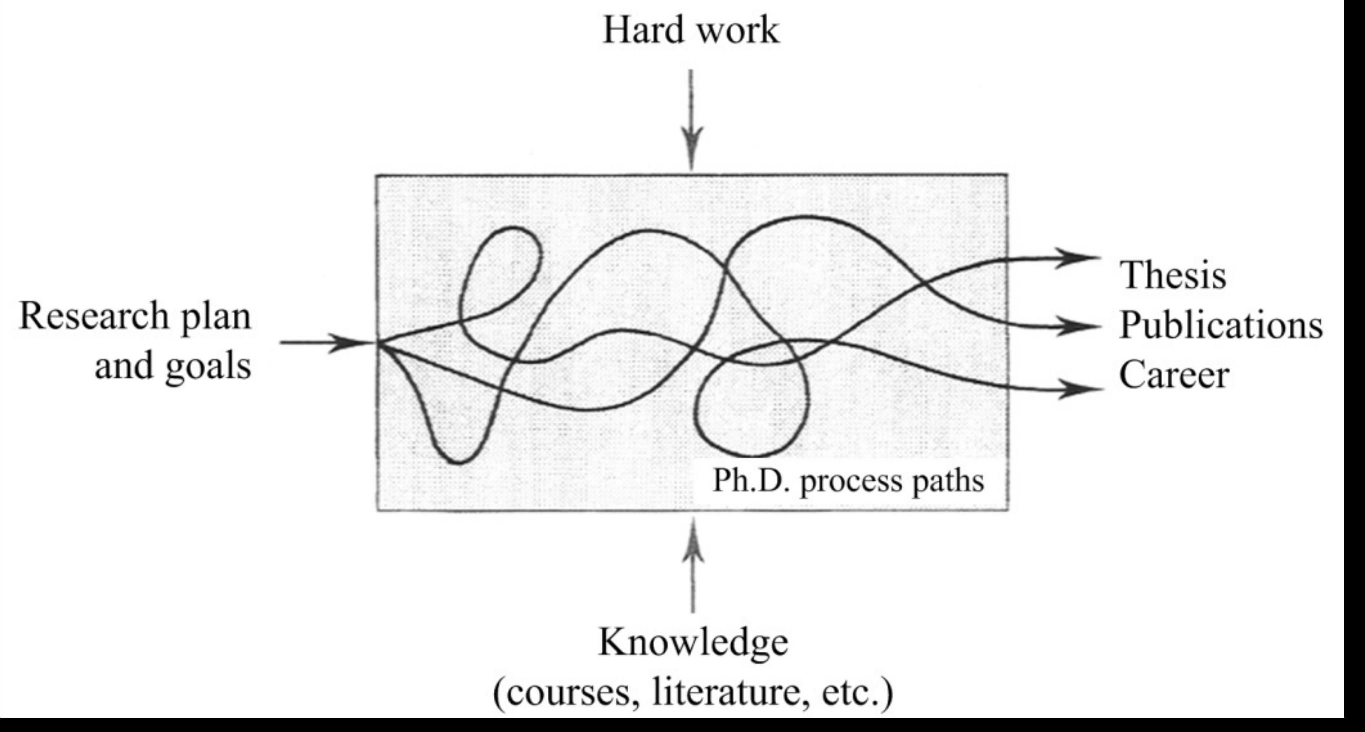
01: **Defining “research”**

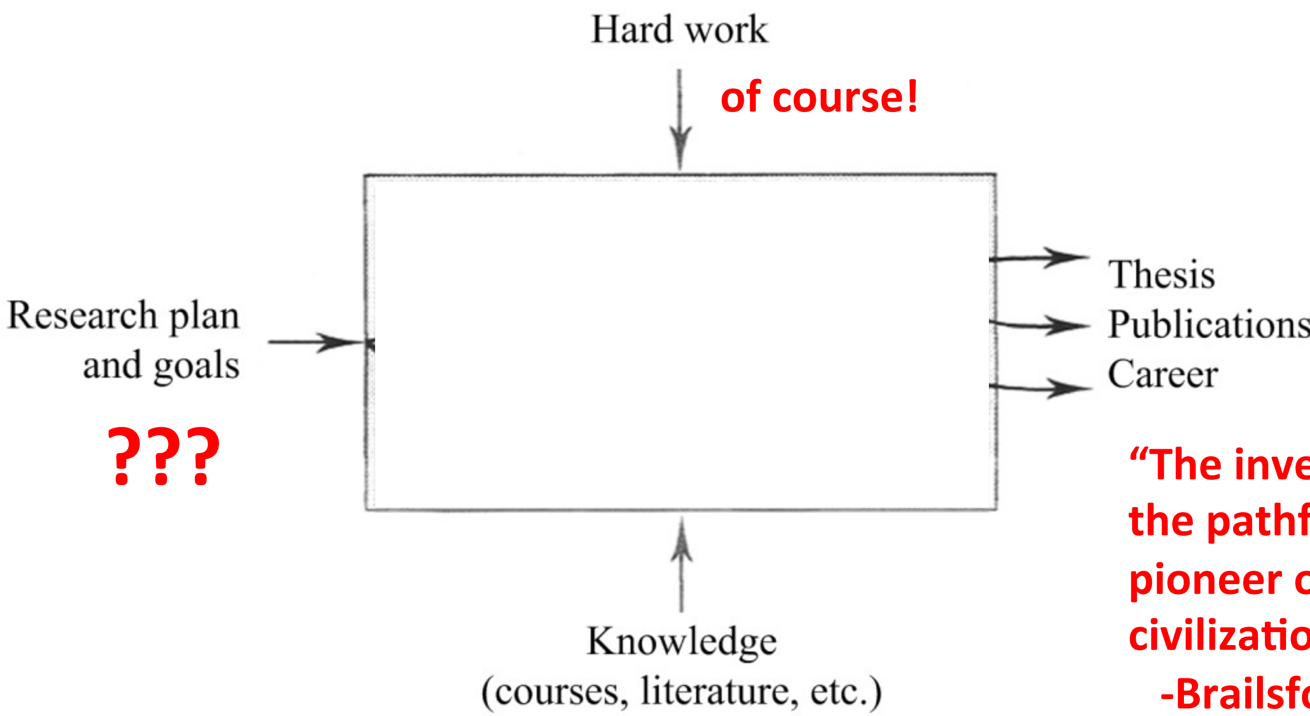
January 13, 2012

Announcements

- Please say your name when you make a comment
- Pre-class tasks are due 2pm Thursday



Hard work
Research plan
and goals
Thesis
Publications
Career
Ph.D. process paths
Knowledge
(courses, literature, etc.)



of course!

???

IMPACT!

"The investigator is the pathfinder and the pioneer of new civilizations"
-Brailsford Robertson

What do I need to know?
What do others know already?

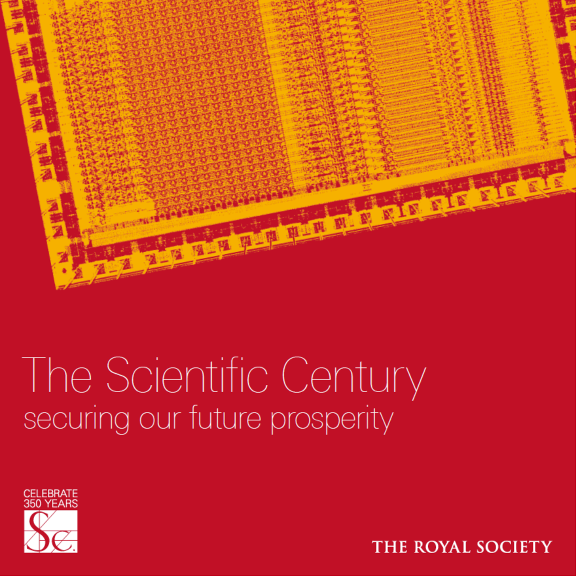
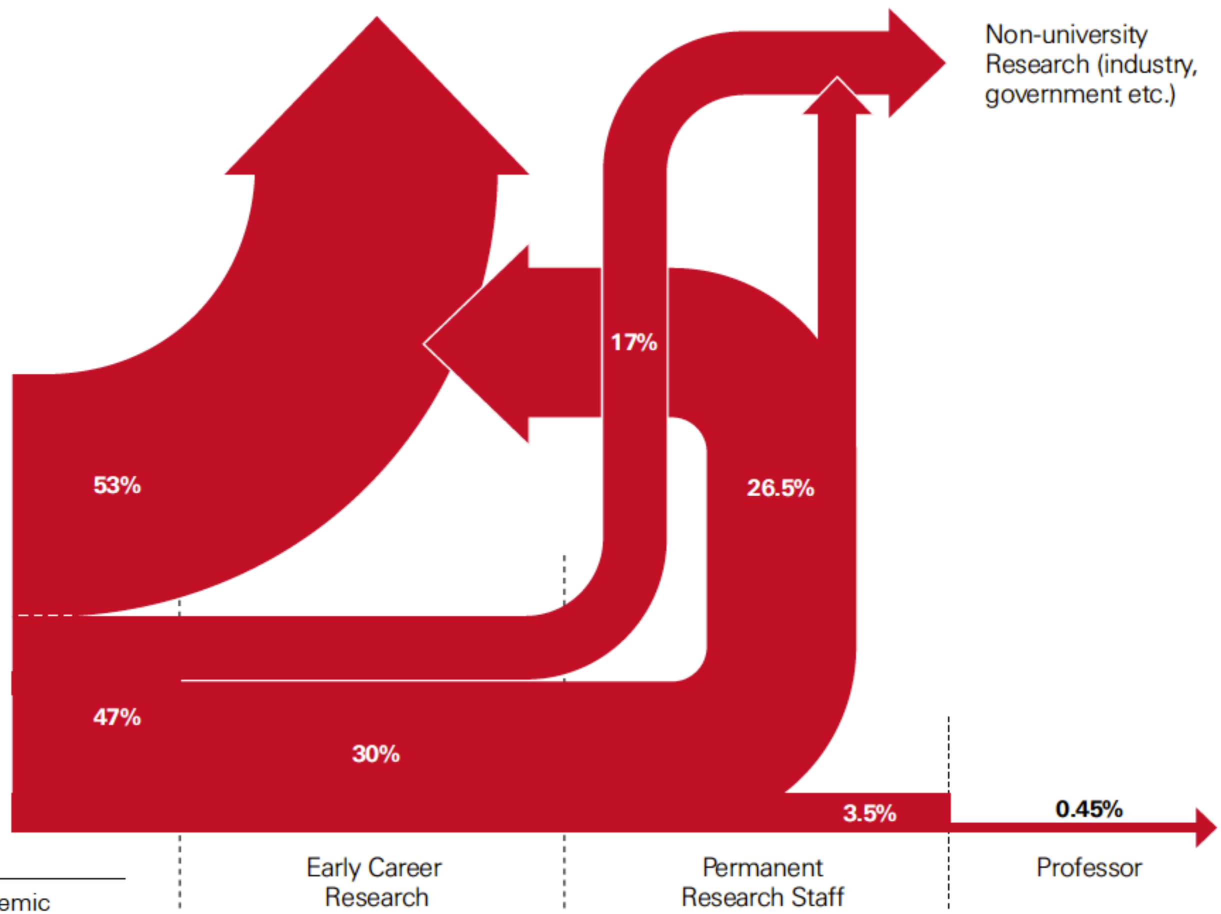


Figure 1.6 **Careers in and outside science**



This diagram illustrates the transition points in typical academic scientific careers following a PhD and shows the flow of scientifically-trained people into other sectors. It is a simplified snapshot based on recent data from HEFCE[33], the Research Base Funders Forum[34] and from the Higher Education Statistics Agency's (HESA) annual Destinations of Leavers from Higher Education' (DLHE) survey. It also draws on Vitae's analysis of the DLHE survey[35]. It does not show career breaks or moves back into academic science from other sectors.

Today's topics

- What are some attributes of researchers?
- What is "good" research?
  - Process
  - Outcomes
- What is your learning style?

"If you really want to be a first class scientist you need to know yourself, your weaknesses, your strengths, and your bad faults…"

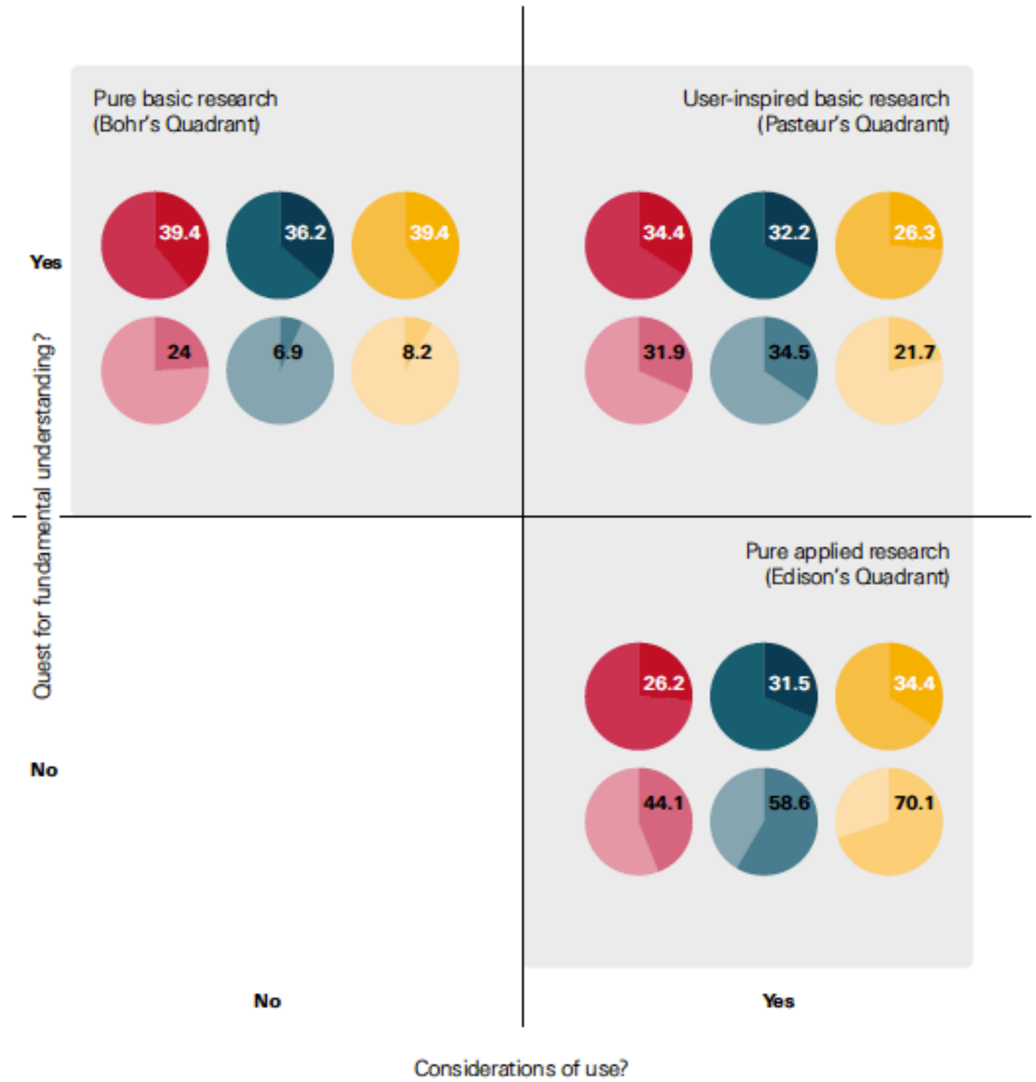
-Richard Hamming

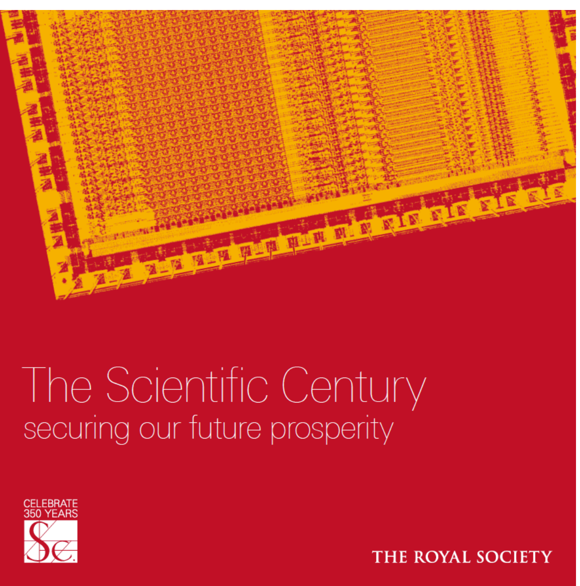
Types of research

- Fundamental vs. applied
- Experiment vs. theory

- *Considerations* of use – always!

Figure 1.8 **How UK academics classify their own work**[42]

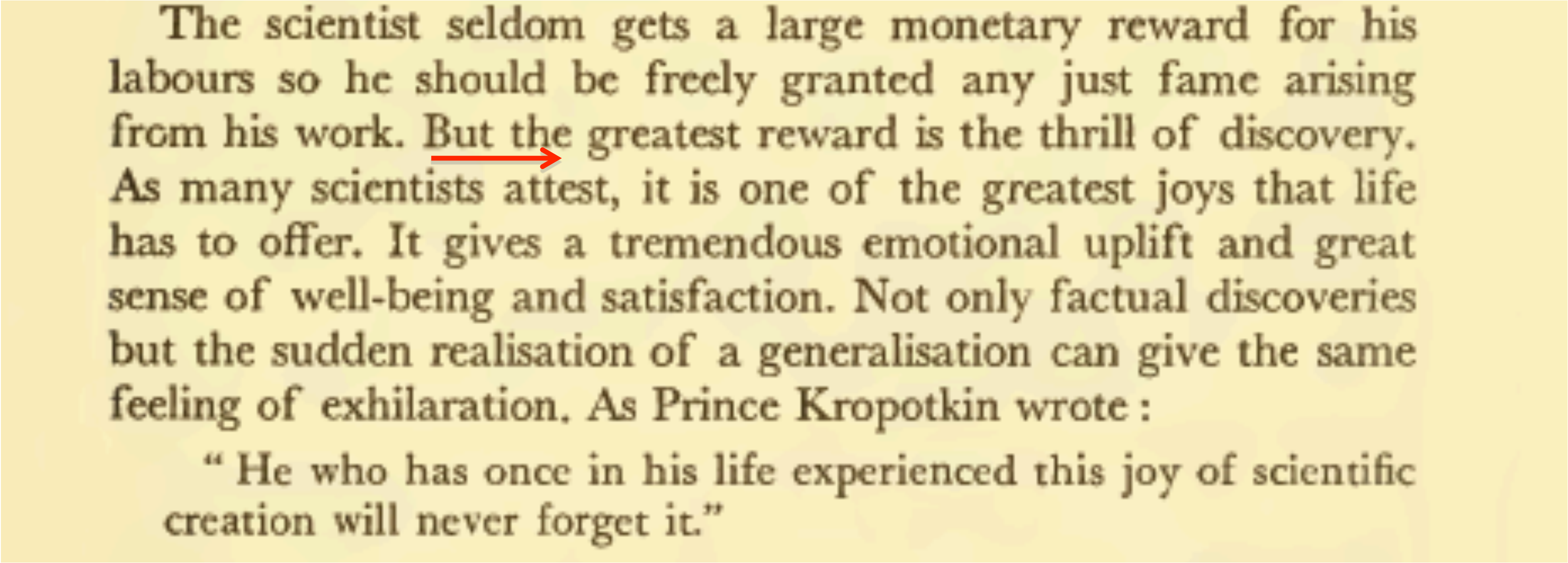




We are pioneers

In many respects the research worker resembles the pioneer. He explores the frontiers of knowledge and requires many of the same attributes: enterprise and initiative, readiness to face difficulties and overcome them with his own resourcefulness and ingenuity, perseverance, a spirit of adventure, a certain dissatisfaction with well-known territory and prevailing ideas, and an eagerness to try his own judgment.

The thrill of discovery


The scientist seldom gets a large monetary reward for his labours so he should be freely granted any just fame arising from his work. But the greatest reward is the thrill of discovery. As many scientists attest, it is one of the greatest joys that life has to offer. It gives a tremendous emotional uplift and great sense of well-being and satisfaction. Not only factual discoveries but the sudden realisation of a generalisation can give the same feeling of exhilaration. As Prince Kropotkin wrote:

> "He who has once in his life experienced this joy of scientific creation will never forget it."

…requires persistence

The stimulus of a discovery immediately wipes out all the disappointments of past frustrations and the scientist works with a new-found vigour. Furthermore, some stimulus is felt by his colleagues and so one discovery makes the conditions more propitious for further advances. But unfortunately things do not always turn out like this. Only too often our joy is short-lived and found to be premature. The consequent depression may be deep, and here a colleague can help by showing understanding and encouragement. To "take it" in this way without being beaten is one of the hard lessons the young scientist has to learn.

Unfortunately research has more frustrations than successes and the scientist is more often up against what appears to be an impenetrable barrier than making progress. Only those who have sought know how rare and hard to find are those little diamonds of truth which, when mined and polished, will endure hard and bright. Lord Kelvin wrote:

> "One word characterises the most strenuous of the efforts for the advancement of science that I have made perseveringly during fifty-five years; that word is failure."

Michael Faraday said that in the most successful instances less than one in ten of the hopes and preliminary conclusions are realised. When one is depressed, some cold comfort might be derived from the experience of those two great scientists. It is well for the young scientist to realise early that the fruits of research are not easily won and that if he is to succeed he will need endurance and courage.

http://en.wikipedia.org/wiki/Wladimir_Klitschko

Hamming says…

- You must focus on an important problem
  - "set out to do something significant"
  - "If what you are doing is not important, and if you don't think it is going to lead to something important, why are you (at Bell Labs) working on it?"

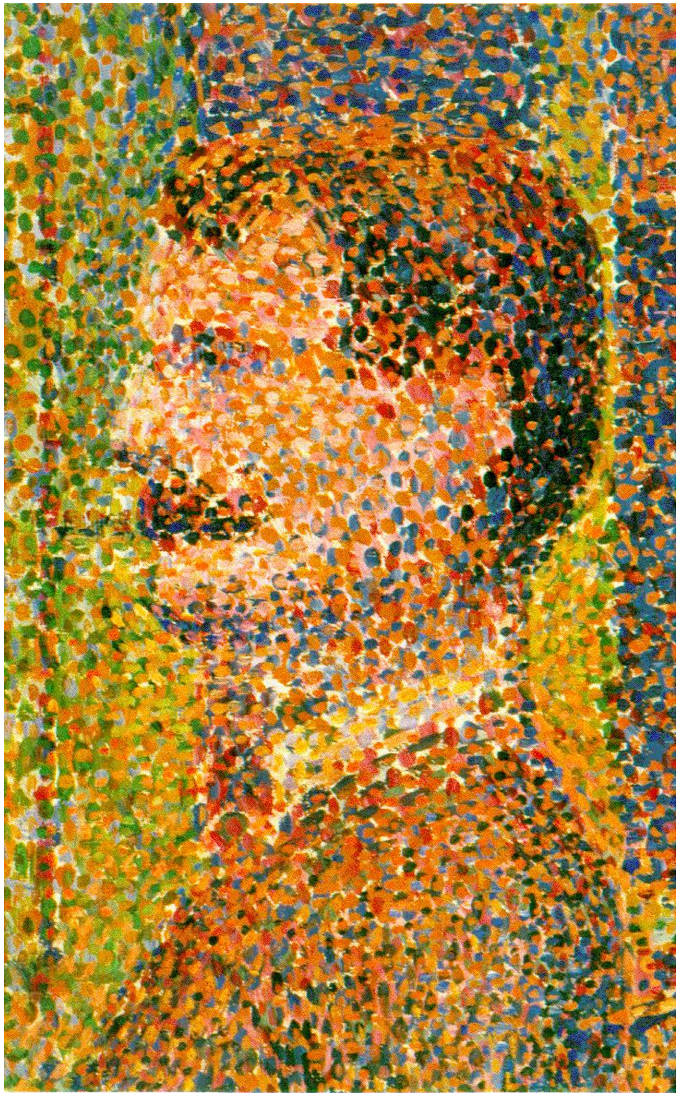
- Great scientists
  - Have courage: "They will go forward under incredible circumstances; they think and continue to think".
  - Have tremendous drive.
  - Are opportunistic: "…when an opportunity opens up, get after it and they pursue it". Beveridge also says this in terms of immersing yourself completely at the critical moments.
  - Are committed to their work (and their problem).

"Science is rarely advanced by what is known in current jargon as a 'breakthrough', rather does our increasing knowledge depend on the activity of thousands of our colleagues throughout the world who add small points to what will eventually become a splendid picture much in the same way the Pointillists built up their extremely beautiful canvasses."

-Howard Florey

[Nobel Prize Chemistry 1945, co-discovery of penicillin]

Georges Seurat, A Sunday Afternoon on the Island of La Grande Jatte (1884)



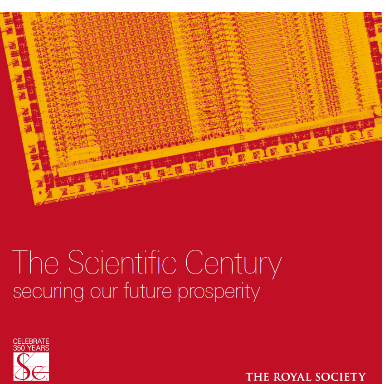
Georges Seurat

Case study 1.4

From Faraday to the iPod

Michael Faraday was a leading light of 19th century science. He began his career as secretary to Sir Humphry Davy, himself a formidable chemist and inventor. Faraday then joined the Royal Institution, where his experiments allowed him to elucidate the principles of electromagnetism and build the first dynamo. Explaining a discovery to then Chancellor of the Exchequer William Gladstone, Faraday was asked, 'But after all, what use is it?' He famously, but perhaps apocryphally, replied, 'Why sir, there is every probability you will be able to tax it'.

Faraday's ideas were taken forward by James Clerk Maxwell, Lord Kelvin and numerous others, including Albert Fert and Peter Grünberg. Fert and Grünberg received the 2007 Nobel Prize in Physics for work on giant magnetoresistance, showing that tiny changes in magnetism can generate large changes in electrical resistance. Their 1988 discovery revolutionised the way that computers store information. The minuscule hard drives inside laptops and the earliest iPods would have been impossible without Faraday's pioneering work more than 150 years earlier.



And,

SLIDE 5: CITATION FREQUENCY DISTRIBUTIONS

Citation Frequency Distribution 1900-August, 2005
(articles cited at least once)

Number of Citations	Approx # of Items Receive Citations	% of WOS
>10,000	61	0.00%
5,000-9,000	120	0.00%
4,000-4,999	116	0.00%
3,000-3,999	215	0.00%
2,000-2,999	664	0.00%
1,000-1,999	3,887	0.02%
900-999	1,232	0.00%
800-899	1,762	0.01%
700-799	2,614	0.01%
600-699	4,077	0.02%
500-599	6,637	0.03%
400-499	12,557	0.06%
300-399	27,059	0.14%
200-299	74,025	0.37%
100-199	343,269	1.73%
50-99	953,064	4.83%
25-49	2,006,529	10.1%
15-24	2,226,603	11.2%
10-14	2,106,995	10.6%
5-9	3,891,542	19.5%
2-4	4,931,952	24.7%
1	3,343,789	16.7%
Items Cited	**19,938,769**	**100.1%**

For a more realistic view of citation frequencies, slide 5 shows that from 1900-2005, about one half of one percent of cited papers were cited over 200 times. Out of about 38 million source items about half were not cited at all. Keep in mind that "items" includes not only substantive articles but also ephemera mentioned earlier. Therefore, these data provide a distorted picture for high impact journals where the number of uncited publications is much smaller.

The assignment

Come up with 5 words representing each of the themes below.

- The practice of doing good research, e.g., "doing good research is…"
- Good research when you evaluate it, e.g., "his/her research is good because it is…"
- Attributes of a good researcher, e.g., "you' re a good researcher because…"

Let's look at each category

(spreadsheet here)

Conflicting traits?

interest and enthusiasm for discovery. The most successful scientists are capable of the zeal of the fanatic but are disciplined by objective judgment of their results and by the need to meet criticism from others. Love of science is likely to be accompanied

Bancroft gives the following illustrations of the outlook of the different types of scientist. Examples of the systematic type are Kelvin and Sir W. Hamilton, who said,

"Accurate and minute measurement seems to the non-scientific imagination a less lofty and dignified work than looking for something new, yet nearly all the grandest discoveries are made this way",

"In physical sciences the discovery of new facts is open to any blockhead with patience and manual dexterity and acute senses."

Contrast this last statement with one made by Davy:

"I thank God I was not made a dextrous manipulator; the most important of my discoveries have been suggested to me by my failures."

Most mathematicians are the speculative type. The following remarks are attributed to Newton, Whewell and Gauss respectively:

"No great discovery is ever made without a bold guess,"

"Advances in knowledge are not commonly made without some boldness and licence in guessing,"

"I have the result but I do not yet know how to get it."

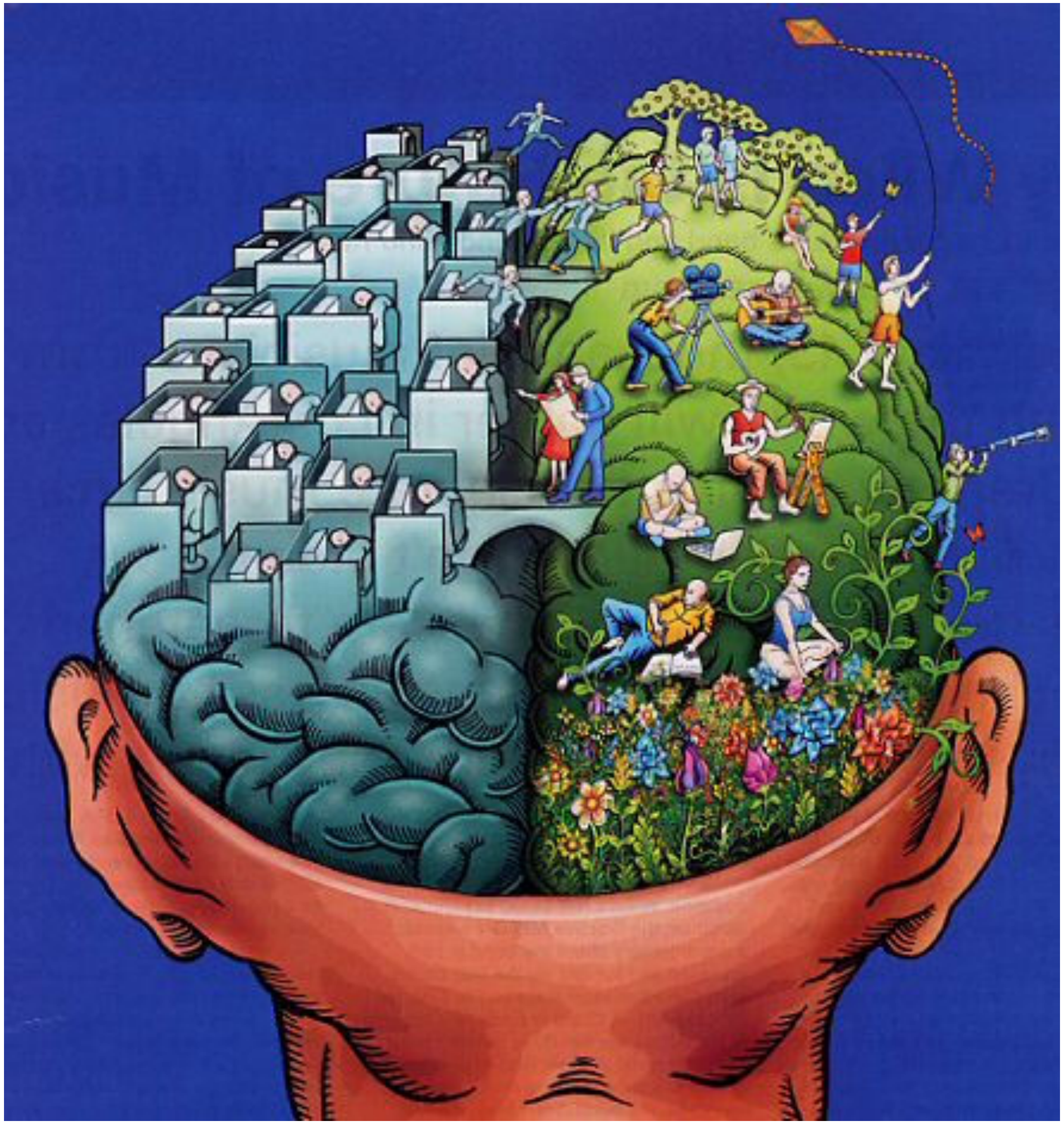
Beveridge, The Art of Scientific Investigation

The two-headed scientist

interest and enthusiasm for discovery. The most successful scientists are capable of the zeal of the fanatic but are disciplined by objective judgment of their results and by the need to meet criticism from others. Love of science is likely to be accompanied by scientific taste and also is necessary to enable one to persist in the face of frustration.

Beveridge, The Art of Scientific Investigation

Left vs. right brain

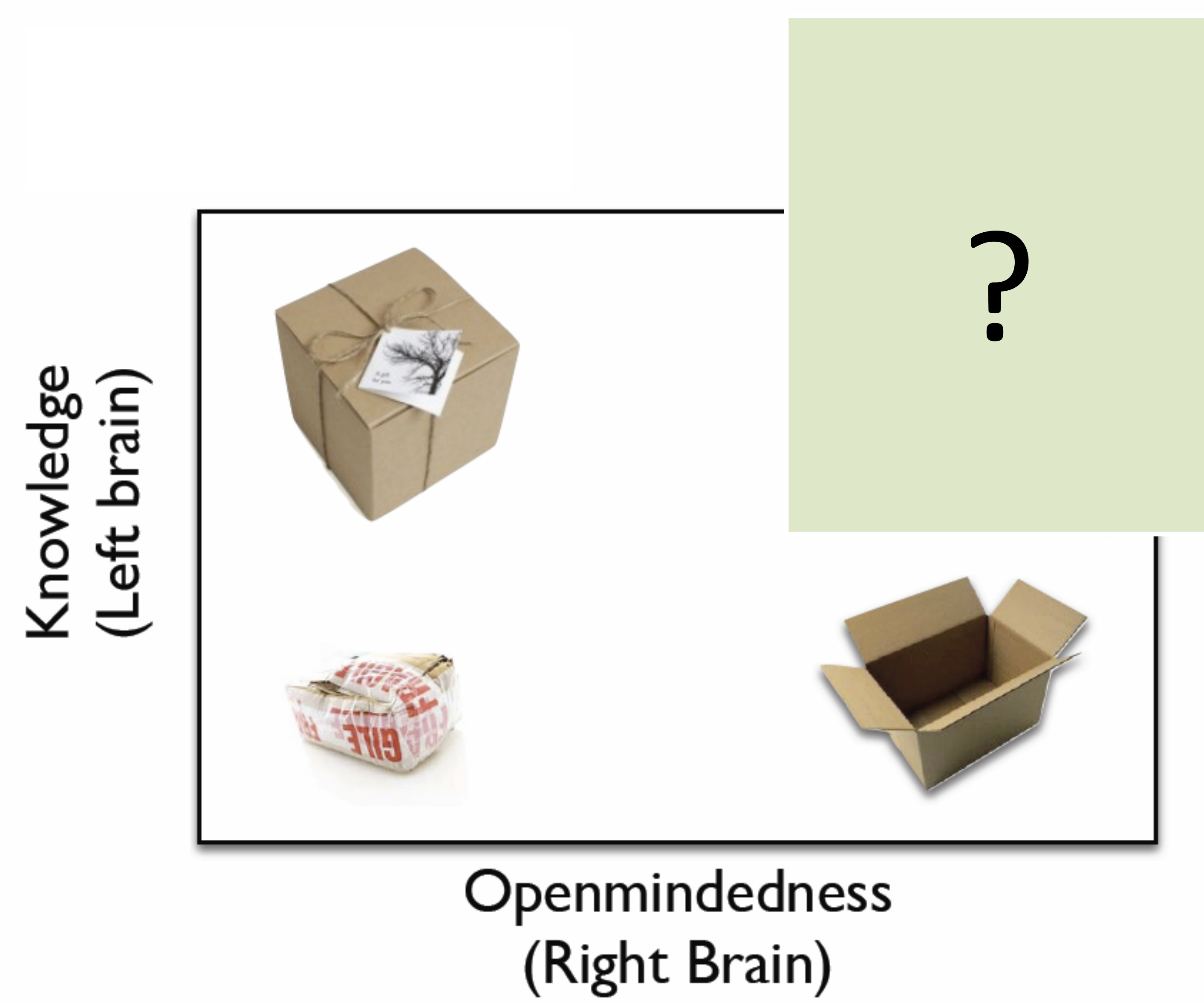


http://www.roblambert.com/wp-content/uploads/2007/10/left-brain-right-brain.jpg

Left vs. right brain attributes

LEFT (Analytic)	RIGHT (Global)
Successive Hemispheric Style	Simultaneous Hemispheric Style
1. Verbal	1. Visual
2. Responds to word meaning	2. Responds to tone of voice
3. Sequential	3. Random
4. Processes information linearly	4. Processes information in varied order
5. Responds to logic	5. Responds to emotion
6. Plans ahead	6. Impulsive
7. Recalls people's names	7. Recalls people's faces
8. Speaks with few gestures	8. Gestures when speaking
9. Punctual	9. Less punctual
10. Prefers formal study design	10. Prefers sound/music background while studying
11. Prefers bright lights while studying	11. Prefers frequent mobility while studying

Combining the best of both sides



Continuous learning is an essential attribute of the research process

Learning styles

Visual

Auditory

Kinaesthetic

Impact and inspiration

The frugal way

George Whitesides CAMBRIDGE, MASSACHUSETTS

The promise of cost-conscious science

Western science, particularly academic science, is culturally obsessed with superlatives, and often separated from technology: the most accurate measure of time, the most detailed accounting of a genome, the most distant star, the highest-energy particle. Why? Superlatives are necessary in some areas, and easy to keep score with in others. And there are technologies (such as GPS) that absolutely require extreme precision.

But superlatives tend to be expensive. Should cost be an issue in science? If knowledge is a treasure beyond price, perhaps obtaining it should be similarly cost-unconstrained—an idea enthusiastically supported by expensive fields such as high-energy physics. And even the most expensive science is cheap relative to, say, a war or a tsunami. Yet science in 2012 and beyond will be evolving a new variant of itself: frugal science, designed to generate knowledge (and technology based on that knowledge) with cost as an integral part of the subject.

The idea of including "cost" in science is perhaps déclassé in Western research universities, but it is based on an important change in the world. The 80% of the global population that is poor (and has long been excluded from science, technology and the benefits of both) would like to join the party. China, India and Brazil have already muscled their way into technology, and other less-developed countries will follow.

Behind the argument between "superlative" and "cost-effective" lie differences of opinion about the purpose of science. Is it the job of science to generate knowledge as an abstract good, with the benefits to the society that pays for it unpredictable, or should science at least think of serving society?

In the West, the answer is often two words: "quantum mechanics". Its development revolutionised both science and technology, and was indeed a product of pure curiosity. But there have been only one or two such events in fundamental science in the past century (genomics may eventually be as important); and the birth of quantum mechanics was not expensive, although its applications in technology were.

In the rich world, maintaining a distinction between curiosity-driven science and applications-driven technology may or may not be an affordable luxury. In the developing world, there are pressing problems whose solutions require relevant science and technology now.

George Whitesides: professor of chemistry and principal investigator, Whitesides Research Group, Harvard University

2012 IN BRIEF

Computer geeks and universities salute and mourn **Alan Turing**, born a century ago

Quick, pass me the screwdriver!

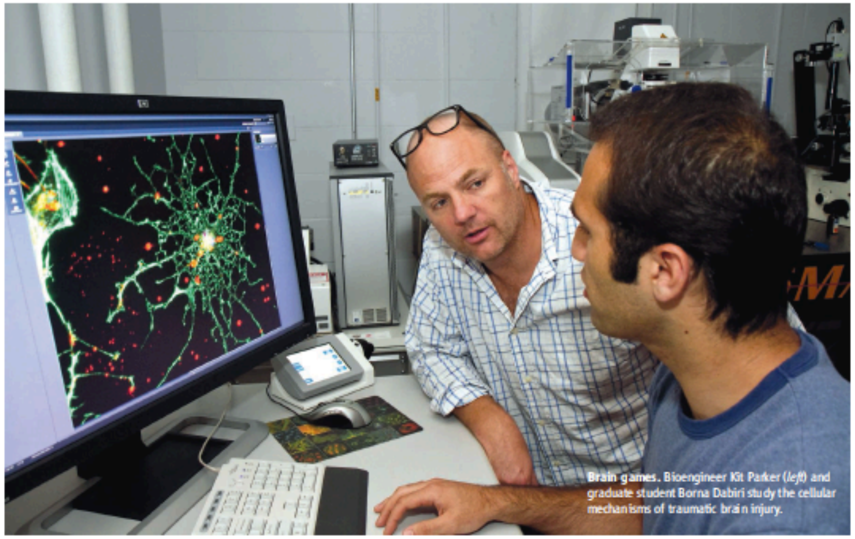
Health care is one example. Western medicine does many things well, but it is not affordable in, or very useful to, most poor populations. What then should be the technology base for affordable health care? Answering that question requires the development of science that is conscious of cost from the beginning—a frugal health care that might, perhaps, be more related to Western public health than to end-of-life, high-tech medicine. What about other problems: the management of megacities, development of radically effective ways of delivering education, or providing water and energy? All of these problems can be phrased as technologies, which will require an appropriate foundation in science—and that must include cost. The race may not be to the swift, but rather to the cheap.

The race may not be to the swift, but rather to the cheap

There is another reason to be encouraging frugal science: jobs. Frugal science has a chance of yielding cheap products, and thus jobs and other understandable benefits. The developing world is pioneering telecoms systems with structures quite different from those used in the rich world. The Shenzhen gene factories, using American technology, are among the lowest-cost producers of genomic information. The Tata Nano car represents a creative step towards low-cost personal transport. And the science that leads to affordable health care for Africa may provide some of the best approaches to reducing the no-longer-affordable cost of health care in America.

Foundations (Gates, Wellcome and others) are already developing frugal medicine, and much of the health-care spending in developing countries is on technology that is, of necessity, frugal. The science base for this—low-cost diagnostics, epidemiology and nutrition informed by mobile-phone reporting—is developing rapidly. Tata, GM, Toyota and their kin are all thinking about radically different concepts for the car: smaller, lighter, cheaper. To sell in world markets, affordability may in future be the first requirement, not an afterthought.

"But is it science?" ask the sceptics. Perhaps "No", under the old definitions of chemistry, physics and biology. But "Yes", as a new discipline, with an intellectual skeleton based on understanding complexity and simplicity, and on developing strategies for integrating information, including economic information, originating in entirely different fields. It will probably get a reluctant welcome at first in the mandarin research universities of America and Europe, but it may flourish in Beijing, Mumbai and Cairo. And where it flourishes best may determine whose grandchildren have jobs. ■



Brain games. Bioengineer Kit Parker (*left*) and graduate student Borna Dabiri study the cellular mechanisms of traumatic brain injury.

PROFILE: KIT PARKER

Engineering a New Line of Attack On a Signature War Injury

By jolting neurons in the lab, an Army officer and bioengineer hopes to gain ground on traumatic brain injury

When hijacked planes slammed into the World Trade Center towers in 2001, Kevin Kit Parker knew he had to do something. He'd always had a patriotic streak, and years earlier, while a graduate student in applied physics at Vanderbilt University in Nashville, Tennessee, Parker had enrolled in the Army Reserve Officers' Training Corps (ROTC). By the time of the attacks, he was a postdoctoral fellow, working on cardiac electrophysiology at Johns Hopkins University in Baltimore, Maryland, and in the middle of hunting for his first faculty position. He felt certain the country would soon be going to war, and despite having several job interviews on his calendar, he transferred to a unit he knew would be deployed. "I wanted to get in the game," he says.

While waiting to deploy, Parker accepted a job at Harvard University. With considerable trepidation, he asked the dean who'd just hired him for an immediate leave of absence to go to Afghanistan. It was a very unusual request, says then-dean Venkatesh Narayanamurti. Few, if any, Harvard professors have taken combat leave since World War II. But Narayanamurti admired Parker's dedication to national service. "I knew right away I would support him," he says.

By fall 2002, Parker was leading a team that patrolled a 900-square-kilometer swath between Kandahar and the Pakistan border, providing aid to villagers and searching for Taliban and Al Qaeda fighters. He finally started his job at Harvard in the summer of 2003, then deployed again in 2008, putting postdocs in charge of running the lab in his absence. His deployments caused Parker to reconsider the focus of his research and to establish a project on a signature injury of the wars in Iraq and Afghanistan: traumatic brain injury (TBI). He has been back to Afghanistan twice more as part of a panel of experts convened to assess how the military handles TBI and combat stress.

The Pentagon estimates that more than 200,000 U.S. troops have experienced TBIs in the recent conflicts, mostly from roadside bombs and other improvised explosive devices (IEDs). The long-term effects of these brain injuries won't be known for decades, but there are already worrisome hints that TBI may compound the effects of combat stress and predispose veterans to the type of early-onset dementia seen in football players with a history of head injuries (*Science*, 29 July 2011, pp. 514 and 517). Despite the urgency of the problem, frustratingly little is known about the mechanisms by which an explosive blast injures the brain, Parker says. "I kept seeing guys get hit, and I thought, all right, I'll take a look at this and see if I can get a better angle on the problem."

Mission shift

On a recent morning, Parker's students and postdocs mill about a conference room before their weekly lab meeting. They pour coffee and set out a plate of jalapeño bagels for Parker, who likes to goad others into eating spicy food. He arrives a few minutes late, wearing torn jeans and a red Harvard baseball cap with the bill folded into a sharp crease. A commanding presence at just under 6'6" (2 meters), Parker has a booming voice that bears more than a trace of his upbringing in west Tennessee. He launches into a list of lab business he's scribbled on a whiteboard. Some Italian researchers have asked about collaborating; so has a team from Merck, the pharmaceutical giant. And Parker has just returned from a molecular medicine conference in Korea. "Y'all make some damn fine fried chicken over there," he says to one of his Korean-born postdocs. "Hyungsuk, do you make that stuff at home?" When he shakes his head no, Parker pretends to be heartbroken. A second later, he's back to his list.

When Parker first arrived at Harvard, his main academic interest was the physical forces that determine how cells and tissues build themselves. His lab did cardiac tissue engineering, and that's still the focus for about two-thirds of his group. At the lab meeting, postdoc Anna Grosberg presents a computational tool she's developed for quantifying the alignment of sarcomeres, the protein fibers that make up muscle cells. How the fibers line up affects how a muscle contracts, and Parker thinks the tool could be useful for clinical pathologists or companies interested in engineering cardiac tissue for drug screens or therapies. In quick asides, he quizzes David Coon, who handles industry relations and intellectual property issues for the lab, about the commercialization prospects, and asks Sean Sheehy, a grad student with a computer science background, how hard it would be to incorporate Grosberg's metric into a graphical software package. When Sheehy says it's doable, Parker jokingly tells him: "This is your project now, baby!"

Ideas and projects spring up freely in the lab. A cotton-candy machine inspired a new way for making nanofiber scaffolds on which to grow cells (and a 2010 paper in *Nano Letters*). Back in his office, Parker shows off a movie on his computer of a more recent project: an artificial jellyfish. Cut from a polymer sheet coated with rat heart muscle cells, its form lacks the organic curves of the real thing, but the ghostly flap of tissue pulses across the screen with surprisingly lifelike motion.

Parker sees his fledgling TBI research project as a moral obligation. He saw IED explosions firsthand in Afghanistan, and he has buddies who've suffered the consequences. When Colonel Geoffrey Ling, the program manager who oversees TBI research at the Defense Advanced Research Projects Agency (DARPA), asked Parker in 2006 if he'd ever thought about studying TBI, he demurred at first. "I said, 'There have to be better people than me; I'm not a brain guy,' " Parker says. But as he started reading the scientific literature, he was struck by how little was known about what happens at the cellular level in a TBI.

In the thick of it. Parker, here searching for IEDs in Afghanistan, has changed the course of his research after two tours of duty.

Concussion on a chip

One prevalent idea has been that a blast wave or physical blow to the head tears the membranes of neurons, allowing positive ions to rush in and overexcite neurons to the point of killing them. Based on his experience with tissue engineering, Parker suspected something else might be going on instead, or in addition. He was surprised to see nothing in the research literature about integrins, proteins in the membrane of all cells that connect a cell's internal protein skeleton to the scaffold of proteins outside the cell, the so-called extracellular matrix. Parker reasoned that the force of a blast could propagate through this network of proteins, interfering with integrins and the many cell-signaling pathways they interact with.

The first challenge was figuring out how to go about studying TBI in the lab. Researchers have studied TBI by issuing blows to the heads of rats, pigs, and other animals, but it's not clear how well those experiments replicate what the human brain experiences in a car crash or explosive blast. Moreover, Parker says, "if I start blowing up goats at Harvard, I'm not going to last long." As an alternative, his lab has devised an arsenal of devices that can subject cultured neurons or slices of brain tissue to carefully calibrated forces. "We need to think of ways to replicate this on the bench top so you can mainstream the science," Parker says.

Their early work supports the idea that integrins may play a role in TBI. In one study, graduate student Matthew Hemphill and others put cultured rat neurons on a stretchy, square sheet of silicone that could be given a short tug by a high-precision motor. These tugs subjected the neurons to forces that the researchers estimated would be similar to those generated inside the head of a soldier exposed to an IED blast. Within a few minutes, microscopic swellings appeared on the spindly axons and dendrites that send and receive messages from neighboring neurons. Axonal injury is a hallmark of TBI, and a diffusion tensor imaging study by a different group published 2 June 2011 in *The New England Journal of Medicine* found evidence of axon damage in U.S. soldiers who suffered TBIs in Iraq. Additional experiments with the cultured rat neurons implicated a particular integrin signaling pathway in this damage. Treating the neurons with a drug that inhibits a component of this pathway called Rho-kinase reduced damage to neurons after a simulated blast, the researchers reported in *PLoS ONE* in July 2011.

In another study, published 2 August 2011 in the *Proceedings of the National Academy of Sciences*, a team led by then-postdoc Patrick Alford used the same setup to investigate the effects of a simulated blast on blood vessels. In this case, the researchers used rat muscle cells from the lining of blood vessels. When subjected to a sudden stretch, these cells flipped a genetic switch that made them more likely to contract and promoted their proliferation. Both effects would tend to clamp down on blood vessels,

Downloaded from www.sciencemag.org on January 5, 2012

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How would you want the world to remember you?

3 NOVEMBER 2010

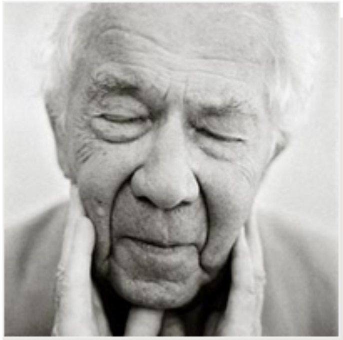
by Nath

Or to quote a chemistry PhD student from the University of the Philippines being a Nobel laureate, how would you want the world to remember you?"

The student is Ian Harvey Arellano and that question is one of the ten most questions according to the NPG (Nature Publishing Group) that was submit Nobel Questions-Lindau Answers' website. There are a total of 205 submitt 14,304 votes are casts. These questions "ranged from scientifc queries abo and theories, to more general considerations about life, politics, funding, ir *with the question of Ian)* epitaphs"[1].

How did some of the Nobel Laureates answer ? [2]

Some are modest...



Christian René de Duve, Physiology or Medicine 1974

I have no such ambition. *In the history of science, my contributions are minor and would have been made by someone else had I not stumbled on them first. They already appear in textbooks without mention of my name. I am no Galileo, Newton, Darwin, Einstein or Watson and Crick. But I have had fun and have been rewarded beyond my deserts. So be it.*

And some are even more modest...

I do not think the world will remember any of us. *When you work in cosmology, you think with a perspective of billions of years. How many people do we remember from 1,000 years ago? How many from 10,000 years ago? How many from 1 million years ago? etc. So now the question is more like that about Ozymandias [from Percy Shelley's poem]. After a thousand or so years nothing is left of the great works but a few broken relics. What will be left in a billion years?* ***The point is not about being remembered or about doing science to win a Nobel prize — you do science because you want to be a scientist.*** *Likewise, you live your life in a way you think is good and good for you.*

George Fitzgerald Smoot, Physics 2006

How to be a "genius"? (10,000 hours guy)

"It's complicated explaining how genius or expertise is created and why it's so rare.

But it **isn't magic**, and it **isn't born**. It happens because some critical things line up so that a person of good intelligence can put in the **sustained, focused effort it takes to achieve extraordinary mastery**.

These people don't necessarily have an especially high IQ, but they almost always have **very supportive environments**, and they almost always have **important mentors**.

And the one thing they always have is this **incredible investment of effort**."

-K. Anders Ericsson

Florida State University

Learning to do good research is hard

- Research itself is an intrinsically difficult task
- There are many component skills to learn, e.g., understanding the literature, setting up your experiments, data analysis, interpretation…
- There is often a long time-scale on rewards
- Ultimately, and at many levels, you are responsible for directing your own education

David Jensen, U. Massachusetts, http://kdl.cs.umass.edu/courses/rmcs/

Homework

- No readings!
- Do the learning styles questionnaire and bring it to class.
- 1-2 paragraph summary of your research topic (submit via ctools), due 2pm Thursday
- Bring a laptop next week (if you don't have one, hope you can share)

- Next time: gathering information (i.e., searching the literature)