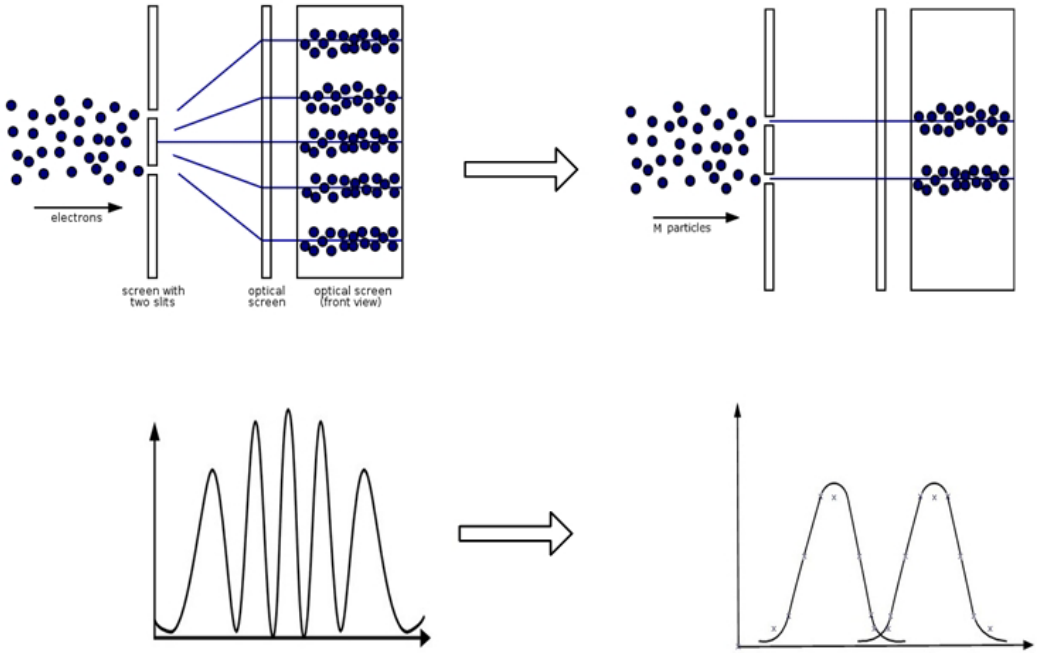

Figure 1-On the right is the expected results if light behaves in Newtonian fashion as particles or "corpuscles." On the left is the actual results indicative of wave-like behavior and interference.

Once Einstein proved that light energy is both a particle and a wave, Louise-Victor de Broglie proposed that this duality is also true of matter. To test this hypothesis, an electron beam was subjected to a similar double slit experiment, and sure enough, a wavelike interference pattern emerged for electrons. When de Broglie's hypothesis was confirmed for electrons, it led to the crystallization of wave-particle duality, which maintains that all matter and energy have simultaneous wave and particle characteristics (5).

Erwin Schrodinger was the first to interpret particle interference patterns and explain the wave characteristic of matter. He suggested that although matter usually moves in the patterns predicted by classical physics, interference patterns reflect the possibility that it could do something unexpected. For example, even though Newtonian law states that the paper you are reading right now will remain in your hand until you put it down, Quantum Mechanical solutions suggests the probability that it can suddenly vanish from your grasp and reappear on the moon. According to Schrodinger, the paper's interference pattern would represent the probability that your paper would be in any possible position. It would include the chance that your paper would be in your hand, outer space, or the circus. For particles with large mass (like you, or I) the wavelike characteristics are overwhelmed by the particle-like characteristics, and the probabilities shrink to

infinitesimally small that you are I are anywhere other than where we think we are. However, for electrons, whose masses are exceedingly small, the wavelike characteristic cannot be ignored, and probability functions play a huge role in their behavior (3). Modern atomic theory, in contradistinction to the classical Bohr Model, no longer talks

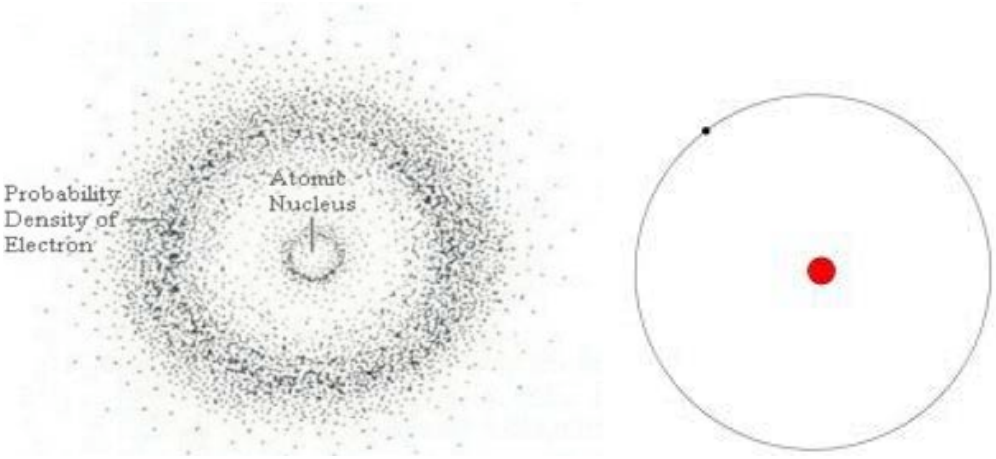

Figure 2: Electron Cloud Model of atom on left vs. Bohr model on the right.

about electrons in orbits, but rather electron clouds that represent all the probable locations of an electron (Figure 2).

Schrodinger's theory goes hand-in-hand with Heisenberg's uncertainty principle, which states that particles have no set spin, velocity, or position until they're measured. Particles don't have precise positions or momenta; the more one is absolutely defined, the more the other is indeterminable, because the act of measuring necessarily disturbs the particle (3).

Heisenberg's principle is shocking in that it implies that particles exist in a state of limbo until scientists poke them into being with measuring apparatus. Until then, they occupy all possibilities simultaneously. This goes against the very basis of classical physics: things cannot exist in two places at once. It also goes against human experience: cars are parked either in the garage or in the driveway, not in both (3).

The disparity between our perceived reality and quantum reality is explained by decoherence. Decoherence is the suppression of wave qualities caused by environmental interaction. Constant bombardment by surrounding matter forces particles to select one of infinite possible positions, at which point the classical model kicks in. Because super-atomic systems are larger and more complicated than individual particles, they interface more with ambient matter. Systems solidify, interference collapses, and quantum weirdness plays no role in everyday life (1).

One application of quantum mechanics is in the field of computing. Computing, at its heart, is a physical process. Physical input, in the form of electronic pulses, passes through transistors and yields physical output, and the result is a calculation. In binary coding, these pulses have values of either 0 or 1; based on the circuiting, codes can yield different outputs or check for certain conditions. Complex combinations of these algorithms combine to form computer programs, including the one used to type this paper (2) (Figure 3).

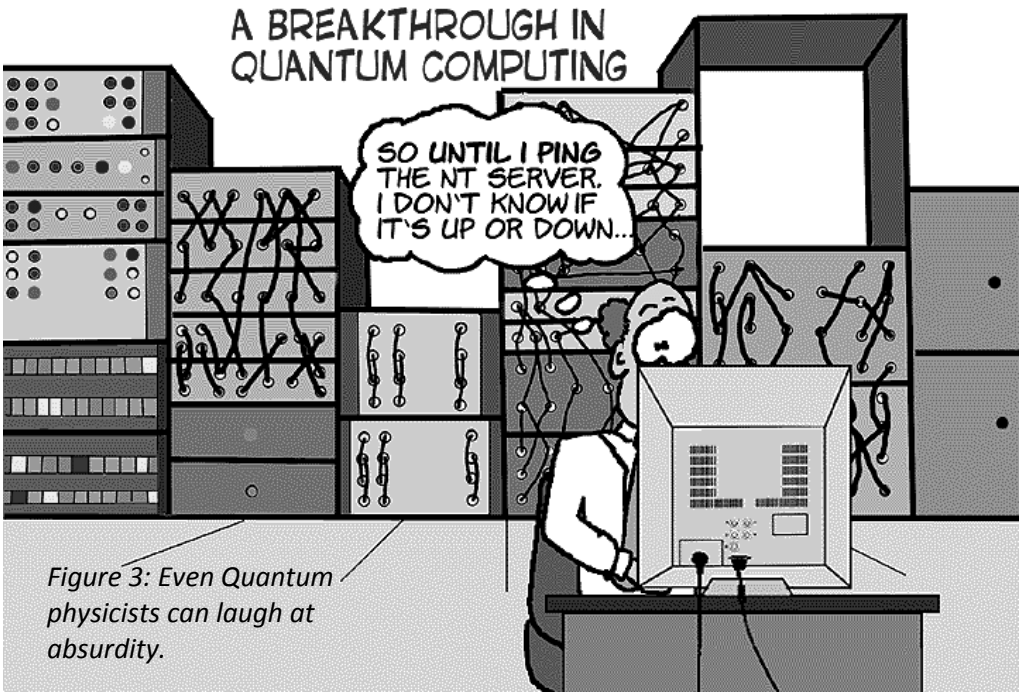

Figure 3: Even Quantum physicists can laugh at absurdity.

Of course, the computing just described is based on classical physics. Today's computers are limited in their power and function. If quantum mechanics were applied to the field of computing, science would see a tremendous increase in computational ability. For example, the superposition of various quantum states would enable the factorization of large numbers, a currently unfeasible operation, because particles would exist as both 0's and 1's simultaneously, allowing the computer to rapidly progress through parallel situations. Instead of testing numbers individually, quantum computers could verify multiple factors at once (2).

Quantum computers would also see maximized memory capabilities. In classical computing, memory is stored in basic informational units called bits. Bits are assigned values of either 0 or 1, and can hold one number each. In contrast, quantum bits—or qubits, as the pun goes—can hold more than one value at a time (2). A single qubit can be

both 0 and 1, while two qubits could simultaneously hold four values: 00, 01, 10, and 11. Each additional bit doubles the amount of possible states, and quantum computer of 300 qubits could hold 2^{300} values– more than the number of atoms in the universe (6)!

While quantum computing is lovely in theory, environmental decoherence renders its application complicated. It is difficult for scientists to work with particles while preserving their quantum qualities. However, this year's Nobel Prize winners for physics, David J. Wineland and Serge Haroche, have independently invented methods for manipulating individual particles while preserving their quantum mechanical properties. It appears that a computer revolution is within our grasp (6).

Many people question the value of theoretical science. They see it as a waste of time and resources. In defiance of this view, quantum computing is the greatest retort. It is the developing story of a romantic, perhaps hotheaded, pursuit of knowledge that paved the way for technological advances beyond contemporary imagination.

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Figure 2: http://cheminfo2011.wikispaces.com/file/view/Electron_Cloud.png/281739626/365x330/Electron_Cloud.png
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DESIGNING FOR DANGER

RIVKA KURTZ '13

On David Owen's first day in Colombia, the very man he had come to interview shot him in the abdomen. Such behavior had been reported as typical of the man, Miguel Caballero, who had no qualms about taking aim at his employees on a regular basis. But things were not as they might have seemed. Caballero is known to be a very special type of designer, one who specializes in producing clothes that serve as designer body armor. Anytime he levels a gun at an employee, the would-be victim is always decked out in the ritziest of body armor, just as David Owen was the day he willingly presented himself to be shot (6). While Caballero deserves significant credit for his entrepreneurial genius and outlandish demonstrations of his product, he does not deserve the credit for being the first to develop bullet stopping materials. No, the credit for that goes to a woman who first discovered the innovative fibers of Kevlar in the DuPont lab forty-nine years ago (4).

Stephanie Kwolek was aiming to find a fiber that would weigh less than metals and still possess enough durability to be a material effectively used in cars, planes, and other vehicles. The idea was that such light, yet strong materials would not weigh down vehicles as much as metals would, and would lessen the vehicles' thirst for gasoline (4). Yet Kwolek is famous for her discovery of a ceramic, a material most people think of as a fragile one often painted in arts and crafts classes. In fact, ceramics are generally defined as substances that are both inorganic and nonmetallic. As any pottery enthusiast would know, ceramics can be rather delicate, but still survive remarkably well when exposed to extremely high temperatures (8, p. 437). Kwolek's story begins on an ordinary day in the lab where she was laboring to create fibers that would save the world from gas shortages of the future (Figure 1). Kwolek's work involved creating polymers, which are chains of molecules (8, p. 428), dissolving them in liquids, and spinning the liquids in a machine called the spinneret, which would bully the mixtures into fibers. On one particular lucky day, Kwolek was having a hard time dissolving her polymers. She finally hit

Figure 1: Stephanie Kwolek at work in her lab at

upon a solvent that dissolved one of the polymers into an unusually watery, cloudy solution that looked as though it had particles floating in it even though it was filtered. When the solution was spun, it formed fibers of unprecedented strength that when baked not only withstood the heat as any valid ceramic would, but actually became stronger. Kwolek's discovery caused a great stir of excitement among her colleagues at the DuPont lab that day. A new super-fiber had been discovered, one strong enough to resist bullets and light enough to be worn as body armor. The super-fiber was named Kevlar (4).

Kevlar's strength is due to the chemical phenomenon called crosslinking. When polymer chains bond to each other, or "crosslink," the material stiffens as more ties are forged between the chains (Figure 2). Kevlar's molecular structure is such that each polymer chain is hydrogen-bonded to the next. This linked formation not only adds to Kevlar's durability, but also gives sheets of Kevlar molecules their fiber structure (8, p. 434-435) (Figure 2).

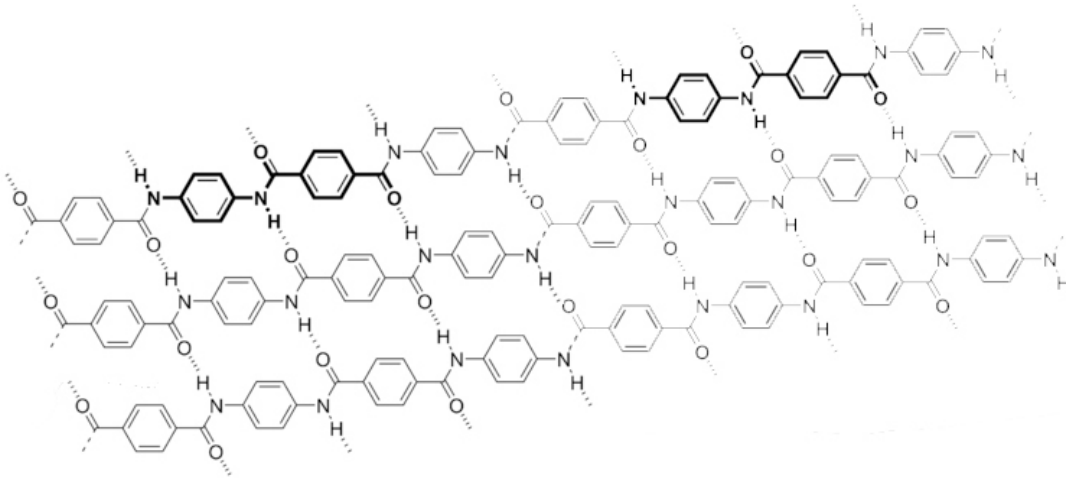

Figure 2: The monomer unit of Kevlar is outlined in bold. The crosslinks between the polymers is indicated by dotted lines.

Kevlar is widely used in body armor worn by police officers, popular because of its lightweight qualities and conformity to police officers' comfort and needs. A relatively new line of Kevlar body armor, Kevlar XP, is comprised of several layers. The first few layers ensnare the bullet, and the shock of the impact is absorbed by the other fibers of the armor (5) (Figure 3). Another older form of Kevlar body armor, Kevlar Correctional, is designed to withstand knives and other spiked weapons. While the strength of Kevlar Correctional's fabric prevents the fibers in the weave from snapping or being pushed aside in much the same way as Kevlar body armor designed for ballistic protection does, the weave of Kevlar Correctional is tighter. Sharp objects like knives are narrow and focused, unlike bullets which come wide and malleable. The tighter and thinner weave of

Kevlar Correctional is necessary to block the smaller, pointier edges of spiked weapons (2). Subsequent to the development of Kevlar Correctional, the company Second Chance combined the Kevlar Correctional with other fabrics to create an effective multi-threat protection vest, successful against both ballistic and stab attacks (7).

Figure 3: A .44 magnum bullet is stopped within three layers of Kevlar XP.

Then there are characters like Caballero who revamp the image of protective bulletproof getup. If you're looking for a bulletproof coat with all the pockets you could ever need, or a bulletproof white linen tunic, you'd better swing by Caballero's shop the next time you visit Colombia. But as different as Caballero's stock is in appearance from standard issue Kevlar vests, all bullet-stopping fabrics employ the same polymer characteristics; working in tandem, the fibers are strong enough to withstand the bullet's energy, and direct the force away from the point of impact (6).

So take your pick. You can purchase one of Caballero's creations, perhaps one of his golf shirts that sell for approximately $12,000 (6), or you can stick with the more traditional DuPont developed Kevlar products. And you can still dress in high fashion even if you don't go with a Caballero line; Point Blank's SPIDER vest is available for purchase in several colors, including navy blue, woodland camo, and OD green (7).

Material	Density [g cm^{-3}]	Strength [Gpa]	Elasticity [%]	Toughness [MJ m^{-3}]
MA silk*	1.3	1.1	27	180
Flag silk*	1.3	0.5	270	150
Insect silk#	1.3	0.6	18	70
Nylon 6.6	1.1	0.95	18	80
Kevlar 49	1.4	3.6	2.7	50
Carbon fiber	1.8	4	1.3	25
Steel	7.8	1.5	0.8	6

*European garden spider *Araneus diadematus*.

#Silkworm *Bombyx mori*.

Figure 4: Mechanical properties of natural and synthetic fibers.

The development of strong materials still continues, both for new fibres and for ways to use them. Originally Kevlar was designed for use as a replacement for steel in radial tires but its uses have endlessly expanded from cord on the airbags of the mars pathfinder to lighter stronger sports equipment like tennis racquets and skis. As the need for strong lightweight materials increases, the range of uses for this material will surely accommodate the demand. Despite its strength and light weight, Kevlar still has some disadvantages. Its limited flexibility and compression makes it stiff , causing the wearer suffers a loss of movement. It also absorbs water and when it does, it is more susceptible to environmental degradation. There are still improvements, which can be made (9).

Again nature is providing the inspiration in the form of spider silk. Stronger than steel, more elastic than rubber, spider silk is tougher than any man-made material, and if made into body armour, would be three times stronger than Kevlar (3) (Figure 4 above).

Until recently, the only way to gather enough of the material is to farm the spiders, and that has proven very difficult given the fact that arachnids are violently territorial, and impractical in terms of the economic expenditures involved. Scientists have gotten around that hiccup by using the technique of recombinant gene technology, where they have inserted the gene for the manufacture of spider silk into goats, where it expressed when they lactate and produce milk. (Figure 5). These goats are capable of producing 15 g of spider silk per liter of milk, ensuring an adequate supply of silk for any future uses that come down the pike (9).

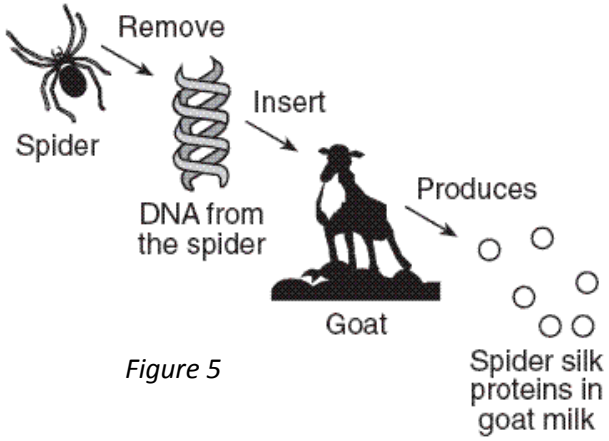

Figure 5

With over 41,000 described species of spiders, most spinning multiple types of silk, the search is on for the spider species that produces the most exceptionally strong and elastic silk. Researchers travelled to the jungles of Madagascar and tested the silk of "Darwin's Bark Spider," *Caerostris darwini* and found that its silk is two times stronger than any previously described silk and over ten times better than Kevlar (1). Who knows—the next time you go bungee jumping, it might be spider silk that saves your hide and provides the thrill.

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Figure 2: http://chempolymerproject.wikispaces.com/Kevlar-E-nydw

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PUTTING AMPUTEES BACK ON THEIR FEET

TZIVIA MILLER ‘13

It’s yoga time. Six of my campers are already in the down-dog pose. But Jake is still lying on his mat. The move is too difficult for him with his prosthetic. Jake’s leg was removed when he was an infant; he’s had his prosthetic for over 6 years and still, he can’t walk without his crutches. He falls a lot, and cannot run, kick, or sit in a pretzel like his peers. His new leg, while better than no leg, is a large, obtrusive nuisance.

More than ever before, people are finding themselves without limbs. Medical advancements now save many more victims of war – be it wars of guns, or disease, or trauma - who previously would have died of their wounds. Instead, as a result of modern medicine, their bodies are reassembled, and they now survive, albeit oftentimes without a limb. The thought of losing an anatomical part, such as a lower limb, is devastating to most people. When it happens, amputation causes a threefold loss in terms of function, sensation and body image (1). And while almost every other field in medicine has seen advancements in the past few decades, the technology for artificial limbs hasn't improved much since World War II (2).

Dr. Todd Kuiken, Director of Amputee Services at The Rehabilitation Institute of Chicago, realized the devastation amputation causes, and the lack of anything much better than an artificial pole to attach to the remaining stump, and in the case of hands, a hook with glove overly (Figure 1). He set out to find a new solution to restore normal function to those who’ve lost a limb. He wanted to come up with a way to attach the prosthetic limb to the central nervous system, allowing amputees to control their new limbs as they would have controlled their old ones – naturally, mentally, and intuitively.

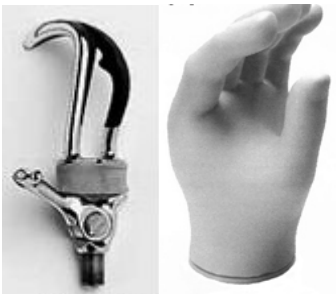

Figure 1

Kuiken focused on this issue of muscle control. His lab came up with the targeted muscle reinnervation (TMR) surgery, which attempts to utilize the brain commands that still attempt to reach the missing limb. Brain signals still travel down these nerves, but they end at the amputation stump and are no longer received by any muscle. Scientists posited that if these nerve signals were to be connected to different muscles sites, they would cause

other muscles to move, producing signals which can be used to control a myoelectric prosthesis (4).

The first person to undergo TMR surgery was an upper arm amputee. Without his arm, his chest muscle was useless. So surgeons attached his severed arm nerves to his chest muscle. Now, when he signals his arm to move, his chest muscles twitch with different contractions for different arm and hand movements. Then, by attaching electrodes to the amputee's chest, scientists were able to locate and differentiate different contractions for the movements of the arm – elbow bending, elbow straightening, hand opening, hand closing, wrist movement, and different hand grasps. The electrodes then translate these twitches to signals for the prosthetic arm's movements. Not only does this prosthetic give an amputee more control over specific joints than the previous prostheses provided, but it also allows the amputee to control his artificial limb mentally, without extra physical exertion(4) (Figure 2).

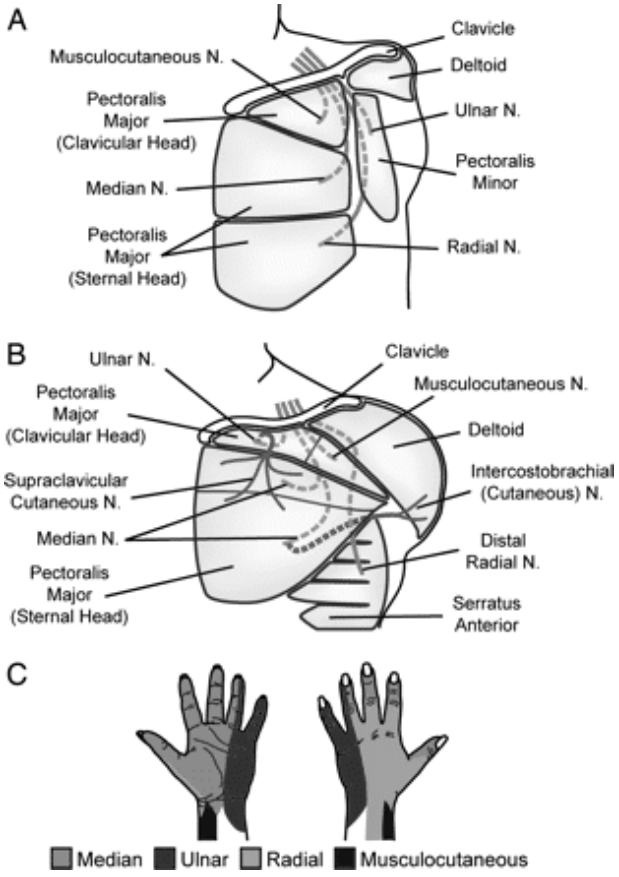

*Figure 2: Schematics of the TR surgeries. Green, arm nerves; blue, skin sensory nerves; dotted lines, nerves routed beneath muscles. (*A*) Patient BSD. The pectoralis muscles were denervated, fat over his chest muscle was removed, and the four major arm nerves were sewn to the remnant nerves of each muscle segment. (*B*) The nerve transfers were performed differently in patient STH. To increase the likelihood of sensory reinnervation, skin nerves were cut, and the distal ends were sewn to the hand nerves to provide neural conduits for the regenerating nerve fibers. (*C*) Diagrams of skin sensation provided by each nerve in the normal hand.(5)*

These findings seem exciting, but there is even more work to be done in perfecting the TMR prostheses. In a promising development, scientists found that patients who have undergone the nerve-transfer surgery over time began to feel touch on their chest as if their arm was being touched. Further investigation has shown that patients were able to perceive different temperatures, textures, pressures, and vibrations on these new chest muscles and assign them to their missing limb. They sense that these stimuli are being placed on their missing limb, and can even pinpoint the sensation to a specific area on the arm or hand. Scientists eventually hope to be able to provide feedback from the prosthesis to the reinnervated skin so that amputees would, for the first time, be able to "feel" again without their natural arm (4; 5) (Figure 3).

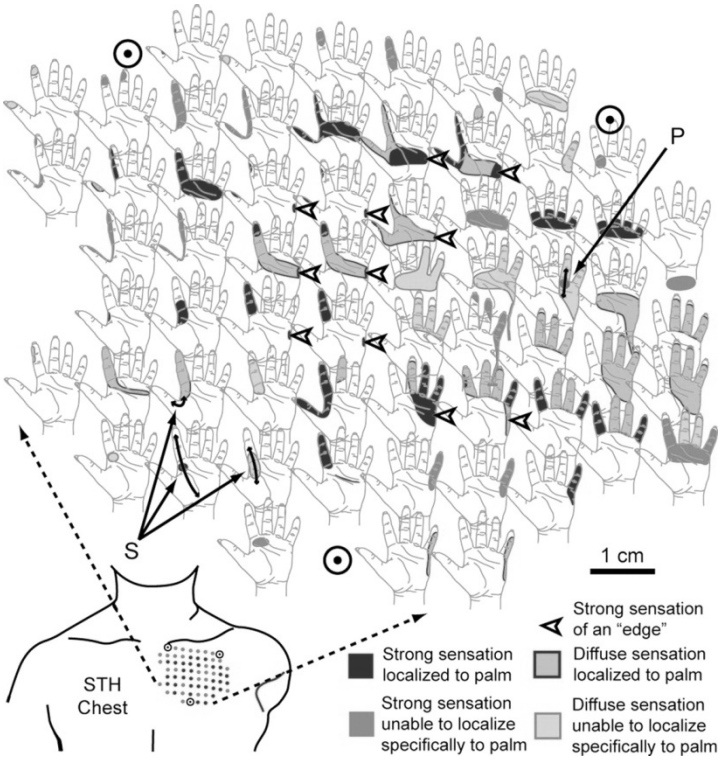

Figure 3: The reinnervated chest skin of patient STH showing sensations referred to the missing limb elicited by indentation of the skin by a cotton-tipped probe. Red, referred sensation points localized to the palm side of the hand. Blue, points where a general diffuse feeling of pressure was felt within the hand. Circled points orient the diagram. P, proprioceptive sensation of fourth finger joint position. S, sensation of skin stretch. Double-headed arrows, direction of stretch. Arrowheads, edge sensation (5).

While the prosthetics of the future are largely being developed to restore function and body image to amputees, a new question is arising over whether these new prostheses would be preferable to a biological arm. John Fergason, chief of prosthetics at the Army Center for the Intrepid at Fort Sam in Houston, Texas, says that "there's a lot of controversy that [an amputee soldier's] prosthetics might be so advanced that he has an advantage over a

person's natural limbs". Still, he's quick to admit that they are still quite far from potential issue. "Amputation is so complex in what it does to your body that it's a very long recovery". "At this point," he adds, "the aspect of a super soldier is still a long way off…You're not going to see anyone decide 'Boy, I think I'd like to get a bionic leg because they're so fantastic" (3).

Still, the idea that technology may be able to create super human is tantalizing food for thought despite the ethical questions it raises. At present, this groundbreaking technology will hopefully improve the lives of thousands of people. With these new advancements, amputees will have a rosier future, in which the limb they have lost is restored back to what it once was. This technology is about improving the quality of life for members in our society, and at the same time, it's about allowing them to once again be productive members of society.

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Figure 1: http://www.rehab.research.va.gov/jour/2012/494/smit494.html

THE INTERNET'S UNSUSTAINABLE SECRET

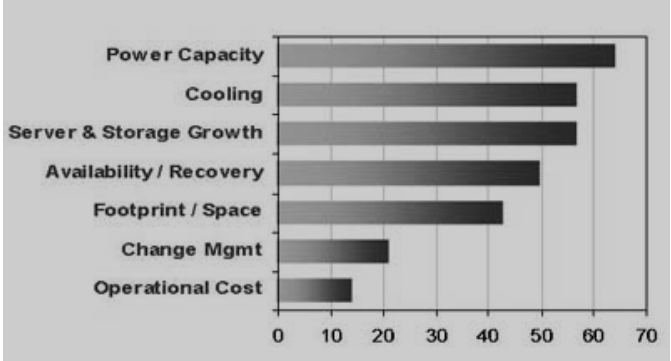
RIVKA SALHANICK '14

We turn off the lights when we leave the room; print double-sided to conserve paper; recycle our empty milk containers. We diligently behave as responsible guardians of the environment to save money and energy. One would assume that behemoth IT conglomerates, such as Google and YouTube, would be similarly invested in developing the most efficient way to conduct their businesses. Or that data analysts at Target, Wal-Mart, and Stop and Shop, whose stock and trade is information, would be equally careful about how much data they store. Target, for example, analyzes the data it stores about its customers to customize each person's shopping experience according to their habits and preferences. Target can even tell when a woman is pregnant before she tells her husband (1). But, how much of our natural resources are being spent when they move, store, and process the millions of terabytes of information that are flowing constantly across the Internet "*cloud*"?

Imagine my surprise when I discovered their dirty secret. Data is not stuck somewhere in the two inches of space of a flat-screen computer. All data stored online is stored in a very physical place and space: Data centers (Figure 1). These buildings filled with computing servers are chewing up millions of kilowatts of energy every year (3). The major internet players, such as Google, Amazon, and Facebook, own large data centers, and smaller businesses usually rent space from them. In 2006, data centers consumed 1.5% of the national energy expenditure, amounting to about 61 billion kilowatt hours and $4.5 billion, and that number is only rising (2). Each data center consumes more power than a medium sized town. Data center energy usage accounts for half of the power expended in IT industry (3). With the growing importance of IT technologies, the power requirements will rise in the future. How will this infrastructure support such a growth?

Figure 1: One small section of the servers (lined up on the racks) of one of Google's Data Center located around the world.

Figure 2: The top current challenges to data centers



Where does all this energy go and what is it used for? Closer inspection reveals the necessity for intricate cooling networks for servers' heat generation (7). The cooling system is crucial, as the servers expend high amounts of heat, and require a certain temperature. Energy efficiency in this area is crucial, but seriously lacking. Backup and cooling systems account for 55% of the energy used in a data center (5) and is the second largest challenge (Figure 2). The way to assess efficiency is Power Usage Effectiveness (PUE)—the energy input divided by the energy used for the actual computing and processing. Ideally, that figure should stand at net zero, with the PUE at 1.0 (7). However, most facilities have a higher ratio with much more energy devoted to cooling, backup, and lighting, than the actual computing. Research has found that servers can stand higher temperatures than the businesses have allowed them up to now. Despite this, the managers are worried of a possible shutdown and associated billions of dollars of business disruptions. Maximum efficiency for cooling systems requires an effective monitoring system of the temperature, pressure, and humidity, to make sure the right temperature of air is going to the right places (Figure 3). One company saved $7,666,000 in annual electric bills by installing sensors throughout the facility for this purpose (8). Although IT industries may have money and resources now, it is important to think of the future infrastructure.

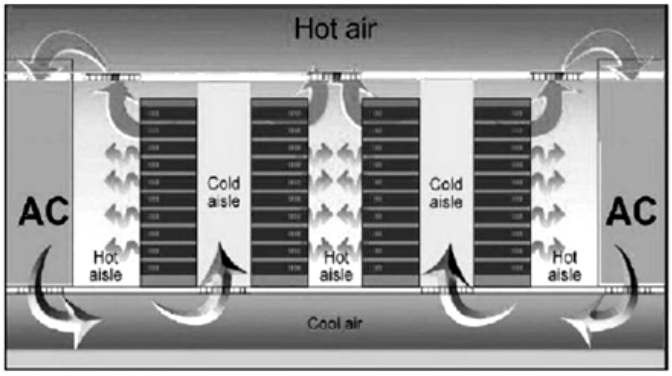


Figure 3: Typical air flow in a traditional data ceneter.

An economical and resourceful cooling solution is a hydrothermal energy and cooling system (6). This is a sustainable approach that will efficiently provide water as a cooling source and an energy provider. The center will need to be situated near a water source. Tunnels dug underground will then conduct water in and out of the building's pipes. The naturally cold water (39°F) will save up to 90% of energy currently used in a cooling system. Turbines and heat exchangers will produce

electric energy from the water temperature differences between the surfaces and lower down (Figure 4).

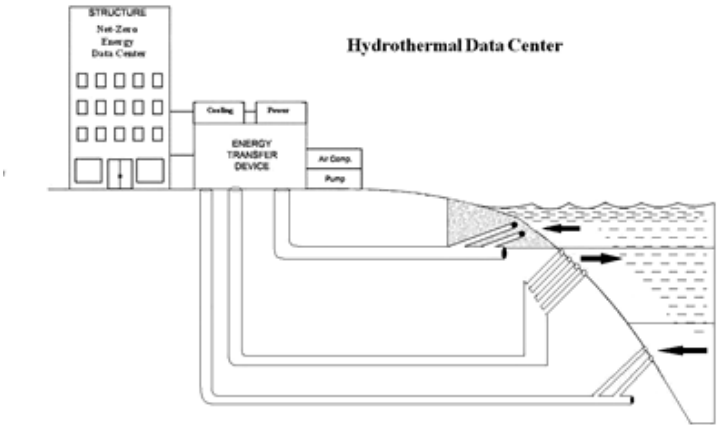


Figure 4: The above illustrates the concept of a large data center using tunnel boring and directional drilling to access and discharge cold and warm seawater or lake water. The cold water will be used for cooling the data center. Turbines and heat exchangers will generate clean electric power by utilizing the temperature difference of warm surface water and deep cold water. This power is used to

In addition, data centers use the typical air conditioners and fans that you would in your house. These machines, while efficient and useful in a house setting, are definitely not what a large data center should use. The importance of temperature to the servers requires a carefully modulated cooling and heating system. The rows and rows of servers require a specifically made industrial system.

Another area that needs to be investigated is the “comatose” servers. Many data centers have servers that are “comatose”, using power while not processing any data. In one survey in 2010 of over 300 servers, three-quarters of them were using less than 10% of their computing capability (4). Most data centers average less than 12% utilization rates (percentage of servers’ possible computing ability actually used for computing), with about 90% of the brainpower in a typical data center unused while still consuming energy. Data centers have vegetating servers in case of a surge of activity, which they can quickly accommodate. The solution is to queue large jobs and schedule these jobs to be done at certain times. This strategy can raise the utilization rate to nearly 100% 24 hours a day. They can also consolidate data into a smaller amount of servers, reducing the cost and energy expenditure, possibly by half (4). However, many large companies would rather spend the money than risk downtime and delays, which will lose business and profit. At present, energy and electricity seem inexhaustible. 70% of energy for data centers comes from fossil fuels. If we can target more energy production through renewable resources—solar, wind, and hydroelectric power—we can create an industry that will last into the future. As the importance of data centers in the IT industry grows,

their infrastructure must be revisited and reconfigured. Hiding them out in Washington or West Virginia is a short-sighted solution

A new and innovative breakthrough in data storage that completely revamps the whole system has been found by Drs. Nick Goldman and Ewan Birney of the European Bioinformatics Institute (EBI). Dr. Goldman quaintly states that "...The cost of storage is rising, but our budgets are not" (9). As always, Hashem has presented to us, through nature, a complex and stable way of storing information: DNA. Dr. Goldman and a group of researchers worked on an idea that would translate the binary information (zeros and ones) into ternary information (A,T, G, C). Mistakes that have been made in this system before include the problem of general repetitions in the nucleotide sequence (ex. AAA). However, this system bases what number to recode the information as by what base was presented most recently (Figure 5). The DNA is then cut into overlapping chunks, further stabilizing the information. This artificial DNA has its disadvantages. It reads back the information very slowly, which makes it incompatible with quick-Internet access. However, it is fine for long-term storage. Secondly, the cost is quoted to be about $12,400 per megabyte stored. However, in contrast with ephemeral storage devices such as floppy-drives and discs, DNA is lasting. It has lasted for thousands of years so far. "So long as life—and biologists—endure, someone should know how to read it."(9).

Previous base written	Digit to be encoded		
	0	*1*	*2*
A	C	G	T
C	G	T	A
G	T	A	C
T	A	C	G

Figure 5

In the final analysis, the consumers are driving this massive new business. In 2011, two data storage managing companies estimated that three quarters of the data produced was by ordinary consumers (3). We want direct results and we want them quickly. However, the data we save virtually should be considered just as physical as the data we save on our hard drive. Perhaps, on our side of the bargain, we can be a bit more vigilant. The safety and sustainability of our own homes is not the only thing we should worry about. We want to avoid a burst in the bubble.

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Figure 2, 3: http://www.imexresearch.com/newsletters/mar07pwrcool.htm

Figure 4: http://www.cotherma.com/The%20Prospect%20of%20Hydrothermal%20Net-Zero%20Energy%20Data%20Centers%2014JUL11.pdf

Figure 5: http://media.economist.com/sites/default/files/imagecache/290-width/images/print-edition/20130126_STC950.png

YAWNING: BEYOND BOREDOM

MIRIAM SCHUSTER ‘14

Everyone yawns at some point during the day without giving it a second thought. Although quite commonplace, yawning is actually a highly contagious social behavior amongst humans. Even fetuses yawn in utero for about four to six seconds during each instance of yawning (5). Research into this seemingly mundane activity, that appears to be both spontaneous and contagious, has revealed that yawning actually has manifestations in neurodevelopment and brain biology.

Researchers study the phenomenon of yawning in order to understand its purpose and its effect upon our bodies. Brain cooling theory was proposed to explain the results of a study which revealed that spontaneous yawn frequency correlates with seasonal temperatures. The authors posit that the function of a yawn is to cool down the brain. As can be seen in figure 1, the frequency of yawning during the summer drops because during the summer the air brought in is about the same temperature as body temperature, so very little brain cooling takes place; hence the necessity for yawning diminishes. In the winter however, significant brain cooling can occur with each yawn and so yawn frequency increases. Heat leaves the brain as cool air is brought in with each yawn. This theory posits that yawning could serve to regulate brain temperature (figure 1)(8).

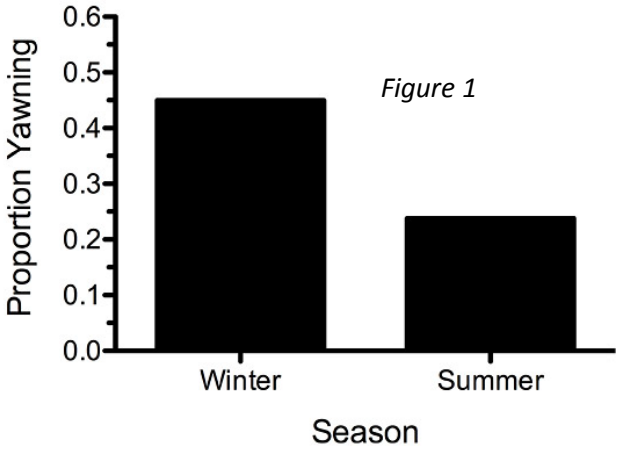

Figure 1

Aside from the spontaneous yawn that regulates brain temperature; contagious yawning is a reaction of the mirror neurons in a person’s brain. Mirror neurons cause an individual to reflect another person’s yawn (9). For example, when you see someone yawning when he or she is tired, even if you are not tired, your mirror neurons are stimulated by the yawn and reflect it back. Mirror neurons are brain cells that are activated when humans (and some animals) observe an action being performed by another of their own species and reflect back the same action. These mirror neurons have been found in the premotor cortex, the supplementary motor area, the primary somatosensory cortex and the left inferior parietal lobe of the brain (Figure 2). There is much controversy regarding where these mirror neurons are found because of inconsistent test results and what role these mirror neurons really play. It has been

shown that mirror neurons take care of thought related actions such as responding to someone else's actions and imitation (10).

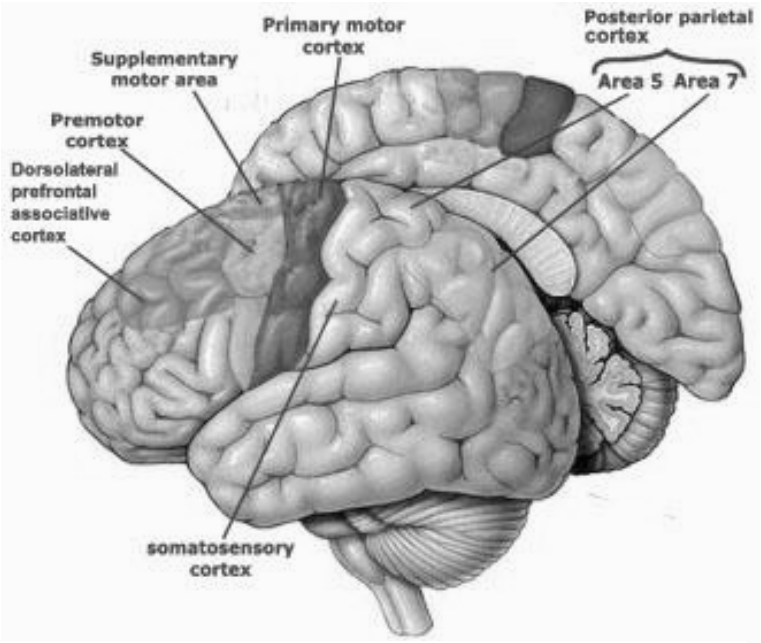

Figure 2: Anatomy of the Human brain where mirror neurons are found.

Aside from reflecting actions, such as yawns, mirror neurons have been seen as a driving force of empathy (3), because they reflect the emotions of people and animals around them. Additionally, it has been speculated that there is greater contagious yawning among Homo sapiens than in animals, because humans have closer emotional contact with one another (6). Therefore, relatives are more likely to yawn out of contagion than two strangers meeting each other for the first time.

Results of a test conducted on the differences between the mirror neurons in macaques and the mirror neurons in humans, show that while macaques respond to object related, or goal oriented, actions, such as moving ones arm or smacking ones lips, human mirror neurons respond to non object directed movements, such as yawning, smiling and other communicative forms of expression. The mirror neurons in macaques and humans respond differently based on their perception of "meaningful [actions] compared to meaningless actions" (1) (Figure 3).

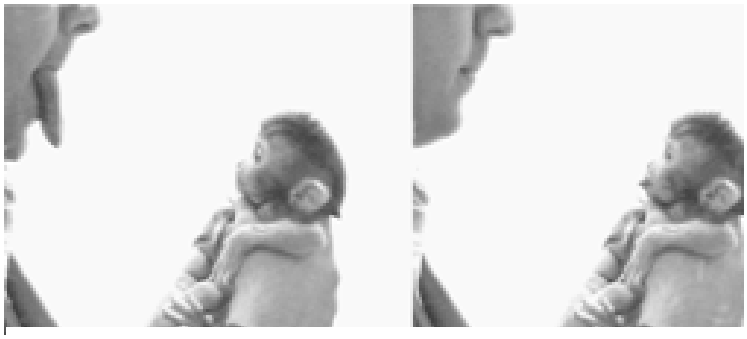

Figure 3: Macaques will imitate tongue thrusting but not yawning because of differences in their mirror neurons.

In addition, other studies have shown that yawning in humans and macaques reflects empathy between themselves and others of their own species. This is why humans do not yawn when they see a cat yawn (1). Contagious yawning, then, can be considered a correlational measure of empathy (6). In empathy disorders such as autism, there is impairment in contagious yawning precisely because yawning displays a measure of empathy, (6) which those with autism lack. Perhaps further studies of contagious yawning in children with autism would lead to a deeper understanding of this disorder.

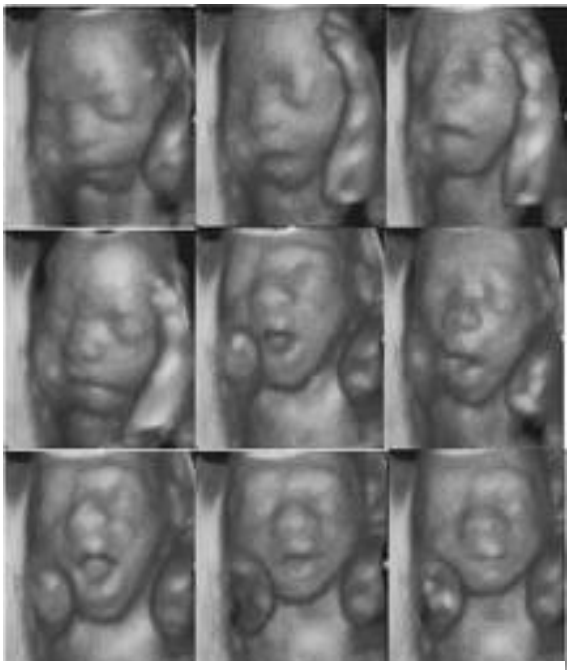

Figure 4: Single fetal yawn captured a various stages of the yawn.

Fetal yawning, however, is clearly not contagious in nature because fetuses are not exposed to other humans and therefore cannot observe their behavior (Figure 4). Fetal yawning is also unrelated to temperature regulation because the fetus is already in a temperature-regulated environment. Instead, fetal yawning may be linked to maturing of the brain in mid to late gestation (4). This has been shown to be true because at about week 24 of gestation, during which the brain development intensifies, there is an increase in the amount of yawning in the fetus. Studies have shown the differences between a fetal yawn and a similar action of regular mouth opening or stretch and therefore they were able to differentiate between the two. The researchers were testing to see at what stage fetuses yawn and to which process is yawning linked: arousal or maturation. They found that fetal yawning decreases over time, as seen in the graph below, which would mean that the yawning is linked to maturation and not specifically arousal (4) (Figure 5).

Yawning is also related to the jaw movements of the fetus, which are imperative to the prenatal development (Figure 5). Scientists are also able to use the progress of yawning in fetuses to know when the fetuses are awake because the fetuses have been shown to yawn after a period of rest when it is ready for activity (5). This differs from yawning in children older than the age of five and adults, who yawn when they are simply tired or bored. Studies of children between ages of infancy and five years old reveal that children do not

have contagious yawning, yet, they do have frequent spontaneous yawning (2). It has been suggested that children's yawning is remnant of neonatal yawning, which indicates a continuation in the development of these mechanisms started in utero (9).

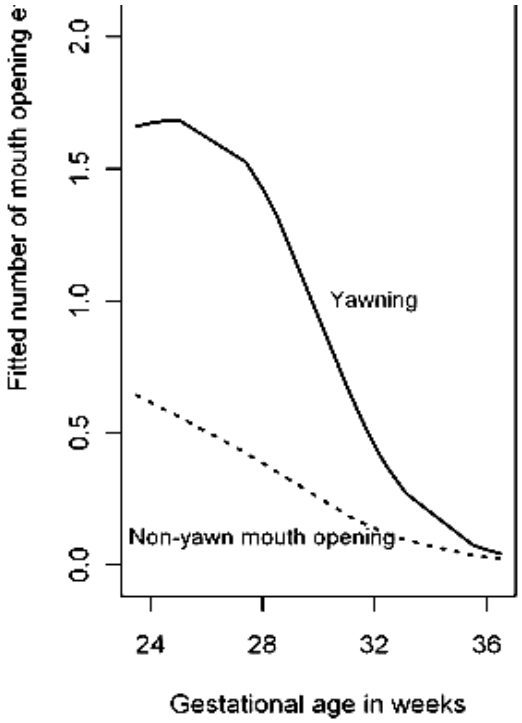

Figure 5: Fetal yawning and nonyawn mouth opening vs. gestational age. Peak yawning activity occurs at 24 weeks and is correlated to fetal development.

Studies of the frequency and timing of fetal yawning have revealed that yawning repeatedly, in the course of one day, during the stages of maturation of the brain, (which is in the first and second trimesters) indicates fetal anemia (5) (7). This is because the fetus is yawning for one purpose only, to help bring oxygen to its heart and lungs. Not only are yawns useful in diagnosing fetal conditions, they are also helpful in diagnosing certain diseases that affect children and adults. It has been found that children and adults with autism and schizophrenia are deficient in their contagious yawning, possibly due to a malfunction in their mirror neurons (9) that originated with their fetal brain development.

Through research into something as mundane as yawning, doctors have deepened their understanding of human psychological and developmental behaviors. Spontaneous yawning is not simply spontaneous, as it is performed to regulate temperature. Additionally, in attempt to better understand empathy, many studies have been conducted on adults, children and fetuses to determine what effect mirror neurons have on contagious yawning. In the future, doctors may be able to measure patterns and frequency of fetal yawning to diagnose and initiate intervention and prevention therapies. Even activities that on the surface are simple and commonplace, when subjected to scientific scrutiny, show that there is so much waiting to be discovered that can address our problems and improve our lives. So go ahead and yawn—cool your brain and exercise your empathy.

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