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Science in Society

COVER IMAGE

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Abstract network.

Adjustments by Steven Chen '15.

SUBMISSIONS

The *DUJS* welcomes submissions from all Dartmouth undergraduates. Please see dujs.dartmouth.edu for more information on the submission process. Letters to the Editor and requests for correction may be e-mailed to the *DUJS* or sent to:

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ABOUT US

The *DUJS* prints quarterly journals that include science news and review articles, along with research by undergraduates. Weekly Dartmouth Science News articles are also posted to *DUJS Online*.

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Note from the Editorial Board

Dear Reader,

Science is often perceived in a solely academic or educational lens. We forget that science is not an isolated aspect of society, but something far more pervasive. It is the study and exploration of the sciences that form the basis of the information and tools, which define how we live. Thus, for this issue of the *Dartmouth Undergraduate Journal of Science*, we examine this connection between science and society.

Our staff review articles this issue tackle an array of topics. Yoo Jung Kim discusses ways in which medicine can be personalized to every patient. Amanda Zieselman describes the placebo effect, and the medical validity of using non-treatment. Evelyn Maldonado's article studies the intricate relationship between music and the brain. And Suyash Bulchandani addresses on sports equipment unites science with athletics.

A discussion of cognitive enhancers can be found in Andrew Foley's article on neurologic drugs. Rui Shu has written a review on the development of optogenetics and magnetism in neuroscience research. Scott Gladstone examines the science and current research behind many popular science-fiction technologies. Finally, Derek Racine investigates the development of the Internet, and a few of its modern social applications.

Independent undergraduate research also plays an important role in the *DUJS*, and we are excited to feature three submissions. Sharang Biswas has written an essay discussing the history and events surrounding the discovery structure of DNA; Ben Hughey and Alexandra Giese summarize their research on glacial movement; and Robin Costello, Nina Frankel, and Madilyn Gamble report on the feeding adaptions and sexual dimorphism of lionfish. Our featured faculty interview in this issue comes from Sienna Craig, Associate Professor of Anthropology, who discusses her study of non-traditional medicine in Nepal and Tibet.

Lastly, we conducted our first annual International Science Essay Contest this fall, and received 80 excellent submissions from 20 countries. We would like to congratulate all of participants for their hard work. Our first place winner, Christian Nakazawa of Owings Mills, MD, and second place winner, Shreya Ahuja of Dallas, TX, have their essays featured in this issue.

We would like to extend a special thank you to the Undergraduate Admissions Office and Maria Laskaris, Dean of Admissions, for bringing the *DUJS* and our ISEC to high schools around the world. In addition, we would like to thank Jane Quigley, Head Librarian of the Kresge Physical Sciences Library, for assisting in the expansion of our distribution network.

Thank you for reading the *DUJS*, and we hope you enjoy this issue.

Sincerely,
The *DUJS* Editorial Board

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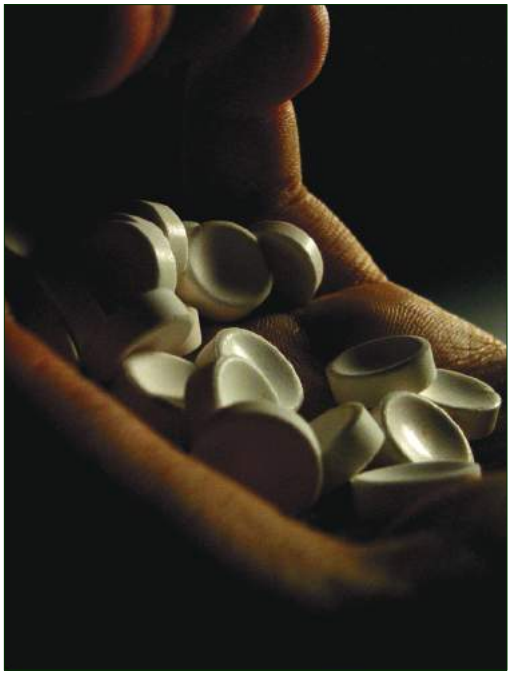

Table of Contents

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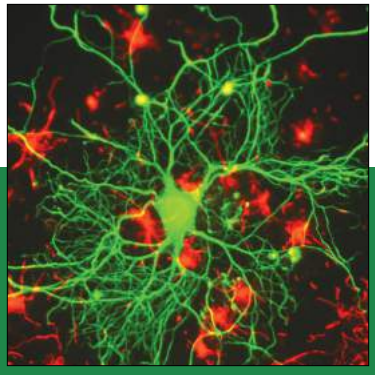

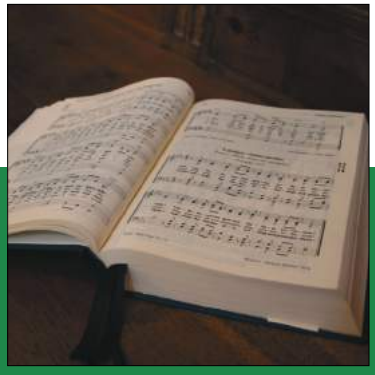

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COMPILED BY KYLE HEPPENSTALL, ANDREW FOLEY, SCOTT GLADSTONE AND XIONGFEI ZHANG

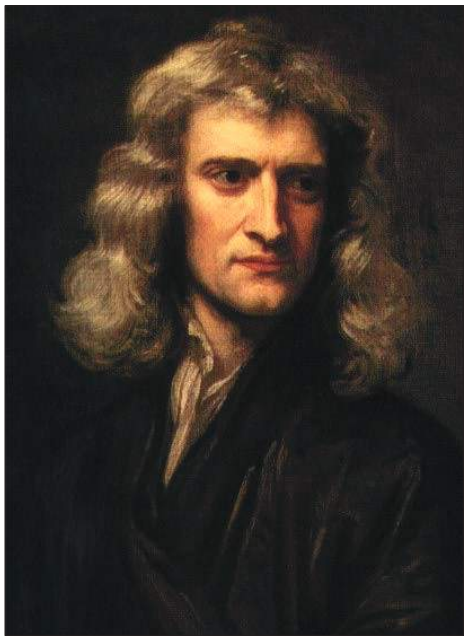
Physics

Time and the Laws of Nature

Lee Smolin, Professor of Physics at the University of Waterloo, spoke at Dartmouth this fall on the concept of time and the evolution of physical laws. Smolin, a theoretical physicist, asserted that scientific laws must have changed over time in order to effectively describe the apparent nature of the universe.

Together with his colleague Roberto Unger, Smolin attempted to address the definition of a scientific law. "Must laws be timeless or can laws change over time?" He described the concept of the Newtonian paradigm, which asserts that the entire physical world is composed of systems with states that are affected by dynamic laws. In Newtonian paradigm, a theory must cover all the possible states a system that can be found in and account for how these states change over time.

Smolin believes that the application of a subsystem of Newtonian paradigm theories and laws to the universe is incorrect. According to Smolin, the application of subsystem laws to the universe is a cosmological fallacy that results in gaps and irrationalities called cosmological dilemmas. Smolin states that scientific laws, as the most fundamental descriptions of nature, must be applicable to the whole universe and not just to special cases.



Isaac Newton's physical laws may form the basis of modern understanding of physics, but they overlook the relevance of time to scientific law.

Two popular axioms in modern physics that Smolin and Unger challenge are that time is an illusion and that our universe is just one of many universes. The two believe in "monoworldism," a theory that purports that there is only one universe. They reject the idea that time is an illusion and believe that the reality of time means that everything that is real exists in the present. They emphasize the importance of the present and argue against the irrelevance of time to physical law.

Biology

The Origin of Life

In 1952, Miller and Urey synthesized amino acids from inorganic precursors by simulating early Earth conditions. This created a new field called astrobiology, the study of how life arose in a seemingly inhabitable universe. The field and its development was the topic of a lecture titled "The Origin of Life" given by Marcelo Gleiser, Dartmouth Professor of Physics and Astronomy, at the E.E. Just Science Symposium this fall.

Hydrogen and helium were the only elements that existed during the universe's early history. Gleiser explained that all other elements, including oxygen, silicon, iron, and other key components of the Earth were formed by nuclear fusion in the center of stars. Supernovae from dying stars injected these new elements into space. Gravity then clumped the resulting stardust into planets. Earth's formation and development in particular were characterized by bombardment from comets and radiation, which injected additional elements unto the planet. With these ingredients, elements formed simple but crucial molecules like methane and ammonia. Spherical drops of lipids akin to the membranes of modern cells shielded chemical reactions from the outside environment. These conditions eventually allowed for the development of RNA. Early RNA was self-replicating and over time eveolved into DNA-based life.

Around 2.5 billion years ago, early autotrophic cyanobacteria started oxygenating Earth's carbon dioxide-rich atmosphere. This new environment was conducive to eukaryotic and multicellular life, resulting in more specialized organisms over the ages. However, Gleiser stresses that life does not strive to evolve into more "advanced" or "cognitive" forms. One cannot predict that natural selection will "create an elephant out of a bacterium," Gleiser says.

The chances of life developing on one of the planets surrounding the billions of stars in billions of galaxies are astronomically high. However, most extra-terrestrial life is probably simple and underground. Although only a tiny fraction of all life is intelligent, the degrees of sophistication even within that tiny fraction are huge. Hence, Gleiser suggests: "We likely are not the most advanced beings in the universe—for all we know, humans are meant to liven up some alien civilization's space 'Petri dish.'"

Anthropology

The Grandmother Hypothesis: An Explanation for Human Development

Kirsten Hawkes, Professor of Anthropology at the University of Utah, recently presented her research supporting the Grandmother Hypothesis at Dartmouth's E.E. Just Symposium. The Grandmother Hypothesis states that the longevity of human females during post-reproduction years allows them to help raise their grandchildren, thereby increasing the chance that grandchildren will propagate this post-reproduction longevity trait. The grandmother hypothesis is an exception to conventional natural selection theory which considers selection irrelevant after reproduction.

Hawkes explains that human mothers

Image courtesy of NASA (accessed 25 Oct. 2012)

An image of Andromeda, Messier 31, the galaxy cluster which contains our Milky Way. The probability that other life forms exist in Andromeda are high, according to Professor Glesier

differ from chimpanzee mothers in the manner they raise their children. While chimpanzees and other primates tend to raise their offspring alone, human mothers receive help from others like members of their the immediate family. This allows human mothers to have more children and with greater frequency. A chimpanzee mother has to wait until its offspring is totally independent, which can take a total of five to six years. In contrast, a human mother can reproduce before her current child can fend for itself.

Hawkes asserts that, over time, humans have evolved to be more social than other primates because human mothers have to pay attention to several children at once. This unique childrearing environment may partially explain why humans have an innate desire to be connected to each other .

Mathematics

Cracking Down on Crime with Applied Mathematics

Andrea Bertozzi, a Professor of Mathematics at the University of California, Los Angeles, presented her research on the mathematics of crime at Dartmouth College this fall. Bertozzi's research is on the development of algorithmic predictive models of crime patterns in urban regions,

Beginning her work with the Los Angeles Police Department (LAPD), Bertozzi used quantitative models to predict where crimes were most likely to occur in the city. Informed by Bertozzi's models, LAPD patrols now receive alerts before each shift on predicted hotspots. According to Bertozzi, targeted patrols like these contributed to decreases in crime rates by up to 27 percent.

Bertozzi's models began with routine activity theory. Routine activity theory states that crimes are more likely to occur where more offenders encounter potential targets. By mapping potential offenders and targets on 2-D grids, Bertozzi creates models that simulate crime patterns. Factors used to estimate the likeliness of a crime include the attractiveness of a location to crime and the security of potential targets.

Bertozzi and her team also use census data, crime density estimations, and high-resolution image processing to inform their models. By considering the expected decrease in attractiveness of a target over time and informing recent crimes into the models, Bertozzi's models strive to hone in on localized criminal hotspots in real time. In an added layer of complexity, Bertozzi's models also predict how effective police forces will likely be able to respond to a crime.

Bertozzi's most recent project has been mapping gang networks in Los Angeles. She attempts to model gang boundaries by simulating violence and retaliations. Using these models, Bertozzi has presented important evidence on unsolved gang crimes and suspet crimes to the police.

Although Bertozzi and her team only started working with the LAPD seven years ago, large advances have already been made in using mathematics to fight crime. As crime continues to evolve, Bertozzi's team plans to continue to advance their models and mapping techniques.

Medicine

Cognitive-Behavioral Intervention as a Way to Treat Alcoholism

For most medical conditions, financial concerns are the biggest barrier to the effective delivery of treatment. However, other more complicated factors can make it difficult for those with substance use disorders to seek therapy. One of the greatest challenges for a substance abuser can be the act of convincing himself that he needs outside help.

Tracy Stecker, Professor of Community and Family Medicine at the Geisel School of Medicine, explored the use of cognitive-behavioral intervention (CBT) to influence the rate of treatment initiation among alcoholics in a recent paper. The results indicated that the participants who received CBT were three times more likely than those who did not to attend treatment sessions within a three-month period.

Cognitive-behavioral therapy operates under the assumption that cognitions, feelings, and behaviors all interact with one another, and therefore seeks to influence patients' outlook towards treatment by changing beliefs related to the care.

In Stecker's study, individuals were divided randomly into a control group assigned to read a pamphlet about the dangers of alcohol use, or an intervention group assigned to receive CBT.

In the control group, only 11 respondents (12%) sought medical treatment and an additional 13 attended AA meetings. In the group that had undergone CBT, 25 respondents (30%) received treatment while 17 went to AA meetings. An odds ratio of 3.14 was recorded, indicating a clear increase in treatment-seeking behavior from patients that underwent CBT. This success suggests CBT as an effective option for alcoholics who need additional encouragement in seeking therapy.

In the future, an expansion of CBT application in influencing treatment-seeking behavior could provide for a gradual dip in the number of substance abuse patients without care.

Personalized Medicine

How Modern Medicine can Improve

YOO JUNG KIM

Imagine that you receive a reminder from the doctor's office for an annual checkup. After mulling it over, you make an appointment to see your primary care provider. She runs through a routine physical and notices nothing amiss, but based on your family history of cancer as written on your digital health record, she pauses to feel for abnormal growth.

Sure enough, your physician detects a lump on your neck, a lump so small that you hadn't noticed it before. After administering a local anesthetic, she extracts a small amount of fluid from the suspicious area and sends the specimen off to the laboratory for a biopsy.

A day later, your physician delivers the bad news: you have cancer. Fortunately, based on a genetic analysis of your specimen, the laboratory has determined the exact subtype of cancer and the known mechanisms that spur on its growth; the prognosis is positive. Moreover, using a genetic database containing millions of known genetic reaction to chemical compounds, your physician has compiled a list of possible treatments that maximizes efficacy with minimum harmful side effects.

And most, if not all, of the costs of diagnosis and treatment is covered by your insurance provider.

As of now, the above scenario seems suited for a futuristic medical utopia, when various components of health care—from diagnosis to reimbursement—will be tailored to the individual patient. But developments are already underway towards personalized medicine: a medical model that allows for the customization of healthcare, with all decisions and practices tailored to the individual patient via use of genetic information.

Currently, personalized medicine exists only in fragments, at varying stages of development. For the full realization of personalized medicine for all, scientific development, medical translation, health delivery and health policy must be coalesced into a streamlined form.

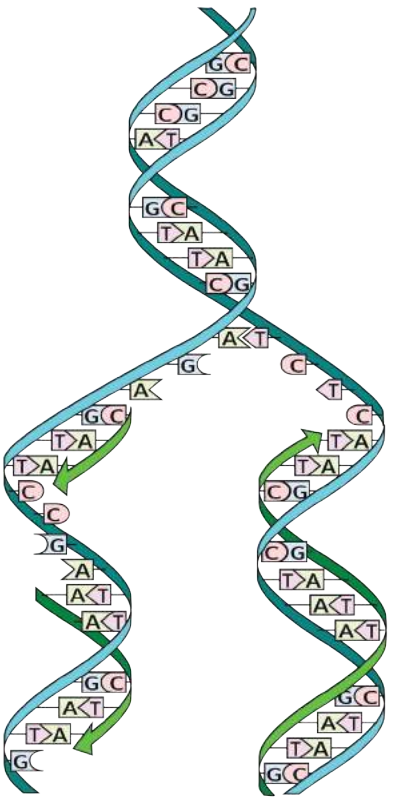


Image courtesy of Madprime. Retrieved from http://commons.wikimedia.org/wiki/File:DNA_replication_split.svg (accessed 11 Oct. 2012)

Figure 1: Schematic of DNA replication, a process investigated for the Human Genome Project.

Personalized Medical Diagnosis

The Human Genome Project

In 2003, the Human Genome Project completed its primary goal of mapping the approximately 20,000 to 25,000 genes of the human genome. The project's completion led to a flurry of speculation of the future of medicine incorporating genomic analysis. While we have yet to meet these expectations, advances in medical genetics have enabled a more detailed understanding of the impact of genetics in disease.

Specifically, the Human Genome Project revealed the importance of single nucleotide polymorphisms (SNPs) in accounting for the genetic variability among individuals (Fig. 1). More specifically, Genome-Wide Association Studies (GWAS) have enabled the examination of genetic variations and their effects; by analyzing common genetic variants in different individuals, variants associated with complex traits—particularly diseases—can be identified (1).

However, GWAS is not without criticism. Opponents have criticized GWAS of insufficiently explaining genetic variation in populations and for not delivering much knowledge of clinical utility. Proponents have pointed out the GWAS design in human populations "has led to new discoveries about genes and pathways involved in common diseases and other complex traits, provided a wealth of new biological insights, led to discoveries with direct clinical utility, and facilitated basic research in human genetics and genomics." Furthermore, future technological advances will allow entire genomes to be sequenced for affordable prices, generate additional genes, pathways, and biological insights, and identify causal mutations (1).

Thus, despite its criticisms, the Human Genome Project and GWAS have laid the scientific foundations and set off the public imagination on the possibility of personalized medicine.

Whole Genome Sequencing

Last July, the New York Times published a story about cancer biologist Dr. Lukas Wartman, a genetic researcher at the Washington University in St. Louis who had developed Acute Lymphoblastic Leukemia (ALL), the very cancer that he had been studying in his lab.

Fortunately for Dr. Wartman, his institute came to his aid. Dr. Timothy Ley, the associate director of Washington University's genome institute, called upon his lab to see whether they could find a "rogue gene" that was spurring Dr. Wartman's cancer. To observe the inner workings of his body, the team sequenced the complete genomic makeup of both his cancerous and healthy cells. By comparing the two sequences, the team deduced that a mutation had caused a gene to be overexpressed; the researchers even identified a promising new drug that might turn off the rogue gene causing the cancer.

While the drug was originally tested and developed for advanced kidney cancer patients, Dr. Wartman used it to

successfully treat his leukemia. He is now in remission (2).

While whole genome sequencing is currently available to the public on a small scale, experts believe that its widespread use may not be too far off in the future. Until then, more specific and limited means of genomic diagnosis are available.

Currently available diagnostics

Molecular diagnosis already has a rich precedence in oncology. Novel molecular experimental methods have enabled tests for markers, genes, proteins, and protein pathway activation expression profiles; these, combined with identification of somatic mutations in cancer cells, have allowed for better defined prognosis and suggestions of effective treatment options.

For a diagnosis assessing an individual's risk to both common and uncommon diseases, a small-scale personalized diagnosis through DNA analysis is currently available. Biotechnological companies have achieved this by synchronizing the rapidly growing body of pharmacogenomic knowledge with commercial gene sequencing and analysis.

For instance, 23andMe, a Silicon Valley biotech firm, provides rapid genetic testing and counseling for the concerned and the curious who have the money to spend (Fig. 2). Founded by Anne Wojcicki, wife of Sergey Brin, the company has been profiled by popular publications such as *Collins*' "The Language of Life: DNA and the Revolution in Personalized Medicine" and *Time*, which awarded 23andMe the 2008 "Invention of the Year."

For a flat fee of $299, the company ships its customers a kit to collect saliva samples. Within 2-3 weeks of the kit's receipt, the customers receive an analysis of their personal genetic variations over the Internet, including carrier status, disease risk, and drug response. While 23andMe has resisted government regulation for years, the company has moved to ask the Food and Drug Administration to approve its drug test as a medical service, which, if successful, may boost scientific credibility and acceptance within medical and scientific circles that have questioned its usefulness (3, 4).

Yet, while 23andMe offers historic, unprecedented access to the possible implications of one's genetic information, genes does not necessarily equate to destiny. Scientists have long debated whether disorders are written into our genetics (nature) or picked up through environmental exposure (nurture). Today's scientific consensus allows for both through the concept of epigenetics, in which environmental factors—ranging from molecular methylation and acute chemical exposure to long-term diet and lifestyle choices—can affect the expression of our genes.

The Development of Personalized Therapies

Population-Based Medicine, A step towards personalized medicine?

Historically, the crossing of science and race evokes centuries of scientific racism in which the vogue scientific methods of the time—ranging from phrenology to physical anthropology to modern-day genetics—were applied to justify racial oppression.

Yet, the scientific community has once again raised the question of race in a way that may prove beneficial to all—race-based medicinal therapies. By stepping away from the current one-size-fits-all modality, race-based medicinal therapies can target specific populations and provide a stepping stone towards personalized medicine. However, these developments may come at a cost: race-based therapies can have unintended side effects on our social fabric.

Tay-Sachs Disease: Community-targeted therapies

Race-based therapies are already utilized within populations facing increased genetic susceptibility to medical conditions. For instance, Tay-Sachs disease is an autosomal recessive neurodegenerative disorder in which harmful quantities of a fatty substance build up in the brain due to insufficient activity of an enzyme that catalyzes the biodegradation of the fatty substance (5). The disorder is observed primarily in Cajun, French Canadian, and Ashkenazi Jewish populations. The first program to prevent Tay-Sachs originated decades ago in Jewish synagogues and community centers of Baltimore and Washington D.C., which pushed for testing of potential carriers. The idea spread to cities throughout the United States and led to the virtual prevention of Tays-Sachs disease within the Jewish population through mate selection (6).

Population-targeted studies are nothing new in epidemiology, considering that members of certain ethnicities share similar diets, values, lifestyle choices, and genetic traits. However, problems arise when science correlates race with genetics.

BiDil: Drugs for African Americans

Race-based therapies have also appeared in the pharmaceutical industry. In June 2005, the F.D.A. approved the first drug to be intended for one racial group—African Americans. BiDil, manufactured by Nitromed, is a combination of two generic vasodilator drugs (isosorbide dinitrate/hydralazine hydrochloride) that prevent heart failure by relaxing blood vessels.

The effects of the drug combination were observed under the African American Heart Failure Trial (A-HeFT), which demonstrated a 43 percent reduction in mortality rate for African Americans' heart failure patients treated with the dual-drug combination (7).

The potent combination of race and medicine has also raised academic backlash. Following the study's publication in the New England Journal of Science, ethicists pointed out that A-HeFT enrolled only self-identified African Americans, which may be a reflection of socio-cultural—rather than strictly genetic—characteristics. Moreover, scientists contended that because the study did not investigate the effects of the drug combination on a non-African American population, researchers cannot convincingly conclude that BiDil works unilaterally on the African American population (8). Perhaps most concerning to society at large, critics have condemned the study for "scientizing" race (8).

Proponents of BiDil have fought back against the allegations, noting that that race-based therapies treat race as a crude marker for genetic variations that have yet

Image courtesy of Boseritwik. Retrieved from http://upload.wikimedia.org/wikipedia/en/3/39/23andme_logo.png (accessed 11 Oct. 2012)

Figure 2: 23andMe is a biotechnology company that provides personal genetic testing for consumers.

to be discovered.

Overall, race-based medicine presents an ethical dilemma. While our public society has strived to minimize racial differences, racialized medicine may enable certain populations to receive more effective treatments.

Pharmacogenomics: Promising personal medicine

While general personalized medicine may be years away, active research is being undertaken to study how an individual's genetic inheritance affects the body's response to drugs, a field known as pharmacogenomics (9). By better analyzing a patient's individual genetic makeup, doctors can prescribe the best drug therapy and the appropriate dosage for the treatment and avoid any unintended side effects (9). Current methods of pharmacogenetics include genotyping for genes involved in the action and metabolism of drugs.

Furthermore, pharmacogenomics may have important implications in health policy (Fig. 3). Each year in the United States, about 106,000 deaths and 2.2 million serious incidents are caused by adverse drug reactions (ADR) (10). ADRs can also lead to the withdrawal of drugs from the market, leading to millions of dollars in wasted development, trial, marketing, and litigation costs for drug companies and federal grant-giving agencies.

Widespread adoption of personalized medicine may enable more efficient medical trials. Scientists anticipate that by linking genetics and proteomics with the body's reaction to external chemical agents, researchers could create more powerful medicines and safer drugs, as well as discover appropriate drug dosages, advanced screening for disease, and better vaccines.

Image courtesy of Ayena. Retrieved from http://commons.wikimedia.org/wiki/File:Pills.JPG (accessed 12 Oct. 2012)

Figure 3: Personalized medicine holds a tremendous amount of potential on targeting difficult diseases.

Policy and Delivery

Health Policy: Regulating the interface between NIH, academia, and private biotech companies

The actualization of personalized medicine will require effective cooperation between academia and industry through "sharing of data, expertise, resources, and tools" (11). In an example of modern-day collaborative drug development, the NIH Therapeutics for Rare and Neglected Diseases Program (TRND) tests promising compounds by bearing the financial and research burden of the high-risk preclinical development phase, which pharmaceutical companies may be reluctant to undertake (12). Scientists hope that this type of active collaboration will accelerate the development of new therapies for rare diseases and identify molecularly distinct variations of common diseases, leading to new treatments options (12).

Yet within the intersection of federal research agencies, academia, and biotechnology—where individual players have different motivations—conflicts of interest are inevitable. In 1980, the passage of the U.S. "Bayh-Dohl University and Small Business Patent Act" enabled universities, private businesses, and non-profit organizations to retain ownership of an invention from research funded by a federal agency. While the legislation enabled more biotech companies to attract investment capital in science and accelerated commercialization of federally funded inventions, improper proprietary patents may stifle progression of research.

For instance, imagine a tangible intellectual property (IP)—such as a cell line—discovered by a biotech company with federal research funding. The IP may be a lucrative product that the biotech company can patent under Bayh-Dohl Act to develop commercial products; on the other hand, the patent may prohibit laboratories from gaining access to an essential research tool, presenting a potential conflict of interest between proprietary rights and the freedom of research and innovation.

The viability of personalized medicine will require research focused on associations between drug response, genetic variation and drug development (11). This type of research and development will be most effective through cross-institutional collaboration and access to research tools for continuation of research (11). As such, the federal government will have to balance the freedom of research with the protection of proprietary rights.

Conclusion

Although the promise of personalized medicine is exciting, it currently exists only in disconnected components. The advent of the Human Genome Project fueled hopeful speculations, leading to genome-wide studies to connect genetic variations with physical traits. Enterprising new startups have embraced the spirit of personalization through the development of personalized diagnosis, which may become more commonly utilized as a medical diagnostics tool with their acceptance by the FDA. However, the realization of personalized medicine is still hampered by limitations in funding and logistics. In order to bring personalized medicine into reality, scientific development, medical translation, health delivery and health policy must come together in effective forms.

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References

1. P. M. Visscher, M. A. Brown, M. I. McCarthy, J. Yang, Am J Hum Genet. 90, 7–24, (2012).
2. In Treatment for Leukemia, Glimpses of the Future (2012). Available at http://www.nytimes.com/2012/07/08/health/in-gene-sequencing-treatment-for-leukemia-glimpses-of-the-future.html?pagewanted=all (July 2012)
3. How it works (2012). Available at https://www.23andme.com/howitworks2/ (July 2012)
4. 23andMe personalized DNA test seeks FDA approval (2012). Available at http://www.cbsnews.com/8301-504763_162-57483267-10391704/23andme-personalized-dna-test-seeks-fda-approval/ (July 2012)
5. NINDS Tay-Sachs Disease Information Page (2011). Available at http://www.ninds.nih.gov/disorders/taysachs/taysachs.htm (July 2012)
6. H. Ostrer, Legacy: A Genetic History of the Jewish People (Oxford University Press, New York, ed. 1, 2012). [first edition]
7. A. L. Taylor *et al.*, N Engl J Med. 351, 2049-2057, (2004).
8. J. Kahn, Am J Bioeth. 5, W1-5, (2006).
9. Pharmacogenomics (2011). Available at http://www.ornl.gov/sci/techresources/Human_Genome/medicine/pharma.shtml (July 2012)
10. J. Lazarou, B. Pomeranz, P. N. Corey, JAMA, 279, 1200-1205, (1998).
11. R. Gupta, J. P. Kim, J. Spiegel, and S. M. Ferguson, Personalized Med. 1, 115-124, (2004).
12. M. A. Hamburg F. S. Collins, N Engl J Med, 363, 301-304, (2010).

Sienna Craig

Associate Professor of Anthropology

ANNIE HUANG

Image courtesy of Sienna Craig

Sienna Craig, Associate Professor of Anthropology, with one of her research assistants in Qinghai Province, China.

Can you tell us about your current research on traditional Tibetan medicine?

I'm working on a couple of projects right now. I just published a book, Healing Elements: Efficacy and the Social Ecologies of Tibetan Medicine which is based on about a decade of research working with Tibetan doctors in Nepal and Tibetan areas in China. On Sunday (Oct 14, 2012), I'm going to Xining, which is the capital of Qinghai province in China, where I've worked for the last couple of years on a collaborative research project looking at the ways Tibetan doctors, Tibetan formulas, Tibetan ideas about health and illness are globalizing – traveling to new parts of the world, to new patients, and to new markets.

I'm going back to Xining now to run a research methods workshop, the goal of which is to bring medical anthropology, field methods and ethnographic approaches to some of the Masters and Ph.D. students at the Qinghai Tibetan Medical College, and also to the Tibetan Medical Hospital in Xining so that they can think about incorporating them into their own work and research. The research that has been done on Tibetan medicine in a hospital setting is primarily in China but is also in other places.

Can you tell us about some of your collaborative projects?

In anthropology, we have four subfields. We have cultural anthropologists, which includes medical anthropologists like myself. We have sociolinguists, people who study the relationship between language and culture; archeologists who study human history and ancient civilizations; and biological or physical anthropologists whose research ranges from human evolution to primatology and paleontology.

My National Science Foundation-funded research project brings two main subfields together. The principal investigator is biological anthropologist Cynthia Beall, who is at Case Western Reserve University. Aside from me, another cultural anthropologist and a demographer, Geoff Childs, based at Washington University – St. Louis is also working on this project, which examines the relationship between genetics and the fertility of ethnically Tibetan women in northern Nepal

Cynthia Beall has worked in the Andes as well as on the Tibetan Plateau for more than 30 years. Her main scientific contribution has focused on human adaptation to living at altitude. Part of what she has discovered is that not only are there specific cultural adaptations Tibetans have acquired to living in high and extreme environments, but it's also an example of natural selection in a living population: over time, Tibetans have genetically adapted to living at altitudes. In particular, part of what Cynthia and colleagues of hers, geneticists, have discovered genetic markers in Tibetan populations that not only seem to be correlated with the ways that Tibetans carried oxygen in their blood, (hemoglobin levels), but also, in the case of women with these markers, with reproductive outcomes. Our project is testing the hypothesis that women with these genetic markers will have better reproductive outcomes than those who do not. But many other things affect whether or not a child lives or dies at altitude. To put it in a different way, a remote, resource-challenged part of a poor country, like Nepal, is bound to introduce other complicating factors to women's fertility, their reproductive histories, and their children's rates of survival. This is where Geoff and I come in. We know the two areas in Nepal where we are doing this work very well and have good rapport with local people. We were not only helping Cynthia to collect the biological data that she needs to answer those genetic questions, but also connecting this information to household demographic data, economic surveys, family histories, and reproductive histories.

For this project we interviewed hundreds of ethnically or culturally Tibetan women in Northern Nepal last summer, asking them about their histories of childbirth, when they got married, and many other questions. We asked them a wide range of questions to get a clearer picture of the cultural, socioeconomic,

and biological factors that impact fertility and child survival. In addition to the surveys and the qualitative interviews, we also collected biometric data such as hemoglobin levels and oxygen saturation, and took non-invasive saliva samples of the women in the primary study, all of whom are 40 years of age or older. These data are now being entered and analyzed.

How did you become interested in Nepal and Tibet?

When I was an undergraduate at Brown, I went on a study abroad program my junior year through the SIT (School for International Training) programs, which some Dartmouth students end up going on. It was a program based in Nepal, and I spent four months in Nepal on this program I was a religion major as an undergraduate, not an anthropology major. I came to Nepal with an interest in the relationships between Hinduism and Buddhism and wanting to learn more about how diverse, really, this relatively small country in South Asia sandwiched between India and China is.

I really fell in love with the country and began learning about the history and politics of the country and began learning the Nepali language. Then, I got a Fulbright when I graduated from Brown to go back to pursue a project that I started on the study abroad program. That one-year grant led to three years of living in the country and starting to learn Tibetan language, and everything sort of went from there. That was the gateway for me to really get into considering anthropology and this part of the world as the focus of my life and of my professional work.

You are involved with Tibetan culture in non-academic ways as well. Can you talk a little bit about Drokpa?

Drokpa means "nomad" in Tibetan. It is a small NGO that my husband and I founded in 1998. We found this nonprofit after both of us spent more than three years in Nepal. We both had received Fulbright fellowships, and we'd done research and worked for conservation and development organizations in Nepal. It was just the beginning of this shift toward NGOs, for better or for worse, as models of health care and education delivery.. We wanted to try to engage with the communities and people who had welcomed us into their lives in a long- term way, not just around research, but also around practical engagements in health, education, and alternative energy for the people that we knew and became close with. Drokpa is a very small organization, and it is completely volunteer work – like each of our third or fourth job.

Other projects that I've been involved in through Dropka is working with a network of Tibetan doctors in Nepal, with clinics and schools, with medicinal plant cultivation projects that the doctors have started, and engaging in knowledge exchange, in creating opportunities for doctors throughout the region to meet each other and strategize. Through Dropka, we see ourselves as catalysts for these kinds of connections. It is an extremely small, very mom-and-pop organization, but we channel money and other resources to projects that we feel like we know well and can monitor well in Nepal, places in China, and other places like that.

What is "One Heart World-Wide" and what is your role?

One Heart World-Wide (OHW) is another non-profit organization with which I have been involved since 2002. It is dedicated to saving the lives of mothers and infants, one birth at a time, and serves primarily indigenous communities that are remote and often politically marginalized. Each year between 350,000 and half a million women still die while trying to give birth. Many more newborns and infants under the age of one also die. It doesn't have to be this way.

One Heart addresses those issues by investing in skilled birth attendant training, technological inputs for birthing centers and health posts, and creating what we call a network of safety from the household to the tertiary care hospital within the countries where One Heart works – currently Nepal and Mexico, and formerly in the Tibet Autonomous Region (TAR), China. I'm a chair of OHW's medical advisory board. One Heart is providing additional training to existing health workers and helping to improve the hospital conditions in districts or regional hospitals that already exist. They are also working with local doctors and health care practitioners.

As background, One Heart began as a project that was really just focused on the TAR, specifically within and around Lhasa,. One Heart has moved out of Tibet and has been taken over by a local organization, which is about one of the best outcomes that you can have for a project like this. This happened, though, for political reasons because 2008 was a very volatile year in China, especially in Tibetan areas, in part because of the Olympics. It became too difficult for an American NGO to work in Tibetan areas in China.

The good thing is that that project is

Image courtesy of Sienna Craig

Professor Craig with research assistants in Mustang, Nepal, in the summer 2012.

still going. Local midwives and community health workers are still benefiting from the training that One Heart has provided in real collaboration with the state and regional health authorities. But One Heart, as a foreign organization, is not working there anymore. Now One Heart is working in a couple of different parts in Nepal. One place is called Dolpo, which is also a culturally Tibetan area, even though it is within the borders of Nepal. It actually leads right up to the border of Tibet. They are also working amongst Tarahumata, indigenous communities in the Copper Canyon in the state of Chihwahwa, Mexico.

What exactly is complementary and alternative medicine?

Complementary and Alternative medicine, or CAM, is really a way of talking about different approaches to health and illness, that departs from anything that we might consider conventional western medicine or "biomedicine. CAM therapies include including acupuncture, Chinese herbal medicine, homeopathy, naturopathy, Ayurveda, Tibetan medicine, and many other practices. It is a kind of catchall term that is useful, but only to a certain degree.

CAM is becoming more and more popular around the world, as people turn to non-conventional or non-biomedical approaches to deal with their health problems. But the idea that you can fit everything that is not conventional biomedicine under one umbrella is a problem, and it is an illustration of the ways that biomedicine – which is an incredibly diverse thing in itself – has essentially more power and authority to dictate what will be considered legitimate forms of care. But CAM as a category also has policy, research and legal implications. For instance, the National Institutes of Health in this country now have a big section that is devoted to testing and evaluating the safety and efficacy of CAM therapies, exploring differing complementary and alternative therapies for problems one might define according to conventional medicine – things like rheumatoid arthritis, fibromyalgia, or severe back-pain. Slowly conventional medicine practitioners and researchers are opening up space for things like acupuncture or other forms of therapy to be a part of that healing picture. Still, the NIH and other organizations like it is very much weighted toward the epistemologies, methods, and ways of discerning evidence that emerges from western science.

Why did you decide to become a cultural anthropologist?

Had I not gone to Nepal as an undergraduate, and had I not gotten an opportunity to go back to Nepal after I finished my B.A., I probably would have had a different life trajectory. I may have gone back to Nepal at some point, but I really cannot separate becoming a cultural anthropologist from having a relationship to Nepal and other parts of Asia. That being said, I think the more I studied anthropology, both through field work and classes I had as an undergraduate and in graduate school, the more I came to think about what it means to be human. It was a compelling way to think about the world. That said, while I enjoy being in the department of anthropology and talking to other anthropologists, I also enjoy being the anthropologist in the midst of doctors, development workers, or other environments. This requires me to think about the dynamics between people.

Controlling the Neuron

The Development and Relevance of Optogenetics and Magnetism in Neuroscience

RUI SHU

One of the central goals of neuroscience is to understand the cellular mechanism underlying the circuitry of brain. The key obstacle to achieving this lies in our lack of understanding autonomous cell-type specific functions. This presents a serious problem, as the brain consists of a multitude of different cell-types.

Neural Excitability

By the end of the twentieth century—decades after the theory of neural connectivity was established by Ramon Cajal—a considerable amount of progress has been made in the field of neuroscience (1). The mid-twentieth century saw the invention of the voltage, current, and patch-clamps. To date, these tools are used by neuroscientists' greatest tools to record neural electrophysiological properties (2).

One of the hallmark characteristics of neurons is its ability to receive and generate unidirectional electrical signals. A neuron's electrical signal is generated by channel-mediated influx of ions. Channels can be typically separated into two distinct classes: ligand-gated channels and voltage-gated channels (3). These ion channels, embedded in the cell membrane, provide a hydrophilic environment through which specific, charged molecules can cross the otherwise hydrophobic membrane. As their names imply, ligand-gated and voltage-gated channels, respectively, open or close when bounded to a particular molecule or when the local voltage difference across the plasma membrane (membrane potential) passes a particular threshold.

The ability to receive a signal from a presynaptic neural or sensory cell is dependent on the activity of ligand-gated channels. Ligand-gated channels are found in the cell body and dendrites at both synaptic and extrasynaptic sites. Within the synapse, they perform the specific task of receiving neurotransmitters. These neurotransmitters, when released into the synaptic cleft, bind to their corresponding receptors, which subsequently cause an ionic flux—effectively translating a chemical signal into an electrical signal. Receptors such as AMPA (2-amino-3-(5-methyl-3-oxo-1,2-oxazol-4-yl)propanoic acid) and NMDA (N-methyl-D-aspartate) generate an influx of cations, positively charged ions. Such net electrical currents into the cell are termed Excitatory Post-Synaptic Currents (EPSCs), while net electrical currents out of the cell (e.g. mediated by GABA receptors) are Inhibitory Post-Synaptic Currents (IPSCs). As their names imply, EPSCs raise the membrane potential and increase a neuron's likelihood to fire, while IPSCs perform the inverse. These currents travel from the post-synaptic sites into the cell body, where they summate at the axon hillock (the base of an axon) and alter the membrane potential. Once the membrane potential crosses a certain threshold, the voltage-gated ion channels situated in the axon hillock open, causing a cascade of membrane depolarization down the axon, known as an action potential. Once the signal reaches the axon terminal, the depolarization triggers a calcium influx that then mediates the release of neurotransmitter toward the next cell. They cycle then repeats.

When and how a neuron fires action potentials are thus critical to our understanding of neural circuitry. Clamping has enabled neuroscientists to measure crucial parameters that contribute both to how a single neuron works and how it operates within a system. The determination of membrane potentials, receptor composition, membrane resistance/capacitance, action potential thresholds, ion channel kinetics and countless other intrinsic and extrinsic neuronal properties depend on the diligent application of voltage/current/patch clamp techniques.

The Big Problem

The aforementioned clamping techniques are only a means of measuring a pre-conditioned system. If the system were left unaltered, then results from such techniques would merely amount to an observational study of a system.

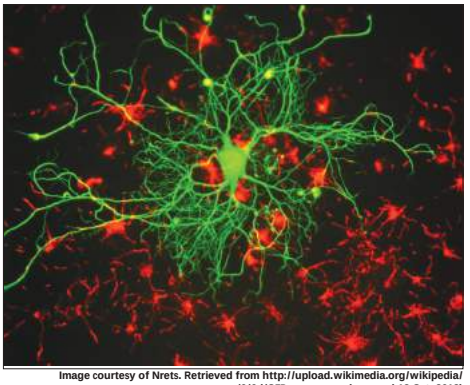

Image courtesy of Nrets. Retrieved from http://upload.wikimedia.org/wikipedia/commons/0/0d/GFPneuron.png (accessed 13 Oct. 2012)

Figure 1: GFP expressing pyramidal cell in mouse cortex.

In order to ascertain the impact of a component within a complex system, we must treat the component as a variable and conduct experiments that compare the consequences of having the component present versus removing the component.

Neuroscientists have made strides in performing such experiments (2, 5). They have measured ionotropic receptor activity by injecting receptor agonists while holding the neuron at various voltage potentials. This generates receptor-mediated current vs. voltage curves (I-V curves) that show how membrane potential influences ligand-gated channel activity. Through the focal application of specific antagonists and agonists for various receptors, we looked at the consequences of activating/inactivating specific receptors. Through the use of a stimulating electrode, we observe the changes in electrophysiological properties following the application of specific stimulation patterns to a region of neurons.

However, neuroscientists lack a technique that allows control of a specific neuron's firing pattern. Such an ability would provide us with considerable insight into the function of specific neurons within a neural circuit of different cell types. By the early 2000s, known methods of activating neurons were unable to resolve cell-type specific functions (6). Neither agonist application nor electrical stimulation provides the specificity required to selectively activate a desired neural subpopulation within a circuit—let alone perform it in a minimally invasive manner.

It was not until 2005 that the first successful technique for performing such an act was developed. We now term this technique optogenetics.

Optogenetics: The Literature

Even before the 1980s, scientists had begun to consider the issue of controlling individual types of neuronal cells. Francis Crick, one of the scientists credited with the discovery of DNA's double helical structure, noted that one of the major challenges facing neuroscience was the ability to control one type of cell while not affecting others. In 1999, Crick published an article that emphatically recommended neuroscientists to make greater use of the tools of molecular biology (7). The Human Genome Project raised great expectation as to what molecular biology could offer to the field of neuroscience. Amongst his predictions for "possible future tools," Crick recommended the use of a light signal to rapidly activate/inactivate one or more types of neuron. Such an innovation, however, remained contingent on the speculation that "molecular biologists could engineer a particular cell type to be sensitive to light in this way" (7).

While there were many possible limitations preventing the development of such a method, the key components of one possible design were already available.

The first paper to demonstrate an approach akin to Crick's suggestions was published in 2002 (8). Zemelman, *et al.* utilized a three-gene system (coined "chARGe"), which they then transfected into neurons. By placing the exogenous genes under specific promoters, they were able to ensure expression of the system in select cell populations. In the select populations, the exogenous genes are translated and transcribed into the proteins that enable "chARGed" neurons to be activated by light. These neurons were capable of sustaining light-induced depolarization, as well as action potentials. The only limitation was the speed of the system: because the system relies on a complex signal transduction, there exists a high latency period between photostimulation and neural activation. They delay could be on the order of several seconds. This, coupled with the multi-component nature of the system, makes the "cHARge" system unsuitable for milli-second control of neural activity. The key, then, was to find a system capable of generating faster and more reliable responses.

By the 1970s, scientists had begun studying the mechanism of light-driven ion pumps found in microbes. These pumps, known as opsins, were capable of rapidly pumping ions across the membrane after illumination. Bacteriorhodopsin and halorhodopsin were among the first opsins to be discovered (9). Respectively, they pumped protons out of cells in response to green light and pumped chloride into cells in response to orange light. By virtue of their mechanism, these opsins caused hyperpolarization of the cell membrane by making the cytoplasmic face of the membrane increasingly negative in charge. A key breakthrough occurred in 2003, when a recently discovered cation-dependent opsin was expressed in Human Embryonic Kidney (HEK) cells and shown to successfully depolarize the cells upon photostimulation. The opsin in question, Channelrhodopsin-2, would drive the establishment of the field of optogenetics.

Optogenetics: The Attempt

The first successful demonstration of incorporating exogenous rhodopsins into neurons was published by Boyden, *et al.* in a 2005 technical report in *Nature: Neuroscience* (10). Out of a selection of rhodopsins, the Boyden lab decided to focus on the expression and application of Channelrhodopsin-2 (ChR2) in neurons. This light-gated cation had a negligibly small latency speed, capable of allowing cation influx 50 μs after the application of blue light (450-490 nm). ChR2's fast kinetics and ability to depolarize the membrane potential thus made it a prime candidate for optogenetics (10).

After transfecting hippocampal neurons with vectors containing a ChR2-fused-fluorescent-protein (YFP), imaging revealed that ChR2 had successfully been expressed on the cell membrane. Physiologically, ChR2 requires the presence of all-trans retinal, which—upon illumination— photoisomerizes from trans to 13-cis in order to activate the channel (20). But stimulation of infected neurons by blue light without the addition of retinal showed strong inward currents during whole-cell patch-clamp recordings, suggesting that vertebrate tissue contained naturally generated all-trans retinal. A potential issue that ChR2 would become inactivated after long durations of stimulation proved to be insignificant, as function recovered after 5 seconds of inactivation. One problem with neural activity under steady stimulation by blue light was the deregulation of action potentials. The realization that short exposures of blue light reliably generated single action potentials led to the development of a new protocol focusing on the use of a pulsed-light strategy.

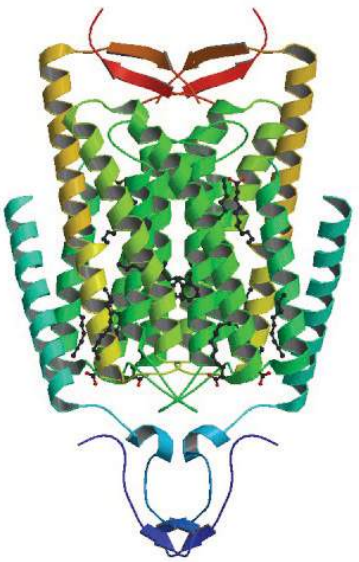

Image from the RCSB PDB (www.pdb.org) of PDB ID Channelrhodopsin. H.E. Kato, F. Zhang, O. Yizhar, C. Ramakrishnan, T. Nishizawa, K. Hirata, J. Ito, Y. Aita, T. Tsukazaki, S. Hayashi, P. Hegemann, A.D. Maturana, R. Ishitani, K. Deisseroth, O. Nureki, *Nature*, 482, 369-374, 2012 (accessed 13 Oct. 2012)

Figure 2: A model of channelrhodopsin.

Such a strategy meant that neural activity could be controlled at the level of single spike-generation. This meant that it was, in principle, possible to photostimulate ChR2+ neurons into mimicking natural neural activity. A Poisson-distributed series of light pulses was set up, successfully eliciting a train of spikes mimicking natural activity. To determine the appropriate exposure time for each light pulse, the Boyden lab titrated the light pulse duration until the neurons could reliably generate spikes. Quantification of spike reliability as a function of pulse-frequency showed that a pulse-series with a lower mean frequency showed greater likelihood of light-evoked spiking than a higher frequency pulse-series. The occasional failure of light-evoked spiking was mostly likely the result of channel inactivation during the pulse-series delivery. But what if multiple neurons were tested at the same time? A conceivable problem lies in the great heterogeneity in neurons: different neurons have marked differences in intrinsic properties, such as membrane capacitance and resistance. These differences may likely cause different neurons to spike differently under the same current-influx conditions. Yet, when comparing the spike-train patterns of

the seven ChR2+ neurons, it was evident that the neurons fired in similar ways, suggesting the possibility of generating a concerted spike train in a heterogeneous neural population. The experiment showed not only the capacity to generate and control spike trains, but also the relative ease of adjusting the photostimulation settings to fit the experimenter's purpose—exemplifying the convenience of a light-mediated technique.

To test the limits of ChR2-mediated spiking, neurons were photostimulated to generate spike trains at various frequencies. While spike latency remained consistent, spike probability was expectedly lower at higher frequencies. Although this imposes a restriction to the range of spike frequencies accessible by ChR2-mediated spiking, Boyden et. al. (2005) believes the physiologically relevant range of firing frequencies was within the limitations.

To test whether ChR2 could control synaptic transmission, ChR2 neurons were recorded with a voltage clamp at a typical neural resting potential. As expected, photostimulation led to reliable EPSCs and IPSCs in a frequency-dependent manner.

Given the applications of ChR2, the final test was whether ChR2+ neurons displayed any side effects, especially with their electrophysiological properties. Vector expression of ChR2 for over a week did not seem to affect membrane resistance or resting potential. Current injections induced similar membrane potential shifts in ChR2+ and ChR2- neurons. Prolonged depolarizing current injection also induced similar spiking patterns, suggesting that ChR2 expression does not influence intrinsic electrophysiological properties. Staining of live neurons with propidium iodide (membrane-impermeant DNA-binding dye) showed similar percentage of staining in ChR2+ and ChR2- neurons, suggesting ChR2 expression also does not impair cell health. The absence of noticeable side effects in ChR2+ neurons thus validated the use of ChR2 for studying neurons in a physiologically relevant manner.

While optogenetics has provided a gateway into the world of neural control, it left a curious problem. A salient limitation of optogenetics is its inconvenient dependency on a specific range within the electromagnetic spectrum. The original suggestion by Crick recommended the use of longer wavelengths (such as infrared) that would penetrate deeper into tissues. The rhodopsins currently in use, however, have optimal stimulation frequencies within the visible light range. This, unfortunately, meant that neurons embedded within thick layers of tissues cannot be easily controlled, due to the inability for visible light to penetrate deeply through our tissues. Even if a light source were invasively administered into the tissue, the visible light stimulus would quickly attenuate with distance. In hopes of resolving this issue, Huang, et al (2010) attempted a different approach, using heat-activated channels instead.

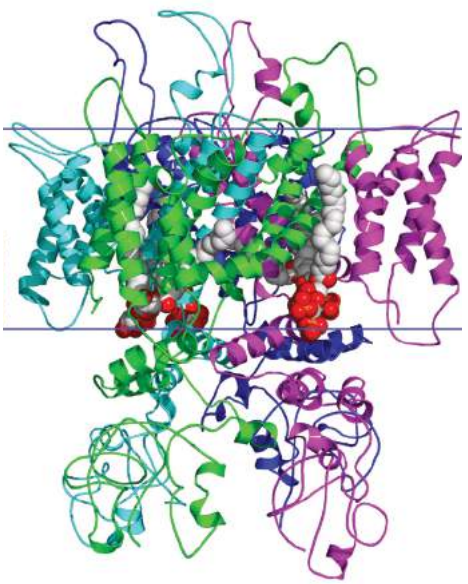

Image retrieved from http://upload.wikimedia.org/wikipedia/commons/0/0b/Trpv1_pip2_bilayer.png (accessed 13 Oct. 2012)

Figure 3: A model of TRPV1.

Heat-activated Channels: The Literature

Scientists have long been aware of the existence of heat-activated channels. Heat-activated ion channels are abundant on thermoreceptors – sensory cells that activate in a temperature-dependent manner (11).

The activation of such ion channels by direct heating of the cell culture, however, is practically infeasible. Heat-sensitive channels such as TRPV1 activate at temperatures above 42°C. Not only would the activation lack precise timing, the culture would also have to be greatly removed from physiological conditions (12). The approach to using these channels relied on the application of nanoparticles, instead.

Aside from light signals, magnetic signals were also considered to be a viable candidate for controlling neural activity. As with light, the application of magnetic fields only interacts weakly with biological molecules (13). This ensures that the application of the magnetic field would typically not interfere with the biological system. The trick then lies in locally translating the magnetic field into a different stimulus that can interact with the system.

One possible way to achieve this is to use nanoparticles that generate heat upon stimulation by coupling a magnetic field with radio frequency (RF) pulses – heat which can then be used to activate a heat-sensitive receptor (14). The question then, becomes whether such nanoparticles can be localized to the heat-sensitive ion channels and whether the concentration of nanoparticles required might inadvertently cause bulk heating of the entire culture.

Heat-activated Channels: The Attempt

In 2010, the Pralle lab at the University of Buffalo submitted a paper that demonstrated the successful use of magnetic fields to control neural activity (13). However, before this attempt, they checked the nanoparticles against bulk heating. A key issue to this feat was finding a means of differentiating the local temperature near the nanoparticles from the bulk solution temperature. A molecular approach to measuring temperature was necessary. Taking advantage of the temperature-dependent nature of most fluorophores' fluorescence intensity, they determined the reduction in fluorescence intensity (of DyLight549 and YFP) as a function of temperature increase (15). Then, by tagging DyLight549 to manganese ferrite ($MnFe_2O_3$, a nanoparticle) and dissolving YFP into solution, the fluorescent proteins could be used to measure the local and bulk temperature increase respectively. Using a literature-recommended concentration of $MnFe_2O_3$, it was possible to heat the nanoparticles at a significant rate without heating the bulk solution, suggesting that the use of $MnFe_2O_3$ in cells might not cause bulk heating of the culture.

The next challenge was to localize the nanoparticles either directly to TRPV1 (a heat-sensitive) channels or to the plasma membrane so that a high local density of nanoparticles is achieved for sufficient heating of the membrane surface to activate the TRPV1 channels. Making use of the high binding affinity of streptavidin to biotin (16), they engineered cells into

expressing the membrane protein marker AP-CFP-TM containing three key domains: a biotin acceptor site (AP), an extracellular fluorescent protein (CFP) for imaging, and a transmembrane domain (TM) for embedding the protein in the plasma membrane. After expression, AP-CFP-TM would then be enzymatically biotinylated in order to bind to the streptavidin-conjugated-nanoparticle. DyLight549 would again be conjugated to the nanoparticle to read the local temperature. After addition of the nanoparticle to the culture, imaging of DyLight549 showed that the nanoparticles selectively bound to the plasma membrane of AP-CFP-TM+ HEK 293 cells. Further expression of a Golgi-targeted GFP showed that nanoparticle heating was localized to the plasma membrane, rapidly dissipated with distance, and thus did not affect GFP intensity.

To test whether the application of RF magnetic field would indeed activate TRPV1 receptors, cytosolic calcium concentrations were measured in HEK cells. After a brief application of the RF magnetic field, calcium concentration dramatically increased 15-fold (from 100 nM to 1.6 μM). Since cells that were TRPV1+/nanoparticle- and TRPV1-/nanoparticle+ did not experience the same calcium influx, the data suggested that the calcium influx was the result of TRPV1 channels activity induced in the presence of heated nanoparticles. RF magnetic field-evoked calcium influx was comparable to that evoked by application of capsaicin (TRPV1 also activates in its presence), showing channel activation within seconds of signal application. The final test, then, was whether such an activation of TRPV1+ neurons could actually depolarize the neuron enough to reach the action potential threshold. Using a voltage-sensitive dye, membrane potential shifts were measured in $MnFe_2O_3$-labeled/TRPV+ hippocampal neurons. Upon application of RF magnetic field, the dye quickly induced membrane depolarization followed by action-potential-type depolarization, thus successfully demonstrating the neural activity control by means of a magnetic field.

Conclusions

The development of techniques to control neural activity has greatly influenced and will continue to influence the field of neuroscience. Seven years since the first published efforts of optogenetics, it has already been put to use in the basic sciences. Additional rhodopsins, such as halorhodopsins and archaerhodopsins, have also been applied for optogenetic studies, offering not only the multi-color activation of neurons but also its inactivation, e.g. halorhodopsin pumps chloride inward (17). Within medical science, optogenetics has also been applied to better resolve the mechanism by which deep brain stimulations alleviate the effects of Parkinson's (9, 18). Slowly, we might begin to see more uses for remote-controlled neurons as well. As it is, activation by RF magnetic fields involves many components, which causes a significant latency between field induction and neural activation. Furthermore, the exposure times needed to sufficiently heat TRPV1 are presently much longer than the pulse-durations necessary for ChR2 activation. This means that while such an approach can be used to alter mean neural activity, control of single spike activity (as in optogenetics) is yet out of reach. Remote-control, however, has been used more successfully in other areas of medical science, such as the induction of gene expression (19). But as technology continues to advance, we may see ever greater use of these tools in the field of neuroscience.

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References

1. W. H. McMenemey, "Santiago Ramon y Cajal," *Proc. R. Soc. Med.* **46**(3), 173-177 (1953).
2. F. Bretschneider, J. R. D. Weille, *Introduction to Electrophysiological Methods and Instrumentation* (Elsevier Ltd, ed. 1, 2006).
3. J. B. Reece, N. A. Campbell, *Biology* (Benjamin Cummings, Boston, MA, ed. 8, 2010).
4. D. Voet, J. G. Voet, Biochemistry. (Wiley & Sons, New York, NY ed. 4, 2010).
5. B. P. Bean, *The Action Potential in Mammalian Central Neurons*, *Nat. Rev. Neurosci.* **8**, 451-465 (2007).
6. Deisseroth, K. *Optogenetics*, Nature Methods, 8(1), 26-29. (2011).
7. F. Crick, F. R. S. Om, "The Impact of Molecular Biology on Neuroscience," *Phil. Trans. R. Soc. Lond.*, **354**, 2012-2025, (1999).
8. B. V. Zemmelman, G. A. Lee, M. Ng, G. Miesenbock, "Selective Photostimulation of Genetically ChARGed Neurons," *Neuron* **33**, 15-22. (2002).
9. E. Boyden, "A History of Optogenetics: The Development of Tools for Controlling Brain Circuits with Light," *F1000 Biol Reports* **3**, 11. (2011).
10. E. S. Boyden, F. Zhang, E. Bamberg, G. Nagel, K. Deisseroth, "Millisecond-Timescale, Genetically Targeted Optical Control of Neural Activity," *Nat. Neurosci.* **8**(9), 1263-1268. (2005).
11. M. J. Caterina *et al.* "The capsaicin receptor: a heat-activated ion channel in the pain pathway," *Nature* **389**, 816–824. (1997).
12. Life Technologies, Temperature (2012). Available at http://www.invitrogen.com/site/us/en/home/References/gibco-cell-culture-basics/cell-culture-environment/temperature.html (09 August 2012).
13. H. Huang, S. Delikanli, H. Zeng, D. Ferkey, A. Pralle, "Remote control of ion channels and neurons through magnetic-field heating of nanoparticles," *Nat. Nanotechnol.* **5**, 602-606. (2010).
14. S. Sun *et al.* "Monodisperse MFe_2O_4 (M = Fe, Co, Mn) nanoparticles. *J. Am. Chem. Soc.* **126**, 273–279 (2004).
15. A. Holmberg, A. Blomstergren, O. Nord, M. Lukacs, J. Lundeberg, M. Uhlén, "The biotin-streptavidin interaction can be reversibly broken using water at elevated temperatures," *Electrophoresis*, **26**(3), 501-510 (2005).
16. T. Karstens, K. Kobs, "Rhodamine B and Rhodamine 101 as reference substances for fluorescence quantum yield measurements." *J. Phys. Chem.* **84**, 1871–1872. (1980).
17. X. Han, E. S. Boyden, "Multiple-Color optical Activation, Silencing, and Desynchronization of Neural Activity, with Single-Spike Temporal Resolution," *PLoS One*, **2**(3), e299 (2007).
18. V. Gradinaru, M. Murtaza, K. Thompson, J. M. Henderson, K. Deisseroth, "Optical Deconstruction of Parkinsonian Neural Circuitry," *Science*, **17**, 354-359. (2009).
19. S. A. Stanley *et al.*, "Radio-wave heating of iron oxide nanoparticles can regulate plasma glucose in mice," *Science* **4**, 604-608. (2012).
20. P. Hegemann, W. Gartner, R. Uhl, "All-trans retinal constitutes the functional chromophore in *Chlamydomonas* rhodopsin," *Biophys. J.* **60**(6), 1477-1489. (1991).

The Development of the Internet

Understanding the History and Relevance of the World Wide Web

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Over the past 10 years, social networking has gradually assimilated into daily life. Yet, few question how the Internet, or digitization of our interactions came to be. By understanding this global network and its history, we can gain insight about how our society regards networking technology today and how its use may evolve in the near future.

History

The origins of the Internet can be traced to a series of memos written by J.C.R. Licklider, Professor of Electrical Engineering at MIT, in August of 1962 In these memos, Licklider discussed the concept of a globally interconnected set of computers that he termed the "Intergalactic Network" (4). His idea relied on a few crucial developments. One of the most important was the improvement of computational tasking. Prior to 1957, computers only worked on one task at a time. This limitation, called batch processing, was bypassed when the idea of time-sharing emerged. Time-sharing allows for a single computer to be operated by multiple users at once. This discovery established the groundwork for information communication. The origins of this method can be traced to the Defense Advanced Research Project Agency (DARPA) which was founded in 1958. One of DARPA's first projects was to plan a large-scale computer network to increase the rate of information exchange. This project would eventually become the ARPANET, whose development began in 1966 with the founding of the Information Processing Techniques Office (IPTO) head by Licklider. While there, Licklider assisted in the development of the time-sharing method. He also convinced many others, including Ivan Sutherland, Bob Taylor, and Lawrence Roberts, of the importance of an interconnected system. The major obstacle at the time in achieving this vision was deciding how to share information between computers. Two strategies were proposed: circuit switching and packet switching.

Image courtesy of Leonard Kleinrock. Retrieved from http://en.wikipedia.org/wiki/File:Leonard-Kleinrock-and-IMP1.png (accessed 3 October 2012)

Figure 1: Leonard Kleinrock in front of the first IMP.

Circuit Switching

Circuit switching is a method that establishes a connection between two computers via a continuous wire circuit. The system protocol provides for constant transfer of data that is protected from competing users (7). However, this technique is inefficient because it requires peak bandwidth at all times, meaning that high levels of computational power would be required to allow the information to flow at a continuously maximized rate. This issue was discovered in 1965 when Roberts connected two computers, the TX-2 at MIT and the Q-32 at Santa Monica, via a circuit switching system.

Packet Switching

Packet switching was proposed by Leonard Kleinrock in 1961, at the time a graduate student at MIT. This method serves as an alternative data transfer method to circuit switching. It groups all transmitted data, regardless of type, into blocks of information called packets (6). Each packet includes an address that is used to route itself to the correct location within a computer network. The main problem with packet switching is that packets are sent individually. As a result, they are sometimes delivered out of order. The major benefit of this technique, as opposed to circuit switching, is that it makes maximal use of available bandwidth for all communication and is thus highly efficient. Multiple users can simultaneously send information over the same network, keeping the rate of exchange high at all times.

ARPANET

By 1969, host-to-host communication was established via ARPANET with the connection of computers at Stanford and UCLA (2). Rather than communicating directly, mainframe computers used smaller computers called Interface Message

Processors (IMPs) to handle all the network activities. Thus, the mainframe computers were only in charge of the initialization of programs and retrieval of data files. For the first connection, the Network Work Group (NWG) developed the Network Control Protocol (NCP), which described the procedure for sending and interpreting messages between computers. Later, the more efficient Transmission Control Protocol (TCP) replaced the NCP. The advantage of the TCP was that it featured the additional requirement of a verification of file transfer, which decreased errors associated with packet loss and failure to reach the intended destination.

Internet

As Cold War tensions grew, fear of a nuclear attack led to concerns about the breakdown of communication networks. The original design of domestic communication networks relied on a central node that was potentially vulnerable to attack. As such, the development of decentralized network architecture became a primary objective of the U.S. government. While radio waves had been used to send messages in the past, scientists realized that these waves would not survive disruptions in the air space caused by a nuclear explosion. At first, radio frequency waves of longer wavelength, known as long waves, were seen as the solution to this problem. They are not as easily distorted by environmental inconsistencies. However, their short range rendered them ineffective. Rather, the solution was a distributed network utilizing several computers called nodes. When information was sent over the network, it passed through a series of nodes before arriving at its final destination. Thus, this system provided multiple paths of communication that could withstand the destruction of some of the nodes. It was

Image courtesy of Coolcaesar. Retrieved from http://en.wikipedia.org/wiki/File:First_Web_Server.jpg (accessed 3 October 2012)

Figure 2: The first web server of the World Wide Web.

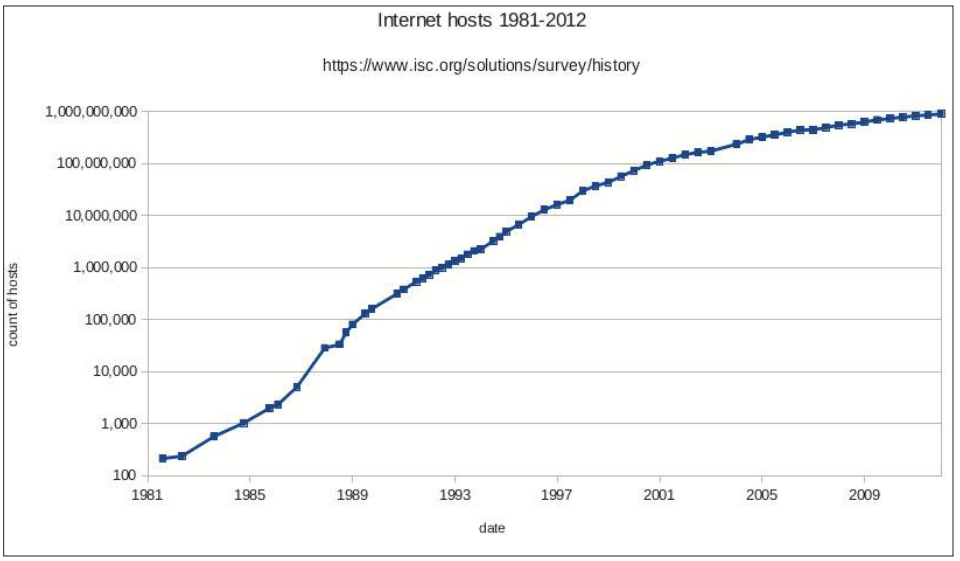

Image courtesy of Ke4roh. Retrieved from http://en.wikipedia.org/wiki/File:Internet_host_count_1988-2012_log_scale.png (accessed 3 October 2012)

Figure 3: Graph of Internet hosts from 8/1/1981 to 1/12012.

during this time that the term "Internet" came into use, as communication occured between multiple networks rather than from just one machine to another.

The setup of this web was such that, during communications, the computers between the sender and the receiver would not to interfere with the message, but simply serve as transfer nodes. The procedure, on a basic level, would allow a message to pass through all machines by making use of a layered channel. Nevertheless, as different networks arose, so too did discrepancies in protocol. As such, the International Organization for Standardization (ISO) designed the Open System Interconnection (OSI) model, which attempted to standardize networks and divide channels into separate layers. As more computers became connected, the TCP assimilated the preferences of the OSI model to produce the superior TCP-IP model, a standard that guaranteed compatibility between networks. In 1990, the last of the ARPANET hardware was removed, and the Internet was up and running.

How It All Works

As a simplified model, the Internet can be said to behave like a electrical wire with various conducting attachments. Connected to this main wire are more than a million special computers (servers) that communicate directly with each other (collectively called a network). Every server has a unique Internet Protocol (IP) address. Like a postal address, an IP address provides a means for packets of data to arrive at the correct destination. Because actual IP addresses are difficult to remember, they are instead given user-friendly names like www.amazon.com, www.facebook.com, or www.wikipedia.org, called Uniform Resource Locators (URLs). The computers that ordinary users connect with are called clients because they are connected indirectly to the Internet through an Internet Service Provider (ISP). A client accesses webpages by communicating through its ISP to a server, which, after receiving a request, sends the file information back to the computer; webpages are simply files on a server's hard drive.

In reality, everything connected to the Internet has an IP address: computers, servers, and all the equipment in between, such as routers. Routers are devices that direct packets around the Internet, helping them to reach their final destination. Each packet is wrapped in several layers, the first of which consists of the IP address of the computer. As a router passes a packet from client to server, it adds its own IP address to the packet. When the server sends information back, the layers of IP addresses are unwrapped until the information returns to your computer.

While the Internet has existed for a couple decades, many of its most influential applications have only recently been discovered. Online commerce, social media, and education have shown that the Internet has uses for businesses, individuals, and government.

Amazon

Founded in 1994, Amazon began as an online bookstore based out of the garage of founder Jeff Bezos (1). With the venture

Retrieved from http://en.wikipedia.org/wiki/File:Original-facebook.jpg (accessed 3 October 2012)

Figure 3: The original Facebook website. Facebook was launched less than a decade ago, in 2004.

capital of investors Nick Hanauer and Tom Alburg, Amazon entered the matinstream Internet. Amazon survived the burst of the dot-com-bubble of the 1990s, but it was not until Bezos added the option to write book reviews on the website that Amazon became the Internet titan it is today. By 1997, Amazon had generated more than $15 million in revenue and was open for public consumption. The website then commenced the movement toward its current business model when it expanded its merchandize to include the sale of CDs and movies. By 1998, electronics, video games, toys, and many other products had been added to the online store. This trend has continued to date, with millions of items ranging from clothes and beauty products to house supplies and electronics now available for purchase on Amazon. In 1999, Time Magazine named Bezos "Person of the Year," recognizing the company's extraordinary success. Today, Amazon stands as the largest online store in the world and is credited with popularizing online shopping as we know it (1).

Facebook

Facebook established a new medium for online social interactions. The company was founded in 2004 by Mark Zuckerberg and a few of his friends as undergraduates at Harvard (5). Originating as a means for cataloguing Harvard students through their pictures, Facebook's popularity and potential for expansion to other colleges were made quickly apparent. Later that year, the website was opened to the rest of the Ivy League and gradually to all universities across North America. Over the next eight years, Facebook would become a sensation, revolutionizing online social activity with more than 800 million active users (5).

Wikipedia

Wikipedia was originally created in 2001 to complement NuPedia, an earlier project by Jimmy Wales to produce an online, free-content encyclopedia that was edited only by experts (3). Wale's goal was that Wikipedia could supplement academic articles without the rigorous quality requirements known to delay academic publications. While this idea was initially met with some resistance, its popularity was quickly recognized. By 2003, the number of English Wikipedia articles surpassed 100,000. Today, as the world's sixth most popular website, Wikipedia features over 23 million articles in 284 languages and is estimated to receive more than 10 billion page views every month (3).

Conclusion

While the technical details surrounding the implementation of the Internet are complex, the overarching concepts are simple and elegant. Knowledge of these ideas grants us the ability to understand not only how the Internet came to be, but also the possibilities it holds for our future. As computing power improves, there is no doubt that the Internet will continue to play a fundamental role in business, daily life, and society.

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References

1. "Amazon.com, Inc. History." Funding Universe Available at http://www.fundinguniverse.com/company-histories/amazon-com-inc-history (14 October 2012).
2. M. Hauben, "History of ARPANET." History of ARPANET. Available at http://www.dei.isep.ipp.pt/~acc/docs/arpa.html (14 October 2012).
3. "History of Wikipedia." Wikipedia. Wikimedia Foundation, n.d. Available at http://en.wikipedia.org/wiki/History_of_Wikipedia (14 October 2012).
4. Pelkey, James. "Networking: Vision and Packet Switching 1959 - 1968 Intergalactic Vision to Arpanet." Entrepreneurial Capitalism and Innovation: A History of Computer Communications 1968-1988. Available at http://www.historyofcomputercommunications.info/Book/2/2.1-IntergalacticNetwork_1962-1964.html (14 October 2012).
5. S. Phillips, "A Brief History of Facebook," The Guardian (24 July 2007). Available at http://www.guardian.co.uk/technology/2007/jul/25/media.newmedia (14 October 2012).
6. Roberts, Lawrence G. "The Evolution of Packet Switching." Available at http://www.packet.cc/files/ev-packet-sw.html (14 October 2012).
7. Q. J. Zhang, F. Farahmand, "Circuit Switching" (2007). Available at http://web.ccsu.edu/technology/farahmand/ccsu/courses/cet543/resources/ch69_circuit_switcing.pdf> (14 October 2012).

The Musical Brain

How the Human Mind Understands Music

EVELYN MALDONADO

Cultures throughout history have each had various forms of musical expression. This consistancy reflects a natural human affinity to music. The scientific study of our relationship to music is rooted in analysis of the brain. An ever expanding area of modern research, the effects of music on our brains are being found to be increasingly complex. Music has the ability to activate many different areas of the brain. In particular, it is seen to have its strongest effects on those areas involved in internal imagery, auditory perception, and motor functions.

Musical Imagery

Music is widespread and prevalent in daily life, and influences even those who don't actively seek it. In his book, *Musicophilia*, Oliver Sacks, Professor of Neurology at New York University, states: "This barrage of music puts a certain strain on our exquisitely sensitive auditory systems, which cannot be overloaded without dire consequences." One of these consequences, he explains, is the "brainworm"—a repeating loop of music in the brain that can recur from a couple of minutes to a few days. Brainworms are generally 15 to 20 second long stretches of music. Sacks finds that these brainworms behave similarly to a tic or seizure because music enters a part of the brain that causes it to play repeatedly. He compares these brainworms to well-known examples of sensory overstimulation. One example would be the feeling people get of rocking back and forth after having been on a boat for a prolonged period. Sacks states that the human mind is attracted to repetition, and the brainworm is a manifestation of that affinity (1).

Musical imagery is the internal music we hear in our minds. Imagery can be the involuntary playing of brainworms to the conscious recall of melodies. A study by Kraemer et al. found that individuals imagining music were found to activate their auditory cortex. Subjects were played both familiar and unfamiliar songs with short gaps of two to five seconds while their brain activity was scanned using functional magnetic resonance. The silent gaps in songs familiar to the listener were found to activate the auditory association areas of the brain more than unfamiliar songs. When subjects listened to familiar songs with no lyrics, activity was also recorded in the primary auditory cortex. Even though the subjects had no instruction or warning of the pauses in music, they only reported hearing gaps in unfamiliar songs. This suggests that participants unconsciously filled the gaps in familiar songs (2).

The accuracy with which a musical segment is remembered is also a notable characteristic of musical imagery. This is quite different from visual memory, which is comparatively unreliable. Each individual builds his visual world around interpretations of the outside environment. As such, visual memory can be altered by the mind. However, the musical characteristics of a piece, including "its tempo, its rhythm, its melodic countours, even its timbre and pitch—tend to be preserved with remarkable accuracy" (1). According to Robert Zatorre, a Professor of Neurology at McGill University, "the phenomenology of this effect suggests that musical imagery

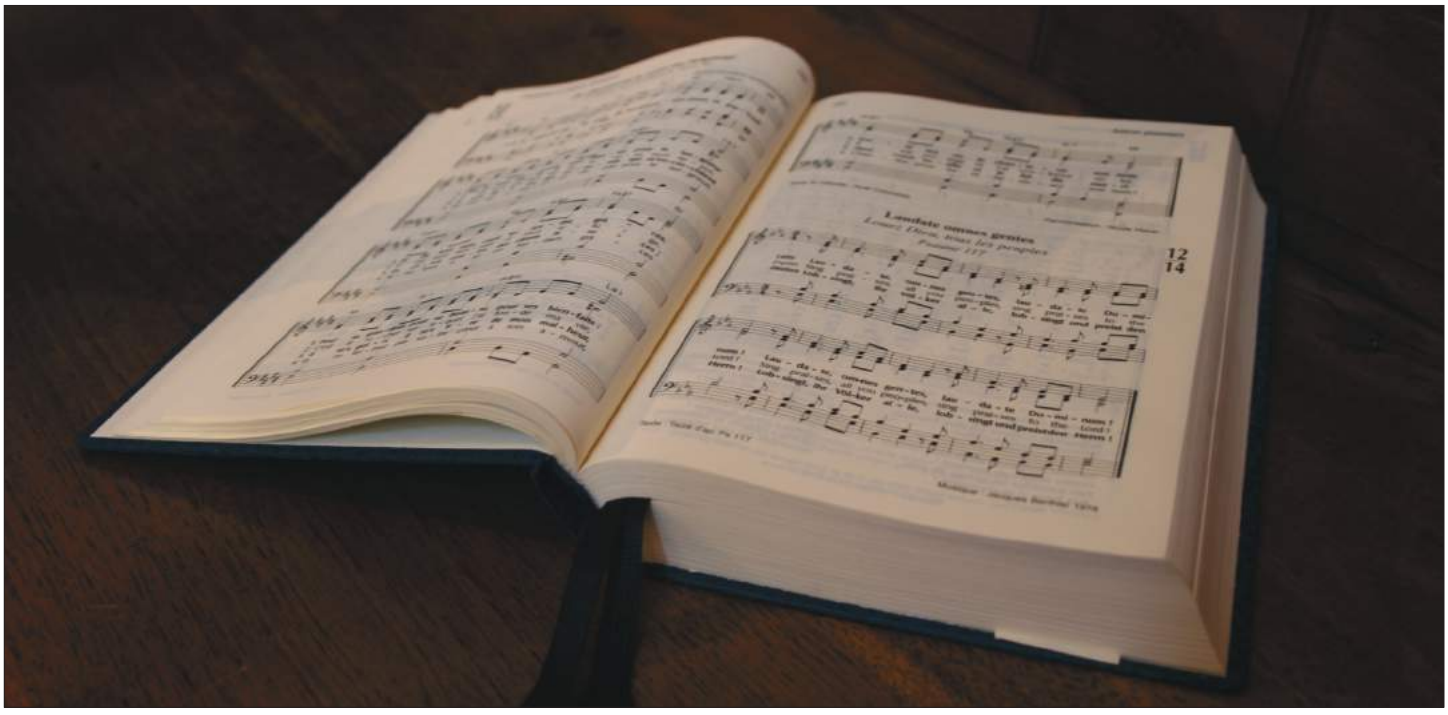

Image courtesy of Davide Restivo. Retrieved from http://www.flickr.com/photos/somemixedstuff/2897763743 (accessed 25 October 2012)

Figure 1: Studies show that musicians who are reading music show activity in the auditory cortex of their brains that is comparable to if they would if they were actually playing music.

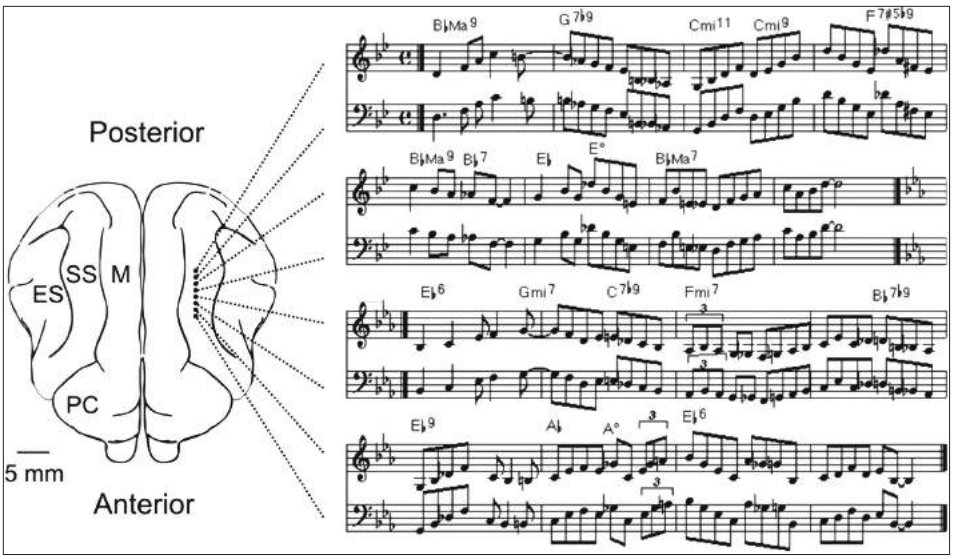

Image retrieved from http://dujs.dartmouth.edu/fall-2009/music-in-the-brain-the-mysterious-power-of-music (accessed 25 October 2012)

Figure 2: We do not possess a music "center" that processes all musical input. Our brains are programmed to comprehend and enjoy music from a variety of regions that vary from individual to individual.

retains many of the properties of real perception…but that it is not confusable with real hearing" (3). A specialist in musical effects on the brain, Zatorre studied this characteristic of musical imagery by assessing the speed of musical processing (4). Zatorre asked subjects to judge a pitch change in two syllables of a well-known song. Not only did the subjects show that they had an internal representation of pitch structure by responding correctly, but the time that elapsed before they responded was a near-linear function of the time between two syllables in the music played (4). This experiment suggests that musical imagery takes place in something close to real time.

The physiological connections musical imagery has to the brain is also notable (4). Zatorre examined this aspect of musical imagery by studying individuals with cortical excision in the superior temporal gyrus, an area in the temporal lobe that contains the auditory cortices. In patients with damage to the right cerebral hemisphere, both musical perception and imagery were affected and their performance on pitch judgment for both heard and imagined music was worse than the performances of those without damage to this area (4). However, patients with lesions on the left side were able to complete the tasks at a level comparable to that of the control group (4). By observing the dysfunctional pitch judgment in patients with damage to the right hemispheric superior temporal gyrus, Zatorre was able to connect that neural area with both musical imagery and perception.

Zatore built on these conclusions by conducting neuroimaging studies on functional subjects. Individuals were scanned while being asked to perform the same type of pitch judgment. Activity was observed in the superior temporal gyri on both sides of the brain as subjects listened to and imagined the tunes, suggesting that sensory areas in the brain might be responsible for musical imagery. In another neuroimaging experiment, listeners were asked to continue a familiar musical excerpt in their minds after hearing only the first few notes. In this study, activity was recorded in the superior temporal gyrus of the right hemisphere as the patient imagined the music. Since the music chosen for the experiment was instrumental and left out verbal associations, Zatorre concluded that mechanisms in the right-hemisphere involve melodic processing (3).

A Kinetic Melody

Of all mammals, close interaction between the motor and auditory systems in the brain is only seen in humans. Humans are able to anticipate and synchronize musical beats as well as to understand and internalize rhythmic patterns. Even when there is not a pattern present, such as in the sounds of a clock ticking at constant intervals, the brain can create its own pattern. The motor cortex and subcortical motor systems in the basal ganglia and cerebellum are not only activated when we move to music, but also through the acts of listening to, or imagining music. This connection between music and sensorimotor movement extends even to human rhythmic patterns of walking and dancing. According to Sacks, "keeping time, physically and mentally, depends on interactions between the auditory and the dorsal premotor cortex – and it is only in the human brain that a functional connection between the two cortical areas exists" (1).

Neuroimaging studies have been especially insightful in studying this connection (4). In one investigation, non-musicians were taught how to play an easy song on a keyboard. After learning the song, activity was found in both the auditory cortex and premotor areas of subjects when the piece was played (4). This was not the case when the subjects listened to a melody they had not learned (4). In other experiments, activity in the supplementary motor area (SMA) and premotor areas was reported in both non-musicians when they imagined hearing musical excerpts and musicians when they imagined performing a piece. This strongly suggests that musical imagery contains both motor and auditory elements (4). For example, trained musicians are able to induce motor imagery while listening to or imagining a piece they have rehearsed many times. There have also been findings of activity in the premotor cortices and SMA even when listeners have not rehearsed motor associations with a musical piece or set of rhythms. This suggests that these areas play a role in unconscious rhythm tracking. (4)

Music Therapy

Since music is able to recruit and connect numerous parts of the brain, music therapy has succeeded over many other conventional forms of therapy. In particular, they are found to work well in helping treat aphasia, Parkinsonism, and dementia (1). In the cases of many of Sacks' patients, individuals in the advanced stages of these disorders retained much of their ability to respond to music (1).

The localized speech area of the brain is the premotor zone in the brain's dominant frontal lobe. Damage to this area can cause aphasia. Though many patients with damage to the premotor zone can barely speak or struggle to form fluid sentences, some still retain the ability to sing the words of songs. Therefore, it is possible for some patients to become reacquainted with speech when it is inserted into music. The right hemisphere, which usually has only very basic speech capabilities, can be transformed by music to produce speech.

In Parkinson patients, the basal ganglia are damaged, thereby preventing initiation of movement, speech, or even thoughts. Parkinsonism is thus a movement disorder and patients consequently are unable to exercise full command over their body's movements. However, studies finds that many Parksinson patients who can ordinarily barely initiate actions on their own, are capable of dancing and singing with the aid of musical cues (1). This effect was observed again when patients were asked to walk with another person in a rhythmic tempo (1). When the other person stopped walking, the subject would lose the ability to continue walking. An important aspect of musical therapy is finding the proper kind of music that the patient will respond to. Sacks thus states that: "If music is present, its tempo and speed take precedence over the Parkinsonism, and allow Parkinson patients to return, while the music lasts, to their own rate of moving, that which was natural for them before their illness. Music resists all attempts at hurrying or slowing, and imposes its own tempo" (1). In fact, some patients were able to accomplish this solely through initiating musical imagery with an outward suggestion of a musical composition (1).

Even in patients with varying stages of dementia—a degenerative loss of affect memory, language, and critical thinking functions—responses and connections to music have been observed. Sacks remarks: "Musical perception, musical sensibility, musical emotion, and musical memory can survive long after other forms of memory have disappeared. Music of the right kind can serve to orient and anchor a patient when almost nothing else can" (1) The aim of musical therapy is to use old tunes, in hopes of evoking emotions, memories, and responses from the patient. Once dementia becomes more advanced, this form of musical memory may not be as successful, but the auditory-motor relationship of rhythm can still remain in the form of movement and dancing. If music therapy takes place in a group setting, the previously detached patients are able to bond with the therapist and members of the group through the synchronization of familiar music in communal singing and dancing, according to Sacks (1). Music thus provides a form of stimulation for dormant patients and helps them to step briefly outside their diseases (1).

Conclusion

The neural effects of music, familiar and unfamiliar, voluntary and involuntary, are universal in the human population. Regardless of musical ability, humans are united through similar neural responses to the playing, singing, and imagining of music. Music is an intrinsic part of our neural function and its recruitment of numerous parts of the brain makes its presence pervasive in our lives.

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References

1. O. Sacks, Musicophilia: Tales of Music and the Brain (Vintage Books, New York, NY, 2008).
2. D. J. M. Kraemer, C. N. Macrae, A. E. Green, W. M. Kelley, "Sound of silence activates auditory cortex," *Nature* **434**, 158 (2005).
3. R. J. Zatorre, Music and the Brain. *Ann. NY Acad. Sci.* **999**, 4-14 (2003).
4. R. J. Zatorre, J. L. Chen, V. B. Penhune, "When the brain plays music: auditory- motor interactions in music perception and production," *Nat. Rev. Neurosci.* **8**, 547-558 (2007).

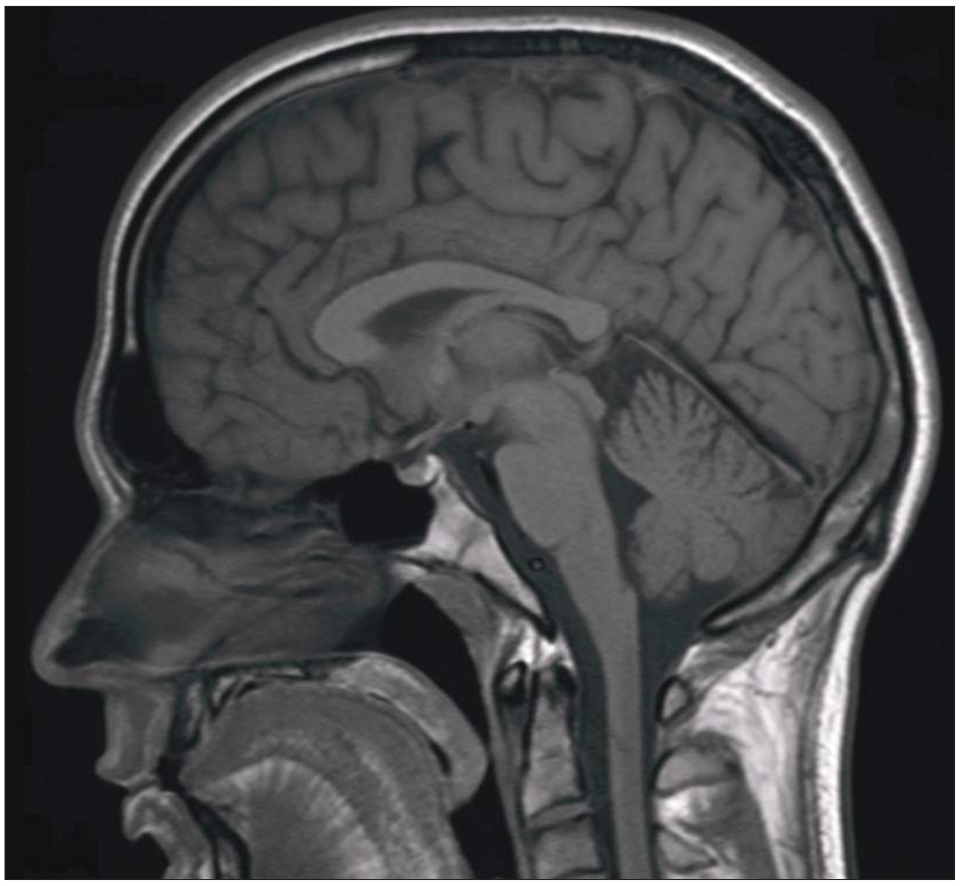

Image courtesy of Helmut Januschka. Retrieved from http://commons.wikimedia.org/wiki/File:Mrt_big.jpg (accessed 25 October 2012)

Figure 3: MRI scan of the side of the head.

The Placebo Effect

The Medicinal Power of Placebo Use

AMANDA ZIESELMAN

A placebo is an inert form of treatment that has a biological effect on the body. The placebo effect has been shown to improve symptoms in a way similar to active medication. Placebos can be used as therapeutic procedures to treat individual patients but are mainly used today as controls in clinical research and trials (1). Benjamin Franklin carried out the first trials utilizing placebos in 1784, under the direction of King Louis XVI (2). However, their use did not become commonplace in research until World War II when Lieutenant Colonel Henry Beecher used them to study how emotions affect healing (2). The patient's perceived medical improvement is where placebos are shown to be truly useful. The placebo itself, being chemically inert, does not have an intrinsic value to a patient. It is the extrinsic circumstances surrounding the placebo, such as trust and care between physicians and their patients that give it a social and physical value resulting in the placebo effect. Thus, placebos hold the ability to transform our biomedical culture from focusing solely on developing impersonal technology and miracle drugs to also developing stronger doctor-patient relationships and a greater emphasis on the individual.

It is not the medical properties of a placebo—be it in the form of a pill, injection, or sham surgery—that directly affect the patient, but rather the power of suggestion and the meaning surrounding it. The outside influence, that is, the ideas and notions that patients have about a treatment, form the mechanisms of the placebo effect (1). These mechanisms are not just subjective, but also biological. Recent neuroimaging technology has shown that the brain releases neurotransmitters, which carry out the healing process, even when a patient has received a placebo (1). This shows that a patient's knowledge, or presumed knowledge, of a procedure plays a large role in the efficacy of the treatment. Another crucial element to the placebo effect is the empathy of the doctor involved (3). Patients desire a more personal relationship with doctors and do not want to be left entirely to their own devices, even when it seems no medical treatment will be effective. Thus, knowing the patient beyond a medical sense contributes greatly to the meaningfulness and the efficacy of the response (4). The healing process is not solely about the medicine; it is also about the symbolism and the ritual that accompany treatment (1). Different societies across the globe have accepted various symbols, including seemingly bizarre methods of treatments such as undressing in front of strangers and swallowing non-food items, as effective medical treatments. When rituals are filled with meaning they can serve as placebos (4).

Research on Placebos

Various scientists have conducted studies on placebos, the results of which emphasize the importance of *meaning* in medicine. Fabrizio Benedetti of the University of Turin Medical School was one of the first scientists to carry out what is known as an "open-hidden" study to show the direct benefit of a doctor's presence (5). His study showed that patients who unknowingly received a drug demonstrated less relief than patients who received the same drug after a physician had told them it would decrease symptoms (5). A study run by Ted Kaptchuk, director of the Program in Placebo Studies & the Therapeutic Encounter at Beth Israel Deaconess Medical Center in Boston, took this result one step further (5). In his study of the placebo effect on Irritable Bowel Syndrome (IBS), he separated IBS patients into three groups (5). The first was the control group; these patients were placed on a waiting list and received no treatment (5). The second

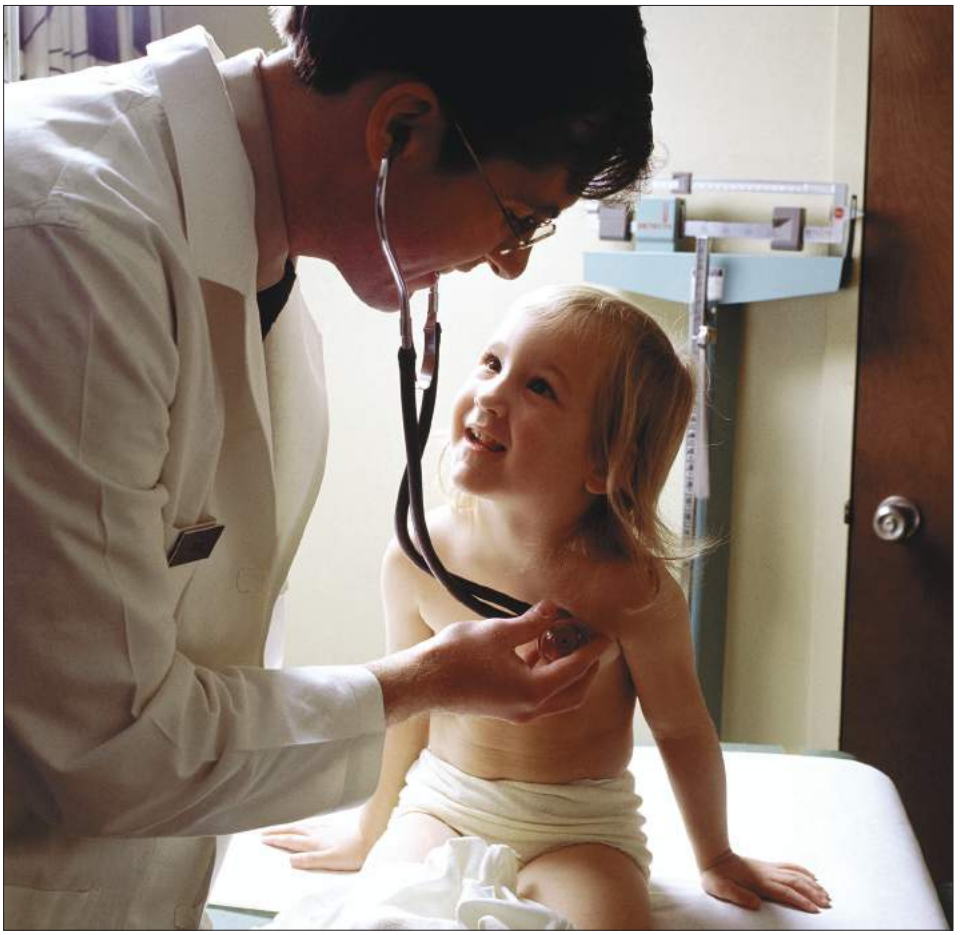

Figure 1: A doctor personally examines a young patient. Studies show that doctors who show a personal interest in their patients see greater improvement in their patients than doctors who don't.

group was seen by empathetic doctors but given fake acupuncture (5). The third group was seen by formal, business-like doctors and also treated with sham acupuncture (5). All three groups were reevaluated after three weeks. 28 percent of the first group, 62 percent of the second group, and 44 percent of the third group reported improvements in their pain symptoms (5). As Kaptchuk concluded, the study demonstrates that "connecting with the patient, rapport and empathy […] that few extra minutes is not just icing on the cake. It has biology" (5). Even though no group actually received therapy known to heal, the patients who were tended to by compassionate staff showed improvements analogous to those of patients receiving common active IBS drugs. These studies exhibit how instituting placebos in medical practice can directly reinforce the importance of the doctor-patient relationship in our society.

Modern technology has provided new opportunities for studying the placebo effect, which may further the acceptance of placebo use in society. A placebo is no longer restricted to the form of a simple pill or injection. Now, it may even be seen in the form of surgery. Knee-surgeon Bruce Moseley, who serves as the team doctor of the Houston Rockets, has used placebo arthroscopic knee surgery with great success (3). The knees of patients who received the placebo surgery healed at the same rate as the knees of those who underwent actual surgery. The placebo patients continued to improve even after they were told the surgery was a sham (3). This underscores the idea that doctor credibility and trust play key roles in the placebo effect (3). Additionally, due to developments in neuroimaging technology, clinical trials are now able to track the release of chemicals by the brain following placebo intake. In one such case, the brains of patients with Parkinson's disease receiving a placebo drug were observed by PET scans to release an amount of dopamine comparable to brains of patients receiving therapeutic doses of active drugs, such as levodopa (4). In general, Kaptchuk and other researchers have found evidence that much of the placebo effect is mental, as larger pills have greater efficacy than smaller ones, two pills more than one, and brand-names more than generics (2). Furthermore, injections work better than capsules, which work better than pills, and colored pills are more effective than white pills (2). All in all, these studies display that conditioning, expectations, and learned behaviors all influence the efficacy of treatment.

Opposition to Placebos

Despite the effectiveness of placebos displayed in these studies, many remain opposed to their usage in medicine, largely on the basis of ethical issues. Robert Temple, director of the Office of Medical Policy of FDA's Center for Drug Evaluation, stated that the FDA will not approve the use of placebos simply because they are not drugs (2). Many major drug companies share his view; however, they also are likely to have an underlying motive, as placebos would create profit obstacles (5). Another objection to placebos is the fear of deceiving and misleading patients (3). Placebos are often seen as a form of fraud, for in order to prescribe a placebo a patient cannot know that they are receiving an inert treatment (5). Professionals are afraid that the use of placebos may be seen as skimping on care, but, in a sense, it is just the opposite (5). Prescribing a placebo requires a doctor to truly desire to help the patient even if there is nothing that modern medicine can offer. Nevertheless, some people, such as philosopher Sissela Bok, argue that the deception, no matter what the reason, is deeply unethical. Bok declares, "to permit a widespread practice of deception […] is to set the stage for abuses and growing mistrust" (1). Those who share this view feel that the mainstream use of placebos will jeopardize the current medical system and doctor-patient relationship, while, in actuality, placebos are more likely to enhance it.

Critics have suggested that placebos may raise problems regarding safety and regulation; however, with a proper system of regulation, these issues would no longer be of concern. One fear regarding placebos is that insurance companies will manipulate their use, as coverage of placebos would be far cheaper than coverage of active medication (5). But if government regulations were instituted to prohibit agencies from favoring placebos over drugs, this would cease to be a valid argument. In addition, an important argument against placebos is that they are not always successful. However, drugs are approved even without one hundred percent efficacy and with potentially severe side effects, whereas placebos never bring the risk of any side effects. Placebos have become well accepted in clinical research, and all effects of drugs in these trials must surpass that of a placebo to be approved by the FDA, meaning that the placebo effect can be as great as or higher than the effects of active drugs being tested. In these situations, placebos should be allowed as a form of treatment. If the FDA approves placebos, the public will have even greater faith in the placebo effect, possibly leading to better symptom relief. The benefits of placebo use would far outweigh any perceived harms.

The Implementation of Placebos

Placebos have been shown to activate quantifiable changes in neurotransmitters, immune regulators, and hormones (4). Thus, even if the effect is "all in your head," that mentality leads to a measurable biological result (2). Relief of symptoms is not just subjectively felt, it can be monitored by the release of chemicals from the brain, and such a reaction is shown to occur even when a patient is treated with a placebo (5). The incessant medicalization our society has come to accept as the norm is not the sole path to medical "progress."

Placebos show that the brain can learn through conditioning to heal with significantly less medication than is currently seen to be necessary (2). The placebo effect has enormous implications for the medical field in that it illustrates how medicalization may be the wrong aspect of healing to focus on. As displayed by placebo studies, the level of empathy in medical care has a great influence on the therapeutic process. Reevaluating and reaffirming the doctor-patient relationship may do more for society than a constant search for miracle drugs (5). Ted Kaptchuk, the director of the Harvard Program in Placebo Studies, and Wayne Jonas, the president of the Samueli Institute, a non-profit medical research organization, concur that placebo research has demonstrated the importance of considering "both the science and the art of medicine, to think about disease as illnesses, and not to rely solely on short-term, high-tech solutions" (2). Changing the social medical mindset to concentrate more on such ideas will allow our medical system to focus more on the individual and less on technology. This shift will lead to the transformation of American medicine.

Unfortunately, a major ethical issue still surrounding placebo use is that of informed consent. It is difficult to obtain

Figure 2: Doctor injects test subject with placebo as part of the Tuskegee Syphilis Study.

consent from patients for placebos without revealing the nature of the placebo (1). Scientists and physicians have long struggled with this dilemma, but there are now standards of ethics put into place in order to protect patients against potential abuses. It is now necessary for experiments conducted using public funding to be approved by ethics committees at the area of research (1). These committees ensure that safety of patients remains the highest priority in any clinical study.

In order to institute placebo use into the medical mainstream, the ethical debate must be solved. This debate focuses mainly around the issue of consent and how to obtain patient permission to treat with a placebo without ruining the placebo effect. One recently introduced option is alternating between medicine and placebo in treatment (5). This way, fewer drugs are used, and the patient can know and consent to being given a placebo without jeopardizing treatment, as the patient is not informed of when he is being given medicine or a placebo. In a clinical study done in support of this idea, patients who alternated between applying a topical pain cream and a placebo cream experienced the same level of relief as patients who received up to four times more of the active drug (5). The effect is due to classical conditioning and the way the brain can learn to associate a placebo with relief and send healing signals even when the treatment is inert (5). Another way to handle the issue of consent is to have patients sign an official form. For instance, pediatricians could distribute these forms to the guardians of minors and once the patients become adults, primary care physicians could redistribute consent forms. The forms would allow for a blanket request for or denial of the use of placebo treatment, should it ever be deemed helpful for a patient. A patient may change his or her decision at any time, but the form would be required at every doctor's office. The institution of this form would allow placebo use to become a regular and accepted part of medical care.

Placebos should not face great opposition in becoming a common practice. While critics denounce them as mere sugar pills, the general public would embrace their use. This is due to the fact that society has begun to view placebos as based off of the "entire ritual of treatment, the complete interaction between doctor and patient" (2). This outlook derives from recently discovered biological mechanisms of the placebo effect. Because the public can now see that the placebo effect is real, there is no longer a fear of deception. Without this fear of deception, there is less public wariness about the undermining of the doctor-patient relationship (3). There are multiple documented examples of patients requesting placebos, from a son begging for a placebo as a last resort to help his cancer-stricken father to the more famous case of journalist Norman Cousins (3). Cousins was diagnosed with ankylosing spondylitis and given only a one out of five hundred chance of survival (3). However, he decided to take matters into his own hands, and, with the support of his doctor, delved into a regimen of positive thinking and laughter (3). Cousins made a full recovery (3). These examples display the patient and caregivers' desire to utilize the placebo effect and thus support the idea of introducing placebo use into primary medical care.

Conclusion

Establishing placebo use in American medicine is in the best interest of multiple parties. Patients will benefit because placebo treatment will decrease the cost of medical care and increase the personal component of the doctor-patient relationship. Doctors will benefit through an increase in patient trust and an ability to conserve resources. Ultimately, society as a whole will benefit from a decrease in government-related medical costs and taxes and, most importantly, a renewed focus on the individual in healthcare.

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References

1. D. Moerman, Meaning, medicine and the 'placebo effect.' Cambridge University Press, New York, NY. (2002).
2. M. Specter, "The power of nothing: Could studying the placebo effect change the way we think about medicine?" *The New Yorker*, **87**, 30-36 (December 2011).
3. A. Harrington, *The Cure Within: A History of Mind-Body Medicine.* (W.W. Norton & Company Inc., New York, NY, 2008).
4. S. Pohlman, N. J. Cibulka, J. L. Palmer, R. A. Lorenz, L. Smithbattle, "The placebo puzzle: examining the discordant space between biomedical science and illness/healing," *Nurs. Inq.* (2012). Available at http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1800.2012.00592.x/full (October 15, 2012).
5. R. Tuhus-Dubrow, The magic cure. The Boston Globe. (May 2010). Available at http://www.boston.com/bostonglobe/ideas/articles/2010/05/09/the_magic_cure/ (October 15, 2012).

Pop Science

Science Fiction to Science Fact: A Look at Sci-Fi's Favorite Innovations

SCOTT GLADSTONE

Science fiction has captivated the minds of young readers for generations, inspiring the curious to dream of time travel, cloaking machines, tractor beams, and any technological advancement imaginable. Avid fans of science fiction share a collective desire to live in a world with these technologies. Some have even used science fiction as a steppingstone to a career in developing and investigating their childhood pastimes, determining the feasibility of Asimov's and Verne's ideas. While most technologies of science fiction remain decades or centuries away, these fantasies contain real scientific concepts. Some are even closer to becoming reality than most would believe.

Time Travel

TARDIS: Time And Relative Dimension in Space. Any fan of the popular British series *Doctor Who* can tell you TARDIS is the name of the iconic, 1960's police-box spaceship that the Doctor and his companions use to travel around the universe . The machine is able to bend space and time, granting the travelers access to anywhere and any point in history. While a device with that type of potential is not yet within reach, no individual needs a time machine to experience time travel (1).

At the most basic level, every living being is a traveler of time. We all spend our lives progressing in four dimensions: the well-known length, width, and depth dimensions of space and the more enigmatic fourth dimension of time. Space cannot exist without time and vice-versa; each dimension serves as a measureable check on the others, collectively forming the basis of the space-time continuum (2). Thus, each individual travels through space differently and takes a unique path through time. This is the most basic explanation of the relativity of time principle and helps to clarify why some things appear to progress faster than others.

One of the most cited examples of this time-relativity phenomenon is the observation that global positioning satellites appear to gain a third of a billionth of a second every day (1). With the Earth as a reference point, time seems to move faster in orbit due to the increased distance between the satellite and the center of mass of the Earth. The planet's mass applies a regressive gravitational force on space and, due the interconnection of space and time, also applies the same force on time (3). This effect is known as gravitational time dilation (3). Time relativity and gravitational time dilation apply most clearly in modeling hypothetical travel around a black hole. A black hole is a massive, infinitely dense point where gravity pulls so strongly that not even light can escape. A small object with the mass of four million suns is a good analogy for a black hole (4). Theoretically, if orbit around a black hole were possible, time would be experienced at half of Earth's normal rate. A five-year journey around the black hole Sagittarius A would seem like a decade to those on Earth (1).

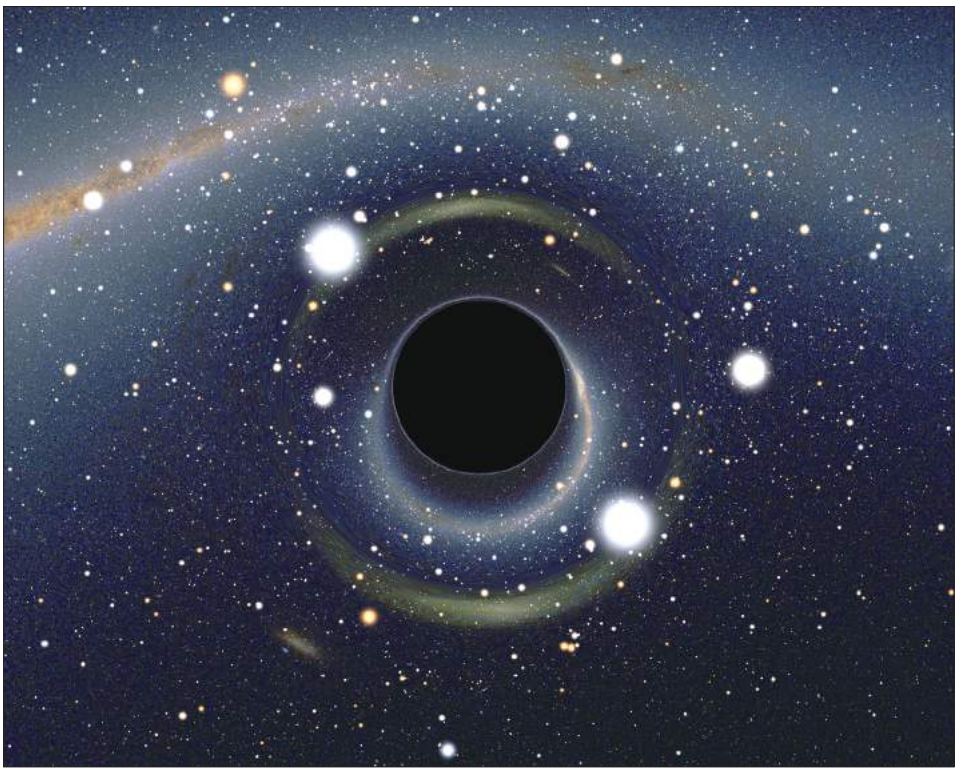

Image courtesy of Alain Riazuelo. Retrieved http://commons.wikimedia.org/wiki/File:BH_LMC.png (accessed 25 October 2012)

Figure 1: Gravitational distortions caused by a black hole in front of the Large Magellanic cloud. This phenomenon reflects the interconnected nature of space and time.

While we can consider the possibilities of faster temporal progression, the more interesting aspect of time travel is not to the future, but to the past. Many physicists hold the belief that time is a linear chain of cause and effect dominated by the law of causality: every action causes a specific response and reaction. Scientists cite this law as the reason that time travel is impossible. For example, it would be difficult to imagine a reality in which an individual could die of a gunshot wound before being shot (1). Yet, if this causality theory is disregarded, room can be made for theoretical ideas such as an Einstein-Rosen bridge, more commonly known as a wormhole. A wormhole is a "tube" that connects two regions of space-time and is believed to be formed by the attractive masses of two black holes (5). The idea is that if someone fell into one side of a wormhole, he or she would exit in a different part of space-time.

Assuming that the time traveler's body resisted being torn apart and the immense energy needed to make this travel was overcome, there are several paradoxes that still exist (1). Consider the following situation: a man travels back in time today

with the mission of killing his grandfather, thus preventing him from ever being born. The commonly accepted outcome of this act is that, regardless of what the man tries, he will not be able to kill his grandfather; the universe will "compensate" for his temporal displacement. Perhaps the gun the man uses will not fire, or the bullet will pass through his grandfather's body, or the laws of physics will break down to prevent the act from occurring (5). Thus, the man has found himself at the zenith of a temporal paradox: the governing laws of the universe cease to exist in order to prevent the collapse of space-time. Another commonly cited paradox is the time loop: a woman travels back in time today, arrives yesterday, and attempt to proceed through the rest of her life. Will she ever be able to avoid getting into her time machine and traveling back to yesterday? The answer, as of yet, remains unknown (6). For now, time travel is trapped to the imagination, to be accessed or discovered impossible in the years to come.

Tractor Beams

A tractor beam is a device capable of moving objects from a distance without any direct physical interaction. While the ability to conveniently pick up, hold, and move a macroscopic object at a distance is still constrained to science fiction, this technology is no longer entirely fantasy. A research group at MIT led by Matthew Lang and David Appleyard has invented a device known as optical tweezers, which have the capacity to perform "tractor beam-like" functions to individual cells on the surface of a microchip (7). The idea behind the device is that a highly focused laser beam can provide a force, on the order of piconewtons, to physically hold and move microscopic objects (8). The researchers tested this theory on silicon chips, overcoming the challenge of their transparency by only using infrared light. Aside from working on microchips, the group is also applying this technology to biology, physics, and chemistry, testing experiments such as placing single neuron cells on sensors to read electrical outputs and influencing the motion of E. coli cells in vitro.

NASA has recently taken an interest in this technology, investing $100,000 to examine three laser-based approaches to manipulating objects from a distance. The main purpose of the research is to investigate new means of gathering samples for analysis in future space-rover missions; the development of this technology would allow NASA to "enhance science goals and reduce mission risk," according to NASA scientist Paul Stysley (9). Along with MIT's optical tweezers, research in this field also includes study of solenoid beams and Bessel beams. Unlike the optical tweezers that require an atmosphere in order to trap objects in a laser beam, these other devices use laser beams with spiral- and cone-shaped intensity beams to capture objects. Both the solenoid and the Bessel beams have been successfully tested in the laboratory and may be produced on a larger scale in the future (9).

Temporal Cloaking

The idea of hiding an object is nothing new, yet it is a concept that has intrigued the mind for generations. Not only does this technology exist, but it also presents itself on a far wider scale than initially imaginable: researchers have also found a way to hide events in time.

Researchers at Cornell University led by applied physics professor Alexander Gaeta have demonstrated the invention of a "temporal cloak." According to Gaeta, "the trick is to create a gap in the beam of light, have the hidden event occur as the gap goes by, and then stitch the beam back together," (10). The cloak works via what Gaeta and his colleagues call a time lens, which manipulates and focuses signals in time, analogous to the way a glass lens focuses light in space. This technique, called "four-wave mixing," uses two beams of light, a signal, and a pump that are sent together through an optical fiber (10). More simply, the scientists speed up and slow down different parts of a light beam to create a short space in which a hidden event can occur.

Currently, this technology is capable of hiding an event for 15 picoseconds, but the group hopes to increase the time up to 10 nanoseconds in the near future. While the researchers joke that the device is not quite ready to conceal "illicit activities," Gaeta notes that the technique has applications in fiber-optic data transmission and data processing. He hypothesizes, "it might allow inserting an emergency signal without interrupting the main data stream, or multitasking operations in a photonic computer where light beams on a chip replace wires," (10, 11). Gaeta says the experiment was inspired by a theoretical proposal for a space-time cloak, or "history editor," published by Martin McCall, professor of physics at the Imperial College of London.

Conclusion

It is thought-provoking and exhilarating that many technologies seen only in science fiction are becoming realities. While time travel still may be a far-off fantasy, the possibility of one day wielding a personal tractor beam or concealing one's activities beneath a temporal cloak may be close at hand. In order to make these technologies a reality, it will take diligence, dedication, ingenuity, and a small, science fiction-based spark of inspiration.

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References

1. K. Bonsor, R. Lamb, How Time Travel Works (2000). HowStuffWorks. Available at http://science.howstuffworks.com/science-vs-myth/everyday-myths/time-travel.htm (August 2012).
2. "Space-time." (2012) Encyclopædia Britannica. Encyclopædia Britannica Online Academic Edition. Available at http://www.britannica.com/EBchecked/topic/557482/space-time (September 2012).
3. "Time Dilation" (2012). The Big View. Available at http://www.thebigview.com/spacetime/spacetime.html (September 2012).
4. H.R. Smith, Black Holes (2012). NASA Educational Technology Services. Available at http://www.nasa.gov/audience/forstudents/k-4/stories/what-is-a-black-hole-k4.html (September 2012).
5. "The Basics of Relativity" (2012). Physics of Time Travel. Available at http://courses.ma.org/sciences/lanik/time_travel/index.html (July 2012).
6. D. Lewis, The Paradoxes of Time Travel. America Philosophical Quarterly.13:2, 145-152 (1976).
7. D. Chandler, A light touch: Researchers move cells on a chip with laser light. MIT Tech Talk.52:8, 1-2 (2007).
8. D. Appleyard, M. Lang, Active particle control through silicon using conventional optical trapping techniques. Lab on a Chip.7, 1837-1840 (2007).
9. "NASA examines 'tractor beams' for sample gathering" (2011). BBC News. Available at http://www.bbc.co.uk/news/science-environment-15535115 (September 2012).
10. B. Steele, 'Time cloak" makes events vanish (2012). Futurity. Available at http://www.futurity.org/top-stories/'time-cloak'-makes-event-vanish/ (September 2012).
11. R. Waugh, Off the clock: scientists create cloaking device that 'hides' whole events – making time itself disappear (2012). Available at http://www.dailymail.co.uk/sciencetech/article-2082266/First-demonstration-time-cloaking-Scientists-create-device-hide-events.html (September 2012).

Technology in Sports Equipment

Understanding the Influence of Technology on Athletic Performance

SUYASH BULCHANDANI

Image courtesy of Frank Steele. Retrieved from http://en.wikipedia.org/wiki/File:Dave_Zabriskie_-_USA_Pro_Time_Trial.jpg (accessed 25 October 2012)

Figure 1: Professional cyclist Dave Zabriskie rides a racing bicycle during a time trial. The solid rear wheel reduces the number of air current eddies which slow cyclists at high speeds.

Through better nutrition and training, the athletes of today are becoming faster and stronger. Old records are constantly being broken, and new ones set. While the vast majority of these achievements are likely due to the athelete themselves, improvements in sports technology have also played a notable role (1). New sports gear technologies have especially been relevant to the sports of rowing, cycling, swimming and tennis, giving rise not only to new records, but also ways in which the sport is played.

Cycling

At top speed, nintey percent of an elite cyclist's energy is used to counter air-resistance (2). By comparison, 3 to 7 percent of a runner's energy is spent overcoming air-resistance (3). Cycling behind a competitor or teammate, or drafting, can reduce drag on a cyclist by up to 38 percent (3). However, since most cycling teams already practice this technique, cyclists today are searching for new ways to reduce air-resistance and differentiate themselves from their competitors.

A rough formula used to calculate the drag of a cyclist is 0.5qCA, q being the air density, C being the drag coefficient, and A being the projected cross-sectional area of the front of the bike and rider. The cross-sectional area is the variable cycling teams can best modify and reduce, and has the been focus of recent technological improvements. Using wind tunnels and computer models, engineers have found that something as simple as attaching a water bottle on the lower part of the bicycle frame rather than the upper part, can have a major impact on reducing drag (2).

Engineers have also improved handlebars, primarily by smoothing over the edges. In 1992, the standard racing handlebars of the time contributed to 10% of the drag created by the bicycle (2). Over the years, engineers have been able to dramatically reduce the drag created by the handlebars. For example, aerobars (handlebars that are low and forward that a cyclist rests his elbows on) have been shown to reduce the time taken to race across 15 kilometers in a time trial by 60 seconds (2). The handlebars of a bicycle are the first part of the bicycle to cut through the air, so minimizing turbulence is essential (2). Although smoothing over the edges barely reduces the projected cross-sectional area, it does prevent recirculating currents and eddies from forming in front of the cyclist's body. This helps the cyclist better cut through the air (2).

The wheels of a bicycle also have a large effect on the airflow around a bike (2). Racing bicycles have thinner tires to reduce the cross-sectional area of the front of the bicycle. More significant improvements have come from changing the spokes in wheels (13, 14). When a wheel spins at high speed, the spokes rapidly cut through the air, and the drag incurred slows down the wheel (2). Additionally, a large number of spokes cutting through the air disturbs the air current flowing around the bike, creating eddies which reduce the overall aerodynamics of the bicycle (2).

A simple solution to this problem is to remove the spokes entirely, and make the wheel a solid disk (2). While this increases the weight of the wheel, new lightweight materials mean that the positive impact of removing spokes far outweighs the detriment on performance due to additional weight (2). Solid disk wheels are used on all bicycles during indoor racing events. However, such wheel are not used outdoors (2). In the presence of a cross wind, solid wheels act like sails, throwing the rider off course. As a result, 3-spoked wheels that allow air to pass through them are favored for outdoor races (2). These provide reduction in drag, while still preventing cross-winds from being a problem.

Bicycles are approaching the limit of how thin they can be. Over the last decade engineers have shifted their focus from reducing the projected cross-sectional area to ensuring that air flows smoothly around the cyclist (2). The most advanced helmets aim to smoothen out the area between the cyclist's head and upper back. These helmets protrude from behind the cyclist's head covering the cyclist's neck, and thus eliminating the dip between head and upper back. This ensures that air turbulence

is minimized and eddies and recirculating currents are not formed behind the cyclist's head (5).

Rowing

Elite rowers face a similar dilemma as cyclists. They have to contend with drag from water, which creates 12 times the resistance of air (6). Manufacturers of top-end racing hulls, or shells, claim that the difference between shells can be the difference between first and second place (7).

Shell manufacturers are constantly looking for the perfect combination of high rigidity, balance, low surface area, and smoothness. Unfortunately, not all of these attributes can be achieved simultaneously. For example, the surface of the shell that comes into contact with the water, known as the wetted area, causes 80 percent of the drag (8). However, reducing the wetted area leads to a trade-off in stability, and a smoother material may be less rigid (8). A rigid hull is important, because the more a hull bends and torques, the less efficiently power is transferred from the rower to the water (9).

Much of the technology that has gone into reducing the friction between the shell and the water flowing past it comes from racing yachts, which often get their technology from the aerospace industry (10). An example of this is the riblet. Riblets are v-shaped grooves that run along the side of the shell parallel to the direction of water flow (10). Developed by NASA, they are "no deeper than a scratch," but can cut drag by up to 8 percent (10).

No matter how rigid the racing shells are, sweep shells still experience oscillating non-zero transverse movement, or wiggle (11). In sweeping, each rower has only one oar. Although rowers are traditionally lined up so that they row on alternate sides, this does not achieve the symmetry in power application that is required to remove wiggle (11). In 2009, Cambridge University asked a member of its mathematics department, John Barrow, to solve the problem of wiggle in an eight-man sweeping boat. The issue occurs because despite alternating rowers, the forces on the shell are unbalanced. This is because the four rowers on one side are on average closer to the bow than the four rowers on the other side (11).

Figure 2 shows four possible rowing configurations where the transverse waves created by the rowers cancel each other out, eliminating wiggle (provided each rower is applying the same amount of force). Interestingly, two of the configurations found by Professor John Barrow were experimented with in the 1950s (11). While configurations "a" and "d" were completely new, configuration "b" was already known as a "bucket" rig and was used in Germany in the 1950s. Configuration "c" was used by the Italian Olympic team, which subsequently won gold at the Melbourne Olympic Games in 1956 (11). However, one of the reasons that these rigs are unlikely to be used is that they only manage to eliminate wiggle if each rower is applying an equal amount of power on each stroke—an unlikely scenario (11).

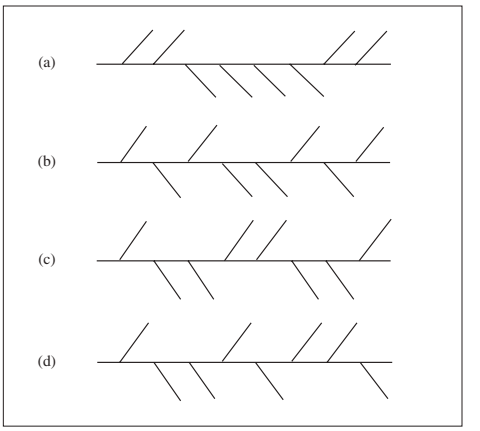

Image courtesy of John D. Barrow

Figure 2: Four possible rowing configurations which have zero transverse moment.

Swimming

Another sport that struggles with water resistance is swimming. After the 2008 Beijing Olympics, official competition rules were changed to reduce the effect high tech swimsuits had on race times. This change came in response to the astounding 42 swimming world records that were broken in the Beijing Olympics. Thirty-eight of these new records were broken by swimmers wearing the Speedo LZR (12).

The Speedo LZR is made of nylon-elastane. Nylon-elastane is extremely light and helps compress the swimmer's body into a more hydrodynamic shape (12). Although compression is not new to racing suits, the LZR suit has three times the compression power at half the weight of the suit used in the previous Olympic Games (12). The compression is so strong it takes 20 minutes to squeeze one's body into the suit (12). This compression not only smoothes out the swimmer's body, but it also helps support the swimmer's hips, which hang lower and increase drag as a swimmer tires (12).

Instead of sewn seams, which disrupt water flow and increase drag, the swimsuit is held together using ultrasonic welding, which according to Speedo reduces drag by 6 percent (12). The suit is also composed of polyurethane panels that are placed at high friction points on the suit. This further reduces drag by a stunning 24 percent (12).

Tests have shown that swimmers wearing the LZR consume 5 percent less oxygen to achieve the same performance—a clear indication of the reduction in effort required by the swimmer (13). Although the suits were banned in 2009 under the new restrictions that only allow male swimmers to wear swimsuits that go from waist to knee, they are a clear example of a technology that is revolutionizing a sport (14).

Tennis

Reducing drag is not the only way sports benefit from scientific advances. Tennis racquets have undergone two major transformations over the past twenty years. Racquet heads became larger, and strings have become better at helping players generate spin on the ball (15). A large racquet head gives a player more reach, and enlarges the "sweet spot" on the racquet (16). Contact at a racquet's sweet spot, which is located at the center of its head, results in the greatest conservation of energy of the ball upon impact, meaning that the ball moves more quickly (16).

Racquet head enlargement has only occurred recently because a larger racquet head requires greater string tension. More tension is needed to keep the strings taught across a longer distance, which in turn requires that frames be stronger (17). Bigger, stronger frames, formerly meant heavier, thicker racquets. Heavy racquets with thick frames suffer from an increase in air resistance during the swing and are detrimental to players who are looking to make fast serves and swings.

The shift in frame material first from steel to aluminum, and then from aluminum to graphite and foam, resulted in frames that are stronger and stiffer without being thicker (17). However, despite being strong enough to withstand increased string tension, graphite racquets were heavy. The relatively recent incorporation of titanium in modern racquet frames, truly allowed frames to become larger, lighter, and thinner (17).

Image courtesy of Guzmán Lozano. Retrieved from http://www.flickr.com/photos/15650492@N08/4623704120 (accessed 25 October 2012)

Figure 3: Professional tennis player Rafael Nadal hits a topspinning backhand. The development of copolyester strings revolutionized tennis by allowing for the rapid, high-spin shots which characterize today's game.

Although racquets have become lighter and bigger, the biggest improvement in tennis racquets has come from improved strings (17). A player who can generate high amounts of spin is able to hit shots that drop down onto the court (much like a curveball in baseball). Hitting a shot that curves down allows players to hit harder shots without the fear that the ball will land outside the court. Studies have shown that adding 100 rotations per minute to the rate at which the ball spins reduces flight distance by 6 to 12 inches (17). Co-polyester strings have been shown to create 20% more topspin than nylon strings (17). Counterintuitively, they create more topspin despite reducing friction between racquet and the ball. Co-polyester strings slide with, rather than grip the ball along the racquet face (17). The strings then snap back and add spin to the ball after the ball has changed direction (17). The use of co-polyester has had an astounding effect. In the words of Andre Agassi, "the advent of a new elastic co-polyester string, which creates vicious topspin, has turned average players into greats, and greats into legends" (15).

Technology has helped athletes hit better shots and race faster. Still, competition has not fundamentally changed: it remains the man, not the tool, that must win.

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References

1. Exploratorium, "The Science of Cycling: Aerodynamics & Drafting." Available at http://www.exploratorium.edu/cycling/aerodynamics1.html (15 October 2012).
2. R. A. Lukes, S. B. Chin, S. J. Haake, "The Understanding and Development of Cycling Aerodynamics," *Sports Engineering*, **8**(2), 59-74 (2005).
3. W. D. McArdle, F. I. Katch, V. L. Katch, *Essentials of Exercise Physiology* (Lippincott Williams & Wilkins, Philadelphia, PA, Vol. 1, 2000), pp. 282.
4. Hyperphysics, "Air Friction." Available at http://hyperphysics.phy-astr.gsu.edu/hbase/airfri.html (15 October 2012).
5. R. Cahill, "Resistance in Swimming" (21 June 2011). Available at http://www.livestrong.com/article/475663-resistance-in-swimming (15 October 2012).
6. Vespoli USA, "Vespoli: History" (2008). Available at http://www.vespoli.com/history (15 October 2012).
7. Vespoli USA, "Boat Science: How Do Hulls from Different Makers Compare?" (2008). Available at http://www.vespoli.com/innovation/67-boatsciencehulls (15 October 2012).
8. Pocock Racing Shells, "Rowing Shell Glossary: Performance & Boat Feel" (05 March 2012). Available at http://www.pocock.com/rowing-boat-information/rowing-shell-glossary3 (15 October 2012).
9. "NASA riblets for Stars & Stripes." Available at http://www.nasa.gov/centers/langley/news/factsheets/Riblets.html (15 October 2012).
10. MIT Technology Review, "Mathematician Solves Rowing Boat 'Wiggle' Problem" (20 November 2009). Available at http://www.technologyreview.com/view/416386/mathematician-solves-rowing-boat-wiggle-problem (15 October 2012).
11. ThomasNet, "Polyurethane and Sports: An Unrivaled Advantage." Available at http://www.thomasnet.com/articles/plastics-rubber/polyurethane-sport-technology (15 October 2012).
12. M. Luebbers, "Speedo Fastskin LZR Racer - The Fastest Swim Suit in the World for 2008!" (2008). Available at http://swimming.about.com/od/swimsuits/qt/speedo_lzr_race.html (15 October 2012).
13. BBC Sport, "Hi-tech suits banned from January" (31 July 2009). Available at http://news.bbc.co.uk/sport2/hi/other_sports/swimming/8161867.stm (15 October 2012).
14. A. Agassi, *Open: An Autobiography* (Knopf, New York, NY, 2009), pp. 178
15. C. Bowers, "Spin Doctor's Cure For Tension." (29 December 1996). Available at http://www.independent.co.uk/sport/spin-doctors-cure-for-tension-1316396.html (15 October 2012).
16. B. Strauss, "Building a Better Racket: Into the Laboratory for the Secrets of Spin" (26 August 2012). Available at http://www.nytimes.com/2012/08/27/sports/tennis/latest-advances-to-tennis-racket-put-new-spin-on-the-game.html?_r=1 (15 October 2012).
17. A. Agassi, *Open: An Autobiography* (Knopf, New York, NY, 2009), pp. 179

The Ups and Downs of Cognitive Enhancers

A Study of Common Cognitive Enhancers

ANDREW FOLEY

The human brain is an exceptionally plastic structure, able to form and re-form connections in response to individual experiences and interactions with the outside world. One of the most important ways in which humans are able to control their mental experience today is through the use of cognitive enhancers—substances that noticeably alter and improve function in specific areas of the brain. While a plethora of experiences and drugs have been noted to alter one's cognitive ability, only a few well-defined and documented cognitive enhancers seem to dominate recent academic study and today's commercial market. Among these drugs known to enhance focus and attention in the short-term are such stimulants as those used to treat attention deficit disorder (e.g. Ritalin and Adderall), caffeine, and even illegal substances like cocaine. While mainstream cognitive enhancers have been the subject of most scientific study, the spectrum of substances that can be classified as cognitive enhancers is far more broad. The class of chemicals that interfere with normal brain functions is incredibly varied and the effect of these substances on the human brain is near impossible to entirely predict or identify. Thus, research regarding all types of cognitive enhancers continues to develop.

Image courtesy of Julius Schorzman. Retrieved from http://en.wikipedia.org/wiki/File:A_small_cup_of_coffee.JPG (accessed 25 October 2012)

Figure 1: A cup of coffee has around 100mg of caffeine. Caffeine remains one of the most common cognitive enhancers consumed around the world.

Ritalin

Ritalin is one of the more controversial classes of cognitive enhancers widely used today. Commonly prescribed to treat attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD), Ritalin is a member of a class of drugs known as stimulants. More specifically, Ritalin, along with other ADD drugs like Adderall or Dexedrine, is classified as an amphetamine. In particular, Ritalin is the brand name of the generic chemical methylphenidate, a direct derivative of amphetamine (1). Amphetamines have been shown to function more effectively as short-term cognitive enhancers than other stimulants, like caffeine. In a paper by Bernard Weiss and Victor Laties in the early 1960s, amphetamines were found to be "vastly superior to caffeine at improving human performance in a variety of mental and physical activities" (1). Even in people who do not experience any form of ADD, amphetamines can help to improve focus and efficiency while performing tasks. Quite simply, appropriate doses of amphetamines like Ritalin, Adderall, or even methamphetamine (a commonly abused street drug), administered over a short period of time can enhance cognitive function for nearly all activities. However, amphetamine use over the long-term can have serious negative consequences. In the short term, the side effects are few and manageable—insomnia and decreased appetite are the most commonly noted short-term side effects of amphetamine use. Side effects of long-term amphetamine use are more pronounced and include addiction and increasing tolerance for the drug, which imply a psychological need to take more frequent and larger doses as amphetamine use progresses.

Diller describes the appeal of Ritalin and drugs like it as "feelings of euphoria; a sense of power, alertness, excitement, or heightened clarity; an ability to deny the need for rest" (1). Ritalin is classified as a Schedule II stimulant under the Federal Controlled Substances Act (CSA). In order to be classified as such, a drug like Ritalin must exhibit "a high potential for abuse […] have currently accepted medical use in treatment in the United States, and […] show that abuse may lead to severe psychologic or physical dependence" (2). The feeling of focus and control associated with Ritalin, as well as its availability through medical prescription, makes it highly susceptible to abuse. Currently, the high risk for abuse of Ritalin makes it both more difficult to get and less commonly used than other cognitive enhancers.

Caffeine

Caffeine is perhaps the most popular and widely used of drugs that alter cognition. It occurs naturally in over 60 species of plants, and has been consumed

by humans for centuries in different forms (3). Many people use caffeine every day for its effects as a mild stimulant. Most of the world's caffeine consumption is in the form of coffee, tea and soft drinks. In the U.S., coffee accounts for about 75 percent of caffeine consumption, tea for about 15 percent, and caffeinated sodas for about 10 percent (3). Caffeine is unique in that few regard it as a "drug" due to its relatively mild effects when compared with other more potent stimulants. However, many praise caffeine as a significant cognitive enhancer, with the ability to enhance focus, increase alertness, and generally improve psychological functioning. According to Barry Smith and Kenneth Tola, the popularity of caffeine today is "typically attributed to its stimulant effects, though its role in slowing and smoothing habituation and in enhancing and sustaining attentional focus may also be factors" (3).

The effects of caffeine on cognitive performance have been studied in several different areas, including information processing, memory, and complex cognitive functioning. The vast array of ways that caffeine can affect these different forms of mental functioning can quickly complicate the role of caffeine as a "cognitive enhancer." For example, while many studies have shown that caffeine "enhances problem-solving and improves logical reasoning," it remains largely unclear whether caffeine has a positive or negative overall impact on memory, an important part of learning and, therefore, daily cognitive functioning (3). When considering caffeine, it is important to remember that all chemicals that are presumed to enhance cognitive function, have—either directly or indirectly—a drawback to their use. This may seem obvious—a cognitive enhancer with no negative side effects would be overwhelmingly popular. No such drug currently exists, and the use of cognitive enhancers such as caffeine requires analysis of the drug's positive and negative effects.

Image courtesy of Patrick Mallahan III. Retrieved from http://en.wikipedia.org/wiki/File:Adderall_XR_20mg.jpg (accessed 25 October 2012)

Figure 2: Adderall XR 20mg capsules. Adderall is a prescription drug, commonly abused for their cognitive effects

Even cognitive functions typically found to benefit from caffeine use can suffer sometimes. An example of this can be seen in the impact of caffeine on information processing. As mentioned previously, caffeine has often been found to improve problem solving, enhance logical reasoning, and even partially reverse age-related deficits in cognitive functioning (3). However, Smith and Tola note that: "most of the studies reporting positive effects of caffeine in information-processing tasks have used primarily or exclusively male subjects" (3). Studies involving the impact of caffeine on both males and females were more frequently associated with no effect or even detrimental effect on information processing. The confounding role of gender in some caffeine studies is just one example of the difficulties of establishing a clear cognitive benefit of any drug. Cognitive enhancers such as caffeine often impact different people in different ways. Moreover, the method of administration, the dose, and the frequency of consumption also play a large role in determining the overall effect of the drug in enhancing cognitive function. For example, some studies have shown that high doses of caffeine can actually interfere with performance during complex tasks (3).

The effect of caffeine has also been studied with regard to memory. Like information-processing experiments, caffeine's impact on memory formation and recall has been studied with mixed results. Confounding variables such as gender, age, and dose taken play a large role in determining the outcomes of each of these individual studies as well. In the case of the interaction between caffeine and memory, the "memory assessment method" (i.e. recall or recognition,) as well as the time frame (whether the memory is assessed immediately or following some time delay), seems to play a significant role in determining the results (3). Experimental trends indicate that caffeine seems to be most effective at enhancing delayed recall, recognition memory, and verbal memory. However, caffeine has also been shown to decrease immediate recall in some cases, such as with word lists (3).

Current Research Limitations

All of the discussed studies on caffeine dealt with one-time tests of subjects who had consumed or abstained from the drug. The issue of controlling for previous exposure to the drug, or of predicting the future impact of the drug through continued, regular use remains a significant one. Since most people in developed parts of the world have been exposed to caffeine or consume it regularly, it can be very difficult to establish a strong control group on whom caffeine has had no significant impact. As the daily influences on the brain are many, it can also be very difficult to tell whether other confounding variables impact the cognitive functioning of a routine caffeine user. In fact, they almost certainly do. For example, the amount of sleep that one gets can very easily affect cognitive functioning, and while caffeine can offset the effects of a lack of sleep in the short-term, over a longer period of time these effects may begin to more clearly manifest, regardless of the presence or absence of caffeine.

Caffeine tolerance and the decreasing benefit to cognitive marginal functioning with prolonged caffeine use is also of concern. In fact, some researchers claim that caffeine has the potential to be highly addictive and to be abused by some users (3). Tolerance can be a good measure of whether a drug is actually "addictive" or not. Some studies maintain that regular or heavy caffeine use does not lead to a tolerance—that the effect of caffeine on non-users and regular users is much the same (3). However, other studies have shown that caffeine tolerance is, in fact, a real problem and can develop "perhaps in as little as five days" (3).

Just as the positive impacts of caffeine use are hotly debated, the negative impacts seem uncertain at this point. While some of this can be attributed to a lack of proper research regarding caffeine tolerance and addiction, much of the problem results from an inability to account for the myriad of confounding variables that are a constant in research regarding cognitive function. It is impossible to isolate two individuals with an identical cognitive experience, and it is therefore difficult to establish a true control group. From this perspective, it is best to consider cognitive enhancers as a part of a larger scheme—the goal of research on this front is not to isolate a single, direct influence of any chemical with the potential to enhance cognitive function, but instead to establish a general positive or negative correlation between cognitive output and the use of a substance.

Image courtesy of Wmahan. Retrieved from http://commons.wikimedia.org/wiki/File:Ginseng_in_Korea.jpg (accessed 25 October 2012)

Figure 3: Ginseng on sale in a South Korean market. Ginseng is popular in Asia for its purported medicinal properties, such as enhancing cognitive functioning. Scientists have classified it as a nootropic.

Nootropics

Research regarding attention deficit drugs like Ritalin and common stimulants like caffeine, while incomplete, has been fairly extensive. However, there are other chemicals with the potential to enhance cognitive function that are less well represented in the scientific literature. For an overview on these types of substances, it is best to look at the relatively newly-established field of "nootropics." Dwivedi *et al.* describes nootropics as: "drugs, supplements, nutraceuticals, and functional foods that are purported to improve mental functions such as cognition, memory, intelligence, motivation, attention, and concentration" (5). This definition is quite broad and would include all classes of cognitive enhancers. However, the term "nootropic" is generally reserved for use in the description of less traditional substances. In many ways, the most defining aspect of a true nootropic is that is has not been well-defined. The proto-typical example would be ginseng, a naturally occuring root with strong cultural significance. Nootropics are "purported" to enhance cognitive functioning, but as in the case of caffeine and Ritalin, an abundance of confounding variables and (especially in the case of nootropics) a lack of research makes it difficult to tell just how effective these substances may be(5).

Nonetheless, the use of nootropics is developing rapidly. Yet many researchers are hesitant to associate themselves with it because to do so seems as if they are stepping away from hard scientific research into the realm of traditional natural medicine. Nootropics have been employed as alternative treatments in cases of degenerative brain disorders such as Alzheimer's or Parkinson's disease, with some success (4). Ultimately, the struggle to identify substances that might enhance brain function is a very difficult one, but one that some researchers are excited to pursue. Malik *et al.* notes that: "many academic researchers are dedicating their efforts to identify compounds that can help in restoring impaired cognitive functions, either directly or through the cure of the pathologies that produce cognitive dysfunction" (4).

Conclusion

While some are more optimistic than others, it is apparent that research regarding the use of cognitive enhancers, especially on a regular basis, is lacking. It is still difficult to identify long-term effects of the use of many cognitive enhancers that are relatively new to the scene, such as attention deficit drugs and various nootropics. Even caffeine, which has been in use for centuries, remains to be fully understood. It seems logical that, for the time being, an appropriate balance is important in the use of cognitive enhancers. "Too much of a good thing" is very much a concern in the use of cognitive enhancers. This is seen to be true of stimulants such as Ritalin and caffeine, which may lead to tolerance, addiction, and ultimately a negative impact on cognitive functioning. Where enhancers have been most effective is in the treatment of disorders affecting cognitive functioning, as in the case of ADD or degenerative diseases such as Alzheimer's or Parkinson's. Especially in the case of neurodegenerative diseases, the risk of using new and relatively unknown cognitive enhancers can be outweighed by their potential to improve the health of the consumer.

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References

1. L. Iversen, *Speed, Ecstasy, Ritalin: The Science of Amphetamines* (Oxford University Press, New York, NY, 2006).
2. L. L. Greenhill, B. Osman, *Ritalin: Theory and Practice* (Mary Ann Liebert, Inc. Publishers, Larchmont, NY, ed. 2, 2000).
3. G. A. Spiller, *Caffeine* (CRC Press LLC, New York, NY, 1998).
4. R. Malik *et al.* "Towards Better Brain Management: Nootropics," *Curr. Med. Chem.* **14**, 123-131 (2007).
5. Dwivedi *et al.* A Traditional Approach to Herbal Nootropic Agents: an Overview. IJPSR (2012); Vol. 3(3): 630 -636
6. L. H. Diller, *Running on Ritalin* (Bantam Books, New York, NY, 1998).
7. P. B. Dews, *Caffeine* (Springer-Verlag, Berlin, Germany, 1984).

The Sublime Cow and the Maltese Cross

SHARANG BISWAS

Ava Helen Pauling, wife of esteemed Chemist Linus Pauling, described early x-ray images of DNA (Figure 1) as such: "From the bull's-eye, a striking arrangement of short, horizontal smears stepped out along the diagonals in the shape of an X or a Maltese cross."

The image is titled "Photograph 51", taken by Rosalind Franklin in 1952.

It was also the most sublime image of a cow ever to be published at the time

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The ceiling of The Eagle pub in Cambridge, England, boasts an impressive example of crystallised history: the warm and inviting wood is adorned with notes scribed with lighters, candles and lipstick by World War II veterans. It's a thought-provoking sight. The chaotic swirl of signatures and messages screams with an almost desperate need; the forgotten dead seem to rise out of their graves and strain to be remembered.

Unfortunately for the soldiers, on 28, February 1953, their graffiti was overshadowed by another piece of history solidifying under their special ceiling. The Eagle's patrons would have recognised two of the regulars: an Englishman whose unmistakeable and hard-to-miss "booming enthusiasm" outstripped his frame, and a lanky 25-year-old with protruding ears and a prominent Adam's apple, who looked vaguely Irish, but was in fact American. The former was Francis H. C. Crick, a lesser-known theoretical physicist with an energetic fascination for how X-rays could be used to understand "the chemical physics of biology". His colleague was James D. Watson, an inexperienced geneticist who had gained his Ph.D. only three years ago. It is unlikely that any of the pub's Saturday morning customers expected their lunch to be interrupted by Crick's powerful voice announcing: "We have found the secret of life."

The pair was talking about DNA (or deoxyribonucleic acid), the heritable genetic material that is found in all living organisms. Watson and Crick had managed to develop a model for the three-dimensional structure of this vital macromolecule: two antiparallel backbones of sugar-phosphate twisting and coiling each other into a double-helix, with the organic bases adenine, cytosine, thymine and guanine nestled within.

The paper that the two scientists published the following April was deceptively brief, a mere one page. "The omissions in the paper by Watson and myself are also striking," Crick later wrote, reviewing his own paper. "The structure is produced like a rabbit out of a hat with no indication as to how we arrived at it." Indeed, the formulation of the double helix structure was an arduous process, and according to Crick, "…partly a matter of luck, and partly good judgement, inspiration and persistent application."

Luck played a significant part in the DNA drama: during a short stint in Naples in 1951, Watson chanced upon another English physicist, Maurice Wilkins, and learned that the highly-organised DNA molecule could diffract X-rays as if it were a crystal. Unsettled by this knowledge, Watson quickly grew bored of his new postdoctoral fellowship studying protein structures at the Cavendish Laboratory in Cambridge. Watson found that Crick, whom he met at Cavendish, shared his idea that uncovering the structure of DNA was of paramount importance.

It is perhaps lucky for the pair that Crick's loud exuberance created friction within the lab. Crick had seriously upset the head of the lab, Sir Lawrence Bragg, by suggesting that his own ideas, and not Bragg's, had spurred the discovery of a novel method of protein analysis. As a result, Watson and Crick moved further away from proteins and spent more time with DNA.

However, "that fall of 1951, we had no reason to hope that we would be more than minor players in DNA research," wrote Watson. It was here that luck played another major role.

Rosalind Franklin, a Cambridge-trained scientist, had joined Wilkins' lab the previous year. Thick eyebrows and a subtly masculine face hid an exceedingly sharp mind; Franklin soon began producing startlingly clear X-ray images of DNA, and positing her own theories of the molecule's structure with admirable mathematical rigour.

Wilkins and Franklin had a distant relationship, despite working in the same lab. When Watson was visiting Wilkins in London, Wilkins retrieved from his desk her Photograph 51, the clearest X-ray image of DNA to date, and showed Watson what he thought was undeniable evidence of the shape of DNA. Wilkins had not gained Franklin's permission to reveal her images.

The images sparked something in Watson. According to Ava Helen Pauling, "the pattern shouted helix."

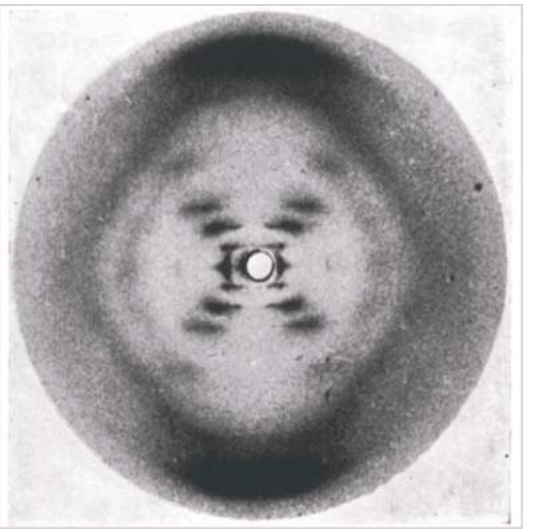

Image courtesy of http://1.bp.blogspot.com/-cSNcwJRPt2E/Tjg408F4ePI/AAAAAAAACwg/wj0TjrnlEp4/s1600/DNARosalindFranklineFoto51MEU.jpg (accessed 21 May 2012)

Figure 1: Rosalind Franklin and an X-ray diffraction image of DNA. Franklin produced the clear X-ray images of DNA that Watson and Crick used to determine the structure of DNA.

Image courtesy of A. Barrington Brown. Retrieved from http://fineartamerica.com/featured/watson-and-crick-a-barrington-brown-and-photo-researchers.html (accessed 21 May 2012)

Figure 2: James Watson and Francis Crick with their DNA model at the Cavendish Laboratories in 1953.

The photograph proved critical to informing Watson and Crick's understanding of the DNA molecule. Nevertheless, shouting or not, the precise helical structure of the precious molecule evaded the pair for another fourteen months. Inspired by Wilkins' revelation, the pair built physical models of the constituents of DNA and agonised over how the organic bases were paired, whether the sugar-phosphate chains were on the inside or the outside, and what stabilising forces were present. However frustratingly elusive the structure may have been, boring it was not. One of Watson and Crick's greatest fears had been that the DNA molecule would end up being "dull". Fortunately, Watson wrote, "the finding of the double helix thus brought us not only joy but great relief. It was unbelievably interesting…"

On April 25, 1953, scientific powerhouse-journal *Nature* published three different papers on the structure of nucleic acids, among them, the now famous "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid", by J.D. Watson and F.H.C. Crick. Nine years later, Watson, Crick and Wilkins shared a Nobel Prize in Physiology, for their contributions to the understanding of DNA and genetics.

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The New York Times of 1953 called Photograph 51 "a whirlpool of light and shade". It depicts DNA taken from a cow thymus. In a way, it depicts the entire animal; it is the most perfect possible snapshot of a cow, complete with every detail of the cow's anatomy, life-processes and habits. It is also a symbol. It depicts the human quest to understand life.

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References

1. BBC News | Science/Nature | 'Secret of life' discovery turns 50. 27 February 2003. Web. 3 April 2012. <http://news.bbc.co.uk/2/hi/science/nature/2804545.stm>. (Oct. 1, 2012).
2. "Clue to Chemistry of Heredity Found." New York Times 13 June 1953: 17. Print.
3. Crick, Francis H. C. "The Double Helix: A Personal View." Nature (1974): 766-769. Print.
4. Gosling, Rosalind E. Franklin & R. G. "Molecular Configuration in Sodium Thymonucleate." Nature (1953): 740-741. Print.
5. Maddox, Brenda. Rosalind Franklin: the Dark Lady of DNA. HarperCollins Publishers, 2002. Print.
6. Ocellated> A Day in Cambridge. 16 July 2009. Web. 3 April 2012. <http://www.ocellated.com/2009/07/16/a-day-in-cambridge/>. (Oct. 1, 2012).
7. Rosalind Franklin. 2010. Oregon state University Libraries. Web. 2 April 2012. <http://osulibrary.orst.edu/specialcollections/coll/pauling/dna/people/franklin.html>. (Oct. 1, 2012).
8. Rosenfield, Israel, Edward Ziff and Borin Van Loon. DNA: A Graphic Guide to the Molecule that Shook the World. New York: Columbia University Press, 2011. Print.
9. The Eagle Pub in Cambridge. 2011. Web. 3 April 2012. <http://gkpubs.co.uk/pubs-in-cambridge/eagle-pub/>. (Oct. 1, 2012).
10. Watson, James D. and Francis H. C. Crick. "Genetic Implications of the Structure of Deoxyribonucleic Acid." Nature (1953): 964-967. Print.
11. "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acids." Nature (1953): 737-738. Print.
12. Watson, James D. Genes, Girls and Gamow: After the Double Helix. New York: Alfred A. Knopf, 2002. Print.
13. Nobelprize.org. n.d. Nobel Lecture. 2 April 2012. <http://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/press.html>. (Oct. 1, 2012).
14. The Double Helix: A Personal Account of the Discovery of the Structure of DNA. New York: Atheneum, 1968. Print.

Quantifying Glacier Retreat on Baranof Island

Tracking Glacial Movement through Remotely Sensed Data

BEN HUGHEY AND ALEXANDRA GIESE

As mountain glaciers melt in response to anthropogenic climate change, they are making a significant contribution to global sea level rise. This paper investigates the history of growth and recession of the Jobildunk Glacier on Baranof Island, in Southeast Alaska. A series of 16 Landsat images and one aerial photo supply a temporal span from 1974 to 2010. Using a modified version of the box method for calculating glacial retreat, we were able to quantify the size of Jobildunk Glacier for 17 individual years over the 36-year time frame. The analysis reveals that the glacier has retreated approximately 860 m since 1974, at a rate of 14 m/year during 1974 – 2001 and an accelerated rate of 48 m/year during 2001 – 2010. Potential reasons for this acceleration include a warming climate, the formation of a proglacial lake and the development of a calving ice cliff terminus.

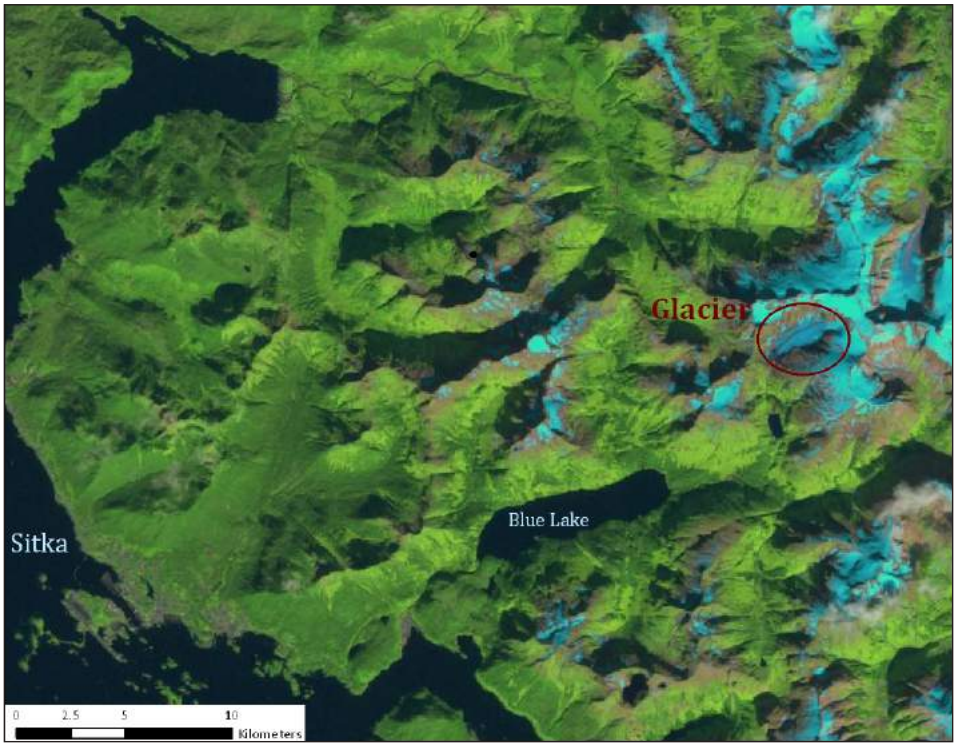

Figure 2: The Jobildunk Glacier in the Blue Lake watershed outside of Sitka. Landsat ETM image from 9 September 2001.

Introduction

Mountain glaciers in Southeast Alaska are of global importance due to their quick response to fluctuations in climate and their significant contribution to global sea level rise. Since glaciers are sensitive to changes in temperature and precipitation, they serve as powerful indicators of climate change (1-3). For a number of years, glacier melt has been accelerating worldwide, leading to global sea level rise (SLR). Between the years of 1951 and 2003, meltwater from mountain glaciers and ice caps contributed 0.51 mm/year to SLR (4). However, that rate of contribution has increased; between 1994 and 2003, the contribution to SLR was estimated to be 0.93 mm/year (4). Recent modeling efforts estimate that from 2001 to 2100, wastage of glaciers and ice caps will amount to an estimated 0.12 +/- 0.04 m contribution to SLR, with the majority coming from glaciers in Arctic Canada, Alaska, and coastal Antarctica (5). It is also projected that the total glaciated area will shrink by 21 +/- 6%, with some areas expected to lose as much as 75% of their current volume (5).

Alaska is a particularly critical region when considering the future of glacier melt and SLR. The state contains approximately 75110 km^2 glaciers; these glaciers, though representing only 13% of global glaciated area, contribute 50% of the SLR from mountain glaciers (6).

Temperate glaciers are comprised of ice near its melting point. Glaciers in coastal areas like in Southeast Alaska, which are typically characterized by high rates of precipitation and very moderate temperatures, are especially responsive to changes in climate (7). Despite their extreme climatic sensitivity, none of the glaciers on the islands of the Alexander Archipelago have been studied in detail (8). In order to gain a better understanding of the causes of glacier retreat in Southeast Alaska glaciers, we chose to explore the history of the Jobildunk Glacier on Baranof Island (9). This glacier was selected in part for its proximity to the city of Sitka (Fig. 2), which would permit easy access for follow-up field measurements . Additionally, some preliminary data had been collected on Jobildunk Glacier by Jonathan Kriess-

Figure 1: Sitka on Baranof Island in Southeast Alaska (24).

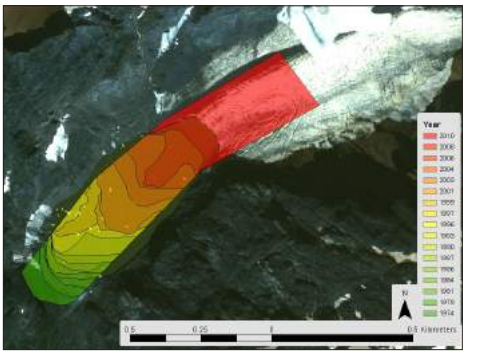

Figure 3: Glacier terminus positions by year (24).

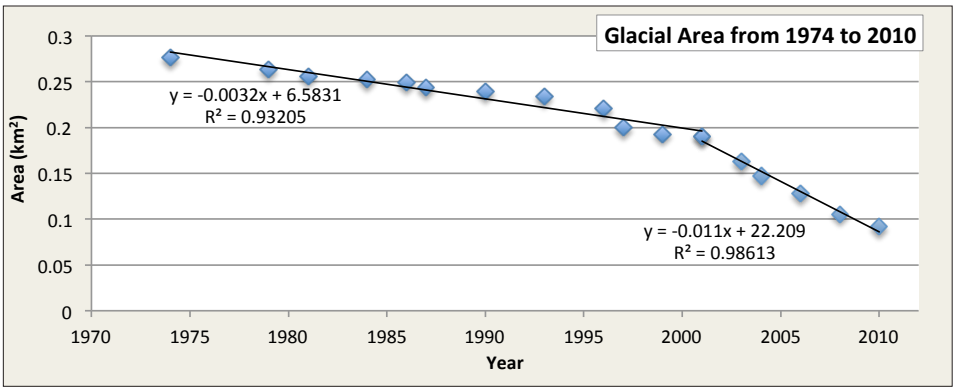

Figure 4: Glacier area (km^2) over time. A marked increase in the rate of retreat is apparent around the year 2001.

Tomkins with support from the Sitka Conservation Society. The Jobildunk Glacier is located approximately 16 km from the open ocean on either side of Baranof Island and is part of the Blue Lake watershed. Blue Lake is a major source of drinking water and hydroelectric power for the city of Sitka. As a result, the health of the glaciers in its catchment basin is of concern to the Sitka residents who depend on Blue Lake as a consistent water source. In 2010, the Jobildunk Glacier measured approximately 945 m at the centerline. It is located at a latitude of 57° 6' N with an elevation ranging from approximately 700 m at its terminus to 800 m at its headwall. In this study, we will be investigating a history of the Jobildunk Glacier's growth and recession in recent decades to understand and quantify its retreat.

Methods

This study employed Landsat imagery due to its uniformity and historic availability. Sixteen images, shot by the Multispectral Scanner (MSS), Thematic Mapper (TM) and Enhanced Thematic Mapper (ETM), provided a temporal span from 1974 to 2010. Additionally, we analyzed a high-resolution U.S. Forest Service aerial photo from 1997 (10). Lastly, a multispectral Worldview scene from 2010 was used as a visual reference to study glacier characteristics (11).

Given that snow cover is present for most of the year at Jobildunk Glacier's elevation, all images were sourced from the end of the ablation season (August, September, or October, depending on availability), allowing us to minimize the potential error from misinterpreting snow as glacial ice.

After examining several images, it became clear that the traditional 'centerline' method would not be the most appropriate approach for this study (12). The Jobildunk Glacier's terminus geometry throughout the past several decades was too dynamic to be captured accurately by a single line. Since the location of the glacier tongue varied laterally from year to year, we decided to employ a modified version of the 'box' method. Similar to the approach of Moon and Joughin, which involved digitizing ice front positions referenced within a three-sided box, we created a reference frame to overlay on each image (14). Our frame, though, is not a box but rather a polygon which better approximates the curve of the glacier; a straight rectangle would miss the southward turn of the flowline and not include the full temporal span of termini positions. The downglacier end of the polygon extends past the earliest and most extensive terminus line (i.e. 1974), while the upglacier end is located behind the most recent and shortest terminus position (i.e. 2010). The reference polygon is narrow enough to avoid the sides of the glacier; accordingly, reported area changes are solely reflective of changes in glacier length. Another advantage of our method relative to the centerline approach is that tracing errors are reduced by averaging over a larger number of pixels. With the centerline method, glacier length changes cannot be detected in finer increments than pixel size (14).

Results

We found that the Jobildunk Glacier retreated dramatically between the years 1974 and 2010 (Fig. 3). Since surface area measurements are recorded within a reference area superimposed on the glacier, reported values represent surface area change only within that reference area rather than over the entire surface, meaning these values represent relative rather than absolute loss. Over the 36-year time-frame, the glacier lost 5,140 m^2/year, corresponding to a retreat of approximately 23 m/year in glacier terminus position. This rate was not constant, however; near the turn of the century, retreat accelerated (See Figure 4). Between 1974 and 2001, glacier area declined at an average rate of 3,200 m^2/year (R2 = 0.932), while after 2001 the rate was 11,000 m^2/year (R2 = 0.986). These correspond to length changes of 14 m/year and 48 m/year, respectively.

Discussion: Process

Delineation of the glacier terminus introduced an inherent error into our analysis due to the 79×79 m and 30×30 m resolution of the Landsat MMS and TM/ETM images, respectively. Terminus tracing was necessarily subjective, but the authors reduced uncertainty through discussion of glacier geometries for the majority of images. The short time intervals between the images (a maximum of 5 yr. and a minimum of 1 yr., with mean = 2.25 yr.) also assisted in terminus recognition (i.e. some consistency in location and geometry was expected year-to-year). The U.S. Forest Service aerial mosaic in the middle of the data series was a particularly useful reference and provided a check for identified terminus locations pre- and post-1997. In addition to the resolution, the presence of a medial moraine presented difficulty in distinguishing the terminus (15). In the area of the moraine, we simply interpolated the well-defined terminus on either side, keeping the approximate geometry dictated by the debris-free ice regions.

Due to the inherent subjectivity and uncertainty associated with terminus delineation in the 17 images, we elected to group authors' measurements by time such that any systematic biases in interpretation would be present only between the groupings. Giese delineated the termini between 1974 and 1999, while Hughey conducted the remainder of the tracings through 2010. Thus, any systematic difference in tracing technique would affect only the change observed in glacier length between the 1999 and 2001 images. We conducted a quantitative assessment of this error through repeated tracing of the 1987 Landsat TM image, which had a resolution, quality, and contrast largely representative of the dataset as a whole. Hughey and Giese traced the terminus 14 times each, with time between interpretations. The standard

deviations for Hughey's and Giese's error measurements were 2,073 m^2 and 2,550 m^2.

Discussion: Results

Results show a significant trend in glacier terminus retreat—and corresponding surface area—between 1974 and 2010, with an increase in rate beginning near the year 2001.

Given that temperate glacier ice is near its melting point and, therefore, particularly sensitive to climate perturbations, we would expect the Jobildunk Glacier to respond quickly to variations in the temperature record. However, the rate of retreat exhibits no significant correlation with the ablation season (16) temperature record, a climatological variable with demonstrated influence in similar cases (17). Furthermore, if the primary mechanism of retreat were climate forcing, we would expect the Jobildunk Glacier to exhibit a closer response to the Pacific Decadal Oscillation (PDO) index. The PDO is an atmospheric and oceanic circulation pattern that, when in a positive (or 'warm') phase, results in higher air and sea surface temperatures in Southeast Alaska (18). The Lemon Creek Glacier (19), an alpine glacier above Juneau, has been shown to have a strong correlation between mass balance and the PDO index (17). During the positive PDO period of 1976 to 1998, the Lemon Creek gained mass only twice; however, from 1999 to 2001, three consecutive years of positive mass balance were recorded, coincident with a swing in the PDO period to cooler temperatures (19). Although temperature anomalies in Sitka are correlated with the PDO index (see Figure 4), the Lemon Creek record contrasts with our observations, which show a dramatic increase in the rate of retreat during a 'cool' PDO phase. Though the PDO index does turn positive in 2002 for a short period of time, the acceleration in retreat both anticipates and outlasts the upswing in temperatures from 2002 to 2006, suggesting that climate forcing is not the primary causal mechanism of inter-annual variation in the rate of retreat.

Even though the temperature record in Sitka does not strongly correlate with glacial retreat, given the evidence of glacier sensitivity to climate elsewhere in Alaska (17, 21), regional climate patterns likely affected the Jobildunk Glacier throughout our study period. It is possible that the turn to a positive PDO phase in 1976 was a significant contributing factor in the initial formation of proglacial lake.

Since the recent changes in the pattern of retreat observed in the Jobildunk glacier do not follow the expected fluctuations of the PDO, it is likely that a different mechanism is responsible. Kirkbride has identified the deepening of proglacial lakes as a critical threshold for retreat rates (22). Landsat imagery from the 1970s, as well as the 1929 and 1948 aerial photographs not used in the retreat analysis, show that the Jobildunk glacier terminated on land. In the early 1980s, however, images begin showing a lake at the terminus of the glacier. Kirkbride suggests that shallow proglacial lakes contribute to a slight increase in the rate of terminal retreat, but rapid retreat does not begin until the lake deepens to allow calving ice cliffs to form (22). Before 2001, when the terminus position of Jobildunk glacier would have constrained the lake to less than half its current size, it is possible the lake was shallow enough, such that the terminus was more stable. Though we do not observe any distinct retreat acceleration coincident with lake formation, this may be a result of having insufficient imagery predating the lake. If our terminus time series could be extended back, it is possible that a change in retreat rate would emerge. It is also possible that the glacier saw little to no retreat acceleration as a result of its transition to a lake-terminating state until the lake was large and deep enough to pass the threshold permitting terminus destabilization and large volumes of calving.

Conclusion

Retreat of the glacier in this study since 1974 is incontrovertible; the changes in glacier length far exceed the uncertainties inherent to the interpretation of coarse resolution Landsat imagery. We find that the glacier area shrunk 3,200 m^2/year between 1974 and 2001 and 11,000 m^2/year between 2001 and 2010, measured within a reference area. This study sought to quantify only the changes in glacier length, and, thus, a more appropriate measure of retreat may be: 14 and 48 m/year. Extrapolating this average retreat rate into the future gives only 26 years before glacier disappearance. It is unlikely the glacier will disappear within this timeframe, given that the glacier may eventually retreat into shallower water and the terminus would stabilize; however, the number serves to provide a sense of the retreat rate. Also illustrative of the magnitude of retreat is a first-order approximation of total surface area change over the entire surface of the glacier, which indicates a 40 percent reduction between 1974 and 2010.

Since our method does not incorporate changes in either the lateral shrinking of the glacier or its thinning, we cannot draw robust, quantitative conclusions about changes in glacier volume or even total surface area. However, terminus retreat is commonly correlated with glacier thinning and volume decline, and this study clearly shows a dramatic retreat in glacier terminus position. Forming a more comprehensive understanding of the glacier's shrinkage over the past several decades requires future investigations of total surface area change as well as ice elevation change. Airborne laser altimetry would be an accurate method of determining thickness of the glacier

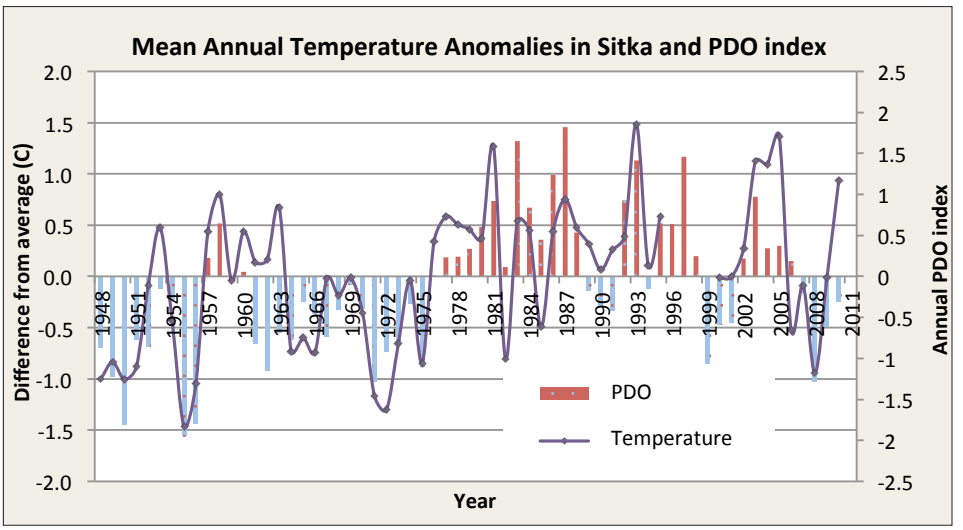

Figure 5: PDO phases color-coded as blue for negative, red for positive (25). Sitka climate data from Japonski airport weather station (26).

(23). Bathymetric measurements of the proglacial lake could aid in substantiating the theory of ice calving as a mechanism for rapid retreat.

Although we did not find a relationship between changes in climate and glacier retreat for the Jobildunk Glacier, it is possible that the effect of the lake masked the influence of temperature fluctuations. The multiple other glaciers on Baranof Island merit studies of their own. Research is needed to show if glaciers on the island not terminating in proglacial lakes exhibit a stronger response to climate forcing.

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References

1. B. Fitzharris *et al.*, "Behaviour of New Zealand glaciers and atmospheric circulation changes over the past 130 years" *The Holocene* **2**, 97-106 (1992).
2. W. Haeberli, M. Hoelzle, "Application of inventory data for estimating characteristics of and regional climate-change effects on mountain glaciers: a pilot study with the European Alps." *Ann. Glaciol.* **206** (1995).
3. J. Oerlemans, B. Reichert, "Relating glacier mass balance to meteorological data by using a seasonal sensitivity characteristic," *J. Glaciol.* **4**, 1-6 (2000).
4. M. B. Dyurgerov, M. F. Meier, "Glaciers and the changing earth system: a 2004 snapshot," *Arctic Alpine Res.* OP-58 (2005)
5. V. Radic, R Hock, "Regionally differentiated contribution of mountain glaciers and ice caps to future sea level rise," *Nat. Geosci.* **4**, 91-94 (2011).
6. M. Meier, M. Dyurgerov, "How Alaska affects the world," *Science* **297**, 350-351 (2002).
7. M. Shulski, G. Wendler, The Climate of Alaska (U. Alaska Press, Fairbanks, AK, 2007).
8. B. Molnia, "Glaciers of North America -- Glaciers of Alaska," in R. Williams, J. Ferrigno, Satellite image atlas of glaciers of the world: USGS 1386-K (2008).
9. Jobildunk Glacier is named after a glacial cirque on New Hampshire's Mount Moosilauke.
10. Image identified and dated with help from Craig Buehler, Sitka Ranger District, USFS.
11. Worldview imagery provided by CRREL. This image was not used to digitize a terminus as it duplicated a Landsat scene that provided sufficient resolution.
12. I. Howat *et al.*, "Rapid retreat and acceleration of Helheim Glacier, east Greenland," *Geophys. Res. Lett.* **32**, L22502 (2005).
13. J. Kargel *et al.*, "Multispectral imaging contributions to global land ice measurements from space," *Remote Sens. Environ.* **99**, 187-219 (2005).
14. T. Moon, I. Joughin, "Changes in ice front position on Greenland's outlet glaciers from 1992 to 2007," *J. Geophys. Res.* **113**, F02022 (2008).
15. E. Gjermundsen *et al.*, "Assessment of multispectral glacier mapping methods and derivation of glacier area changes, 1978-2002, in the central Southern Alps, New Zealand, from ASTER satellite data, field survey and existing inventory data." *J. Glaciol.* **57**, 667-683 (2011).
16. Ablation season approximated by months of April through September, following Criscitiello (17).
17. A. Criscitiello, M. Kelly, B. Tremblay, "The response of Taku and Lemon Creek Glaciers to climate," *Arct. Antarct. Alp. Res.* **42**, 34-44 (2010).
18. C. Bitz, D. Battisti, "Interannual to decadal variability in climate and the glacier mass balance in Washington, Western Canada, and Alaska," *J. Climate* **12**, 3181–3196 (1999).
19. The Lemon Creek Glacier is relatively small, close to the ocean and about 150 km from Sitka, making it an ideal candidate for comparison.
20. M. Miller, M. Pelto, "Mass Balance Measurements On The Lemon Creek Glacier." (2011). Available at http://www.nichols.edu/departments/glacier/Lemon.html (May 20, 2012).
21. S. Hodge *et al.*, "Climate variations and changes in mass of three glaciers in western North America," *J. Climate* **11**, 2161–2179 (1998).
22. M. Kirkbride, "The temporal significance of transitions from melting to calving termini at glaciers in the central Southern Alps of New Zealand," *The Holocene* **3**, 232-240 (1993).
23. A. Arendt *et al.*, "Rapid wastage of Alaska glaciers and their contribution to rising sea level," *Science* **297**, 382–386 (2002).
24. National Climate Data Center (NOAA), Climate Data Online. (2012). Available online at http://www.ncdc.noaa.gov/cdo-web/ (May 20, 2012).
25. N. Mantua, The Pacific Decadal Oscillation (PDO). (2012). Available at http://jisao.washington.edu/pdo/ (May 20, 2012).
26. Background imagery from National Geographic World Basemap, ESRI ArcMap 10.

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Allometric Scaling of Morphological Feeding Adaptations and Extreme Sexual Dimorphism in Energy Allocation in Invasive Lionfish

A Study of Pterois Volitans

ROBIN COSTELLO, NINA FRANKEL AND MADILYN GAMBLE

Lionfish (*Pterois volitans*) are a rapidly spreading invasive marine species in the Western Atlantic. High feeding success and reproductive output are potential mechanisms that allow lionfish to be such successful invaders. In order to better understand these mechanisms, we studied the allometry of morphological features involved in lionfish feeding ecology (specifically pectoral fin length and gape area), using fat mass as a metric of feeding success. We expected shorter lionfish to have longer pectoral fins, larger gape areas, and more fat stored than expected for their length. This allometric pattern would give smaller lionfish a feeding advantage, allowing them to grow to a large size quickly and outcompete other reef piscivores. Since we expected increased pectoral fin length and gape area to increase feeding success, we expected lionfish with longer pectoral fins and larger gape areas relative to length to have relatively more fat. We found that 1) shorter fish have longer pectoral fins, larger gape areas, and more fat mass than expected for their size, 2) lionfish with longer pectoral fins and larger gape areas for their length do not have more fat than expected for their length, and 3) females of a given body size had significantly lower fat mass than males. Our results indicate that compensatory allometric scaling of morphological features involved in feeding may give shorter lionfish a competitive advantage over native piscivores. We also found that fat mass is not necessarily indicative of feeding success. Finally, adult females may be investing more energy in reproduction than in growth or fat storage. Because lionfish reproduce continually while other reef piscivores reproduce seasonally, this intense allocation of energy into reproduction may play a critical role in the invasive success of lionfish in the Caribbean.

Introduction

Biological invasions are homogenizing the world and occurring more frequently as human activity increases on an international scale (1). Despite the overall increase in non-native introductions, introductions of marine fish species are surprisingly rare (2). Lionfish (*Pterois volitans*) are the first non-native marine fish species to invade the Western Atlantic (3, 4). This lionfish invasion represents one of the most rapid marine fish invasions in documented history (5). Anecdotal evidence blames the introduction of lionfish on releases from aquaria in South Florida (4). Since introduction in the 1990s, lionfish have spread north to Bermuda and south to Jamaica (4, 6). Albins and Hixon (2008) performed the first experimental study investigating the impact of this invasion, demonstrating that lionfish predation decreased native coral reef fish recruitment by 79%. This study showed that lionfish feeding ecology is a vital factor in understanding the success of their invasion. Previous studies have documented that lionfish use their long pectoral fins to corral fish and benthic invertebrates into their mouths (5). Lionfish also blow a jet stream of bubbles to mimic a current, tricking fish into swimming headfirst into their mouths (7). Such novel predation strategies potentially allow lionfish to grow rapidly and outcompete other piscivorous fish for prey and resources, contributing to their success.

Figure 1: *Pterois volitans* on the Owen's Island reef, Little Cayman Island. Photo by Nina Frankel.

To investigate which characteristics of lionfish contribute to their feeding success in invaded communities, we measured two feeding-related morphological features: pectoral fin length and gape area. Additionally, we assumed that the mass of fat stores in a lionfish would serve as a metric of feeding success. If these morphological features and fat stores follow an allometric growth pattern where smaller fish have longer pectoral fins, larger gape areas, and/or larger fat stores than expected for their size, this would indicate that selection has favored greater prey-capture ability in smaller lionfish. Because this allometric pattern would give smaller lionfish a feeding advantage, lionfish could grow to a large size quickly outcompeting other reef piscivores. If lionfish's feeding success is directly related to feeding morphological features, we would expect lionfish with longer pectoral fins and larger gape areas for their size to have more fat stores than expected for their size. Alternatively, sex may be a better predictor of fat stores than morphological features. Unlike most piscivorous Caribbean fish, lionfish do not spawn once or twice a year. Instead, studies suggest that lionfish reproduce during all seasons (8) and may be capable of reproducing every four days (3). Thus, if sex is a better predictor of fat than morphology, we would expect females to have less fat than males due to allocation of energy to reproduction instead of growth.

Methods

On 1 March 2012, lionfish (n = 41) were culled at the Rock House Bay dive site off Little Cayman Island. The fish were speared by divers at a depth of approximately 55 feet. On 2 March 2012, additional lionfish (n = 4) were obtained at approximately the same depth from the Locher's dive site off Little Cayman.

On 2-3 March 2012, we dissected the lionfish, measuring mass, total length, gape height, gape width and pectoral fin length. Total length (TL) was measured as the distance from the front of the mouth to the end of the caudal fin. Gape length and width were measured from the inside edges of the mouth. Pectoral fin length (PFL) was measured from the base of the fin to its longest point. Fish mass was measured

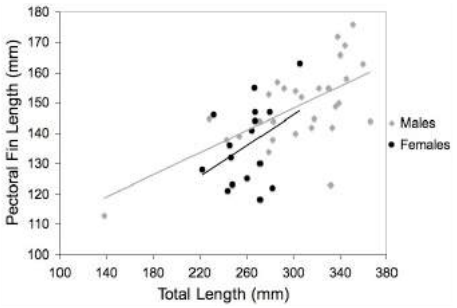

Figure 2: Pectoral fin length significantly increases with total length for males but not for females.

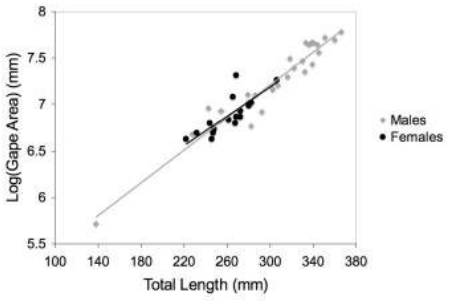

Figure 3: Gape area significantly increases with total length in both males and females.

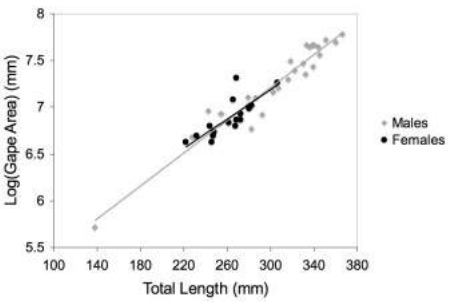

Figure 4: Fat mass significantly increases with total length for males but not for females.

to the nearest 0.1 gram using an OHaus Explorer balance. Gape area (GA) was obtained by multiplying gape height and gape width. We identified each lionfish as male or female based on observation of the gonads and removed the internal organs, including the intestines, liver and all fat (stomachs were removed separately). We cut out the lobes of fat from the rest of the organs and weighed the fat to a precision of 0.0001 grams using an OHaus Adventurer balance.

Statistical Analyses

Fat mass was square root transformed and GA was log transformed for normality. A multiple regression was used to determine which morphological characteristics (PFL, GA, TL, or sex) best predicted fat mass. To analyze various pairwise relationships, we regressed TL on PFL, GA, and fat mass, separately for male (n = 29) and female (n=16) lionfish.

To account for the effect of fish length on PFL, GA, and fat mass, we took the residuals of each of the regressions mentioned above regardless of statistical significance. For the remainder of this paper, we will refer to these residuals as relative PFL, relative GA, and relative fat mass. We performed two linear regressions with relative PFL and relative GA as predictors of relative fat mass. These regressions were performed separately for males and females. We also calculated residuals of fat mass by length regardless of sex and performed a t-test to determine if this relative fat mass differed between males and females. All statistical analyses were performed using JMP 9 software (SAS Institute, Cary, NC).

Results

The mean TL was 304 ± 8.8 mm for males and 261.3 ± 5.2 mm for females (mean ± 1 S.E.). TL ranged from 138 to 366 mm for males and from 222 to 306 mm for females. Since lionfish reach sexual maturity at lengths of 100 mm for males and 180 mm for females (9), all lionfish included in our study were adults.

The multiple regression analysis indicated that sex was the only significant predictor of fat mass ($t = -2.97$, $df = 40$, $P = 0.005$). None of the other main effects significantly predicted fat mass (TL: $t = 1.70$, $df = 40$, $P = 0.098$; GA: $t = -0.60$, $df = 40$, $P = 0.554$; PFL: $t = 1.58$, $df = 40$, $P = 0.123$).

For univariate analyses, PFL significantly increased with TL for males ($r^2 = 0.40$, $df = 27$, $P < 0.001$, Fig. 2) but not for females ($r^2 = 0.15$, $df = 14$, $P = 0.132$, Fig. 2). The slope of this regression for males ($m=0.18$) was less than 1. GA significantly increased with TL for both males and females ($r^2 = 0.93$, $df = 27$, $P < 0.001$; $r^2 = 0.62$, $df = 14$, $P < 0.001$, respectively; Fig. 3). The slope of these regressions for both males ($m = 0.009$) and females ($m = 0.008$) was less than 1. Fat mass significantly increased with TL for males ($r^2 = 0.41$, $df = 27$, $P < 0.001$, Fig. 4), but not for females ($r^2 = 0.01$, $df = 14$, $P = 0.7278$, Fig. 4). The slope of this regression for males ($m = 0.01$) was less than 1.

Relative PFL did not significantly predict relative fat mass for either males ($r^2 = 0.06$, $df = 27$, $P = 0.209$) or females ($r^2 = 0.11$, $df = 14$, $P = 0.1995$). Relative GA did not significantly predict relative fat mass for either males ($r^2 = 0.03$, $df = 27$, $P = 0.367$) or females ($r^2 = 0.05$, $df = 14$, $P = 0.416$). Relative fat mass regardless of sex was significantly greater in males than females ($t = 5.06$, $df = 40.1$, $P < 0.001$).

Discussion

Our results indicate significant differences in growth allometries between male and female lionfish. However, since the slopes of all allometric relationships were less than 1 or not significantly different from 0, smaller fish, regardless of sex, have longer pectoral fins, larger mouths, and more fat stores relative to their length. This suggests either that shorter lionfish may be compensating for their small size, or that shorter lionfish have been selected to have larger feeding features that could increase their feeding success. It is not known whether their piscivorous competitors (such as groupers, jacks, and snappers) exhibit similar allometric scaling of morphological features that are important for feeding. If lionfish are the only reef piscivores to display these compensatory patterns, shorter lionfish may be able to use their relatively longer pectoral fins and larger mouths to grow at a faster rate than their competitors.

Despite this potential compensatory mechanism, the fact that lionfish of both sexes with relatively longer pectoral fins and larger mouths do not have relatively more fat suggests that these morphological characteristics may be less important to feeding success than we had hypothesized. Feeding success could depend more on diet or behavioral adaptations than on morphological features. Since small lionfish primarily eat crustaceans and large lionfish are primarily piscivores (5), diet may affect fat stores in differently sized lionfish. Also, predation pressure may play a greater role than feeding success in selecting for relatively longer pectoral fins in shorter lionfish. Alternatively, prey may not be limiting lionfish in the Western Atlantic. A lack of interspecific competition for food could explain why lionfish with relatively longer pectoral fins and larger mouths do not have more fat than their less well-endowed conspecifics.

Fat stores may not be a good indicator of feeding success in lionfish and could be influenced more by energy allocation than by feeding success. The fact that TL does not predict PFL or fat mass in females suggests that female lionfish are allocating energy differently than males. Females may switch from investing energy in somatic growth and fat storage to investing

in reproduction once they reach sexual maturity, as occurs seasonally in other fish species that spawn once or twice a year (10). Lionfish reproduction is not well studied, but it is estimated that lionfish can produce between 20,000 and 30,000 eggs as often as every 4 days, year-round (3). This would require a relatively constant energy allocation to egg production in females, which would explain why females have significantly lower fat stores than males.

Given the fitness trade-off between investing in reproduction and survival, it is surprising that female lionfish do not face extremely high mortality in exchange for allocating so much energy towards reproduction. Release from predation, disease, and parasites in the Western Atlantic post-introduction could allow female lionfish to invest high amounts of energy into reproduction without incurring survival costs (6).

Feeding ecology and reproductive success are vital components in understanding how non-native species invade certain ecosystems. Compensatory allometry of morphological features in smaller size classes could give lionfish a competitive advantage over other coral reef predators, contributing to their success as invaders. The apparent switch in energy allocation from growth and fat stores to reproduction in adult females warrants future studies including both juveniles and adults. In female lionfish, the apparent intense energy allocation into reproduction without decreased survival likely contributes to the incredible success of lionfish as an invasive species in the Caribbean. Future studies should investigate the trade-off between reproduction and survival in lionfish in their native environment to see how it compares to Western Atlantic populations. The combination of abnormally high reproductive success with morphological adaptations that could give smaller lionfish a feeding advantage over other reef piscivores may play a crucial role in the invasive success of lionfish in the Caribbean.

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References

1. J. T. Carlton, J. B. Geller, "Ecological roulette: the global transport of nonindigenous marine organisms," *Science* **261**, 78-82 (1993).
2. A. N. Cohen, J. T. Carlton, "Accelerating invasion rate in a highly invaded estuary," *Science* **279**, 555-557 (1998).
3. J. A. Morris, "The biology and ecology of invasive indopacific lionfish." Ph.D. dissertation. North Carolina State University, Raleigh, NC. 168p. (2009).
4. P. E. Whitfield, T. Gardner, S. P. Vives, M. R. Gilligan, W. R. Courtenay, G. C. Ray, J. A. Hare, "Biological invasion of the Indo-Pacific lionfish *Pterois volitans* along the Atlantic coast of North America" *Marine Ecol-Prog. Ser.* **235**, 289-297 (2002).
5. J. A. Morris, J. L. Atkins, "Feeding ecology of invasive lionfish (*Pterois volitans*) in the Bahamian archipelago," *Environ. Biol. Fish.* **86**, 389-398 (2009).
6. R. Ruiz-Carus, R. E. Matheson, D. E. Roberts, P. E. Whitfield, "The western Pacific red lionfish, *Pterois volitans* (Scorpaenidae), in Florida: Evidence for reproduction and parasitism in the first exotic marine fish established in state waters" *Biol. Conserv.* **128**, 384-390 (2006).
7. M. A. Albins, P. J. Lyons, "Invasive red lionfish *Pterois volitans* blow directed jets of water at prey fish," *Marine Ecol-Prog. Ser.* **448**, 1-5 (2012).
8. J. A. Morris, J. L. Akins, A. Barse, D. Cerino, D. W. Freshwater, S. J. Green, R. C. Munoz, C. Paris, P. E. Whitfield, "Biology and Ecology of the Invasive Lionfishes, *Pterois miles* and *Pterois volitans*," Proceedings of the 61st Gulf and Caribbean Fisheries Institute (2009).
9. J. A. Morris, P. E. Whitfield, "Biology, ecology, control and management of the invasive Indo-Pacific lionfish: an updated integrated assessment," NOAA Technical Memorandum NOS NCCOS 99 (2009).
10. D. N. Reznick, B. Braun. Fat cycling in the mosquitofish (*Gambusia affinis*): fat storage as a reproductive adaptation, *Oecologia* **73**, 401-413 (1987).
11. M. A. Albins, P. J. Lyons, "Invasive red lionfish *Pterois volitans* blow directed jets of water at prey fish" *Marine Ecol-Prog. Ser.* **448**: 1-5 (2012).

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1st Place: Neuroscience and the Law

McDonogh School, Owings Mills, MD

CHRISTIAN NAKAZAWA, 12TH GRADE

Over the past two decades, advances in brain-imaging technology have allowed neuroscientists to investigate the once inscrutable human brain in greater detail than ever before. Cognitive neuroscientists' growing understanding of the complicated mechanisms of the brain, aided by increasingly sophisticated brain-imaging tools, has brought into question the extent to which we control our behavior, and the extent to which it is determined by the physical structure of our brains. While this question promises to inform a large range of disciplines in science and medicine, one area where it has already been brought to bear with profound implications is in the emerging field of neurolaw. By introducing new perspectives regarding how responsible criminals really are for their actions, neurolaw has begun to change the criminal justice system within the United States. Neuroscience also holds the promise of changing the judicial system further through neuropredictive technologies, which could assess the likelihood that a criminal would commit a crime in the future, and fMRI-based lie detection, which could be used to determine whether a defendant or a witness is telling the truth. Finally, recent findings in neuroscience could challenge traditional legal assumptions of free will and the very foundations of the judicial system itself.

On March 30th, 1981, John W. Hinckley, Jr. shot President Ronald Reagan in an attempt to assassinate him. In the ensuing legal case, United States of America v. John W. Hinckley, Jr., the defense argued that Hinckley was not responsible for the attack on the grounds that he was schizophrenic (1). The defense introduced computer-assisted tomography (CAT) scans of Hinckley's brain that they argued showed evidence of schizophrenia in the form of permanent brain shrinkage. Hinckley was found not guilty by reason of insanity (NGRI). The Hinckley case, which was the first time brain-imaging technology appeared within a United States court, marked the beginning of a new marriage between neuroscience and law.

Since then, both brain-imaging technologies and neuroscientists' knowledge of the brain have improved significantly. CAT scans of the brain have been superseded by more advanced technologies such as function magnetic resonance imaging (fMRI). Neuroscientists can now link specific regions of the brain to the control of certain behaviors. These findings have radical implications for the criminal justice system within America because they raise questions of how responsible criminals really are for their actions.

For example, studies by Joshua Greene and other neuroscientists at Princeton University have shown that regions of the frontal and parietal cortexes are active in particular types of moral decision-making (2-3). Suppose that fMRI scans reveal abnormalities in those regions of a murderer's brain. Should the murderer be found NGRI on the grounds that he cannot tell right from wrong? Or, consider a 2007 study suggesting that certain regions of the prefrontal cortex are involved in forming intentions to act (4). Should criminals with defects in this area be committed to mental institutions instead of being incarcerated? It is easy to see how findings such as these could change how the law views criminal responsibility. In fact, this is already is beginning to happen. In 2009, rapist and serial killer Brian Dugan was tried for the death penalty after pleading guilty to the 1983 rape and murder of a ten year-old girl (5). The defense introduced testimony from a University of New Mexico neuroscientist who said that he believed that fMRI scans of Dugan's showed that Dugan had suffered from psychopathy from birth and that Dugan's mental illness may have caused him to commit the crime. Dugan's case was the first time that a court had accepted fMRI scans as evidence.

However, some argue that, at present, testimony including fMRI evidence should not be taken into consideration by courts (6-7). Sinnott-Armstrong *et al.* claim that fMRI scans showing abnormalities in the brain are not sufficient to be used as evidence for reduced sentencing or NGRI (6). According to a paper published by Sinnott-Armstrong *et al.*, because individual brains are so different from one another, most people will have fMRI scans that differ from the group averages used as baselines in studies. Additionally, Sinnott-Armstrong argues that even highly accurate fMRI machines are prone to large numbers of false positives:

"…consider a population of 10,000 with a 1% base rate of a functional abnormality that leads to murder. […] That means that 100 people in the population have the relevant functional abnormality and 9,900 do not. If an fMRI test for this functional abnormality has 95% specificity, then it will still test positive in 5% of the 9900 who lack that abnormality, which is 495 false alarms – 495 people who test positive but do not really have the relevant functional abnormality."

Sinnott-Armstrong also remarks that no causative link has been demonstrated between abnormal fMRI scans and behavior, only correlative ones. Finally, the paper notes that just because impairment of the brain enables a criminal impulse that does not mean that a defendant cannot ignore that impulse.

Scientists' knowledge of what causes brain defects and mental states that are linked to criminal activity is also improving. Recent studies have shown a correlation between adverse experiences in childhood and altered brain function as an adult (8-10). The 1995-96 Adverse Childhood Experiences (ACE) Study examined the childhoods of 9,508 adults and assigned them scores based on the extent to which they had undergone "adverse childhood experiences," including being subjected to physical, verbal, or sexual abuse; witnessing domestic violence; having parents who were divorced, alcoholic, addicted to drugs, incarcerated, or suicidal; and living in poverty (11). The ACE Study and subsequent studies found that adults with higher ACE Scores were, among other things, more likely to have attempted suicide, engage in sexually risky behaviors, be addicted to tobacco, alcohol, or other substances, and suffer from depression, schizophrenia, or other mental illnesses (11). In 2006, researchers including Vincent J. Felitti and Robert F. Anda, two of

the researchers who conducted the original ACE Study, found that adults with higher ACE Scores overwhelmingly demonstrated "impairment in multiple brain structures and functions" including the amygdala, the hippocampus, and the prefrontal cortex, suggesting that these abnormalities are behind the aberrant behavior of people with high ACE Scores (8). Such research on the causes of brain defects may soon play a role in how judges and juries determine the culpability of criminals. It may also play a part in the actual treatment of criminals, notes leading neuroscientist and co-director of the MacArthur Foundation Law and Neuroscience Project Michael Gazzaniga (12). "The goal" he says, "is to understand abnormal states [of people with brain defects] and attempt to design therapies and other interventions that might lead them to a so-called normal status" (12).

Neuroscience could also inform the criminal justice system by assessing the likelihood that criminals will recidivate by committing violent crimes in the future, or what Nadelhoffer *et al.* term "neuropredicting" (13). Nadelhoffer *et al.* argue that increasingly sophisticated methods of data collection, e.g. the "neural intermediate phenotype strategy" used to collect information about how genes affect brain function, and analysis, e.g. the multi-voxel pattern analysis technique used to interpret fMRI scans, combined with researchers' growing understanding of the brain, are making neuroprediction progressively more feasible. Nadelhoffer *et al.* also raise several interesting questions regarding the legality and morality of neuroprediction. Would nonconsensual neuroprediction be in violation of the Fourth Amendment by constituting an unreasonable and overly intrusive search? Would it be considered a violation of the Fifth Amendment on the grounds that it forces a person to give witness against his or her self? What if neuroprediction was used not just on criminals but also on civilians? Could we force individuals who were determined to have a high risk of committing violent crime in the future to undergo therapy or even institutionalize them before they broke the law? These are the types of questions that will likely continue to arise as neuroscience's influence upon our society grows.

A more direct way in which neuroscience could affect the legal system is through fMRI-based lie-detection. In laboratory settings, scientists have been able to use fMRI to detect lies with upwards of ninety-percent accuracy, causing many to consider whether fMRI might be employed as a form of lie-detection in court (14). To date, no United States court has allowed fMRI scans to be used legally as a form of lie-detection (15). Most recently, in August, a Maryland judge ruled that lie-detection using fMRI would not be allowed as evidence in the case of Gary Smith, a former Army Ranger who allegedly killed his roommate (15). However, in 2001, an Iowa court allowed the use of electroencephalography (EEG) based lie detection (6). Currently, the general attitude of the neuroscience community toward fMRI-based lie-detection seems to be that it should not be admitted in court due to the fact that it has not proven to be accurate enough in real-world (as opposed to laboratory) settings (16-19). However, University of Virginia School of Law professor Fred Schauer argues that although the accuracy of fMRI-based lie-detection is not sufficient enough to be used as evidence in the conviction of criminals, it is sufficient to raise the possibility that a defendant is innocent due to the presence of reasonable doubt (19).

Neuroscience's recent engagement with law over the question of how responsible we are for our actions has spilled into the age-old debate over the existence of free will. Dartmouth College philosopher and neuroscientist Adina Roskies argues that while neuroscience can provide evidence that our brains are deterministic, it cannot provide definitive proof for the absence of free will (20). New findings in neuroscience, Roskies says, are likely to change only how people view the existence of free will. Greene and Cohen disagree and argue that cognitive neuroscience will increasingly show that we are purely nature and nurture (21). Greene and Cohen contend that as the public begins to realize that "the combined effects of genes and environment determine all of our actions," the criminal justice system will change from a retributive one that seeks to punish lawbreakers to a restorative one that seeks to heal not only the damage caused by criminals, but also the criminals themselves.

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References

1. S. Taylor, Jr., CAT scans said to show shrunken Hinckley Brain. The New York Times, 2 June, A1 (1981).
2. J. D. Greene, R. B. Sommerville, L. E. Nystrom, J. M. Darley, J. D. Cohen, "An fMRI Investigation of Emotional Engagement in Moral Judgment," *Science* **293**, 2105-2108 (2001).
3. J. D. Greene, L. E. Nystrom, A. D. Engell, J. M. Darley, J. D. Cohen, "The Neural Bases of Cognitive Conflict and Control in Moral Judgment," *Neuron* **44**, 389-400 (2004).
4. J. Haynes *et al.*, Reading Hidden Intentions in the Human Brain. *Curr. Biol.* **17**, 323-328 (2007).
5. V. Hughes, "Science in court: Head case," *Nature* **464**, 340-342 (2010).
6. W. Sinnott-Armstrong, A. Roskies, T. Brown, E. Murphy, "Brain Images as Legal Evidence," *Episteme* **5**, 359-373 (2008).
7. S. Morse, "Brain Overclaim Syndrome and Criminal Responsibility: A Diagnostic Note" *Ohio State Journal of Criminal Law*, **3**, 397-412 (2006).
8. R. F. Anda *et al.*, "The enduring effects of abuse and related adverse experiences in childhood," *Eur. Arch. Psy. Clin. N.* **265**, 174-186 (2006).
9. M. H. Teicher, C. M. Anderson, A. Polcan, "Childhood maltreatment is associated with reduced volume of the hippocampal subfields CA3, dentate gyrus, and subiculum," *Proc. Natl. Acad. Sci. U.S.A.* **109**, E563-E572 (2012).
10. M. M. Kishiyama, W. T. Boyce, A. M. Jimenez, L. M. Perry, R. T. Knight, "Socioeconomic Disparities Affect Prefrontal Function in Children," *J. Cogn. Neurosci.* **21**, 1106-1115 (2009).
11. V. J. Felitti *et al.*, "Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study," *Am. J. Prev. Med.* **14**, 245-258 (1998).
12. M. S. Gazzaniga, "The Law and Neuroscience," *Neuron* **60**, 412-15 (2008).
13. T. Nadelhoffer *et al.*, "Neuroprediction, Violence, and the Law: Setting the Stage," *Neuroethics* **5**, 67-99 (2012).
14. F. A. Kozel *et al.*, "Detecting Deception Using Functional Magnetic Resonance Imaging," *Biol. Psychiat.* **58**, 605-613 (2005).
15. M. Laris, "Debate on brain scans as lie detectors highlighted in Maryland murder trial," *The Washington Post*, 26 August, E2 (2012).
16. P. R. Wolpe, K. R. Foster, D. D. Langleben, "Emerging Neurotechnologies Lie-Detection: Promises and Perils," *Am. J. Bioethics* **5**, 39-49 (2005).
17. M. C. T. Lee *et al.*, "Lie detection by functional magnetic resonance imaging," *Hum. Brain Mapp*. **15**, 157-164 (2002).
18. C. Davatzikos, K. Ruparel, Y. Fan, D. Shen, M. Acharyya, "Classifying spatial patterns of brain activity with machine learning methods: application to lie detection," *Neuroimage* **28**, 663-668 (2005).
19. F. Schauer, "Can Bad Science be Good Evidence: Neuroscience, Lie-Detection, and Beyond" *Cornell Law Rev.* **95**, 1191-1219 (2010).
20. A. Roskies, "Neuroscientific challenges to free will and responsibility," *Trends Cogn. Sci.* **10**, 419-423 (2006).
21. J. D. Greene, J. D. Cohen, "For the law, neuroscience changes nothing and everything." *Philos. T. R. Soc. Lon. B* **359**, 1775-1785 (2004).

2nd Place: Humpty Dumpty without the King's Men

The Hockaday School, Dallas, TX

SHREYA AHUJA, 11TH GRADE

Humpty Dumpty sat on a wall.
Humpty Dumpty had a great fall.
And all the king's horses and all the king's men
Couldn't put Humpty together again.
~Mother Goose

Equating the human brain to an anthropomorphic egg from a children's nursery rhyme may seem odd, but the comparison is apt for victims of traumatic brain injury (TBI). Like Humpty Dumpty, who fell and shattered into millions of pieces, these patients often suffer widespread damage across the brain; like Humpty Dumpty, who could never be put back together again, those who have suffered trauma to the head sustain lifelong physical, cognitive, and psychosocial impairments. There remains, however, one fundamental distinction between the two: all of the king's horses and all of the king's men tried to save the one and only Humpty Dumpty. It was a valiant and commendable effort. The same cannot be said about the treatment of 1.7 million annual TBI patients in the United States (1). People are five times more likely to incur a traumatic brain injury than multiple sclerosis, spinal cord injury, HIV/AIDs, and breast cancer combined, and yet no army fights for them or attempts to piece them back together (2). These patients are often forced to patch their lives on their own. The treatment of traumatic brain injuries is a profound public health concern, and a mounting one at that. From 2002 to 2006, TBI-related ER visits increased by 46%, hospitalizations increased by 34%, and deaths increased by 27% (3). The characteristics uniquely attributed to traumatic brain injuries that research, funding, and social acceptance for these patients is limited.

TBI patients share only one similarity—their status as TBI patients; barring that, they vary across the board in cause, severity, diagnosis, and treatment, making it a grueling task to research their heterogeneous condition. Traumatic brain injuries stem from motor vehicle accidents, falls, assaults, and impact-related events such as sports and war injuries, each of which generate a range of mild to severe behavioral and mental alterations, depending on the areas of the brain that are injured. Since the phrase "traumatic brain injury" functions as an overarching label for a diverse patient population, grouping together all types of brain damage that occur in this manner, symptoms exhibited by TBI patients are often times extensive yet undetectable. They face many impairments, including those in memory, decision making, planning, sequencing, judgment, attention, communication, literary skills, thought processing speed, problem solving skills, organization, self-perception, thought flexibility, safety awareness, and/or new learning (2). However, neuroimaging and neuropsychological evaluations possess considerable limitations in the diagnostic sensitivity and specificity necessary for such distinct and expansive incapacities. Executive function (e.g., planning, decision-making) deficits are difficult to identify with standardized tests alone; in addition, patients often perform with pronounced inconsistency due to neurologic, emotional, and contextual factors, ensuring the difficulty of interpreting test results at face value. Raising the already trying challenge of treating and researching these patients, the recovery process prolonged but unpredictable, with patients making neurological improvements during the initial weeks, months, and even years following the injury. Thus, assessments completed early on in recovery many not be accurate of the individual's strengths and weaknesses. Take two hypothetical teenage boys who were in car accidents, and whose injuries look identical on paper—their brain scans show the same site of injury—but one might recover well enough to go to college and have meaningful relationships, while the other won't (4). It's hard to explain why, except that each case is different—each injury is different and each brain is different. In this way, the expression "traumatic brain injury" serves not as an identifier of a condition, but as a generalization of injuries too nonspecific for neurologists and other clinicians to successfully treat and research.

Effective treatment—short-term and long-term—is restricted by the lack of financial support from the government and private insurance agencies. For the 5.3 million Americans, around 2% of the nation's population, currently suffering from TBI, the government has meagerly spent roughly three dollars for the treatment and services of each brain injury survivor (2, 5). In their eyes, "cognitive deficits are not really considered medical problems," as exposed by Cathy Crimmins in *Where is the Mango Princess?*, a book that details the course of her husband's TBI and some of the ubiquitous struggles that TBI survivors and their family must face (6). TBI patients have invisible wounds, Crimmins says, and that is perhaps their greatest stumbling block. No one can see their injury; they appear normal from the exterior, therefore people assume that they must be so internally as well. Crimmins recounts her ongoing battle with her health maintenance organization (HMO) just to obtain minimal benefits for her husband Alan, who was run over by a speedboat in a boating accident at a lake. Not only did the insurance company deny her an air ambulance to transport her husband from Canada to the United States after his injury, claiming "[they] were not so sure [her] husband's condition warrant[ed] an air ambulance," but they also refused him more than three weeks in rehabilitation when his injury required at least three months of treatment (6). The HMO's sole concern was that Alan could now walk around independently, not realizing that he was still inept at behaving appropriately, making sense in conversations, and handling stress or excitement without becoming agitated. Crimmins often times found herself wishing that there was a visual aspect to her husband's injury like a cast or crutches so that people could see his impairment, and not voice statements such as "gee, he doesn't look that bad" (6). Many might argue that her experience was an exception, but it is clear that an absolute

disregard for cognitive impairments in the TBI patient population as a whole is an ongoing trend in today's society. Those who cannot afford state-of-the-art rehabilitation centers cannot count on support from Medicare, Medicaid, or insurers. While these programs may cover brain surgeries and intensive care necessary to save the lives of such patients, they consistently skimp on benefits for rehabilitation programs that would allow patients to relearn abilities destroyed by brain trauma. In fact, research shows that as the demand for medical care decreases post injury, the demand for nonmedical services and support spikes immediately after the patient's discharge, pending through the time in their lives when insurance coverage expires and they attempt to integrate into the community, up until the time of death.

Besides being "invisible" to observers, TBI is a difficult condition to garner support for in the community; rather than invoking sympathy, it frequently repels societal acceptance. TBI patients have been known to "indulg[e] in the grossest profanity (which was not previously [their] custom)." Upon the onset of her husband's disease, Crimmins describes her husband as "mean and all nasty like," referring to him as "another Alan." For this same reason, TBI survivors and their spouses have a high divorce rate: 75% (6). The TBI patients' inappropriate behavior and unremitting tempers, which people often forget are not voluntary actions but rather a construction of their injury, expel them as outcasts in society as well as in their homes. Few care to fund or research or foster what they perceive as a vulgar population of patients; few care to spread social awareness about them either. Instead, the majority of TBI survivors, especially war veterans, are cast aside, and they often struggle to assimilate back into society (4). As particularly high-functioning individuals with TBI attempt to resume their usual daily activities, the environment places increasing demands upon them. Occasionally, a TBI survivor returns to the workplace. At first, coworkers celebrate the return of their colleague who has overcome a terrible accident and survived in what Crimmins dubs the "halo effect." They may even cover for him by helping him out with his extra workload so as to ease him back into the routine. "Then, after a few months, the changes in his short term memory and ability to juggle projects or his weird penchant for cornering them at the coffee machine and telling them long, tedious stories begins to wear on them" (6). Essentially, coworkers get tired of mopping up after their collegue's mistakes and doing extra work because he is not up to speed. They have assumed, mistakenly, that he is all put back together again. After then, after a year or so, the once triumphant TBI patient will quit either in frustration or fatigue, or perhaps he'll be fired because of unfavorable evaluations. "Case studies of brain-injured people who try to return to work without help chronicle how those workers often lose their jobs years down the road, and by that time no one really attributes it to the brain injury because they think all that was over a long time ago" (6). What people don't realize, though, is that the TBI patient is a patient for life.

The characteristics inherent to traumatic brain injury condemned those suffering from the condition to a lifetime of difficulties. Not only is TBI complicated to diagnose and treat, but rehabilitation is not adequately funded. Even if patients independently salvage enough of their old selves to consider rejoining the community, their TBI has socially ostracized them to the point of limited recovery. Society's approach toward and misunderstanding of TBI victims have condemned them to suffer alone. The leading cause of death and disability in the United States, affecting people of all ages, races, ethnicities, and incomes, has but a minority of healthcare professionals championing for their cause. TBI patients are lost to all but a tiny, yet growing cluster of beacons for hope and change. Dr. Melissa Duff, one of such beacons, is a researcher at the University of Iowa Hospitals and Clinics. She founded the first national TBI patient registry in 2011 (4). In an interview, Dr. Duff says that the TBI registry is a mechanism to "know more about who's going to get better, how can we help them get better, and what we can do to put all brain-injury survivors on a better life trajectory" (4, 7). Her registry indicates the beginnings of interest in clinical research that translates into treatment and hope, beyond saving of lives of such patients. She is one of the king's men endeavoring to save the Humpty Dumpties of today. It is a valiant and commendable effort, but one that requires an entire army— more researchers, more funding, more awareness— to succeed.

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References

1. D.J. Thurman *et al.*, Traumatic brain injury in the United States: a report to Congress. CDC Injury Center (2001).
2. K. Croft, lecture presented at graduate program in Neuroscience, University of Iowa, IA. 11 October 2007.
3. Get the Stats on Traumatic Brain Injury in the United States. (CDC). http://www.cdc.gov/traumaticbraininjury/pdf/Bluebook_factsheet-a.pdf
4. M. Duff. Personal communication. July 15-27 2012. "Shreya, I'm writing to grant you permission to use any portion of our personal communications this summer in your essay for the DUJS International Science Essay Competition. Good luck, and let me know if I can provide any additional information."
5. J.A. Langlois *et al.*, The epidemiology and impact of traumatic brain injury: a brief overview. J Head Trauma Rehabilitation, 375-378 (2006).
6. C. Crimmins. Where is the Mango Princess? A Journey Back from Brain Injury. (Vintage Books, New York, 2000).
7. J. Riehl. UI Neuroscientists Establish Patient registry to study Traumatic Brain Injuries. (University of Iowa Graduate College Office of External Relations, Iowa, 2011) http://news-releases.uiowa.edu/2011/august/080111brain_injury_registry.html

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