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Catalyst

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ALSO IN THIS ISSUE:

Astrocytes: Spotlight on the Brain's Rising Star

EMT Burnout: The Health of Healthcare Providers

FROM THE Editors

Dear Reader,

Welcome to the tenth annual edition of *Catalyst*, Rice University's Undergraduate Science Journal. Our mission is to foster scientific communication and showcase student perspectives on a broad range of scientific topics. Our publication is written, edited, and designed entirely by undergraduate students and we focus on making science exciting and engaging to all audiences, whether you are a scientist or just a casual reader.

This year, for our landmark tenth issue, we have created our largest issue yet. As an organization, Rice Catalyst has expanded immensely in pursuing our goal of facilitating scientific communication. We have created several initiatives on campus, such as the *Catalyst* Scientific Communication Symposium (CS^2 for short) which showcases the oral presentation skills of students presenting about their own research or other scientific topics. We have also reached out beyond Rice's hedges this year, partnering with the Energy Institute High School and the Young Women's College Preparatory Academy in Houston ISD to create a new publication: *Catalyst Eureka*. Rice Catalyst members guide high school students at each of these schools to produce articles similar to the articles that appear in *Catalyst*, teaching skills in scientific communication and learning about mentorship themselves. The first issue of *Catalyst Eureka* has already been released, and issue two will be released later this spring. Through these initiatives, we hope to further our mission to increase scientific literacy both within and outside Rice University.

The progress and expansion we have undergone this year would not have been possible without the support of the Rice community, our partners, our mentors, and our absolutely amazing staff. In particular, we would like to thank the Rice Center for Civic Leadership, the Program in Writing and Communication, and the Student Activities President's Programming Fund for their continued generous support of Rice Catalyst's endeavors. Of course, we also want to especially thank Dr. Dan Wagner, our faculty sponsor who has provided us with invaluable advice and guidance throughout this entire process.

We are proud of what Rice Catalyst has become and are excited to see how it grows in the future, but until then, we hope you enjoy this year's issue of *Catalyst*!

Alex Alexander and Ajay Subramanian
Catalyst Co-Editors-in-Chief
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BIOLOGICAL BLOODHOUNDS:

SNIFFING OUT CANCER

JESSICA WAGNER

Fifty years ago, doctors needed to see cancer to diagnose it - and by then, it was usually too late to do anything about it. Newer tests have made cancer detection easier and more precise, but preventable cases continue to slip through the cracks, often with fatal consequences. However, a new test has the potential to stop these types of missed diagnoses - it can detect cancer from a single drop of blood, and it may finally allow us to ensure patients receive care when they need it.

Blood platelets are a major component of blood, best known for their ability to stop bleeding by clotting injured blood vessels. However, blood platelets are far more versatile than previously understood. When cancer is formed in the human body, the tumors shed molecules such as proteins and RNA directly into the bloodstream. The blood platelets come in contact with these shed molecules and will absorb them. This results in an alteration of the blood platelets' own RNA. Persons with cancer will therefore have blood platelets that contain information about the specific cancer present. These "educated" blood platelets are called tumor educated platelets, or TEPs. Recently, TEPs have been used to aid in the detection of specific cancers, and even to identify their locations.[1]

In a recent study, a group of scientists investigated how TEPs could be used to diagnose cancer. The scientists took blood platelets from healthy individuals and from those with either advanced or early stages of six different types of cancer and compared their blood platelet RNA. While doing so, the researchers found that those with cancer had different amounts of certain platelet RNA molecules. For example, the scientists discovered that the levels of dozens of specific non-protein coding RNAs were altered in patients who had TEPs. The further analysis of hundreds of different RNA levels, from the nearly 300 patients in the study, enabled the scientists to distinguish a cancer-associated RNA profile from a healthy one. Using these results, the team created an algorithm that could classify if someone did or did not have cancer with up to 96% accuracy.[1]

NOT ONLY COULD THE TEPS DISTINGUISH BETWEEN HEALTHY INDIVIDUALS AND THOSE WITH A SPECIFIC CANCER, BUT THEY COULD ALSO IDENTIFY THE LOCATION OF THE CANCER.

Not only could the TEPs distinguish between healthy individuals and those with a specific type of cancer, but they could also identify the location of the cancer. The patients in the study had one of six types of cancer: non-small-cell lung cancer, breast cancer, pancreatic cancer, colorectal cancer, glioblastoma, or hepatobiliary cancer. The scientists analyzed the specific TEPs associated with the specific types of cancer and created an algorithm to predict tumor locations. The TEP-trained algorithm correctly identified the location of these six types of cancer 71% of the time.[1]

The authors of the study noted that this is the first blood-borne factor that can diagnose cancer and pinpoint the location of primary tumors. It is possible that in the near future, TEP-based tests could lead to a new class of extremely accurate liquid biopsies. Nowadays, many cancer tests are costly, invasive, or painful. For example, lung cancer tests require an X-ray, sputum cytology examination, or tissue sample biopsy. X-rays and sputum cytology must be performed after symptoms present, and can often have misleading results. Biopsies are more accurate, but are also highly painful and relatively dangerous. TEP-based blood tests have the potential to both obviate the need for these techniques and provide more granular, clinically useful information. They can be performed before symptoms are shown, at low cost, and with minimal patient discomfort, making them an ideal choice to interdict a growing tumor early.

The information that TEPs have revealed has opened a gate to many potential breakthroughs in the detection of cancer. With high accuracy and an early detection time, cancer blood tests have the potential to save many lives in the future.

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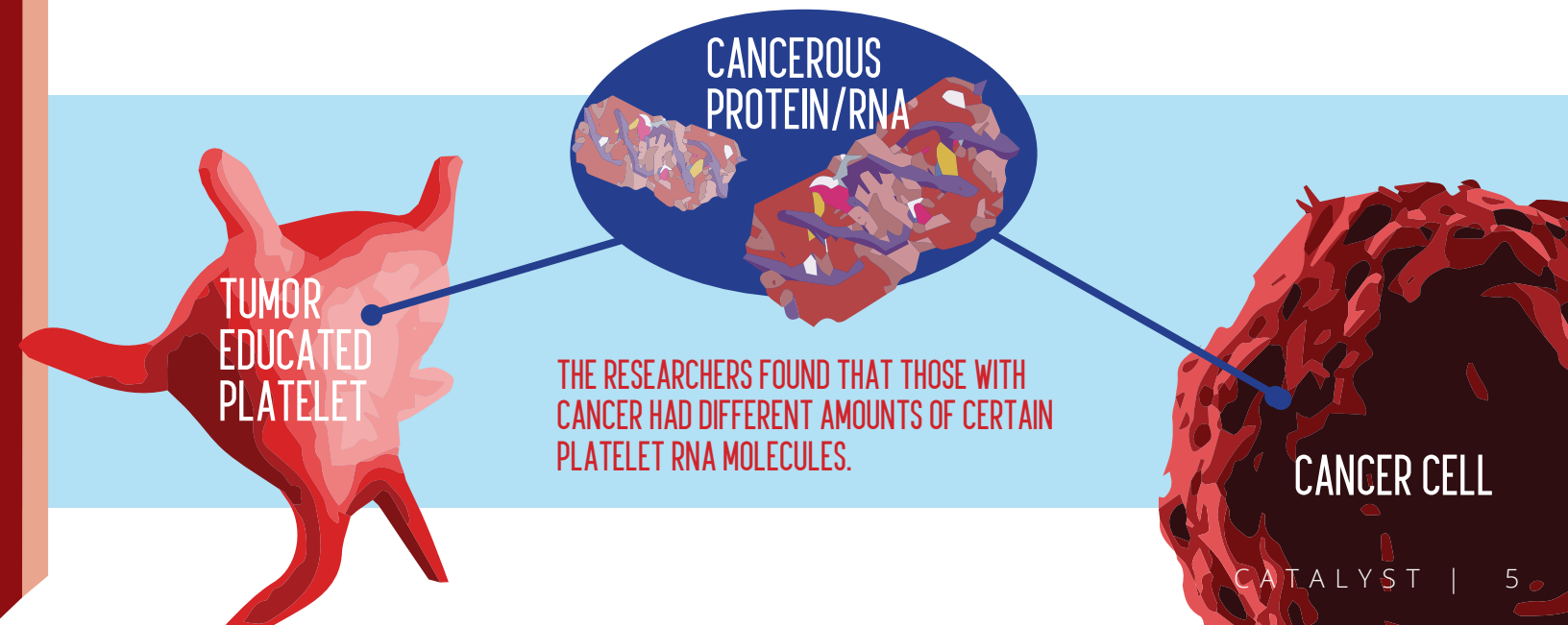


THE RESEARCHERS FOUND THAT THOSE WITH CANCER HAD DIFFERENT AMOUNTS OF CERTAIN PLATELET RNA MOLECULES.

who says TIME TRAVEL isn't possible?

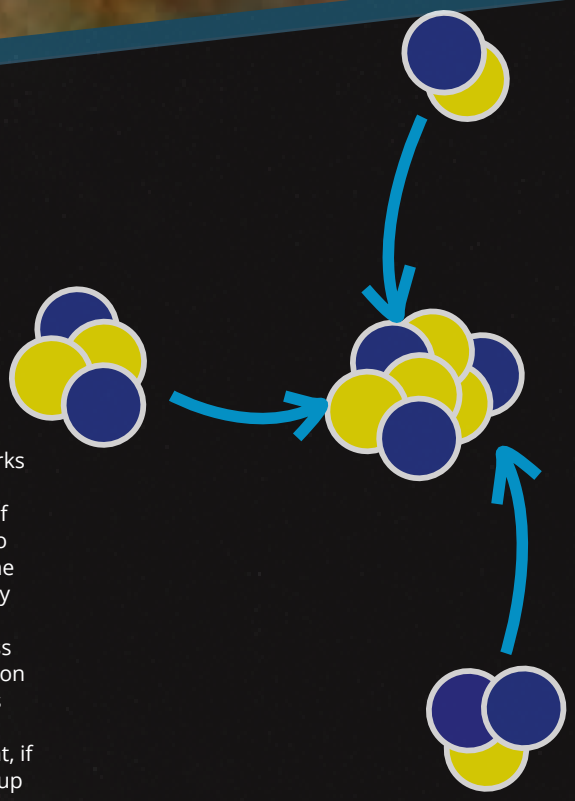
AKASH GUPTA

There are several challenges that must be overcome when attempting to travel to another star, let alone another galaxy. However, with today's technology and understanding of physics, we can envision potential ways to make interstellar travel, and even time travel, a reality, giving rise to the question of why other potential civilizations have not invented and made use of it yet. This is especially suspicious because considering the immensity of the universe, there are bound to be other intelligent civilizations, begging the famous question of the Fermi Paradox, "So where is everybody?" It's answer would enable us to evolve into an interstellar or intergalactic species, while failing to do so could spell our demise.

Einstein's theory of special relativity is where the cosmic speed limit (the speed of light) was first introduced. His theory also gives rise to the concept of time dilation, which states that time runs slower for those traveling extremely fast than it does for those on Earth, and that distances shrink when traveling at high speeds.[1] So, when a spaceship is traveling close to the speed of light, time measured aboard runs slower than it would on clocks at rest. This can play an important role in interstellar travel, because it can allow travelers moving close to the cosmic speed limit to age slower than those on Earth. For example, if a spaceship left Earth in the year 2100 and made a roundtrip to the star Vega at 90% the speed of light, it would return in Earth year 2156, but only 24 years would have passed for the crew of the ship.[2] Because of time dilation, journeys could be made to very distant places, and the crew would age very little. Due to this amazing effect, one could theoretically travel to the black hole at the center of the Milky Way Galaxy, 28,000 light years away, and only age 21 years, if traveling fast enough.[2] At a high enough percentage of the speed of light, you would be able to reach Andromeda (2.5 million light years away), and return to Earth only 60 years older while 5 million years have passed on Earth.[2] Clearly, time dilation is a real form of time travel to the future, assuming relativistic speeds are achievable. Therefore, it follows that the main obstacle for this method is reaching a percentage of the speed of light where time dilation becomes significant, requiring enormous amounts of energy.

Though obtaining the energy required for interstellar travel may seem like a far off goal, it will definitely be possible to travel great distances at great speeds in the near future with the science and technology that we have today. The first of these technologies are rockets that use nuclear energy as power. According to Albert Einstein's equation, $E=mc^2$, any small amount of mass can release a very large amount of energy. In fact, through the use of nuclear fission, only 0.6 grams of Uranium (less than the weight of an M&M) was sufficient to level Hiroshima during World War II.[3] Nuclear fission makes use of the lost mass when an atomic nucleus splits into two. Nuclear fusion, on the other hand, involves two atomic nuclei fusing into one, releasing ten times the energy of fission. This process is the source of energy for the sun, occurring at its core. Nuclear fusion, if controlled, is a viable source of energy in the future. Just using the hydrogen present in the water coming out of one faucet could provide enough energy for the United States' current needs, a staggering 2,850,000,000,000 joules/second.[2]

"**time dilation** is a real form of time travel to the future, assuming relativistic speeds are achievable"



In order to conduct nuclear fusion, an environment similar to the center of the sun must be created, with the same temperatures and pressures. Gas must be converted into an highly ionized state known as plasma. Recently, MIT was able to use their Alcator C-Mod tokamak reactor's extreme magnetic fields to create highest plasma pressures ever recorded.[4] In addition , a 7-story reactor in southern France, 800 times larger than MIT's reactor, is set to be completed in 2025 and will have magnets that are each as heavy as a Boeing 747.[5] Nuclear fusion could one day provide limitless energy for a spacecraft, accelerating it to relativistic speeds. Enormous scoops could be attached to the spacecraft to collect interstellar hydrogen gas throughout the journey, allowing travel to the distant corners of the galaxy.

Another technological development to facilitate interstellar travel is the EM drive, which is purported to be an electromagnetic thruster. This form of propulsion is highly controversial because it seemingly violates Newton's 3rd law and thus the Law of Conservation of Momentum, which together say that for something to move in one direction, an equal and opposite force must be exerted in the opposite direction. The EM drive is thought to use electromagnetic waves as fuel and create thrust through microwaves within the engine cavity that push on the inside and cause the thruster to accelerate in the opposite direction.[6] Simply put, the EM drive is able to go in one direction without a propellant or an opposite force pushing it. It has been tested multiple times, most notably by NASA's Eagleworks Lab. The EM drive has repeatedly been measured to produce a small amount of thrust, making it difficult for scientists to dismiss the possibility that it works.[7] The thrust seemingly cannot be explained by our current understanding of physics, but the Eagleworks Lab has nevertheless submitted its results to be published soon in the American Institute of Aeronautics and Astronautics' Journal of Propulsion and Power. This Eagleworks experiment, if shown to be reproducible, would open up opportunities for researchers around the world to conduct further experimentation. In August, plans were announced to test the EM drive in space, which would be the most robust test of its efficacy to date. The EM drive could one day provide an essentially limitless supply of thrust on a spacecraft without the need for propellant, allowing it to constantly accelerate until it reached relativistic speeds.

These are only two examples of technologies that could make interstellar travel possible. In the next few decades, we can look forward to more innovative research that will push the boundaries of science and redefine interplanetary, interstellar, and intergalactic travel. If relativistic speeds are achieved, humans could travel thousands, if not millions of years into the future by aging much slower than the rate at which time would actually pass on Earth. So who says we can't time travel? Certainly not science!

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ALGAE POND SCUM OR ENERGY OF THE FUTURE?

BY AMY KURITZKY

In many ways, rising fuel demands indicate positive development--a global increase in energy accessibility. But as the threat of climate change from burning fuel begins to manifest, it spurs the question: How can the planet meet global energy needs while sustaining our environment for years to come? While every person deserves access to energy and the comfort it brings, the population cannot afford to stand by as climate change brings about ecosystem loss, natural disaster, and the submersion of coastal communities. Instead, we need a technological solution which will meet global energy needs while promoting ecological sustainability. When people think of renewable energy, they tend to picture solar panels, wind turbines, and corn-based ethanol. But what our society may need to start picturing is that nondescript, green-brown muck that crowds the surface of ponds: algae.

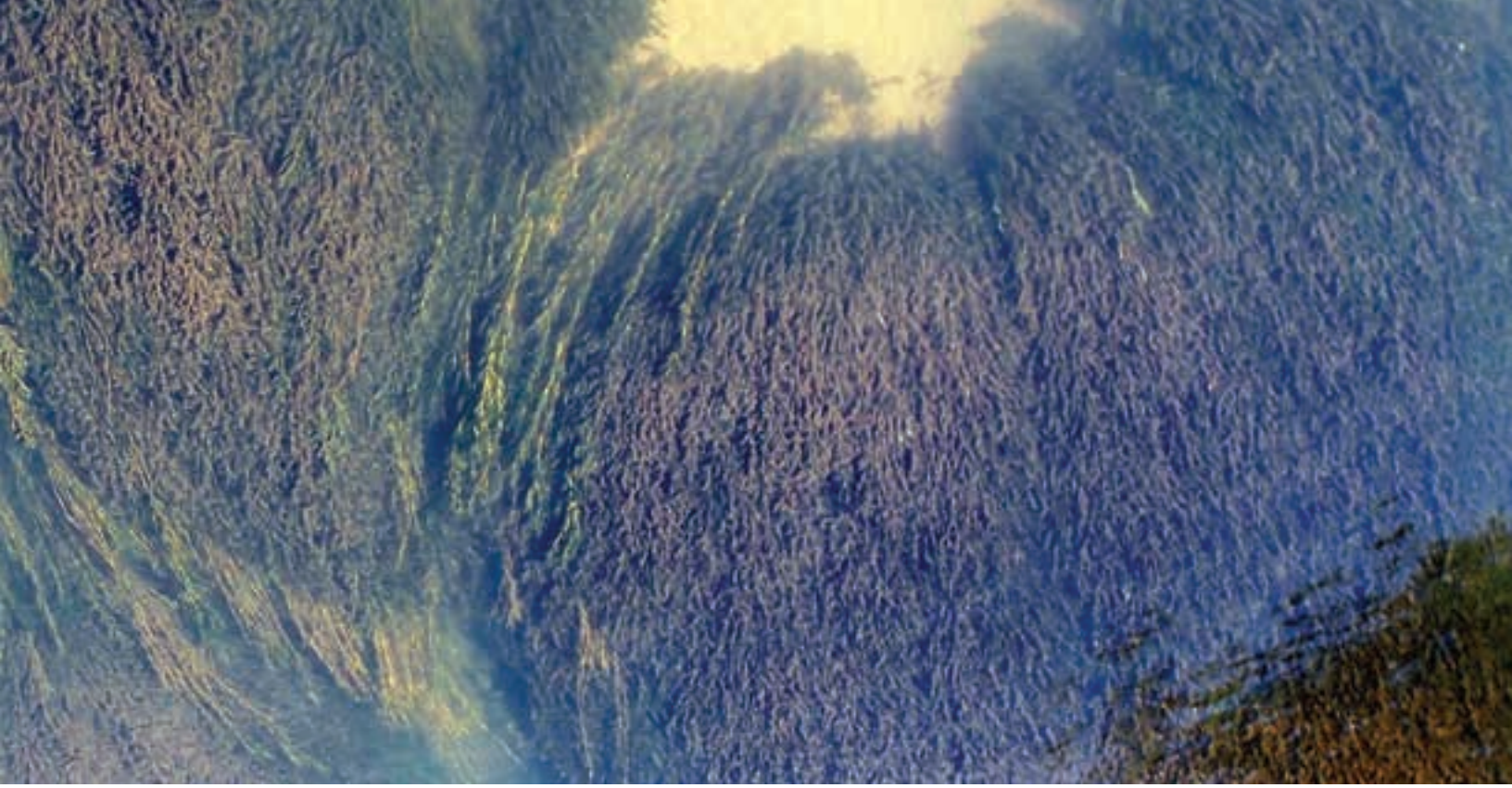
Conventional fuel sources, such as oil and coal, produce energy when the carbon they contain combusts upon burning. Problematically, these sources have sequestered carbon for millions of years, hence the term fossil fuels. Releasing this carbon now increases atmospheric CO_2 to levels that our planet cannot tolerate without a significant change in climate. Because fossils fuels form directly from the decomposition of plants, live plants also produce the compounds we normally burn to release energy. But, unlike fossil fuels, living biomass photosynthesizes up to the point of harvest, taking CO_2 out of the atmosphere. This coupling between the uptake of CO_2 by photosynthesis and the release of CO_2 by combustion means using biomass for fuel should not add net carbon to the atmosphere.[1] Because biofuel provides the same form of energy through the same processes as fossil fuel, but uses renewable resources and does not increase atmospheric carbon, it can viably support both societal and ecological sustainability.

> "[TO MEET GLOBAL ENERGY NEEDS], WHAT OUR SOCIETY MAY NEED TO START PICTURING IS THAT NONDESCRIPT, GREEN-BROWN MUCK THAT CROWDS THE SURFACE OF PONDS: ALGAE."

If biofuel can come from a variety of sources such as corn, soy, and other crops, then why should we consider algae in particular? Algae double every few hours, a high growth rate which will be crucial for meeting current energy demands.[2] And beyond just their power in numbers, algae provide energy more efficiently than other biomass sources, such as corn.[1] Fat composes up to 50 percent of their body weight, making them the most productive provider of plant oil.[3,2] Compared to traditional vegetable biofuel sources, algae can provide up to 50 times more oil per acre.[4] Also, unlike other sources of biomass, using algae for fuel will not detract from food production. One of the primary drawbacks of growing biomass for fuel is that it competes with agricultural land and draws from resources that would otherwise be used to feed people.[3] Not only does algae avoid this dilemma by either growing on arid, otherwise unusable land or on water, but also it need not compete with overtaxed freshwater resources. Algae proliferates easily on saltwater and even wastewater.[4] Furthermore, introducing algae biofuel into the energy economy would not require a systemic change in infrastructure because it can be processed in existing oil refineries and sold in existing gas stations.[2]

However, algae biofuel has yet to make its grand entrance into the energy industry. When oil prices rose in 2007, interest shifted towards alternative energy sources. U.S. energy autonomy and the environmental consequences of carbon emission became key points of discussion. Scientists and policymakers alike were excited by the prospect of algae biofuel, and research on algae drew governmental and industrial support. But as U.S. fossil fuel production increased and oil prices dropped, enthusiasm waned.[2]

Many technical barriers must be overcome to achieve widespread use of algae, and progress has been slow. For example, algae's rapid growth rate is both its asset and its Achilles' heel. Areas colonized by algae



can easily become overcrowded, which blocks access to sunlight and causes large amounts of algae to die off. Therefore, in order to farm algae as a fuel source, technology must be developed to regulate its growth.[3] Unfortunately, the question of how to sustainably grow algae has proved troublesome to solve. Typically, algae for biofuel use is grown in reactors in order to control growth rate. But the ideal reactor design has yet to be developed, and in fact, some current designs use more energy than the algae yield produces.[5]

Although algae biofuel faces technological obstacles and dwindling government interest, many scientists today still see algae as a viable and crucial solution for future energy sustainability. UC San Diego houses the California Center for Algal Biotechnology, and Dr. Stephen Mayfield, a molecular biologist at the center, has worked with algae for over 30 years. In this time he has helped start four companies, including Sapphire Energy, founded in 2007, which focuses on developing algae biofuels. After receiving $100 million from venture capitalists in 2009, Sapphire Energy built a 70,000-square-foot lab in San Diego and a 220-acre farm in New Mexico. They successfully powered cars and jets with algae biofuel, drawing attention and $600 million in further funding from ExxonMobil. Although diminished interest then stalled production, algal researchers today believe people will come to understand the potential of using algae.[2] The Mayfield Lab currently works on developing genetic and molecular tools to make algae fuel a viable means of energy production.[4] They grow algae, extract its lipids, and convert them to gasoline, jet, and diesel fuel. Mayfield believes his lab will reach a low price of 80 or 85 dollars per barrel as they continue researching with large-scale biofuel production.[1]

The advantage of growing algae for energy production lies not only in its renewability and carbon neutrality, but also its potential for other uses. In addition to just growing on wastewater, algae can treat the water by removing nitrates.[5] Algae farms could also provide a means of carbon sequestration. If placed near sources of industrial pollution, they could remove harmful CO_2 emissions from the atmosphere through photosynthesis.[4] Additionally, algae by-products are high in protein and could serve as fish and animal feed.[5]

At this time of increased energy demand and dwindling fossil fuel reserves, climate change concerns caused by increased atmospheric carbon, and an interest in U.S. energy independence, we need economically viable but also renewable, carbon neutral energy sources.[4] Algae holds the potential to address these needs. Its rapid growth and photosynthetic ability mean its use as biofuel will be a sustainable process that does not increase net atmospheric carbon. The auxiliary benefits of using algae, such as wastewater treatment and carbon sequestration, increase the economic feasibility of adapting algae biofuel. While technological barriers must be overcome before algae biofuel can be implemented on a large scale, demographic and environmental conditions today indicate that continued research will be a smart investment for future sustainability.

"THE ADVANTAGE OF GROWING ALGAE FOR ENERGY PRODUCTION LIES NOT ONLY IN ITS RENEWABLITY AND CARBON NEUTRALITY, BUT ALSO ITS POTENTIAL FOR OTHER USES."

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GMO

HOW SAFE IS OUR FOOD?

BY ANU DWARUMPUDI

For thousands of years, humans have genetically enhanced other living beings through the practice of selective breeding. Sweet corn and seedless watermelons at local grocery stores as well as purebred dogs at the park are all examples of how humans have selectively enhanced desirable traits in other living creatures. In his 1859 book *On the Origin of Species*, Charles Darwin discussed how selective breeding by humans had been successful in producing change over time. As technology improves, our ability to manipulate plants and other organisms by introducing new genes promises both new innovations and potential risks.

Genetically modified organisms (GMOs) are plants, animals, or microorganisms in which genetic material, such as DNA, has been artificially manipulated to produce a certain advantageous product. This recombinant genetic engineering allows certain chosen genes, even those from unassociated species, to be transplanted from one organism into another.[1] Genetically modified crops are usually utilized to yield an increased level of crop production and to introduce resistance against diseases. Virus resistance makes plants less susceptible to diseases caused by insects and viruses, resulting in higher crop yields.

Genetic enhancement has improved beyond selective breeding as gene transfer technology has become capable of directly altering genomic sequences . Using a "cut and paste" mechanism, a desired gene can be isolated from a target organism via restriction enzymes and then inserted into a bacterial host using DNA ligase. Once the new gene is introduced, the cells with the inserted DNA (known as "recombinant" DNA) can be bred to generate an advanced strain that can be further replicated to produce the desired gene product.[1] Due to this genetic engineering process, researchers have been able to produce synthetic insect-resistant tomatoes, corn, and potatoes. Humans' ability to modify crops has improved yields and nutrients in a given environment, becoming the keystone of modern agriculture.[2] Despite these positive developments, skepticism still exists regarding the safety and societal impact of GMOs.

GMO: PLANT, ANIMAL OR MICROORGANISM IN WHICH GENETIC MATERIAL, SUCH AS DNA, HAS BEEN ARTIFICIALLY MANIPULATED TO PRODUCE A CERTAIN ADVANTAGEOUS PRODUCT

The technological advancement from selective breeding to genetic engineering has opened up a plethora of possibilities for the future of food. As scientific capabilities expand, ethics and ideals surrounding the invasive nature of the production of GMOs have given rise to concerns about safety and long-term impacts. According to the Center for Food Safety, GMO seeds are used in 90 percent of corn, soybeans, and cotton grown in the United States.[2] Because GMO crops are so prevalent, any negative ecological interactions involving a GMO product could prove devastating for the environment.

While the dangers of genetic modification are being considered, genetic engineering has proven to have benefits to human health and the farming industry. Genetically modified foods maintain a longer shelf life, which allows for the safe transport of surplus foodstuffs to people in countries without access to nutrition-rich foods. Genetic engineering has supplemented staple crops with vital minerals and nutrients,helping fight worldwide malnutrition. For example, Golden rice is a genetically-modified variant of rice that biosynthesizes beta-carotene, a precursor of vitamin A.[3] This type of rice is intended to be produced and consumed in areas with a shortage of dietary vitamin A, which is a deficiency that kills 670,000 children each year. Despite the controversial risks, genetic engineering of crops promises to continually increase the availability and durability of food.

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TELOMERES

WAYS TO PROLONG LIFE

BY ANDREW STEFANI

Two hundred years ago, the average life expectancy oscillated between 30 and 40 years, as it had for centuries before. Medical knowledge was fairly limited to superstition and folk cures, and the science behind what actually caused disease and death was lacking. Since then, the average lifespan of human beings has skyrocketed due to scientific advancements in health care, such as an understanding of bacteria and infections. Today, new discoveries are being made in cellular biology which, in theory, could lead us to the next revolutionary leap in life span. Most promising among these recent discoveries is the manipulation of telomeres in order to slow the aging process, and the use of telomerase to identify cancerous cells.

Before understanding how telomeres can be utilized to increase the average lifespan of humans, it is essential to understand what a telomere is. When cells divide, their DNA must be copied so that all of the cells share an identical DNA sequence. However, the DNA cannot be copied all the way to the end of the strand, resulting in the loss of some DNA at the end of the sequence with every single replication.[1] To prevent valuable genetic code from being cut off during cell division, our DNA contains telomeres, a meaningless combination of nucleotides at the end of our chromosomal sequences that can be cut off without consequences to the meaningful part of the DNA. Repeated cell replication causes these protective telomeres to become shorter and shorter, until valuable genetic code is eventually cut off, causing the cell to malfunction and ultimately die.[1] The enzyme telomerase functions in cells to rebuild these constantly degrading telomeres, but its activity is relatively low in normal cells as compared to cancer cells.[2]

The applications of telomerase manipulation have only come up fairly recently, with the discovery of the functionality of both telomeres and telomerase in the mid 80's by Nobel Prize winners Elizabeth Blackburn, Carol Grieder, and Jack Sjozak.[3] Blackburn discovered a sequence at the end of chromosomes that was repeated several times, but could not determine what the purpose of this sequence was. At the same time, Sjozak was observing the degradation of minichromosomes, chromatin-like structures which replicated during cell division when introduced to a yeast cell. Together, they combined their work by isolating Blackburn's repeating DNA sequences, attaching them to

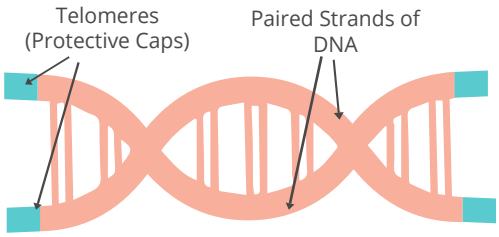

Figure 1: DNA strand with telomere ends

Sjozak's minichromosomes, and then placing the minichromosomes back inside yeast cells. With the new addition to their DNA sequence, the minichromosomes did not degrade as they had before, thus proving that the purpose of the repeating DNA sequence, dubbed the telomere, was to protect the chromosome and delay cellular aging.

Because of the relationship between telomeres and cellular aging, many scientists theorize that cell longevity could be enhanced by finding a way to control telomere degradation and keep protective caps on the end of cell DNA indefinitely.[1] Were this to be accomplished, the cells would be able to divide an infinite number of times before they started to lose valuable genetic code, which would theoretically extend the life of the organism as a whole.

In addition, studies into telomeres have revealed new ways of combating cancer. Although there are many subtypes of cancer, all variations of cancer involve the uncontrollable, rapid division of cells. Despite this rapid division, the telomeres of cancer cells do not shorten like those of a normal cell upon division, otherwise this rapid division would be impossible. Cancer cells are likely able to maintain their telomeres due to their higher levels of telomerase.[3] This knowledge allows scientists to use telomerase levels as an indicator of cancerous cells, and then proceed to target these cells. Vaccines that target telomerase production have the potential to be the newest weapon in combating cancer.[2] Cancerous cells continue to proliferate at an uncontrollable rate even when telomerase production is interrupted. However, without the telomerase to protect their telomeres from degradation, these cells eventually die.

As the scientific community advances its ability to control telomeres, it comes closer to controlling the process of cellular reproduction, one of the many factors associated with human aging and cancerous cells. With knowledge in these areas continuing to develop, the possibility of completely eradicating cancer and slowing the aging process is becoming more and more realistic.

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CORALS IN HOT WATER, LITERALLY.

ANNA KNOCHEL

Coral reefs support more species per unit area than any other marine environment, provide over half a billion people worldwide with socio-economic benefits, and produce an estimated USD $30 billion annually.[1] Many people do not realize that these diverse ecosystems are at risk of extinction as a result of human activity--the Caribbean has already lost 80% of its coral cover in the past few decades[2] and some estimates report that at least 60% of all coral will be lost by 2030.[1] One of the most predominant and direct threats to the health of these fragile ecosystems is the enormous amount of carbon dioxide and methane that have spilled into the atmosphere, warming the planet and its oceans on unprecedented levels.

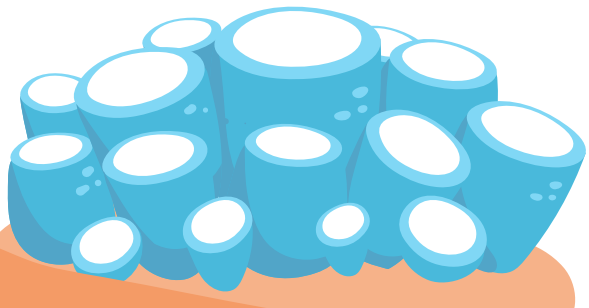
Corals are Cnidarians, the phylum characterized by simple symmetrical structural anatomy. Corals reproduce either asexually or sexually and create stationary colonies made up of hundreds of genetically identical polyps.[3] The major reef-building corals belong to a sub-order of corals, called Scleractinia. These corals contribute substantially to the reef framework and are key species in building and maintaining the structural complexity of the reef.[3] The survival of this group is of particular concern, since mass die-offs of these corals affect the integrity of the reef. Corals form a symbiosis with tiny single-celled algae of the genus Symbiodinium. This symbiotic relationship supports incredible levels of biodiversity and is a beautifully intricate relationship that is quite fragile to sudden environmental change.[3]

The oceans absorb nearly half of the carbon dioxide in the atmosphere through chemical processes that occur at its surface.[4] Carbon dioxide combines with water molecules to create a mixture of bicarbonate, calcium carbonate, and carbonic acid. Calcium carbonate is an important molecule used by many marine organisms to secrete their calcareous shells or skeletons. The increase of carbon dioxide in the atmosphere shifts this chemical equilibrium, creating higher levels of carbonic acid and less calcium carbonate.[4] Carbonic acid increases the acidity of the ocean and this phenomenon has been shown to affect the skeletal formation of juvenile corals.[5] Acidification weakens the structural integrity of coral skeletons and contributes to heightened dissolution of carbonate reef structure.[3]

The massive influx of greenhouse gases into our atmosphere has also caused the planet to warm very quickly. Corals are in hot water, literally. Warmer ocean temperatures have deadly effects on corals and stress the symbiosis that corals have with the algae that live in their tissues. Though coral can procure food by snatching plankton and other organisms with protruding tentacles, they rely heavily on the photosynthesizing organism Symbiodinium for most of their energy supply.[3] Symbiodinium provides fixed carbon compounds and sugars necessary for coral skeletal growth. The coral provides the algae with a fixed position in the water column, protection from predators, and supplementary carbon dioxide.[3] Symbiodinium live under conditions that are 1 to 2° C below their maximum upper thermal limit. Under warmer conditions due to climate change, sea surface temperatures can rise a few degrees above their maximum thermal limit. This means that a sudden rise in sea temperatures can stress Symbiodinium by causing photosynthetic breakdown and the formation of reactive oxygen species that are toxic to corals.[3] The algae leave or are expelled from the coral tissues as a mechanism for short-term survival in what is known as bleaching. Coral will die from starvation unless the stressor dissipates and the algae return to the coral's tissues.[3]

Undoubtedly, the warming of the seas is one of the most widespread threats to coral reef ecosystems. However, other threats combined with global warming may have synergistic effects that heighten the vulnerability of coral to higher temperatures. These threats include coastal development that either destroys local reefs or displaces sediment to nearby reefs, smothering them. Large human populations near coasts expel high amounts of nitrogen and phosphorous into the ecosystem, which can increase the abundance of macroalgae and reduce hard coral cover. Increased nutrient loading has been shown to be a factor contributing to a higher prevalence of coral disease and coral bleaching.[6] Recreational fishing and other activities can cause physical injury to coral making them more susceptible to disease. Additionally, fishing heavily reduces population numbers of many species of fish

Approaches that seemed too radical a decade ago are now widely considered as the only means to save coral reefs from the looming threat of extinction.



that keep the ecosystem in balance. The first documented global bleaching event in 1998 killed off an estimated 16% of the world's reefs; the world experienced the destruction of the third global bleaching event occurred only last year.[1] Starting in mid-2015, an El Niño Southern Oscillation (ENSO) weather event spurred hot sea surface temperatures that decimated coral reefs across the Pacific, starting with Hawaii, then hitting places like American Samoa, Australia, and reefs in the Indian Ocean.[7] The aftermath in the Great Barrier Reef is stunning; the north portion of the reef experienced an average of 67% mortality.[8] Some of these reefs, such as the ones surrounding Lizard Island, have been reduced to coral skeletons draped in macroalgae. With climate change, it is expected that the occurrence of ENSO events will become more frequent, and reefs around the world will be exposed to greater thermal stress.[1]

Some scientists are hopeful that corals may be able to acclimatize in the short term and adapt in the long term to warming ocean temperatures. The key to this process lies in the genetic type of Symbiodinium that reside in the coral tissues. There are over 250 identified types of Symbiodinium, and genetically similar types are grouped into clades A-I. The different clades of these algae have the potential to affect the physiological performance of their coral host, including responses to thermotolerance, growth, and survival under more extreme light conditions.[3] Clade D symbiont types are generally more thermotolerant than those in other clades. Studies have shown a low abundance of Clade D organisms living in healthy corals before a bleaching event, but after bleaching and subsequently recovering, the coral has a greater abundance of Clade D within its tissues.[9,10] Many corals are generalists and have the ability to shuffle their symbiont type in response to stress.[11]

However, there is a catch. Though some algal members of Clade D are highly thermotolerant, they are also known as selfish opportunists. The reason healthy, stress-free corals generally do not have a symbiosis with this clade is that it tends to hoard the energy and organic compounds it creates from photosynthesis and shares fewer products with its coral host.[3] Approaches that seemed too radical a decade ago are now widely considered as the only means to save coral reefs from the looming threat of extinction. Ruth Gates, a researcher at the Hawaii Institute of Marine Biology is exploring the idea of assisted evolution in corals. Her experiments include breeding individual corals in the lab, exposing them to an array of stressors, such as higher temperatures and lower pH, and picking the hardiest survivors to transplant to reefs.[12] In other areas of the globe, scientists are breeding coral larvae in labs and then releasing them onto degraded reefs where they will hopefully settle and form colonies. Governments and policy makers can create policies that have significant impact on the health of reefs. The creation of marine protected areas that heavily regulates or outlaws harvesting of marine species offers sanctuary to a stressed and threatened ecosystem.[3] There is still a long way to go, and the discoveries being made so far about coral physiology and resilience are proving that the coral organism is incredibly complex.

The outlook on the future of healthy reefs is bleak; rising fossil fuel consumption rates mock the global goal of keeping rising temperatures below two degrees Celsius. Local stressors such as overfishing, pollution, and coastal development cause degradation of reefs worldwide. Direct human interference in the acclimatization and adaptation of corals may be instrumental to their survival. Rapid transitions to cleaner sources of energy, the creation of more marine protection areas, and rigid management of reef fish stocks may ensure coral reef survival. If humans fail in this endeavor, one of the most biodiverse and productive ecosystems on earth that has persisted for millions of years may come crashing to an end within our lifetime.

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MODELING CLIMATE CHANGE:

by Jackson Stiles

> *"It is a unique and exciting opportunity to be able to study a geological era so similar to our own and apply discoveries we make from that era to our current environment."*

Believe it or not, we are still recovering from the most recent ice age that occurred between 21,000 and 11,500 years ago. And yet, in the past 200 years, the Earth's average global temperature has risen by 0.8ºC at a rate more than ten times faster than the average ice-age recovery rate.[1] This increase in global temperature, which shows no signs of slowing down, will have tremendous consequences for our planet's biodiversity and overall ecology.

Climate change is caused by three main factors: changes in the position of the Earth's continents, variations in the Earth's orbital positions, and increases in the atmospheric concentration of "greenhouse gases", such as carbon dioxide.[2] In the past 200 years, the Earth's continents have barely moved and its orbit around the sun has not changed.[2] Therefore, to explain the 0.8 ºC increase in global average temperature that has occurred, the only reasonable conclusion is that there has been a change in the concentration of greenhouse gases.

After decades of research by the Intergovernmental Panel on Climate Change (IPCC), this theory was supported. The IPCC Fourth Assessment Report concluded that the increase in global average temperature is very likely due to the observed increase in anthropogenic greenhouse gas concentrations. Also included in the report is a prediction that global temperatures will increase between 1.1 ºC and 6.4 ºC by the end of the 21st century.[2]

Though we know what is causing the warming, we are unsure of its effects. The geologists and geophysicists at the US Geological Service (USGS) are attempting to address this uncertainty through the Pliocene Research, Interpretation, and Synoptic Mapping (PRISM) program.[3]

The middle of the Pliocene Era occurred roughly 3 million years ago-- a relatively short time on the geological time scale. Between the Pliocene era and our current Holocene era, the continents have barely drifted, the planet has maintained a near identical orbit around the sun, and the type of organisms living on earth has remained relatively constant.[2] Because of these three commonalities , we can draw three conclusions. Because the continents have barely drifted, global heat distribution through oceanic circulation is the same. Additionally, because the planet's orbit is essentially the same, glacial-interglacial cycles have not been altered. Finally, because the type of organisms has remained relatively constant, the biodiversity of the Pliocene is comparable to our own.

While the eras share many similarities, the main difference between them is that the Pliocene was about 4 ºC warmer at the equator and 10 ºC warmer at the poles.[4] Because the Pliocene had similar conditions to today, but was warmer, it is likely that at the end of the century, our planet's ecology may begin to look like the Pliocene. This idea has been supported by the research done by the USGS's PRISM.[3]

It is a unique and exciting opportunity to be able to study a geological era so similar to our own and apply discoveries we make from that era to our current environment. PRISM is using multiple techniques to extract as much data about the Pliocene as possible. The concentration of magnesium ions, the number of carbon double bonds in organic structures called alkenones, and the concentration and distribution of fossilized pollen all provide a wealth of information that can be used to inform us about climate change. However, the single most useful source of such information comes from planktic foraminifera, or foram.[5]

Foram, abundant during the Pliocene era, are unicellular, ocean-dwelling organisms adorned with calcium shells. Fossilized foram are extracted from deep-sea core drilling. The type and concentration of the extracted foram reveal vital information about the temperature, salinity, and productivity of the oceans during the foram's lifetime.[5] By performing factor analysis and other statistical analyses on this information, PRISM has created a model of the Pliocene that covers both oceanic and terrestrial areas, providing a broad view

Images from Hgrobe via Wikimedia Commons and Foram Art Gallery

A GIFT FROM THE PLIOCENE

of our planet as it existed 3 million years ago. Using the information provided by this model, scientists can determine where temperatures will increase the most and what impact such a temperature increase will have on life that can exist in those areas.

> *"Our temperatures are increasing at a much more rapid rate..."*

Since its inception in 1989, PRISM has predicted, with proven accuracy, two main trends. The first is that average temperatures will increase the most at the poles, with areas nearest to the equator experiencing the least amount of temperature increase.[5] The second is that tropical plants will expand outward from the equator, taking root in the middle and higher latitudes.[5]

There are some uncertainties associated with the research behind PRISM. Several assumptions were made, such as the idea of uniformitarianism, which states that the same natural laws and physical processes that occur now were true in the past. The researchers also assumed that the ecological tolerances of certain key species, such as foram, have not significantly changed in the last 3 million years. Even with these normalizing assumptions, an important discrepancy exists between the Pliocene and our Holocene: the Pliocene achieved its temperature at a normal rate and remained relatively stable throughout its era, while our temperatures are increasing at a much more rapid rate.

The film industry has fetishized climate change, predicting giant hurricanes and an instant ice age, as seen in the films 2012 and The Day After Tomorrow. Fortunately, nothing as cataclysmic will occur. However, a rise in global average temperature and a change in our ecosystems is nothing to be ignored or dismissed as normal. It is only through the research done by the USGS via PRISM and similar systems that our species can be prepared for the coming decades of change.

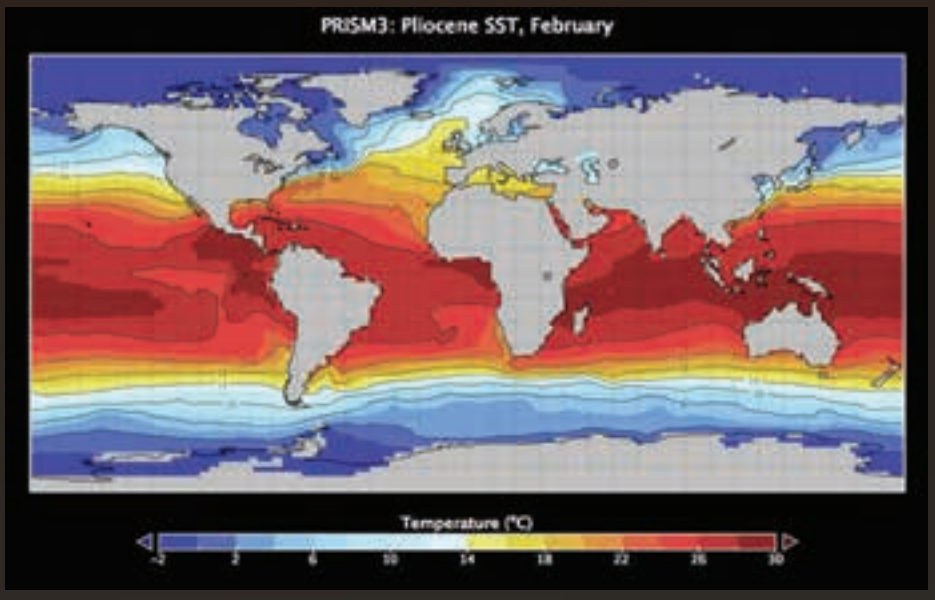

Figure 1. Ocean surface level temperatures during the mid-Pliocene. This data can serve as an indicator for temperatures at the end of the century.

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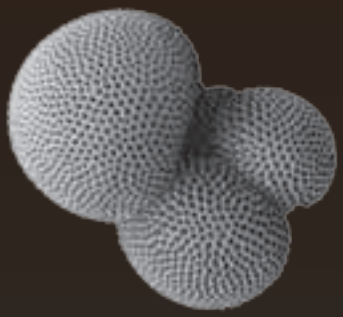

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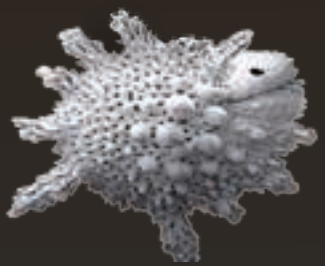


calcarina

WEARABLE TECH IS THE NEW BLACK

BY AVANTHIKA MAHENDRABABU

What if our clothes could detect cancer? That may seem like a far fetched, "only applicable in a sci-fi universe" type of concept, but such clothes do exist and similar devices that merge technology and medicine are actually quite prominent today. The wearable technology industry, a field poised to grow to $11.61 billion by 2020[1], is exploding in the healthcare market as numerous companies produce various devices that help us in our day to day lives such as wearable EKG monitors and epilepsy detecting smart watches. Advancements in sensor miniaturization and integration with medical devices have greatly opened this interdisciplinary trade by lowering costs. Wearable technology ranging from the Apple Watch to consumable body-monitoring pills can be used for everything from health and wellness monitoring to early detection of disorders. But as these technologies become ubiquitous, there are important privacy and interoperability concerns that must be addressed.

Wearable tech like the Garmin Vivosmart HR+ watch uses sensors to obtain insightful data about its wearer's health. This bracelet-like device tracks steps walked, distance traveled, calories burned, pulse, and overall fitness trends over time.[2] It transmits the information to an app on the user's smartphone which uses various algorithms to create insights about the person's daily activity. This data about a person's daily athletic habits is useful to remind them that fitness is not limited to working out at the gym or playing a sport—it's a way of life. Holding tangible evidence of one's physical activity for the day or history of vital signs empowers patients to take control of their personal health. The direct feedback of these devices influences patients to make better choices such as taking the stairs instead of the elevator or setting up a doctor appointment early on if they see something abnormal in the data from their EKG sensor. Connecting hard evidence from the body to physical and emotional perceptions refines the reality of those experiences by reducing the subjectivity and oversimplification that feelings about personal well being may bring about.

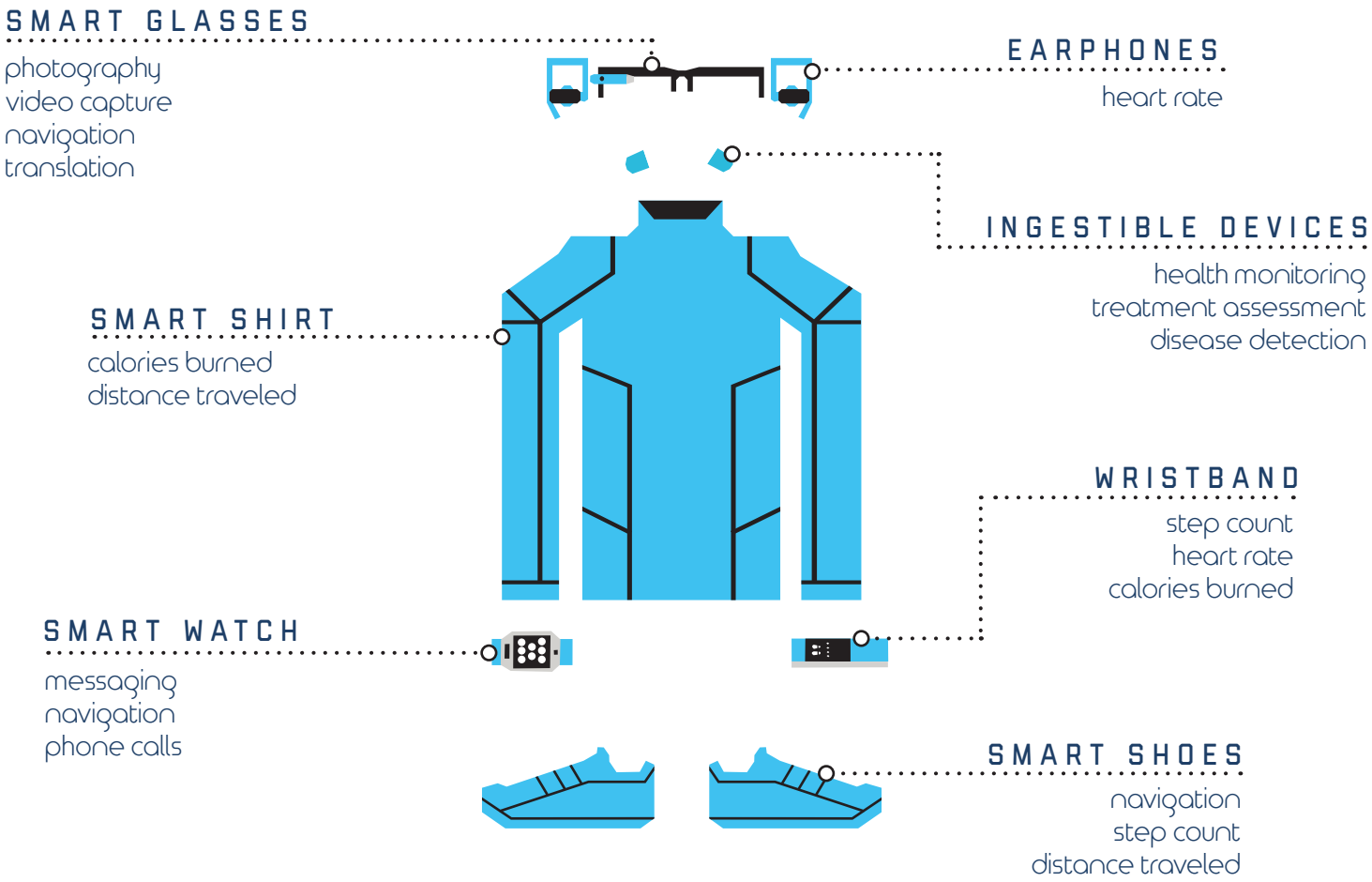
HOLDING TANGIBLE EVIDENCE OF ONE'S PHYSICAL ACTIVITY FOR THE DAY OR HISTORY OF VITAL SIGNS EMPOWERS PATIENTS TO TAKE CONTROL OF THEIR PERSONAL HEALTH.

Not only can wearable technology gather information from the body, but these devices can also detect and monitor diseases. Diabetes, the 7th leading cause of death in the United States,[3] can be detected via AccuCheck, a technology that can send an analysis of blood sugar levels directly to your phone.[4] Analysis software like BodyTel can also connect patients with doctors and other family members who would be interested in looking at the data gathered from the blood test.[5] Ingestible devices such as the Ingestion Event Marker take monitoring a step further. Designed to monitor medication intake, the pills keep track of when and how frequently patients take their medication. The Freescale KL02 chip, another ingestible device, monitors specific organs in the body and relays the organ's status back to a Wi-Fi enabled device which doctors can use to remotely measure the progression of an illness. They can assess the effectiveness of a treatment with quantitative evidence which makes decision-making about future treatment plans more effective.

Many skeptics hesitate to adopt wearable technology because of valid concerns about accuracy and privacy. To make sure medical devices are kept to the same standards and are safe for patient use, the US Food and Drug Administration (FDA) has begun to implement a device approval process. Approval is only granted to devices that provably improve the functionality of traditional medical devices and do not pose a great risk to patients if they malfunction[6]. In spite of the FDA approval process, much research is needed to determine whether the information, analysis and insights received from various wearable technologies can be trusted.

THE WEARABLE TECHNOLOGY INDUSTRY, A FIELD POISED TO GROW TO $11.61 BILLION BY 2020 IS EXPLODING IN THE HEALTHCARE MARKET

Privacy is another big issue especially for devices like fitness trackers that use GPS location to monitor user behavior. Many questions about data ownership (does the company or



the patient own the data?) and data security (how safe is my data from hackers and/or the government and insurance companies?) are still in a fuzzy gray area with no clear answers[7]. Wearable technology connected to online social media sites, where one's location may be unknowingly tied to his or her posts, can increase the chance for people to become victims of stalking or theft. Lastly, another key issue that makes medical practitioners hesitant to use wearable technology is the lack of interoperability, or the ability to exchange data, between devices. Data structured one way on a certain wearable device may not be accessible on another machine. Incorrect information might be exchanged, or data could be delayed or unsynchronized, all to the detriment of the patient.

Wearable technology is changing the way we live our lives and understand the world around us. It is modifying the way health care professionals think about patient care by emphasizing quantitative evidence for decision making over the more subjective analysis of symptoms. The ability for numeric evidence about one's body to be documented holds people accountable for the actions. Patients can check to see if they meet their daily step target or optimal sleep count, and doctors can track the intake of a pill and see its effect on the patient's body. For better or for worse, we won't get the false satisfaction of achieving our fitness goal or of believing in the success of a doctor's recommended course of action without tangible results. While we have many obstacles to overcome, wearable technology has improved the quality of life for many people and will continue to do so in the future.

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CRISPR:

The phrase "genetic engineering," mired in science fiction and intrigue, often brings to mind a mad scientist manipulating mutant genes or a Frankenstein-like creation emerging from a test tube. Brought to light by heated debates over genetically modified crops, genetic engineering has long been viewed as a difficult, risky process fraught with errors.[1]

With the 2012 discovery of CRISPRs, short for clustered regularly interspaced sport palindromic repeats, by Jennifer Doudna of Berkeley, the world of genetic engineering has been turned on its head.[2] Praised as the "Model T" of genetic engineering, CRISPR is transforming what it means to edit genes and in turn, raising difficult ethical and moral questions along with it.[3]

CRISPR itself is no new discovery. The repeats are sequences used by bacteria and microorganisms to protect against viral infections. Upon invasion by a virus, CRISPR identifies the DNA segments from the invading virus, processes them into "spacers," or short segments of DNA, and inserts them back into the bacterial genome.[4] When the bacterial DNA undergoes transcription, the resulting RNA is a single-chain molecule that acts as a guide to destroy viral material. In a way, the RNA functions as a blacklist for the bacteria cell: re-invasion attempts by the same virus are quickly identified using the DNA record and subsequently destroyed. That same blacklist enables CRISPR to be a powerful engineering tool. The spacers act as easily identifiable flags in the genome, allowing for extremely accurate precision when manipulating individual nucleotide sequences in genes.[5] The old biotechnology system can be perceived as a confused traveler holding an inaccurate, with a general location and vague person to meet. By the same analogy, CRISPR provides a mugshot of the person to meet and the precise coordinates of where to find them. Scientists have taken advantage of this precision and now use modified proteins, often Cas-9, to activate gene expression as opposed to cutting the DNA, an innovative style of genetic engineering.[6] Traditional genetic engineering can be a shot in the dark- however, with the accuracy of CRISPR, mutations are very rare.[7] For the first time, scientists are able to pinpoint the exact destination of genes, cut the exact desired sequence, and leave no damage. Another benefit of CRISPR is the reincorporation of genes that have become lost, either by breeding or evolution, bringing back extinct qualities: such as mammoth genes in living elephant cells.[8,9] Even better, CRISPR is very inexpensive - around $75 to edit a gene at Baylor College of Medicine - and accessible to anyone with biological expertise, starting with graduate students.[11] Thus, the term "Model T of genetic engineering" could hardly be more appropriate.

> PRAISED AS THE "MODEL T" OF GENETIC ENGINEERING. CRISPR IS TRANSFORMING WHAT IT MEANS TO EDIT GENES.

CRISPR stretches the boundaries of bioengineering. One enterprising team from China led by oncologist Dr. Lu You has already begun trials on humans. They plan on injecting cells modified with CRISPR-Cas9 system into patients with metastatic non-small cell lung cancer: patients who otherwise have little hope of survival.[12] Extracted T cells, critical immune cells, will be edited with the CRISPR-Cas9 system to identify and "snip" out a gene that encodes PD-1, a protein that acts as a check on the cell's capacity to launch an immune response, to prevent attacks on healthy cells. Essentially, Lu's team is creating super-T-cells: ones that have no mercy for any suspicious activity. This operation is very risky: for one, CRISPR's mechanisms are not thoroughly understood, and mistakes with

A TIMELINE OF CRISPR:

1987 *Short direct repeats found in E.coli*

2002 *"CRISPR" coined by Jansen et al to describe repeats*

2005 *Spacer sequences found to be viral in nature*

2007 *First evidence of CRISPR-Cas partnership*

2008 *DNA found to be the target of CRISPR-Cas systems*

2010 *CRISPR-Cas systems are found to be able to cut DNA*

THE DOUBLE-EDGED SWORD AT THE FOREFRONT OF GENETIC ENGINEERING

BY CHRISTINA TAN

gene editing could have drastic consequences.[11] Secondly, the super T cells could attack in an autoimmune reaction, leading to degradation of critical organs. In an attempt to prevent an extreme autoimmune response, Lu's team will extract the T-cells from the tumor itself, as those T-cells have already specialized in attacking cancer cells. To ensure patient safety, the team will proceed with great caution: they will examine the effects of three different dosage regimens on ten patients, watching closely for side effects and responsiveness.

> **ESSENTIALLY, LU'S TEAM IS CREATING SUPER-T-CELLS: ONES THAT HAVE NO MERCY.**

Trials involving such cutting-edge technology raise many questions: with ease of use and accessibility, CRISPR has the potential to become a tool worthy of science fiction horror. Several ethics groups have raised concerns over the ease of use involved with CRISPR: they worry that the technology could be used by amateurs and thus yield to dangerous experiments. Indeed, China had already greenlighted direct editing of human embryos, creating international uproar and a moratorium on further testing.[13] But that editing could lead to new breakthroughs: CRISPR could reveal how genes regulate early embryonic development, leading to a better understanding of infertility and miscarriages.[14]

This double-edged nature of benefit and risk defines CRISPR-Cas9's increasing relevance at the helm of bioengineering. The momentum behind CRISPR and its endless application continues to build and break open long-unanswered questions in biology, disease treatment, and genetic engineering. Still, with that momentum comes caution: with CRISPR's discoveries come increasingly blurred ethical distinctions.

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DESIGN BY Christina Tan
EDITED BY Meredith Brown

2011 *CRISPR-Cas classification system made*

2012 *Jennifer Doudna applies CRISPR-Cas9 to genetic engineering*

2013 *CRISPR-Cas9 research applications explode in popularity*

2014 *CRISPR-Cas9 is used on human embryonic stem cells*

2015 *CRISPR becomes Science Magazine's Breakthrough of the Year*

2016-ONWARD *Possible applications of CRISPR in the future include GMOs, cancer treatment, plastic-forming yeast, vaccine plants, & more*

SURVIVING WITHOUT THE SIXTH SENSE

By Swathi Rayasam

Though references to the "sixth sense" often bring images of paranormal phenomena to mind, the scientific world has bestowed this title to our innate awareness of our own bodies in space. Proprioception, the official name of this sense, is what allows us to play sports and navigate in the dark. Like our other five senses, our capability for spatial awareness has become so automatic that we hardly ever think about it. But scientists at the National Institute of Health (NIH) have made some breakthroughs about a genetic disorder that causes people to lack this sense, leading to skeletal abnormalities, balance difficulties, and even the inability to discern some forms of touch.[1]

The gene PIEZO2 has been associated with the body's ability to sense touch and coordinate physical actions and movement. While there is not a substantial amount of research about this gene, previous studies on mice show that it is instrumental in proprioception.[2] Furthermore, NIH researchers have recently attributed a specific phenotype to a mutation in PIEZO2, opening a potential avenue to unlock its secrets.

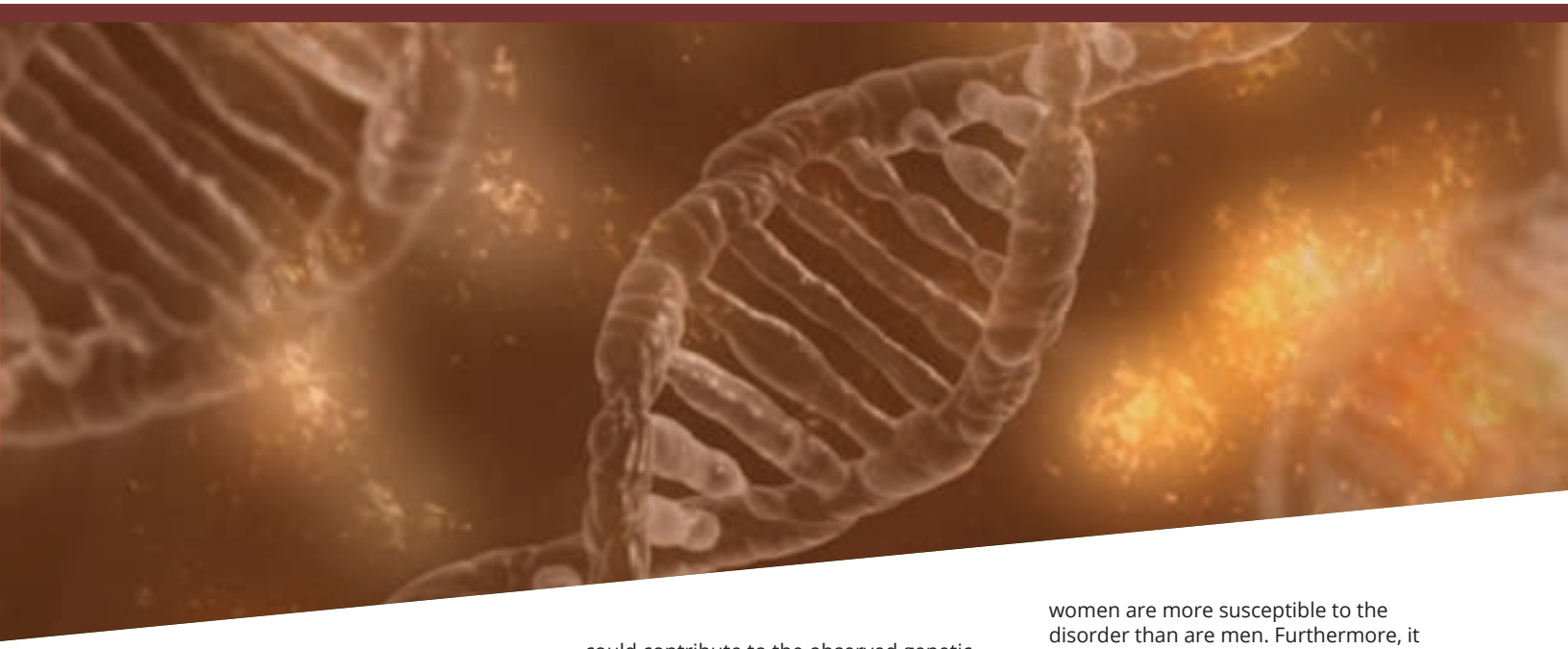
Pediatric neurologist Carsten G. Bönnermann, the senior investigator at the NIH National Institute of Neurological Disorders and Stroke, had been studying two patients with remarkably similar cases when he met Alexander Chesler at a lecture. Chesler, an investigator at the NIH National Center for Complementary and Integrative Health, joined Bönnermann in performing a series of genetic and practical tests to investigate the disorder.[1]

The subjects examined were an 8-year-old girl and an 18-year-old woman from different backgrounds and geographical areas. Even though these patients were not related, they both exhibited a set of similar and highly uncommon phenotypes. For example, each presented with scoliosis - unusual sideways spinal curvature - accompanied by fingers, feet, and hips that could bend at atypical angles. In addition to these physical symptoms, the patients experienced difficulty walking, substantial lack of coordination, and unusual responses to physical touch.[1]

These symptoms are the result of PIEZO2 mutations that block the gene's normal activity or production. Using full genome sequencing, researchers found that both patients have at least one recessively-inherited nonsense variant in the coding region of PIEZO2.[1] But because these patients represent the first well-documented cases of specific proprioceptive disorders, there is not an abundance of research about the gene itself. Available previous studies convey that PIEZO2 encodes a mechanosensitive protein - that is, it generates electrical nerve signals in response to detected changes in factors such as cell shape.[2] This function is responsible for many of our physical capabilities, including spatial awareness, balance, hearing, and touch. In fact, PIEZO2 has even been found to be expressed in neurons that control mechanosensory responses, such as perception of light touch, in mice. Past studies found that removing the gene in mouse models caused intolerable limb defects.[2] Since this gene is highly homogeneous in humans and in mice (the two versions are 95% similar), many researchers assumed that humans could not live without the gene either. According to Bönnermann and Chesler, however, it is clear that this PIEZO2 mutation does not cause a similar fate in humans.

"The gene PIEZO2 has been associated with the body's ability to sense touch and coordinate physical actions and movement"

Along with laboratory work, Bönnermann and Chesler employed techniques to further investigate the tangible effects of the mutations. Utilizing a control group for comparison, the researchers presented patients with a set of tests that examined their movement and sensory abilities. The results were startling, to say the least. The patients revealed almost a total lack of proprioception when blindfolded. They stumbled and fell while walking and could not determine which way their joints were moving without looking. In addition, both failed to successfully move a finger from their noses to a target. The



absence of certain sensory abilities is also astonishing - both patients could not feel the vibrations of a tuning fork pressed against their skin, could not differentiate between ends of a caliper pressed against their palms, and could not sense a soft brush across their palms and bottom of their feet. Furthermore, when this same soft brush was swept across hairy skin, both of the patients claimed that the sensation was prickly. This particular result revealed that the subjects were generally missing brain activation in the region linked to physical sensation, yet they appeared to have an emotional response to the brushing across hairy skin; these specific brain patterns directly contrasted with those of the control group participants. Additional tests performed on the two women revealed that the patients' detection of pain, itching, and temperature was normal when compared to the control group findings, and that they possessed nervous system capabilities and cognitive functions appropriate for their ages.[1]

Because the patients are still able to function in daily life, it is apparent that the nervous system has alternate pathways that allow them to use sight to largely compensate for their lack of proprioception.[3,4] Through further research, scientists can tap into these alternate pathways when designing therapies for similar patients. Additionally, the common physical features of both patients shed light on the fact that PIEZO2 gene mutations could contribute to the observed genetic musculoskeletal disorders.[3] This suggests that proprioception itself is necessary for normal musculoskeletal development; it is possible that abnormalities developed over time as a result of patients' postural responses and compensations to their deficiencies.[4]

"PIEZO2 gene mutations could contribute to the observed genetic musculoskeletal disorders"

In an era when our lives depend so heavily on our abilities to maneuver our bodies and coordinate movements, the idea of lacking proprioception is especially concerning. Bönnermann and Chesler's discoveries open new doors for further investigation of PIEZO2's role in the nervous system and musculoskeletal development. These discoveries can also aid in better understanding a variety of other neurological disorders. But, there is still much unknown about the full effects of the PIEZO2 mutation. For example, we do not know if musculoskeletal abnormalities injure the spinal cord, if the gene mutation poses additional consequences for the elderly, or if women are more susceptible to the disorder than are men. Furthermore, it is very likely that there are numerous other patients around the world who present similar symptoms to the 8-year-old girl and 18-year-old woman observed by Bönnermann and Chesler. While researchers work towards gaining a better understanding of the disease and developing specific therapies, these patients must focus on other coping mechanisms, such as reliance on vision, to accomplish even the most basic daily activities. Because contrary to popular perception, the sixth sense is not an ability to see ghosts; it is so much more.

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DESIGN BY Albert Han
EDITED BY Allison Chang

THE HEALTH OF HEALTHCARE PROVIDERS

BY DANIEL NGO

A CAR CRASH. A HEART ATTACK. A DRUG OVERDOSE.

No matter what time of day, where you are, or what your problem is, emergency medical technicians (EMTs) will be on call and ready to come to your aid. These health care providers are charged with providing quality care to maintain or improve patient health in the field, and their efforts have saved the lives of many who could not otherwise find care on their own. While these EMTs deserve praise and respect for their line of work, what they deserve even more is consideration for the health issues that they themselves face. Emergency medical technicians suffer from a host of long-term health issues, including weight gain, burnout, and psychological changes.

The daily "schedule" of an EMT is probably most characterized by its variability and unpredictability. The entirety of their day is a summation of what everyone in their area is doing, those people's health issues, and the uncertainty of life itself. While there are start and end times to their shifts, even these are not hard and fast--shifts have the potential to start early or end late based on when people call 911. An EMT can spend their entire shift on the ambulance, without time to eat a proper meal or to get any sleep. These healthcare providers learn to catch a few minutes of sleep here and there when possible. Their yearly schedules are also unpredictable, with lottery systems in place to ensure that someone is working every day, at all hours of the day, while maintaining some fairness. Most services will have either 12 or 24 hour shifts, and this lottery system can result in EMTs having stacked shifts that are either back to back or at least within close proximity to one another. This only enhances the possibility of sleep disorders, with 70 percent of EMTs reporting having at least one sleep problem.[1] While many people have experienced the effects of exhaustion and burnout due to a lack of sleep, few can say that their entire professional career has been characterized by these feelings. EMTs have been shown to be more than twice as likely than control groups to have moderate to high scores on the Epworth Sleepiness Scale (ESS), which is correlated with a greater likelihood of falling asleep during daily activities such as conversing, sitting in public places, and driving.[1] The restriction and outright deprivation of sleep in EMTs has been shown to cause a large variety of health problems, and seems to be the main factor in the decline of both physical and mental health for EMTs.

> **AN EMT NEEDS TO BE READY AROUND THE CLOCK TO RESPOND, WHICH MEANS THERE REALLY ISN'T ANY TIME TO SIT DOWN AND HAVE A PROPER MEAL.**

A regular amount of sleep is essential in maintaining a healthy body. Reduced sleep has been associated with an increase in weight gain, cardiovascular disease, and weakened immune system functions. Studies have shown that, at least in men, short sleep durations are linked to weight gain and obesity, which is potentially due to alterations in hormones that regulate appetite.[2,3] Due to this trend, it is no surprise that a 2009 study found that sleep durations that deviated from an ideal 7-8 hours, as well as frequent insomnia, increased the risk of cardiovascular disease.

The fact that EMTs often have poor diets compounds that risk. An EMT needs to be ready around the clock to respond, which means there really isn't any time to sit down and have a proper meal. Fast food becomes the meal of choice due to its convenience, both in availability and speed. Some hospitals have attempted to improve upon this shortcoming in the emergency medical service (EMS) world by providing some snacks and drinks at the hospital. This, however, creates a different issue due to the high calorie nature of these snacks. The body generally knows when it is full by detecting stretch in the stomach, and signaling the brain that enough food has been consumed. In a balanced diet, a lot of this space should be filled with fruits, vegetables, and overall low calorie items unless you are an athlete who uses a lot more energy. By eating smaller, high calorie items, an EMT will need to eat more in order to feel full, but this will result in the person exceeding their recommended daily calories. The extra energy will often get stored as fat, compounding the weight gain due to sleep deprivation. Studies involving the effects of restricted sleep on the immune system are less common, but one experiment demonstrated markers of systemic inflammation which could, again, lead to cardiovascular disease and obesity.[2]

Mental health is not spared from complications due to long waking periods with minimal sleep. A study was conducted to test the cognitive abilities of subjects experiencing varying amounts of sleep restriction;the results showed that less sleep led to cognitive deficits, and being awake for more than 16 hours led to deficits regardless of how much sleep the subject had gotten.[4] This finding affects both the EMTs, who can injure themselves, and the patients, who may suffer due

The stress in the everyday job of an EMT creates a poor environment for mental health.

With unpredictable and variable schedules, EMTs lack sufficient sleep.

EMTs experience weight gain due to a poor diet, which is a consequence of the lack of sufficient sleep and of the fast paced nature of their job.

WHILE MANY GO INTO THE HEALTHCARE FIELD TO HELP OTHERS, EXHAUSTION AND DESENSITIZATION CREATE A SORT OF CYNICISM IN ORDER TO DEFEND AGAINST THE ENORMOUS EMOTIONAL BURDEN THAT COMES WITH TREATING PATIENTS DAY IN AND DAY OUT.

to more errors being made in the field. First year physicians, who similarly can work over 24 hour shifts, are subject to an increased risk of automobile crashes and percutaneous (skin) injuries when sleep deprived.[5]

These injuries often happen when leaving a shift. A typical EMT shift lasts from one morning to the next, and the EMT will leave his or her shift during rush hour on little to no sleep, increasing the dangerous possibility of falling asleep or dozing at the wheel. A similar study to the one on first year physicians mentioned prior studied extended duration work at critical-care units, and found that long shifts increased the risk of medical errors and lapses in attention.[6] In addition to the more direct mental health problems posed by the continuous strain, EMTs and others in the healthcare field also face more personal issues, including burnout and changes in behavior. A study on pediatric residents, who face similar amounts of stress and workloads, established that 20% of participants were suffering from depression, and 75% met the criteria for burnout, both of which led to medical errors made during work.[7] A separate study found that emergency physicians suffering from burnout also faced high emotional exhaustion, depersonalization, and a low sense of accomplishment.[8] While many go into the healthcare field to help others, exhaustion and desensitization create a sort of cynicism in order to defend against the enormous emotional burden that comes with treating patients day in and day out.

Sleep deprivation, long work duration, and the stress that comes with the job contribute to a poor environment for the physical and mental health of emergency medical technicians and other healthcare providers. However, a recent study has shown that downtime, especially after dealing with critical patients, led to lower rates of depression and acute stress in EMTs.[9] While this does not necessarily ameliorate post-traumatic stress or burnout, it is a start to addressing the situation. Other possible interventions would include providing more balanced meals at hospitals that are readily available to EMTs, as well as an improved scheduling system that prevents or limits back to back shifts. These concepts can apply to others facing high workloads with abnormal sleeping schedules as well, including college students, who are also at risk for mood disorders and a poorer quality of life due to the rigors of college life.[10]

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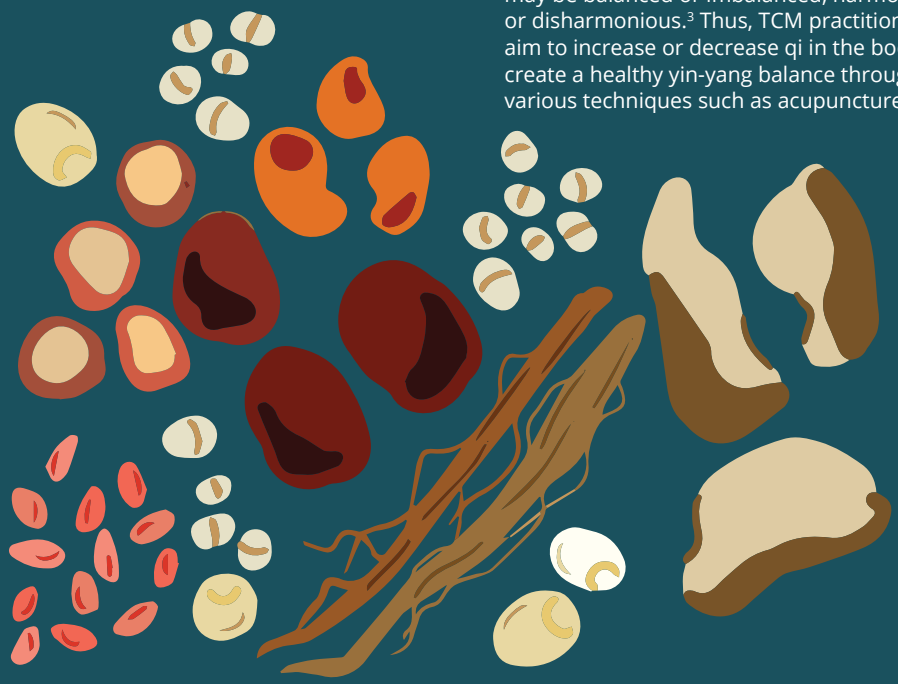
EAST JOINS WEST

THE RISE OF INTEGRATIVE MEDICINE

JEANIE KIM

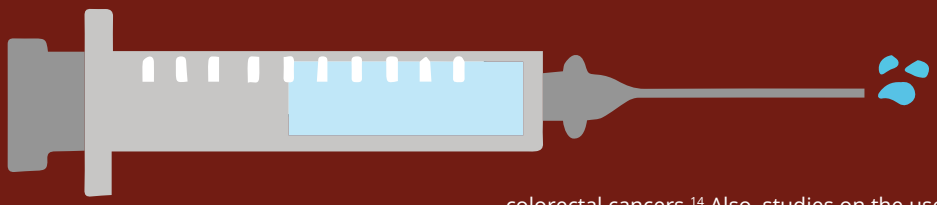
An ancient practice developed thousands of years ago and still used by millions of people all over the world, Traditional Chinese Medicine (TCM) has undoubtedly played a role in the field of medicine. But just what is TCM? Is it effective? And can it ever be integrated with Western medicine?

The techniques of TCM stem from the beliefs upon which it was founded. The theory of the yin and yang balance holds that all things in the universe are composed of a balance between the forces of yin and yang. While yin is generally associated with objects that are dark, still, and cold, yang is associated with items that are bright, warm, and in motion.[1] In TCM, illness is believed to be a result of an imbalance of yin or yang in the body. For instance, when yin does not cool yang, yang rises and headaches, flushing, sore eyes, and sore throats result. When yang does not warm yin, poor circulation of blood, lethargy, pallor, and cold limbs result. TCM aims to determine the nature of the disharmony and correct it through a variety of approaches. As the balance is restored in the body, so is the health.[2]



Another fundamental concept of TCM is the idea of qi, which is the energy or vital force responsible for controlling the functions of the human mind and body. Qi flows through the body through 12 meridians, or channels, that correspond to the 12 major organ systems, and 8 extra meridians that are all interconnected with the major channels. Just like an imbalance between yin and yang, disruption to the flow causes disease, and correction of the flow restores the body to balance.[2] In TCM, disease is not viewed as something that a patient has. Rather, it is something that the patient is. There is no isolated entity called "disease," but only a whole person whose body functions may be balanced or imbalanced, harmonious or disharmonious.[3] Thus, TCM practitioners aim to increase or decrease qi in the body to create a healthy yin-yang balance through various techniques such as acupuncture, herbal medicine, nutrition, and mind/body exercise (tai chi, yoga). Eastern treatments are dismissed by some as superfluous to the recovery process and even harmful if used in place of more conventional treatments. However, evidence exists indicating Eastern treatments can be very effective parts of recovery plans.

The most common TCM treatments are acupuncture, which involves inserting needles at precise meridian points, and herbal medicine, which refers to using plant products (seeds, berries, roots, leaves, bark, or flowers) for medicinal purposes. Acupuncture seeks to improve the body's functions by stimulating specific anatomic sites—commonly referred to as acupuncture points, or acupoints. It releases the blocked qi in the body, which may be causing pain, lack of function, or illness. Although the effects of acupuncture are still being researched, results from several studies suggest that it can stimulate function in the body and induce its natural healing response through various physiological systems.[4] According to the WHO (World Health Organization), acupuncture is effective for treating 28 conditions, while limited but probable evidence suggests it may have an effective value for many more. Acupuncture seems to have gained the most clinical acceptance as a pain reduction therapy. Research from an international team of experts pooled the results of 29 studies on chronic pain involving nearly 18,000 participants—some had acupuncture, some had "sham" acupuncture, and some did not have acupuncture at all. Overall, the study found acupuncture treatments to be superior to both a lack of acupuncture treatment and sham acupuncture treatments for the reduction of chronic pain, suggesting that such treatments are a reasonable option for afflicted patients.[5] According to a study carried out at the Technical University of Munich, people with tension headaches and/or migraines may find acupuncture to be very effective in alleviating their symptoms.[6] Another study at



the University of Texas M.D. Anderson Cancer Center found that twice weekly acupuncture treatments relieved debilitating symptoms of xerostomia--severe dry mouth--among patients undergoing radiation for head and neck cancer.[7] Additionally, acupuncture has been demonstrated to both enhance performance in the memory-related brain regions of mild cognitive impairment patients (who have an increased risk of progressing towards Alzheimer's disease),[8] and to provide therapeutic advantages in regulating inflammation in infection and inflammatory disease.[9]

Many studies have also demonstrated the efficacy of herbal medicine in treating various illnesses. Recently, the WHO estimated that 80% of people worldwide rely on herbal medicines for some part of their primary health care. Researchers from the University of Adelaide have shown that a mixture of extracts from the roots of two medicinal herbs, Kushe and Baituling, works to kill cancer cells.[10] Furthermore, scientists concluded that herbal plants have the potential to delay the development of diabetic complications, although more investigations are necessary to characterize this antidiabetic effect.[11] Finally, a study found that Chinese herbal formulations appeared to alleviate symptoms for some patients with Irritable Bowel Syndrome, a common functional bowel disorder that is characterized by chronic or recurrent abdominal pain and does not currently have any reliable medical treatment.[12]

Both TCM and Western medicine seek to ease pain and improve function. Can the two be combined? TCM was largely ignored by Western medical professionals until recent years, but is slowly gaining traction among scientists and clinicians as studies show that an integrative approach has been effective. For instance, for patients dealing with chronic pain, Western medicine can stop the pain quickly with medication or interventional therapy, while TCM can provide a longer-lasting solution to the underlying problem with milder side effects and a greater focus on treating the underlying illness.[13] A study by Cardiff University's School of Medicine and Peking University in China showed that combining TCM and Western medicine could offer hope for developing new treatments for liver, lung, bone, and colorectal cancers.[14] Also, studies on the use of traditional Chinese medicines for the treatment of multiple diseases like bronchial asthma, atopic dermatitis, and IBS showed that an interdisciplinary approach to TCM may lead to the discovery of new medicines.[15]

TCM is still a developing field in the Western world, and more research and clinical trials on the benefits and mechanisms of TCM are being conducted. While TCM methods such as acupuncture and herbal medicine must be further examined to be accepted as credible treatment techniques in modern medicine, they have been demonstrated to treat various illnesses and conditions. Therefore, while it is unlikely for TCM to be a suitable standalone option for disease management, it does have its place in a treatment plan with potential applications alongside Western medicine. Utilizing TCM as a complement to Western medicine presents hope in increasing the effectiveness of healthcare treatment.

WESTERN MEDICINE CAN STOP THE PAIN QUICKLY WITH MEDICATION OR INTERVENTIONAL THERAPY, WHILE TCM CAN PROVIDE A LONGER LASTING SOLUTION TO THE UNDERLYING PROBLEM WITH MILDER SIDE EFFECTS AND A GREATER FOCUS ON TREATING THE UNDERLYING ILLNESS.

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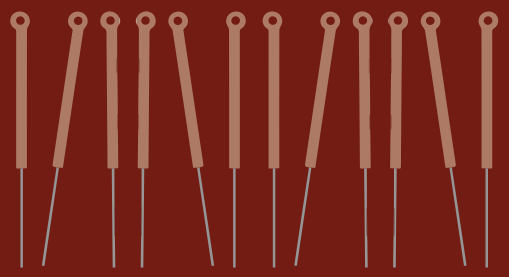

DESIGN BY Juliana Wang
EDITED BY Jackson Stiles

REWRITING THE GENETIC CODE

BY ALBERT TRUONG

DNA, or deoxyribonucleic acid, is at the root of all life as we know it. Using just four component nucleotide bases, DNA contains all the information needed to build any protein. To make a protein, DNA is transcribed into mRNA, which is in turn "translated" into a protein by molecules called ribosomes. More specifically, the mRNA is "read" by ribosomes in groups of three base pairs called codons, each of which codes for one of 20 possible amino acids. The set of rules that determines which codon codes for which amino acid is called the genetic code, and it is common to almost all known organisms--everything, from bacteria to humankind, shares the same protein expression schema. It is this common code that allows synthetic biologists to insert one organism's genes into another to create transgenic organisms; generally, a gene will be expressed the same way no matter what organism possesses it. Interestingly, some scientists are attempting to alter this biological norm: rather than modifying genes, they are attempting to modify the genetic code itself in order to create genetically recoded organisms, or GROs.

This modification is possible due to the redundancy of the genetic code. Because there are 64 possible unique codons and only 20 amino acids found in nature, many amino acids are specified by more than one codon. Theoretically, then, researchers should be able to swap every instance of a particular codon with a synonymous one without harming a cell, then repurpose the eliminated codon.1 This was proven possible in a 2013 paper by Lajoie et al. published in Science; in it, a team of scientists working with E. coli cells substituted all instances of the codon UAG, which signals cells to stop translation of a protein, with the functionally equivalent sequence UAA. They then deleted release factor 1 (RF1), the protein that gives UAG its stop function. Finally, they reassigned the function of UAG to code for a non-standard amino acid (NSAA) of their choice.[1]

In a more recent paper, Ostrov et al. took this recoding even further by excising seven codons from the E. coli genome, reducing it to 57 codons. Because there are 62,214 instances of these codons in the E. coli genome, researchers couldn't directly excise them from the E. coli DNA with typical gene-editing strategies. Instead, they resorted to synthesizing long stretches of the modified genome, inserting them into the bacteria, and testing to make sure the modifications were not lethal. At time of publishing, they had completed testing of 63% of the recoded genes and found that most of their changes had not significantly impaired the bacteria's fitness, indicating that such large changes to the genetic code are feasible.[2]

Should Ostrov's team succeed in their recoding, there are a number of possible applications for the resulting GRO. One would be the creation of virus-resistant cells.[1, 2,3] Viral DNA injected into recoded bacteria would be improperly translated if it contained the repurposed codons due to the modified protein expression machinery the GRO possesses. Such resistance was demonstrated by Lajoie in an experiment in which he infected E. coli modified to have no UAG codons with two types of viruses: a T7 virus that contained UAG codons in critical genes, and a T4 virus that did not. As expected, the modified cells showed resistance to T7, but were infected normally by T4. The researchers concluded that more extensive genetic code modifications would probably make the bacteria immune to viral infection entirely.[2] Using such organisms in lieu of unmodified ones in bacteria-dependent processes like cheese- and yogurt-making, biogas manufacturing, and hormone production would reduce the cost of those processes by eliminating the hassle and expense associated with viral infection.[3,4] It should be noted that while GROs would theoretically be resistant to infection, they would also be unable to "infect" anything themselves. If GRO genes were to be taken up by other organisms, they would also be improperly translated as well, making horizontal gene transfer impossible. This means that GROs are "safe" in the sense that they would not be able to spread their genes to organisms in the wild like other GMOs can.[5]

GROs could also be used to make novel proteins. The eliminated codons could be repurposed to code for amino acids not found in nature, or non-standard amino acids (NSAAs). It is possible to use GRO's to produce a range of proteins with expanded chemical properties, free from the limits imposed by strictly using the 20 standard amino acids.[2,3] These proteins could then be used in medical or industrial applications. For example, the biopharmaceutical company Ambrx develops proteins with NSAAs for use as medicine to treat cancer and other diseases.[6]

While GRO's can do incredible things, they are not without their drawbacks. Proteins produced by the modified cells could turn out to be toxic, and if these GROs manage to escape from the lab into the wild, they could flourish due to their resistance to viral infection.[2,3] To prevent this scenario from happening, Ostrov's team has devised a failsafe. In previous experiments, the researchers modified bacteria so that two essential genes, named adk and tyrS, depended on NSAAs to function. Because NSAAs aren't found in the wild, this modification effectively confines the bacteria within the lab, and it is difficult for the organisms to thwart this containment strategy spontaneously. Ostrov et al. intend to implement this failsafe in their 57-codon E. coli.[2]

Genetic recoding is an exciting development in synthetic biology, one that offers a new paradigm for genetic modification. Though the field is still young and the sheer amount of DNA changes needed to recode organisms poses significant challenges to the creation of GROs, genetic recoding has the potential to yield tremendously useful organisms.

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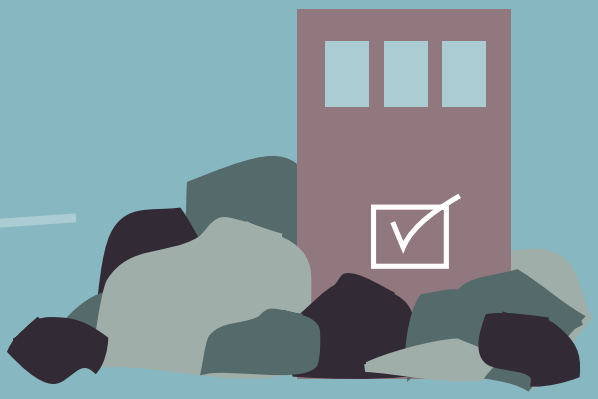
Icon by Tim Madle via the Noun Project

DESIGN BY Jason Dennis, Vidya Giri
EDITED BY Aseem Utrankar



BY RISHI SURESH

HEALTHCARE REFORM FOR THE MENTALLY ILL

Neuropsychiatric illnesses are some of the most devastating conditions in the world. Despite being non-communicable, mental and neurological conditions are estimated to contribute to approximately 30.8% of all of the years lived in disability.[1] Furthermore, in developed nations like the United States, mental disorders have been reported to erode around 2.5% of the yearly gross national product, which fails to account for the opportunity cost of families who have to take care of patients long-term.[1] If left untreated, many patients with neuropsychiatric illnesses cannot find gainful employment; their aberrant behavior is stigmatized and prevents forward professional and personal advancement. In fact, about three times as many individuals living with mental illnesses are in prisons rather than rehabilitative psychiatric institutions.[2]

Though the Affordable Care Act has substantially decreased the amount of uninsured individuals in the U.S., there are still millions of people who fall into something called the Medicaid gap.[3] People in this group make too much money for Medicaid, but too little money to be able to qualify for government tax credits in purchasing an insurance plan. In an attempt to fix this 'hole,' the federal government offers aid to states in order to expand their Medicaid programs as needed.[4] States that have accepted the Medicaid expansion sponsored by the federal government, have seen sudden reductions in their populations of uninsured people, which has directly improved quality of life for the least fortunate people in society. However, in the many states that continue to reject federal aid, the situation is considerably worse—especially for the mentally ill.

Mental health patients are especially vulnerable to falling into the Medicare gap. Many patients suffering from psychiatric conditions often are unable to find serious employment. According to a report by the Department of Health and Human Services in March 2016, there are 1.9 million low-income, uninsured individuals with mental health disorders who cannot access proper healthcare resources.[5] These impoverished psychiatric patients are originally eligible for Medicare. However, once their treatment takes and they become employed, they might pass the Medicare income threshold. If their private health insurance does not cover the cost of their psychiatric treatments, patients will relapse, creating a vicious cycle that is exceptionally difficult to break out of.[6]

"ABOUT THREE TIMES AS MANY INDIVIDUALS LIVING WITH MENTAL ILLNESSES ARE IN PRISONS RATHER THAN REHABILITATIVE PSYCHIATRIC INSTITUTIONS."

Furthermore, many psychiatric illnesses often initially present during adolescence or early adulthood, which is right around the time students leave home to go to college. So, during initial presentation, many students lack the proper support system necessary to deal with their condition, causing many to drop out of college or receive poor grades. Families often chalk up these conditions to poor adjustments to a brand new college environment at home, preventing psychiatric patients from properly receiving treatment.[6] Alone, many students with psychiatric conditions delay seeking treatment, fearing being labeled as "crazy" or "insane" by their peers.

Under the status quo, psychiatric patients face significant barriers to care. As the Medicaid gap is unfortunately subject to political maneuverings, it probably will not be fixed immediately. However, the United States could fund the expansion of Assertive Community Treatment programs, which provide medication, therapy, and social support in an outpatient setting.[7] Such programs dramatically reduce hospitalization times for psychiatric patients, alleviating the costs of medical treatment. Funding these programs would help insurance issues from being a deterrent to treatment.

In the current system, psychiatric patients face numerous deterrents to receiving treatment, from lack of family support to significant social stigma. Having access to health insurance be a further barrier to care is a significant oversight of the current system and ought to be corrected.

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DESIGN BY Evelyn Syau
EDITED BY Jacqueline Locarno

astrocytes

SHINING THE SPOTLIGHT ON THE BRAIN'S RISING STAR

KELSEY SANDERS

WE HAVE WITHIN US the most complex and inspiring stage to ever be set: the human brain. The cellular components of the brain act as players, interacting through chemical and electrical signaling to elicit emotions and convey information. Although most of our attention has in the past been focused on neurons, which were erroneously presumed to act alone in their leading role, scientists are slowly realizing that astrocytes—glial cells in the brain that were previously assumed to only have a supportive role in association with neurons—are so much more than merely supporting characters .

Though neurons are the stars, most of the brain is actually composed of supportive cells like microglia, oligodendrocytes, and, most notably, astrocytes. Astrocytes, whose formal name is a misnomer given that modern imaging technology reveals they actually maintain a branch-like shape rather than a star-like one, exist as one of three mature types in the grey matter, white matter, or retina. Structurally, the grey matter astrocyte variant exhibits bushy, root-like tendrils and a spherical shape. The white matter variant, commonly found in the hippocampus, favors finer extensions called processes. The retinal variant features an elongated structure.[1]

Functionally, astrocytes were previously believed to play a solely supportive role, as they constitute a large percentage of the glial cells present in the brain. Glial cells are essentially all of the non-neural cells in the brain that assist in basic functioning; they themselves are not electrically excitable. However, current research suggests that astrocytes play far more than merely a supporting role in the brain. Astrocytes and neurons directly interact to interpret stimuli and store memories[4], among many other yet undiscovered tasks.

Although astrocytes are not electrically excitable, astrocytes communicate with neurons via calcium signaling and the neurotransmitter glutamate.[2] Calcium signaling works whereby intracellular calcium in astrocytes is released upon excitation and is propagated in waves that move through neighboring astrocytes and neurons. Neurons experience a responsive increase in intracellular calcium if they are directly touching affected astrocytes, as the signal is communicated via gap junctions rather than synaptically. Such signaling is unidirectional; calcium excitation can move from astrocyte to neuron, but not from neuron to astrocyte.[3] The orientation of astrocytes in different regions of the brain and their proximity to neurons allows them to form close communication networks that help information travel throughout the central nervous system.

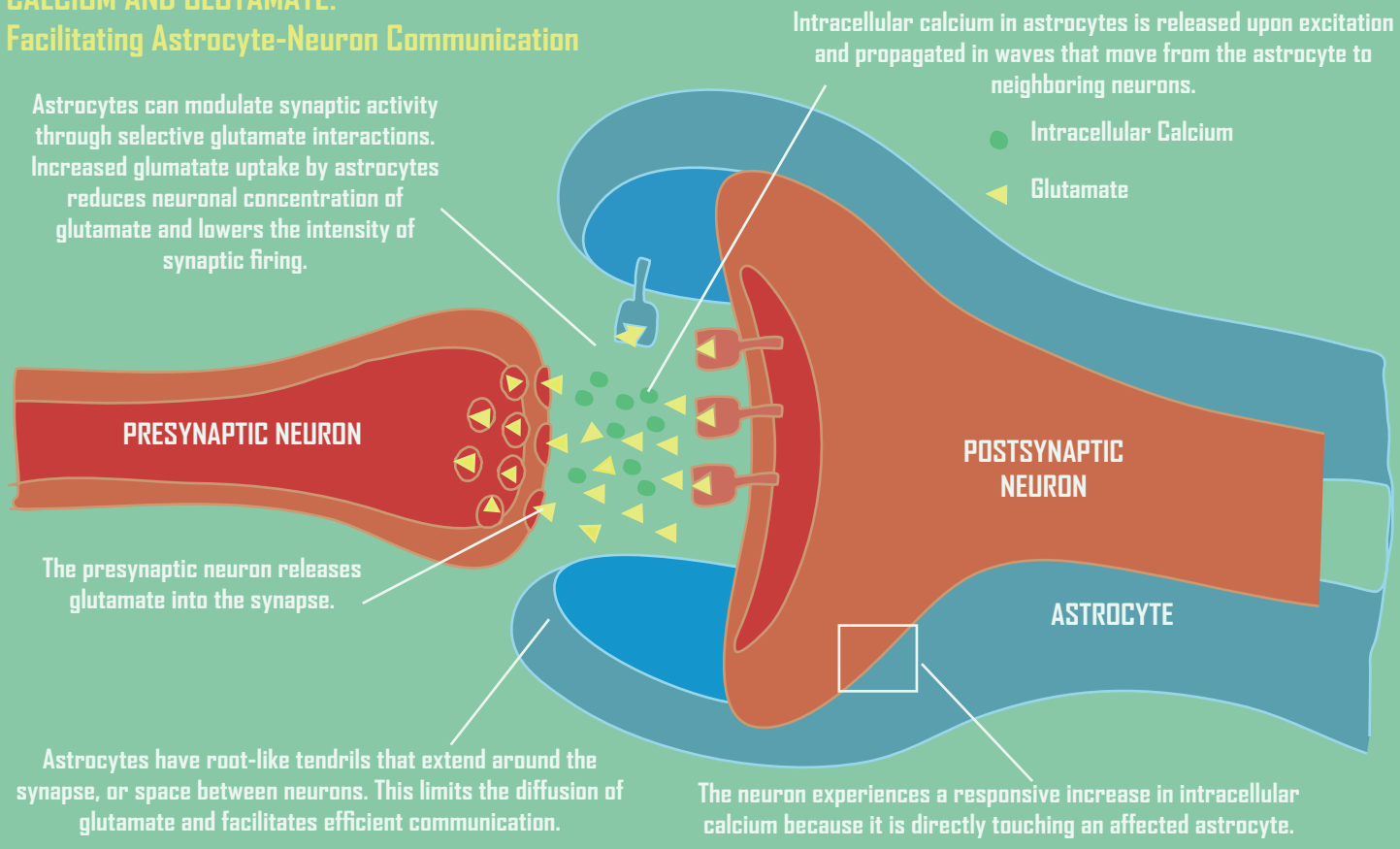
Astrocytes in the hippocampus play a role in memory development. They act as an intermediary cell in a neural inhibitory circuit that utilizes acetylcholine, glutamate, and Gamma-Aminobutyric Acid (GABA) to solidify experiential learning and memory formation. Disruption of cholinergic signaling, signaling relating to acetylcholine, prohibits the formation of memories in the dentate gyrus of the hippocampal formation. Astrocytes act as mediators that convert cholinergic inputs into glutamatergic activation of neurons.[4] Without the assistance of astrocytic networks in close association with neurons, memory formation and long-term potentiation would be far less efficient if even still possible.

Astrocytes' ability to interpret and release chemical neurotransmitters, especially glutamate, allows them to regulate the intensity of synaptic firing in neurons.[5] Increased glutamate uptake by astrocytes reduces synaptic strength in associated neurons by decreasing neuronal concentration of glutamate.[6] Regulation of synaptic strength in firing is crucial for healthy brain function. If synapses fire too much or too powerfully, they may overwhelm the brain. Conversely, if synapses fire too infrequently or not strongly enough, messages might not make their way throughout the central nervous system. The ability of astrocytes to modulate synaptic activity through selective glutamate interactions puts them in an integral position to assist in consistent and efficient transmission of information throughout the human body.

Through regulation of neurotransmitters and psychoactive chemicals in the brain, astrocytes are able to maintain homeostasis in the central nervous system. Potassium buffering and balancing of pH are the major ways that astrocytes assist in maintaining optimal conditions for brain function.[7] Astrocytes are able to compensate for the slow re-uptake of potassium by neurons, thus decluttering the extracellular space of free potassium in response to neuronal activity. Re-uptake of these ions is extremely important to brain function as synaptic transmission by neurons relies on electrically switching membrane potentials along neuronal axons.

Due to their role in synaptic regulation and their critical position in the brain network, astrocytes also have the potential to aid in therapies for dealing with neurological disorders. For example, epileptic seizures have been found to be related to an excitatory loop between neurons and astrocytes. Focal ictal discharges, the brain activity responsible for epileptic seizures, are correlated to hyperactivity in neurons as well as an increase in intracellular calcium in nearby astrocytes; the calcium

CALCIUM AND GLUTAMATE:
Facilitating Astrocyte-Neuron Communication



oscillations then spread to neighboring astrocyte networks to perpetuate the ictal discharge and continue the seizure. Astrocytes in epileptic brain tissues exhibit structural changes that may favor such a positive feedback loop. Inhibition of calcium uptake in astrocytes, and consequent decrease in release of glutamate and ATP, is linked to suppression of ictal discharges, and therefore linked to a decrease in the severity and occurrence of epileptic seizures.[8] Furthermore, it is evident that astrocyte activity also plays a role in memory loss associated with Alzheimer's Disease. Although astrocytes in the hippocampus contain low levels of the neurotransmitter GABA under normal conditions, hyperactive astrocytes near amyloid plaques in affected individuals exhibit increased levels of GABA that are not evident in other types of glial cells. GABA is the main inhibitory neurotransmitter in the brain, and abnormal increases in GABA are associated with Alzheimer's Disease; introducing antagonist molecules has been shown to reduce memory impairment, but at the cost of inducing seizures.[9] Since there is a shift in GABA release by astrocytes between normal and diseased individuals, astrocytes could be as the key to remedying neurodegenerative conditions like Alzheimer's.

In addition to aiding in treatment of neurological disorders, astrocytes may also help stroke victims. Astrocytes ultimately support damaged neurons by donating their mitochondria to the neurons.[10] Mitochondria produce adenosine triphosphate (ATP) and act as the energy powerhouse in eukaryotic cells; active cells like neurons cannot survive without them. Usually neurons accommodate their exceptionally large energy needs by multiplying their intracellular mitochondria via fission. However, when neurons undergo stress or damage, as in the case of stroke, the neuron is left without its source of energy. New research suggests that astrocytes come to the rescue by releasing their own mitochondria into the extracellular environment in response to high levels of the enzyme CD38, so that damaged neurons can absorb the free mitochondria and survive the damage.[11] Astrocytes also help restore neuronal mitochondria and ATP production post-insult by utilizing lactate shuttles, in which astrocytes generate lactate through anaerobic respiration and then pass the lactate to neurons where it can be used as a substrate for oxidative metabolism[12]. Such a partnership between astrocytes and neurons presents researchers with the option of using astrocyte-targeted therapies to salvage neuronal systems in stroke victims and others afflicted by ailments associated with mitochondrial deficiencies in the brain.

Essentially, astrocytes are far more than the background supporters they were once thought to be. Before modern technological developments, the capabilities and potential of astrocytes were left woefully unnoticed. Astrocytes interact both directly and indirectly with neurons through chemical signaling to create memories, interpret stimuli, regulate signaling, and, maintain a healthy central nervous system. A greater understanding of the critical role astrocytes play in the human brain could allow scientists to develop astrocyte-targeted therapeutic practices. As astrocytes slowly inch their way into the spotlight of neuroscientific research, there is so much yet to be discovered.

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DESIGN BY Evelyn Syau, Vidya Giri
EDITED BY Rebecca Chen

FIRE THE LASERS

BY NIGEL EDWARD

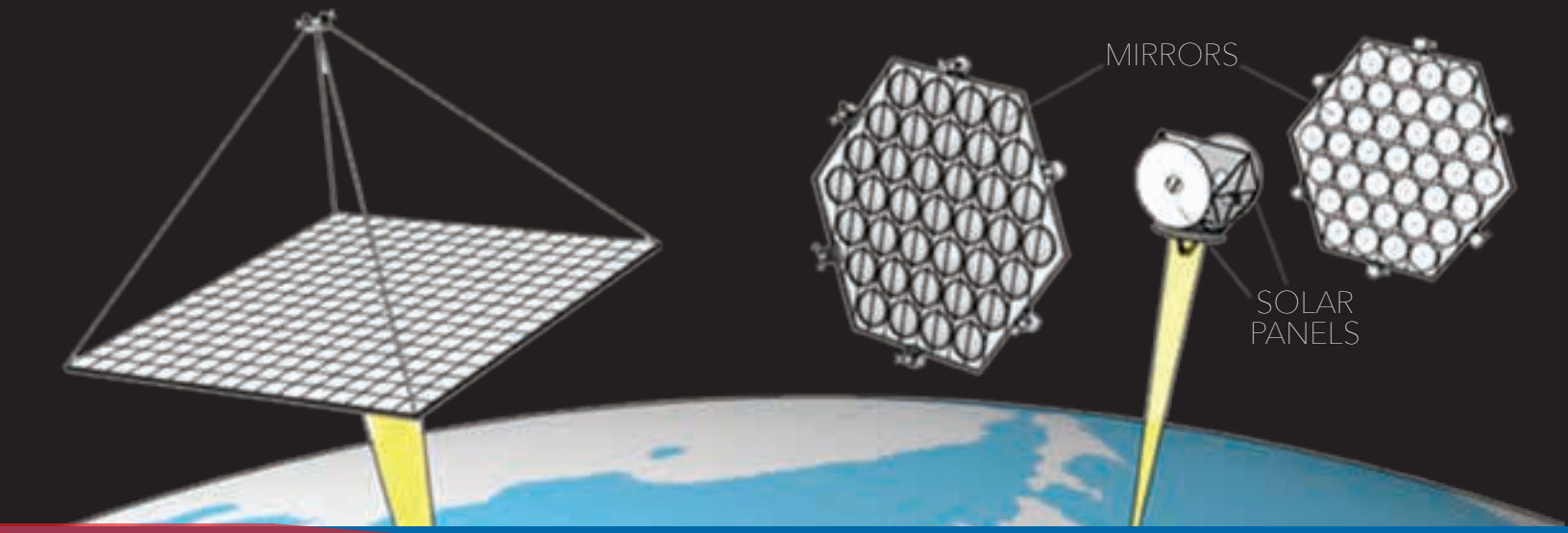
Imagine a giant solar harvester flying in geosynchronous orbit, which using solar energy, beams radiation to a single point 36, 000 km away. It would look like a space weapon straight out of Star Wars. Surprisingly, this concept might be the next so-called "moonshot" project that humanity needs to move forward. In space-based solar power generation, a solar harvester in space like the one discussed above would generate DC current from solar radiation using photovoltaic cells, and then convert it into microwaves. These microwaves would then be beamed to a rectifying antenna (or a rectenna) on the ground, which would convert them back into direct current (DC). Finally, a converter would change the DC energy to AC to be supplied into the grid.[1]

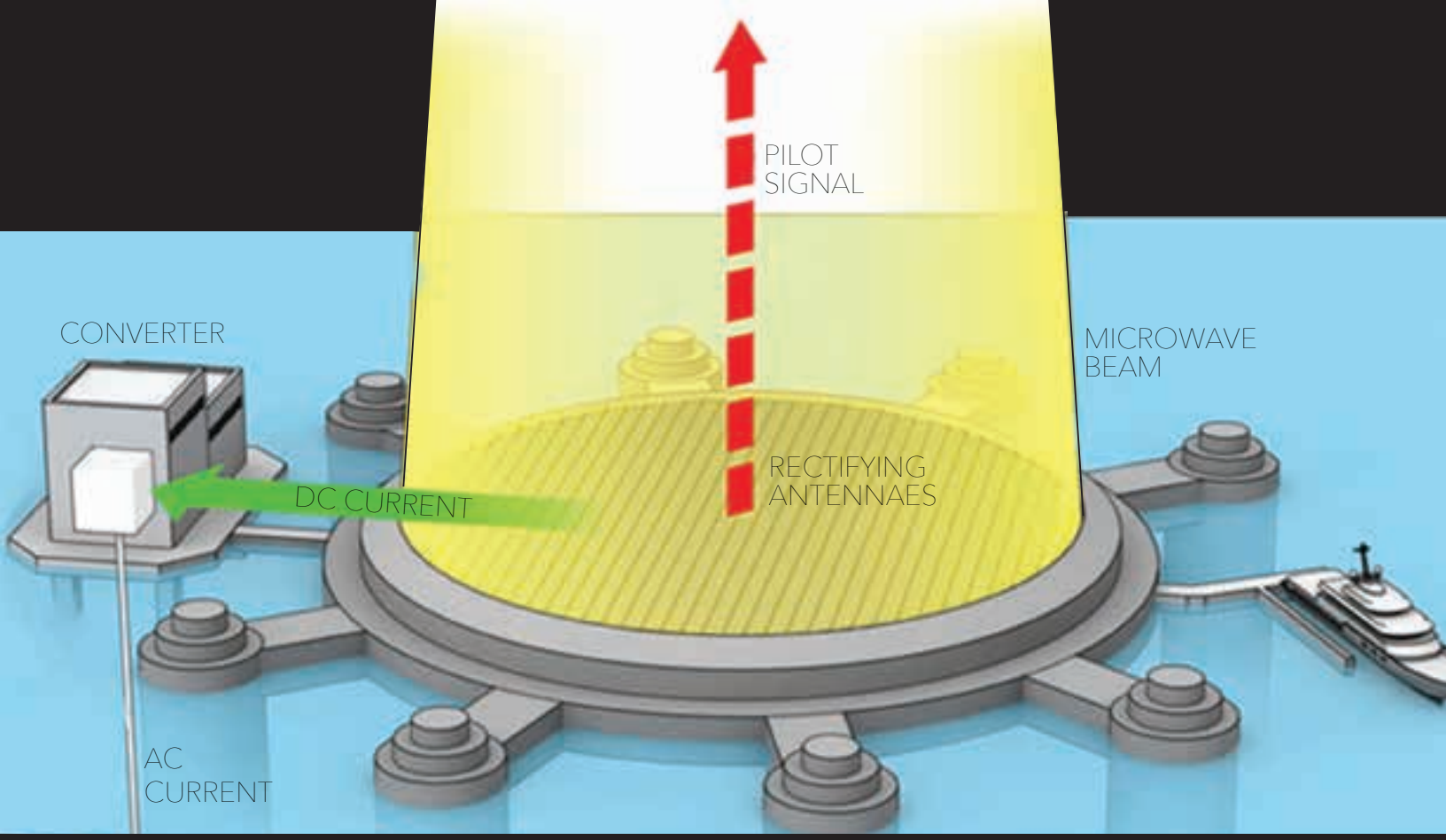
With ever-increasing global energy consumption and rising concerns of climate change due to the burning of fossil fuels, there has been increasing interest in alternative energy sources. Although renewable energy technology is improving every year, its current energy capacity is not enough to obviate the need for fossil fuels. Currently, wind and solar sources have capacity factors (a ratio of an energy source's actual output over a period of time to its potential output) of around 34 and 26 percent, respectively. In comparison, nuclear and coal sources have capacity factors of 90 and 70 percent, respectively.[2] Generation of energy using space solar power satellites (SSPSs) could pave the path humanity needs to move towards a cleaner future. Unlike traditional solar power, which relies on favorable weather conditions, SSPSs would allow continuous, green energy generation.

> UNLIKE TRADITIONAL SOLAR POWER, WHICH RELIES ON FAVORABLE WEATHER CONDITIONS, SPACE SOLAR POWER SATELLITES WOULD ALLOW CONTINUOUS, GREEN ENERGY GENERATION.

Although space-based solar power (SBSP) might sound pioneering, scientists have been flirting with the idea since Dr. Peter Glaser introduced the concept in 1968. Essentially, SBSP systems can be characterized by three elements: a large solar collector in geostationary orbit fitted with reflective mirrors, wireless transmission via microwave or laser, and a receiving station on Earth armed with rectennas.[3] Such an implementation would require complete proficiency in reliable space transportation, efficient power generation and capture, practical wireless transmission of power, economical satellite design, and precise satellite-antenna calibration systems. Collectively, these goals might seem insurmountable, but taken separately, they are actually feasible. Using the principles of optics, scientists are optimizing space station design to maximize energy collection.[4] There have been advancements in rectennas that allow the capture of even weak, ambient microwaves.[5] With the pace of advancement speeding up every year, it's easy to feel like the future of renewable energy is rapidly approaching. However, these advancements will be limited to literature if there are no global movements to utilize SBSP.

Japan Aerospace Exploration Agency (JAXA) has taken the lead in translating SBSP from the page to the launch pad. Due to





its lack of fossil fuel resources and the 2011 incident at the Fukushima Daiichi nuclear plant, Japan, in desperate need of alternative energy sources, has proposed a 25-year technological roadmap to the development of a one-gigawatt SSPS station. To accomplish this incredible feat, Japan plans on deploying a 10,000 metric ton solar collector that would reside in geostationary orbit around Earth.6 Surprisingly, the difficult aspect is not building and launching the giant solar collector; it's the technical challenge of transmitting the energy back to earth both accurately and efficiently. This is where JAXA has focused its research.

Historically, wireless power transmission has been accomplished via laser or microwave transmissions. Laser and microwave radiation are similar in many ways, but when it comes down to which one to use for SBSP, microwaves are a clear winner. Microwaves have longer wavelengths (usually lying between five and ten centimeters) than those of lasers (which often are around one micrometer), and are thus better able to penetrate Earth's atmosphere.[6] Accordingly, JAXA has focused on optimizing powerful and accurate microwave generation. JAXA has developed kW-class high-power microwave power transmission using phased, synchronized, power-transmitting antenna panels. Due to current limitations on communication technologies, JAXA has also developed advanced retrodirective systems, which allow high-accuracy beam pointing.[7] In 2015, JAXA was able to deliver 1.8 kilowatts accurately to a rectenna 55 meters away which, according to JAXA, is the first time that so much power has been transmitted with any appreciable precision . Although this may seem insignificant compared to the 36,000 km transmissions required for a satellite in geosynchronous orbit, this is huge achievement for mankind. It demonstrates that large scale wireless transmission is a realistic option to power electric cars, transmission towers, and even satellites. JAXA,continuing on its roadmap, plans to conduct the first microwave power transmission in space by 2018.

LARGE SCALE WIRELESS TRANSMISSION IS A REALISTIC OPTION TO POWER ELECTRIC CARS, TRANSMISSION TOWERS, AND EVEN SATELLITES.

Although the challenges ahead for space based solar power generation are enormous in both economic and technical terms, the results could be revolutionary. In a manner similar to the introduction of coal and oil, practical SBSP systems would completely alter human civilization. With continuous green energy generation, SBSP systems could solve our energy conflicts and allow progression to next phase of civilization. If everything goes well, air pollution and oil spills may merely be bygones.

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DESIGN BY Brianna Garcia
EDITED BY Aseem Utrankar

transplanting time.

by sara ho

Nowadays, it is possible for patients with organ failure to live for decades after receiving an organ transplant. Since the first successful kidney transplant in the 1950s,[1,2] advances in the procedure, including the improvement of drugs that facilitate acceptance of the foreign body parts,[3] have allowed surgeons to transplant a wider variety of organs, such as the heart, lungs, liver, and pancreas.[2,4] Over 750,000 lives have been saved and extended through the use of organ transplants, an unthinkable feat just over 50 years ago.[2] Limitations to organ transplantation, such as the lack of available organs, and the development of new advancements that can improve the process promote ongoing discussion regarding the ethics of transplants.

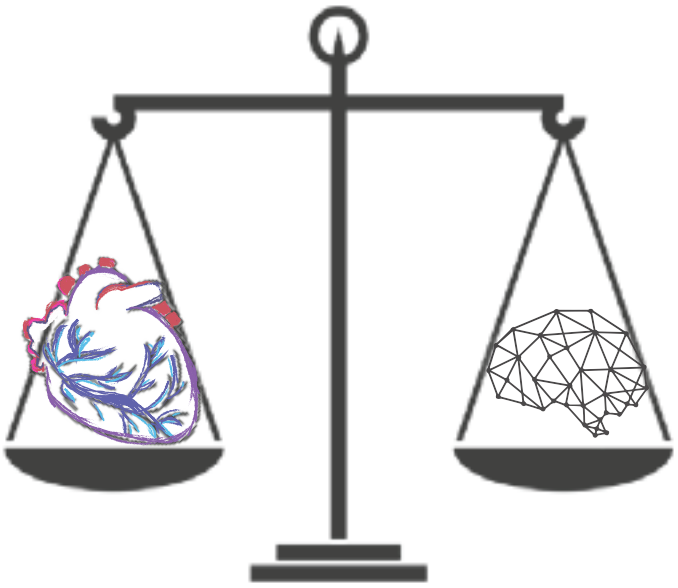
The idea behind an organ transplant is simple. When both the recipient and the new organ are ready, surgeons detach the blood vessels attached to the failing organ before putting the new one in its place by reattaching the patient's blood vessels to the functioning organ. To prevent rejection of the new organ, the recipient will continue to take immunosuppressant drugs.[3] In exchange for this lifelong commitment, the patient often receives a longer, more enjoyable life.[2]

The organs used in transplants usually originate from a cadaver or a living donor.[1-3] Some individuals are deterred from becoming an organ donor because they are concerned that doctors will not do their best to save them if their organs are needed. This concern is further complicated by blurred definitions of "dead"; in one ethically ambiguous situation, dying patients who are brain dead may be taken off of life support so that their organs may be donated.[1-3] Stories of patients who reawaken from comas after being pronounced "dead" may give some encouragement, but a patient's family and doctors must decide when to give up that hope. Aside from organs received from the deceased, living donors, who may be family, friends, or strangers to the recipient, may donate organs that they can live without, such as a lung or a kidney.[1-3] However, the potential injuring of a healthy person for the sake of another may contradict the oath that doctors take, which instructs physicians to help, not harm their patients.[1]

One of the most pressing issues today stems from the following question: who receives the organs? The transplant waiting list is constantly growing because the number of organs needed greatly exceeds the number of organs that are available.[1-3] Unfortunately, 22 patients die every day while they are waiting for a new organ.[4] Because the issue of receiving a transplant is time-sensitive, medical officials must decide who receives a transplant first. Should the person who needs a transplant the most have greater priority over another who has been on the waiting list longer? Should a child be eligible before a senior? Should a lifelong smoker be able to obtain a new lung? Currently, national policy takes different factors into account depending on the organ to be transplanted. For example, other than compatibility requirements, patients on the waiting list for liver transplants are ranked solely on their medical need and distance from the donor hospital.[4] On the other hand, people waiting for kidneys are further considered based on whether they have donated a kidney previously, their age, and their time spent on the waiting list.[4]

Despite various efforts to increase the number of organ donors through education and legislation, the supply of organs does not meet the current and increasing need for them.[1-3] As a result, other methods of obtaining these precious resources are currently being developed, one of which is the use of animal organs, a process known as xenotransplantation. Different animal cells, tissues, and organs are being researched for use in humans, giving some hope to those on the waiting list or those who do not quite qualify for a transplant.[2,3] In the past, surgeons have attempted to use a primate's heart and liver for transplantation, but the surgical outcomes were poor.[2] Other applications of animal tissue are more promising, such as the use of pigs' islet cells, which can produce insulin, in humans.[2]

"SHOULD THE PERSON WHO NEEDS A TRANSPLANT THE MOST HAVE GREATER PRIORITY OVER ANOTHER WHO HAS BEEN ON THE WAITING LIST LONGER?"



However, a considerable risk of using these animal parts is that new diseases may be passed from animal to human. Additionally, animal rights groups have protested the use of primates as a source of whole organs.[2] Another possible solution to the deficit of organs is the use of stem cells, which have the potential to grow and specialize. Embryonic stem cells can repair and regenerate damaged organs, but harvesting them destroys the source embryo.[2,3] Although the embryos are created outside of humans, there are objections to their use. What differentiates a mass of cells from a living person? Fortunately, adult stem cells can be used for treatment as well.[2] Researchers have developed a new method that causes adult stem cells to return to a state similar to that of the embryonic stem cells, although the efficacy of the induced adult stem cells compared to the embryonic stem cells is still unclear.[7]

Regardless of the continuous controversy over the ethics of transplantation, the boundaries for organ transplants are being pushed further and further. Head transplants have been attempted for over a century in other animals, such as dogs,[5] but several doctors want to move on to work with humans. To attach a head to a new body, the surgeon would need to connect the old and new nerves in the spinal cord so that the patient's brain could interact with the host body. Progress is already being made in repairing severe spinal cord injuries. In China, Dr. Ren Xiaoping plans to attempt a complete body transplant, believed by some to be currently impossible.[6] There is not much information about the amount of pain that the recipient of a body transplant must endure,[5] so it may ultimately decrease, rather than increase, the patient's quality of life. Overall, most agree that it would be unethical to continue, considering the limited success of such projects and the high chance of failure and death.

Organ transplants and new developments in the field have raised many interesting questions about the ethics of the organ transplantation process. As a society, we should determine how to address these problems and set boundaries to decide what is "right."

"DESPITE VARIOUS EFFORTS TO INCREASE THE NUMBER OF ORGAN DONORS THROUGH EDUCATION AND LEGISLATION, THE SUPPLY OF ORGANS DOES NOT MEET THE CURRENT AND INCREASING NEED FOR THEM."

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Icons from Nikhil Dev, Julia Amadeo, Sergey Patutin via the Noun Project

DESIGN BY Dora Cheng
EDITED BY Katrina Cherk

VENOM, M.D.

by **NICK FALKENBERG**

Nature, as mesmerizing as it can be, is undeniably hostile. There are endless hazards, both living and nonliving, scattered throughout all parts of the planet. At first glance, the world seems to be quite unwelcoming. Yet through science, humans find ways to survive nature and gain the ability to see its beauty. A fascinating way this is achieved involves taking one deadly element of nature and utilizing it to combat another. In labs and universities across the world today, scientists are fighting one of the world's most devastating diseases, cancer, with a surprising weapon: animal toxins.

Various scientists around the globe are collecting venomous or poisonous animals and studying the biochemical weapons they synthesize. In their natural forms, these toxins could kill or cause devastating harm to the human body. However, by closely inspecting the chemical properties of these toxins, we have uncovered many potential ways they could help us understand, treat, and cure various diseases. These discoveries have shed a new light on many of the deadly animals we have here on Earth. Mankind may have gained new friends—ones that could be crucial to our survival against cancer and other illnesses.

Take the scorpion, for example. This arachnid exists in hundreds of forms across the globe. Although its stinger is primarily used for killing prey, it is often used for defense against other animals, including humans. Most cases of scorpion stings result in nothing more than pain, swelling, and numbness of the area. However, there are some species of scorpions that are capable of causing more severe symptoms, including death.[1] One such species, *Leiurus quinquestriatus* (more commonly known as the "deathstalker scorpion"), is said to contain some of the most potent venoms on the planet.[2] Yet despite its potency, deathstalker venom is a prime target for cancer research. One team of scientists from the University of Washington used the chlorotoxin in the venom to assist in gene therapy (the insertion of genes to fight disease) to combat glioma, a widespread and fatal brain cancer. Chlorotoxin has two important properties that make it effective against fighting glioma. First, it selectively binds to a surface protein found on many tumour cells. Second, chlorotoxin is able to inhibit the spread of tumours by disabling their metastatic ability. The scientists combined the toxin with nanoparticles in order to increase the effectiveness of gene therapy.[3,4]

Other scientists found a different way to treat glioma using deathstalker venom. Researchers at the Transmolecular Corporation in Cambridge, Massachusetts produced an artificial version of the venom and attached it to a radioactive form of iodine, I-131. The resultant compound was able to find and kill glioma cells by releasing radiation, most of which was absorbed by the cancerous cells.[5] There are instances of other scorpion species aiding in cancer research as well, such as the *Centruroides tecomanus* scorpion in Mexico. This species' toxin contains peptides that

> **The scientists combined the toxin with nanoparticles in order to increase the effectiveness of gene therapy.**

have the ability to specifically target lymphoma cells and kill them by damaging their ion channels. The selective nature of the peptides makes them especially useful as a cancer treatment as they leave healthy cells untouched.[6]

Scorpions have demonstrated tremendous medical potential, but they are far from the only animals that could contribute to the fight against cancer. Another animal that may help us overcome this disease is the wasp. To most people, wasps are nothing more than annoying pests that disturb our outdoor life. Wasps are known for their painful stings, which they use both for defense and for hunting. Yet science has shown that the venom of these insects may have medicinal properties. Researchers from the Institute for Biomedical Research in Barcelona investigated a peptide found in wasp venom for its ability

how some of **the world's deadliest toxins** fight cancer

to treat breast cancer. The peptide is able to kill cancer cells by puncturing the cell's outer wall. In order to make this peptide useful in treatment, it must be able to target cancer cells specifically. Scientists overcame the specificity problem by conjugating the venom peptide with a targeting peptide specific to cancer cells.[7] Similar techniques were used in Brazil while scientists of São Paulo State University studied the species *Polybia paulista*, another organism from the wasp family. This animal's venom contains MP1, which also serves as a destructive agent of the cell's plasma membrane. When a cell is healthy, certain components of the membrane should be on the inner side of the membrane, facing the interior of the cell.

However, in a cancerous cell, these components, (namely, the phospholipids phosphatidylserine (PS) and phosphatidylethanolamine (PE)) are on the outer side of the membrane. In a series of simulations, MP1 was observed to selectively and aggressively target membranes that had PS and PE on the outside of the cell. Evidently, using targeted administration of wasp toxins is a viable method to combat cancer.[8]

Amazingly enough, the list of cancer-fighting animals at our disposal does not end here. One of the most feared creatures on Earth, the snake, is also among the animals under scientific investigation for possible medical breakthroughs. One group of scientists discovered that a compound from the venom of the Southeast Asia pit viper (*Calloselasma rhodastoma*) binds to a platelet receptor protein called CLEC-2, causing clotting of the blood. A different molecule expressed by cancer cells, podoplanin, binds to CLEC-2 in a manner similar to the snake venom, also causing blood clotting.

Why does this matter? In the case of cancer, tumors induce blood clots to protect themselves from the immune system, allowing them to grow freely. They also induce the formation of lymphatic vessels to assist their survival. The interaction between CLEC-2 and podoplanin is vital for both the formation of these blood clots and lymphatic vessels, and is thus critical to the persistence of tumors. If a drug is developed to inhibit this interaction, it would be very effective in cancer treatment and prevention.[9] Research surrounding the snake venom may help us develop such an inhibitor.

Even though there may be deadly animals roaming the Earth, it is important to remember that they have done more for us than most people realize. So next time you see a scorpion crawling around or a wasp buzzing in the air, react with appreciation, rather than with fear. Looking at our world in this manner will make it seem like a much friendlier place to live.

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health

#FIRST WORLD PROBLEMS

BY MAHESH KRISHNA

I am a first generation American, as both of my parents immigrated here from Myanmar, a third world country. There had been no occurrence of any Inflammatory Bowel Disease (IBD) in my family, yet I was diagnosed with Ulcerative Colitis at the beginning of my sophomore year of high school. Since IBD is known to be caused by a mix of genetic and environmental factors,[1, 2] what specifically triggered me to develop Ulcerative Colitis? Was it the food in America, the air I was exposed to, a combination of the two, or neither of them at all? Did the "environment" of the first world in the United States cause me to develop Ulcerative Colitis?

IBD is a chronic autoimmune disease, characterized by persistent inflammation of the digestive tract and classified into two separate categories: Ulcerative Colitis and Crohn's Disease.[3] Currently, there is no known cure for IBD, as its pathogenesis (i.e. the manner in which it develops) is not fully understood.[1] Interestingly, the incidence of IBD has increased dramatically over the past century.[1] A systematic review by Molodecky et al. showed that the incidence rate of IBD was significantly higher in Western nations. This may be due to better diagnostic techniques or the growth of environmental factors that promote its development. This could also suggest that there may be certain stimuli in first world countries that can trigger pathogenesis in individuals with a genetic predisposition to IBD.

Environmental factors that are believed to affect IBD include smoking, diet, geographic location, social status, stress, and microbes.[1] Smoking has had varying effects on the development of IBD depending on the form; smoking is a key risk factor for Crohn's Disease, while non-smokers and ex-smokers are usually diagnosed with Ulcerative Colitis.[4] There have not been many studies investigating the causal relationship between diet and IBD due to the diversity in diet composition.[1] However, since IBD affects the digestive system, diet has long been thought to have some impact on the pathogenesis of the disease.[1] In first world countries, there is access to a larger variety of food, which may impact the prevalence of IBD. People susceptible to the disease in developing countries may have a smaller chance of being exposed to "trigger" foods. In addition, IBD has been found in higher rates in urban areas versus rural areas.[1,4,5] This makes sense, as cities have a multitude of potential disease-inducing environmental factors including pollution, poor sanitation, and microbial exposure. Higher socioeconomic status has also been linked to higher rates of IBD.[4] This may be partly due to the sedentary nature of white collar work, which has also been linked to increased rates of IBD.[1] Stress used to be viewed as a possible factor in the pathogenesis of IBD, but recent evidence has indicated that it only exacerbates the disease.[3] Recent research has focused on the microorganisms in the gut, called gut flora, as they seem to have a vital role in the instigation of IBD.[1] In animal models, it has even been observed that pathogenesis of IBD is not possible in a germ-free environment.[1] The idea of the importance of microorganisms in human health is also linked to the Hygiene Hypothesis.

THE HYGIENE HYPOTHESIS STATES THAT THE LACK OF INFECTIONS IN WESTERN COUNTRIES IS THE REASON FOR AN INCREASING AMOUNT OF AUTOIMMUNE AND ALLERGIC DISEASES. THE IDEA BEHIND THE THEORY IS THAT SOME INFECTIOUS AGENTS GUARD AGAINST A WIDE VARIETY OF IMMUNE-RELATED DISORDERS.

The Hygiene Hypothesis states that the lack of infections in western countries is the reason for an increasing amount of autoimmune and allergic diseases.[6] The idea behind the theory is that some infectious agents guard against a wide variety of immune-related disorders.[6] Animal models and clinical trials have provided some evidence backing the Hygiene Hypothesis, but it is hard to causally attribute the pathogenesis of autoimmune and allergic diseases to a decrease in infections, since first world countries have very different environmental factors than third world countries.[6]

The increasing incidence of IBD in developed countries is not yet fully understood, but recent research points towards a complex combination of environmental and genetic factors. The rise of autoimmune disease diagnoses may also be attributed to better medical equipment and facilities and the tendency of people in more developed countries to regularly get checked by a doctor. There are many difficulties in researching the pathogenesis of IBD including isolating certain environmental factors and obtaining tissue and data from third world countries. However, there is much promising research and it might not be long until we discover a cure for IBD.

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DESIGN BY Juliana Wang
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ENGINEERING EDEN

TERRAFORMING A SECOND EARTH

MEREDITH BROWN

Today's world is faced with thousands of complex problems that seem to be insurmountable. One of the most pressing is the issue of the environment and how our over-worked planet can sustain such an ever-growing society. Our major source of energy is finite and rapidly depleting. Carbon dioxide emissions have passed the "irreversibility" threshold. Our oceans and atmosphere are polluted, and scientists predict a grim future for Mother Earth if humans do not change our wasteful ways. A future similar to the scenes of "Interstellar" or "Wall-E" is becoming increasing less fictitious. While most of the science world is turning to alternative fuels and public activism as vehicles for change, some radical experts in climate change and astronomy suggest relocation to a different planet: Mars. The Mars rover, Curiosity, presents evidence that Mars has the building blocks of a potential human colony, such as the presence of heavy metals and nutrients nestled in its iconic red surface. This planet, similar in location, temperature, and size to Earth, seems to have the groundwork to be our next home. Now is when we ponder: perhaps our Earth was not meant to sustain human life for eternity. Perhaps we are living at the tail end of our time on Earth.

Colonizing Mars would be a project beyond any in human history, and the rate-limiting step of this process would be developing an atmosphere that could sustain human, animal, and plant life. The future of mankind on Mars is contingent on developing a breathable atmosphere, so humans and animals could thrive without the assistance of oxygen tanks, and vegetation could grow without the assistance of a greenhouse. The Martian atmosphere has little oxygen, being almost 95.7 percent carbon dioxide. It is also one percent of the density of Earth's atmosphere, so it provides no protection from the Sun's radiation. Our atmosphere, armed with a thick layer of ozone, absorbs or deflects the majority of radiation before it hits our surface. Even if a human could breathe on the surface of Mars, he or she would die from radiation poisoning or cancer. Fascinating ways to address this have been discussed, one being mass hydrogen bombing across the entire surface of the planet, creating an atmosphere of dust and debris thick enough to block ultraviolet radiation. This feat can also be accomplished by physically harnessing nearby asteroids and catapulting them into the surface. The final popular idea is the use of mega-mirrors to capture the energy of the sun to warm up the surface to release greenhouse gases from deep within the soil[1].

> "EVEN IF A HUMAN COULD BREATHE ON THE SURFACE OF MARS, HE OR SHE WOULD DIE FROM RADIATION POISONING OR CANCER."

However, bioengineers have suggested another way of colonizing Mars—a way that does not require factories or asteroids or even human action for that matter. Instead, we would use genetically modified plants and algae to build the Martian atmosphere. The Defense Advanced Research Projects Agency (DARPA) is pursuing research in developing these completely new life forms[2]. These life forms would not need oxygen or water to survive, but instead would synthesize a new atmosphere given the materials already on Mars. The bioengineering lab at DARPA has developed a software called DTA GView which has been called a "Google Maps of Genomes." It acts as a library of genes, and DARPA has identified genes that could be inserted into extremophile organisms. A bacteria called *Chroococcidiopsis* is resistant to wide temperature changes and hypersalinity, two conditions found on Mars[3]. *Carnobacterium spp* has proven to thrive under low pressure and in the absence of oxygen. These two organisms could potentially be genetically engineered to live on Mars and add vital life-sustaining molecules to the atmosphere.

Other scientific developments must occur before these organisms are ready to pioneer the human future on Mars. Curiosity must send Earth more data regarding what materials are present in Mars' soil, and we must study how to choose, build, and transport the ideal candidate to Mars. Plus, many argue that our scientific research should be focused on healing our current home instead of building a new one. If we are willing to invest the immense scientific capital required to terraform another planet, we would likely also be able to mediate the problem of Earthly pollution. However, in such a challenging time, we must venture to new frontiers, and the bioengineers at DARPA have given us an alternative method to go where no man or woman has ever gone before.

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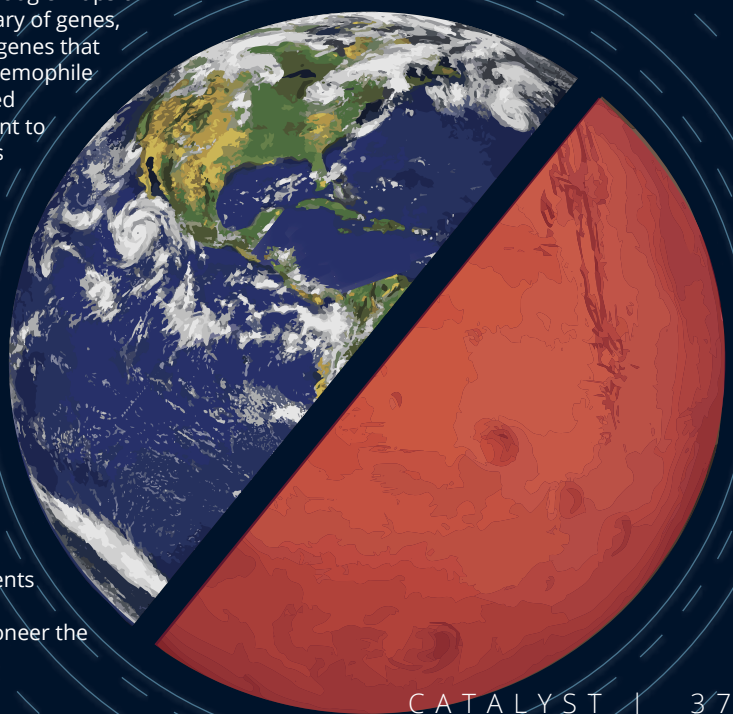


ZIKA AND FETAL VIRUSES:

SHARING MORE THAN A MOTHERLY BOND

BY NATASHA MEHTA

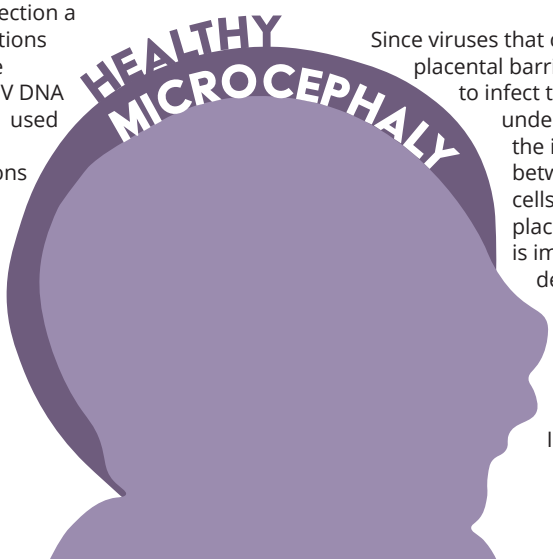
Zika is a blood-borne pathogen primarily transmitted through mosquito bites and sexual activities. Pregnant women infected by Zika can pass the virus to their fetus, causing microcephaly, a condition in which the baby has an abnormally small head indicative of abnormal brain development. With the outbreak of the Zika virus and its consequences for pregnant women and their babies, much research has focused on how the infection leads to microcephaly in fetuses.

Current Zika research has been focused on uncovering methods for early detection of Zika in pregnant women and educating the public on safe sexual practices to contain the vector of transmission to just mosquitoes.[1] However, to truly end the Zika epidemic, there are three critical steps that need to be taken. First, researchers must determine the point at which maternal infections harm the neurological development of fetuses in order to ensure treatment is administered to the mothers before the brain damage becomes irreversible. Subsequently, researchers must determine the mechanism through which Zika spreads from mother to fetus. After this step, researchers can begin developing therapies to protect the fetus from Zika once the mother is already infected and also start creating a preventative vaccine. Although Zika seems like a mysterious new illness, there are several other well-studied viral infections that affect pregnancies, such as cytomegalovirus (CMV). CMV infection during pregnancy also leads to severe fetal brain damage. Previous research techniques could provide clues for researchers trying to understand more about Zika, and learning more about Zika will better equip us for handling prenatal viral outbreaks in the future.

TO TRULY END THE ZIKA EPIDEMIC THERE ARE 3 CRITICAL STEPS THAT NEED TO BE TAKEN.

The current detection of microcephaly of infants with Zika-infected mothers involves fetal ultrasound as early as 18 weeks into the gestation period.[2] However, this is a late diagnosis of fetal Zika infection and at this point the brain abnormalities caused by the virus are irreversible. Ultrasounds and MRI scans of infants with confirmed CMV infection can detect these neurological abnormalities as well.[3] However, these brain lesions are also irreversible, making early detection a necessity for CMV infections as well. Fortunately, the presence of CMV or CMV DNA in amniotic fluid can be used for early diagnosis, and current treatment options include administration of valacyclovir or hyperimmunoglobulin in the window before the fetus develops brain lesions.[4] Researchers must try to identify fetal Zika infection as early as possible as opposed to relying on fetal microcephaly as the sole diagnostic tool. Some potential early detection methods include testing for Zika in the urine of pregnant women as soon as Zika symptoms are present, as opposed to screening the fetus for infection.[5]

Discovering the mechanism through which Zika infects the fetus is necessary to develop therapies to protect the fetus from infection. Many viruses that are transferred to the fetus during pregnancy do so by compromising the immune function of the placental barrier, allowing the virus to cross the placenta and infect the fetus. The syncytiotrophoblast is the epithelial covering of placental embryonic villi, which are highly vascular finger-like projections that increase the surface area available for exchange of nutrients and wastes between the mother and fetus.[6] In one study, experiments found that infection of extravillous trophoblast cells decreased the immune function of the placenta, which increased fetal susceptibility to infection.[7] Determining which cells in the placenta are infected by Zika could aid research into preventative treatments for fetal infection.



Since viruses that cross the placental barrier are able to infect the fetus, understanding the interaction between immune cells and the placental barrier is important for developing therapies against Zika that increase fetal viral resistance. In one study,

researchers found that primary human trophoblast cells use cell-derived vesicles called exosomes to transfer miRNA, conferring placental immune resistance to a multitude of viruses to other pregnancy-related cells.[8] miRNAs are responsible for regulating gene expression, and different miRNAs exist in different cells so that those cells will have specific functions and defenses. Isolating these miRNA exosomes, using them to supplement placental cell strains, and subsequently testing whether those cells are more or less susceptible to Zika could support the development of drugs that bolster the placental immune defense mechanism already in place. Since viral diseases that cross the placenta lead to poor fetal outcome, developing protective measures for the placenta is imperative, not only for protection against Zika but also for protection against new viruses without vaccinations.[9]

Combating new and more elusive viral outbreaks is difficult, but understanding and preventing viral infection in fetuses is like taking a shot in the dark. Although the prospects for infants infected by Zika are currently poor, combining the research done on other congenital infections paints a more complete picture on viral transmission during pregnancy. Instead of starting from scratch, scientists can use this information to determine the tests that can detect Zika, the organs to examine for compromised immune system function, and the treatment types that have a higher probability of effectiveness. Zika will not be the last virus that causes birth defects, but by combining the efforts of many scientists, we can get closer to stopping fetal viral infection once and for all.

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GREEN SEA TURTLES

A SHELL OF WHAT THEY ONCE WERE

KIRA CHEN

Sea turtles appear in many cultures and myths, and are often beloved symbols of longevity and wisdom. However, in spite of the cultural respect shown towards them, green sea turtles have gradually become endangered due to factors such as nesting habitat loss, pollution, egg harvesting, climate change, and boat strikes. Now, there's a new, even more dangerous threat on the block: herpes. And no, it's not the herpes you're thinking of - this kind, known as fibropapillomatosis (FP), is much, much worse.

FP has been observed across all species of sea turtles for years, but it has recently become especially widespread among green sea turtles (Chelonia mydas). The alarming incidence of FP is exacerbating the decline of this already vulnerable population. Among green sea turtles, the number of cases of FP increased 6000% from the 1980s to the mid-1990s, with FP becoming so globally pervasive that the outbreak has been classified as "panzootic," the animal equivalent of "pandemic." Now, you might think, "That sounds bad, but why are these turtles dying?" In humans, herpes is unpleasant, but it is seldom life-threatening. Unfortunately, in green sea turtles, the outlook isn't nearly as optimistic. FP causes the development of tumors on the soft tissues, the shells, and even the eyes of infected turtles. When these growths are left untreated, they can grow to immense sizes, impairing the animal's vital activities, such as breathing and swallowing. So, while the tumors aren't directly lethal, they invite hordes of secondary infections and pathogens that ultimately result in death.

To make matters worse, treatment for FP is still in development. A landmark study identified the specific pathogen responsible for FP as Chelonid herpesvirus 5 (ChHV5), a close relative of human genital herpes.[1] This discovery was the first step to a cure, but it raised an important question - how had this variant of herpesvirus become so prevalent? Until recently, the answer to that question was elusive.

Fortunately, several recent discoveries offered new explanations for FP's rise. One study reported a significant positive correlation between serum concentrations of heavy metals and the severity of FP, as well as a significant negative correlation between serum cholesterol concentrations and FP.[2] In a related find, a team at the University of São Paulo discovered that many green sea turtles have been exposed to organochlorine compounds, which are known to have carcinogenic effects.[3] Further research could potentially determine a direct causal relationship between the development of FP and exposure to heavy metals or organochlorine compounds. If such a relationship were found, projects that strive to decrease the prevalence of said compounds in the turtles' habitats could prove effective in mitigating the spread of FP.

So what's the prognosis for the green sea turtle? Unfortunately, even knowing what we now know, it may not be good. A study by Jones et al. found almost all of the infected turtles are juveniles, potentially creating a big problem for the population.[4] Jones believes the most optimistic explanation for this trend is that current adults and hatchlings have never been exposed to the disease, so only one generation (the juveniles) has been infected. Another optimistic possibility is that once infected turtles recover from the disease, they will simply acquire immunity as adults. However, there is another, devastating possibility: all of the affected juveniles will perish before they reach adulthood, leaving only the unaffected alive and dooming the species. In a heartbreaking aside, Jones reported that FP "grows on their [the turtles'] eyes, they can't see predators, they can't catch food, so sometimes they slowly starve to death — it's not a nice thing for the turtles to experience... Severely affected turtles are quite skinny and have other pathogens affecting them – that's why they die."

Eradicating such a devastating disease will no doubt take many more years of specialized research, and significant efforts are needed immediately to rehabilitate the green sea turtle population. Luckily, conservation groups such as The Turtle Hospital, located in the Florida Keys, are making an active effort to save infected sea turtles. They perform surgeries that remove FP tumors, rehabilitate the turtles, and then release them back into the wild. In addition, they collaborate with universities to study the virus and educate the public on sea turtle conservation. To date, the Turtle Hospital has successfully treated and released over 1,500 sea turtles.[8] Through the hard work of conservation organizations and researchers across the globe, we may still be able to save the green sea turtle.

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TOUCHING LIVES

BY JACK TROUVÉ

Everyday you use a device that has haptic feedback: your phone. Every little buzz for notifications, key presses, and failed unlocks are all examples of haptic feedback. Haptics is essentially tactile feedback, a form of physical feedback that uses vibrations. It is a field undergoing massive development and applications of haptic technology are expanding rapidly. Some of the up-and-coming uses for haptics include navigational cues while driving, video games, virtual reality, robotics, and, as in Dr. O'Malley's case, in the medical field with prostheses and medical training tools.

Dr. Marcia O'Malley has been involved in the biomedical field ever since working in an artificial knee implant research lab as an undergraduate at Purdue University. While in graduate school at Vanderbilt University, she worked in a lab focused on human-robot interfaces where she spent her time designing haptic feedback devices. Dr. O'Malley currently runs the Mechatronics and Haptic Interfaces (MAHI) Lab at Rice University, and she was recently awarded a million dollar National Robotics Initiative grant for one of her projects. The MAHI Lab "focuses on the design, manufacture, and evaluation of mechatronic or robotic systems to model, rehabilitate, enhance or augment the human sensorimotor control system."[1] Her current research is focused on prosthetics and rehabilitation with an effort to include haptic feedback. She is currently working on the MAHI EXO- II. "It's a force feedback exoskeleton, so it can provide forces, it can move your limb, or it can work with you," she said. The primary project involving this exoskeleton is focused on "using electrical activity from the brain captured with EEG... and looking for certain patterns of activation of different areas of the brain as a trigger to move the robot." In other words, Dr. O'Malley is attempting to enable exoskeleton users to control the device through brain activity.

Dr. O'Malley is also conducting another project, utilizing the National Robotics Initiative grant, to develop a haptic cueing system to aid medical students training for endovascular surgeries. The idea for this haptic cueing system came from two different sources. The first part was her prior research which consisted of working with joysticks. She worked on a project that involved using a joystick, incorporated with force feedback, to swing a ball to hit targets.[2] As a result of this research, Dr. O'Malley found that "we could measure people's performance, we could measure how they used the joystick, how they manipulated the ball, and just from different measures about the characteristics of the ball movement, we could determine whether you were an expert or a novice at the task... If we use quantitative measures that tell us about the quality of how they're controlling the tools, those same measures correlate with the experience they have." After talking to some surgeons, Dr. O'Malley found that these techniques of measuring movement could work well for training surgeons.

The second impetus for this research came from an annual conference about haptics and force feedback. At the conference she noticed that more and more people were moving towards wearable haptics, such as the Fitbit, which vibrates on your wrist. She also saw that everyone was using these vibrational cues to give directional information. However, "nobody was really using it as a feedback channel about performance," she said. These realizations led to the idea of the vibrotactile feedback system.

Although the project is still in its infancy, the current anticipated product is a virtual reality simulator which will track the movements of the tool. According to Dr. O'Malley, the technology would provide feedback through a single vibrotactile disk worn on the upper limb. The disk would use a voice coil actuator that moves perpendicular to the wearer's skin. Dr. O'Malley is currently working with Rice psychologist Dr. Michael Byrne to determine which frequency and amplitude to use for the actuator, as well as the timing of the feedback to avoid interrupting or distracting the user.

Ultimately, this project would measure the medical students' smoothness and precision while using tools, as well as give feedback to the students regarding their performance. In the future, it could also be used in surgeries during which a doctor operates a robot and receives force feedback through similar haptics. During current endovascular surgery, a surgeon uses screens that project a 2D image of the tools in the patient. Incorporating 3D views would need further FDA approval and could distract and confuse surgeons given the number of screens they would have to monitor. This project would offer surgeons a simpler way to operate. From exoskeletons to medical training, there is a huge potential for haptic technologies. Dr. O'Malley is making this potential a reality.

"SOME OF THE UP-AND-COMING USES FOR HAPTICS INCLUDE NAVIGATIONAL CUES WHILE DRIVING, VIDEO GAMES, VIRTUAL REALITY, ROBOTICS, AND, AS IN DR. O'MALLEY'S CASE, IN THE MEDICAL FIELD WITH PROSTHESES AND MEDICAL TRAINING TOOLS."

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DESIGN BY Juliana Wang
EDITED BY Rachita Pandya

THE DEPRESSIVE AFTERMATH OF BRAIN INJURY

BY DEEPU KARRI

One intuitively knows that experiencing a brain injury is often painful and terrifying; the fact that it can lead to the onset of depression, however, is a lesser known but equally serious concern. Dr. Roberta Diddel, a clinical psychologist and member of the adjunct faculty in the Psychology Department at Rice University, focuses on the treatment of individuals with mental health issues and cognitive disorders. In particular, she administers care to patients with cognitive disorders due to traumatic brain injury (TBI). Dr. Diddel acquired a PhD in clinical psychology from Boston University and currently runs a private practice in Houston, Texas. Patients who experience TBI often experience depression; Dr. Diddel uses her understanding of how this disorder comes about to create and administer potential treatments.

Traumatic brain injury (TBI) affects each patient differently based on which region of the brain is damaged. If a patient has a cerebellar stroke, affecting the region of the brain which regulates voluntary motor movements, he or she might experience dizziness and have trouble walking. However, that patient would be able to take a written test because the injury has not affected higher order cognitive functions such as language processing and critical reasoning.

Dr. Diddel said, "Where you see depression the most is when there is a more global injury, meaning it has affected a lot of the brain. For example, if you hit your forehead in a car accident or playing a sport, you're going to have an injury to the front and back parts of your brain because your brain is sitting in cerebrospinal fluid, causing a whiplash of sorts. In turn, this injury will cause damage to your frontal cortex, responsible for thought processing and problem solving, and your visual cortex, located in the back of your brain. When your brain is bouncing around like that, you often have swelling which creates intracranial pressure. Too much of this pressure prevents the flow of oxygen-rich blood to the brain. That can cause more diffuse brain injury."

WHERE YOU SEE DEPRESSION THE MOST IS WHEN THERE IS A MORE GLOBAL INJURY

In cases where people experience severe brain injury such as head trauma due to an explosion or a bullet, surgeons may remove blood clots that may have formed in order to relieve intracranial pressure and repair skull fractures.[4] They may also remove a section of the skull for weeks or months at a time to let the brain swell, unrestricted to the small, cranial cavity. That procedure alone significantly reduces the damage that occurs from those sorts of injuries and is especially useful in the battlefield where urgent care trauma centers may not be available.

Depression is a common result of TBI. The Diagnostic and Statistical Manual of Mental Disorders (DSM) defines depression as a loss of interest or pleasure in daily activities for more than two weeks, a change in mood, and impaired function in society.[1] These symptoms are caused by brain-related biochemical deficiencies that disrupt the nervous system and lead to various symptoms. Usually, depression occurs due to physical changes in the prefrontal cortex, the area of the brain associated with decision-making, social behavior, and personality. People with depression feel overwhelmed, anxious, lose their appetite, and have a lack of energy, often because of depleted serotonin levels. The mental disorder is a mixture of chemical imbalances and mindstate; if the brain is not correctly functioning, then a depressed mindstate will follow.

THE US SAW ABOUT 2.5 MILLION CASES OF TRAUMATIC BRAIN INJURY IN 2010 ALONE

Dr. Diddel mentioned that in many of her depressed patients, their lack of motivation prevents them from addressing and improving their toxic mindset. "If you're really feeling bad about your current situation, you have to be able to say 'I can't give in to this. I have to get up and better myself and my surroundings.' People that are depressed are struggling to do that," she said.

The causes of depression vary from patient to patient and often depends on genetic predisposition to the disease. Depression can arise due to physical changes in the brain such as the alterations in the levels of catecholamines, neurotransmitters that works throughout the sympathetic and central nervous systems. Catecholamines are broken down into other neurotransmitters such as serotonin, epinephrine, and dopamine, which are released during times of positive stimulation and help increase activity in specific parts of the brain. A decrease in these chemicals after an injury can affect emotion and thought process. Emotionally, the patient might have a hard time dealing with a new disability or change in societal role due to the trauma. Additionally, patients who were genetically loaded with genes predisposing them to depression before the injury are more prone to suffering from the mental disorder after the injury.[2, 3]

Depression is usually treated with some form of therapy or antidepressant medication. In cognitive behavior therapy (CBT), the psychologist tries to change the perceptions and behavior that exacerbate a patient's depression. Generally, the doctor starts by attempting to change the patient's behavior because it is the only aspect of his or her current situation that can be described. Dr. Diddel suggests such practices to her patients, saying things like "I know you don't feel like it, but I want you to go out and walk everyday." Walking or any form of exercise increases catecholamines, which essentially increases the activity of serotonin in the brain and improves the patient's mood. People who exercise as part of their treatment regimen are also less likely to experience another episode of depression.

The efficacy of antidepressant medication varies from patient to patient depending on the severity of depression a patient faces. People with mild to moderate depression generally respond better to CBT because the treatment aims to change their mindset and how they perceive the world around them. CBT can result in the patient's depression gradually resolving as he or she perceives the surrounding stimuli differently, gets out and moves more, and pursues healthy endeavors. Psychologists usually begin CBT, and if the patient does not respond to that well, then they are given medication. Some medications increase serotonin levels while others target serotonin, dopamine, and norepinephrine; as a result, they boost the levels of neurotransmitters that increase arousal levels and dampen negative emotions. The population of patients with moderate to severe depressions usually respond better to antidepressant medication. Medication can restore ideal levels of neurotransmitters, which in turn encourages the patient to practice healthier behavior.

DEPRESSION IS STILL AN ENIGMA TO PHYSICIANS AND RESEARCHERS ALIKE

According to the Center for Disease Control and Prevention, the US saw about 2.5 million cases of traumatic brain injury in 2010 alone.[5] That number rises every year and with it brings a number of patients who suffer from depression in the aftermath.[5] Though the mental disorder has been studied for decades and treatment options and medications are available, depression is still an enigma to physicians and researchers alike. No two brains are wired the same, making it very difficult to concoct a treatment plan with a guaranteed success rate. The work of researchers and clinical psychologists like Dr. Diddel, however, aims to improve the currently available treatment. While no two patients are the same, understanding each individual's depression and tailoring treatment to the specific case can vastly improve the patient's outcome.

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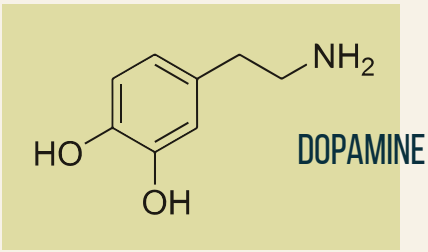
DESIGN BY Lin Guo
EDITED BY Shrey Agarwal



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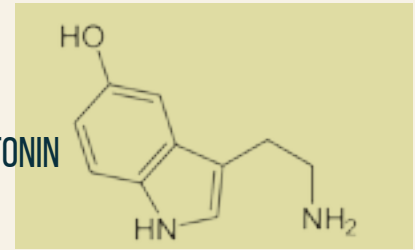

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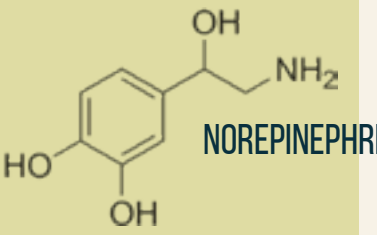

NOREPINEPHRINE

TACTILE LITERACY

THE LASTING IMPORTANCE OF BRAILLE

JENNIFER LEE

On June 27th, 1880, a baby girl was born. At nineteen months old, the little girl contracted a severe fever, and once the fever dissipated, she woke up to a world of darkness and silence. This little girl was Helen Keller. By the age of two, Helen Keller had completely lost her sense of sight and hearing.

Over a century later, it is estimated that 285 million people are visually impaired worldwide, of which 39 million are blind.[1] Blindness is defined as the complete inability to see with a corrected vision of 20/200 or worse.[2] For Keller to absorb the information around her, she relied on the sensation of touch. The invention of the braille alphabet by Frenchman Louis Braille in the early 1800s allowed Keller to learn about the world and to communicate with others. Like Keller, the majority of the visually impaired today rely on braille as their main method of reading.

The technological advances of smartphones, artificial intelligence, and synthetic speech dictations have opened a whole new world for blind readers. With the advent of the electronic information age, it's easy to think that blind people don't need to rely on braille anymore to access information. In fact, braille literacy rates for school-age blind children have already declined from 50 percent 40 years ago to only 12 percent today.[3] While current low literacy rates may be in part due to the inclusion of students with multiple disabilities that inhibit language acquisition, these statistics still reveal a major concern about literacy amongst the visually impaired. To substitute synthetic speech for reading and writing devalues the importance of learning braille.

TACTILE READERS DO RELY ON SUBLEXICAL STRUCTURES AND HAVE SIMILAR COGNITIVE PROCESSES TO PRINT READERS... THE BELIEF THAT BRAILLE IS OLD-FASHIONED AND NOT NEEDED ANYMORE IS FAR FROM THE TRUTH.

"There are many misunderstandings and stereotypes of braille readers," says Dr. Robert Englebretson, Professor of Linguistics at Rice University. "When a person reads, they learn about spelling and punctuation, and it's the exact same for tactile readers. Humans better process information when they actively process it through reading instead of passively listening.

Dr. Englebretson is also blind, and one part of his research agenda is a collaborative project with Dr. Simon Fischer-Baum in Psychology and pertains to understanding the cognitive and linguistic importance of braille to braille readers. He explores the questions surrounding the nature of perception and reading and explores the ways the mind groups the input of touch into larger pieces to form words.

In order to understand how written language is processed by tactile readers compared to visual readers, Dr. Englebretson conducted experiments to find out if braille readers exhibit an understanding of sublexical structures, or parts of words, similar to that of visual readers. An understanding of sublexical structures is crucial in recognizing letter groupings and acquiring reading fluency. Visual readers recognize sublexical structures automatically as the eye scans over words, whereas tactile readers rely on serially scanning fingers across a line of text.

To explore whether the blind have an understanding of sublexical structures, Dr. Englebretson studied the reaction time of braille readers in order to judge their understanding of word structures.

The subjects were given tasks to determine whether the words were real or pseudowords, and the time taken to determine the real words from the pseudowords were recorded. The first experiment tested the ability for braille readers to identify diagraphs or parts of words, and the second experiment test the ability for braille readers to identify morphemes, or the smallest unit of meaning or grammatical function of a word. For braille readers, Dr. Englebretson and his team developed a foot pedal system that enabled braille readers to indicate their answer without pausing to click a screen as the visual readers did. This enabled the braille readers to continuously use their hands while reading. From the reaction times of the braille readers when presented with a morphologically complex word, the findings show evidence of braille readers processing the meaning of words and recognizing these diagraphs and morphemes.[4]

"What we discovered was that tactile readers do rely on sublexical structures and have similar cognitive processes to print readers," says Dr. Englebretson. "The belief that braille is old-fashioned and not needed anymore is far from the truth. Tactile reading provides an advantage in learning just as visual reading does."

Dr. Englebretson also gathered a large sample of braille readers and videotaped them reading using a finger tracking system. Similar to an eye tracking system that follows eye movements, the finger tracking system used LED lights on the backs of fingernails to track the LED movements over time using a camera. The movements of the LED lights on the x-y coordinates are then plotted on a graph. This system can track where each finger is, how fast they are moving, and the movements that are made during regressions, or the right-to-left re-reading movement of the finger.[5] While this test was independent from the experiment about understanding sublexical structures, the data collected offers a paradigm for researchers about braille reading.

The outcome of these studies has not only scientific and academic implications, but also important social implications. "At the scientific level, we now better understand how perception [of written language] works, how the brain organizes and processes written language, and how reading works for tactile and visual readers," says Dr. Englebretson. "Through understanding how tactile readers read, we will hopefully be able to implement policy on how teachers of blind and visually impaired students teach, and on how to guide the people who are working on updating and maintaining braille."

With decreasing literacy rates among braille readers, an evidence-based approach to the teaching of braille is as critical as continuing to implement braille literacy programs. With an understanding of braille, someone who is blind can not only access almost infinite pages of literature, but also make better sense of their language and world.

WITH DECREASING LITERACY RATES AMONG BRAILLE READERS AN EVIDENCE-BASED APPROACH TO THE

TEACHING OF BRAILLE IS AS CRITICAL AS CONTINUING TO IMPLEMENT BRAILLE LITERACY PROGRAMS.

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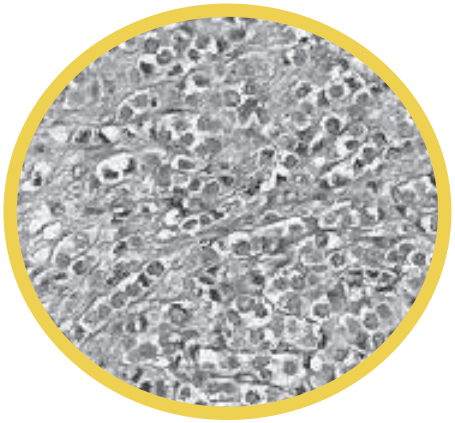
DESIGN BY Ashley Gentles
EDITED BY Ruchi Gupta

(Title braille reads "tactile")



MICROBES:

To millions around the world, the word 'cancer' evokes emotions of sorrow and fear. For decades, scientists around the world have been trying to combat this disease, but to no avail. Despite the best efforts of modern medicine, about 46% of patients diagnosed with cancer still pass away as a direct result of the disease.[1] However, the research performed by Dr. Michael Gustin at Rice University may change the field of oncology forever.

Cancer is a complex and multifaceted disease that is currently not fully understood by medical doctors and scientists. Tumors vary considerably between different types of cancers and from patient to patient, further complicating the problem. Understanding how cancer develops and responds to stimuli is essential to producing a viable cure, or even an individualized treatment.

Dr. Gustin's research delves into the heart of this problem. The complexity of the human body and its component cells are currently beyond the scope of any one unifying model. For this reason, starting basic research with human subjects would be detrimental. Researchers turn instead to simpler eukaryotes in order to understand the signal pathways involved in the cell cycle and how they respond to stress.[2] Through years of hard work and research, Dr. Gustin's studies have made huge contributions to the field of oncology.

Dr. Gustin studied a species of yeast, Saccharomyces cerevisiae, and its response to osmolarity. His research uncovered the high osmolarity glycerol (HOG) pathway and mitogen-activated protein kinase (MAPK) cascade, which work together to maintain cellular homeostasis. The HOG pathway is much like a "switchboard [that] control[s] cellular behavior and survival within a cell, which is regulated by the MAPK cascade through the sequential phosphorylation of a series of protein kinases that mediates the stress response."[3] These combined processes allow the cell to respond to extracellular stress by regulating gene expression, cell proliferation, and cell survival and apoptosis. To activate the transduction pathway, the sensor protein Sln1 recognizes a stressor and subsequently phosphorylates, or activates, a receiver protein that mediates the cellular response. This signal transduction pathway leads to the many responses that protect a cell against external stressors. These same protective processes, however, allow cancer cells to shield themselves from the body's immune system, making them much more difficult to attack.

Dr. Gustin has used this new understanding of the HOG pathway to expand his research into similar pathways in other organisms. Fascinatingly, the expression of human orthologs of HOG1 proteins within yeast cells resulted in the same stimulation of the pathway despite the vast evolutionary differences between yeast and mammals. Beyond the evolutionary implications of this research, this illustrates that the "[HOG] pathway defines a central stress response signaling network for all eukaryotic organisms".[3] So much has already been learned through studies on Saccharomyces cerevisiae and yet researchers have recently discovered an even more representative organism. This fungus, Candida albicans, is the new model under study by Dr. Gustin and serves as the next step towards producing a working model of cancer and its responses to stressors. Its more complex responses to signalling make it a better working model than

PARTNERS IN CANCER RESEARCH

SAMANTHA CHAO

Saccharomyces cerevisiae.[4] The research that has been conducted on Candida albicans has already contributed to the research community's wealth of information, taking great strides towards eventual human applications in the field of medicine. For example, biological therapeutics designed to combating breast cancer cells have already been tested on both Candida albicans biofilms and breast cancer cells to great success.[5]

This research could eventually be applied towards improving current chemotherapy techniques for cancer treatment. Eventual applications of this research are heavily oriented towards fighting cancer through the use of chemotherapy techniques. Current chemotherapy techniques utilize cytotoxic chemicals that damage and kill cancerous cells, thereby controlling the size and spread of tumors. Many of these drugs can disrupt the cell cycle, preventing the cancerous cell from proliferating efficiently. Alternatively, a more aggressive treatment can induce apoptosis, programmed cell death, within the cancerous cell.[6] For both methods, the chemotherapy targets the signal pathways that control the vital processes of the cancer cell. Dr. Gustin's research plays a vital role in future chemotherapy technologies and the struggle against mutant cancer cells.

According to Dr. Gustin, current chemotherapy is only effective locally, and often fails to completely incapacitate cancer cells that are farther away from the site of drug administration where drug toxicity is highest. As a result, distant cancer cells are given the opportunity to develop cytoprotective mechanisms that increase their resistance to the drug.[7] Currently, a major goal of Dr. Gustin's research is to discover how and why certain cancer cells are more resistant to chemotherapy. The long-term goal is to understand the major pathways involved with cancer resistance to apoptosis, and to eventually produce a therapeutic product that can target the crucial pathways and inhibitors. With its specificity, this new drug would vastly increase treatment efficacy and provide humanity with a vital tool with which to combat cancer, saving countless lives in the future.

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DESIGN BY Gloria Kim
EDITED BY David Chiang

"The long-term goal is to understand the major pathways involved with cancer resistance to apoptosis, and to eventually produce a therapeutic product that can target the crucial pathways and inhibitors."

COGNITIVE NEUROSCIENCE

COGNITIVE NEUROSCIENCE is a branch of science that addresses the processes in the brain that occur during cognitive activity. The discipline addresses how psychological and cognitive activities are caused by and correlated to the neural connections in our brain. It bridges psychology and neuroscience.

Dr. Simon Fischer-Baum, an assistant professor and researcher at Rice University, co-directs the neuroplasticity lab at the BioScience Research Collaborative. He received his B.A. in Neuroscience and Behavior from Columbia University in 2003 and received his Ph.D. in Cognitive Sciences from Johns Hopkins University in 2010.

Dr. Fischer-Baum describes his research as the "intersection of psychology and neuroscience and computer science to some extent." He is interested in instances of how we understand and pronounce a word once we see it. He also studies memory and how information is encoded in the brain. In his opinion, functional magnetic resonance imaging (fMRI) and other tools of cognitive neuroscience are extremely relevant to cognitive psychology despite public perception. For example, he believes that there is a "serious disconnect" as a result of the belief that the methods and findings of cognitive neuroscience do not apply to cognitive psychology. Cognitive psychologists have been attempting to discover the variation between the different levels of processing and how information travels between these levels. Cognitive neuroscience can help achieve these goals through the use of fMRIs.

fMRI shows which parts of the brain are active when the subject is performing a task. During any task, multiple regions of the brain are involved, with each region processing different types of information. For example, reading a word involves processing both visual information and meaning; when you are reading a word, multiple regions of the brain are active. However, one problem with fMRIs is that while they demonstrate what regions of the brain are active, they do not convey what function each region is carrying out. One of the main objectives of Dr. Fischer-Baum's work is to pioneer new

ONE OF THE MAIN OBJECTIVES OF DR. FISCHER-BAUM'S WORK IS TO PIONEER NEW METHODS SIMILAR TO COMPUTER ALGORITHMS TO DECODE WHAT DATA FROM AN FMRI TELLS US ABOUT WHAT TASKS THE BRAIN IS PERFORMING.

methods similar to computer algorithms to decode what data from an fMRI tells us about what tasks the brain is performing. "I want to be able to take patterns of activity and decode and relate it back to the levels of representation that cognitive psychologists think are going on in research," Dr. Fischer-Baum explains.

Recently, Dr. Fischer-Baum published a study of a patient who suffered severe written language impairments after experiencing a hemorrhagic stroke. Although this patient's reading of familiar words improved throughout the years, he still presented difficulties in processing abstract letter identity information for individual letters. Someone who is able to utilize abstract letter representations can recognize letters independent of case or font; in other words, this person is able to identify letters regardless of the whether they are upper case, lower case, or a different font. In the studied patient, Dr. Fischer-Baum's team observed contralesional reorganization. Compromised regions of the left hemisphere that contained orthography-processing regions (regions that process the set of conventions for writing a language) were organized into homologous regions in the right hemisphere. Through the use of fMRI, the research team determined that the patient's residual reading ability was supported by functional take-over, which is when injury-damaged functions are taken over by healthy brain regions. These results were found by scanning the brain of the patient as he read and comparing the data with that of a control group of young healthy adults with normal brain functions.

While Dr. Fischer-Baum has made substantial progress in this project, the research has not been without challenges. The project began in 2013 and took three years to complete, which is a long time for Dr. Fischer-Baum's field of study. Due to this, none of the co-authors from Rice University know each other despite all working on the project at some point in time with another. Because of the amount of time spent on the project, many of the students rotated in and out while working on various parts; the students never worked on the project at the same time as their peers. In addition, the project's interdisciplinary approach required the input of many collaborators with different abilities. All of the Rice undergraduate students that worked on the project were from different majors although most were from the Cognitive Sciences Department and the Statistics Department. At times, this led to miscommunication between the different students and researchers on the project. Since the students came from different backgrounds, they had different approaches to solving problems. This led to the students at times not being harmonious during many aspects of the project.

Another major setback occurred in bringing ideas to fruition. "You realize quickly when you begin a project that there are a million different ways to solve the problem that you

A GLIMPSE OF THE FUTURE BY JOSHUA HOBBS

are researching, and trying to decide which is the right or best way can sometimes be difficult," Dr. Fischer-Baum said. As a result of this, there have been a lot of false starts, and it has taken a long time in order to get work off the ground. How did Dr. Fischer-Baum get past this problem? "Time, thinking, discussion, and brute force," he chuckled. "You realize relatively quickly that you need to grind it out and put in effort in order to get the job done."

Despite these obstacles, Dr. Fischer-Baum has also undertaken other projects in order to keep his mind busy. In one, he works with stroke patients with either reading or writing deficits to understand how written language is broken down in the mind. He studies specific patterns in the patients' brain activity to investigate how reading and writing ability differ from each other. In another of Dr. Fischer-Baum's projects he works with Dr. Paul Englebretson of the Linguistics Department in order to research the brain activity of blind people as they read Braille. "There is a lot of work on how the reading system works, but a lot of it is based on the perspective of reading by sight," Dr. Fischer-Baum acknowledged. "I am very interested to see how the way we read is affected by properties of our visual system. Comparing sight and touch can show how much senses are a factor in reading."

Ultimately, Dr. Fischer-Baum conducts his research with several goals in mind. The first is to build an approach to cognitive neuroscience that is relevant to the kinds of theories that we have in the other cognitive sciences, especially cognitive psychology. "While it feels like studying the mind and studying the brain are two sides of the same coin and that all of this data should be relevant for understanding how the human mind works, there is still a disconnect between the two disciplines," Dr. Fischer-Baum remarked. He works on building methods in order to bridge this disconnect.

In addition to these goals for advancing the field of cognitive neuroscience, there are clinical implications as well to Dr. Fischer-Baum's research. Gaining more insight into brain plasticity following strokes can be used to build better treatment and recovery programs. Although the research requires further development, the similarity between different regions and their adaptations following injury can lead to a better understanding of the behavioral and neural differences in patterns of recovery. Additionally, Dr. Fischer-Baum aims to understand the relationship between spontaneous and treatment-induced recovery and how the patterns of recovery of language differ as a result of the initial brain injury type and location. Through the combined use of cognitive psychology and fMRI data, the brains of different stroke patients can be mapped and the data can be used to create more successful treatment-induced methods of language recovery. By virtue of Dr. Fischer-Baum's research, not only can cognitive neuroscience be applied to many other disciplines, but it can also significantly improve the lives of millions of people around the world.

DESIGN BY Priscilla Li
EDITED BY Shannon Wang

THROUGH THE COMBINED USE OF COGNITIVE PSYCHOLOGY AND FMRI DATA, THE BRAINS OF DIFFERENT STROKE PATIENTS CAN BE MAPPED AND THE DATA CAN BE USED TO CREATE MORE SUCCESSFUL TREATMENT-INDUCED METHODS OF LANGUAGE RECOVERY.

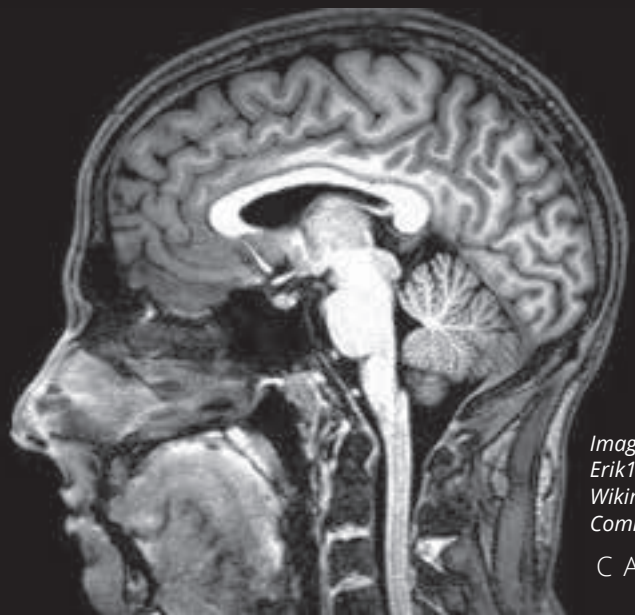

Image from Erik1980 via Wikimedia Commons

The Fight Against Neurodegeneration: The Humans Behind the Science

By Kevin Chang

"You know that it will be a big change, but you really don't have a clue about your future." A 34-year-old postdoctoral researcher at the Telethon Institute of Genetics and Medicine in Italy at the time, Dr. Sardiello had made a discovery that would change his life forever. Eight years later, Dr. Sardiello is now the principal investigator of a lab in the Jan and Dan Duncan Neurological Research Institute (NRI) where he continues the work that had brought him and his lab to America.

Throughout his undergraduate career, Sardiello knew he wanted to be involved in some manner with biology and genetics research, but his passion was truly revealed in 2000: the year he began his doctoral studies. It was during this year that the full DNA sequence of the common fruit fly was released, which constituted the first ever complete genome of a complex organism. At the time, Sardiello was working in a lab that used fruit flies as a model, and this discovery served to spur his interest in genetics. As the golden age of genetics began, so did Sardiello's love for the subject, leading to his completion of a PhD in Genetic and Molecular Evolution at the Telethon Institute of Genetics and Medicine. It was at this institute that his team made the discovery that would bring him to America: the function of Transcription Factor EB, colloquially known as TFEB.

Many knew of the existence of TFEB, but no one knew of its function. Dr. Sardiello and his team changed that. In 2009, they discovered that the gene is the master regulator for lysosomal biogenesis and function. In other words, TFEB works as a genetic switch that turns on the production of new lysosomes, an exciting discovery.[1] Before the discovery of TFEB's function, lysosomes were commonly known as the incinerator or the garbage can of the cell, as these organelles were thought to be essentially specialized containers that get rid of cellular waste. However, with the discovery of TFEB's function, we now know that lysosomes have a much more active role in catabolic pathways and the maintenance of cell homeostasis. Sardiello's groundbreaking findings were published in Science, one of the most prestigious peer reviewed journals in the scientific world. Speaking about his success, Sardiello said, "The bottom line was that there was some sort of feeling that a big change was about to come, but we didn't have a clue what. There was just no possible measure at the time."

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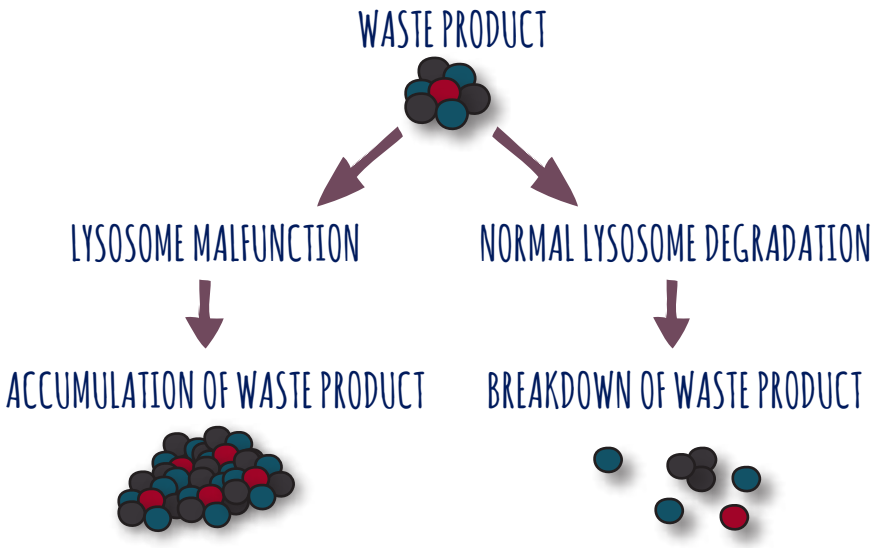
Riding the success of his paper, Sardiello moved to the United States and established his own lab with the purpose of defeating the family of diseases known as Neuronal Ceroid Lipofuscinosis (NCLs). NCLs are genetic diseases caused by the malfunction of lysosomes. This malfunction causes waste to accumulate in the cell and eventually block cell function, leading to cell death. While NCLs cause cell death throughout the body, certain specialized cells such as neurons do not regenerate. Therefore, NCLs are generally neurodegenerative diseases. While there are many variants of NCLs, they all result in premature death after loss of neural functions such as sight, motor ability, and memory.

"With current technology," Sardiello said, "the disease is incurable, since it is genetic. In order to cure a genetic disease, you have to somehow bring the correct gene into every single cell of the body." With our current understanding of biology, this is impossible. Instead, doctors can work to treat the disease, and halt the progress of the symptoms. Essentially, his lab has found a way using TFEB to enhance the function of the lysosomes in order to fight the progress of the NCL diseases.

In addition to genetic enhancement, Sardiello is also focusing on finding drugs that will activate TFEB and thereby increase lysosomal function. To test these new methods, the Sardiello lab uses mouse models that encapsulate most of the symptoms in NCL patients. "Our current results indicate that drug therapy for NCLs is viable, and we are working to incorporate these strategies into clinical therapy," Sardiello said. So far the lab has identified three different drugs or drug combinations that may be viable for treatment of this incurable disease.

While it might be easy to talk about NCLs and other diseases in terms of their definitions and effects, it is important to realize that behind every disease are real people and real patients. The goal of the Sardiello Lab is not just to do science and advance humanity, but also to help patients and give them hope. One such patient is a boy named Will Herndon. Will was diagnosed with NCL type 3, and his story is one of resilience, strength, and hope.



When Will was diagnosed with Batten Disease at the age of six, the doctors informed him and his family that there was little they could do. At the time, there was little to no viable research done in the field. However, despite being faced with terminal illness, Will and his parents never lost sight of what was most important: hope. While others might have given up, Missy and Wayne Herndon instead founded The Will Herndon Research Fund - also known as HOPE - in 2009, playing a large role in bringing Dr. Sardiello and his lab to the United States. Yearly, the foundation holds a fundraiser to raise awareness and money that goes towards defeating the NCL diseases. Upon its inception, the fundraiser had only a couple of hundred attendees- now, only half a decade later, thousands of like-minded people arrive each year to support Will and others with the same disease. "Failure is not an option," Missy Herndon said forcefully during the 2016 banquet. "Not for Will, and not for any other child with Batten disease." It was clear from the strength of her words that she believed in the science, and that she believed in the research.

"I have a newborn son," Sardiello said, recalling the speech. "I can't imagine going through what Missy and Wayne had to. I felt involved and I felt empathy, but most of all, I felt respect for Will's parents. They are truly exceptional people and go far and beyond what anyone can expect of them. In face of adversity, they are tireless, they won't stop, and their commitment is amazing."

When one hears about science and labs, it usually brings to mind arrays of test tubes and flasks or the futuristic possibilities of science. In all of this, one tends to forget about the people behind the test bench: the scientists that conduct the experiments and uncover the next step in the collective knowledge of humanity, people like Dr. Sardiello. However, Sardiello isn't alone in his endeavors, as he is supported by the members of his lab.

> "SCIENCE SHOULDN'T BE DETACHED FROM THE HUMANS WORKING TO ADVANCE IT, BUT RATHER INTEGRATED WITH THE MEN AND WOMEN WORKING TO MAKE THE WORLD A BETTER PLACE."

Each and every one of the researchers in Marco's lab is an international citizen, hailing from at least four different countries in order to work towards a common cause: Parisa Lombardi from Iran, Lakshya Bajaj, Jaiprakash Sharma, and Pal Rituraj from India, Abdallah Amawi, from Jordan, and of course, Marco Sardiello and Alberto di Ronza, from Italy. Despite the vast distances in both geography and culture, the chemistry among the team was palpable, and while how they got to America varied, the conviction that they had a responsibility to help other people and defeat disease was always the same.

Humans have always been predisposed to move forwards. It is because of this propensity that humans have been able to eradicate disease and change the environments that surround us. However, behind all of our achievements lies scientific advancement, and behind it are the people that we so often forget. Science shouldn't be detached from the humans working to advance it, but rather integrated with the men and women working to make the world a better place. Dr. Sardiello and his lab represent the constant innovation and curiosity of the research community, ideals that are validated in the courage of Will Herndon and his family. In many ways, the Sardiello lab embodies what science truly represents: humans working for something far greater than themselves.

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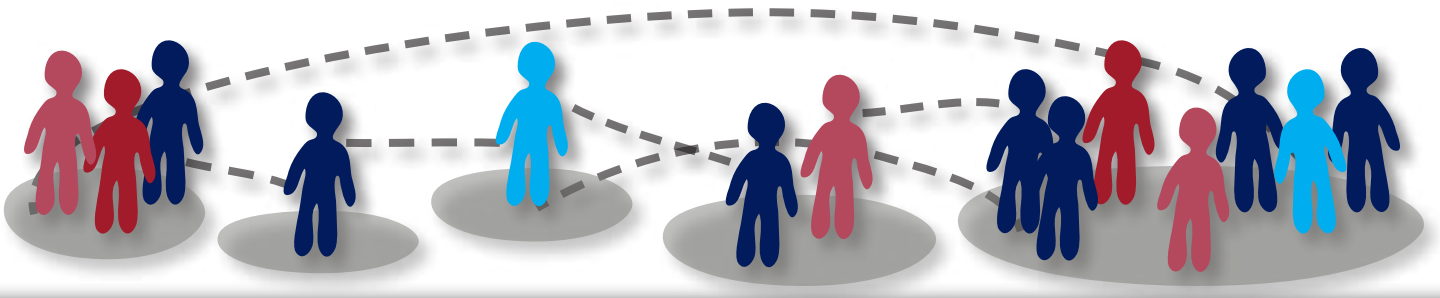
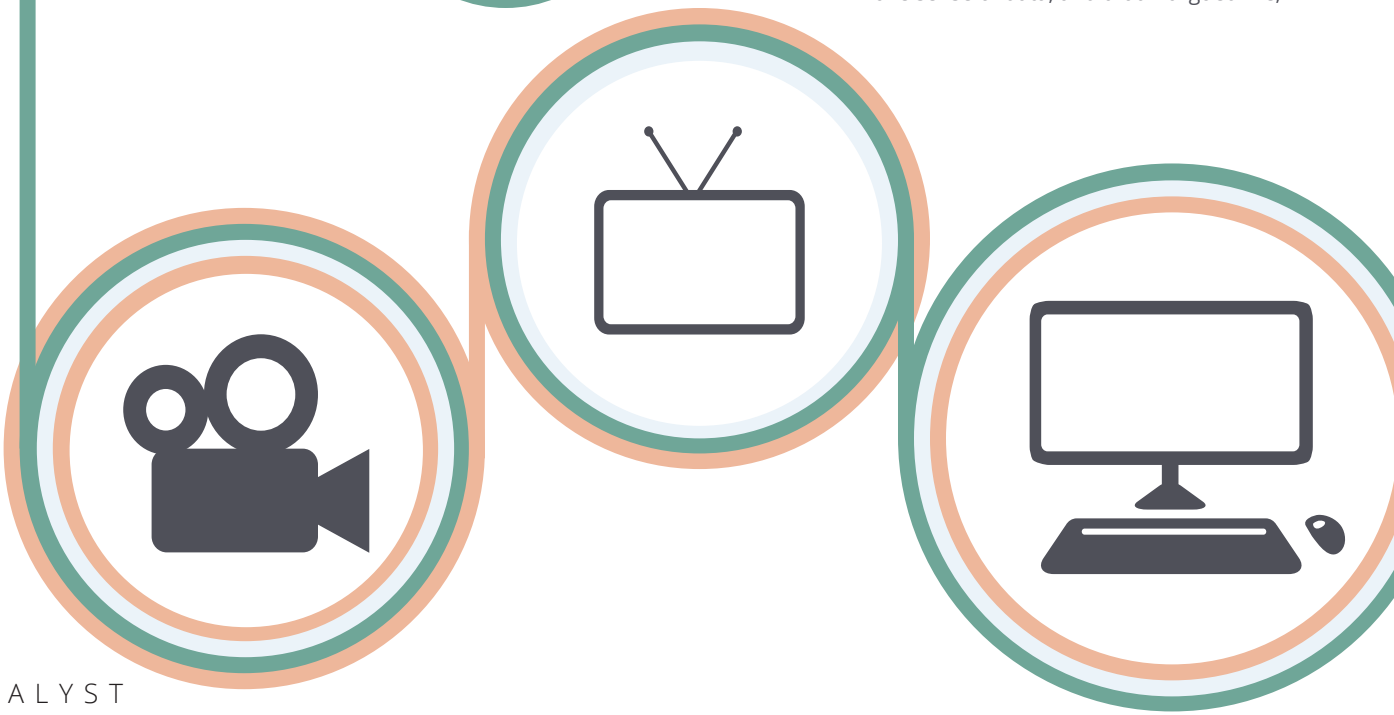


visualizing THE FUTURE OF MEDICINE

NAIMAH SARWAR

What do you do when you get sick? Most likely you schedule a doctor's appointment, show up, and spend ten to fifteen minutes with the doctor. The physician quickly scans your chart, combines your narrative of your illness with your medical history and his or her observations so that you can leave with diagnosis and prescription in hand. While few give the seemingly routine process a second thought, the very way in which healthcare providers approach the doctor-patient experience is evolving. There is a growing interest in the medical humanities, a more interdisciplinary study of illness. According to Baylor College of Medicine, the aim of the medical humanities is "understanding the profound effects of illness and disease on patients, health professionals, and the social worlds in which they live and work."[1] Yet medical humanities is somewhat of a catch all term. It encompasses disciplines including literature, anthropology, sociology, philosophy, the fine arts and even "science and technology studies."[1] This nuanced approach to medicine is exactly what Dr. Kirsten Ostherr, one of the developers of Rice University's medical humanities program, promotes.

Dr. Ostherr uses this interdisciplinary approach to study the intersection of technology and medicine. She has conducted research on historical medical visualizations through media such as art and film and its application to medicine today. Originally a PhD recipient of American Studies and Media Studies at Brown University, Dr. Ostherr's interest in medicine and media was sparked while working at the Department of Public Health at Oregon Health Sciences University, where researchers were using the humanities as a lens through which they could analyze health data. "I noticed that the epidemiologists there used narrative to make sense of data, and that intrigued me,"



she said. This inspired Dr. Ostherr to use her background in media and public health to explore how film and media in general have affected medicine and to predict where the future of medical media lies. While the integration of medicine and media may seem revolutionary, it is not a new concept. In her book, *Medical Visions*, Dr. Ostherr says that "We know we have become a patient when we are subjected to a doctor's clinical gaze," a gaze that is powerfully humanizing and can "transform subjects into patients."[2] With the integration of technology and medicine, this "gaze" has extended to include the visualizations vital to understanding the patient and decoding disease. Visualizations have been a part of the doctor-patient experience for longer than one might think, from X-rays in 1912 to the electronic medical records used by physicians today.[3]

In her book, Dr. Ostherr traces and analyzes a series of different types of medical visualizations throughout history. Her research begins with the study of scientific films of the early twentieth century, and their attempt to bridge the gap between scientific knowledge and the general public.[2] The use of film in medical education was also significant in the 20th century. These technical films helped facilitate the globalization of health and media in the postwar era. Another form of medical visualizations that emerged with the advent of medicine on television. At the intersection of entertainment and education, medical documentary evolved into "health information programming" in the 1980's which in turn transitioned into the rise of medical reality television.[2] The history of this diverse and expanding media, she says, proves that the use of visualizations in healthcare and our daily lives has made medicine "a visual science."

One of the main takeaways from Dr. Ostherr's historical analysis of medical visualizations was the deep-rooted relationship between visualizations and their role in spreading medical knowledge to the average person. While skeptics may argue against this characterization, "this is a broad social change that is taking place," Dr. Ostherr said, citing new scientific research emerging on human centered design and the use of visual arts in medical training. "It's the future of medicine," she said. There is already evidence that such a change is taking place: the method of recording patient information using health records has begun to change. In recent years there has been a movement to adopt electronic health records due to their potential to save the healthcare industry millions of dollars and improve efficiency.[4] Yet recent studies show that the current systems in place are not as effective as predicted.[5] Online patient portals allow patients to keep up with their health information, view test results and even communicate with their health care providers, but while these portals can involve patients as active participants in their care, they can also be quite technical.[6] As a result, there is a push to develop electronic health records with more readily understandable language.

In order to conduct further research in the field including projects such as the development of better, easier to understand electronic health records, Dr. Ostherr co-founded and is the director of the Medical Futures Lab. The lab draws resources from Baylor College of Medicine, University of Texas Health Science Center, and Rice University and its diverse team ranges from humanist scholars to doctors to computer scientists.[7] The use of technology in medicine has continued to develop rapidly alongside the increasing demand for personalized, humanizing care. While it seems like there is an inherent conflict between the two, Dr. Ostherr believes medicine needs the "right balance of high tech and high touch" which is what her team at the Medical Futures Lab (MFL) works to find. The MFL team works on projects heavily focused on deconstructing and reconstructing the role of the patient in education and diagnosis.[7]

The increasingly integrated humanistic and scientific approach to medicine is revolutionizing healthcare. As the Medical Futures Lab explores the relationship between personal care and technology, the world of healthcare is undergoing a broad cultural shift. Early on in their medical education, physicians are being taught the value of incorporating the humanities and social sciences into their training, and that science can only teach one so much about the doctor-patient relationship. For Dr. Ostherr, the question moving forward will be "what is it that is uniquely human about healing?" What are the limitations of technology in healing and what about healing process can be done exclusively by the human body? According to Dr. Ostherr, the histories of visualizations in medicine can serve as a roadmap and an inspiration for the evolution and implementation of new media and technology in transforming the medical subject into the patient.

Visualizations have been a part of the doctor patient experience for longer than one might think from X rays in 1912 to the electronic medical records used by physicians today.

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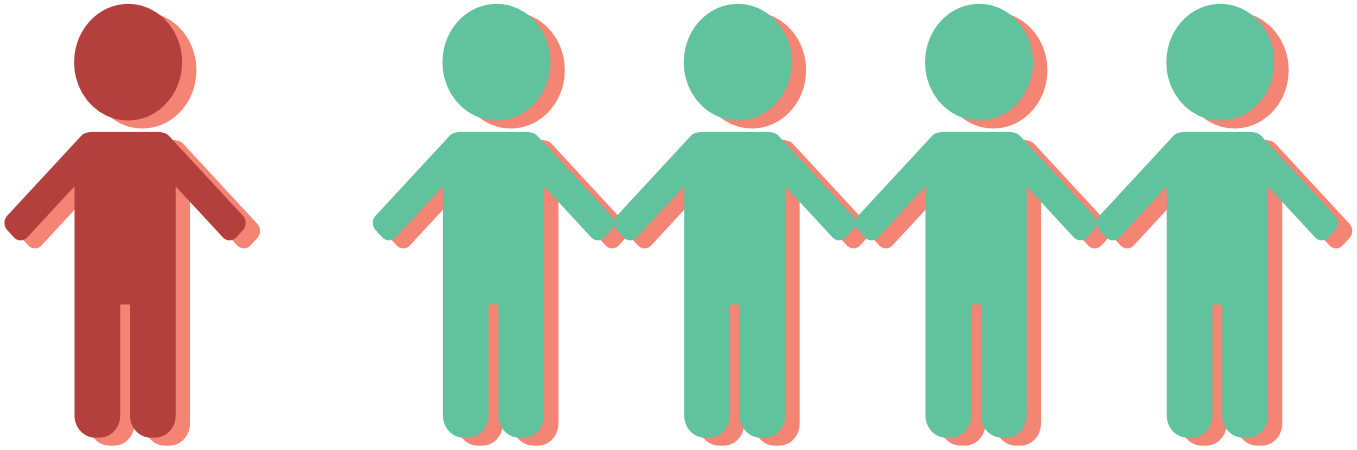
DESIGN BY Kaitlyn Xiong
EDITED BY Ruchi Gupta

THE SECRET BEHIND SOCIAL STIGMA

BY JACQUELINE LOCARNO



How do you accurately quantify something as subjective and controversial as discrimination? What about stigma—a superficial mark imposed upon a prototypical group of individuals? How do you attempt to validate what is seemingly invisible? Dr. Michelle "Mikki" Hebl and her team in the Industrial/Organizational (I/O) department of social psychology at Rice University attempt to answer these questions.

In the world of social psychology, where human interactions are often unpredictable, researchers must get creative to control variables as much as possible while simultaneously mimicking real-life situations. Dr. Hebl integrates both laboratory procedures and field studies that involve standardized materials. "My research is fairly novel," she notes. Unlike the majority of existing stigma and discrimination research, which depends on self-reported assessments, her studies examine real, non-simulated social interactions. Although her approach seeks to provide more realistic and unbiased settings, "it's messier," she adds, laughing about the many trials discarded due to uncontrollable circumstances. That attitude—optimistic, determined, and creative—is held proudly by Dr. Hebl. It is clear that her lab's overall mission—to reduce discrimination and increase equity—is worth undertaking.

> Discrete recording devices worn by the subjects revealed a pattern of decreased word count per sentence and shorter interactions for the stigmatized group.

Dr. Hebl and her team focus on a form of behavior they call "interpersonal discrimination," a type of discrimination that occurs implicitly while still shaping the impressions we form and the decisions we make.[1] This kind of bias, rooted in stereotypes and negative social stigma, is far more subtle than some of the more well-known, explicit forms of discrimination. For example, in a field study evaluating bias against homosexual applicants in Texas, Dr. Hebl found that the members of both the experimental and control group, who were wearing hats that said "Gay and Proud" and "Texan and Proud" respectively, did not experience formal bias when entering stores to seek employment. For example, none of the subjects were denied job applications. What she did find, however, was a pattern of interpersonal reactions against the experimental group. Discrete recording devices worn by the subjects revealed a pattern of decreased word count per sentence and shorter interactions for the stigmatized group. Their self-reports further

indicated on average a higher perceived negativity and lower perceived employer interest.1 In another study evaluating obesity-related stigma, results showed that obese individuals—in this case subjects wearing obese prosthetic suits—experience similarly negative interactions.[2]

While many of her studies evaluated biases in seeking employment, Dr. Hebl also explored the presence of interpersonal discrimination against lesser-known groups that experience bias. One surprising finding indicated negative stigmatization against cancer survivors.[3] In other studies, the team found patterns relating to stereotypicality; this relatively new phenomena explores the lessened interpersonal discrimination against those who deviate from the stereotypical prototype of their minority group, i.e. a more light-skinned Hispanic male.[4] A holistic review of her research reveals a pattern of discrimination against stigmatized groups on an implicit level. Once researchers like Dr. Hebl find these patterns, they can investigate them in the lab by further isolating variables to develop a more refined and widely-applicable conclusion.

> A holistic review of her research reveals a pattern of discrimination against stigmatized groups on an implicit level.

What can make more subtle forms of bias so detrimental is the ambiguity surrounding them. When someone discriminates against another in a clear and explicit form, one can easily attribute the behavior to the person's biases. On the other hand, when this bias is perceived in the form of qualitative behavior, such as shortened conversations and body language, it raises questions regarding the person's intentions. In these cases, the victim often internalizes the negative treatment, questioning the effect of traits that they cannot control—be it race, sexual orientation, or physical appearance. This degree of uncertainty raises conflict and tension between differing groups, thus potentially hindering progress in today's increasingly diverse workplaces, schools, and universities.[5]

Dr. Hebl knew that exploring the presence of this tension between individuals was only the first step. "One of the most exciting aspects of social psychology is that just learning about these things makes you inoculated against them," she said. Thus emerges the search for practical solutions involving education and reformation of conventional practices in the workplace. Her current work looks at three primary methods: The first is acknowledging biases on an individual level. This strategy involves individuation, or the recognition of one's own stigma and subsequent compensation for it.[6] The second involves implementing organizational methods in the workplace, such as providing support for stigmatized groups and awareness training.[7] The third, which has the most transformative potential, is the use of research to support reformation of policies that could protect these individuals.

"I won't rest...until we have equity," she affirmed when asked about the future of her work. For Dr. Hebl, the ultimate goal is education and change. Human interactions are incredibly complex, unpredictable, and difficult to quantify. But they influence our daily decisions and actions, ultimately impacting how we view ourselves and others. Social psychology research suggests that biases, whether we realize it or not, are involved in the choices we make every day: from whom we decide to speak to whom we decide to work with. Dr. Hebl saw this and decided to do something about it. Her work brings us to the complex source of these disparities and suggests that understanding their foundations can lead to a real, desirable change.

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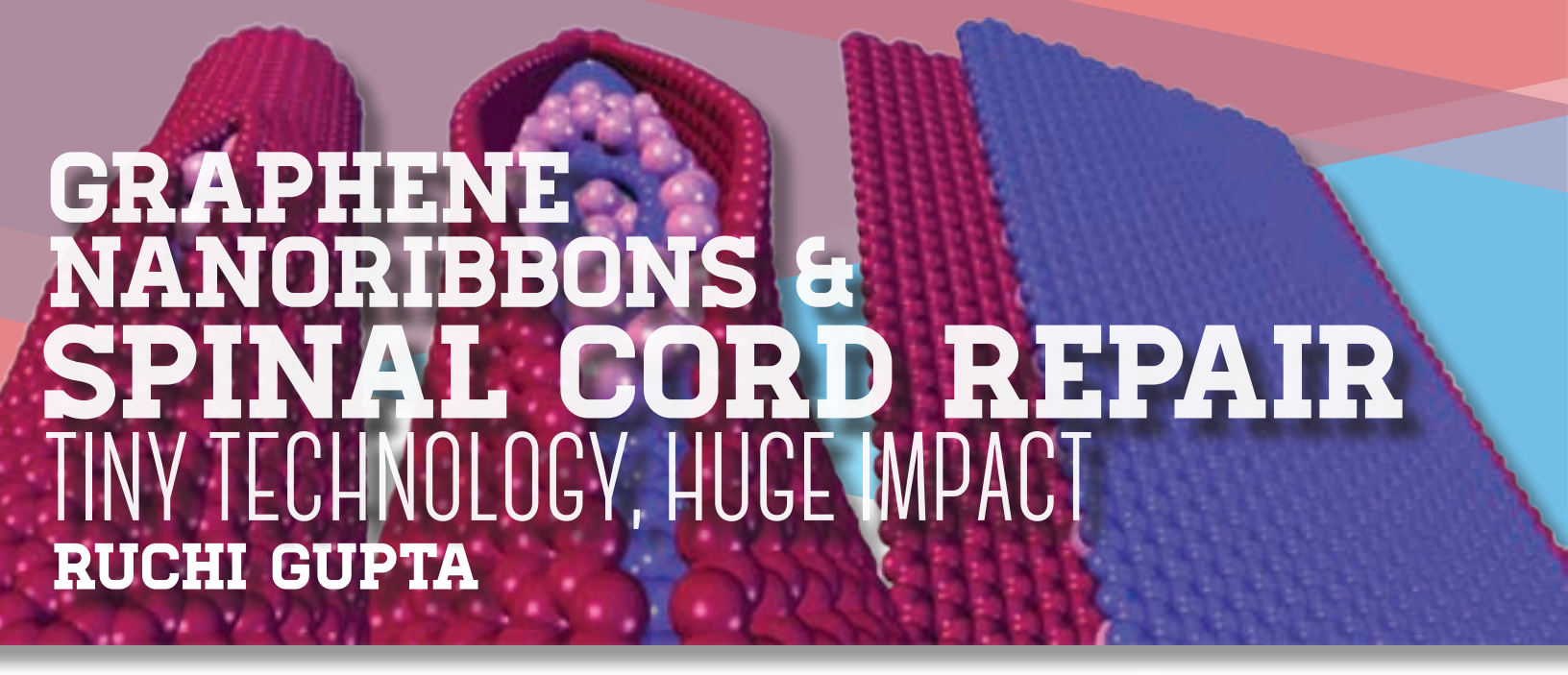

GRAPHENE NANORIBBONS & SPINAL CORD REPAIR

TINY TECHNOLOGY, HUGE IMPACT

RUCHI GUPTA

The same technology that has been used to strengthen polymers[1], de-ice helicopter wings[2], and create more efficient batteries[3] may one day help those with damaged or even severed spinal cords walk again. The Tour Lab at Rice University, headed by Dr. James Tour, is harnessing the power of graphene nanoribbons to create a special new material called Texas-PEG that may revolutionize the way we treat spinal cord injuries; one day, it may even make whole body transplants a reality.

Dr. Tour, the T.T. and W.F. Chao Professor of Chemistry, Professor of Materials Science and NanoEngineering, and Professor of Computer Science at Rice University, is a synthetic organic chemist who mainly focuses on nanotechnology. He currently holds over 120 patents and has published over 600 papers, and was inducted into the National Academy of Inventors in 2015.[4] His lab is currently working on several different projects, such as investigating various applications of graphene, creating and testing nanomachines, and the synthesizing and imaging of nanocars. The Tour Lab first discovered graphene nanoribbons while working with graphene back in 2009.[5] Their team found a way to "unzip" graphene nanotubes into smaller strips called graphene nanoribbons by injecting sodium and potassium atoms between nanotube layers in a nanotube stack until the tube split open. "We fell upon the graphene nanoribbons," says Dr. Tour. "I had seen it a few years ago in my lab but I didn't believe it could be done because there wasn't enough evidence. When I realized what we had, I knew it was enormous."

This discovery was monumental: graphene nanoribbons have been used in a variety of different applications because of their novel characteristics. Less than 50 nm wide (which is about the width of a virus), graphene nanoribbons are 200 times stronger than steel and are great conductors of heat and electricity. They can be used to make materials significantly stronger or electrically conductive without adding much additional weight. It wasn't until many years after their initial discovery, however, that the lab discovered that graphene nanoribbons could be used to heal severed spinal cords.

The idea began after one of Dr. Tour's students read about European research on head and whole body transplants on Reddit. This research was focused on taking a brain dead patient with a healthy body and pairing them with someone who has brain activity but has lost bodily function. The biggest challenge, however, was melding the spine together. The neurons in the two separated parts of the spinal cord could not communicate with one another, and as a result, the animals involved with whole body and head transplant experiments only regained about 10% of their original motor function. The post-graduate student contacted the European researchers, who then proposed using the Tour lab's graphene nanoribbons in their research, as Dr. Tour's team had already proven that neurons grew very well along graphene.

"When a spinal cord is severed, the neurons grow from the bottom up and the top down, but they pass like ships in the night; they never connect. But if they connect, they will be fused together and start working again. So the idea was to put very thin nanoribbons in the gap between the two parts of the spinal cord to get them to align," explains Dr. Tour. Nanoribbons are extremely conductive, so when their edges are activated with polyethylene glycol, or PEG, they form an active network that allows the spinal cord to reconnect. This material is called Texas-PEG, and although it is only about 1% graphene nanoribbons, this is still enough to create an electric network through which the neurons in the spinal cord can connect and communicate with one another.

The Tour lab tested this material on rats by severing their spinal cords and then using Texas-PEG to see how much of their mobility was recovered. The rats scored about 19/21 on a mobility scale after only 3 weeks, a remarkable advancement from the 10% recovery in previous European trials. "It was just phenomenal. There were rats running away after 3 weeks with a totally severed spinal cord! We knew immediately that something was happening because one day they would touch their foot and their brain was detecting it," says Dr. Tour. The first human trials will begin in 2017 overseas. Due to FDA regulations, it may be awhile before we see trials in the United States, but the FDA will accept data from successful trials in other countries. Graphene nanoribbons may one day become a viable treatment option for spinal injuries.

This isn't the end of Dr. Tour's research with graphene nanoribbons. "We've combined our research with neurons and graphene nanoribbons with antioxidants: we inject antioxidants into the bloodstream to minimize swelling. All of this is being tested in Korea on animals. We will decide on an optimal formulation this year, and it will be tried on a human this year," Dr. Tour explained. Most of all, Dr. Tour and his lab would like to see their research with graphene nanoribbons used in the United States to help quadriplegics who suffer from limited mobility due to spinal cord damage. What began as a lucky discovery now has the potential to change the lives of thousands.

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Image courtesy of Tour Group

DESIGN BY Monika Karki, Vidya Giri
EDITED BY Jeff Michel

DETECTION OF GUT INFLAMMATION + TUMORS USING PHOTOACOUSTIC IMAGING

CHRISTINE TANG

ABSTRACT

Photoacoustic imaging is a technique in which contrast agents absorb photon energy and emit signals that can be analyzed by ultrasound transducers. This method allows for unprecedented depth imaging that can provide a non-invasive alternative to current diagnostic tools used to detect internal tissue inflammation.[1] The Rice iGEM team strove to use photoacoustic technology and biomarkers to develop a noninvasive method of locally detecting gut inflammation and colon cancer. As a first step, we genetically engineered Escherichia coli to express near-infrared fluorescent proteins iRFP670 and iRFP713 and conducted tests using biomarkers to determine whether expression was confined to a singular local area.

INTRODUCTION

In photoacoustic imaging, laser pulses of a specific, predetermined wavelength (the excitation wavelength) activate and thermally excite a contrast agent such as a pigment or protein. The heat makes the contrast agent contract and expand producing an ultrasonic emission wavelength longer than the excitation wavelength used. The emission wavelength data are used to produce 2D or 3D images of tissues that have high resolution and contrast.[2]

The objective of this photoacoustic imaging project is to engineer bacteria to produce contrast agents in the presence of biomarkers specific to gut inflammation and colon cancer and ultimately to deliver the bacteria into the intestines. The bacteria will produce the contrast agents in response to certain biomarkers and lasers will excite the contrast agents, which will emit signals in local, targeted areas, allowing for a non-invasive imaging method. Our goal is to develop a non-invasive photoacoustic imaging delivery method that uses engineered bacteria to report gut inflammation and identify colon cancer. To achieve this, we constructed plasmids that have a nitric-oxide-sensing promoter (*soxR/S*) or a hypoxia-sensing promoter (*narK* or *fdhf*) fused to genes encoding near-infrared fluorescent proteins or violacein with emission wavelengths of 670 nm (iRFP670) and 713 nm (iRFP713). Nitric oxide and hypoxia, biological markers of gut inflammation in both mice and humans, would therefore promote expression of the desired iRFPs or violacein.[3,4]

RESULTS AND DISCUSSION

ARABINOSE

To test the inducibility and detectability of our iRFPs, we used *pBAD*, a promoter that is part of the arabinose operon located in *E. coli*.[5] We formed genetic circuits consisting of the *pBAD* expression system and iRFP670 and iRFP713 (Fig. 1a). AraC, a constitutively produced transcription regulator, changes form in the

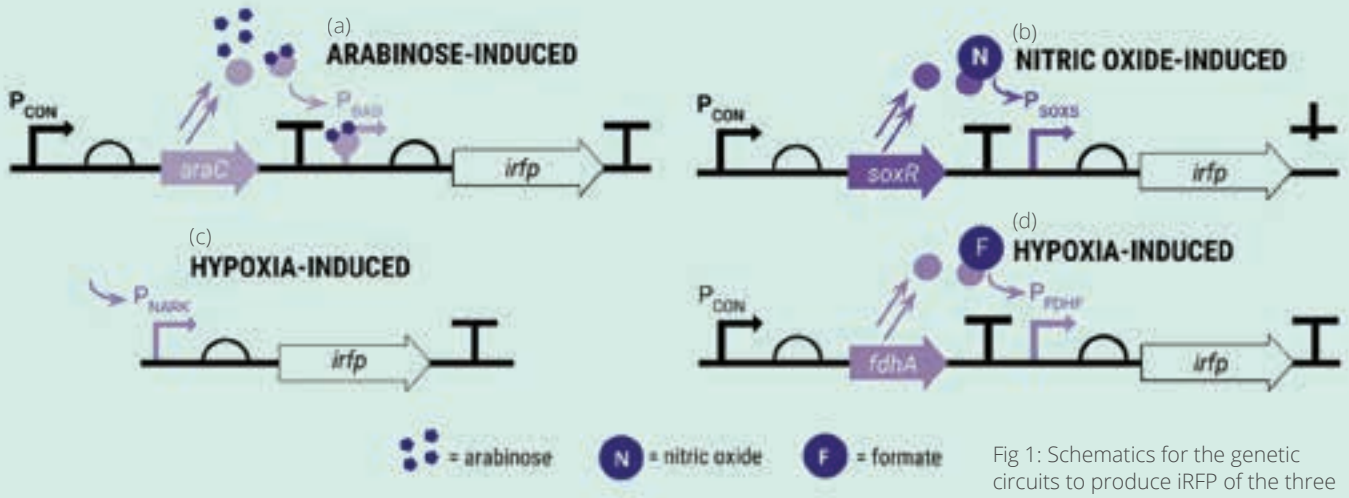


Fig 1: Schematics for the genetic circuits to produce iRFP of the three different inducers: (a) aribanose, (b) nitric oxide, (c and d) hypoxia

presence of arabinose sugar, allowing for the activation of the *pBAD* promoter.

Fluorescence levels emitted by the iRFPs increased significantly when placed in wells containing increasing concentrations of arabinose (Figure 2). This correlation suggests that our selected iRFPs fluoresce sufficiently when promoters are induced by environmental signals. The results of the arabinose assays showed that we successfully produced iRFPs; the next steps were to engineer bacteria to produce the same iRFPs under nitric oxide and hypoxia.

NITRIC OXIDE

The next step was to test the nitric oxide induction of iRFP fluorescence. We used a genetic circuit consisting of a constitutive promoter and the *soxR* gene, which in turn expresses the *soxR* protein (Figure 1b). In the presence of nitric oxide, *soxR* changes form to activate the promoter *soxS*, which activates the expression of the desired gene. The source of nitric oxide added to our engineered bacteria samples was diethylenetriamine/nitric oxide adduct (DETA/NO).

Figure 3 shows no significant difference of fluorescence/OD600 between DETA/NO concentrations. This finding implies that our engineered bacteria were unable to detect the nitric oxide biomarker and produce iRFP; future troubleshooting includes verifying promoter strength and correct sample conditions. Furthermore, nitric oxide has an extremely short half-life of a few seconds, which may not be enough time for most of the engineered bacteria to sense the nitric oxide, limiting iRFP production and fluorescence.

HYPOXIA

We also tested the induction of iRFP fluorescence with the hypoxia-inducible promoters *narK* and *fdhf*. We expected iRFP production and fluorescence to increase when using the *narK* and *fdhf* promoters in anaerobic conditions (Figure 1c and d).

However, we observed the opposite result. A decreased fluorescence for both iRFP constructs in both promoters was measured when exposed to hypoxia (Figure 4). This finding suggests that our engineered bacteria were unable to detect the hypoxia biomarker and produce iRFP; future troubleshooting includes verifying promoter strength and correct sample conditions.

FUTURE DIRECTIONS

Further studies include testing the engineered bacteria co-cultured with colon cancer cells and developing other constructs that will enable bacteria to sense carcinogenic tumors and make them fluoresce for imaging and treatment purposes.

VIOLACEIN HAS ANTI-CANCER THERAPY POTENTIAL

Violacein is a fluorescent pigment for in vivo photoacoustic imaging in the near-infrared range and shows anti-tumoral activity.[6] It has high potential for future work in bacterial tumor targeting. We have succeeded in constructing violacein using Golden Gate shuffling and intend to use it in experiments such as the nitric oxide and hypoxia assays we used for iRFP670 and 713.[7]

INVASIN CAN ALLOW FOR TARGETED CELL THERAPY

Using a beta integrin called invasin, certain bacteria are able to invade mammalian cells.[8-9] If we engineer *E. coli* that have the beta integrin invasion as well as the genetic circuits capable of sensing nitric oxide and/or hypoxia, we can potentially allow the *E. coli* to invade colon cells and release contrast agents for photoacoustic imaging or therapeutic agents such as violacein only in the presence of specific biomarkers.[10] Additionally, if we engineer the bacteria that exhibit invasin to invade colon cancer cells only and not normal cells, then this approach would potentially allow for a localized targeting and treatment of cancerous tumors. This design allows us to create scenarios with parameters more similar to the conditions observed in the human gut as we will be unable to test our engineered bacteria in an actual human gut.

Fig 2: Arabinose induces iRFP production by pBAD promoter

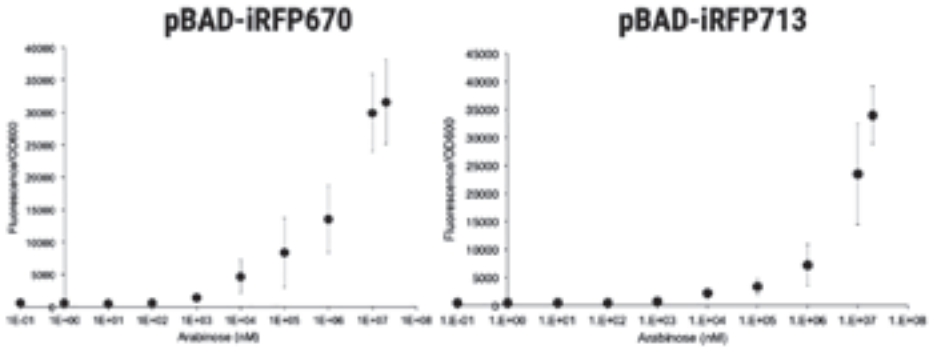


Fig 3: iRFP production by Sox R/S promoter is not induced by nitric oxide analog

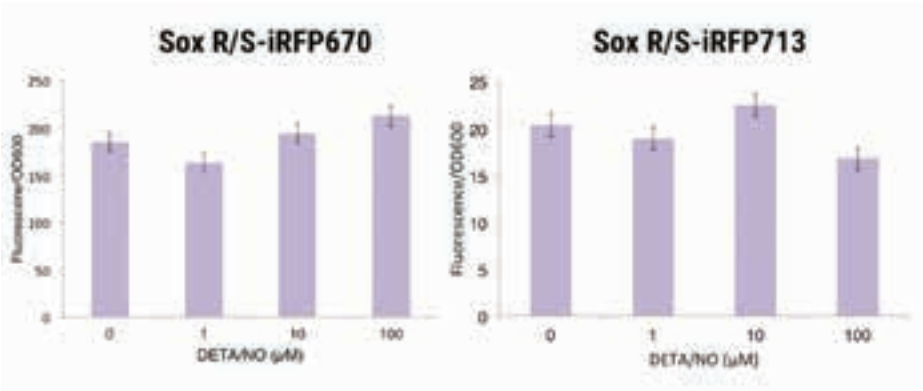
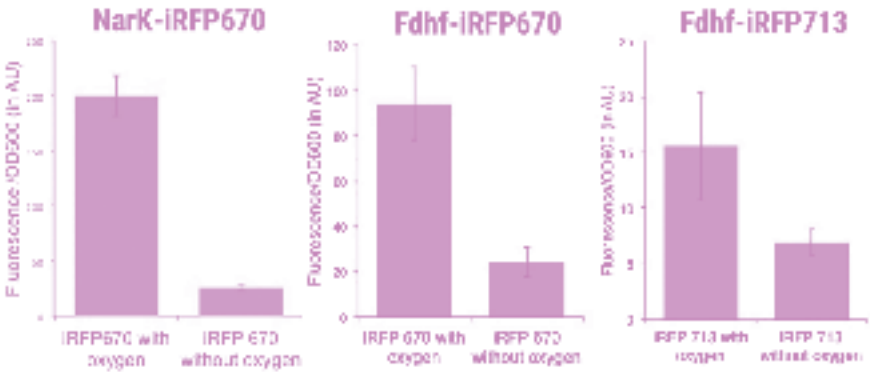


Fig 4: iRFP production by Fdhf or NarK is not induced by hypoxic conditions



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If you would like to know more information about our project and our team, please visit our iGEM wiki at: http://2016.igem.org/Team:Rice.

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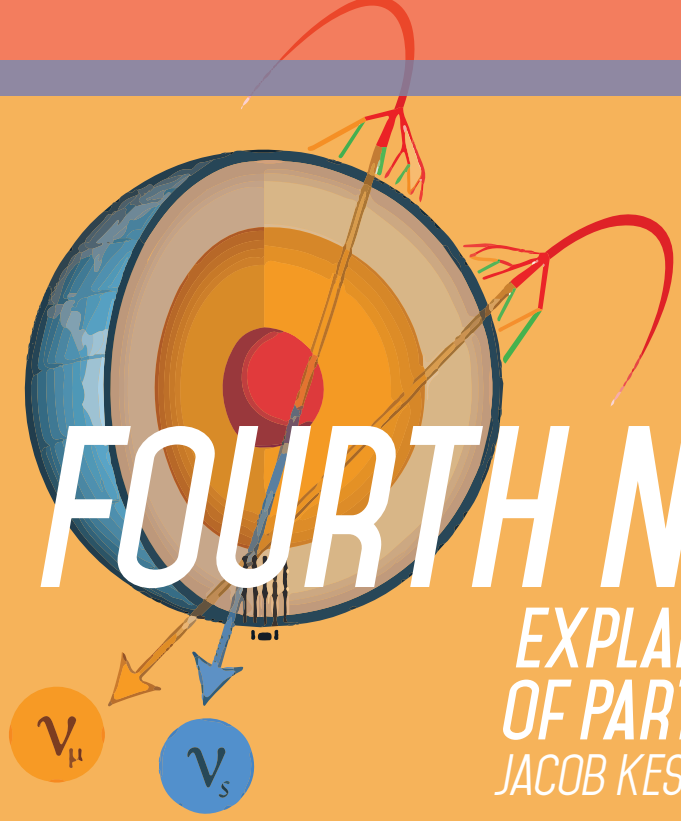

Fig 1: A diagram of the IceCube detection facilities at the South Pole. It demonstrates where upgoing neutrinos would originate from and how those crossing the core would be most likely to oscillate into sterile neutrinos due to the large gravitational force.[3]

A FOURTH NEUTRINO?

EXPLAINING THE ANOMALIES OF PARTICLE PHYSICS

JACOB KESTEN

ABSTRACT

The very first neutrino experiments discovered that neutrinos exist in three flavors and can oscillate between those flavors as they travel through space. However, many recent experiments have collected anomalous data that contradicts a three neutrino flavor hypothesis, suggesting instead that there may exist a fourth neutrino, called the sterile neutrino, that interacts solely through the gravitational force. While there is no conclusive evidence proving the existence of a fourth neutrino flavor, scientists designed the IceCube laboratory at the South Pole to search for this newly hypothesized particle. Due to its immense size and sensitivity, the IceCube laboratory stands as the most capable neutrino laboratory to corroborate the existence of these particles.

INTRODUCTION

Neutrinos are subatomic, ubiquitous, elementary particles that are produced in a variety of ways. Some are produced from collisions in the atmosphere between different particles, while others result from the decomposition and decay of larger atoms.[1,3] Neutrinos are thought to play a role in the interactions between matter and antimatter; furthermore, they are thought to have significantly influenced the formation of the universe.[3] Thus, neutrinos are of paramount concern in the world of particle physics, with the potential of expanding our understanding of the universe. When they were first posited, neutrinos were thought to have no mass because they have very little impact on the matter around them. However, decades later, it was determined that they have mass but only interact with other matter in the universe through the weak nuclear force and gravity.[2]

Early neutrino experiments found that measuring the number of neutrinos produced from the sun resulted in a value almost one third of the predicted value. Coupled with other neutrino experiments, these observations gave rise to the notion of neutrino flavors and neutrino flavor oscillations. There are three flavors of the standard neutrino: electron (v_e), muon (v_μ), and tauon (v_T). Each neutrino is a decay product that is produced with its namesake particle; for example, v_e is produced alongside an electron during the decay process.[9] Neutrino oscillations were also proposed after these results, stating that if a given type of neutrino is produced during decay, then at a certain distance from that spot, the chance of observing that neutrino with the properties of a different flavor becomes non-zero.[2] Essentially, if v_e is produced, then at a sufficient distance, the neutrino may become either v_μ or v_T. This is caused by a discrepancy in the flavor and mass eigenstates of neutrinos.

In addition to these neutrino flavor states, there are also three mass eigenstates, or states in which neutrinos have definite mass. Through experimental evidence, these two different states represent two properties of neutrinos. As a result, neutrinos of the same flavor can be of different masses. For example, two electron neutrinos will have the same definite flavor, but not necessarily the same definite mass state. It is this discrepancy in the masses of these particles that actually leads to their ability to oscillate between flavors with the probability function given by the formula $P(ab) = sin^2(2q)sin^2(1.27Dm^2L_vE_v^{-1})$, where a and b are two flavors, q is the mixing angle, Dm is the difference in the mass eigenstate values of the two different neutrino flavors, L_v is the distance from source to detector, and E_v is the energy of the neutrino.[6] Thus, each flavor is a different linear combination of the three states of definite mass.

The equation introduces the important concept of the mixing angle, which defines the difference between flavor and mass states and accounts for neutrino flavor oscillations. Thus, if the mixing angle were zero, this would imply that the mass states and flavor states were the same and therefore no oscillations could occur. For example, all muon neutrinos produced at a source would still be muon neutrinos when $P(mb) = 0$. On the other hand, at a mixing angle of $\pi/4$, when $P(mb) = 1$, all muon neutrinos would oscillate to the other flavors in the probability function.[9]

ANOMALOUS DATA

Some experimental data has countered the notion of three neutrino flavor oscillations.[3] If the experimental interpretation is correct, it would point to the existence of a fourth or even an additional fifth mass state, opening up the possibility of other mass states that can be taken by the hypothesised sterile neutrino. The most conclusive anomalous data arises from the Liquid Scintillator Neutrino Detector (LSND) Collaboration and MiniBooNE. The LSND Collaboration at Los Alamos National Laboratory looked for oscillations between v_m neutrinos produced from muon decay and v_e

neutrinos. The results showed a lower-than-expected probability of oscillation.[6] These results highly suggest either an oscillation to another neutrino flavor. A subsequent experiment at Fermilab called the mini Booster Neutrino Experiment (MiniBooNE) again saw a discrepancy between predicted and observed values of ve appearance with an excess of ν_e events.[7] All of these results have a low probability of fit when compared to the standard model of particle physics, which gives more plausibility to the hypothesis of the existence of more than three neutrino flavors.

GALLEX, an experiment measuring neutrino emissions from the sun and chromium-51 neutrino sources, as well as reactor neutrino experiments gave inconsistent data that did not coincide with the standard model's predictions for neutrinos. This evidence merely suggests the presence of these new particles, but does not provide conclusive evidence for their existence.[4,5] Thus, scientists designed a new project at the South Pole to search specifically for newly hypothesized sterile neutrinos.

ICECUBE STUDIES

IceCube, a particle physics laboratory, was designed specifically for collecting data concerning sterile neutrinos. In order to collect conclusive data about the neutrinos, IceCube's vast resources and acute precision allow it to detect and register a large number of trials quickly. Neutrinos that come into contact with IceCube's detectors are upgoing atmospheric neutrinos and thus have already traversed the Earth. This allows a fraction of the neutrinos to pass through the Earth's core. If sterile neutrinos exist, then the large gravitational force of the Earth's core should cause some muon neutrinos that traverse it to oscillate into sterile neutrinos, resulting in fewer muon neutrinos detected than expected in a model containing only three standard mass states, and confirming the existence of a fourth flavor.[3]

For these particles that pass upward through IceCube's detectors, the Earth filters out the charged subatomic particle background noise, allowing only the detection of muons (the particles of interest) from neutrino interactions. The small fraction of upgoing atmospheric neutrinos that enter the ice surrounding the detector site will undergo reactions with the bedrock and ice to produce muons. These newly created muons then traverse the ice and react again to produce Cherenkov light, a type of electromagnetic radiation, that is finally able to be detected by the Digital Optical Modules (DOMs) of IceCube. This radiation is produced when a particle having mass passes through a substance faster than light can pass through that same substance.[8]

In 2011-2012, a study using data from the full range of DOMs, rather than just a portion, was conducted.[8] This data, along with other previous data, were examined in order to search for conclusive evidence of sterile neutrino oscillations in samples of atmospheric neutrinos. Experimental data were compared to a Monte Carlo simulation. For each hypothesis of the makeup of the sterile neutrino, the Poissonian log likelihood, a probability function that finds the best correlation of experimental data to a hypothetical model, was calculated. Based on the results shown in Figure 2, no evidence points towards sterile neutrinos.[8]

CONCLUSION

Other studies have also been conducted at IceCube, and have also found no indication of sterile neutrinos. Although there is strong evidence against the existence of sterile neutrinos, this does not completely rule out their existence. These experiments have focused only on certain mixing angles and may have different results for different mixing angles. Also, if sterile neutrinos are conclusively found to be nonexistent by IceCube, there is still the question of why

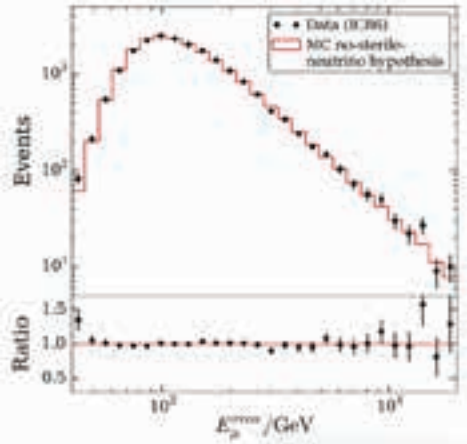

Fig 2: This graph shows the experimental results compared to the MC simulations. It shows the close correlation and how the experimental results highly correspond to a no sterile neutrino hypothesis.[8]

the anomalous data appeared at LSND and MiniBooNE. Thus, IceCube will continue sterile neutrino experiments at variable mixing angles to search for an explanation to the anomalies observed in the previous neutrino experiments.

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THE CREATION OF SUCCESSFUL SCAFFOLDS FOR TISSUE ENGINEERING

MATTHEW WESTER

ABSTRACT

Tissue engineering is a broad field with applications ranging from pharmaceutical testing to total organ replacement. Recently, there has been extensive research on creating tissue that is able to replace or repair natural human tissue. Much of this research focuses on the creation of scaffolds that can both support cell growth and successfully integrate with the surrounding tissue. This article will introduce the concept of a scaffold for tissue engineering; discuss key areas of research including biomolecule use, vascularization, mechanical strength, and tissue attachment; and introduce some important recent advancements in these areas.

INTRODUCTION

Tissue engineering relies on four main factors: the growth of appropriate cells, the introduction of the proper biomolecules to these cells, the attachment of the cells to an appropriate scaffold, and the application of specific mechanical and biological forces to develop the completed tissue.[1]

Successful cell culture has been possible since the 1960's, but these early methods lacked the adaptability necessary to make functioning tissues. With the introduction of induced pluripotent stem cells in 2008, however, researchers have not faced the same resource limitation previously encountered. As a result, the growth of cells of a desired type has not been limiting to researchers in tissue engineering and thus warrants less concern than other factors in contemporary tissue engineering.[2,3]

Similarly, the introduction of essential biomolecules (such as growth factors) to the developing tissue has generally not restricted modern tissue engineering efforts. Extensive research and knowledge of biomolecule function as well as relatively reliable methods of obtaining important biomolecules have allowed researchers to make engineered tissues more successfully emulate functional human tissue using biomolecules.[4,5] Despite these advancements in information and procurement methods, however, the ability of biomolecules to improve engineered tissue often relies on the structure and chemical composition of the scaffold material.[6]

FURTHER RESEARCH IN THE FIELD OF TISSUE ENGINEERING MUST ADDRESS CHALLENGES WITH EXISTING SCAFFOLDS AND IMPROVE THEIR UTILITY FOR REPLACING OR REPAIRING HUMAN TISSUE

Cellular attachment has also been a heavily explored field of research. This refers specifically to the ability of the engineered tissue to seamlessly integrate into the surrounding tissue. Studies in cellular attachment often focus on qualities of scaffolds such as porosity as well as the introduction of biomolecules to encourage tissue union on the cellular level. Like biomolecule effectiveness, successful cellular attachment depends on the material and structure of the tissue scaffolding.[7]

Also critical to developing functional tissue is exposing it to the right environment. This development of tissue properties via the application of mechanical and biological forces depends strongly on finding materials that can withstand the required forces while supplying cells with the necessary environment and nutrients. Previous research in this has focused on several scaffold materials for various reasons. However, improvements to the material or the specific methods of development are still greatly needed in order to create functional implantable tissue. Because of the difficulty of conducting research in this area, devoted efforts to improving these methods remain critical to successful tissue engineering.

In order for a scaffold to be capable of supporting cells until the formation of a functioning tissue, it is necessary to satisfy several key requirements, principally introduction of helpful biomolecules, vascularization, mechanical function, appropriate chemical and physical environment, and compatibility with surrounding biological tissue.[8,9] Great progress has been made towards satisfying many of these conditions, but further research in the field of tissue engineering must address challenges with existing scaffolds and improve their utility for replacing or repairing human tissue.

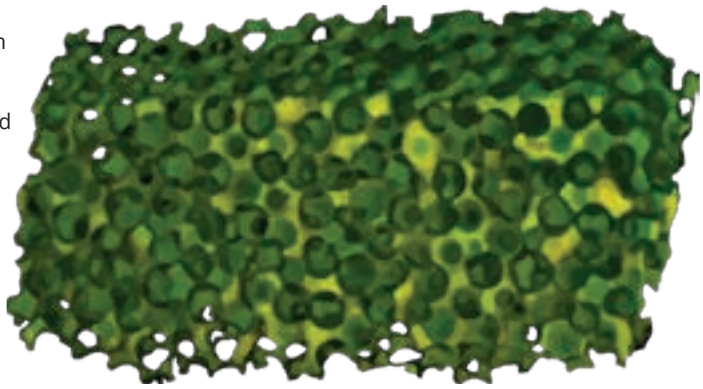
KEY RESEARCH AREAS OF SCAFFOLDING DESIGN

Biomolecules

Throughout most early tissue engineering projects, researchers focused on simple cell culture surrounding specific material scaffolds.[10] Promising developments such as the creation of engineered cartilage motivated further funding and interest in research. However, these early efforts missed out on several crucial factors to tissue engineering that allow implantable tissue to take on more complex functional roles. In order to create tissue that is functional and able to direct biological processes alongside nearby natural tissue, it is important to understand the interactions of biomolecules with engineered tissue.

Because the ultimate goal of tissue engineering is to create functional, implantable tissue that mimics biological systems, most important biomolecules have been explored by researchers in the medical field outside of tissue engineering. As a result, a solid body of research exists describing the functions and interactions of various biomolecules. Because of this existing information, understanding their potential uses in tissue engineering relies mainly on studying the interactions of biomolecules with materials which are not native to the body; most commonly, these non-biological materials are used as scaffolding. To complicate the topic further, biomolecules are a considerably large category encompassing everything from DNA to glucose to proteins. As such, it is most necessary to focus on those that interact closely with engineered tissue.

One type of biomolecule that is subject to much research and speculation in current tissue engineering is the growth factor.[11] Specific growth factors can have a variety of functions from general cell proliferation to the formation of blood cells and vessels.[12,13,14] They can also be responsible for disease, especially the unchecked cell generation of cancer.[15] Many of the positive roles have direct applications to tissue engineering. For example, Transforming Growth Factor-beta (TGF-β) regulates normal growth and development in humans.[16] One study found that while addition of ligands to engineered tissue could increase cellular adhesion to nearby cells, the addition also decreased the generation of the extracellular matrix, a key structure in functional tissue.[17] To remedy this, the researchers then tested the same method with the addition of TGF-β. They saw a significant increase in the generation of the extracellular matrix, improving their engineered tissue's ability to become functional faster and more effectively. Clearly, a combination of growth factors and other tissue engineering methods can lead to better outcomes for functional tissue engineering.



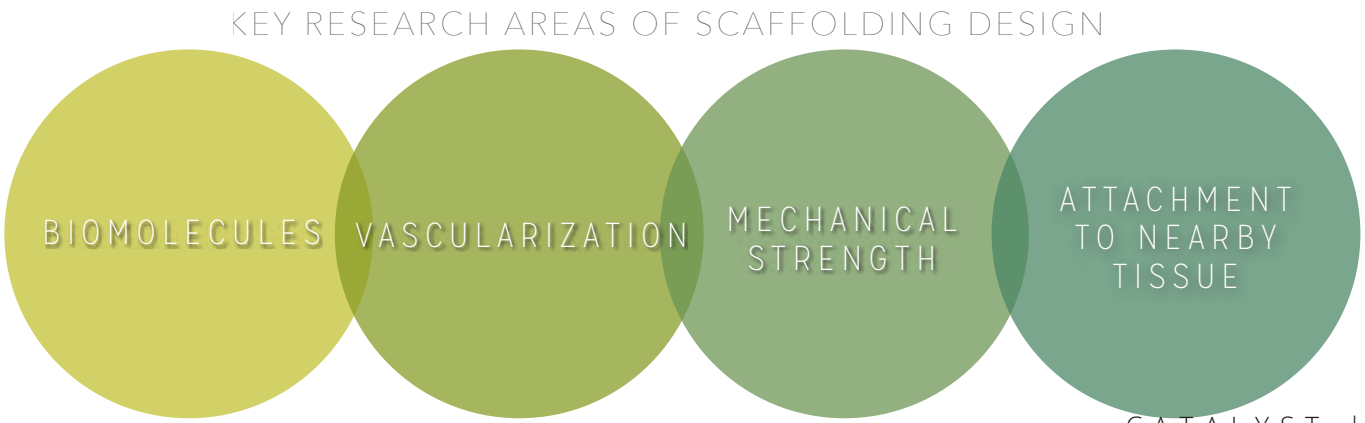
With the utility of growth factors established, delivery methods become very important. Several methods have been shown as effective, including delivery in a gelatin carrier.[18] However, some of the most promising procedures rely on the scaffolding's properties. One set of studies mimicked the natural release of growth factors through the extracellular matrix by creating a nanofiber scaffold containing growth factors for delayed release.[19] The study saw an positive influence on the behavior of cells as a result of the release of growth factor. Other methods vary physical properties of the scaffold such as pore size to trigger immune pathways that release regenerative growth factors, as will be discussed later. The use of biomolecules and specifically growth factors is heavily linked to the choice of scaffolding material and can be critical to the success of an engineered tissue.

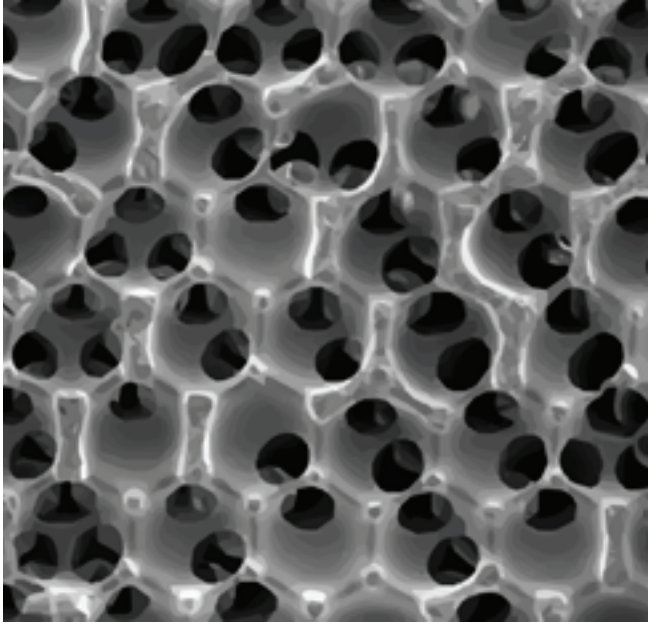
Vascularization

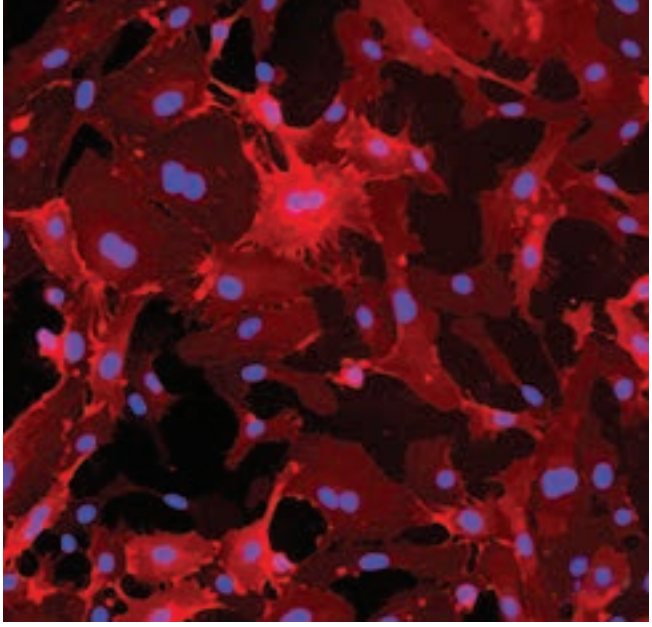
Because almost all tissue cannot survive without proper oxygenation, engineered tissue vascularization has been a focus of many researchers in recent years to optimize chances of engineered tissue success.[20] For many of the areas of advancement, this process depends on the scaffold.[21] The actual requirements for level and complexity of vasculature vary greatly based on the type of tissue; the requirements for blood flow in the highly vascularized lungs are different than those for cortical bone.[22,23] Therefore, it is more appropriate for this topic to address the methods which have been developed for creating vascularized tissue rather than the actual designs of specific tissues.

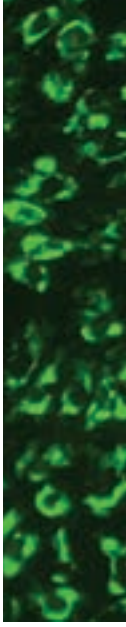
One method that has shown great promise is the use of modified 3D printers to cast vascularized tissue.[24] This method uses the relatively new printing technology to create carbohydrate glass networks in the form of the desired vascular network. The network is then coated with a hydrogel scaffold to allow cells to grow. The carbohydrate glass is then dissolved from inside of the hydrogel, leaving an open vasculature in a specific shape. This method has been successful in achieving cell growth in areas of engineered tissue that would normally undergo necrosis. Even more remarkably, the created vasculature showed the ability to branch into a more complex system when coated with endothelial cells.[24]

However, this method is not always applicable. Many tissue types require scaffolds that are more rigid or have properties different from those of hydrogels. In this case, researchers have focused on the effect of a material's porosity on angiogenesis.[7,25] Several key factors have been identified for blood vessel growth, including pore size, surface area, and endothelial cell seeding similar to that which was successful in 3D printed hydrogels. Of course, many other methods are currently being researched based on a variety of scaffolds. Improvements on these methods, combined with better research into the interactions of vascularization with biomaterial attachment, show great promise for engineering complex, differentiated tissue.









Mechanical Strength

Research has consistently demonstrated that large-scale cell culture is not limiting to bioengineering. With the introduction of technology like bioreactors or three-dimensional cell culture plates, growing cells of the desired qualities and in the appropriate form continues to become easier for researchers; this in turn allows for a focus on factors beyond simply gathering the proper types of cells.[2] This is important because most applications in tissue engineering require more than just the ability to create groupings of cells—the cells must have a certain degree of mechanical strength in order to functionally replace tissue that experiences physical pressure.

CELLS MUST HAVE A CERTAIN DEGREE OF MECHANICAL STRENGTH IN ORDER TO FUNCTIONALLY REPLACE TISSUE THAT EXPERIENCES PHYSICAL PRESSURE

The mechanical strength of a tissue is a result of many developmental factors and can be classified in different ways, often based on the type of force applied to the tissue or the amount of force the tissue is able to withstand. Regardless, mechanical strength of a tissue primarily relies on the physical strength of the tissue and its ability for its cells to function under an applied pressure; these are both products of the material and fabrication methods of the scaffolding used. For example, scaffolds in bone tissue engineering are often measured for compressive strength. Studies have found that certain techniques, such as cooking in a vacuum oven, may increase compressive strength.[26] One group found that they were able to match the higher end of the possible strength of cancellous (spongy) bone via 3D printing by using specific molecules within the binding layers.[27] This simple change resulted in scaffolding that displayed ten times the mechanical strength of scaffolding with traditional materials, a value within the range for natural bone. Additionally, the use of specific binding agents between layers of scaffold resulted in increased cellular attachment, the implications of which will be discussed later.[27] These changes result in tissue that is more able to meet the functional requirements and therefore to be easily used as a replacement for bone. Thus, simple changes in materials and methods used can drastically increase the mechanical usability of scaffolds and often have positive effects on other important qualities for certain types of tissue.

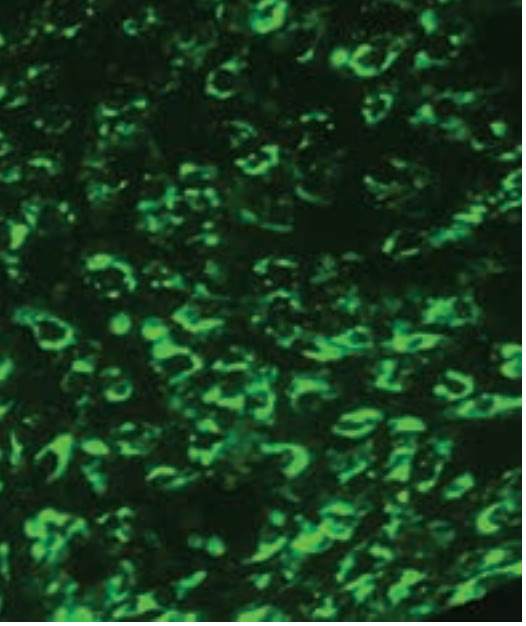
Clearly, not all designed tissues require the mechanical strength of bone; for example, the brain experiences less than one kPa of pressure compared to the forebone's 106 kPa pressure bones experience.[28] Thus, not all scaffolds must support the same amount of pressure, and scaffolds must be made accordingly to accommodate for these structural differences. Additionally, other tissues might experience forces such as tension or torsion based on their locations within the body. This means that mechanical properties must be looked at on a tissue-by-tissue basis in order to determine their corresponding scaffolding structures. But mechanical limitations are only a primary factor in bone, cartilage, and cardiovascular engineered tissue, the latter of which has significantly more complicated mechanical requirements.[29]

Research in the past few years has investigated increasingly complex aspects of scaffold design and their effects on macroscopic physical properties. For example, it is generally accepted that pore size and related surface area within engineered bone replacements are key to cellular attachment. However, recent advances in scaffold fabrication techniques have allowed researchers to investigate very specific properties of these pores such as their individual geometry. In one recent study, it was found that using an inverse opal geometry--an architecture known for its high strength in materials engineering--for pores led to a doubling of mineralization within a bone engineering scaffold.[30] Mineralization is a crucial quality of bone because of its contribution to compressive strength.[31] This result is so important because it demonstrates the recent ability of researchers to alter scaffolds on a microscopic level in order to affect macroscopic changes in tissue properties.

Attachment to Nearby Tissue

Even with an ideal design, a tissue's success as an implant relies on its ability to integrate with the surrounding tissue. For some types of tissue, this is simply a matter of avoiding rejection by the host through an immune response.[32] In these cases, it is important to choose materials with a specific consideration for reducing this immune response. Over the past several decades, it has been shown that the key requirement for biocompatibility is the use of materials that are nearly biologically inert and thus do not trigger a negative response from natural tissue.[33] This is based on the strategy which focuses on minimizing the immune response of tissue surrounding the implant in order to avoid issues such as inflammation, which might be detrimental to the patient undergoing the procedure. This method has been relatively effective for implants ranging from total joint replacements to heart valves.

Avoiding a negative immune response has proven successful for some medical fields. However, more complex solutions involving a guided immune response might be necessary for engineered tissue implants to survive and take on the intended function. This issue of



balancing biochemical inertness and tissue survival has led researchers to investigate the possibility of using the host immune response in an advantageous way for the success of the implant.[34] This method of intentionally triggering surrounding natural tissue relies on the understanding that immune response is actually essential to tissue repair. While an inert biomaterial may be able to avoid a negative reaction, it will also discourage a positive reaction. Without provoking some sort of response to the new tissue, an implant will remain foreign to bordering tissue; this means that the cells cannot take on important functions, limiting the success of any biomaterial that has more than a mechanical use.

Current studies have focused primarily on modifying surface topography and chemistry to target a positive immune reaction in the cells surrounding the new tissue. One example is the grafting of oligopeptides onto the surface of an implant to stimulate macrophage response. This method ultimately leads to the release of growth factors and greater levels of cellular attachment because of the chemical signals involved in the natural immune response.[35] Another study found that the use of a certain pore size in the scaffold material led to faster and more complete healing in an in vivo study using rabbits. Upon further investigation, it was found that the smaller pore size was interacting with macrophages involved in the triggered immune response; this interaction ultimately led more macrophages to differentiate into a regenerative pathway, leading to better and faster healing of the implant with the surrounding tissue.[36] Similar studies have investigated the effect of methods such as attaching surface proteins with similarly enlightening results. These and other promising studies have led to an increased awareness of chemical signaling as a method to enhance biomaterial integration with larger implications including faster healing time and greater functionality.

CONCLUSION

The use of scaffolds for tissue engineering has been the subject of much research because of its potential for extensive utilization in the medical field. Recent advancements have focused on several areas, particularly the use of biomolecules, improved vascularization, increases in mechanical strength, and attachment to existing tissue. Advancements in each of these fields have been closely related to the use of scaffolding. Several biomolecules, especially growth factors, have led to a greater ability for tissue to adapt as an integrated part of the body after implantation. These growth factors rely on efficient means of delivery, notably through inclusion in the scaffold, in order to have an effect on the tissue. The development of new methods and refinement of existing ones has allowed researchers to successfully vascularize tissue on multiple types of scaffolds. Likewise, better methods of strengthening engineered tissue scaffolds before cell growth and implantation have allowed for improved functionality, especially under mechanical forces. Modifications to scaffolding and the addition of special molecules have allowed for increased cellular attachment, improving the efficacy of engineered tissue for implantation. Further advancement in each of these areas could lead to more effective scaffolds and the ability to successfully use engineered tissue for functional implants in medical treatments.

MODIFICATIONS TO SCAFFOLDING AND THE ADDITION OF SPECIAL MOLECULES HAVE ALLOWED FOR INCREASED CELLULAR ATTACHMENT, IMPROVING THE EFFICACY OF ENGINEERED TISSUE FOR IMPLANTATION

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Kseniya Anishchenko

MOLECULAR MECHANISMS BEHIND *ALZHEIMER'S DISEASE & EPILEPSY*

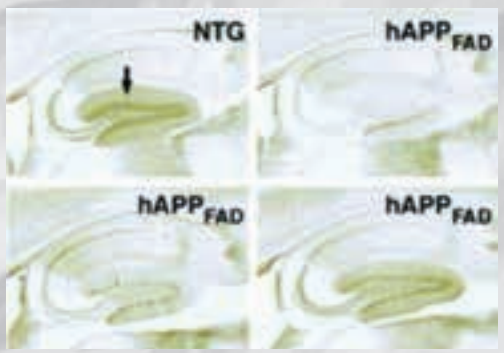
ABSTRACT

Seizures are characterized by periods of high neuronal activity and are caused by alterations in synaptic function that disrupt the equilibrium between excitation and inhibition in neurons. While often associated with epilepsy, seizures can also occur after brain injuries and interestingly, are common in Alzheimer's patients. While Alzheimer's patients rarely show the common physical signs of seizures, recent research has shown that electroencephalogram (EEG) technology can detect nonconvulsive seizures in Alzheimer's patients. Furthermore, patients with Alzheimer's have a 6 to 10-fold increase in the probability of developing seizures during the course of their disease compared to healthy controls.[2] While previous research has focused on the underlying molecular mechanisms of Aβ tangles in the brain, the research presented here relates seizures to the cognitive decline in Alzheimer's patients in an attempt to find therapeutic approaches that tackle both epilepsy and Alzheimer's.

INTRODUCTION

The hippocampus is found in the temporal lobe and is involved in the creation and consolidation of new memories. It is the first part of the brain to undergo neurodegeneration in Alzheimer's disease, and as such, the disease is characterized by memory loss. Alzheimer's is different than other types of dementia because patients' episodic memories are affected strongly and quickly. Likewise, patients who suffer from epilepsy also exhibit neurodegeneration in their hippocampi and have impaired episodic memories. Such similarities led researchers to hypothesize that the two diseases have the same pathophysiological mechanisms. In one study, four epileptic patients exhibited progressive memory loss that clinically resembled Alzheimer's disease.[6] In another study, researchers found that seizures precede cognitive symptoms in late-onset Alzheimer's disease.[7] This led researchers to hypothesize that a high incidence of seizures increases the rate of cognitive decline in Alzheimer's patients. However, much is yet to be discovered about the molecular mechanisms underlying seizure activity and cognitive impairments.

Amyloid precursor protein (APP) is the precursor molecule to Aβ, the polypeptide that makes up the Aβ plaques found in the brains of Alzheimer's patients. In many Alzheimer's labs, the J20 APP mouse model of disease is used to simulate human Alzheimer's. These mice overexpress the human form of APP, develop amyloid plaques, and have severe deficits in learning and memory. The mice also have high levels of epileptiform activity and exhibit spontaneous seizures that are characteristic of epilepsy.[11] Understanding the long-lasting effects of these seizures is important in designing therapies for a disease that is affected by recurrent seizures. Thus, comparing the APP mouse model of disease with the temporal lobe epilepsy (TLE) mouse model is essential in unraveling the mysteries of seizures and cognitive decline.



Levels of reduction of calbindin in the mouse hippocampus.10 NTG is wild-type mice who do not express APP, while the other three photos indicate levels of severity of calbindin loss in APP mice.

SHARED PATHOLOGY OF THE TWO DISEASES

The molecular mechanisms behind the two diseases are still unknown and under much research. An early observation in both TLE and Alzheimer's involved a decrease in calbindin-28DK, a calcium buffering protein, in the hippocampus.[10] Neuronal calcium buffering and calcium homeostasis are well-known to be involved in learning and memory. Calcium channels are involved in synaptic transmission, and a high calcium ion influx often results in altered neuronal excitability and calcium signaling. Calbindin acts as a buffer for binding free Ca^{2+} and is thus critical to calcium homeostasis. Some APP mice have severe seizures and an extremely high loss of calbindin, while other APP mice exhibit no loss in calbindin. The reasons behind this is unclear, but like patients, mice are also very variable.

The loss of calbindin in both Alzheimer's and TLE is highly correlated with cognitive deficits. However, the molecular mechanism behind the calbindin loss is unclear. Many researchers are now working to uncover this mechanism in the hopes of preventing the calbindin loss, thereby improving therapeutic avenues for Alzheimer's and epilepsy patients.

SEIZURES AND NEUROGENESIS

The dentate gyrus is one of the two areas of the adult brain that exhibit neurogenesis.[13] Understanding neurogenesis in the hippocampus can lead to promising therapeutic targets in the form of neuronal replacement therapy. Preliminary research in Alzheimer's and TLE has shown changes in neurogenesis over the course of the disease.[14] However, whether neurogenesis is increased or decreased remains a controversial topic, as studies frequently contradict each other.

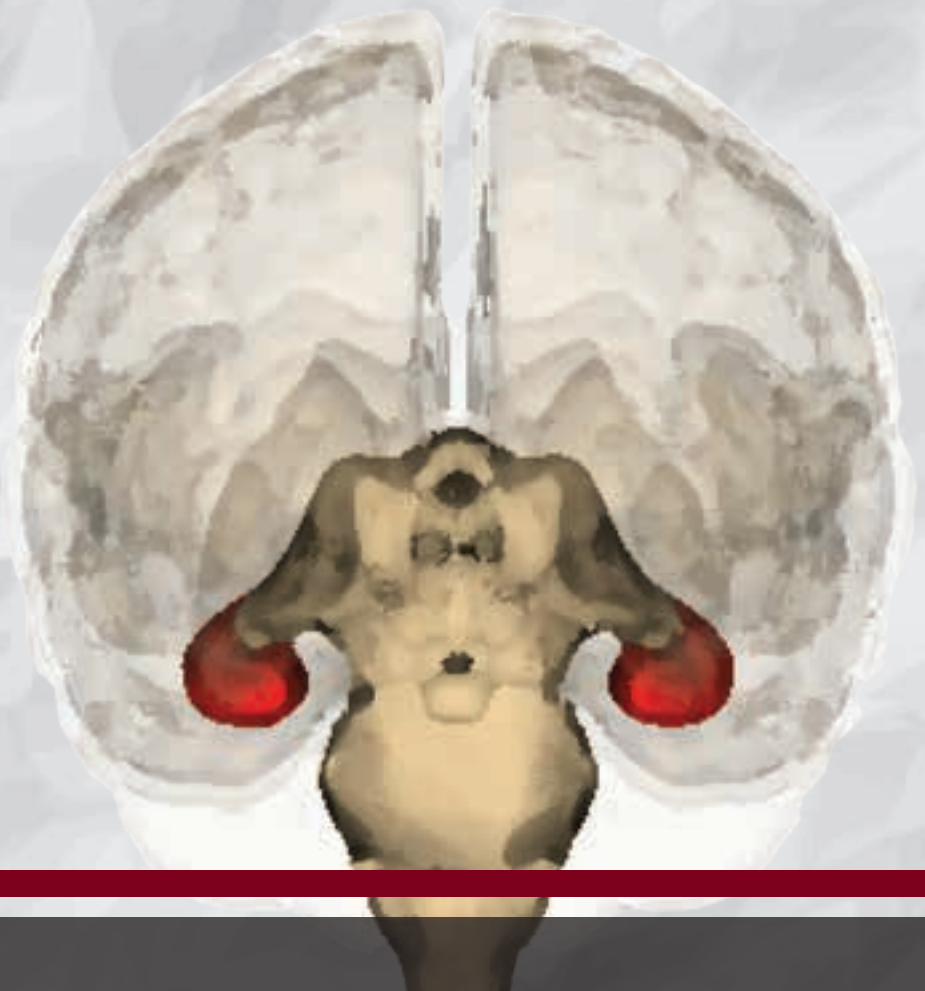
Many researchers study neurogenesis in the context of different diseases. In memory research, neurogenesis is thought to be involved in both memory formation and memory consolidation.[12] Alzheimer's leads to the gradual decrease in the generation of neural progenitors, the stem cells that can differentiate to create a variety of different neuronal and glial cell types.[8] Further studies have shown that the neural stem cell pool undergoes accelerated depletion due to seizure activity.[15] Initially, heightened neuronal activity stimulates neural progenitors to divide rapidly at a much faster rate than controls. This rapid division depletes the limited stem cell pool prematurely. Interestingly enough, this enhanced neurogenesis is detected long before other AD-linked pathologies. When the APP mice become older, the stem cell pool is depleted to a point where neurogenesis occurs much slower compared to controls.[9] This is thought to represent memory deficits, in that the APP mice can no longer consolidate new memories as effectively. The same phenomenon occurs in mice with TLE.

The discovery of this premature neurogenesis in Alzheimer's disease has many therapeutic benefits. For one, enhanced neurogenesis can be used as a marker for Alzheimer's long before any symptoms are present. Furthermore, targeting increased neurogenesis holds potential as a therapeutic avenue, leading to better remedies for preventing the pathological effects of recurrent seizures in Alzheimer's disease.

CONCLUSION

Research linking epilepsy with other neurodegenerative disorders is still in its infancy, and leaves many researchers skeptical about the potential to create a single therapy for multiple conditions. Previous EEG studies recorded Alzheimer's patients for a few hours at a time and found limited epileptiform activity; enhanced overnight technology has shown that about half of Alzheimer's patients have epileptiform activity in a 24-hour period, with most activity occurring during sleep.[1] Recording patients for even longer periods of time will likely raise this percentage. Further research is being conducted to show the importance of seizures in enhancing cognitive deficits and understanding Alzheimer's disease, and could lead to amazing therapeutic advances in the future.

"The dentate gyrus is one of the two areas of the adult brain that exhibit neurogenesis.Understanding neurogenesis in the hippocampus can lead to promising therapeutic targets in the form of neuronal replacement therapy."



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DESIGN BY Gloria Kim
EDITED BY Allison Chang

MACHINE MINDS:

AN EXPLORATION OF ARTIFICIAL NEURAL NETWORKS

BY SHASHANK MAHESH

ABSTRACT

An artificial neural network is a computational method that mirrors the way a biological nervous system processes information. Artificial neural networks are used in many different fields to process large sets of data, often providing useful analyses that allow for prediction and identification of new data. However, neural networks struggle with providing clear explanations regarding why certain outcomes occur. Despite these difficulties, neural networks are valuable data analysis tools applicable to a variety of fields. This paper will explore the general architecture, advantages and applications of neural networks.

INTRODUCTION

Artificial neural networks attempt to mimic the functions of the human brain. Biological nervous systems are composed of building blocks called neurons. In a biological nervous system, biological neurons communicate with axons and dendrites. When a biological neuron receives a message, it sends an electric signal down its axon. If this electric signal is greater than a threshold value, the electrical signal is converted to a chemical signal that is sent to nearby biological neurons.[2] Similarly, while artificial neural networks are dictated by formulas and data structures, they can be conceptualized as being composed of artificial neurons, which hold similar functions to their biological counterparts. When an artificial neuron receives data, if the change in the activation level of a receiving artificial neuron exceeds a defined threshold value, the artificial neuron creates an output signal that propagates to other connected artificial neurons.[2] The human brain learns from past experiences and applies this information from the past in new settings. Similarly, artificial neural networks can adapt their behaviors until their responses are both accurate and consistent in new situations.[1]

While artificial neural networks are structurally similar to their biological counterparts, artificial neural networks are distinct in several ways. For example, certain artificial neural networks send signals only at fixed time intervals, unlike biological neural networks, in which neuronal activity is variable.[3] Another major difference between biological neural networks and artificial neural networks is the time of response. For biological neural networks, there is often a latent period before a response, whereas in artificial neural networks, responses are immediate.[3]

Neural networks are useful in a wide-range of fields that involve large datasets, ranging from biological systems to economic analysis. These networks are practical in problems involving pattern recognition, such as predicting data trends.[3] Neural networks are also effective when data is error-prone, such as in cognitive software like speech and image recognition.[3]

NEURAL NETWORK ARCHITECTURE

One popular neural network design is the Multilayer Perceptrons (MLP) design. In the MLP design, each artificial neuron outputs a weighted sum of its inputs based on the strength of the synaptic connections.[1] Artificial neuron synaptic strength is determined by the formulaic design of the neural network and is directly proportional to weight: stronger and more valuable artificial neurons have a larger weight and therefore are more influential in the weighted sum. The output of the neuron is based on whether the weighted sum is greater than the threshold value of the artificial neuron.[1] The MLP design was originally composed of perceptrons. Perceptrons are artificial neurons that provide a binary output of zero or one. Perceptrons have limited use in a neural network model because small changes in the input can drastically alter the output value of the system. However, most current MLP systems use sigmoid neurons instead of perceptrons. Sigmoid neurons can take inputs and produce outputs of values between zero and one, allowing for more variation in the inputs because these changes do not radically alter the outcome of the model.[4]

In terms of the architecture of the MLP design, the network is a feedforward neural network.[1] In a feedforward design, the units are arranged so signals travel exclusively from input to output. These networks are composed of a layer of input neurons, a layer of output neurons, and a series of hidden layers in between the input and output layers. These hidden layers are composed of internal neurons that further process the data within the system. The complexity of this model varies with the number of hidden layers and the number of inputs in each layer.[1]

In an MLP design, once the number of layers and the number of units in each layer are determined, the threshold values and the synaptic weights in the system need to be set using training algorithms so that the errors in the system are minimized.[4] These training algorithms use a known dataset (the

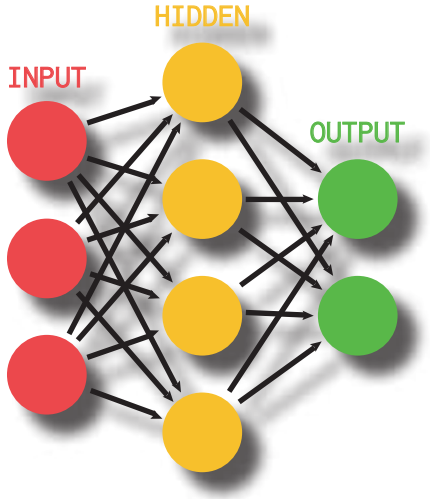


DIAGRAM OF A BASIC MLP DESIGN

training data) to modify the system until the differences between the expected output and the actual output values are minimized.[4] Training algorithms allow for neural networks to be constructed with optimal weights, which lets the neural network make accurate predictions when presented with new data. One such training algorithm is the backpropagation algorithm. In this design, the algorithm analyzes the gradient vector and the error surface in the data until a minimum is found.[1] The difficult part of the backpropagation algorithm is determining the step size. Larger steps can result in faster runtimes, but can overstep the solution; comparatively smaller steps can lead to a much slower runtime, but are more likely to find a correct solution.[1]

While feedforward neural network designs like MLP are common, there are many other neural network designs. These other structures include examples such as recurrent neural networks, which allow for connections between neurons in the same layer, and self-organizing maps, in which neurons attain weights that retain characteristics of the input. All of these network types also have variations within their specific frameworks.[5] The Hopfield network and Boltzmann machine neural network architectures utilize the recurrent neural network design.[5] While feedforward neural networks are the most common, each design is uniquely suited to solve specific problems.

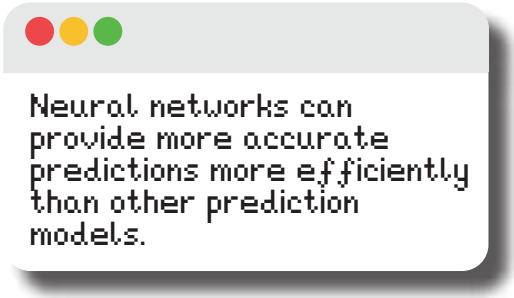
DISADVANTAGES

One of the main problems with neural networks is that, for the most part, they have limited ability to identify causal relationships explicitly. Developers of neural networks feed these networks large swathes of data and allow for the neural networks to determine independently which input variables are most important.[10] However, it is difficult for the network to indicate to the developers which variables are most important in calculating the outputs. While some techniques exist to analyze the relative importance of each neuron in a neural network, these techniques still do not present as clear of a causal relationship between variables as can be gained in similar data analysis methods such as a logistic regression.[10]

Another problem with neural networks is the tendency to overfit. Overfitting of data occurs when a data analysis model such as a neural network generates good predictions for the training data but worse ones for testing data.[10] Overfitting happens because the model accounts for irregularities and outliers in the training data that may not be present across actual data sets. Developers can mitigate overfitting in neural networks by penalizing large weights and limiting the number of neurons in hidden layers.[10] Reducing the number of neurons in hidden layers reduces overfitting but also limits the ability of the neural network to model more complex, nonlinear relationships.[10]

APPLICATIONS

Artificial neural networks allow for the processing of large amounts of data, making them useful tools in many fields of research. For example, the field of bioinformatics relies heavily on neural network pattern recognition to predict various proteins' secondary structures. One popular algorithm used for this purpose is Position Specific Iterated Basic Local Alignment Search Tool (PSI-BLAST) Secondary Structure Prediction (PSIPRED).[6] This algorithm uses a two-stage structure that consists of two three-layered feedforward neural networks. The first stage of PSIPRED involves inputting a scoring matrix generated by using the PSI-BLAST algorithm on a peptide sequence. PSIPRED then takes 15 positions from the scoring matrix and uses them to output three values that represent the probabilities of forming the three protein secondary structures: helix, coil, and strand.[6] These probabilities are then input into the second stage neural network along with the 15 positions from the scoring matrix, and the output of this second stage neural network includes three values representing more accurate probabilities of forming helix, coil, and strand secondary structures.[6]



Neural networks are used not only to predict protein structures, but also to analyze genes associated with the development and progression of cancer. More specifically, researchers and doctors use artificial neural networks to identify the type of cancer associated with certain tumors. Such identification is useful for correct diagnosis and treatment of each specific cancer.[7] These artificial neural networks enable researchers to match genomic characteristics from large datasets to specific types of cancer and predict these types of cancer.[7]

In bioinformatic scenarios such as the above two examples, trained artificial neural networks quickly provide high-quality results for prediction tasks.[6] These characteristics of neural networks are important for bioinformatics projects because bioinformatics generally involves large quantities of data that need to be interpreted both effectively and efficiently.[6]

The applications of artificial neural networks are also viable within fields outside the natural sciences, such as finance. These networks can be used to predict subtle trends such as variations in the stock market or when organizations will face bankruptcy.[8,9] Neural networks can provide more accurate predictions more efficiently than other prediction models.[9]

CONCLUSION

Over the past decade, artificial neural networks have become more refined and are being used in a wide variety of fields. Artificial neural networks allow researchers to find patterns in the largest of datasets and utilize the patterns to predict potential outcomes. These artificial neural networks provide a new computational way to learn and understand diverse assortments of data and allow for a more accurate and effective grasp of the world.

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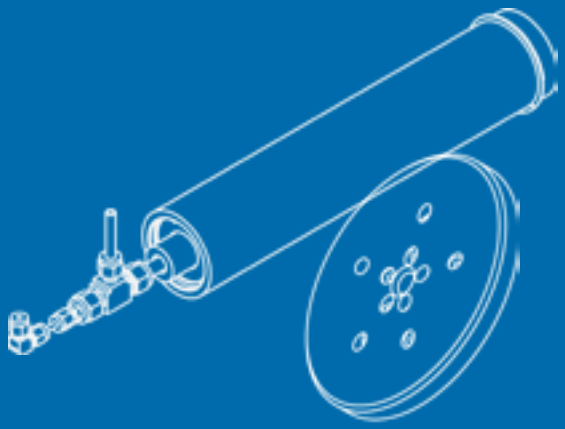


OPTIMIZING IMPULSE AND IN HYBRID

INTRODUCTION

Hybrid rockets—rockets that use a liquid oxidizer and solid fuel cylindrical grains—are currently experiencing a resurgence in research rocketry due to their comparative safety benefit.[1] The unique design of a hybrid rocket enables fuel and oxidizer input regulation, and thus modulation of the combustion chamber pressure.[2] This reduces the risk of explosion.[3] This paper will give a basic overview of the function of a hybrid rocket, the role of injector plate geometry and rocket fuel on thrust, and the results of the Rice Eclipse research team on studying the effect of injector plate geometries and rocket fuel combinations on thrust and impulse. The purpose of this research is to discover a fuel grain and injector plate combination with the thrust necessary to launch a hybrid rocket into suborbital space.

"THE UNIQUE DESIGN OF A HYBRID ROCKET ENABLES FUEL AND OXIDIZER INPUT REGULATION."

SOLID ROCKETS

Most entry-level, low-hazard rockets use solid motors.[4] Solid rockets are generally considered to be the safest option because of the consistent burn profile.5 These rockets have a solid cylinder of fuel in their combustion chamber that contains a blend of rocket fuel and oxidizer.[5] Through the course of flight, the fuel/oxidizer blend gradually depletes like a high power candle until the rocket reaches its apogee.[5] Since the fuel and oxidizer are initially mixed together, it is highly unlikely for a solid rocket to have a concentration of fuel necessary for instantaneous combustion, which would result in an explosion.[5]

LIQUID ROCKETS

Typical rockets that are deployed in space are liquid rockets.[6] These rockets contain tanks of liquid oxidizer and liquid fuel that are atomized in the combustion chamber to burn at the high efficiencies required to achieve the impulse necessary for escape velocity.[7] Particularly, the atomization provides the high surface area-volume ratio that is necessary for an efficient burn and allows the rocket to have the extremely high thrust. The disadvantage of liquid rockets is the huge safety risk they pose.[7] Having a liquid combustion system makes the oxidizer and fuel dangerously close to blending, which can create a concentration of oxidizer-fuel mixture susceptible to a spark and resultant explosion.

HYBRID ROCKETS

Hybrid rockets combine the best of both solid and liquid rockets.6 The liquid oxidizer of the hybrid rocket is atomized over the solid fuel to give a high-thrust yet controlled burn in the combustion chamber.[2] Although the sophistication of hybrid rocket engineering prevents most novice rocket builders from constructing hybrids, Rice Eclipse has constructed the fifth amateur hybrid rocket in America—which we call the MK1.

INJECTOR PLATES

Injector plates are metallic structures that function like spray guns and divide the stream of oxidizer into thousands of small atomized parts.[8] A variety of designs or geometries exist that serve to break up oxidizer flow; the designs we considered in this study are the showerhead and impinging designs.

SHOWERHEADS

Showerhead injectors function similarly to household showerheads.[4] A series of radially placed holes taper inwards as they move through the injector plate, confining the oxidizer fluid to a very small space before releasing it as a spray in the combustion chamber.[8] The fluid atomizes because the oxidizer accelerates as it travels through the constrained small holes but suddenly decelerates as it reaches into the combustion chamber due to the rapid change in pressure.[8] This process of breaking up liquid streams due to sudden resistance to flow is called the venturi effect.[8]

IMPINGING PLATES

The second type of injector plate studied is an impinging injector plate.[4] In this style of injector plate, the holes of the plate are placed facing one another.[9] As the oxidizer flows through the holes of the plate, the streams impinge, or collide at a central location.[9] Upon collision, the streams atomize.[4] It is hypothesized that this plate structure should result in much better performance because of greater atomization compared to a corresponding showerhead plate.[4] For this project, the angle of the impinging holes was chosen to be 30 degrees from the normal in order to optimize impingement and atomization at the end of the pre-combustion chamber.[9]

FUEL GRAINS

Rocket fuels are often made of various materials that complement each other's chemical properties to produce a high efficiency burn.[10] These fuel components are held together in a cylindrical grain through the use of a binder compound that is also consumed in combustion.[11] Therefore, it is important for both the standard fuel components and the binder to burn efficiently.[11] The efficiency of a burn is quantified in the fuel regression rate, which is how fast the fuel grain is depleted.[12] While this rate varies based on combustibility and other chemical properties, it also heavily depends on the surface area available for burning.[12] Fuels with high surface area, like those in a liquid or gaseous state, can achieve high regression rates.[12] Thus, hybrid and solid rocket enthusiasts have been attempting to develop high surface area grains for efficient burns; this is has been previously achieved by using exotic grain configurations designed to maximize the exposure of the grain.[12] Rice Eclipse has taken the different approach by using a standard cylindrical fuel grain that incorporate high regression rate liquefying paraffin with conventional solid rocket fuel. These fuel grains were combusted with a nitrous oxide oxidizer.

PARAFFIN FUEL

Hydroxyl-terminated polybutadiene (HTPB), is the most commonly used rocket fuel for both hybrid and solid rocket motors.[13] In solid rockets, the physical properties of HTPB make it an ideal chemical to both bind the oxidizer into a strong yet elastic fuel grain and serve as source of fuel.[12] However, HTPB does not burn with efficiencies required to accelerate rockets into orbital velocities.[14] To improve pure HTPB grains, researchers have experimented with the addition of paraffin, a waxy compound that burns with a higher regression rate than HTPB, in the fuel grain.[15] Under the high temperatures of the combustion chamber, solid paraffin

CHAMBER PRESSURE ROCKETS

NATHANAEL ASSEFA

wax forms a thin layer of low surface tension liquid on the face of the fuel grain cylinder that is exposed to the oxidizer.16 The layer of liquid vaporizes due to the high flow rate and pressure of the oxidizer, producing the large surface-area-to-volume ratio that is common in solid and liquid rockets.[16] This liquefaction phenomena allows paraffin to produce high regression rate fuels in both hybrid and solid motors.[16] However, paraffin by itself cannot be molded into a fuel grain due to its low viscosity.[16] Thus, the inclusion of HTPB enables the production of a moldable fuel grain that possesses the high regression rate of paraffin wax.[17]

MATERIALS + METHODS

These tests were conducted in Houston, Texas in the MK1 test motor. The maximum combustion chamber pressure of MK1 was set to 500 psi. The motor used a load cell for thrust measurements and an internal pressure sensor for the combustion chamber profile. Each test fire lasted for four seconds, and three fires were conducted per configuration to ensure reproducibility and consistency of data.
We tested two types of fuel grains with HTPB and paraffin grains at 0% paraffin/100% HTPB and 50% paraffin/50% HTPB. All of these tests utilized a nitrous oxide oxidizer. Each of these grain types were cast in the Rice University, Oshman Engineering Design Kitchen.

"RICE ECLIPSE IS USING A STANDARD CYLINDRICAL FUEL GRAIN THAT INCORPORATES HIGH REGRESSION RATE LIQUEFYING PARAFFIN WITH CONVENTIONAL SOLID ROCKET FUEL."

The injector plates were made out of stock steel and were machined in the Rice University, Oshman Engineering Design Kitchen. The values used to drive the design of the injector plate are the desired mass flow rate of the oxidizer: 0.126 kg/s and the desired pressure drop across the injector plate: 1.72 MPa. Graphite nozzles with an entrance diameter of 1.52 in, a throat diameter of 0.295 in, and an exit diameter of 0.65 in were used. Each nozzle is 1.75 in long and has a converging half angle of 40 degrees and a diverging half angle of 12 degrees.

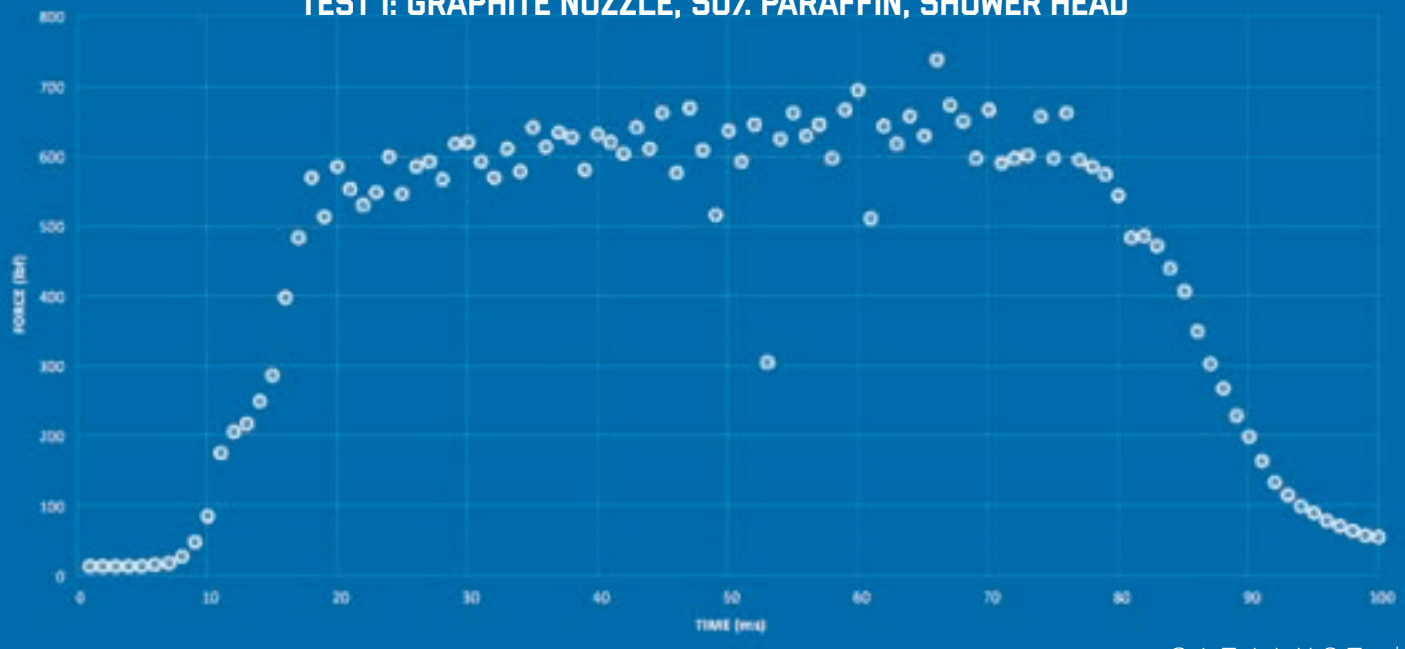
RESULTS

Three different fuel and injector plate combinations were studied. We performed a base case test of 0% paraffin/100% HTPB in a shower head plate. We then studied the effect of adding an impinging plate to the 0% paraffin/100% HTPB grain and went on to test a 50% paraffin/50% HTPB on the shower head palate. The reason we tested these configurations is to see how having a paraffin blended fuel grain and adding an impinging plate independently affected our rocket performance. The three scatter plots below show the thrust from each of the grains during a test fire. Thrust has a directly proportional relationship to the specific impulse of the rocket.

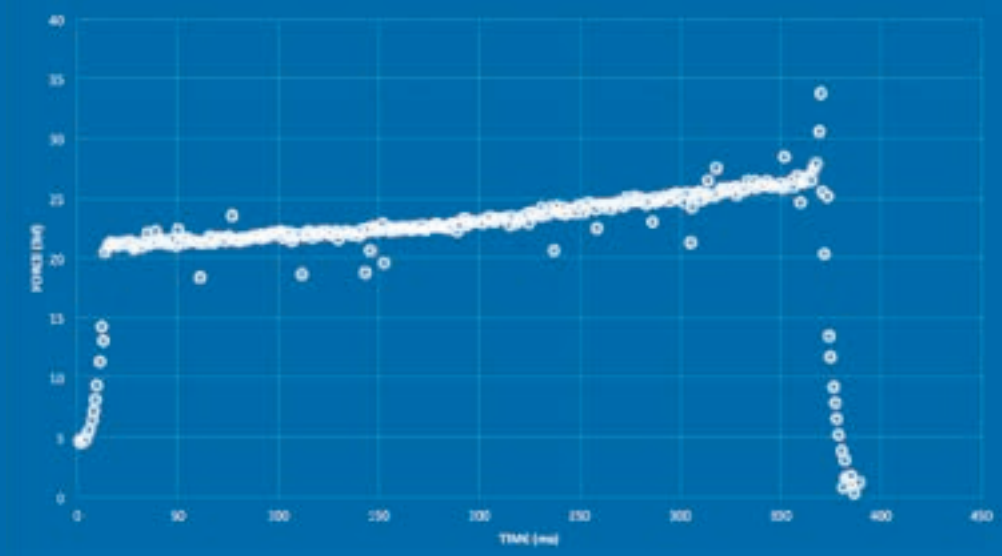
DISCUSSION

50% PARAFFIN TEST

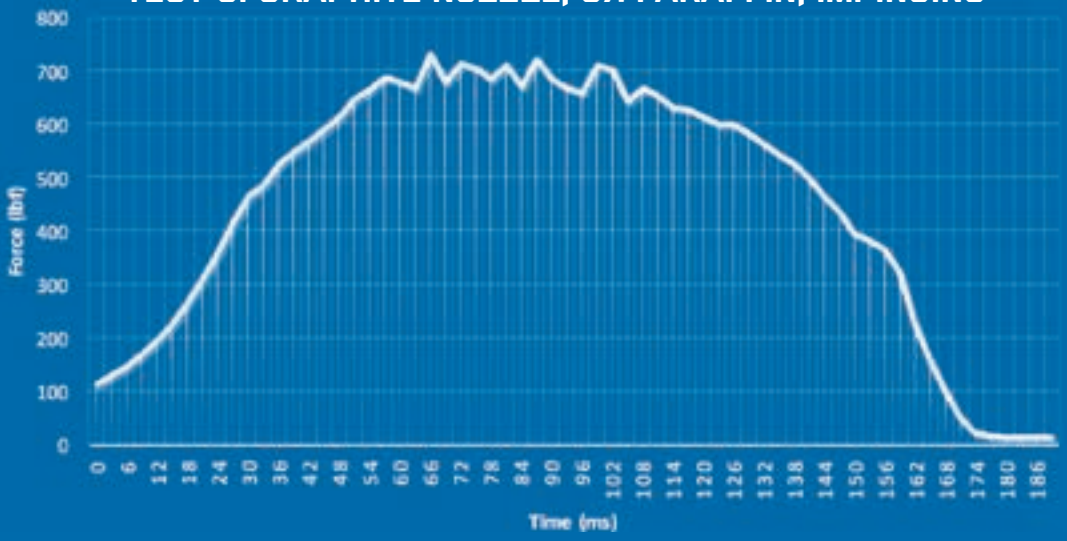
The 50% paraffin grain showed a significant improvement compared to the 0% paraffin base case, increasing the average thrust by 58% from 380 lbf to about 600 lbf. The paraffin fuel



TEST 2: GRAPHITE NOZZLE, 0% PARAFFIN, SHOWER HEAD



TEST 3: GRAPHITE NOZZLE, 0% PARAFFIN, IMPINGING



grain also improved the consistency of the burn due to the even spread of the paraffin grains in the fuel. Although chamber pressure did increase from about 23 psi to 38 psi, this increase in pressure is well below the 50 psi operating capacity of the rocket and would not be a handicap for the fuel grain.

IMPINGING PLATE

The third test fire, which demonstrated the impinging plate, maintained an average thrust of 700 lbf at maximum capacity—the highest average thrust. This is because the impinging injector plate increases the atomization of the oxidizer and the surface area available for combustion, intensifying the resulting burn. This increase in burn efficiency also reduces the overall burn time of the fuel and in this case shortened the fire to about two seconds from a four second burn in the base case.

CONCLUSIONS

The data show that the impinging injector was successful at achieving higher thrust burn. The paraffin fuels also demonstrated improved performance from the traditional HTBP fuel grains. This improvement in performance likely results from the reduced energy barrier to vaporization in the paraffin fuels compared to HTPB. The combination of improved vaporization and atomization allowed the impinging injector plate test results to show significantly better maximum thrust than all other tested plate combinations. Future testing can focus on combining the impinging plate with different concentrations of paraffin to take full advantage of increased atomization and surface area.

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ENDANGERED SLEEP

HOW TO SAVE IT FROM YOUR PHONE

BY CAROLINE LEE

There's nothing that college students immensely value and yet routinely sacrifice as much as sleep. Most people immediately before nodding off for a night's rest will routinely check their phones to set a morning alarm or to scroll through the latest social media feeds. Our mobile devices are now a necessity during every single moment of our lives, from waking up all the way to going to sleep. The National Sleep Foundation found that close to all adults under 30 years old - 96% total - use a technological device in the bedroom a hour before sleeping.[1] So in what ways is using technology before sleep actually harmful and how can these effects be reduced?

Mobile devices, including phones and laptops, have LED screens that emit artificial light with blue wavelength, which is used for its bright illuminating abilities. Within the visible light portion of the electromagnetic spectrum, blue light is closer to UV light with shorter wavelengths.[2] In the daylight, these blue wavelengths boost attention and reaction times; however, blue light at night causes disruptive effects on the body's circadian rhythm. The circadian rhythm controls sleep and wake cycles and responds to changes in light by regulating melatonin, a hormone released by the pineal gland during darkness.[3] Melatonin is especially affected by light because before the invention of electricity, changes in sun brightness determined sleeping patterns. Harvard researchers found that blue light exposure, even compared with equal exposure to green light of comparable brightness, suppressed melatonin for twice as long and shifted circadian rhythms by twice as much.[4]

Besides the screen's light affecting sleep, electromagnetic radiation from cell phone frequencies and cognitive influences of technology are suggested to affect sleep as well. A preliminary study of 70 participants found that exposure to 884 MHZ GSM, a specific frequency used in mobile phones, increased people's time to reach Stage 3 of deep non-REM sleep compared to those given fake exposure.[5] This suggests that electromagnetic radiation exposure, which can result from sleeping with your phone close nearby, has the potential to affect sleep cycle lengths. Additionally, activities including sending emails or texts keeps the brain active and can cause difficulties in entering sleep cycles by stimulating stress or extensive thoughts.

The need to stay connected to the latest news, assignments, and social updates may make it hard to consistently ban electronic devices from the bedroom the hour before sleep. However, there are simple changes that can be made to get the best sleep possible. Apple's new iOS 9.3 has found a way to mitigate the disruptive effects of blue light to help people get better sleep. With Night Shift as a Display and Brightness option, users can set their phones to automatically reduce the amount of blue light and shift the display to warmer colors with yellow and orange wavelengths around bedtime. This feature, if activated properly an hour or two before sleeping, is an easy compromise to make sure that mobile phone use doesn't have a negative impact on the limited amount of sleep-time available.[6] Some other easy changes include placing your phone further away from your bed instead of under the pillow or at arm's length and glancing around your surroundings every few minutes of device use to reduce eye strain. Finally, to mitigate cognitive influences of phone use, try to limit your phone and laptop use to passive activities before bed, such as watching videos, instead of active reading or interaction with emails or texts.[1] With these small changes, we can all maximize our precious sleep whenever we're lucky to have it!

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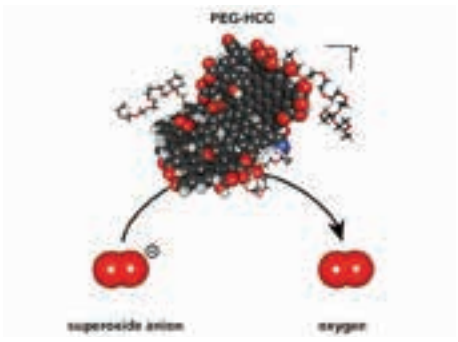
TATTOO THERAPY

RETHINKING TREATMENT OF AUTOIMMUNE DISEASES

BY EVELYN SYAU

How do tattoos relate to nanoparticles and selective inhibition of immune cells? And could this association be applied to a person diagnosed with an autoimmune disease? A recent partnership between Rice University and Baylor College of Medicine—in which scientists at Baylor worked with antioxidant nanoparticles created at Rice—seeks to answer these questions.

Autoimmune diseases have the power to deftly weaken an individual's immune system because a person's T lymphocyte cells can no longer distinguish between normal cells and invading ones, and will subsequently attack both. But Baylor scientists have found a way to circumvent these faulty T cells: using nanoparticles modified with polyethylene glycol (an organic compound made up of ethers[1]), the scientists succeeded in inhibiting the function of defective T cells. This treatment leaves the rest of the individual's immune system intact because other immune cells, like macrophages, did not recognize the nanoparticles and as a result, their functions remained active.



Credit: Errol Samuel/Rice University

The scientists at Baylor then worked with nanoparticles that combine polyethylene glycol with hydrophilic carbon clusters (called PEG-HCCs). PEG-HCCs are especially effective in detecting superoxide molecules, which signal T cells to become activated; PEG-HCCs can also remove superoxide molecules from T cells to prevent activation.[2] A testing of a sample of PEG-HCCs showed that like the modified nanoparticles, the PEG-HCCs only affect T lymphocyte cells.

SCIENTISTS COULD USE NANOPARTICLES TO DELIVER CANCER DRUGS TO TUMORS OR DECREASE THE SUPER-OXIDE OVERPRODUCTION CAUSED BY TRAUMATIC BRAIN INJURIES

To actually inject the PEG-HCCs into patients, scientists placed the particles right underneath the skin. According to Christine Beeton, one of the scientists at Baylor, "PEG-HCCs can be administered for slow release and don't stay in the system for long. This gives us much better control over the circulating half-life." The nanoparticles dispersed within a few days after uptake—long enough to be effective, but not so long that they couldn't be removed if needed.[2]

The ability to selectively inhibit one cell over another through the use of nanoparticles provides exciting new possibilities for medical treatment. Scientists could use nanoparticles to deliver cancer drugs to tumors, or decrease the superoxide overproduction caused by traumatic brain injuries.[3]

The only evidence of such a treatment would be a temporary but visible spot where the nanoparticles were injected. There are two possible courses of action: either the nanoparticles are injected in an area that is not usually seen, or scientists can use micropattern needles and actually shape where the nanoparticles are injected. This sort of "tattoo therapy" can lessen the stress and apprehension that may accompany treatment for autoimmune diseases and instead, become a creative outlet for patients.

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MEGALODON HUGE AND REAL?

BY EMRE YURTBAY

During Shark Week 2013, Discovery Network aired a very misleading documentary in its "Shark after Dark" series called Megalodon: The Monster Shark Lives. The "documentary" led many panicked people around the globe to believe that the Megalodon is "huge and real," prowling the planet's waters ready to make you its next prey. Of course, the events portrayed in Megalodon: The Monster Shark Lives are about as real as those shown in Sharknado, and outrage among scientists and public figures erupted.[1] Wil Wheaton went as far as to say that Discovery "lied to its audience," while marine biologist and self proclaimed "shark scientist" David Shiffman took to Twitter to allay people's fear, proclaiming unequivocally that "#Megalodon is extinct." Because Shark Week did Megalodon a huge injustice, we at Rice Catalyst are here to give you the real facts about the fascinating Megalodon, the monster shark that once lived.

Megalodon, whose name is derived from the Greek for "giant tooth," was the apex predator of the seas for almost 20 million years, feeding on absolutely anything that had the misfortune of sharing its waters. It has been suggested by scientists that Megalodon was "arguably the most formidable carnivore to have ever existed."[2] In general, Megalodon was piscivorous, meaning that its diet consisted mainly of fish (giant fish, of course), but everything from sea lions to truly gargantuan sperm whales made up Megalodon's diet. Great white sharks, formidable killing machines in their own right, were simply food for stronger, faster, and more brutal Megalodons. In tough times when food was scarce, Megalodon turned to cannibalism, eating its own kind to stay alive. The ocean 20 million years ago was a shark-eat-shark world, a Darwinian survival of the fittest scenario in overdrive.

Even more impressive than its feeding habits was the Megalodon's anatomy. Because no true complete fossils of Megalodon exist, it's hard to know precisely just how big this creature got.[3] The scientific consensus puts Megalodon at 68 feet long, bigger than modern day whale sharks.

MEGALODON WAS ARGUABLY THE MOST FORMIDABLE CARNIVORE TO HAVE EVER EXISTED

How could a creature so powerful, so robust, and so savage go extinct? Like with many prehistoric beasts, the culprit was climate change. Around 2.6 million years ago, the time of Megalodon's extinction, the earth was undergoing a period of global cooling and glaciation. Dropping sea levels and cooling ocean temperatures adversely affected Megalodon, which needed warm water temperatures to thrive. At the same time, this cooling affected the prey that Megalodon hunted, such as baleen whales, many of which started to disappear at the same time. Habitat depletion and prey extinction together brought upon the end of the mighty Megalodon.

The ocean will forever be a mysterious place, and the uncharted depths are sure to hold sea life that mankind will not discover for many years, if ever. However, Megalodon almost certainly does not exist anymore, and any suggestion that the monster shark still prowls the waters is false.

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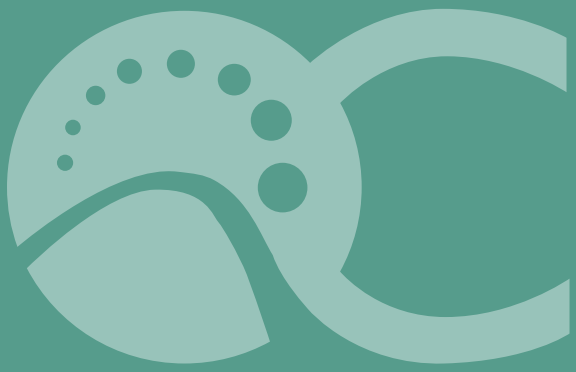

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