DUJS | Dartmouth Undergraduate Journal of Science

FALL 2013 | VOL. XVI | NO. 1

PROTECTION AND SECURITY

Defining safety in the era of science

Cybersecurity: The Ethical Hacker

Faculty interview with Charles Palmer, IBM Research CTO

p. 3

Science as Narrative with Alan Alda

Telling the stories behind scientific discoveries

p. 6

Scientific Dilemmas: The Global Stage

Rethinking nuclear security and mental illnesss

p. 41

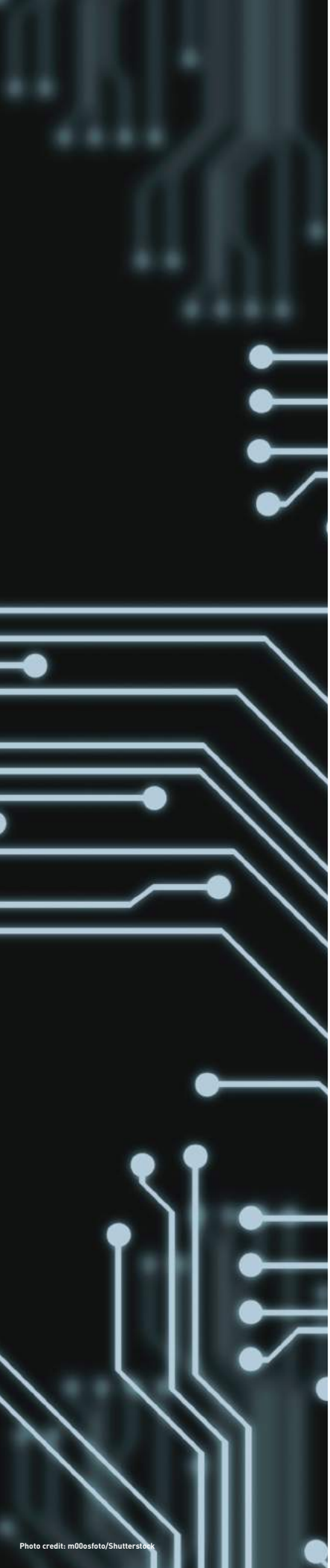


Photo credit: m00osfoto/Shutterstock

Note from the Editorial Board

Dear Reader,

Over the course of history, our perception of protection and security has evolved greatly. Beyond the simple evasion of physical injury, the concept of "safety" has adapted to a technologically-driven world. In the age of biomedicine and computers, we seek protection against pathogens and online identity theft – concerns far removed from those of our ancestors. Even the very protection against injury itself has expanded in the wake of increasingly destructive weapons technology. In light of this evolution, there is no doubt that science and technology intertwine intimately with protection and security, influencing what we wish to protect and to protect against.

In this issue of the *DUJS*, our articles explore "Protection and Security" in a variety of settings. Olivia Dahl reviews the intersection of neuroscience with criminology. Kristen Flint describes the various mechanisms by which contraceptives prevent pregnancy. Stephanie Alden discusses the advances in vaccination research. Annie (Yi) Sun details the technology that farmers employ to prevent citrus greening. John Steward addresses the issue of human enhancements, offering a unique interpretation of the issue's theme. Jessica Barfield highlights new brain-computer interface technologies that can rescue patients from locked-in syndrome. Julia Isaacson elucidates the protective properties of shear thickening fluid, and Shinri Kamei elaborates on the advances in anti-missile systems.

This issue's faculty interview features Charles Palmer, Ph.D., an Adjunct Professor of Computer Science at Dartmouth College and the Chief Technology Officer for Security and Privacy for IBM Research. Here, Dr. Palmer recounts his incredible career in cybersecurity, presenting an inside-story behind the development of ethical hacking. In addition to our faculty interview, *DUJS* is also proud to feature an interview with Alan Alda, the acclaimed actor, writer, and science advocate, who discusses his experience in promoting science communications through his institute, the Alan Alda Center for Communicating Science at Stony Brook University.

Finally, we are pleased to announce the winners of our second annual International Science Essay Competition. We received over 260 submissions from 20 countries and would like to congratulate all of the participants for their excellent work. Our first place winner, Tony Pan, from Lynbrook High School in San Jose, CA, wrote a winning entry on nuclear security. Our second place winner, Navya Dasari, from BASIS Scottsdale in Scottsdale, AZ, wrote an essay on mood disorders. The two runner ups were Sara Camilli from Biotechnology High School in Freehold, NJ, and Rachel Stanziola from MMI Preparatory School in Freeland, PA.

We would like to thank the Office of Undergraduate Admissions and Dean Maria Laskaris for once again bringing the *DUJS* and ISEC to high schools around the world; Jane Quigley, Head Librarian of the Kresge Physical Sciences Library, for her continued assistance in expanding our distribution; and Dr. Christiane Wolforth, the director of the Montgomery Fellows Program at Dartmouth, for arranging the interview with *DUJS* and Mr. Alda.

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

Sincerely,
The DUJS Editorial Board

DUJS
Hinman Box 6225
Dartmouth College
Hanover, NH 03755
(603) 646-8714
http://dujs.dartmouth.edu
dujs@dartmouth.edu

The Dartmouth Undergraduate Journal of Science *aims to increase scientific awareness within the Dartmouth community by providing an interdisciplinary forum for sharing undergraduate research and enriching scientific knowledge.*

EDITORIAL BOARD

President: Yoo Jung Kim '14
Editor-in-Chief: Rui Shu '15

Managing Editors: Steven Chen '15, Scott Gladstone '15, Aaron Koenig '14. Tessa Streeter '14
Assistant Editors: Shinri Kamei '16, Annie (Yi) Sun '16, Na Oh '16, Barry Chen '16
Design Editors: Jocelyn Shyong '16, Rebecca Xu '15
Web Development Team: Derek Racine '14, Shawn (Yifei) Xie '16
Director of Publicity: Carrie Wolf '15
Directors of Programming: Miguel Peña '16, Michael (Siyang) Li '16
Communications: Harrison Han '16
Essay Contest Directors: Josephine Coury '15, Rebecca Burten '16
Cartoon Artist: Jenny (Yuying) Liu '16

STAFF WRITERS

Abigail Chen '17
Alex Przeslawski '17
Ali Siddiqui '17
Alexandra Dalton '16
Clara Guo '17
Eric Tao '16
Esther Wu '16
Hirsh Elhence '17
James Howe VI '17
Jessica Barfield '16
John Steward '15
Jonathan Huang '17
Julia Isaacson '15
Kartikeya Menon '16
Katie Billings '16
Kristen Flint '14
Matthew Jin '17
Melvin King '16
Merritt Losert '17
Nancy Wu '16
Olivia Dahl '14
Pranav Vangala '17
Stephanie Alden '16
Yi He '17
Yvette Zou '16

DESIGN STAFF

Jocelyn Shyong '16
Rebecca Xu '15

ADVISORY BOARD

Alex Barnett - Mathematics
David Bucci - Neuroscience
Marcelo Gleiser - Physics/Astronomy
David Glueck - Chemistry
Carey Heckman - Philosophy
David Kotz - Computer Science
Richard Kremer - History
Maria Laskaris - Undergraduate Admissions
William Lotko - Engineering
Jane Quigley - Kresge Physical Sciences Library
Roger Sloboda - Biological Sciences
Leslie Sonder - Earth Sciences

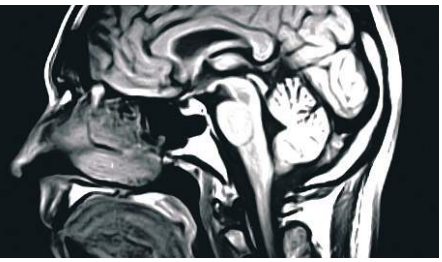
SPECIAL THANKS

Dean of Faculty
Associate Dean of Sciences
Thayer School of Engineering
Provost's Office
R.C. Brayshaw & Company
Undergraduate Admissions

Table of Contents

Faculty Spotlight: Charles Palmer **3**
Scott Gladstone '15

Spotlight: Alan Alda **6**
Shinri Kamei '16 and Rui Shu '15



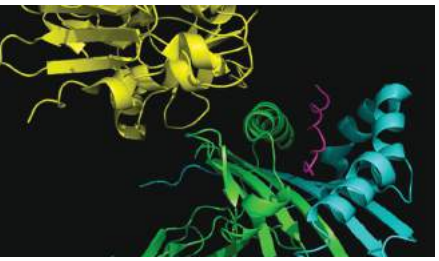
Neurocriminology: The Disease Behind the Crime **10**
Olivia Dahl '14

Contraception: Beyond the Pill **14**
Kristen Flint '14

Vaccines and the Immune System: The Ultimate Protection **18**
Stephanie Alden '16

Protecting the Orange **22**
Annie (Yi) Sun '16

Human Enhancement **25**
John Steward '15



Unlocking the Mind with Brain-Computer Interfaces **31**
Jessica Barfield '16

Liquid Body Armor **34**
Julia Isaacson '15

Countering Man-Portable Air-Defense Systems (MANPADS) **37**
Shinri Kamei '16

INTERNATIONAL SCIENCE ESSAY COMPETITION (ISEC) WINNERS

Nuclear Security and Nanotechnology **41**
Tony Pan

Next to Normal: Mood Disorders, Medicine, and Society **43**
Navya Dasari

BY SCOTT GLADSTONE

Faculty Spotlight: Charles Palmer

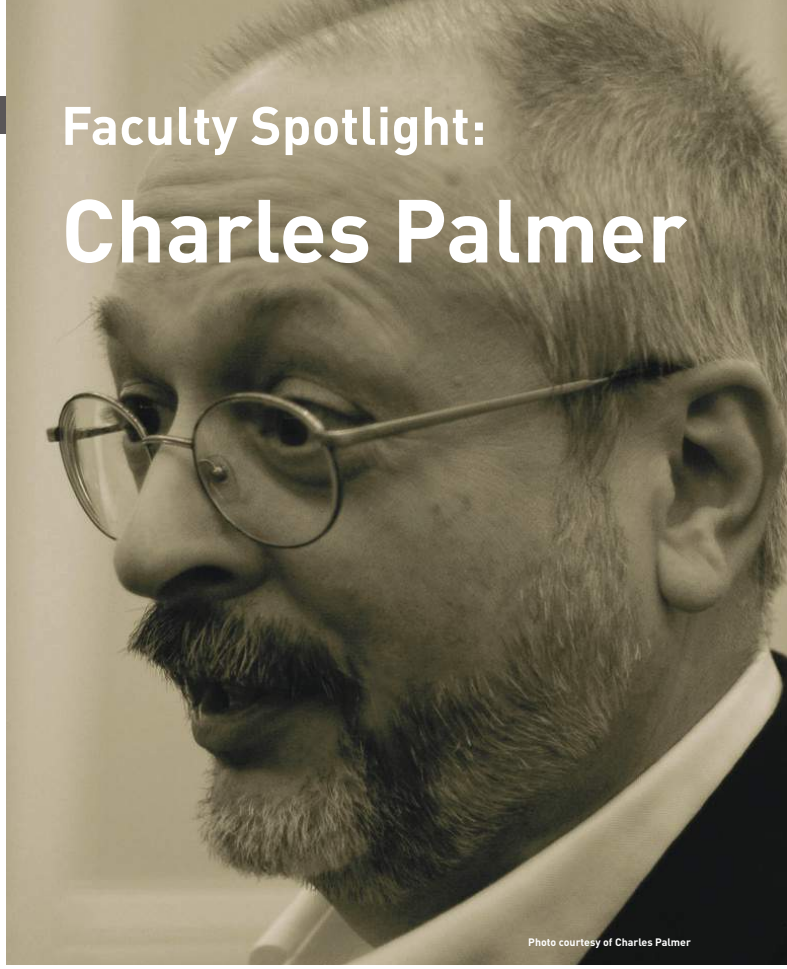


Photo courtesy of Charles Palmer

Introduction

Dr. Charles C. Palmer is an adjunct professor of Computer Science at Dartmouth College, CTO for Security and Privacy for IBM Research, and a member of several government advisory boards. Working in both industry and academia, Dr. Palmer focuses on special projects relating to security and privacy, unique customer challenges, and national security issues (1).

Dr. Palmer was the founding director of IBM's Institute for Advanced Security. Based in Washington, D.C., the Institute helps clients, academics, policymakers, and businesses understand the complex, multidisciplinary issues associated with system security (1). At Dartmouth, Dr. Palmer teaches courses titled Security and Privacy, Database Systems, and Software Design & Implementation to undergraduate and graduate students; he is also past Director of Research and Senior Technical Advisor to the Institute for Information Infrastructure Protection (I3P), which is managed by Dartmouth College (2).

Prior to taking on these roles, Dr. Palmer led the Security and Privacy departments at IBM's Thomas J. Watson Research Center for several years. He continues to work with those teams, assisting with IBM's products, services, and "ethical hacking" ventures. Dr. Palmer received a Ph.D. in Computer Science from Polytechnic University in Brooklyn, NY in 1994 (2). In an interview with the Dartmouth Undergraduate Journal of Science, Dr. Palmer describes his career trajectory and shares some of his thoughts on the current state of security.

On your first day of class teaching CS 55: Security & Privacy, you ask students to define security. How would you define security?

A simple way to describe it is "no surprises." The system does what you expect it to do, no more no less. And that system could be anything – your computer system at home or the automated check out machine at Home Depot.

Do you think that other people would say something different? What is the public's perception of security?

That's tricky. I think most people try to boil it down to their world. For example, if you're in a classified environment, security means that the secrets don't leave. If you're Amazon and you're worried about books, then it means that the secrets – the books – don't leave unless someone pays for them. Most people look at security as a context-specific thing.

And don't forget, the bad guys have security too. They look at it as, "Can I do this and not get caught?" Security is really where you stand. Physical security too – I can stand on the edge of that cliff and assume that the ground is not going to crumble, but at the end of the day, security is what you boil it up to be.

When did you first get started working in security?

I was actually in it for a long time and didn't know it. For example, you're a student and you need to get extra credit on an assignment, so you change the rules of the game…kind of like the Kobayashi Maru test posed to Captain Kirk at Starfleet Academy in the Star Trek series. It was a no-win situation that was supposed to test how he would react in such a situation, so he hacked into the system and changed the scenario so there was an answer. That's sort of how I got started – I didn't think of it as security. I noticed that someone didn't set up a system well and I could exploit it to somebody's advantage, sometimes to my whole class' and sometimes to mine. But I really got into it when IBM said to me, "Why don't you stop that theoretical network design stuff and build a team to go break into customers' systems, under a contract, and see what they did wrong?" Straight out of the movie Sneakers, that's what we started doing.

I've actually found a lot of people in security didn't start there, at least in my generation. Most of us didn't go to college for it; my crack team of ethical hackers at IBM included two computer science majors, a fine arts photography major, a physicist, and a high school graduate. And we 'won' 85% of the time, out of about 2000 gigs. 'Win' meaning that we were able to do more than the customer thought we could do. And the other times, either we were blocked or the customer was so terrified that they tried to change the game, effectively running down the hall ahead of us locking doors. We got to work on both electronic security and physical security, so it was a lot of fun.

You are a Professor in the Dartmouth Computer Science Department, CTO for Security and Privacy for IBM Research, a member of several government advisory boards, and an expert in the field of systems security. How do you feel about balancing research, work, and undergraduate teaching?

It's definitely a challenge. But the good news is that before I came to Dartmouth, I gave up management of my department at IBM because I wanted to get technical again. That allows me to come up here to Dartmouth, pursue teaching, and help to run a Consortium that was based at Dartmouth for a little while.

And now what I do for IBM is go down to Washington talking to customers, policymakers, and so on to help them understand security: what they are trying to do, what works, what won't, what can't…all that sort of thing.

What is "ethical hacking"? How did that come about? Was it IBM's idea?

So the customers actually drove it. They said, "We do want to do this Internet thing, it sounds way cool," but they had also heard about hackers, heard about break ins, heard about people on the inside doing things that they shouldn't – things like changing the price of a product for a friend so they could buy it cheaper. So one of the guys that I eventually hired, Wietse Venema, had written a paper with Dan Farmer titled "Improving the Security of Your System by Breaking Into it." They had done a lot of cool stuff, a bunch of defensive projects including a project called SATAN that was a system administrator tool to test system networks. And, of course, it was misunderstood (given the name and whatnot), but what the world didn't realize is that the bad guys already had tools like this.

So that kind of noise had already started and then the customers started flipping out. At large companies like IBM with big research divisions, we started getting hard problems from customers dealing with mainframes, among a bunch of other concerns. So the guys at the company came down to IBM Research. Of course, we had all read Venema's paper and we looked around and talked to our consultants, and we saw that there were lots of consultants who could help you set up a system securely, but there was no one trained to go in and see if they had actually done it right. So it just sort of made sense – we would do this "hacking for contract" or "hacking for hire" thing. Then someone else in IBM came up with the term "ethical hacking" and it all went on from there.


Image courtesy Charles Palmer

Now all of the big accounting firms, even individual companies, do this. The customers are real excited about it but also terrified. When we go in for an "ethical hack," they are basically handing us the keys to their company; if I can hack you and I tell someone what I did, then they can hack you too. The clients are worried about losing their intellectual property and losing their money, but their biggest concern is that "CNN Moment": They don't want word to get out that they have a problem. And the threat of that "CNN Moment" is profound – anything from changing a website background to orange for Halloween to displaying pornography when a user clicks on a product description. So the customers were ready for a solution.

At that point, we set up a contract. The terms for each company varied from "try anything you want, we're perfect" to "whatever you do, don't hit the 'T' system because it runs the trains." And then they started asking for physical tests: can you find the computer room in a business the size of Berry Library? Can you even get into the building? And then other customers just wanted to know internal things like "do we have wireless networks in this company?" Because, nowadays, anyone can go to Staples and buy a wireless router, sometimes our job was more of an audit where people wanted to know what was going on in their companies.

What does a conversation with a customer of an "ethnical hack" usually look like?

Our first two questions for a customer are always: what do you have and what is it worth to you? What are you protecting, and why? And if you think hard about that, they are very tough questions. These companies would much rather have IBM come in with their professional, trained "white hats" to tell them what they did wrong than have some other guy figure it out. The military has been doing this for years: they make two teams – a "blue team" sets up the defenses and a "red team" tries to break them. The idea has definitely been around.

Now, at the end of the process, when the customer is reflecting on what we've done, they would ask, "So we're secure now?" And we'd respond, "Well, at least for the next few minutes." And that's always the answer because people are involved – you never know what's going to happen. Recently, this type of work has moved much more toward long term, continuous analysis and evaluation, with much more monitoring than there used to be.

Shifting gears away from industry for a second, do you think that the public's view of security is more theatrical than we'd like it to be? Is there anything we can do about that?

Could our security, our personal security, be better? Sure! The biggest challenge we have is that we don't have a culture of security. People are more interested in features and functions than they are in securing their credit card. That decision is hard to believe, and we're getting better, but that's how it is.

We always used to pick on students and say thing like, "Company X is going to see what you put on Facebook." And maybe they will and maybe they won't. But what people put online is forever. I'd be more concerned about a future significant other or children seeing that stuff than an employer.

What are some of the most interesting or fun problems you've tackled during your career?

Certainly ethical hacking was the most fun ever, because you're really actively helping the customer realize just what they were doing. I guess the most fun things are the ones you can demonstrate. Demonstrating cryptography is not that much fun: "now you can read it, poof, now you can't – questions?" That's not real exciting, and it's very hard to prove stuff in that field. But there are plenty of other things that you can actually do to demonstrate how you can fix the security.

One student demonstrated a few years ago that if he took a flash bulb from his camera, held it close to his CPU, and at a certain point in the CPU's processing flashed the bulb, it affected the CPU to the point that he could make it do what he wanted. That's simplifying it a lot, but even so, where does it come from and how did he do that? It's not about breaking things always, but the real fun has been in showing customers how they could improve. I don't know if you watched "the Three Stooges", but the typical thing they do is to poke someone in the eyes. Well, when Curly learned to put his hand vertically between his eyes to protect himself, then Moe had to figure out how to hit him another way. We use that analogy a lot in the industry – we don't just show you how someone can poke you in the eyes, but also how you can protect yourself in the future. And when a customer realizes that it's both possible and not that bad, then you see their business blossom. They can benefit and truly see the economies of scale from it because the bulb finally went on – it's very gratifying. When you work with a customer, client, team member…and the light comes on: that's why I teach! When I see the students out there in my class, some are cross eyed tired and some are just like 'Argh I don't get this', but then I look around and see some students who perk up and I know "he's got it!" and "she's got it!" That's definitely the most fun. When I see someone understand that they can truly make something better by changing their hygiene, making a new password…that's really it.

How do industry and academia effectively work together to progress the state of security today?

Well, to start, industry goals vary wildly. Smaller companies may favor more of a "get it out" approach, even if products are not fully secure or don't completely work. However, that focus has pretty much changed over time. The larger, more established companies – IBM, HP, Microsoft – realize that every bug costs a lot, a lot more than it costs for testing. So these companies have gotten a clue and started worrying about things like brand and whether a customer will come back. That is what's going to determine the future of the company, as opposed to just features and functionality. The customer has to believe you when you say that a system is secure, especially when a history of integrity and security is what you've got to offer.

Now academia is different, but it has to be. It has to be open, encourage experimentation. And that's great. We need that. Where else could you do the stuff that some of the researchers here do? Not that it's illegal, but you need to be in an environment that can tolerate it. Some kinds of research you can't do in industry because it's too disruptive. If I want to test a new piece of software, the best thing that I can think of doing is give it to a bunch of students at a university because they will beat it to death. They may not be looking for security holes, but they will encounter way more bugs than the testers did because they are users. And these users, especially students, are unruly users. And that's good! Where else can you have a student do an experiment where the student walks around campus with a box of candy bars and says, "Tell me your password and I'll give you a candy bar,"? You don't do that at an industrial company or the government. Now granted, maybe students are a weird population, but it's still interesting and it's a great way to get a feel for that stuff.

"The key to security is the weakest link. The weakest link might be the network, the box on your desk, the people . . ."

Academia plays an extraordinarily important role in all of this. Companies are out there to make money for their shareholders, keep things going, etc. If there is a problem that is really hard, even industrial research organizations may not be allowed to work on it because it takes too long. The payoff may be 10 years or 17 years or an unknown amount of time in the future, especially with things like the "science of security." HP, IBM, or the government may look at things like that, but the people who will really investigate are the ones with the time and without the worry of quotas and selling: it's the academics. It's going to be an academic who has the time and the students to worry about these issues. If you think about this all as a "security ecosystem," the academics play a huge role because when you ask, "where did all of this stuff come from?" The answer: those guys.

What would you say to someone interested in pursuing a career in security, be it academic or in industry?

To be good at security, you have to have an interest in systems. Unless you want to go into something very specific like cryptography, you really need to have a "systems view," because the key to security is the weakest link. The weakest link might be the network, the box on your desk, the people – it can be any of that stuff. So that's what we try to do in CS 55: Security and Privacy. We take a step back and say, "Look at this whole thing. This whole thing implements that 'task.' Where are the problems?" There have been a lot of glorious hacks that were very simple and had nothing to do with hardware or software; they had to do with things like impersonating a UPS man, picking up a code book, or looking over someone's shoulder as they typed in a password.

There are lots of ways a system can be broken and we are trying to make it harder and harder, but it's never going to be done. Trying to understand all of the vulnerabilities and plug all of the holes: it can't be finished. So if someone wants to go into this, I would say study networking, operating systems, programming, sociology, policy – just about anything you can imagine is going to be related because this is a multidisciplinary science. You can't just be "Joe Firewall" anymore; that's not going to work. You're going to have to be much more than that to make a difference, and we kind of need you to!

References

1. Charles C. Palmer - IBM Research. (n.d.). *IBM Research, Researcher and Project Pages.* Retrieved October 3, 2013, from http://researcher.watson.ibm.com/researcher/view.php?person=us-ccpalmer

2. Charles C. Palmer. (n.d.). *Dartmouth Computer Science Department.* Retrieved October 1, 2013, from http://www.cs.dartmouth.edu/~ccpalmer/

Communicating Science with Alan Alda

Photo courtesy of Gavin Huang

BY SHINRI KAMEI AND RUI SHU

Introduction

Alan Alda is a director, writer, and widely-acclaimed actor. But to those in academia, he is also a Visiting Professor at the State University of New York at Stony Brook, an advisory board member for the Alan Alda Center for Communicating Science, and long-time advocate of scientific communication (1).

Over the course of his acting career, Mr. Alda has won various accolades, including six Emmy and six Golden Globe Awards for his portrayals in the hit series *M*A*S*H* and *The West Wing* (2). His occasional role as director and writer when on the set of *M*A*S*H* also won him three Directors Guild of America awards, establishing his excellence as actor, writer, and director (2).

Despite his incredible success in *M*A*S*H* and *The West Wing*, Mr. Alda would go on to assert that "best thing [he] ever did in front of a camera" was in fact his hosting of PBS' *Scientific American Frontiers* – because beyond his career in television and film, Mr. Alda is also driven by his lifelong interest in science (1). His involvement in *Scientific American Frontiers* provided him the unique opportunity to interview hundreds of scientists. From these interviews, Mr. Alda soon discovered that scientists are often unsuccessful in conveying their research to the public.

In order to bridge the gap between the scientific community and the public, Mr. Alda played a key role in the creation of the Alan Alda Center for Communicating Science and has led workshops to help scientists communicate science in a more effective manner (1). Because of his contributions to science, the Montgomery Fellows Program at Dartmouth invited him to campus. In an interview with the *Dartmouth Undergraduate Journal of Science*, Mr. Alda reflects on his experiences in promoting science communication and shares his thoughts on the impact of presenting scientific research as stories.

Can you talk a little bit about your work with *Scientific American Frontiers* and how you got into it?

Well, they just wrote me out of the blue

and asked me if I'd be interested in hosting. I thought that they probably meant would I do an on-camera introduction to the show and read the narration, which didn't interest me, because I wanted to talk to the scientists and learn from them, find out what their work was about. So I said I'm interested in doing it if I can talk to the scientists on camera, because then I knew that I could spend the whole day with them. So they took a chance on that because they knew that I wasn't a professional interviewer. That actually was what worked for the show. Because I was just a curious layperson, and I didn't give up until I understood what they were saying.

Why were you so curious about science to begin with? I understand that you read *Scientific American* from fairly early on.

Well, I've always been very curious. Once I started reading about science, it got obsessive, and I was more and more curious about what more there was to know. But it's very disorganized, my understanding of science, because I never studied it. It's just always an amazing, beautiful thing to read about. It's just like a hobby. But now, that interest has grown to something where I see I can be helpful to scientists in helping them communicate better.

In your lecture yesterday, you showed the video of the people in Long Island trying to answer questions about science. I was wondering if you had any ideas about how it might be best to communicate to people who probably aren't going to science lectures. How can we get them more informed about science?

One of the reasons I want to help scientists better communicate in their own voices is so they can go out to the public, so they can go on television, and so they can write pieces for magazines and newspapers – and speak in a language that people can understand. The more that science makes its way into the public consciousness, the more people will see it as part of our culture. It's not an alien thing. They really are on a blind date with it, and it's something that they don't know much about. They don't know if they can trust it. So we need to warm up that relationship and get people connected.

Why did you choose to collaborate with Stony Brook University?

I went around the country trying to interest the presidents of universities in starting a program for science education to include communication education. Stony Brook was the only one that was interested of the ones that I talked to – I didn't talk to many. Once we started to do the work there, we showed that it was helping scientists and that the time was well-spent. And we've seen a lot of other institutions getting interested in it. What we're now trying to promote is communication courses for credit, workshops where graduate students, post-docs, and even faculty members can work out to develop and improve their skills. No matter how good you are, you can always improve. I've been doing this for a while, and I've improved what I've been doing a great deal.

Are you teaching at their journalism school right now?

Yes, I'm called a visiting professor, but I don't have regular classes. Sort of a drive-by teacher. But I mainly do a lot of work like this visit to Dartmouth, where I do workshops, where I try to help spread the word. Mainly to demonstrate what it is that we're trying to do. Partly because I can't just describe how it works. It's one of those things that just has to be experienced. I've had a wonderful visit to Dartmouth. It's been very effective.

"The more that science makes its way into the public consciousness, the more people will see it as part of our culture."

What makes improving communication especially important in science? Why not do it for politics or law?

Yes, that would be a good idea. Everyone needs to communicate better. [Laughing] But I can only do two thousand things at once.

Especially with legal jargon.

In fact, there are websites that help you clean up your legal jargon. There are programs where people are encouraged to do that. I think we'll start with science, which is quite enough. Math is hard too. People just hold their heads when it comes to math. Math is very hard because none of it is in words. Almost none. At least a lot of science is in words. Although many of them are not common words.

Do you think there's potential for the center at Stony Brook to eventually grow to fields beyond just science?

No, no plan at the moment. We're very busy just trying to spread the word on science. Because our hope is to have affiliations and partnerships with universities all across the country that have programs like ours where we can show them what we've learned, and they can show us what they've learned. And we can spread that new knowledge about how to teach communication all over the country so that it can cross-pollinate itself. And I guess you know that we're going to be partnering

Photos courtesy of We hope. Availabel at Wikimedia Commons

Alan Alda received widespread attention and acclaim for his potrayal of Hawkeye Pierce on the show *M*A*S*H* (1972-1983), for which he won five Emmy awards.

with Dartmouth. We already had a meeting a couple of hours ago where we started to work out how we'll communicate with one another and how we'll set up our partnership. And I can't tell you how exciting this is for me. I mean, this is a magnificent institution, and we'll be trading really high-class ideas. I'm really looking forward to it. When you do a workshop, it's a lot like a lab. You develop ideas that you didn't know existed before – ideas to develop these new techniques and pass them on to others, to excite other universities' imaginations, and then to develop even newer, more effective techniques. We'll gather a lot more, we're really excited.

"You're telling the truth, but you're telling it in a way that people find interesting and exciting."

Someone mentioned during the lecture that with global warming, sometimes scientists only convey the why they believe it; he said that what makes it hard to start a serious debate about global warming is that not everyone can understand the how that scientist came to that result.

That's a good observation. The problem is you start getting into detail about your data and how you collect your data and analyze it. You got to find a way to distill that into chunks that they can follow, and that's an interesting problem. And without destroying the accuracy of it, you have to be accurate about what you say but make it comprehensible to people who haven't studied it. They're not ready for the raw data.

How you know is a very interesting thing. For instance – this is more important – if you think about how data is collected for global warming, there are some very interesting stories about that. People braving bad weather, people flying over glaciers. There are interesting stories about how they do that. I covered some of those stories for *Scientific American Frontiers*, and if you can think of ways to deal with the "how they know" as a story, you can find a way to make it accurate and interesting at the same time. That's the case for almost any science. Usually the facts aren't as interesting as the stories behind them if a person's hearing it for the first time without any training.

Do you think another potential issue then is that there can be information overload, that if we start creating interesting stories around every single person's perspective on global warming, people will be so overwhelmed by stories and information that it becomes hard to understand?

That could be, but so far we have very few stories. It'd be nice to hear some stories. You don't make something untrue by telling it as a story. It doesn't become fiction. You find the interesting, true elements that make it a story, and you tell it in that sequence. You're telling the truth, but you're telling it in a way that people find interesting and exciting. A story always has a hero who's trying to accomplish something against obstacles and either succeeds or fails. The hero gets a payoff, either a payoff of success or a payoff of tragic failure. And that's a story. That's the outline of every experiment. It's the outline of every discovery; any scientist's life tends to follow that path. If you pick out those elements, you can find yourself telling the story easily.

Do you think there's a risk of sensationalizing science information and people getting wrong information just because the media is trying to make it more interesting?

Of course that's a danger. And that's one reason why it's valuable for scientists to be such good communicators that they make sure that they tell their stories accurately, and make sure they're not misunderstood by people trying to pass on their work to a public that doesn't have their training. But there are a lot of really good science writers that don't do that. They're trained to tell the real story about the science. Sometimes, though, it's done in quick bites in evening news or they misinterpret it. But the more scientists can communicate in their own voice, the less sensationalism there is.

What exactly is the nature of the partnership between Dartmouth and your center at Stony Brook?

We're going to trade information. We can help with their own program and help them become a part of a larger network.

What other institutions are a part of that network?

The American Chemical Society is already

affiliated, the University of Cincinnati, and two or three others that are probably going to, but I shouldn't talk about them until it's official.

How did the partnership come about, then? Why Dartmouth?

As far as I know, from the work we've done here, people have come to our summer institute where we invite people from many universities. And the idea is for them to get a taste of our institute through three or four days and then decide if they want to go back to their university and start up a similar program. I think that's the beginning of the relationship. There may have even been interest before that.

Haven't you been to Dartmouth before for *Brains on Trail*?

Brains on Trial, and before that, *Scientific American Frontiers*. Maybe 20 years ago with Mike Gazzaniga, a neuroscientist.

You were up here before for an episode of *Scientific American Frontiers*?

Yes, I was interviewing a brain scientist called Michael Gazzaniga for a show called *Brains on Trial*. It showed for a couple of weeks on public television and it's on the web now.

There are many people on the news that are very resistant to science for religious reasons, such as people that don't believe in evolution. Do you think that more effective communication with science would help to bridge that gap a bit? Or do you think that the resistance is stemming from something other than lack of understanding?

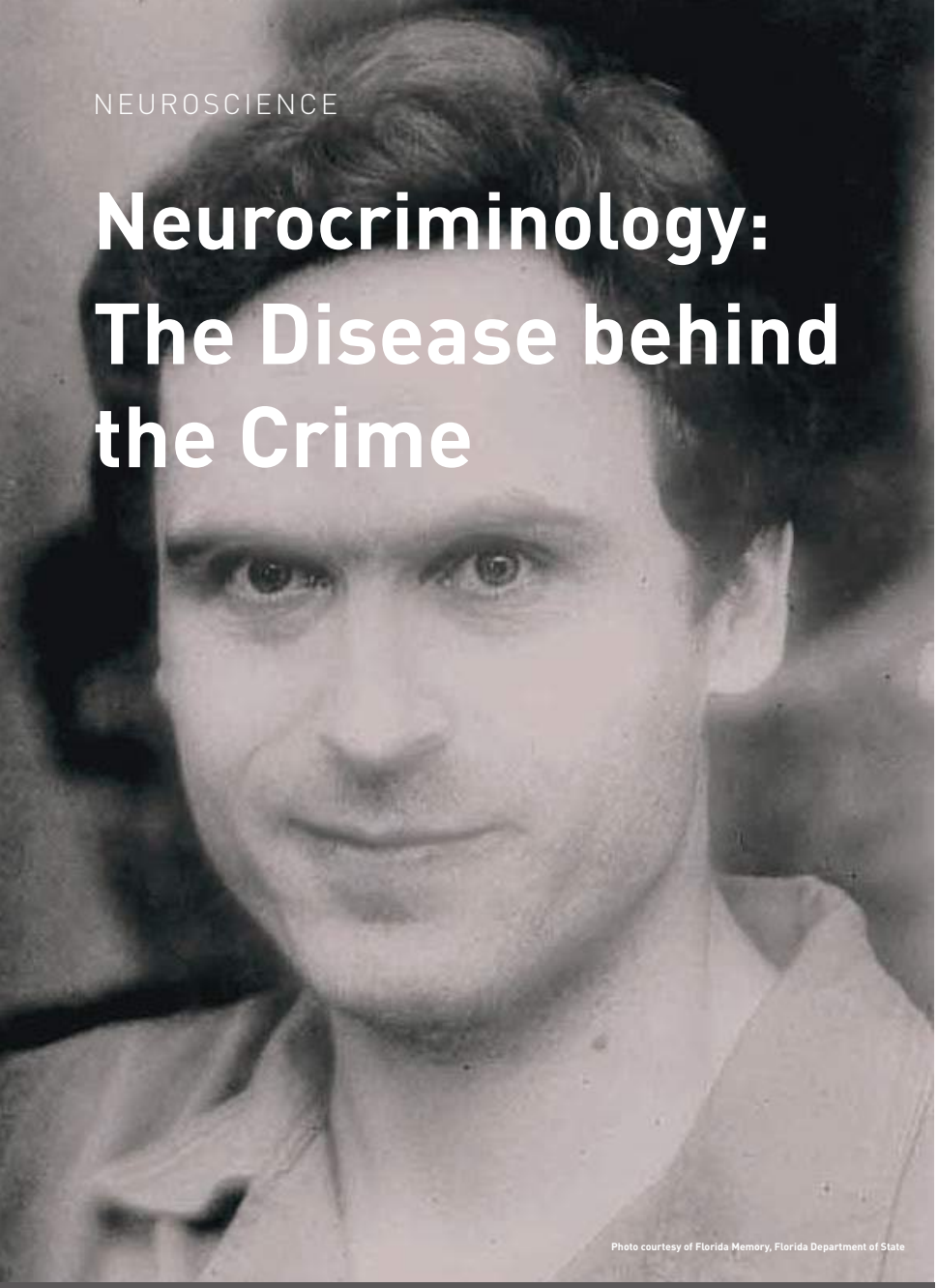
My guess is that good communication would help; the ability to communicate flexibly, not only in one way, would be helpful in getting around points of resistance that now seem insurmountable. And that's what this training does. It makes you very flexible and able to speak about your science in many different ways and get it to still be the same science. It's very helpful because it helps you be able to talk to many different audiences.

References

1. Alan Alda Center for Communicating Science. Alan Alda. Available at http://www.centerforcommunicatingscience.org/alan-alda-2/ (29 October 2013).
2. Alan Alda's Bio (2013). Available at http://www.alanalda.com/alan_alda_actor_bio.htm (29 October 2013).

Photo courtesy of Gavin Huang

Neurocriminology: The Disease behind the Crime



BY OLIVIA DAHL

Figure 1: Ted Bundy, shown above, is one of history's most well-known and brutal serial killers. By many definitions, Bundy would be considered a psychopath.

Introduction

In a sample of psychopathic subjects drawn from a temporary job agency, 52% of psychopaths confessed to having attacked a stranger to the point of bruising or drawing blood from the stranger, 42% admitted to having raped at least one person, and 38% said that they had fired a gun at another person (1). Psychopathy, also known as antisocial personality disorder (APD), is of public interest because alarming statistics like these indicate that psychopaths pose a great risk to the population at large (1-4). APD predisposes psychopaths to violent behavior, both because of their categorical inability to empathize with others and their proclivity for dangerous thrill-seeking. Psychopaths have a host of impairments—they have a stunted ability to forge close relationships, they are perceived as callous and manipulative, and they are able to commit atrocities without remorse. These psychopathic qualities make it unsurprising that psychopaths constitute a disproportionate percentage of prison inmates: while an estimated one percent of the general population has APD, it is estimated that more than 35% of prison inmates have APD (2).

Given the criminal appetite associated with psychopathy, there is incentive to diagnose and monitor the psychopathic population in an effort to prevent crime (2,3,5). Predicting and thereby preventing crime is not a new topic. The movie *Minority Report* is about a futuristic dystopia in which the FBI forms the "Precrime Unit". The unit is devoted to catching would-be killers moments before the crime, using genetically-engineered savants with visions of the future. While the FBI has announced no plans of breeding humans to prevent crime, there is one up-and-coming field focused on predicting crime: neurocriminology (2,3,5).

Neurocriminology concentrates on studying the brains of criminals, putting the psychopathic brain in the spotlight (2,3). The field seeks to identify those with neurological and genetic predispositions for violent behavior and to hopefully engineer a treatment or prevention strategy (2,3). While the field is still burgeoning, genetic and neurological evidence is making its way into the courtroom, raising ethical questions about how genetics, neurological functioning, and child abuse affect a criminal's responsibility (2-4,6).

Recent discoveries in neuroscience are relevant to all stages of criminal justice. It is increasingly possible to predict whether a brain is predisposed to criminal activity, and neuroscience is making steps toward predicting what brain activity in criminals correlates with reoffending (2,3,6,7). A 2013 study concluded that criminals with diminished activity in the anterior cingulate cortex, a brain region associated with executive function, were 4.3 times more likely to reoffend while on parole (7). With the increasingly predictive power of neuroscience, it is necessary to examine the ethical implications of allowing neuroscience into courtrooms. Should a person with a neuroanatomical predisposition for killing receive more or less jail time for committing murder? Should a brain scan that predicts, with a small margin of error, that a convicted criminal is likely to revert to violent crime be sufficient grounds to prevent a person's parole? Should statistics guide sentencing and the granting of parole, or would such a system deny the possibility of free will?

Neuroscience of Psychopathy

Adrian Raine is a leader in neurocriminology as well as a professor at the University of

Pennsylvania and chair of their criminology department (6). Raine explores genetic, environmental, and neurological factors that play into violent criminality in his most recent book, *The Anatomy of Violence* (6). In this book, Raine stipulates that someday all eighteen-year-old men (men because there are nine male murderers for every female murderer) will undergo brain imaging tests to determine their likelihood of succumbing to violent behavior (2,3,5). The reputable criminologist suggests that when neuroscience reaches the point where it can predict a person's penchant for violence with near certainty, those with a neuroanatomical thirst for blood will be sent away from mainstream society to some equivalent of a holding facility (2). He suggests that this holding facility need not be a prison. It could instead be considered more of a highly regulated sleep-away camp for potentially dangerous individuals (2). This prediction is alarming for ethical reasons and is strongly reminiscent of *Minority Report*. Perhaps Raine's hope for a future with confined psychopaths is shaped by his career devoted to studying cold-blooded killers and rapists.

It is little wonder that a man who has spent so much time working with psychopaths hopes for a future without the more dangerous ones on the loose. The psychology of people with APD is chilling; the disorder robs the afflicted of any rich emotion, leaving only the capacity for raw emotions such as fear, anger, boredom, and lust (2,3). Psychopaths are impulsive and irresponsible, which often manifests itself in the form of unprotected sexual promiscuity. Psychopathic irresponsibility is also evidenced by their proclivity for a parasitic lifestyle, where they use their superficial charm to manipulate others into funding their needs and whims (5,7).

One irony of this disorder is that those with APD are often gifted at reading the emotions of others while incapable of experiencing those same emotions themselves (1-3). The psychopathic paucity of emotion can prove advantageous in many arenas. Businessmen who have no reservations about laying off thousands of workers, politicians who feel no twinge of guilt making duplicitous deals—these are just two examples of arenas in which a conscience can be considered a hindrance (8). Psychopathy relegates people to a mechanical existence wherein they consider the emotions of others as no more than a bargaining chip to be played when advantageous. The "successful psychopath" is one who escapes detection, using charm to win people over, all the while satiating his or her craving for stimulation in a variety of ways, sometimes escalating to killing (8).

There are two notable neuroanatomical structures that are deviant in psychopathic brains—the prefrontal cortex (PFC) and the amygdala (1,2,6). The PFC is responsible for executive control, namely inhibition of inappropriate impulses, while the amygdala is critically important in fear conditioning (1). Fear conditioning is tested in lab animals by exposing an animal to an unpleasant or painful situation. The animal is successfully conditioned if it then fears the place in which it experienced the discomfort or any associated stimuli.

Fear conditioning is a simplified version of what happens when people socialize – children learn to avoid a social faux pas by associating social misconduct with discomfort (1). The amygdala and the PFC are critical to this learning process (1,5). A lab rat with a lesioned (surgically removed) amygdala completely loses the ability to learn the associations in fear conditioning. The PFC is involved in fear conditioning in a more subtle way, working by inhibiting the socially unacceptable impulses that have been associated with discomfort. People with APD have been found to have an amygdala that is up to 18% smaller than normal, and studies have found that the psychopathic PFC has a 11% reduction in grey matter (5). These findings point to the theory that APD is a neurodevelopmental disorder that interferes with a person's ability to experience and learn from negative experiences, specifically negative social feedback (2,5). Raine and his colleagues speculate, "Poor conditioning is theorized to be associated with poor development of the conscience."

The Merriam-Webster Dictionary defines empathy as "vicariously experiencing the feelings… of others," and this ability is fundamentally lacking in psychopaths (9). One simple test of empathy measures sympathetic skin conductance response (SCR) while subjects are shows a variety of stimuli (10). The SCR is an electrophysiological indicator of a person's arousal that measures how much the person is sweating. The SCR test can be used to measure a person's distress in response to different types of photos, including relaxing photos of nature and more disturbing photos, like a person's hand getting caught in a closing door (10). The greater a person's SCR, the greater that person's distress. The SCR should be low for emotionally neutral scenes, but it should be elevated when, for example, a person sees photos of a needle going into someone's hand (10). When psychopaths take this test, they exhibit very little change in SCR between the two types of photos (2). They retain a low resting heart rate and a low SCR throughout the photo exhibit, indicating that they are unperturbed when graphically presented with another person's physical pain.

Feeling another person's pain may seem like a lofty behavior, but there is neurological evidence that this might be fundamentally important in development (11). The mirror

"Antisocial personality disorder (APD) is a neurodevelopmental disorder that interferes with a person's ability to experience and learn from negative experiences, specifically negative social feedback."

neuron system (MNS) is a circuit of neurons found in monkeys that activates both when an individual performs a specific action, such as making a fist, and when that individual sees another person perform that same specific action (11). The existence of the MNS suggests that "perceiving similarity between self and others" is so adaptive that our neurons force us to feel what others are doing, at least to some degree. The MNS is believed to play a role even in such critical milestones as learning language (12). One theory of language acquisition suggests that mirror neurons propel babies to mimic the movements of their parents' mouths, expediting their understanding of the relationship between different labiodental configurations and phonemes (12). While there is currently very little literature addressing language development in those with APD, the theory that psychopaths have a dysfunctional MNS is popular and under investigation (2,12).

Between SCR tests, fMRIs scans, and other behavioral measures, there are many different ways of diagnosing psychopathy (2,6). Now the question becomes: how can psychopaths who are likely to commit acts of violence be preempted? And in this new age of neuroscience, how will neurological aberrations be treated in the courtroom? While it is difficult to speculate about how neuroscience will integrate into law in twenty years, there are two recent court cases from the past five years that represent two different roads that neurolaw can take.

"A schoolteacher went to the emergency room complaining that he had a nearly irresistible urge to rape his landlady (13). Doctors were suspicious – this was a man who was scheduled go on trial the very next day for molesting his young stepdaughter . . . "

Neuroscience in Court

A schoolteacher went to the emergency room complaining that he had a nearly irresistible urge to rape his landlady (13). Doctors were suspicious – this was a man who was scheduled go on trial the very next day for molesting his young stepdaughter, and this resembled a ploy to escape trial (13). While the doctors deliberated over how to deal with the man they suspected was faking symptoms, the patient propositioned the nurses publicly and shamelessly in the waiting room. Doctors noticed that the patient walked with a stiff gait and neglected to notice objects in his left field of vision. This was not a ruse; the unnatural gait and hemispatial neglect were sufficient grounds to order an MRI, which brought to light an egg-sized tumor that the patient had developed. The tumor was pressing on the patient's prefrontal cortex, the part of the brain associated with inhibition, which explained why the patient could not put a lid on his vivid and violent sexual fantasies (13).

The discovery of this man's tumor revolutionized his defense. Yes, he had made sexual advances on his stepdaughter, who was just a child (13). But this was a man who had no prior criminal record, who had experienced no pedophilic urges prior to developing this tumor. Once doctors removed his tumor, the patient abruptly lost all pedophilic urges and was profoundly ashamed of his tumorous conduct. The surgery corrected this man's behavior for a while, but when the patient relapsed into hypersexuality, he discovered that his tumor had reappeared. After the second surgery to remove the tumor, the patient's libido returned to socially acceptable levels and his wife allowed him to move back in with her (13).

This appears to be a cut and dry case of a tumor driving a man to criminal conduct, and the results of the defendant's MRI were clearly important to his defense (13). But consider another court case that hinged on genetic testing, tried in 2007 in Italy (14). Abdelmalek Bayout murdered Walter Perez in a bar brawl because Perez had insulted Bayout's kohl makeup. Bayout confessed to his crime, one that would typically have resulted in a sentence of about twelve years in prison. Bayout's lawyer, however, negotiated a significantly lighter sentence because genetic tests showed that Bayout carried five genes that correlated with violent behavior (14). One of the genes that Bayout carried, monoamine oxidase (MAO-A), has come to be known as "The Warrior Gene," because expression of this gene is correlated with elevated levels of aggression and violence. The association between this gene and aggression is still poorly understood – the correlation between MAO-A and aggression varies between ethnic groups, and yet the defendant's ethnicity was not tested (14). *Nature* published an article questioning not only the methodology behind the defense's explanation of genetic predisposition, but also the wisdom of promulgating defense strategies based on "genetic determinism". The defendant, who confessed to murdering someone over an insult, was relieved of one year of his sentence on the grounds that his genes predisposed him to react to stressful situations with violence (14).

More Questions to Consider

The two cases described above seem different. In one, a tumor transformed a previously model citizen into a child molester. In another, the results of a genetic test relieved a murderer of one year of his sentence. Bayout will be released one year earlier than he would be if he were not a carrier of the Warrior Gene, and he will still have a proclivity towards violence when released, if we are to believe that genes so closely determine so complex a behavior as violence (13). If one of these defenses seems more acceptable than the other, what exactly is the difference?

It is difficult to map out what types of neurological tests or genetic predispositions

belong in a courtroom, and it is then even more difficult to determine how such data should affect a verdict. With neuroscience discovering increasingly more about the criminal mind, a revolution in criminal law might be on the horizon. One company offers lie detection services called "No Lie MRI," and while that technology has not been allowed in court to date, there are serious questions to consider (15,16). If it becomes possible to put a murder suspect in an MRI, ask him if he is the killer, and determine based on the scan's results whether he is lying or not, is that a violation of the American right to plead the fifth amendment? Will murder suspects have a right to protect themselves from brain scans?

The roles of insanity and remorse in the death penalty are additional factors to consider. In a 2002 court case, *Atkins v. Virginia*, the Supreme Court ruled that an insane person could not be put to death. When a psychopath is found guilty of murder, should he or she be able to plead insanity and thus escape the death penalty? When a defendant can persuade the judge of his or her genuine remorse, the judge is legally urged to spare that person of the death penalty. Since psychopaths are inherently incapable of remorse, should they go through an adjusted sentencing process? These are just some of the questions we must consider as neuroscience generates more and more information.

CONTACT OLIVIA DAHL AT
OLIVIA.S.DAHL.14@DARTMOUTH.EDU

Figure 2: A sagittal MRI scan of a human brain.

References

1. A. Raine, Reduced Prefrontal Gray Matter Volume and Reduced Autonomic Activity in Antisocial Personality Disorder (2000). *Arch Gen Psychiatry.* Available at http://archpsyc.jamanetwork.com/article.aspx?articleid=481571 (8 August, 2013)
2. A., Raine, *The Anatomy of Violence* (Random House LLC, 2013).
3. E. Lerner, Can Science Predict Criminal Behavior? (2011). Available at http://www.upenn.edu/pennnews/current/2011-03-24/research/can-science-predict-criminal-behavior (9 August, 2013)
4. L. Baker, S. Bezdjian, and A. Raine, Behavioral Genetics: The Science of Antisocial Behavior (2006). *Law and Contemporary Problems.* Available at: http://www.jstor.org/stable/pdfplus/27592122.pdf?acceptTC=true (8 August, 2013)
5. Y. Yang, et al., Localizations of Deformations Within the Amygdala in Individuals With Psychopathy (2009). *Arch Gen Psychiatry.* Available at http://archpsyc.jamanetwork.com/article.aspx?articleid=210298 (10 August, 2013)
6. A. Raine, The Criminal Mind (2013). Available at http://online.wsj.com/article/SB10001424127887323335404578444682892520530.html (10 August, 2013)
7. R. Nuzzo., Brain Scans Can Predict Who Is Likely to Reoffend (2013). *Nature.* Available at http://www.nature.com/news/brain-scans-predict-which-criminals-are-more-likely-to-reoffend-1.12672
8. M. Stout, *The Sociopath Next Door* (Broadway Books, New York, 2005)
9. "empathy." 2012. In *Merriam-Webster.com.* Available at http://www.merriam-webster.com/dictionary/empathy (10 August, 2013).
10. H. Critchley, R. Elliot, C. Mathias and R. Dolan., Neural Activity Relating to Generation and Representation of Galvanic Skin Conductance Responses: A Functional Magnetic Resonance Imaging Study (2013). *The Journal of Neuroscience.* Available at http://www.jneurosci.org/content/20/8/3033.short (11 August, 2013).
11. W. Shoemaker, The Social Brain Network and Human Moral Behavior, (2012). Available at http://onlinelibrary.wiley.com/doi/10.1111/j.1467-9744.2012.01295.x/abstract?deniedAccessCustomisedMessage=&userIsAuthenticated=false (12 August, 2013).
12. J. Hurford, "Lanugage beyond our Grasp: What Mirror Neurons Can and Cannot, Do for the Evolution of Language. *Evolution of a Communication Systems: A Comparative Approach* (Bradford Book, New York, 2004). pp. 298-300. Available at http://books.google.com/books?hl=en&lr=&id=GsSWKPB6KW8C&oi=fnd&pg=PA297&dq=mirror+neurons+language+learning&ots=l9oeRHGpa5&sig=ZfO4uqUk0hLfIxgelpQ_3sJRgXw#v=onepage&q=mirror%20neurons%20language%20learning&f=false (10 August, 2013).
13. N. Thomson, My Brain Made Me Do It (2006). *Legal Affairs.* Available at http://www.legalaffairs.org/issues/January-February-2006/feature_thompson_janfeb06.msp (14 August, 2013).
14. E. Feresin, Lighter Sentence for Murderer with "Bad Genes" (2009). *Nature.* Available at http://www.nature.com/news/2009/091030/full/news.2009.1050.html (14 August, 2013).
15. J. Simson, Functional MRI Lie Detection: Too Good To Be True? (2008). *J. Am. Acad. Psychiatry Law.* Available at: http://www.jaapl.org/content/36/4/491.full.pdf+html (14 August, 2013)
16. H. Greely, "Can MRIs Help Solve Crimes?" National Public Radio, *Talk of the Nation.* Available at http://www.npr.org/templates/story/story.php?storyId=126831150 (14 August, 2013).

Contraception: Beyond the Pill

Figure 1: Condoms are one of the most popular forms of contraceptives.

Image courtesy of CDC

BY KRISTEN FLINT

Introduction

In 2010, the United States celebrated the 50th anniversary of the oral contraceptive pill. Created in 1960 by Margaret Sanger and Katherine McCormick, the oral contraceptive pill was the first form of safe, effective contraception that enabled women to control their reproductive cycles (1). Today, 100 million women use a form of the oral contraceptive pill to prevent pregnancy; the oral contraceptive pill is the contraceptive of choice for about 30% of women using contraception (2,3). The other 70% of women choose from a variety of other contraceptive options, including non-oral hormonal contraceptives, non-hormonal contraceptives, and permanent sterilization. This article will focus on the current options for non-permanent contraceptives and potential future contraceptives.

Contraceptives aim to prevent the fusion of an egg and a sperm by inhibiting one or multiple steps involved in fertilization and implantation. For fertilization to occur, first, the male must produce viable sperm. Sperm are formed in the testes throughout a male's reproductive life (4). During sexual intercourse, the sperm travel through the epididymis and vas deferens, and are ejaculated through the urethra into the female (4). On average, over 100 million sperm are present in the ejaculate, but most are incapable of fertilization due to poor motility or immaturity; 85% of the sperm are incapable of traveling to the egg (4). Once inside the female reproductive tract, the sperm must journey across the cervix and through the uterus to the fallopian tubes where the sperm might find an egg (5). Sperm have a lifespan of 12-48 hours depending on the environment encountered in the female reproductive tract, so for fertilization to occur, the female must either have recently ovulated or release an egg while sperm are present in the reproductive tract (5). Ovulation is controlled by female hormones, specifically luteinizing hormone (LH) and progesterone (6). A surge of LH midway through the menstrual cycle triggers ovulation in women, leaving them at their most fertile (6,7). As the egg travels down the fallopian tube, progesterone levels increase, causing the endometrial lining to thicken to facilitate implantation of a fertilized egg (6). Without the lining, implantation cannot occur, and the egg, even if fertilized, will pass out of the female reproductive tract. In summary, successful fertilization is the result of many

events happening at precise times under precise conditions. Contraceptives alter the timing of these events, or the environmental conditions, to disrupt and prevent fertilization.

Hormonal Contraceptives

Since the days of Sanger and McCormick, a variety of hormonal contraceptives has been developed. Today, the most commonly used contraceptive is the oral contraceptive pill. In his book *The Pill: A Biography of the Drug That Changed the World*, Bernard Asbell argues "the Pill has been swallowed as a daily routine by more humans than perhaps any other prescribed medication in the world" (1). After the first oral contraceptive pill was developed and approved by the FDA, in only five years, one in four married women had used it (1). Today, 100 million women utilize the drug due to its high rate of effectiveness and safety (3).

The oral contraception pill exists in two main forms: progestin-only pills and combined hormonal pills. Combined hormonal pills contain daily doses of progestin and estrogen and usually come in packs of 28 or 21. Both packs have 21 pills that contain active hormone, but where the last seven pills of the 28-pack are inert, 21-pill packs recommend a seven-day period of no pills (8). The seven days without active hormone allow for shedding of the endometrial wall to convey a semblance of the natural menstrual cycle (8). However, the FDA has recently approved several extended cycle pills, which contain lower doses of hormone and can be used without the week of placebo pills to postpone or fully eliminate withdrawal bleeding (9). In combined pills, the progestin keeps LH levels low so that ovulation does not occur, thickens cervical mucus so that sperm cannot cross into the uterus, and thins the endometrial wall so that the uterine environment is more hostile to fertilization and implantation (8,10,11). The estrogen also works to suppress LH levels and prevent ovulation (11).

Progestin-only pills are less widely used than combination pills and are usually reserved for women with medical problems or women experiencing severe side effects from combined pills (8). Like combined pills, progestin-only pills thin the endometrial lining, thicken cervical mucus, and block ovulation, but ovulation may occasionally still occurs (8).

Oral contraceptive pills are very effective at preventing pregnancy. Combined oral contraceptive pills have a failure rate of 0.3% when taken perfectly (correct and consistent use) or a failure rate of 8% when taken typically (10). Progestin-only pills have a slightly higher failure rate because of their inability to fully suppress ovulation (10). However, the failure rate for oral contraceptives can vary greatly if the pills are misused (12).

In addition to preventing pregnancy, oral contraceptives provide many health benefits to women. A study done by the Collaborative Group on Epidemiological Studies of Ovarian Cancer found that women who used oral contraceptives had a reduced risk of developing ovarian cancer for decades after ending use of oral contraceptives (13). Oral contraceptive use also decreases the risk of developing endometrial cancer (10). Additionally, use of oral contraceptives relieves menstrual symptoms in many women by leveling estrogen production, and reduces the amount of bleeding by suppressing growth of the endometrial wall (8).

A third form of the oral contraceptive pill is emergency contraception, commonly known as the "morning-after pill." Emergency contraception is similar to the daily oral contraception pill but contains a significantly higher dose of hormones (8). Thus, emergency contraception inhibits or delays the natural surge of LH that precedes ovulation (9). However, if emergency contraception is used after ovulation, it is ineffective. Emergency contraception has been a controversial issue in the twenty-first century as politicians have argued over who should be able to buy and use emergency contraception (14-16). In a move to increase access to emergency contraception, in 2013, the FDA approved Plan B One-Step, a form of emergency contraception, to be sold over the counter to all individuals aged 15 and older without a prescription (15).

Not all hormonal contraceptives are oral. Many women cannot adhere to the rigorous daily regimen of pills, so they turn to other forms of hormonal contraception. Many hormonal

Image courtesy of BetteDavisEyes. Available at http://commons.wikimedia.org/wiki/File:Ortho_tricyclen.jpg

Figure 2: Some oral contraceptive pills come in packs that contain three weeks' worth of active hormone and one week's worth of placebo pills.

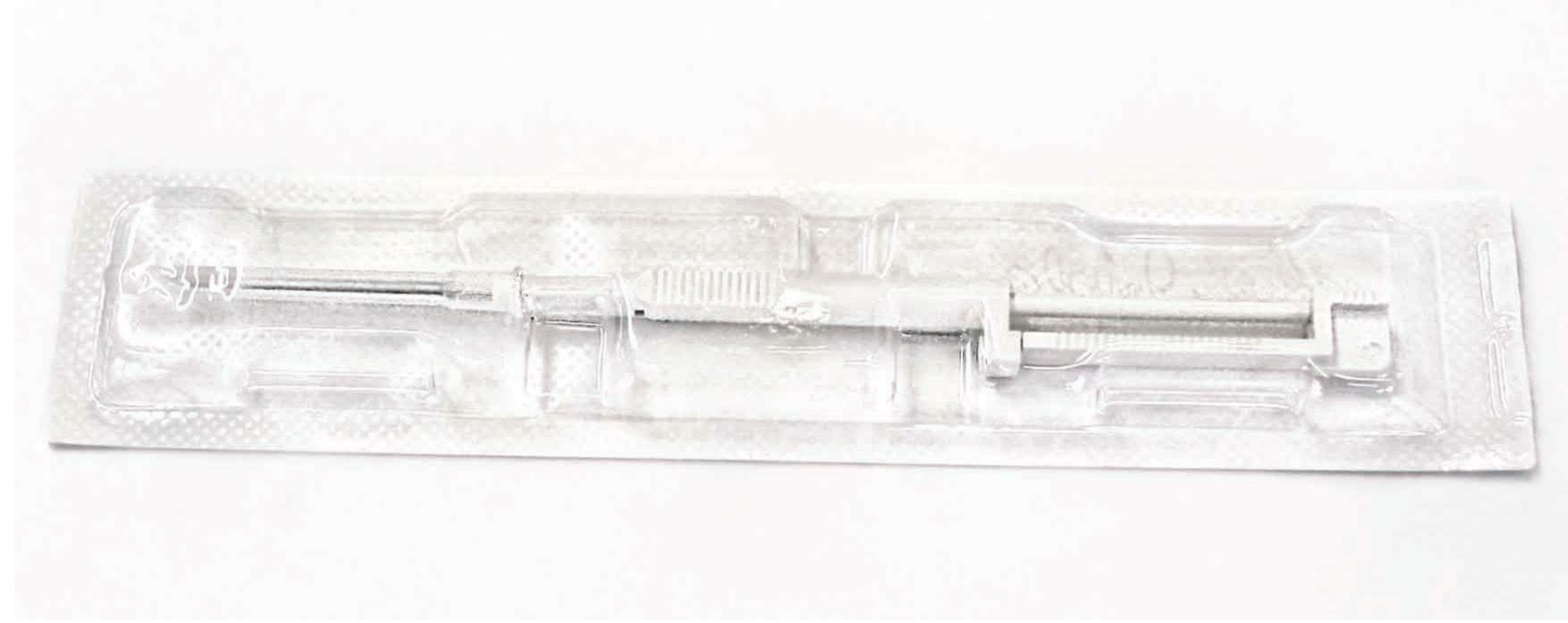


Image courtesy of Ciell. Available at http://commons.wikimedia.org/wiki/File:Implanon.JPG

Figure 3: Hormonal implants such as Implanon (shown above) that release progestin and estrogen are an alternative to oral contraceptive pills.

contraceptives act as the pills do, releasing daily doses of progestin and estrogen, but exist in different physical forms (10). These hormonal contraceptives include patches worn on the skin, rings placed in the vagina, implants that release hormones, and periodic hormonal injections (8).

However, the most effective contraceptive device is the intrauterine device (IUD). The IUD is a device placed in the uterus to change the uterine environment and make it more hostile to fertilization (2,8). IUDs release either the hormone progestin or copper ions to reduce the motility and viability of sperm in order to prevent fertilization (2,10). Once in place, the IUD is an almost 100% effective contraceptive for five years (10).

Non-Hormonal Contraceptives

While hormonal contraceptives block the ability of sperm to reach the egg by altering hormones levels to change the environment of the female reproductive tract, non-hormonal contraceptives physically bar the passage of sperm to the egg. Of the non-hormonal contraceptives, the condom is the most widely used (2). Both male and female condoms exist, the male condom acting as a sheath, and the female condom acting as a pouch (2). Male condoms have a higher success rate than female condoms, and both types protect against the transmission of sexually transmitted diseases (10).

Females also have the option of using diaphragms or cervical caps as a contraceptive. Like condoms, diaphragms and caps are also barriers that prevent sperm from entering the cervix. However, to be most effective, diaphragms and caps must be coated with spermicide before insertion (2). Spermicides contain a detergent that inhibits sperm mobility and ultimately kills the sperm (2). However, the detergent can damage the vaginal wall, which then facilitates transmission of HIV between partners (10). Thus, although they are as effective as condoms at preventing pregnancy, diaphragms and cervical caps are not as popular (2).

Figure 4: One non-hormonal contraceptive option is the diaphragm, which acts a barrier between sperm and the cervix.

Image courtesy of Axefan2. Available at http://commons.wikimedia.org/wiki/File:Contraceptive_diaphragm.jpg

Future Contraceptives

The vast majority of the contraceptive options explored above exist for female use. In fact, the male condom is currently the only non-permanent male contraceptive option, but research into alternatives has yielded some promising results. In 2012, Martin Matzuk et al. developed a small molecule that inhibits the ability of sperm to mature as they move through the male reproductive tract (17). The molecule targets a protein in the testes that is needed for proper development and motility of sperm cells. When the molecule was injected into mice, Matzuk et al. found that the mice developed smaller testes, fewer sperm, and sperm with poorer motility. Matzuk et al. also discovered that upon stopping injections, the mice returned to original testes size and normal sperm function (17). Due to the overlap between mouse and human genes, the small molecule holds great potential as a future contraceptive for human males.

Another potential male contraceptive acts via a mechanism similar to the female oral contraceptive pill: by releasing progestin. In 2003, Leo Turner et al. studied the effects of administering testosterone plus progestin to males as a form of contraception. Turner et al. discovered that men receiving the hormonal combination developed fewer sperm and had a higher contraceptive success rate than men who used condoms (18). In 2009, Vahid Mahabadi et

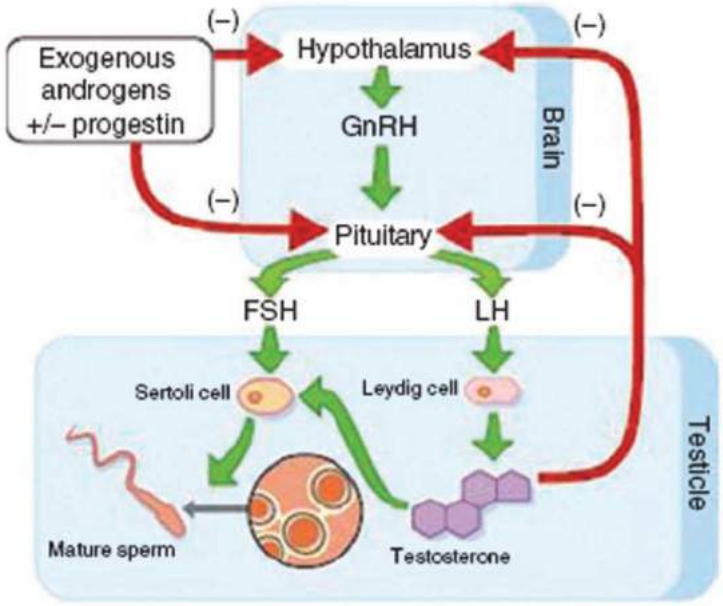


Image courtesy of CDC

Figure 5: The mechanism of action of male hormonal contraception, a potential contraceptive method. The normal hormone cycle is shown with green arrows. Testosterone (exogenous androgens), alone or in combination with a progestin, mimics the negative feedback of natural testosterone in the brain and suppresses the luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which normally promote spermatogenesis.

al. expanded on Turner's research and tested a gel containing nestorone, a type of progestin, and testosterone. Mahabadi et al. found that the gel safely suppressed gonadotropins, or sex hormones, so the gel has the potential to also suppress sperm development (19).

A third approach to male contraceptives centers on the use of ultrasound treatment to block sperm production. In 2012, Catherine VandeVoort and Theodore Tollner investigated the contraceptive effects of ultrasound treatment in the rhesus monkey. VandeVoort and Tollner used ultrasound on the monkeys' scrotums and measured the quality of the monkeys' semen over time. VandeVoort and Tollner observed that the monkeys undergoing the ultrasound treatment developed sperm with less motility, due to misshaped flagella, and lower overall sperm count (20). Applied to humans, ultrasound treatment could be a successful, easy-to-use, non-hormonal contraceptive.

Conclusion

For individuals currently not interested in having children, contraceptives are an important protective measure to consider. Hormonal contraceptives have a higher rate of preventing pregnancy when taken as instructed than do non-hormonal contraceptives, but they do not protect against sexually transmitted diseases. Additionally, hormonal contraceptives have only been developed for women, placing the burden of contraception solely on the female partners. Ongoing research into male contraceptives has revealed several promising options for the future of contraception. The United States recently celebrated the 50th anniversary of female hormonal contraception – in another fifty years, perhaps both sexes will have a form of contraception to celebrate.

CONTACT KRISTEN FLINT AT
KRISTEN.L.FLINT.14@DARTMOUTH.EDU

References

1. B. Asbell, *The Pill: A Biography of the Drug That Changed the World* (Random House, New York, 1995).
2. K. Black, A. Kubba, *Obstetrics, Gynaecology and Reproductive Medicine* 21, 103-106 (2011).
3. Oral Contraceptive Use Worldwide. *Population Reports* 28, 4 (2000).
4. M. Chang, G. Pincus, *Physiological Reviews* 31, 1-26 (1951).
5. C. Freudenrich, M. Edmonds, How Human Reproduction Works (2001). Available at URL http://science.howstuffworks.com/life/human-biology/human-reproduction.htm (19 August 2013).
6. N. Santoro *et al., Am J Physiol Endocrinol Metab* 284, E521-E530 (2002).
7. D. Baird *et al., Fertility and Sterility* 71, 40-49 (1999).
8. P. Blumenthal, A. Edelman, *Obstetrics & Gynecology* 112, 670-684 (2008).
9. P. Casey, S. Pruthi, *The Journal of Family Practice* 57, 797-805 (2008).
10. J. Amy, V. Tripathi, *BMJ* 339, 563-568 (2009).
11. Birth Control In-Depth Report. Available at URL http://health.nytimes.com/health/guides/specialtopic/birth-control-and-family-planning/print.html (18 August 2013).
12. J. Trussel, *Arch Dermatol* 131, 1064-1068 (1995).
13. Collaborative Group on Epidemiological Studies of Ovarian Cancer, Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23 257 women with ovarian cancer and 87 303 controls. *The Lancet* 371, 303-314 (2008).
14. S. Abell, J. Ey, *Clin Pediatr* 48, 341-342 (2009).
15. A. Sifferlin, Plan B One-Step Now For Sale: What You Should Know (2013). Available at URL http://healthland.time.com/2013/08/01/plan-b-one-step-now-for-sale-what-you-should-know/ (20 August 2013).
16. C. Ellertson, *Family Planning Perspectives* 28, 44-48 (1996).
17. M. Matzuk *et al., Cell* 150, 673-684 (2012).
18. L. Turner *et al., J Clin Endocrinol Metab* 88, 4659-4667 (2003).
19. V. Mahabadi *et al., J Clin Endocrinol Metab* 94, 2313-2320 (2009).
20. C. VandeVoort, T. Tollner, *Reprod Biol Endocrinol* 10, 81 (2012).

"The United States recently celebrated the 50th anniversary of female hormonal contraception – in another fifty years, perhaps both sexes will have a form of contraception to celebrate."

Vaccines and the Immune System: The Ultimate Protection

BY STEPHANIE ALDEN

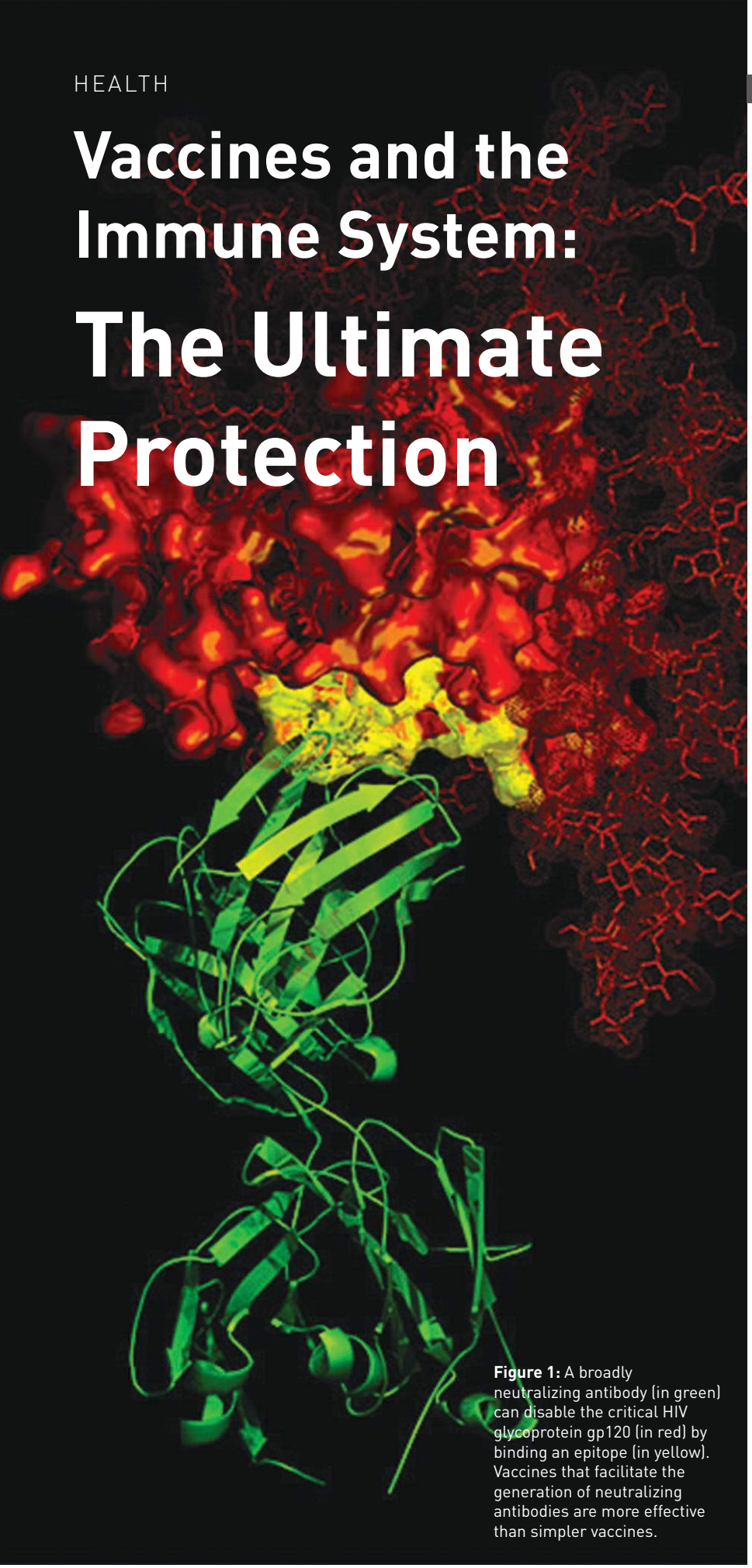


Figure 1: A broadly neutralizing antibody (in green) can disable the critical HIV glycoprotein gp120 (in red) by binding an epitope (in yellow). Vaccines that facilitate the generation of neutralizing antibodies are more effective than simpler vaccines.

Image courtesy of NIAID

Introduction

Vaccines, altered forms of pathogens, enhance immunity by priming a host's immune system, building up memory to improve the "secondary response" (1). The immune system is a network of pathways that protects the body through the innate and the adaptive immune systems (1). While the innate immune system acts as a general "first response" to foreign molecules, the adaptive system is a specific secondary response that develops after exposure to an antigen (1). Researchers focus on improving this secondary response by developing vaccines.

Background

Edward Jenner was one of the first to venture into the field of vaccine development. In 1798, Jenner discovered that inoculations with cowpox, a weaker form of smallpox, helped build resistance to smallpox better than employment of the deadly pathogen itself (2). Almost a century later, Louis Pasteur observed that inoculating chickens with a weakened culture of bacteria built resistance to the disease (2, 3). Since these two discoveries, huge advances have been made in vaccine development.

Scientists now understand the science behind immunity. T cells, responsible for cell-mediated immunity, recognize and bind to antigens that are attached to pathogens (1). They reproduce and develop into T helper cells and cytotoxic T cells, which recruit other cells and kill antigen-presenting cells respectively (1). Unlike T cells, B cells recognize and bind to free antigens (4). They differentiate into plasma cells, which secrete large numbers of specific antibodies for a short period of time, and memory B cells, which stay in the body for a long time (4). Both B cells and T cells differentiate into cells with a memory for a specific antigen, making the secondary response faster and stronger (1).

With the knowledge provided by Jenner, Pasteur, and numerous other scientists, it is now understood that vaccines work through active immunization by stimulating the host to create T cells and B cells specific to the injected pathogen (1). When the body encounters these pathogens again, it can fight them much more effectively. This understanding enables the development of safer, stronger vaccines.

Types of Vaccines

There are many types of vaccines that can successfully prime the immune system, arming the host with an array of memory B and T cells that quickly mount a response and protect the host from infectious diseases.

Live Vaccines

The vaccines created by Jenner and Pasteur were both live and weakened versions of the pathogen, meaning that they still had the ability to reproduce within the host (2). Because live vaccines stay in the host's system longer and more closely resemble the natural virus, they build the strongest immune response (1).

Scientists create attenuated vaccines by weakening pathogens with chemicals and using related animal viruses of weaker pathogenicity in humans (3). Growing the pathogen in conditions unlike those in the body to develop strains that will not be strong enough to cause disease is another common technique (3).

While live, weakened vaccines have their advantages, in some cases they can cause the inoculated individual to develop the disease or can transform into a more dangerous form of the disease (1). This change can occur through mutations in the virus that revert it to its pathogenic state or through recombination with other viruses present in the patient followed by further replication (5). In addition, other viruses can be introduced into the vaccine in the process of weakening the virus; these viruses can infect the patient when the patient is injected with the weakened virus (5). During their production in cell culture or as a result of the attenuation process, some of the first live polio vaccines were contaminated by SV40, a virus found in monkeys that does not harm humans (5). Doctors in the United States have not used the live oral poliovirus vaccine since 2000 due to the risk of permanent paralysis associated with the reversion of the live vaccine to its pathogenic state (6). Each year in the United States, there were six to eight cases of vaccine-associated paralytic polio, and, after successful eradication of the disease resulting from vaccination programs, this risk was higher than the risk of acquiring the disease from the wild-type pathogen (6).

Through improvements in genetic engineering, vaccines containing a combination of live, attenuated virus and protective agents have been created, making these vaccines much safer (3). Researchers have also discovered genes necessary for replication of viruses; by deleting these genes, researchers can prevent replication in the host while allowing for expression of genes in the pathogen that provoke an immune response (7). Scientists are also looking into the use of RNA interference, such as microRNAs, which can block translation of specific RNA sequences to protein (7). By including more microRNA binding sites in vaccines, the engineered virus can be further attenuated (7).

The methods discussed above are still being investigated. Nevertheless, current live vaccines are able to provide sufficient protection. For example, without the live, attenuated measles vaccine, there would be an estimated 2.7 million deaths around the world due to the disease (8).

Inactivated Vaccines

Scientists create inactivated vaccines by "killing" the pathogen with heat or by chemical means (1). By disabling the pathogen in these ways, scientists can prevent replication within the host but still prompt a protective immune response (1). Inactivated vaccines are considered safer than live, attenuated vaccines because they cannot replicate in the host and thus have a lesser chance of causing disease (1). In addition, in the process of killing the target pathogen, all other viruses and pathogens are killed, eliminating another problem associated with the attenuation process (5).

On the other hand, inactivated vaccines require more than one vaccination because of the lower level of exposure to the pathogen. With inactivated vaccines, there is a shorter exposure period because of a lack of replication and the more altered form of the virus (1).

Perhaps one of the most famous inactivated vaccines is the polio vaccine created by Jonas Salk in 1952 (9). Salk created his polio vaccine by inactivating three different strains of the poliovirus (9). Improvements in cell culture and preservation allowed scientists to grow kidney cells from monkeys and infect these cells with a virus (9). After letting the virus replicate and allowing the cells to respond, the infected cells were filtered and inactivated with formaldehyde to kill the polio virus (9). According to the Center for Disease Control, before the inactivated polio vaccine there were "13,000 to 20,000 cases of paralytic polio [...] each year in the United States," but the disease has now been effectively eradicated in the U.S. (8).

Inactivated vaccines targeting HIV are now under development. A research team in Canada has created a whole-killed HIV-1 vaccine, which has a version of the virus that was engineered and then inactivated by researchers (10). Because scientists engineer and modify the disease to make the vaccine, it can be widely produced and is not pathogenic (10). During its Phase 1 clinical trials, this vaccine has been shown to increase the amount of antibody against viral coat proteins that allow HIV to attach to and invade cells, and against proteins that make up the viral core of HIV (10). If these vaccines are successful, they could help some of the 34 million people around the world living with HIV (10).

"A research team in Canada has created a whole-killed HIV-1 vaccine, which has a version of the virus that was engineered and then inactivated by researchers."

Subunit Vaccines

While the inactivated and activated vaccines discussed above include the entire pathogen, subunit vaccines only deliver the specific antigen or antigens that prompt the largest immune response (11). Because subunit vaccines do not

contain all of the elements of the pathogen, they are less likely to have negative side effects (11).

Subunit vaccines are being considered as a potential vehicle for cancer vaccination. Scientists target proteins that are altered or overexpressed in cancel cells (12).

For example, MUC1 is a protein found on the surface of most healthy cells, and it plays a role in various cell functions depending on the agent that binds it (12). However, in cancer patients, this protein is overexpressed, expressed in new locations, and demonstrates abnormal protein-to-protein binding, suggesting a structural change (12). Upon injection with tumor-antigen-associated MUC1, scientists saw increased antibody production, but it is too soon to say whether or not this vaccine is effective.

The only approved cancer vaccine is Provenge (13). Researchers create this vaccine by taking white blood cells from a patient and exposing them to a protein found in prostate cancer cells (13). Upon exposure to these proteins, these blood cells are then put back into the patient (13). This vaccine increases the life expectancy of patients, but does not cure the cancer (13).

While subunit vaccines have proven successful in some cases, they have many faults as well. Because subunit vaccines only contain certain components of entire pathogens, they must be introduced with an adjuvant, an agent that increases the effectiveness of vaccines by enhancing the immune response (7). Adjuvants can elicit antigen expression and direct antigens to locations that will produce the largest immune response (7). Because of complications like the need for adjuvants, some scientists believe that subunit vaccines are not comprehensive enough and are pushing for more investigation into the field of whole-cell vaccines, where killed tumor cells are injected into patients (12).

Recombinant Vector Vaccines

Recently, scientists started developing vaccines by inserting portions of DNA from pathogens into innocuous viruses and injecting these recombinant vectors into patients (11). The weakened or harmless virus can reproduce in the host, simultaneously producing the inserted pathogen's antigens (1). There is still much testing that must be done before recombinant vector vaccines can be used widely, but improvements are happening quickly.

Like those who are working on inactivated vaccines, scientists in the field of recombinant vector vaccines are looking into creating a vaccine for human immunodeficiency virus (HIV), but are following a different path. Currently, researchers find it difficult to cover the variability of HIV between and even within patients due to its fast replication and mutation in a host (14). There are also many different families of HIV, making it difficult to decide which proteins and other factors should be encoded in the virus to prime the immune system (14).

Researchers now believe that employing a mixture of adenoviruses - common human viruses that can efficiently invade human cells - may be the answer (14). By keeping particular promoters and coding sequences in the DNA insertion in the

Figure 2: U.S. Secretary of Health and Human Services Kathleen Sibelius administers oral polio vaccine, not used in the U.S. since 2000 due to rare complications, in New Delhi, India. The U.S. government has been a leading force in achieving global polio eradication, allocating 133.9 million dollars in the 2011 fiscal year to the CDC and USAID for the effort.

adenovirus and having a mixture of these viruses, scientists can cover a wide variety of HIV (14).

In addition to concerns regarding variability of diseases themselves, scientists worry about pre-existing immunity to the viral surrogate used to bear DNA insertions (14). In terms of recombinant vectors, adenoviruses are fairly common, and some people may have gained immunity to adenoviruses through exposure in everyday life (14). Many have tried to choose vectors from less common viruses, but find trouble with certain gene interactions that prevent the new vector virus from successfully producing the desired antigen (14). By replacing certain coding regions, scientists have overcome these boundaries (14).

In one vaccine now in clinical trial in Africa, scientists have inserted part of the HIV virus into a weakened form of the Sendai virus, a virus that causes influenza in rats and is even less harmful to humans (15). The Sendai virus is a viable alternative to adenoviruses; it is less commonly encountered by humans in everyday life, meaning fewer populations are immune to it. After injection with the vaccine, the virus can reproduce within the host and create proteins characteristic of HIV, causing an immune response (15).

Conclusion

Researchers have made huge discoveries since Edward Jenner developed the first vaccine at the end of the 18th century (2). While the immune system can effectively protect individuals in a variety of cases, vaccines can increase this protection. These vaccines range from weakened, but complete versions of viruses to small subunits consisting of essential proteins, and each type has its own strengths and weaknesses. These vaccines have saved the lives of many in the past and, with continuing research, the development of new or improved vaccines will save even more lives in the future.

CONTACT STEPHANIE ALDEN AT
STEPHANIE.L.ALDEN.16@DARTMOUTH.EDU

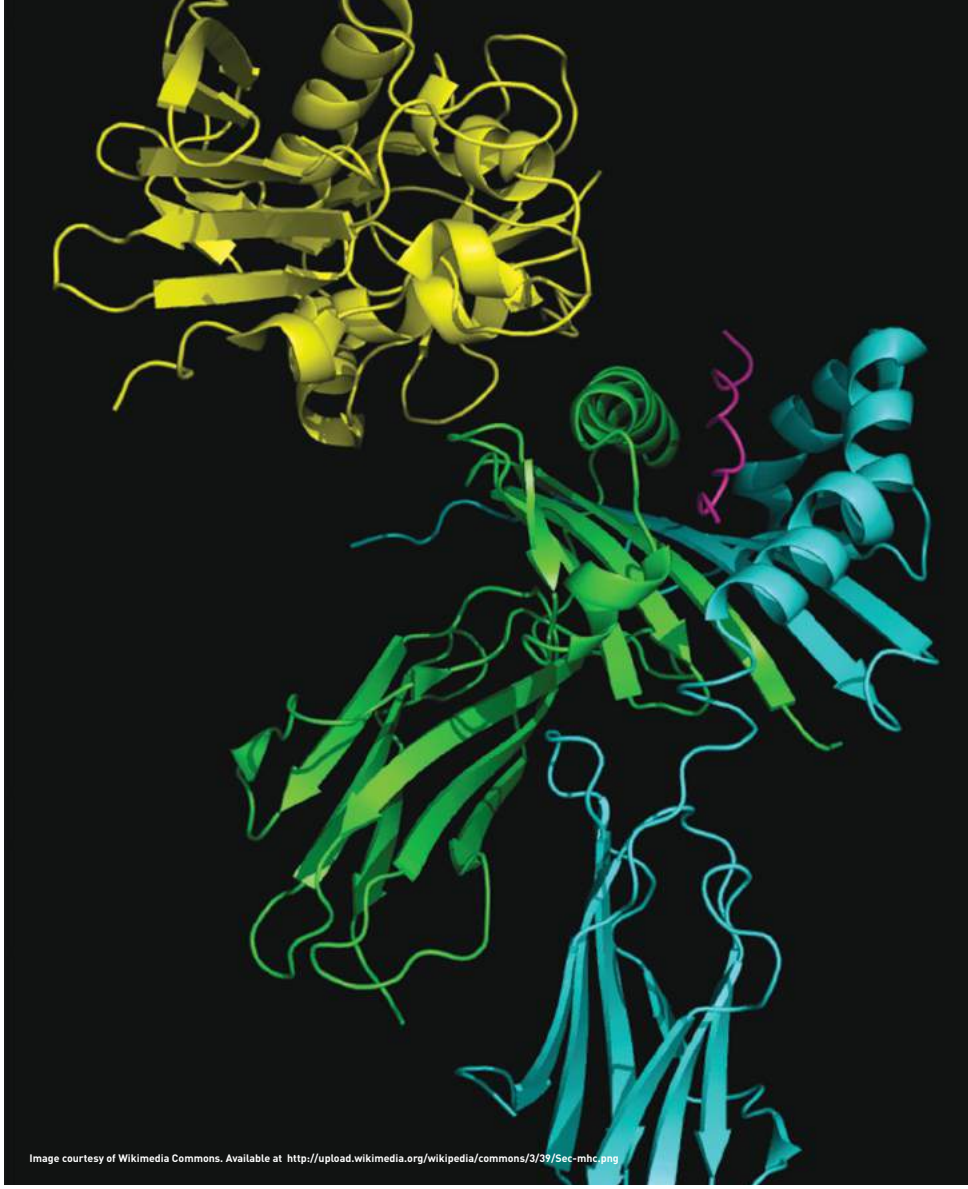


Figure 3: Superantigens – antigens that provoke a futile, nonspecific, and massive immune response by the host – are a potential target for vaccine development. Here, a staphylococcal superantigen (in yellow) obliquely binds an MHC class II protein (in green and cyan) from an antigen-presenting cell outside of the site where antigen fragments are displayed (in purple). Superantigens then bind receptors on cells of the immune system to activate them without regard to their specificities.

References

1. R.A. Goldsby, T.J. Kindt, Barbara A. Osborne, *Immunology* (W. H. Freeman and Company, New York, NY, ed. 6, 2007).
2. M. Lombard, P.P. Pastoret, A.M Moulin, A brief history of vaccines and vaccination. *Rev. sci. tech. Off. Int. Epiz.* **26**, 29-48 (2007).
3. S.A. Plotkin, Vaccines: past, present, and future. *Nature.* **11**, S5-S9 (April 2005).
4. P. Fisher, Immunology Module (2008). Available at http://missinglink.ucsf.edu/lm/immunology_module/prologue/objectives/obj05.html
5. J. Victoria *et al,* Viral Nucleic Acids in Live and Attenuated Vaccine: Detection of Minority Variants and an Adventitious Virus. *J Virol.* **84**. 6033-6040 (April 2010).
6. W. Egan, Testimony at Hearing: SV40 in Polio Vaccine, Washington, D.C., 13 November 2003.
7. F. Vogel, Improving Vaccine Performance with Adjuvants. *Oxford J, Clin Infect Dis.* **30**. S266-S270 (2000).
8. Centers for Disease Control and Prevention, What Would Happen If We Stopped Vaccinations? (June 2013). Available at http://www.cdc.gov/vaccines/vac-gen/whatifstop.htm#intro
9. L. Morganistein, B. Maybury Okonek, Development of Polio Vaccines. Available at http://www.accessexcellence.org/AE/AEC/CC/polio.php
10. S. Scutti, New HIV Vaccine Prove Successful in Phase 1 Human Trial (2013). Available at http://www.medicaldaily.com/new-hiv-vaccine-proves-successful-phase-1-human-trial-commercially-available-soon-255439
11. NIAID, NIH, U.S. Department of Health and Human Services, *Understanding Vaccines: What They Are, How They Work* (NIH, January 2008).
12. S. Boghossian, A. Von-Delwig, Tumor Vaccines, Monoclonals, Proteins, or Whole Cell Therapies. *J Vaccines Vaccin.* **S1:003**. 1-10 (2012).
13. American Cancer Society, Cancer Vaccines (February 2013). Available at http://www.cancer.org/treatment/treatmentsandsideeffects/treatmenttypes/immunotherapy/immunotherapy-cancer-vaccines
14. E. Emini, J. Shiver, Recent Advances in the Development of HIV-1 Vaccines Using Replication-Incompetent Adenovirus Vectors. *Ann Rev Med.* **55.** 355-372 (February 2004).
15. J. Gilmour, "New AIDS vaccine trial launched in UK, Africa." *Nightly News.* By Victoria MacDonald. London, UK: NBC, 2013. Web.

Protecting the Orange

Image courtesy of Böhringer Friedrich. Available at http://commons.wikimedia.org/wiki/File:OrangeOrange.jpg

BY ANNIE (YI) SUN

The Disease

A tiny insect has been spreading disease to millions of Florida orange trees since 2005. The creature, known as the Asian citrus phyllid, is small (about the size of an aphid), feeds forty-five degrees from the surface of leaves, and looks like a small thorn on the orange tree (1). The state had been dreading its arrival for many months as it spread throughout countries such as Mexico, China, and Brazil (the world's largest producer of oranges) (2).

This year, the Asian citrus psyllid *Diaphorina citric* continued its spread of the "citrus greening" disease that has been devastating orange crops throughout the world. It has already spread the disease throughout all 32 of Florida's citrus-growing counties; even states such as Texas, California, and Arizona have been affected (2, 3).

The insect itself acts only as a vector for a bacterium called *Candidatus Liberibacter asiaticus.* Flying rapidly from tree to tree, the psyllid feeds upon the sap of the leaves and inadvertently carries the bacterium within the sap. The insect itself is very hardy, able to carry bacteria for up to a mile without ceasing flight and able to reproduce rapidly. Though they live only for one month, psyllid females may lay up to 800 eggs (1,2).

The trees, once infected, may take years to show symptoms. The leaves turn yellow and fall off. The fruit remains green and falls to the ground prematurely. Eventually, the tree itself succumbs to the disease. Unfortunately, once the tree has been infected, it cannot be cured by any means available to growers. Growers simply must burn or otherwise destroy the tree to prevent the further spread of bacterium-bearing psyllids (1,3).

The effects have been devastating to citrus crops wherever the disease spreads. The U.S. Agriculture Department has classified it next to anthrax and Ebola virus as a potential agent of bioterrorism (1). U.S. Senator Bill Nelson of Florida commented that the $9 billion Florida citrus industry and its thousands of workers are now "totally threatened" and, without a cure, will be eliminated (3).

The Fight

Citrus growers in Florida have already poured $60 million of their own companies' money into researching the disease. The Florida legislature has approved $8 million in research, and Washington State University has initiated a $9 million project to develop genetically altered psyllids resistant to infection from the citrus-greening bacterium (2,3).

In an attempt to bolster morale and show its commitment to the Florida orange, Coca-Cola (owner of Minute-Maid) has announced a plant to invest $2 billion to plant 25,000 acres of new orange groves in Florida (2).

Currently, efforts to combat the disease center around containment. Growers have chopped down hundreds of thousands of infected trees and sprayed an expanding assortment of pesticides on the psyllid. In fact, the industry has tripled pesticide applications in order to kill the psyllids – the increased dosage has become increasingly worrisome and expensive.

One pesticide lost effectiveness as the psyllid had evolved to become resistant, even as the Florida citrus growers begin their petition

to spray young trees multiple times a year in hopes of saving their harvest. The industry has shifted its view towards finding a more permanent solution.

Unfortunately, efforts to find a naturally immune tree to serve as the new progenitor for the Florida orange have failed. The plant pathologist heading a National Research Council task force on the disease remarked that "there is no evidence of immunity" within the scope of "all of cultivated citrus" (1).

Without a natural option, the focus has shifted to laboratory-based approaches. This shift is remarkable given the popularity of oranges in America and the simultaneous skittishness of the American people to support genetically modified organisms (GMO's).

The Challenge

The manipulation of DNA in laboratories often sparks distrust and fear, according to recent research (1,2). However, the total destruction of the Florida orange crop for the forseeable future is too much to risk for all those invested within the industry. And within the scientific community, there already exists a consensus that genetic engineering will be required to defeat citrus greening effectively (2, 3).

The process of creating a transgenic tree would take much of the next decade. It could cost up to $20 million and require rounds and rounds of testing before approval for use in real fields (2).

Traditionally, plant breeding has been used to select for desirable traits already seen in existing plants. Thus, the absence of a naturally resistant orange tree makes this process extremely difficult. The genetic engineering of resistance will require extraction of a foreign genome from a source organism, isolation of the desired gene, cloning to create thousands of copies of the gene, and ultimately the insertion of the gene into orange trees (4).

To ensure that the gene will function well in the new organism—in this case the orange tree—the gene is modified with sequences, such as a promoter, that will be read by the new organism. Various techniques may be used to insert the transgene into tissue cultures of the plant cells; each technique essentially injects the gene into the nucleus of the cell without killing the cell in the process (4).

Then, the growth of the orange tree begins as a single-line cell cultivar that requires two years of growth in a greenhouse before being planted. It would require many years before bearing fruit. Afterwards, the new orange plant may be bred with the original orange plant to pass down the resistance to a greater number of plants than what may be painstakingly grown

Figure 1: View of a Florida orange grove. Millions of orange trees have already been infected in Florida, due to the spread of an incurable plant disease spread by an invasive vector insect.

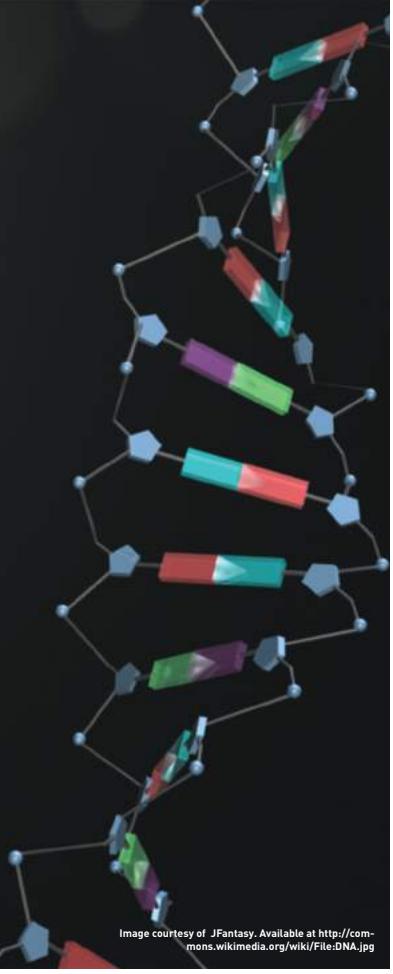


Figure 2: Genetic engineering may be the key to protecting the Florida orange— and orange trees around the world—from a devastating disease.

"Public backlash has erupted as of late due to the "Monsanto effect," a situation where the public disliked farmers using genetically modified plants, such as corn, that were engineered with an internal herbicide."

from cell culture (2, 4).

Difficulties have already arisen in the process. The plants that seem resistant and healthy in the greenhouse often do not fare well in the grove under a variety of environmental conditions. In these confined field trials, the trees are isolated to prevent their transgenes from spreading rampantly (4).

One stopgap technique created by a scientist at the University of Florida can be used as an alternative means of protecting citrus trees until the day that true transgenic trees become functional. The technique involves making an incision in the bark of a healthy, adult orange tree and inserting a virus that contains the gene for citrus-greening resistance. This virus acts to confer some degree of immunity to the tree (2).

If the pestilence were spreading less rapidly, the growers perhaps could expect to wait for natural immunity to arise within the orange trees. Unfortunately, the rate at which the Florida orange is being threatened is too great, and it is likely that the trees will entirely disappear before developing resistance (2).

Whatever the technique, there still exists much public resistance to transgenic crops. Public opinion polls indicate that as many as a half of Americans would refuse to eat any transgenic crop, a third may refuse to eat fruit modified with another plant gene, and very few would accept plants that contained animal or viral DNA (2, 3).

Figure 3: The Asian citrus psyllid carries the bacteria responsible for "citrus greening" in citrus fruits—the fruit do not mature, the leaves wither, and the tree eventually dies.

Public backlash has erupted as of late due to the "Monsanto effect," a situation where the public disliked farmers using genetically modified plants, such as corn, that were engineered with an internal herbicide, *Bacillus thuringiensis* (Bt). While these plants reduced the need for harmful insecticides, there still exists trepidation in the "mixing" of genes resulting in the blending of other characteristics from the gene donor (2).

The possibility that the genetically modified orange juice would not be labeled scares those reluctant to consume food created by "unnatural" means. Currently, the Food and Drug Administration supports voluntary labeling of genetically modified foods; however, the citrus industry in Florida is painfully aware of the backlash that may arise from forcing genetically modified orange juice on the market (2, 5).

Thus far, a gene from the spinach plant is showing the most promising results. The gene, though specifically derived from spinach, exists in many forms in plants and animals and functions to produce a protein that will attach the bacteria. In tests in both groves and greenhouses, the trees with conferred resistance remain resistant while the unaltered trees do not (2).

If these resistant trees manage to gain regulatory approval (the gene has already been thoroughly tested on mice and bees, to no ill effect), then they may be ready for planting by 2015 and ready to produce oranges for juice by 2018. The battle with the pestilence of citrus greening will have lasted 13 years in Florida, due to the infiltration of one bacteria-spreading insect (2).

CONTACT ANNIE (YI) SUN AT
YI.SUN.16@DARTMOUTH.EDU

References

1. Citrus Research Board, "The Insect: Asian Citrus Psyllid" (2013). Available at http://californiacitrusthreat.org/asian-citrus-psyllid.php (26 September 2013).
2. A. Harmon, "A Race to Save the Orange by Altering Its DNA", *The New York Times* (27 July 2013). Available at http://www.nytimes.com/2013/07/28/science/a-race-to-save-the-orange-by-altering-its-dna.html?pagewanted=all&_r=0 (4 August 2013).
3. M. Ricciardi, "Florida Orange Crop 'Totally Threatened' by Bacterium-Carrying Bug" (5 May 2013). Available at http://planetsave.com/2013/05/12/florida-orange-crop-totally-threatened-by-bacterium-carrying-bug/ (4 August 2013).
4. University of Nebraska, "Overview of the Process of Plant Genetic Engineering" (2001). Available at http://agbiosafety.unl.edu/education/summary.htm (27 September 2013).
5. Food and Drug Administration, "Genetically Engineered Plants" (07 April 2013). Available at http://www.fda.gov/Food/FoodScienceResearch/Biotechnology/ucm346030.htm (27 September 2013).

Human Enhancement

Image courtesy of NIH. Art by Gérard de Lairesse (1690)

BY JOHN STEWARD

Introduction

Humans have constantly attempted to improve themselves through technology. Whether it is increased physical attractiveness through cosmetic surgery or decreased likelihood of hereditary disorders in embryos using pre-implantation genetic testing, human enhancement in one form or another is not a foreign concept.

In the context of engineering, human enhancement can be defined as the application of technology to overcome physical or mental limitations of the body, resulting in the temporary or permanent augmentation of a person's abilities and features. By this definition, human enhancement entails both the treatment of disease and disability, as well as the upgrading of human aptitude (1). Furthermore, human enhancement is dichotomous in nature: while it heavily implements theoretical ideas by raising important questions about the human application of a diverse array of emerging technology, it also uses applied science and current technology, often borrowing from interdisciplinary scientific fields and methods.

Enhancing Substances

Several technologies exist today that can be properly classified as human enhancement technology. In addition to cosmetic techniques such as plastic surgery and orthodontics, there are drugs known as lean mass builders that directly improve physical performance by increasing muscle growth and density. These substances include membrane-permeable anabolic-androgenic steroids and the water-soluble growth hormone (GH). Although the two drugs differ in their pharmacodynamics and rates of induced muscle growth, both result in increased anabolism, the activity of pathways that promote protein biosynthesis (2). GH spurs lean muscle growth by increasing both lipolysis (breakdown of lipids) and protein synthesis, and producing insulin-like growth factor 1 (IGF-1) which stimulates overall tissue growth (3). Similarly, anabolic steroids stimulate the formation of new muscle fibers by increasing protein synthesis and causing hypertrophy (enlargement) of skeletal muscle even in the absence of strength training (4). Steroids increase both the cross-sectional area of the muscle and the length of the muscle, by raising the myofibril count and the number of sarcomeres per myofibril, respectively (5). Furthermore, research has shown anabolic steroids increase the activity of mitochondrial enzyme carnitine palmitoyltransferase in fast-twitch (Type II) muscle mitochondria, suggesting that androgens (including anabolic steroids) may have an important physiological role in the regulation of fatty acid oxidation by way of speeding up ATP synthesis (6). With the advent of reverse-engineered biochemicals such as recombinant human growth hormone (rhGH) for the treatment of growth disorders, these drugs have been employed as physical enhancers both legally and otherwise, especially in competitive sports (7).

In addition to drugs that allow heightened physical abilities, nootropic pharmaceuticals can enhance certain mental abilities of an individual. There are several classes of drugs that have been shown to improve cognitive processes such as memory and attention (8). One such class is cholinergic drugs, which affect the neurotransmitter acetylcholine (a facilitator of memory retention and formation) and are usually prescribed to moderate the effects of a variety of memory disorders including Alzheimer's disease (9,10). Acetylcholine may augment the encoding of new memories by not only stimulating long-term potentiation, but also strengthening feed-forward input to the cortex while decreasing excitatory feedback activity (11). Evidence suggests that drugs like acetylcholinesterase inhibitors, which increase the amount and longevity of acetylcholine in the brain, could be effectively implemented in healthy individuals for the purpose of improving memory functions in the absence of genuine medical needs (10).

Additionally, several pharmaceutical companies have been attempting to create a new class of mechanism-based, memory-enhancing drugs using information about the induction and consolidation of the memory encoding process (12). The most recent results of these efforts are known as ampakines, stimulants that improve short-term and long-term memory, as well as attention span and

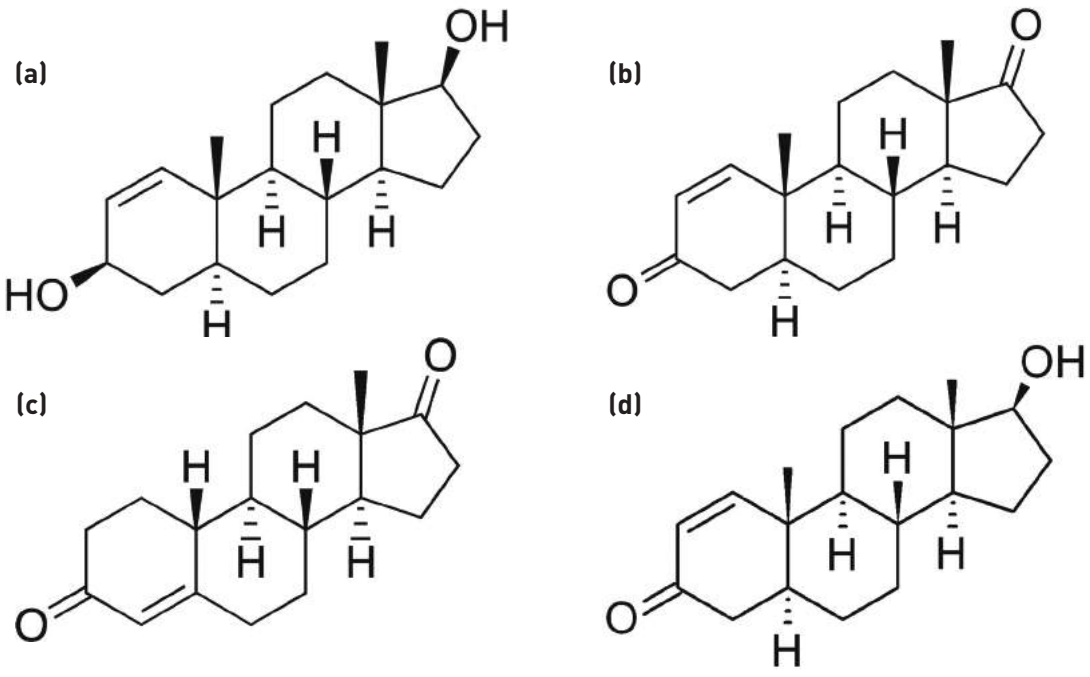


Figure 1: Various types of anabolic-androgenic steroids. (a) 1-androstendiol; (b) 1-androstenedione; (c) 19-norandrostenedione; (d) 1-testosterone

Images courtesy of Wikimedia Commons

alertness. These compounds have a strong affinity for the glutaminergic AMPA receptor, which is important for encoding memory (10). Ampakines have been investigated by DARPA as a potential means of increasing military efficiency, namely by reducing performance degradation due to sleep deprivation (13,14). Another type of stimulant, prescribed clinically to treat attention-deficit hyperactivity disorder (ADHD), is the mixed salts of amphetamine and is often sold under the brand name Adderall. Amphetamine's mechanism of action involves the release of dopamine and norepinephrine, important neurotransmitters involved in the regulation of attention (15). Amphetamine facilitates dopamine neurotransmission in striatal brain regions, which is thought to play a critical role in the therapeutic effects and stimulates the release of vesicular dopamine stores in presynaptic terminals, increasing extracellular dopamine levels (16).

The use of pharmaceuticals by the healthy to enhance mental faculties like memory and attention is a controversial neuroethical issue, as there are both positive and negative implications. In a non-clinical study involving the testing of amphetamine and related stimulants on healthy individuals without ADHD, the drugs were found to have a positive effect on cognition, improving performance on tasks that required sustained attention (16). The use of stimulants as cognitive enhancers is hardly a new idea; the United States Department of Defense distributed amphetamine tablets to troops as recently as the Gulf War (17). However, along with the positive effects of increased focus and productivity, these substances often have negative effects (10).

The negative consequences of using enhancing drugs include unexpected side effects and degenerative societal impacts. Although modern pharmaceuticals go through exhaustive laboratory trials before they are ever implemented clinically, there is still a risk of side effects in certain individuals. Furthermore, even when taking drugs medically prescribed to treat disorders, people can form addictive habits. Allowing the proliferation of enhancing substances could lead to increased drug abuse.

Genetic Engineering

The human enhancement methods discussed hitherto have been pharmaceutical drugs with a mostly temporary duration of effect that are currently regulated and administered for restricted medical use in the United States. In addition to ongoing pharmaceutical engineering efforts, there are many nascent and visionary technologies that could have extensive biological, social, political, and economic impacts if applied to humans for the purpose of enhancement. A number of these techniques are banned, some are not sufficiently developed to be implemented in an enhancing manner, and others are purely theoretical at present due to limits of technology.

With the emergence of biotechnology and recombinant DNA methods, the opportunity for true, permanent enhancement of humans exists on a profound level. Currently, human genetic engineering is legally limited to somatic gene therapy, a technique that involves the injection of a transgene (artificially introduced genetic material) into a somatic (body) cell of an individual to prevent a genetic defect (18,19). Any genetic effect or modification will be restricted to the individual treated and is not inherited by the progeny (18). Somatic gene therapy can be divided into two distinct approaches: *in vivo* and *ex vivo*. *In vivo* gene therapy comprises the introduction of a gene (in the form of a DNA liposome complex, recombinant virus, or DNA plasmid) into an individual to reduce or eliminate a defect (18). *Ex vivo* gene therapy involves removal of target cells from an individual, the subsequent modification of their genetic constitution by inserting a transgenic virus, the reintroduction of altered cells via transfusion, and finally the production of the desired protein or hormone (18). Germ line gene therapy, currently banned for use in humans, refers to the injection of a functional gene into the germ cells of an individual, allowing any genetic modifications made to be passed on to the offspring via gametes (18). Theoretically, this method should be quite effective in counteracting genetic disorders and hereditary diseases, but cannot be used in humans due to the risk of severe side effects and developmental problems because of limitations in current technology (18,20).

These types of gene therapy not only represent the means to cure genetic defects and hereditary disorders, but are also ways in which human genetic enhancement could eventually be performed through related processes. Echoing something encountered in the futuristic world of the video game BioShock, genetic enhancement is a form of positive eugenics that theoretically adds favorable genetic traits, such as disease resistance, strength, physical attractiveness, and even intelligence (18). Although somatic and germ line gene therapy methods can be an effective treatment for a genetic disorder where one mutant gene is the problem, they limit prospects for genetic enhancement because most human traits involve the interactions of many genes and their products. Efficient, directed genetic change to enhance human traits will probably require a technique able to introduce multiple human genes at the same time (21). However, genetic engineering for the purpose

WHAT IS GENE THERAPY?

Somatic gene therapy: injection of artificially introduced genetic material into a somatic cell

***In vivo*:** direct introduction of a gene to reduce or eliminate a defect

***Ex vivo*:** removal of target cells, modification of genetic material by inserting a transgenic virus, reintroduction of altered cells, and production of a desired protein or hormone

of enhancement is still in its infancy, and there are major scientific hurdles to overcome before this technology could be used in humans (22). Genetic enhancement is controversial in that it is no longer therapy for a disorder, but is instead the insertion of additional normal genes to produce a desired change in a characteristic (22). Even more controversial is eugenic genetic engineering, where a 'designer baby' would be created by manipulating any physical or behavioral trait that is controlled by genes using a perfected form of pre-implantation genetic diagnosis (23). However, this is not realistic at present: potentially hundreds of unknown genes that interact in unknown ways likely contribute to each trait and environmental influencers are poorly understood (22). Nonetheless, gene replacement, an emerging technique not yet perfected in humans, allows for excision of an abnormal gene from its chromosome and replacement with a normal gene. It has the potential for use in genetic enhancement, as genes for unfavorable attributes could be replaced with pre-engineered genes for more desirable traits (24).

Just as human genetic engineering techniques produced effective treatments for hereditary disorders, the development of genetic enhancement technology in humans is certainly possible, albeit much more difficult. With the potential to be an incredibly powerful scientific tool, human genetic enhancement would likely have both positive and negative effects. Due to the artificial augmentation of innate physical and mental qualities, genetic enhancement might have an effect on evolution (especially in a germ line enhancement). However, direct control over evolution is unlikely as the evolution of the human species is a nonrandom change in allelic frequencies resulting from selective pressure (25). Furthermore, genetic enhancement in humans would bring into question issues of genetic inequality and create potential for discrimination on a genetic basis. Possibly stemming from the fact that it is a quite nascent technology, there also exist stigma and fear surrounding this biotechnology in modern society. This is a factor that, while protecting humans from the possible dangers of experimental ideas, may concurrently obstruct innovation, scientific progress, and sociocultural evolution.

Images courtesy of Yuichiro C. Katsumoto. Available at http://commons.wikimedia.org/wiki/File:Hybrid_Assistive_Limb,_CYBERDYNE.jpg

Figure 2: This Japanese hybrid assistive limb utilizes a powered exoskeleton.

Enhancing Devices

In addition to drugs and genetic engineering techniques, there are a number of actual and visionary devices that could be used in the near future for the purpose of human enhancement. Many of these apparatuses are being proposed through emerging interdisciplinary scientific fields and have important applications to human enhancement. However, much of this technology is speculative or in its infancy. Nanomedicine has potential for use in human enhancement. Molecular nanotechnology is relevant to human enhancement because of molecular assemblers, theoretical machines that could re-order matter on the molecular or atomic scale to build biocompatible medical nanorobots, by way of positionally-controlled mechanosynthesis guided by molecular machine systems (26). The ability to design, construct, and deploy large numbers of medical nanorobots would facilitate the rapid elimination of disease and the reliable and relatively painless recovery from physical trauma via cell repair (26). Medical nanorobotics could also allow for the convenient correction of genetic defects, thus increasing lifespan (26). Furthermore, it has been hypothesized that diamondoid–based medical nanorobotics would be able to augment the natural capabilities of human biological systems: respirocytes are hypothetical artificial red blood cells composed of a spherical diamondoid pressure tank operated at up to 1000 atm of pressure – able to carry 236 times more oxygen to tissues than an equal volume of natural red blood cells, supplementing or replacing the function of the human body's normal respiratory system (27).

Emerging enhancement technologies could provide functional augmentation for various parts of the human body. The powered exoskeleton is a recently developed technology used to increase the wearer's strength, endurance, and agility (28). Reminiscent of the metal-clad character in the movie *Iron Man*, the exoskeleton includes an outer framework and employs electromechanical technology, featuring sensors that follow the wearer's movements. Microcontrollers then translate the movements into signals fed to a series of hydraulic actuators, emulating and amplifying the force of the movements (28). A common problem with mobile robotic suits like the powered exoskeleton is the extremely limited battery life, although more innovative technologies like lithium–sulfur batteries will be implemented in the future (28). Researchers are investigating the possibility of neural-controlled exoskeletons and integration of humans and robotic machines, as a human-machine interface was established at the neuromuscular level by using the neuromuscular signal (EMG) as the primary command signal for the exoskeleton system (29). As prosthetic technology advances, some scientists are considering the use of advanced prosthetic enhancements (which apply principles of biomorphic robotics), replacing healthy body parts with artificial mechanisms and systems to improve function (30). With the advent of 3D organ printing and improved tissue

engineering techniques, it could be possible to print fully functional replacement organs in the near future (31,32). These 3D printed organs could eventually be genetically modified to have enhanced functions.

Neural Enhancement

Because it directly and invasively interacts with the human brain, neural engineering would have the highest potential for negative effects if it was used for enhancement purposes. Clinical neurostimulation techniques such as deep brain stimulation (DBS) with microelectrodes are already used to treat Parkinson's disease, dystonia, and tremors (33). Also, neural prosthetics include integrated circuits, used to restore cognitive function to individuals with brain tissue loss, and cochlear implants that restore hearing (34). The increased use of these therapeutic methods could lead to the destigmatization of brain implants. Although neural engineering is a nascent science, implants in the prefrontal cortex of monkeys demonstrated a 10% increase in decision-making abilities (35). There would likely be similar neuroenhancement in humans if artificial neurotechnological devices were developed and implanted, possibly allowing humans to acquire superior perception, cognition, motor control, and positive moods (36). Additionally, there are direct communication pathways between an external device and the human brain, known as brain-computer interfaces (BCI), which can allow the brain to directly control a computer when a BCI is linked to the outer layers of the neocortex (37). Given the plasticity of the brain and the increased clinical use of neurostimulation devices and BCIs, it is possible that cybernetic organisms might exist in the future. These 'cyborgs' are humans who have synthetic elements infused in their body – they would be examples of human enhancement taken to the extreme. As early as 2007, a paper questioning the ethics of brain implants stated that "…there can be ethical problems inherent in the proper human uses of technologies and because brain chips are a very likely future technology, it is prudent to formulate policies and regulations that will mitigate their ill effects before the technologies are widespread" (38). Improvements to devices such as neurochips, neurocybernetics (integration of machines into living organisms), and neurobionics (substitution of failed and damaged brain areas with artificial, implantable information processing systems) could make the use of brain-enhancing implants more appealing and practical. There is a possibility that retinal implants and bionic eyes could become so advanced that upgrades to our natural hardware may be advantageous. Bioelectronics and biomechatronics could also be used in human enhancement for the purpose of creating cyborgs. Currently, biocompatible nanoscale wires have been successfully embedded into engineered human tissues in a laboratory (39). Biorobots, with a biological brain and mechanical limbs, would be the ultimate form of cyborg technology, presently only created artificially. Mind uploading (whole brain emulation) and the exocortex are two purely theoretical enhancement technologies. Mind uploading would involve the copying of a conscious mind from a brain to a non-biological form, while an exocortex would involve an artificial external information processer that would augment the cognitive function of the brain.

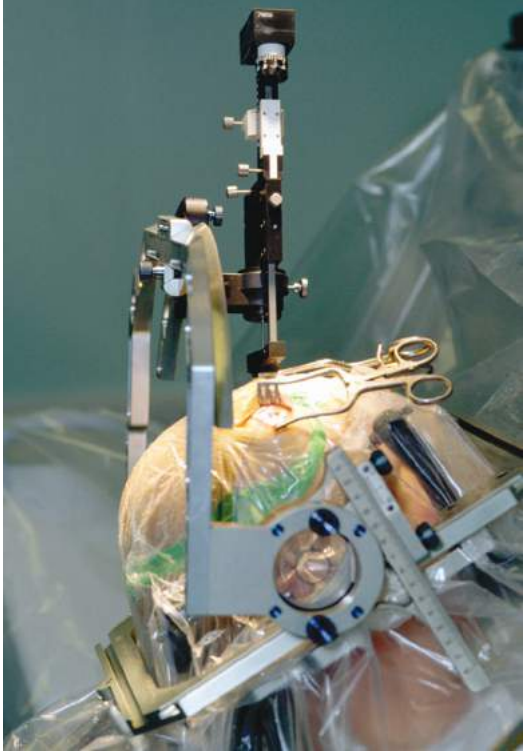


Figure 3: Electrode for deep brain stimulation (DBS) being inserted into the brain of a patient with Parkinson's disease.

Images courtesy of Thomasbg. Available at http://commons.wikimedia.org/wiki/File:Parkinson_surgery.jpg

"Biorobots, with a biological brain and mechanical limbs, would be the ultimate form of cyborg technology, presently only created artificially."

Conclusion

Human enhancement refers to the use of technology designed and implemented not for medical reasons but for enhancing the human body. However, as the enhancing technology becomes more abstract and far-influencing, ethical concerns arise. In addition to possibly affecting the identity of an individual, there are social implications of biological enhancement through science: the wealthy may be the only ones with access, those who choose not to enhance themselves may be ostracized, or the enhancement technology could start an arms race between nations. Also, human ingenuity has given us a means of enhancing our brains through inventions such as written language, printing, and the Internet. Yesterday's science fiction is today's technology, and in a sense, human enhancement is the most extreme

form of protective science. Thus, although the level of biological enhancement is limited by current technology and legal barriers, it is likely that human enhancement will become a controversial socio-scientific issue in the future. Humans must decide if increased physical and mental acuity from human enhancement technologies would be worth the potential side effects and costs to society and personal identity. Although enhancement has drawbacks, it does have the potential to be extremely beneficial and protective to humans, fostering innovation and possibly improving our species.

"Humans must decide if increased physical and mental acuity from human enhancement technologies would be worth the potential side effects and costs to society and personal identity."

CONTACT JOHN STEWARD AT
JOHN.A.STEWARD.15@DARTMOUTH.EDU

References

1. C. Elliott, "What's wrong with enhancement technologies?" (1998). CHIPS public lecture, Center for Bioethics at the University of Minnesota, 26 February, 1998.
2. A. T. Kicman, Pharmacology of anabolic steroids. *Brit. J. Pharmacol.* **154**, 502-521 (June 2008).
3. Actions of anterior pituitary hormones: physiologic actions of GH. Medical College of Georgia (2007).
4. D.C. Taylor, D.E. Brooks, J.B. Ryan, Anabolic-androgenic steroid administration causes hypertrophy of immobilized and nonimmobilized skeletal muscle in a sedentary rabbit model. *Am. J. Sport. Med.* **27**, 718-727 (1999).
5. B. Braun, "Muscle hypertrophy and anabolic agents" (November 2007). Lectures 20 and 21 for Kinesiology 380: Diet, Supplements and Athletic Performance, University of Massachusetts Amherst. Available at http://courses.umass.edu/kin380 (14 August 2013).
6. M. Guzmán *et al.*, Treatment with anabolic steroids increases the activity of the mitochondrial outer carnitine palmitoyltransferase in rat liver and fast-twitch muscle. *Biochem. Pharmacol.* **41**, 833-835 (1991).
7. A. Takeda *et al.*, Recombinant human growth hormone for the treatment of growth disorders in children: a systematic review and economic evaluation. *Health Technol. Asses.* **14**, 1-209 (2010).
8. C. Lanni *et al.*, Cognition enhancers between treating and doping the mind. *Pharmacol. Res.* **57**, 196-213 (2008).
9. M. Eidi *et al.*, Effects of histamine and cholinergic systems on memory retention of passive avoidance learning in rats. *Eur. J. Pharmacol.* **465**, 91-96 (2003).
10. W. Dekkers, M. O. Rikkert, Memory enhancing drugs and Alzheimer's disease: enhancing the self or preventing the loss of it? *Med. Health Care Philos.* **10**, 141-151 (2007).
11. M. E. Hasselmo, The role of acetylcholine in learning and memory. *Curr. Opin. Neurobiol.* **16**, 710-715 (2006).
12. G. Lynch, Memory enhancement: the search for mechanism-based drugs. *Nat. Rev. Neurosci.* **5**, 1035-1038 (2002).
13. W. Saletan, Night of the Living Meds: The U.S. military's sleep-reduction program (2008). Available at http://www.slate.com/articles/health_and_science/human_nature/2008/07/night_of_the_living_meds.html (15 August 2013).
14. E. Williams *et al.*, "Human performance" (Tech. Rep. JSR-07-625, Office of Defense Research and Engineering, Washington, DC, 2008).
15. F. P. Bymaster *et al.*, Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. *Neuropsychopharmacol.* **27**, 699-711 (2002).
16. L. C. Bidwell, F. J. McClernon, S. H. Kollins, Cognitive enhancers for the treatment of ADHD. *Pharmacol. Biochem. Be.* **99**, 262-274 (2011).
17. E. Borin, The U.S. Military Needs Its Speed (2003). Available at http://www.wired.com/medtech/health/news/2003/02/57434 (15 August 2013).
18. E. M. Berger, "Recombinant DNA III: human biology" (2013). Lecture delivered at Dartmouth College, 25 July 2013.
19. P.J. Russell, *iGenetics: A Molecular Approach* (Benjamin Cummings, San Francisco, CA, ed. 3, 2010), pp. 280.
20. T. O. Nielsen, Human germline gene therapy. *McGill J. Med.* **3**, 126-132 (1997).
21. The President's Council on Bioethics, Human Genetic Enhancement (2002). Available at http://bioethics.georgetown.edu/pcbe/background/humangenetic.html (15 August 2013).
22. W. F. Anderson, Human gene therapy: scientific and ethical considerations. *J. Med. Philos.* **10**, 275-291 (1985).
23. D. Simmons, Genetic Inequality: Human Genetic Engineering (2008). Nature Education. Available at http://www.nature.com/scitable/topicpage/genetic-inequality-human-genetic-engineering-768 (15 August 2013).
24. R. M. Sade, G. Khushf, Gene therapy: ethical and social issues. *J. S. C. Med. Assoc.* **94**, 406-410 (1998).
25. K. E. Hanna, Genetic Enhancement (2006). National Human Genome Research Institute. Available at http://www.genome.gov/10004767 (15 August 2013).
26. R. A. Freitas, Jr., Current status of nanomedicine and medical nanorobotics. *J. Comput. Theor. Nanos.* **2**, 1-25 (2005).
27. R. A. Freitas, Jr., A Mechanical Artificial Red Cell: Exploratory Design in Medical Nanotechnology (1999). Foresight Institute. Available at http://www.foresight.org/Nanomedicine/Respirocytes.html (15 August 2013).
28. R. Bogue, Exoskeletons and robotic prosthetics: a review of recent developments. *Ind. Robot.* **36**, 421-427 (2009).
29. J. Rosen, M. Brand, M. B. Fuchs, M. Arcan, A myosignal-based powered exoskeleton system. *IEEE T. Syst. Man Cy. A.* **31**, 210-222 (2001).
30. F. Tenore, R. Etienne-Cummings, Biomorphic circuits and systems: control of robotic and prosthetic limbs. *IEEE BioCAS*, 241-244 (2008). Available at http://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=4696919 (15 August 2013)
31. M. S. Mannoor *et al.*, 3D printed bionic ears. *Nano Lett.* **13**, 2634-2639 (2013).
32. I. T. Ozbolat, Y. Yu, Bioprinting toward organ fabrication: challenges and future trends. *IEEE T. Biomed. Eng.* **60**, 691-699 (2013).
33. J. S. Perlmutter, J. W. Mink, Deep brain stimulation. *Annu. Rev. Neurosci.* **29**, 229-257 (2006).
34. T. W. Berger *et al.*, Restoring lost cognitive function. *IEEE Eng. Med. Biol.* **24**, 30-44 (2005).
35. The futuristic brain implant that makes monkeys smarter (2012). Available at http://theweek.com/article/index/233419/the-futuristic-brain-implant-that-makes-monkeys-smarter (15 August 2013)
36. J. K. Berg-Olson, S. A. Pedersen, V. F. Hendricks, Eds., *A Companion to the Philosophy of Technology* (Wiley-Blackwell, Hoboken, NJ, 2009), pp. 392-396.
37. P. R. Kennedy, R. A. E. Bakay, M. M. Moore, K. Adams, Direct control of a computer from the human central nervous system. *IEEE T. Rehabil. Eng.* **8**, 198-202 (2000).
38. E. M. McGee, G. Q. Maguire, Jr., Becoming borg to become immortal: regulating brain implant technologies. *Camb. Q. Heathc. Ethic.* **16**, 291-302 (2007).
39. P. Reuell, Merging the biological, electronic (2012). Available at http://news.harvard.edu/gazette/story/2012/08/merging-the-biological-electronic (15 August 2013).

Unlocking the Mind with Brain-Computer Interfaces

Image courtesy of Bainbridge State College. Available from http://fsweb.bainbridge.edu/acunningham/AP/AP-img/Nerve-Slide-MotorNeurons.jpg

BY JESSICA BARFIELD

Introduction

Some people afflicted with a severe form of neurological disease are essentially "locked in" their own bodies. They are conscious but cannot move or communicate verbally due to paralysis of nearly all of their voluntary muscles except for their eyes (1); for those with total locked-in syndrome, even the eyes are paralyzed. While many locked-in patients retain awareness and cognitive capabilities, those with central nervous system damage enter into a minimally conscious state, showing fluctuating signs of awareness.

Neurodegeneration, the progressive loss of neuron structure or function, is a notable cause of locked-in syndrome (1). Of the many neurodegenerative disorders, amyotrophic lateral sclerosis and a minimally conscious state are often associated with the locked-in state. But with the recent advancements in technology, researchers can now develop brain-computer interfaces that assist these patients in interacting and communicating with the world.

Lou Gehrig's Disease and Minimally Conscious State

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord (2, 3). Often also called Lou Gehrig's disease (after the hall-of-fame baseball player diagnosed with the disease in the 1930s), ALS affects over 30,000 Americans and has an incidence of 5,600 people per year in the U.S. (1, 2).

The distinct physical defects associated with ALS are easily deducible from its name. "Amyotrophic" means that the muscles have lost their nourishment; when this happens, they become smaller and weaker. "Lateral" indicates that the disease affects the sides of the spinal cord, where the nerves that nourish the muscles are located. Lastly, "sclerosis" means that the diseased part of the spinal cord develops hardened or scarred tissue in place of healthy nerves. The progressive degeneration of the motor neurons in ALS eventually leads to the inability of the brain to initiate and control muscle movement (2, 3).

It is also this loss of motor neurons that makes ALS patients likely to enter a state of being locked in. Motor neurons are nerve cells that control muscle movement, and the neuromuscular system that enables our body to move is made up of the brain, many nerves, and muscles. Unfortunately, ALS damages motor neurons in the brain and spinal cord (1, 2). Specifically, it results in the death of both upper and lower motor neurons in the motor cortex of the brain, the brain stem, and the spinal cord. Over time, ALS causes the motor neurons in the brain and spinal cord to shrink and disappear, causing the muscles to no longer receive the signals that induce movement (1, 2). In the absence of use, the muscles atrophy, becoming smaller and weaker. And when the muscles no longer work, the body becomes paralyzed. But despite paralysis, ALS patients, even at an advanced stage, can still see, hear, smell, and feel; the nerves that carry the sensation of hot, cold, pain, or pressure are not affected by ALS (2, 3). For some people with ALS, the parts of the brain that allow us to think, remember, and learn are also

Figure 1: Motor neurons on a microscope slide. The neuron cell body, dendrites, and axons are clearly visible.

"Researchers can now develop brain-computer interfaces that assist these patients in interacting and communicating with the world."

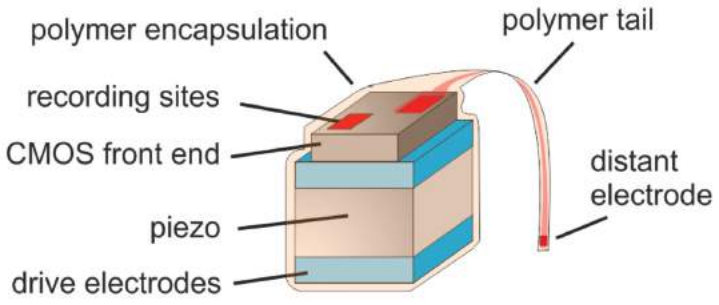


Image courtesy of Dongjin Seo, et. al. Available at http://arxiv.org/pdf/1307.2196v1.pdf

Figure 2: Berkeley researchers have proposed a strucure for neural dust that will improve upon current brain computer interfaces.

affected by the disease (3). Once ALS progresses, the person's central nervous system motor neurons may be so damaged that the person becomes totally paralyzed, essentially locked in his or her own body.

Another severe neurological condition that leads to the loss of the ability to interact and communicate with the world is a minimally conscious state (MCS). People suffering from MCS are so impaired with immobility that they have trouble performing basic life activities. While they are usually able to breathe without a respirator, they lack the means to communicate meaningfully, have bladder and bowel incontinence, and require feeding tubes. MCS patients are also severely cognitively impaired, although they do seem to have some definite, but extremely limited, awareness of themselves and their environment, and limited means of communication (1). They are able to experience pain and suffering to some degree, although the degree of pain and suffering often cannot be determined.

Brain-Computer Interface

Brain cells communicate by producing tiny electrical impulses that facilitate processes such as thought, memory, consciousness, and emotion. Even people who are locked-in and unable to speak or gesture still produce these electrical impulses within the brain areas that plan movements. These signals can be detected by implanted micro-electrodes and computer chips that detect, pick up, and translate these impulses (4, 5). Using this technology, researchers are developing devices to help people with limited motor skills due to neurological damage. These devices will give the patients the opportunity to communicate by reading their brain signals.

Detecting a person's brain activity may allow patients to activate prosthetics or command computers, providing them the ability to regain the functions they have lost to the disease (5, 6). If people afflicted with ALS could control a computer through thought alone, the computer could then serve as an interface for these patients to operate light switches, television, a robotic arm, and communicate to their loved ones – something that over 160,000 people in the United States who cannot move their arms and legs would surely welcome.

Another example of technology that assists people with severe neurological damage is the brain-computer interface, designed to assist patients suffering from MCS (6, 7). Dr. Ali Rezai and colleagues at Ohio State University, and Maysam Ghovanloo at the Georgia Tech Bionics Lab are developing techniques in neuromodulation, or deep brain stimulation (DBS). DBS is a surgical procedure that can create dramatic improvements for a patient suffering from neurological disorders. In a DBS procedure, the surgeon implants millimeter-thin electrodes in the brain and a small device that powers the electrodes in the patient's chest (7). The electrodes deliver tiny electrical signals that block abnormal brain signals. The results produced by Rezai's team have shown that people who have spent years in a near-vegetative state have made dramatic recoveries following treatment to stimulate his or her brain with electrical pulses.

To address deficiencies with current brain-computer interfaces, such as a limitation of implantable recording sites and the degradation of the electrodes' recording performance over time, researchers at Berkeley are developing a system that will allow thousands of ultra-tiny neural-dust chips to be inserted into the brain to monitor neural signals at high resolution (7, 8). The particles of neural dust are no more than 100 micrometers across and each particle is a sensor capable of measuring electrical activity in neurons. The system is covered in polymer to render it biologically neutral and backed by a piezoelectric material that can convert electrical signals into ultrasound (8, 9). The researchers envision a system in which thousands of neural dust sensors are constructed at the tips of fine wire arrays, which would then be inserted directly into brain tissue. Signals from the brain would be detected by a sub-dural transceiver that sits just above and ultrasonically powers the dust chips. The transceiver would then relay the data to an external transceiver resting just outside the skull, which in turn would communicate wirelessly with a computing device (9). Once the sensors are pulled free of the wire, the arrays would withdraw. One of the serious design challenges to overcome in this system is to make sure the system is efficient enough to avoid producing heat between the skull and brain.

Conclusions and Future Directions

For people suffering from neurodegenerative diseases such that they are locked in their body

and unable to interact and communicate directly with the world, a brain-computer interface may provide them with a means to communicate and control prosthesis. For people with MCS, an implantable electrode stimulating the brain may allow them to regain consciousness and awareness of their environment. The development of these brain-computer interfaces could not have been possible without the manufacturing of inexpensive computer hardware and software, the scientific research on the nature and functional correlates of brain signals, and the improved methods for recording these signals. Nevertheless, more research will be needed to develop better brain-computer interfaces that further improve the quality of life for people locked in their own bodies or suffering from MCS.

In summary, brain-computer interfaces may assist those locked in their body with the ability to communicate and interact with the world. As shown by the Berkeley team, the new technology currently under development may greatly assist those with other severe neurological disorders. Given the recent developments in brain-computer interfaces, the future holds great promise for people locked-in their own bodies, aware and awake but unable to move or communicate verbally due to complete paralysis of nearly all voluntary muscles in the body (1). Finally, the use of implantable electrodes within the person's brain may also provide a way to treat those in a MCS.

CONTACT JESSICA BARFIELD AT
JESSICA.K.BARFIELD.16@DARTMOUTH.EDU

References

1. Hardiman, O., and Doherty, C. P., 2011, Neurodegenerative Disorders: A Clinical Guide, Springer Publisher.
2. Lou Gehrig's Disease, Available at http://kidshealth.org/kid/grownup/conditions/als.html, accessed (September 12 2013).
3. Engdahl, S., 2012, Lou Gehrig's Disease: Perspectives on Diseases and Disorders, Greenhaven Press.
4. Graimann, B., Allison, B. Z., and Pfurtscheller, G., 2013, Brain-Computer Interfaces: Revolutionizing Human-Computer Interaction (The Frontiers Collection), Springer; 2011 edition.
5. Wolpaw, J., and Wolpaw, E.W., 2012, Brain-Computer Interfaces: Principles and Practice (Jan 24, 2012), Oxford University Press, USA; 1 edition.
6. Cyberkinetics, Company Web Site, Available at http://www.cyberkineticsinc.com/, accessed (September 14 2013).
7. Ali Rezai, Ohio State University, Deep Brain Stimulation, Available at http://www.osu.edu/features/2013/rezai.html, accessed (September 14 2013).
8. Peckham, M., Your Future Brain-Machine Implant: Ultrasonic Neural Dust, http://techland.time.com/2013/07/17/your-future-brain-machine-implant-ultrasonic-neural-dust/, accessed (August 12 2013).
9. Dongjin Seo, Jose M. Carmena, Jan M. Rabaey, Elad Alon, Michel M. Maharbiz, Neural Dust: An Ultrasonic, Low Power Solution for Chronic Brain-Machine Interfaces, http://arxiv.org/abs/1307.2196, accessed (August 12 2013).

Figure 3: Non-invasive Brain computer interfaces such as the headset shown here can detect electrical impulses without implanting electrodes directly into the brain.

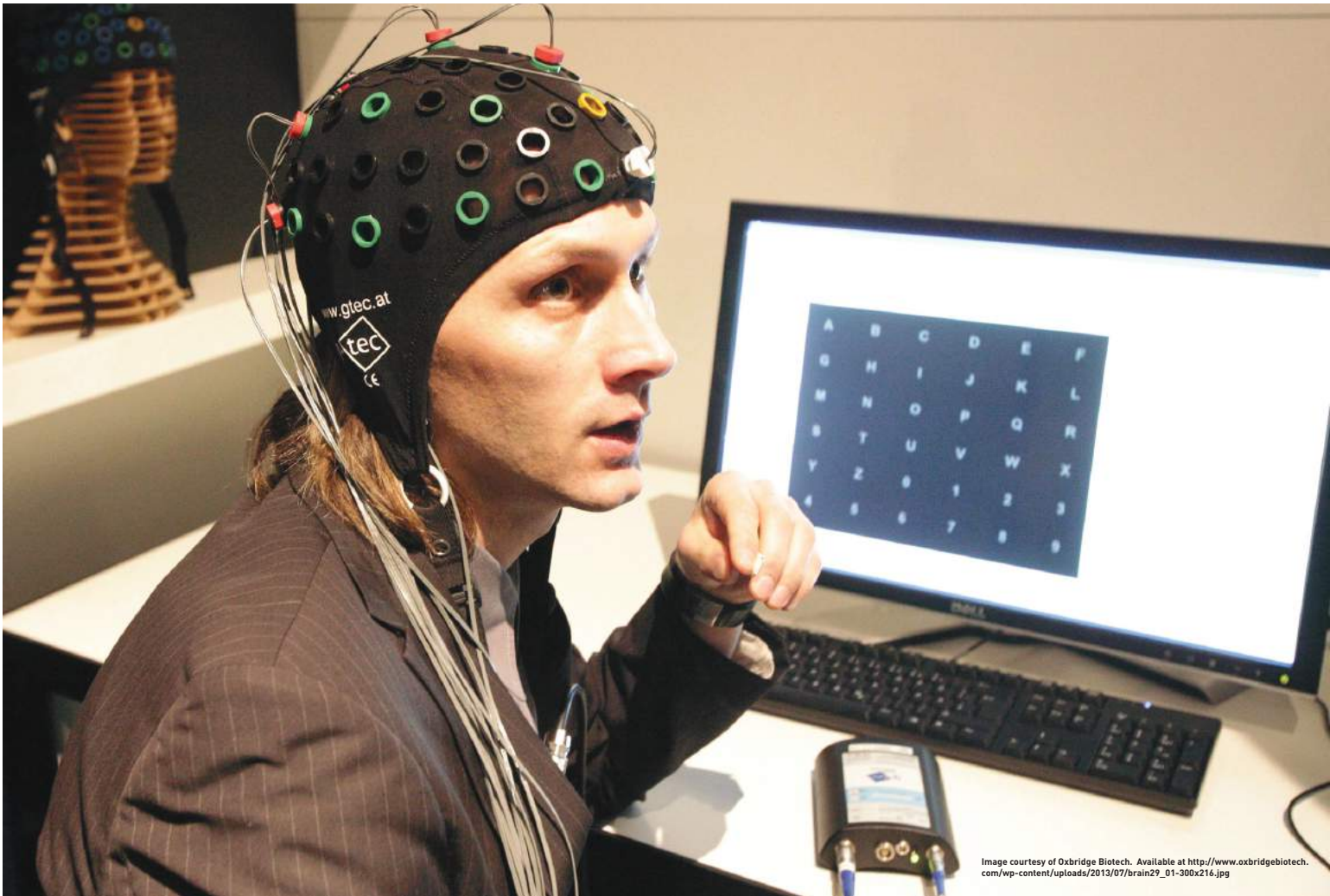


Image courtesy of Oxbridge Biotech. Available at http://www.oxbridgebiotech.com/wp-content/uploads/2013/07/brain29_01-300x216.jpg

Liquid Body Armor

Image courtesy of Rory MacLeod. Available at http://www.flickr.com/photos/macrj/539381838/lightbox/

BY JULIA ISAACSON

Figure 1: Oobleck is a hallmark example of a shear thickening fluid.

Introduction

Increasingly sophisticated weapons continue to pose new threats for soldiers in the frontline. Thus, efforts are underway to develop more protective and reliable body armor. Researchers at the United States Army Research Laboratory recently developed shear thickening fluid (STF), a lightweight and flexible protective material that can do the work of its heavier and bulkier conventional counterparts. The discovery and subsequent implementation of such materials has increased the demand for armor that is not only durable, but also allows for heightened maneuverability and operational effectiveness. According to Eric Wetzel, who led the military research team, "the goal of the technology is to create a new material that is low-cost and lightweight, and that offers equivalent or superior ballistic properties as compared to current Kevlar fabric but has more flexibility and less thickness" (1).

Figure 2: Tradiitonal ballistics armor may include a combination of a soft Kevlar vest and an additional ceramic trauma plate such as the Small Arms Protective Insert shown below.

Image courtesy of U.S. Air Forces. Available at http://www.afcent.af.mil/shared/media/photodb/photos/2013/04/130329-F-KZ210-008.jpg

A Nanoscale Discovery

Shear thickening fluid, colloquially known as "liquid body armor", was developed in 2002 at the United States Army Research Laboratory in Adelphi, Maryland. Two scientists – Norman Wagner, a professor of chemical engineering at the University of Delaware, and Eric Wetzel, a staff member at the laboratory – led the development team. The application for US Patent No. 7,226,878, the patent for "Advanced Body Armor Utilizing Shear Thickening Fluids," was submitted in 2003 and issued four years later (2). Wagner and Wetzel were subseqently awarded the Paul A. Siple Award, the Army's highest award for scientific achievement.

The Technology

Several properties of shear thickening fluid make it desirable for use in protective clothing. Most significantly, STF behaves as a liquid until it is exposed to mechanical stress. At that point, within a matter of milliseconds, it hardens into a solid. Thus, when there is no threat to the wearer's safety, he or she experiences little impairment in flexibility or range of motion. However, a ballistic or penetrative threat instantaneously activates the protective features of the armor (3).

Shear thickening fluid is an application of the rapidly growing field of nanotechnology. STF is a colloid, a mixture in which one substance is dispersed throughout another (4). Liquid body armors employ an STF that consists of 450 nm silica nanoparticles suspended in polyethylene glycol or ethylene glycol, both liquid polymers. The silica particle concentration must be between 55 and 65 percent by volume for optimal protective capabilities (5).

When STF is in liquid form, the weak molecular interactions between the silica particles permit them to move around freely in the liquid polymer without binding to one another. However, a ballistic or penetrative strike to the material (because the energy of impact is much greater than the energy between the metal particles) forces the particles to temporarily assemble into hydroclusters - long irregularly shaped chains of molecules. The hydroclusters subsequently overlap to form a mesh-like structure, which dramatically increases the viscosity of the liquid (6). As soon as the energy from the mechanical stressor disappears, this process reverses itself, and the substance returns to a liquid state.

Shear thickening fluid is considered to be a "non-Newtonian" fluid, a fluid that behaves in a way that contradicts Newton's original theories. Newtonian fluids have a constant viscosity unless exposed to changes in temperature or pressure. Non-Newtonian fluids, in contrast, experience changes in viscosity in situations in which most fluids would not. In the case of STF specifically, its viscosity is dependent on shear stress (6). However not all non-Newtonian fluids exhibit the same physical changes in response to stress – while stress increases the viscosity of STF, it decreases the viscosity of shear thinning fluids, such as paint.

Unique Properties Allow for Increased Protection

The concept of "liquid body armor" can be misleading – there is in fact no external, visible liquid layer. Rather, shear thickening fluid is used to reinforce conventional forms of body armor such as Kevlar. While Kevlar has proven to be effective, 20 to 40 layers of its high-strength aramid fibers are required to stop a bullet, and ceramic tile inserts are necessary in high-threat situations (5). This form of body armor protects the wearer well but decreases flexibility and hinders performance.

The data from a study conducted by the United States Army Research Laboratory showed that four layers of Kevlar impregnated with STF could dissipate the same amount of energy as 14 layers of neat Kevlar. Furthermore, treating the Kevlar with STF adds little extra weight or thickness. Treating four layers of neat Kevlar with STF increases its mass by 2.9 g and its thickness by 0.1 mm. In general, saturated Kevlar can be 45% thinner than neat Kevlar without posing a threat to the wearer's safety (5).

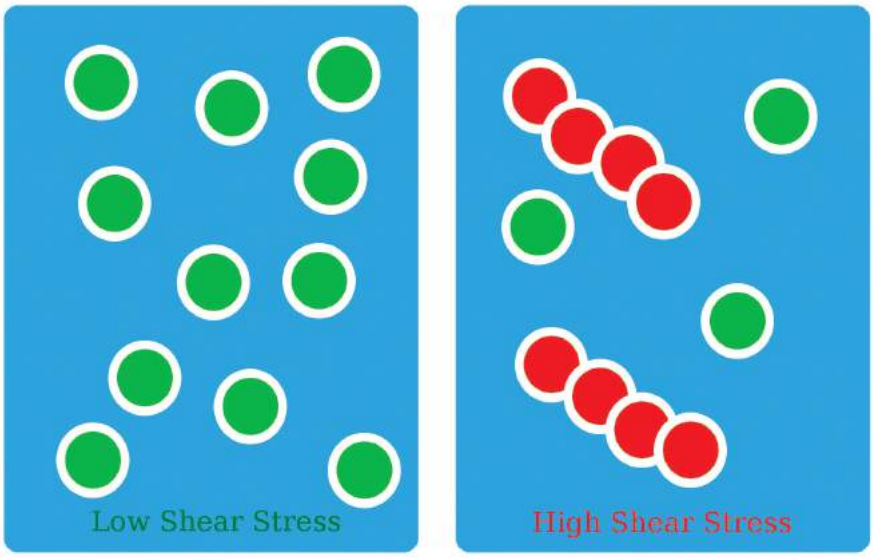


Image courtesy of Rui Shu

Figure 2: Shear thickening fluid behaves as a solid when exposed to mechanical stress because the energy of the impact forces the metal particles in the colloid to form hydroclusters.

In addition to increasing the wearability of conventional body armor, STF saturation also reduces the pain resulting from a bullet strike. This is due to STF's increased energy dissipation capacity. According to BAE Systems, the company currently manufacturing this product, liquid armor disperses mechanical stress over a wider area, restricting the depth of penetration (7). For the lowest impact velocities tested, the saturated Kevlar was never penetrated (5).

STF is applied to conventional ballistic fabrics, such as Kevlar, by diluting the liquid with ethanol, applying the diluted mixture to the fabric, then evaporating the ethanol. Fabrics saturated with STF retain all the desirable properties of unsaturated fabrics.

Far-Ranging Applications

While STF-incorporated armor is not currently ready for combat, its inventors believe that it shows great promise. They predict that STF-saturated fabrics will soon supplement, if not entirely replace, conventional forms of body armor. In addition, this technology will likely be applied to shields, sportswear, and protective clothing for police officers, prison guards, and ambulance crews (7). There is also potential for its use in gloves for medical professionals in order to prevent needlestick

"Shear thickening fluid is considered to be a "non-Newtonian" fluid, a fluid that behaves in a way that contradicts Newton's original theories."

injury and infection.

When asked about the prospects of this technology, Wetzel replied, "The sky's the limit." He continued, "We would first like to put this material in a soldier's sleeves and pants, areas that aren't protected by ballistic vests but need to remain flexible. We could also use this material for bomb blankets, to cover suspicious packages or unexploded ordnance. Liquid armor could even be applied to jump boots, so that they would stiffen during impact to support soldiers' ankles" (8).

"When asked about the prospects of this technology, Wetzel replied, 'The sky's the limit.'"

However, by no means are the applications of shear thickening fluid limited to protective clothing. In the oil industry, shear-strengthening materials are used in combination with other drilling fluids to 'patch' wells in order to control some forms of blowouts (9). Additionally, engineering students at Case Western Reserve University in Ohio used Oobleck, a shear thickening fluid made with cornstarch and water, to fill potholes. The students believed that STF was the ideal material for this project because of its ability to both "fill irregularly-shaped depressions" and to "become rigid in the presence of passing automobiles" (10). BAE systems also plans to "further engineer" STF to ensure high levels of thermal stability and moisture resistance, properties which Kevlar is argued to lack (5).

STF's wide-ranging applications demonstrate the innovative employment of its non-Newtonian properties. The extent of its versatility is bounded only by our creativity, and it will take new minds to expand upon STF's implementation in our society, both as a protective material and beyond it.

CONTACT JULIA ISAACSON AT
JULIA.E.ISAACSON.15@DARTMOUTH.EDU

References

1. A. Manser, UD Researchers Devise Liquid Body Armor Technology. Available at http://www.udel.edu/PR/experts/armor.html (5 September 2013).
2. A. Guerrero, Liquid Body Armor. Available at http://www.nisenet.com/sites/default/files/catalog/uploads/8379/liquid_body_armor.pdf (5 September 2013).
3. Shear Thickening Fluid Showing Promise for Increasing Soldier Protection (8 December 2010). Available at http://www.arl.army.mil/www/default.cfm?video=9 (4 September 2013).
4. Colloid Definition. Available at http://www.merriam-webster.com/dictionary/colloid (21 September 2013).
5. E. Wetzel, N. Wagner, Advanced Body Armor Utilizing Shear Thickening Fluids (3 December 2002). Available at http://www.ccm.udel.edu/STF/PubLinks2/AdvancedBodyArmor_Pres.pdf (2 September 2013).
6. D. Price, Shear-Thickening Fluid (10 May 2012). Available at http://physics.wooster.edu/JrIS/Files/Price_Web_Article.pdf (21 September 2013).
7. Flexible Friend on the Front Line. Available at http://www.baesystems.com/home?_afrLoop=127439853666000 (7 September 2013).
8. T. Johnson, Army Scientists, Engineers Develop Liquid Body Armor (21 April 2004). Available at http://www.military.com/NewsContent/0,13319,usa3_042104.00.html (21 September 2013).
9. McCreary, Shear Fluid Paper. Available at http://paultheengineer.com/print/shearfluidpaper.pdf (19 September 2013).
10. B. Brownell, A Practical Use for Oobleck (2013). Available at http://www.architectmagazine.com/blogs/postdetails.aspx?BlogId=mindmatterblog&postId=107817 (19 September 2013).

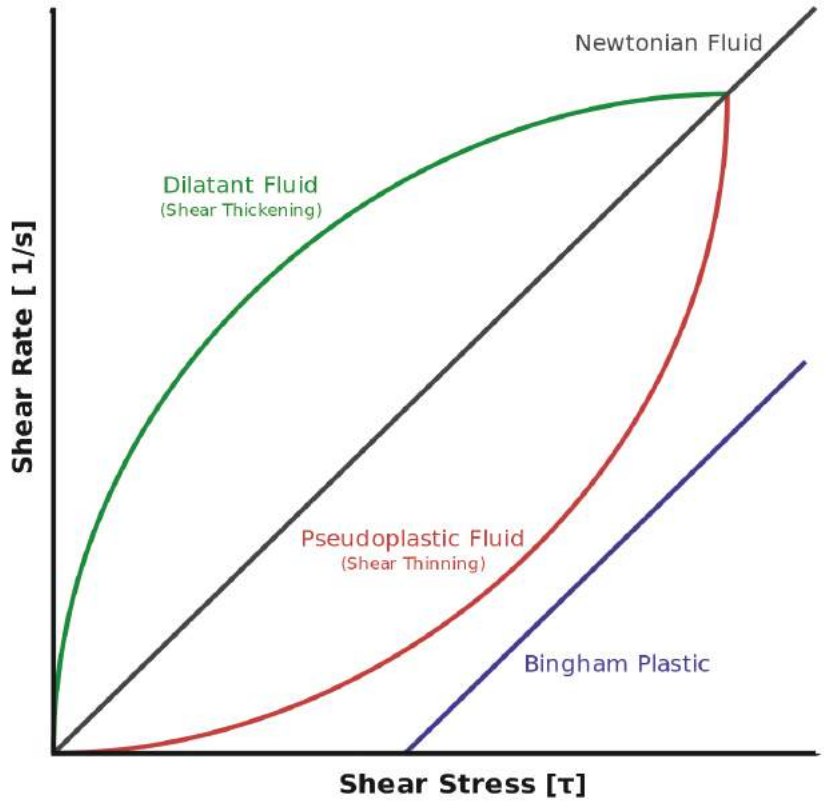


Figure 3: This graph of shear rate versus shear stress shows the dependency of the shear rate on different types of fluid on applied shear stress.

Image courtesy of Wikimedia Commons. Available at http://en.wikipedia.org/wiki/File:Shear_rate_vs._Shear_stress.png

Countering Man-Portable Air-Defense Systems

Image courtesy of Wikimedia Commons. Available at http://commons.wikimedia.org/wiki/File:Redeye_MANPADS.JPEG

BY SHINRI KAMEI

Introduction

With 261 passengers on board, a Boeing 757 takes off from the Moi International Airport in Mombasa, Kenya, on its way to Israel. But right as the plane takes off, two missiles whiz by the left wing of the aircraft. They miss, and the passengers only experience a loud noise. But in an Israeli-owned hotel in the same city, people are not so lucky. 15 die, and a Lebanese terrorist group called the Army of Palestine takes responsibility for both attacks (1).

The missiles fired at the commercial jet that day originated from man-portable air-defense systems (MANPADS). Originally developed during the Cold War as convenient anti-aircraft weapons, MANPADS have since seeped through black markets worldwide (2). Today, several thousand MANPADS do not belong to a national government (2); an estimated 24 terrorist groups have MANPADS, each equipped with an infrared sensor that guides the missile to the hot engine of a target aircraft (3). Since 1973, there have been fifty recorded MANPADS attacks on civilian aircraft, bringing the death toll to 920 (4).

Of the two attacks in Mombasa in 2002, the bombing did prove to be the more destructive. But had the MANPADS been angled slightly differently upon launch, and the infrared tracking system a little more accurate, the death toll would have been 276 instead of 15—almost 19 times greater. Furthermore, at the 2003 Asia-Pacific Economic Cooperation forum, Secretary of State Colin Powell declared that "no threat is more serious to aviation" than MANPADS (5).

Use in Terrorism

The destructive potential of MANPADS has proven itself in a number of high-profile attacks, including the one that began the Rwandan genocide.

In 1994, tensions were high as two warring ethnic groups in Rwanda, the Hutus and the Tutsis, struggled to implement agreed-upon peace accords. The presidents of Rwanda and Burundi flew to Rwanda from a regional summit in Tanzania, but as their plane prepared to land, a missile was launched using MANPADS nearby (2). Junvénal Habyarimana,

Figure 1: A U.S. Marine aims a Redeye anti-aircraft rocket during an air combat straining exercise.

Figure 2: The Russian Igla MANPADS. During launch, an operator rests the back half of the launcher on his shoulder. He looks through the sight assembly to launch and can then "fire and forget," as the warhead is self-guided.

the assassinated Rwandan president, was a dictatorial leader that promoted national hatred against the Tutsis throughout his regime. Habyarimana's death was seen as an attack from the opposition and reignited a civil war. The subsequent genocide that would result in 800,000 deaths over the course of 100 days. It is still unknown who was responsible for the attacks.

How They Work

MANPADS operate by using one of two main guidance mechanisms: passive homing and command guidance. Both systems make MANPADS usable by a single operator, making it a convenient tool for the military and insurgents.

"The Russian Igla's design has been frequently copied in missiles developed by militaries."

In passive homing, the MANPADS missiles take advantage of the infrared rays emitted by the aircraft's engine (4). The warheads are equipped with sensor units that detect this radiation and internal programming that controls the missiles to follow these rays on their own. These "fire and forget" missiles require no operator input after launch and are the most widely used systems. However, their automated function also makes them the most susceptible to decoys. The Russian Igla, pictured in Fig 2., is the most well-known of MANPADS that employed this system, and its design has been frequently copied in missiles developed by militaries.

A passive homing MANPADS consists of a launch tube, a gripstock, and a battery coolant unit (4). Each warhead comes fitted into its own sealed launch tube, as the launch tube is typically disposed of after firing. The launch tube comes with the sight assembly and sockets into which the gripstock fits. The launch tube and warhead are together referred to as the "missile round."

The gripstock, which is the triggering unit, is detachable and fits into the launch tube (4). The battery coolant unit (BCU) is a disposable component inserted into either the gripstock or the launch tube, depending on the model. A thermal battery in the BCU provides energy to the system for 30 to 90 seconds after activation as the missile prepares to launch, and a pressurized gas tank cools the warhead's seeker—perhaps the most critical component of the entire system. A fully assembled MANPADS, complete with loaded launch tube, gripstock, and BCU, is referred to as a weapon round.

Unlike passive homing missiles, command guidance missiles depend on their operator to reach their target (4). Although their overall mechanisms are very similar to that of passive homing weapon rounds, the missiles are lighter and cheaper, as their function is less dependent on systems built into the missiles themselves. Instead, an operator uses a bulkier launch unit from the ground and typically follows the target with a laser beam. The missile follows the laser beam until impact. While this method is more accurate and immune to many defense systems, the system has its limitations. The operator, in keeping the laser fixed on the target, is more susceptible to counter-attacks and has to keep both the missile and the target in his line of sight.

Anti-MANPADS Defense Systems

Both policy and technical developments have sought to mitigate the threat of MANPADS (5). By securing airport perimeters, terrorists with MANPADS can be kept out of range of aircrafts. Changing aircraft departure and approach patterns to a steep climb and a tight spiral down could minimize the amount of time that aircraft remain in range of MANPADS. However, the range of MANPADS is up to 15,000 feet from their launch point. Planes currently remain in range of MANPADS for 25 miles, and securing this area would be wildly expensive. Similarly, retraining pilots to adopt new departure and landing techniques would be expensive and also increase the likelihood of danger in the case of engine failure.

Technical countermeasures against MANPADS can either be classified as active or passive (4). Active countermeasures include systems that are triggered upon missile detection, such as flares. The steering mechanism of passive homing MANPADS pulls

them towards infrared signals released by an airplane's engines (6). Flares, which release a stronger infrared signal than the airplane itself, can misdirect MANPADS missiles. These active systems are comparatively cheap, but the flares are heavy, pushing up fuel costs, and a fire hazard, making them unattractive for commercial aircrafts (4). As anti-missile technology developed, missile technology followed suit. New missile designs included ultraviolet sensors to detect airplanes among their decoys, making flares ineffective.

Another alternative, called laser-based Direct Infrared Countermeasures (DIRCM), attack the infrared sensors themselves (6). On board the aircraft would be a lamp or laser system that, upon detecting an incoming missile, will direct intense infrared energy towards the missile. The missile's infrared sensor would be overpowered and left unable to track the aircraft. However, this system also struggled to keep up with developments in MANPADS design. They offer protection against most generations of MANPADS, but they need to remain up to date with new seeker models. The protective system could otherwise fail to destroy the seeker and instead become a clearer infrared target.

Development of Commercial Systems

In 2004, the Department of Homeland Security (DHS) began a 4 year study on adapting anti-MANPADS systems for commercial aircrafts. Two aerospace defense corporations, BAE Systems and Northrop Grumman (NG) participated in the study to woo DHS for the defense contract.

NG equipped 11 regularly used FedEx cargo aircraft with its Guardian anti-missile system (8). As pictured in Fig 3., NG consolidated their system into a pod that could attach to the bottom of any airplane (9). NG's Guardian system was relatively cheap at a million dollars per plane after the two hundredth or three hundredth airplane compared to DHS's cost requirement of a million dollars per plane after the thousandth airplane. Both NG's Guardian and the BAE's Jeteye systems used laser-based Direct Infrared Countermeasures (DIRCM).

In December 2008, the Department of Homeland Security ultimately signed with BAE systems for $29 million (10). Seven months later, DHS announced that an American Airlines Boeing 767 had been outfitted with the BAE Jeteye infrared missile defense system and that the aircraft had just completed its first flight — from JFK to LA. The design for Jeteye was based on systems used in military aircrafts and involved seeker-jamming laser systems (11). DHS then sought to outfit two more AA 767s with Jeteye in order to confirm the system's sustainability and reliability.

Abandoning the March

The costs of the defense systems proved to be their downfall. Fitting an airplane with such systems can cost between one to four million USD, along with $300,000 each year in operating costs (4). Fitting all U.S. commercial aircrafts with anti-MANPADS would cost about $43 billion over 20 years, so in 2010, the U.S. government ended its funding (3). $276 million had been spent over eight years to research and develop these systems.

Given that there have been no instances of MANPADS attacks on U.S. soil, committing further funding to this nebulous threat is difficult for the government to justify, and some experts also argue that, as a result of the current levels of pilot training as well as the robustness of newer aircraft models, the threat of MANPADS is limited (4).

However, even the million-dollar price tag for each system is not much in the world of aviation; in-flight entertainment systems for aircraft cost three million dollars on average (12). The threat of MANPADS is real but remains largely theoretical, paling in the face of the hundreds of other risks on the DHS's tab. In the future, the choices about protecting America may lie not with the Department of Homeland Security but with commercial airliners. They will be the ones determining what their passengers truly need.

Figure 3: Northrop Grumman's Guardian anti-missile protection system on a FedEx cargo jet. During the race to win the DHS contract anti-MANPADS contract, Northrop Grumman equipped 11 FedEx aircrafts, among others, with its new system.

CONTACT SHINRI KAMEI AT
SHINRI.KAMEI.16@DARTMOUTH.EDU

References

1. Kenya Terror Strikes Target Israelis (2002). Available at: http://news.bbc.co.uk/2/hi/africa/2522207.stm (22 August 2013).
2. D. Kimball, MANPADS at a Glance (2013). Available at: http://www.armscontrol.org/factsheets/manpads (23 August 2013).
3. R. Tiron, Congress Stops Funding Commercial Airline Defense Tech (2010). Available at: http://www.popularmechanics.com/technology/military/missile-defense/manpads-airplane-missile-defense (23 August 2013).
4. M. Ashkenazi *et. al.*, "Brief 47: MANPADS A Terrorist Threat to Civilian Aviation?" (Bonn International Center for Conversion, Bonn, NY, 2013; http://www.bicc.de/uploads/tx_bicctools/BICC_brief_02.pdf).
5. Man-Portable Air Defense System (MANPADS) Proliferation (2013). Available at: http://www.fas.org/programs/ssp/asmp/MANPADS.html (16 September 2013).
6. Australian Government Department of Foreign Affairs and Trade, *Man-Portable Air Defence Systems (MANPADS) Countering the Terrorist Threat* (Australian Strategic Policy Institute, 2008; http://www.dfat.gov.au/security/manpads_countering_terrorist_threat.pdf).
7. BAE Jeteye Anti-Manpads System Installed on American Airlines Plane (2008). Available at: http://www.satellitetoday.com/publications/st/2008/07/28/bae-jeteye-anti-manpads-system-installed-on-american-airlines-plane/ (10 September 2013).
8. J. Doyle, BAE, NG Bid to Test counter-MANPADS on Airliners (2007). Available at: http://abcnews.go.com/Technology/story?id=3603787&page=1 (10 September 2013).
9. M. McCarter, Northrop Grumman Completes C-MANPADS Tests (2008). Available at: http://www.hstoday.us/briefings/industry-news/single-article/northrop-grumman-completes-c-manpads-tests/6e65a2af6aab849669b11b64900a41d6.html (10 September 2013).
10. M. Ahlers, Anti-missile system to be tested on passenger planes (2008). Available at: http://edition.cnn.com/2008/TRAVEL/01/04/missile.tests/ (10 September 2013).
11. C. Howard, BAE Systems applies military technology to commercial airliner defense system (2006). Available at: http://www.militaryaerospace.com/articles/print/volume-17/issue-10/news/bae-systems-applies-military-technology-to-commercial-airliner-defense-system.html (10 September 2013).
12. S. Schechner, Airlines Entertain Tablet Ideas (2012). Available at: http://online.wsj.com/article/SB10000872396390443916104578020601759253578.html (10 September 2013).
13. Short Range SAM Divison, *MANPADS Components*. Available at: http://www.fas.org/irp/dia/manpads_components.pdf (16 September 2013).

Figure 4: A C-130 deploys infrared flares as decoys against heat-seeking MANPADS missiles.

Image courtesy of Wikimedia Commons. Available at http://commons.wikimedia.org/wiki/File:AC-130_Training.jpg

Nuclear Security and Nanotechnology

TONY PAN [LYNBROOK HIGH SCHOOL, SAN JOSE, CA]

Introduction

The 13-day confrontation between the Soviet Union and the United States during October of 1962 was marked by the nuclear stalemate that became known as the closest the world has ever been to a nuclear conflict (1). Since then, international pacts such as the 1970 Non-Proliferation Treaty (NPT) and the 1991 Strategic Arms Reduction Treaty (START) have been passed to prevent a recurrence of the October Crisis. However, as the global use of nuclear technology for generating energy grows increasingly common, incidents such as the Fukushima Dai-ichi nuclear meltdown remind us of the terrors of potential nuclear disasters. The deployment of nuclear plants perpetuates the risk of nuclear accidents and nuclear proliferation (2). But rather than forgo the use of the world's largest source of emission-free energy and second-largest producer of electricity, the incorporation of nanotechnology into nuclear science offers hope for the future of nuclear energy and security.

The repercussions of nuclear catastrophes stemming from inadequate security measures can reverberate around the world years after the actual incidents. The United Nations' International Atomic Energy Agency (IAEA) declared that the recent Fukushima crisis has "escalated to its worst level since a massive earthquake and tsunami crippled the plant more than two years earlier" as storage tanks continue to leak radioactive water (3). Although an earthquake provided the ultimate trigger for the incident, the damage could also be attributed to human negligence at multiple levels, according to the Tokyo Electric Power Company (TEPCO). These included the ill-advised decision to release volatile hydrogen gas to vent steam (that later reacted with oxygen in the second containment structure, resulting in structure-damaging explosions and a radioactive leak) and pumping saltwater to cool reactor temperatures (which damaged the reactors) (4). Today, contamination has risen to a level five times the maximum human exposure capacity. Yet this crisis is still far from the worst-case scenario; an accidental release of the remaining radioactive material within the plant could have generated far greater health and environmental hazards (5). Given that the decommissioning of the plant would require an additional 40 years, the possibility of another nuclear mishap seems greater than ever.

At first glance, the problems stemming from the use of nuclear energy seem daunting. Yet they can be divided into three central concerns: future nuclear meltdowns, nuclear proliferation, and international nuclear security. All of these categories involve issues of international relations, environmental sustainability, and health. At the heart of solution lies nanotechnology, the manipulation of matter on the atomic and nuclear scale.

Future Nuclear Meltdowns

At the time of the Fukushima Incident, Japan was ranked as the third leading country in scientific research and technology, suggesting that Japan should have been one of the countries most capable of dealing with a nuclear catastrophe (6). Its failure to do so, however, points to the possibility of additional nuclear meltdowns in the future, especially considering the growing number of countries interested in developing nuclear power plants (7). These nations are eager to claim the economic and environmental benefits associated with nuclear energy but have been a source of concern since many of the countries lack experience in dealing with nuclear technology, making them less reliable at responding efficiently to a nuclear emergency compared to their developed counterparts (7).

Instead of depending solely on emergency procedures, however, pre-emptive measures must also be taken. Researchers at the Los Alamos research institute have made progress in producing self-repairing substances within nuclear reactors utilizing the unique properties of nanocrystalline materials (10). These virus-sized copper particles consist of a series of nanosized particles (called grains) and the interfaces between them (called grain boundaries) and possess the ability to absorb and eliminate any defective particles (10). This characteristic was observed when scientists monitored defects and grain boundaries in a series of computer simulations in which particles were exposed to radiation. Researchers expected to see the standard phenomenon responsible for the failure of nuclear reactors: the formation of wide spaces in between the individual atoms (called vacancies) as a direct result of the radioactive energy displacing the particles out of place, causing brittleness and swelling in the material that eventually causes the nuclear reactors to fail (10). Instead, scientists discovered that particles underwent a process now dubbed the "loading-unloading" process:

> *"On the shorter timescales, radiation-damaged materials underwent a 'loading' process at the grain boundaries, in which interstitial atoms became trapped—or loaded—into the grain boundary. After trapping interstitials, the grain boundary later 'unloaded' interstitials back into vacancies near the grain boundary. In so doing, the process annihilates both types of defects—healing the material."*

This finding debunked the belief that nanocrystalline grain boundaries can only accumulate interstitial atoms, encouraging further studies into the functions and capabilities of self-healing regarding nanoengineered material surfaces. Most importantly, the low energy threshold required for this mechanism to take place consolidates this process as a viable addition for future designs of much more radiation-tolerant nuclear structures (10). Should the allure of national development continue to drive interest in erecting nuclear power plants in developing countries, the self-restoring capabilities of nanocrystalline materials could decrease the number of nuclear accidents by proactively enriching nuclear structures before an emergency response is necessary.

Nuclear Contamination

Another problem posed by nuclear energy use is nuclear waste. Environmentalists over the decades have lobbied against nuclear

power plants because of the radioactive byproducts of nuclear energy. The chief concerns of nuclear waste have boiled down to the assertions that radioactive uranium lasts for hundreds of thousands of years, allowing its radiation to permeate bodies of water, wildlife, and agriculture. Much of the nuclear waste may take an upward of 240,000 years before it becomes safe to approach. Although institutions such as the Nuclear Security Summit and the IAEA are doing their best to maintain the safety of nuclear plants, the IAEA has acknowledged that it cannot possibly prevent all problems (7).

In spite of this global hurdle, Professor Huai-Yong Zhu from the Queensland University of Technology supports theory that could drastically lower radioactive emissions. A nanofiber comprised of inorganic titanic oxide, he claims, can lock radioactive material from exposure to water and wildlife, surpassing the current methods of using microporous minerals (known as zeolites) and clay to absorb radiation (12). Professor Zhu said that "one gram of the nanofibers can effectively purify at least one [metric ton] of polluted water." When used conjunctively with silver oxide nanocrystals, these nanofibers were able to capture and incapacitate harmful radioactive ions known to induce cancer (12).

In a similar effort, former Los Alamos National Laboratory engineer Liviu Popa-Simil revealed that harmful radiation could also be translated into usable electricity. When radioactive matter runs through nanotube complexes packed with gold and coated by lithium hydride, a stream of high-energy electrons is produced. This stream can eventually come in contact with electrodes, which allow the electric current to flow (13). This practice allows electricity to be harvested from both high-radiation centers (such a nuclear waste dump) and directly from radiation emitted from a nuclear reactor, potentially easing a major environmental consequence of nuclear energy. Continued development of Popa-Simil's concept may be instrumental in bridging the gap between nuclear energy and nuclear security. By mitigating the consequences of nuclear waste, nuclear energy can be utilized without the constant fear of environmental destruction.

International Nuclear Security

The Seoul Nuclear Security Summit, comprised of 53 world leaders, meets yearly to discuss national and international issues regarding nuclear security. In spite of having advanced international nuclear security objectives in response to the Fukushima incident, the summit has found it difficult to reach a global consensus due to differing national opinions regarding nuclear proliferation and weaponry. With 473 nuclear power plants and over 17,000 nuclear weapons distributed internationally, the numbers continue to grow, escalating the chances of domestic and international nuclear disasters. In the year 2000 alone, nearly 310 tons of usable, weapons-grade uranium was produced worldwide (to put this into perspective, just 8 kilograms is sufficient to manufacture a Nagasaki-scale bomb) (8). Although the bulk of the 1,600 tons of highly enriched uranium (HEU) and 500 tons of plutonium are separated and securely guarded by the world's two largest nuclear giants–United States and Russia–the remaining radioactive substances are scattered among thirty-some countries and susceptible to theft (7). Increased proliferation of nuclear weapons pushes the world closer and closer to global nuclear war.

While nanotechnology possesses the capability of restricting many of the environmental implications of nuclear waste, no international organization can guarantee that each sovereign nation will handle its radioactive material responsibly. What nanotechnology can guarantee, however, is a reliable detection system in the event that nuclear warheads are fired. Researchers at Louisiana Tech University have developed a multi-channel nanoparticle device that is capable of alpha, beta, gamma, and neutron detection (11). Taking advantage of the fact that fissionable bombs emit all five of the given types of radiation, scientists can convert each species into electrons through physical mechanisms (including charge conversion, and thermonuclear fusion reactions) to pinpoint the exact radioactive isotope (11). Such information might be crucial for an immediate response in the event of danger. With the use of multiple high-flux regions, particles can be successfully identified as one of four different types of radiation (11). The developed glass microdevice harbors a patterning that discriminates between all types of radioactive waves, a property crucial for determining the exact composition of the nuclear material (11). This detection mechanism proves to be superior to modern technologies because of its additional ability to detect beta and gamma radiation despite lead-shielding. The device produced successful results when tested with a cobalt gamma source and is undergoing continual refinement. The adaptation of this particular nuclear response system worldwide will curb the threat of a nuclear launch and drastically reduce the chance of nuclear turmoil.

Through a multi-faceted approach to enforcing nuclear security centered around nanotechnology, the hopes of a consequence-free nuclear future is becoming a reality. By increasing the synergy between nuclear science and nanotechnology, the world can advance its understanding of nanotechnology and take control over nuclear power.

CONTACT TONY PAN AT TON YPAN19@GMAIL.COM

References

1. B. G. Marfleet, *Political Psychology. 21*(3), 545-558 (2000).
2. Problems of Nuclear Reactors. Available at hyperphysics.phyastr.gsu.edu/hbase/nucene/nucprob.html (25 September 2013).
3. K. Takenaka, J. Topham, Japan's nuclear crisis deepens, China expresses 'shock' (2013). Available at http://www.reuters.com/article/2013/08/21 (29 September 2013).
4. E. Strickland, What Went Wrong in Japan's Nuclear Reactors (2013). Available at http://spectrum.ieee.org/tech-talk/energy/nuclear/explainer-what-went-wrong-in-japans-nuclear-reactors (29 September 2013).
5. L. Abrams, How everything went so wrong at Fukushima (2013). Available at http://www.salon.com/2013/08/23/how_everything_went_so_wrong_at_fukushima/ (29 September 2013).
6. World's top 10 technology driven nations (2011). Available at http://www.rediff.com/business/slide-show/slide-show-1-tech-worlds-top-10-technology-driven-nations/20110331.htm#3 (29 September 2013).
7. F. Jishe, Why global nuclear security is a major issue (2012). Available at http://www.china.org.cn/opinion/2012-03/29/content_25017459.htm (29 September 2013).
8. L. L. Morrison, Issues: Nuclear Energy & Waste: Nuclear Energy Fact Sheet. Available at http://www.wagingpeace.org/menu/issues/nuclear-energy-&-waste/nuclear-energy-fact-sheet.php (29 September 2013).
9. Nanoscience and nanotechnologies: opportunities and uncertainties. Available at www.nanotec.org.uk/report/Nano%20report%202004%20fin.pdf (29 September 2013).
10. J. Rickman, Safer nuclear reactors could result from Los Alamos research (2010). Available at http://nanotechnologytoday.blogsssable at ftp://ftp.iaea.org/dist/inis/full-text/korea/39004834.pdf (29 September 2013).
12. G. T, Nanotechnology For Safe Storage Of Nuclear Waste And Containing Radiation Damage (2011). Available at http://www.medindia.net/news/Nanotechnology-for-Safe-Storage-Of-Nuclear-Waste-And-Containing-Radiation-Damage-92794-1.htm (29 September 2013).
13. P. McKenna, Nanomaterial turns radiation directly into electricity (2008). Available at http://newscientist.com/article/dn13545#.Uko0G2QaYvo (29 September 2013).

Next to Normal: Mood Disorders, Medicine, and Society

NAVYA DASARI (BASIS SCOTTSDALE, SCOTTSDALE, AZ)

Mental illnesses are the leading causes of disability in the United States, with bipolar disorder and major depressive disorder affecting 2.6% and 6.7% of American adults respectively. But despite this prevalence, the struggles of those who suffer from mood disorders have long been avoided in public discussion (1). Recently, however, increased publicity both from high-profile sufferers of mood disorders and discussions about violence in our society have brought this issue and the importance of their treatment into the limelight. The number of people whose mental health issues have been misdiagnosed, mistreated, or simply not monitored, signifies the need for urgent action. *Next to Normal,* a 2009 musical about a suburban mother named Diana Goodman who struggles with bipolar disorder, provides a framework through which its audience can examine the status and implications of mental health care within our society. Such an examination elucidates clear goals for the future, including a destigmatization of mood disorders, more sympathetic public policy, an interdisciplinary approach to psychiatric research, and a greater focus on the families of the mentally ill, in order to create a system that better responds to the needs of those who suffer from depression, bipolar disorder, and other mental illnesses.

"What makes you think I'd lose my mind?
I'm no sociopath,
I'm no Sylvia Plath" (2).

In this scene from the musical, Diana lashes out at her doctor, angrily refusing the therapy he recommends; she cannot relate to the popular images of mental illness, and therefore cannot accept that she has one. The character's denial highlights the way stigmatization and stereotyping of mental illness have prevented people from seeking the treatment they need, with both social and professional stigmas continuing to reinforce such feelings of shame and guilt over mental illness. A recent study on bipolar disorder found that over 50% of Argentinean patients believed that the public was afraid of persons with bipolar disorder (3). In another study, a third of patients across seven Western countries reported being discriminated against because of their mental illness (4). In yet another survey, 66% of people with bipolar disorder agreed with the statement "I feel ashamed of my mental illness," and many of the public (29% across America) believed that people with mood disorders were "not normal, even when treated." Only 17% of patients with bipolar disorder reported being able to speak with their employer about their mental illness (5). And despite the importance of law enforcement having an understanding of mental disorders, a study revealed that 60% of police officers believed the mentally ill to be more dangerous than the rest of the population, and 67% believed they should be permanently hospitalized (6). Such statistics reveal a strong presence of stigma against people suffering from mood disorders.

Unfortunately, race continues to play a large role in whether or not an individual receives mental health care. Asian American teenagers, especially girls, suffer the highest rates of depression in their age group, and yet they are the least likely to seek treatment for that disorder (7). And as reported by the Center for Disease Control, 19% of Asian American teens contemplate suicide, compared to 16% of teens across ethnic groups (8). University of Pennsylvania psychiatrist Dr. Zheya Yu explains that much of the gap between the rates of depression and treatment stems from the cultural stigmatization by parents, who feel that a child with depression could reflect poorly on them and their family. Asian parents, who typically expect high achievement from their children, may not want to accept that there is a problem with their child. This can manifest in refusal to seek help or even in refusal to complete treatment, in cases where the parent and/or child are aware of the mental illness. The cultural gap between the East and West with regard to mental illness is illustrated further by the criminalization of attempted suicide in India, with survivors facing up to a year of imprisonment. However, a new Indian Mental Health Care Bill introduced in August seeks to remove this penalty, which seems to indicate progress in the perception of mental illness in Asian cultures (9).

Prominent voices in the media continue to spread false information about mental health and mental health services, contributing to the confusion of those suffering from disorders and those who surround them. As recently as June 2013, an article in *The Daily Caller* asserted that what psychologists call "anxiety" and "depression" are really just "stress" and "sadness," and suggested "stoicism, hard work, marriage, prayer and personal initiative" as alternatives to psychiatric treatment (10). Such misinformation can easily add to the guilt and shame experienced by people who find that those traditional coping mechanisms do not alleviate the symptoms of their disorder. But the reasons Americans do not utilize mental health services run deeper than just stigma. According to the 2013 report by the U.S. Substance Abuse and Mental Health Services Administration, over 50% of Americans cannot afford treatment, even with insurance (11). It is important to note that the high costs of mental health services actually hurt the economy; as early as 2000, the World Health Organization noted that in terms of productivity loss, mental disorders cost 4% of a developed country's GNP, which in the U.S. would be approximately

$636 billion (12).

"The memories will wane, the aftershocks remain.
You wonder which is worse, the symptom or the cure" (13).

In *Next to Normal*, Diana responds negatively to electroconvulsive therapy (ECT), one of the most effective current treatments for depression and bipolar disorder; while it successfully mitigates the effect of her trauma, the memory dysfunction-- a key side effect of ECT – leaves her feeling empty. But whether or not the benefits of ECT outweigh the risks has been a matter of contention since the 1980s, partially because the mechanisms of depression – and its treatment – are still not completely clear. The traditional perspective on depression has been that low serotonin levels cause depression, and thus scientists believe that antidepressants function by raising serotonin levels. However, recent research suggests this is not the case, that an imbalance of neurotransmitters cannot be the sole cause of depression; for example, patients with depression were not found to have consistently lower serotonin levels (14). However, lowering serotonin levels had a significant effect on the mood of people with a family history of depression, suggesting a strong genetic component to the disorder. The mechanisms behind antidepressants have been further called into question by Irving Kirsch's 1997 experiments on the placebo effect in depression, in which he observed that 75% of the antidepressant effect could be achieved with a placebo (15). Together, these studies showed that those who responded positively to antidepressants often had milder forms of depression, and serotonin seemed to play a large role for these patients. In the 1980's, Fred Gage approached the problem from a different angle when he found that the adult brain produces new neurons in the hippocampus, a part of the brain involved in memory and, to a certain degree, emotion. Later experiments on mice found that Prozac worked only with the production of new neurons within the hippocampus, and when this production was blocked, Prozac had no effect; the experiments, when replicated in 2011 with monkeys, achieved the same results (14). So how might the new information about the hippocampus be connected with what we know about serotonin? The answer may lie in the subcallosal cingulate, an area of the brain connected with the hippocampus and rich in serotonin transporters, which regulates responses to emotional stress (16). Electric stimulation of this area was reported to cause a powerful mood change in 75% of depressed patients. All this suggests that serotonin may actually change the circuitry of the brain itself, affecting how the subcallosal cingulate regulates a malfunctioning hippocampus. To fully understand how depression works, and to come to a proper conclusion about its treatment, scientists will have to combine the studies of cognitive psychology, neuroscience, and genetics, but until that occurs, patients must choose between the available treatments – including ECT – using the information they currently have.

Although its side effects and high relapse rate make many patients wary of the treatment, ECT has been shown to mitigate severe cases of depression on which antidepressants have had no effect (as antidepressants work in only 30% of cases) (17). Recent studies, however, may illuminate the mechanisms behind ECT's effects, possibly opening research pathways for alternative therapies. In fMRI scans of depressed patients who received ECT, the treatment appeared to reduce the connection between brain regions associated with emotion and those associated with cognitive function (18). While such an explanation addresses the involvement of neural circuitry, research has not yet extended this finding to a connection with serotonin levels. Either way, it doesn't seem that the fears surrounding ECT will disappear anytime soon; an FDA panel recently refused recommendations that ECT be reclassified as a Class II medical device, which would decrease restrictions and regulations on its production and use (19). Instead, ECT will retain its designation as a Class III procedure – one with the highest risks. With more knowledge of the biology behind both depression and its treatments, scientists may be able to either improve the function of ECT and antidepressants, or develop a replacement therapy with greater benefit and fewer risks.

"With you always beside me to catch me when I fall,
I'll never get to know the feel of solid ground at all" (20).

The scene where Diana leaves her family, citing her need to recover on her own, represents the climax of the familial struggle central to the musical and illuminates the greater need for counseling and support of families of people with depression and bipolar disorder. The negative impacts of stigma and ineffective treatment of Diana's disorder are only exacerbated by the familial dysfunction in her home; meanwhile, Diana is unable to respond to her daughter Natalie's feelings of alienation from her family or her husband Dan's attempts to remain optimistic in the face of their troubles. Often, family members are not involved in diagnosis, despite being twice as likely as the patient to recognize manic symptoms (21). Families of violent patients have also expressed helplessness in connecting with their family member's treatment or finding support for their family. The need for both patient privacy and family support makes the situation difficult to resolve. For example, while many of the laws that block parents from interfering with their children's mental health treatment were intended to enable children to receive treatment more easily, they can actually have the opposite effect in more severe cases, when the parent is the one seeking help for their child (22). In addition, coming to terms with the tragedy of a patient's suicide can be extremely difficult for families who are unable to obtain answers about what happened from their family member's doctor. A balance must be achieved between allowing patients agency and safety in their treatment and enabling families to feel confident about their loved one's treatment.

Due to their major implications for community and economy, mood disorders and their treatments must be treated as a major public health issue in order to promote global emotional health, well-being, and productivity. With the situation as problematic as it is both socially and clinically, it is easy for people with these disorders, as well as their friends and family, to feel discouraged about the future. But campaigns and programs for destigmatizing mood disorders, interdisciplinary research, and increased lobbying

have begun to move the cause in a better direction. After all, while pointing out the flaws in the system and society, the musical *Next to Normal* ends on an inspiring note: with the hope that we will *"find the will to find our way, knowing that the darkest skies will someday see the sun... There will be light"* (23).

CONTACT NAVYA DASARI AT NAVYA.DASARI.12@GMAIL.COM

References

1. National Institute of Mental Health, The Numbers Count: Mental Disorders in America (2013). Available at http://www.nimh.nih.gov/health/publications/the-numbers-count-mental-disorders-in-america/index.shtml (20 September 2013)..
2. A. Ripley, "Didn't I See This Movie?" Tom Kitt. Next to Normal: Original Cast Recording (2009).
3. V.R. Mileva et al., Neuro. Dis. Treat. **9**, 31-40 (2013).
4. Schizophrenia Ireland, Survey: Thinking Ahead. World Federation for Mental Health (2006).
5. Depression and Bipolar Support Alliance, Fighting Stigma (2013). Available at http://www.dbsalliance.org/site/PageServer?pagename=help_advocacy_stigma (20 September 2013).
6. European Commission by David McDaid. Countering the stigmatisation and discrimination of people with mental health problems in Europe. Directorate-General for Health & Consumers, European Union (2012).
7. National Alliance on Mental Illness, Asian American Teenage Girls Have Highest Rates of Depression (2011). Available at http://www.nami.org/Template.cfm?Section=press_room&template=/ContentManagement/ContentDisplay.cfm&ContentID=115681 (17 September 2013).
8. K. Kam, Cultural Stigma Hurts Asian American Teens With Depression (2013). Available at http://newamericamedia.org/2013/09/cultural-stigma-hurts-asian-american-teens-with-depression.php (17 September 2013).
9. Mental Health Care Bill 2013: Suicide Attempt Decriminalised, Patients Can Seek Quality Treatment (2013). Available at http://www.ibtimes.co.in/articles/500767/20130822/mental-health-care-bill-2013-suicide-attempt.htm (24 September 2013).
10. N. Munro, Obama urges public to use government mental health programs (2013). Available at http://dailycaller.com/2013/06/03/obama-urges-public-to-use-government-mental-health-programs/ (20 September 2013).
11. S. Mukherjee, STUDY: Americans Just Can't Afford Mental Health Treatment (2013). Available at http://thinkprogress.org/health/2013/01/24/1489091/americans-just-cant-afford-mental-health-treatment/ (17 September 2013).
12. Unite for Sight, Introduction to Global Mental Health: Effects of Mental Health on Individuals and Populations (2013). Available at http://www.uniteforsight.org/mental-health/module1 (17 September 2013).
13. A. Tveit, "Aftershocks." Tom Kitt. Next to Normal: Original Cast Recording (2009).
14. S. Mukherjee, The Science and History of Treating Depression (2012). Available at http://www.nytimes.com/2012/04/22/magazine/the-science-and-history-of-treating-depression.html (17 September 2013).
15. J.C. Coyne, Irving Kirsch: Deja Vu All Over Again? (2012). Available at http://www.psychologytoday.com/blog/the-skeptical-sleuth/201203/irving-kirsch-d-j-vu-all-over-again (24 September 2013).
16. E.R. Kandel, The New Science of Mind (2013). Available at http://www.nytimes.com/2013/09/08/opinion/sunday/the-new-science-of-mind.html (24 September 2013).
17. Shock Therapy Makes a Comeback (2008). Accessed (20 September 2013).
18. R. Rettner, Shock Therapy's Effect On Depressed Brain Explained By New Electroconvulsive Therapy Study (2012). Available at http://www.huffingtonpost.com/2012/03/20/shock-therapy-brain-depression-study_n_1367203.html (20 September 2013).
19.D. Wilson, F.D.A. Panel Is Split On Electric Shock Risks (2011). Available at http://www.nytimes.com/2011/01/29/health/29shock.html (17 September 2013).
20. A. Ripley, "So, Anyway." Tom Kitt. Next to Normal: Original Cast Recording (2009).
21. H. E. Marano, Depression: A Family Matter (2002). Available at http://www.psychologytoday.com/articles/200303/depression-family-matter (17 September 2013).
22. G. Fields, Families of Violent Patients: 'We're Locked Out' of Care (2012). Available at http://online.wsj.com/news/articles/SB10001424127887323463704578495154217291958 (17 September 2013).
23. Next to Normal: Original Broadway Cast, "Light." Tom Kitt. Next to Normal: Original Cast Recording (2009).

About the Winners

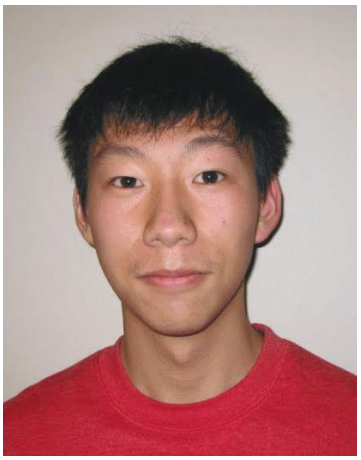
This year marks our second annual International Science Essay Competition. The submissions we received spanned a vast range of topics, each with a unique interpretation of the following prompt:

> *Scientific dilemmas today occur on a global stage and require international cooperation. Please choose one pressing scientific issue and explain: the problem as it exists today, the point it can reach before action must be taken, some potential courses of action to combat the problem, and the global implications of solving or avoiding the issue.*

With over 260 submissions from 20 countries, we would like to congratulate the ISEC winners for their exceptional entries:

Tony Pan, from Lynbrook High School in San Jose, CA; Navya Dasari, from BASIS Scottsdale in Scottsdale, AZ; Sara Camilli, from Biotechnology High School in Freehold, NJ; and Rachel Stanziola, from MMI Preparatory School in Freeland, PA.

In addition to featuring the 1st and 2nd place essays in this print issue, the *DUJS* is presenting two mini-interviews with the first and second place winners.



1st Place: Tony Pan

How do you feel about winning first place in the DUJS ISEC?

I've always had a passion for the sciences and writing, and I decided that ISEC would be the perfect opportunity to demonstrate my abilities in both fields. Winning first place was a huge honor for me, and it felt great to know that a team of accomplished authors and editors acknowledged the quality of my writing.

What did you learn while writing your essay?

Writing my essay helped me realize how interconnected different disciplines of science really are. I was very excited to learn how important ideas can be applied in multiple contexts. I was able to expand my capability as a thinker and develop creativity in science. I also became more aware of the role science plays in today's world and how it affects the way we live our lives.

What do you hope to study in college?

I hope to major in materials science engineering or chemical engineering and minor in computer science in college.

2nd Place: Navya Dasari

How do you feel about winning second place in the DUJS ISEC?

I am really honored to have my essay selected for second place. I worked hard on the essay and really enjoyed researching and writing it, so I'm glad that the *DUJS* found it valuable. I feel strongly about advancing the mental health care system, as I've seen firsthand how important it is. If my essay could spark more discussion about these issues, it would make me really happy.

What did you learn while writing your essay?

While writing the essay, I learned how deep the stigma and discrimination surrounding bipolar disorder and depression really go. I gained knowledge that allows me to identify areas in which progress can be made. The biology behind depression and its treatments is fascinating, and I finished the essay with a better understanding of the brain and how crucial interdisciplinary research is to the study of depression.

What do you hope to study in college?

As someone who is both a captivated psychology student and research assistant in a neuro-oncology lab, I've developed a strong passion for neuroscience, and I hope that I can continue to pursue this interest in college.

DUJS | Dartmouth Undergraduate Journal of Science

ESTABLISHED 1998

ARTICLE SUBMISSION

What are we looking for?

The *DUJS* is open to all types of submissions. We examine each article to see what it potentially contributes to the Journal and our goals. Our aim is to attract an audience diverse in both its scientific background and interest. To this end, articles generally fall into one of the following categories:

Research

This type of article parallels those found in professional journals. An abstract is expected in addition to clearly defined sections of problem statement, experiment, data analysis and concluding remarks. The intended audience can be expected to have interest and general knowledge of that particular discipline.

Review

A review article is typically geared towards a more general audience, and explores an area of scientific study (*e.g.* methods of cloning sheep, a summary of options for the Grand Unified Theory). It does not require any sort of personal experimentation by the author. A good example could be a research paper written for class.

Features (Reflection/Letter/Essay/Editorial)

Such an article may resemble a popular science article or an editorial, examining the interplay between science and society. These articles are aimed at a general audience and should include explanations of concepts that a basic science background may not provide.

Guidelines:

1. The length of the article should be under 3,000 words.
2. If it is a review or a research paper, the article must be validated by a member of the faculty. This statement can be sent via email to the *DUJS* account.
3. Any co-authors of the paper must approve of submission to the *DUJS*. It is your responsibility to contact the co-authors.
4. Any references and citations used must follow the *Science* Magazine format.
5. If you have chemical structures in your article, please take note of the American Chemical Society (ACS)'s specifications on the diagrams.

For more examples of these details and specifications, please see our website:
http://dujs.dartmouth.edu

For information on citing and references, please see:
http://dujs.dartmouth.edu/dujs-styleguide

Specifically, please see *Science Magazine's* website on references:
http://www.sciencemag.org/feature/contribinfo/prep/res/refs.shtml

Dartmouth Undergraduate Journal of Science
Hinman Box 6225
Dartmouth College
Hanover, NH 03755
dujs@dartmouth.edu

ARTICLE SUBMISSION FORM*

Please scan and email this form with your research article to dujs@dartmouth.edu

Undergraduate Student:

Name:_____ Graduation Year: _____

School _____ Department _____

Research Article Title:

_____

_____

Program which funded/supported the research _____

I agree to give the *Dartmouth Undergraduate Journal of Science* the exclusive right to print this article:

Signature: _____

Faculty Advisor:

Name: _____ Department _____

Please email dujs@dartmouth.edu comments on the quality of the research presented and the quality of the product, as well as if you endorse the student's article for publication.

I permit this article to be published in the *Dartmouth Undergraduate Journal of Science*:

Signature: _____

*The *Dartmouth Undergraduate Journal of Science* is copyrighted, and articles cannot be reproduced without the permission of the journal.

Visit our website at dujs.dartmouth.edu for more information

DARTMOUTH UNDERGRADUATE JOURNAL OF SCIENCE
Hinman Box 6225
Dartmouth College
Hanover, NH 03755
USA

http://dujs.dartmouth.edu

dujs@dartmouth.edu

ISSN 2167-7883
01>
9 772167 788169