Columbia Science Review

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Mirror Neurons
Monkey-See, Monkey-Do

Magnificent Desolation?
The Search for Extraterrestrial Life

Squaring the Circle
The Ancient Delian Problem

Martin Chalfie
An Interview with the Nobel Prize Winner

Columbia Science Review

The Columbia Science Review

The Columbia Science Review strives to increase knowledge and awareness of science and technology in the Columbia community by presenting engaging and informative approaches to contemporary science and technology that include, but are not limited to:

- Exploration into contemporary issues of science, including research, policy, and opinion
- Features on current faculty
- Opportunity for students to publish their scientific research

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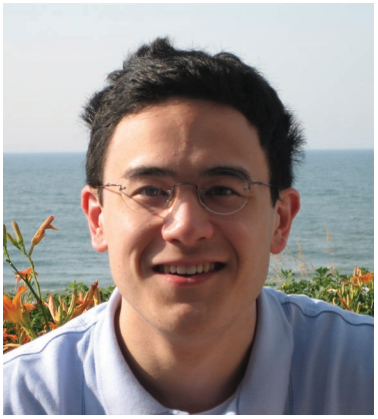
The Curious Case of the Beans: G6PDD

COVER PICTURE: Using genes from various organisms, scientists at Harvard University have developed a technique to light up brain cells in mice. These brain cells are from the dentate gyrus, a part of the brain associated with memory, and each one randomly expresses fluorescent proteins of different colors. Credit: Livet and Lichtman, Harvard University.

Letters



Despite nearly 400 years of success, science still faces tremendous challenges in obtaining the popular support of many. A key problem of science is that it has always seemed detached from the human condition. Unlike enduringly popular religion, which has promised everything from eternal life to salvation for our sins, science is often viewed as a cold, unfeeling stance towards the universe; a concept lacking humanity, and thus, enthusiastic adherents. But this is not true.

Science lies at the very core of what makes us human. Let us call it Humanism instead. Humanists remind us that the human condition is universal, and most importantly, that it can be improved through our mutual cooperation and the ability of the human mind through the scientific inquiry of nature.

Science is one of the greatest forces for good in the world that we have ever discovered. But I believe this is obscured because we miss the Humanism that underlies it. It is the most basal human faith, one that recognizes our biological commonality, one that celebrates the awesome beauty and mystery of our universe, and one whose objective is the advancement of our collective condition without exclusion. Its central tenant is faith in the human ability to understand, to question, to wonder, and to use that great wonder as a source of inspiration, that we might find, however elusive, the truths of our existence, and the peace of our mortality. Personally, I find this the most reassuring and altogether most fulfilling of endeavors, which I hope in all its majesty calms even the most restless of spirits, even the most parochial of critics.

Science is for everyone; it is a shared part of our human experience. At the Columbia Science Review, we hope this common bond, this 'voice of life,' calls you to come and learn.

-Jonathan L. Mo, Editor-in-Chief

As with every issue of the Columbia Science Review, we strive to explore...well... science! But what is science? Commonly defined as an objective study of the physical world, the human race has developed a method—the scientific method—for regulating this investigative process. The great success of this method in allowing us to make conclusions about the environment we inhabit has led us to neglect many subjective discussions of science, rendering countless studies, ideas and proposals invalid. So what do we lose in our often blind pursuit of objectivity, if anything at all? Is there a place for rock music in formulating new genetic sequencing techniques? Could sculpture add to our of quantum theory? Does poetry allow further conceptualization of an intricate computer code? Conversely, could knowledge of a plant cell's components inspire acrylic painting? Could identification of a novel animal species in the Amazon give rise to a new movie script?

It is with these questions that I would like to dedicate this issue to you, the reader, so that you may expand your frame of reference with respect to whichever discipline you have chosen for study. Academic disciplines have never been more interconnected, and they continue to meld and mesh every day, creating new and exciting ideas in the process. The perpetual formation of these junctures is redefining the word science and I call upon you to use this issue of CSR as a platform for further exploration of this interdisciplinary, amorphous, and limitless word.

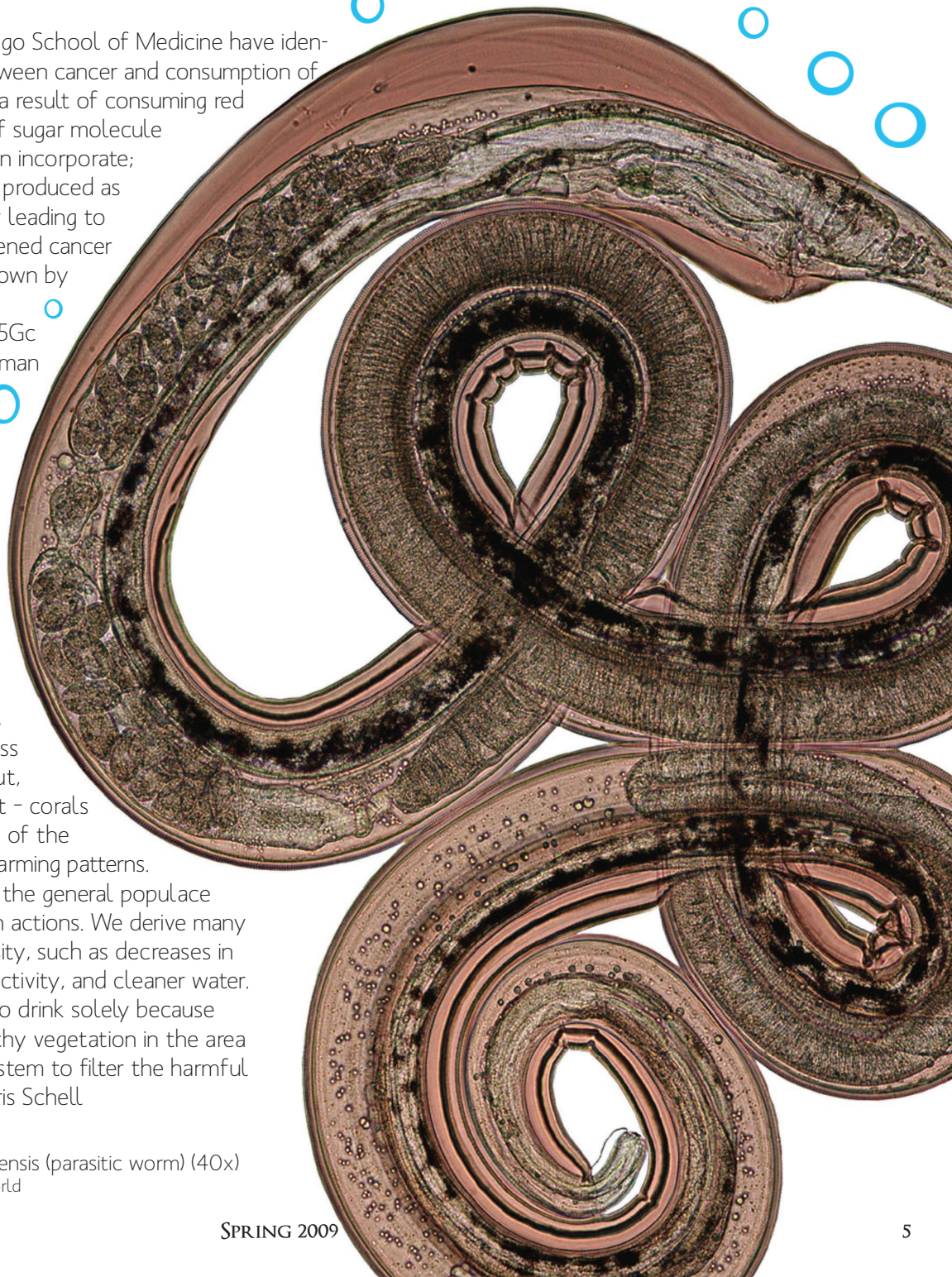
-Niccola Pérez, President

Cocktail Science

Believe it or not, animals can rain from the sky. This relatively common meteorological phenomenon has been occurring in Honduras for more than a century on a yearly basis between the months of May and July. Live fish literally rain down from the sky during a violent thunderstorm accompanied by strong winds and heavy rain. Although there is no valid scientific explanation for this bizarre phenomenon, many locals believe that Father Jose Manuel Subirana, a Spanish Catholic missionary, rains the fish down upon Honduras to provide food for the poor and malnourished. Can you think of a better (and cooler) way to go fishing? -Pradeep Bandaru

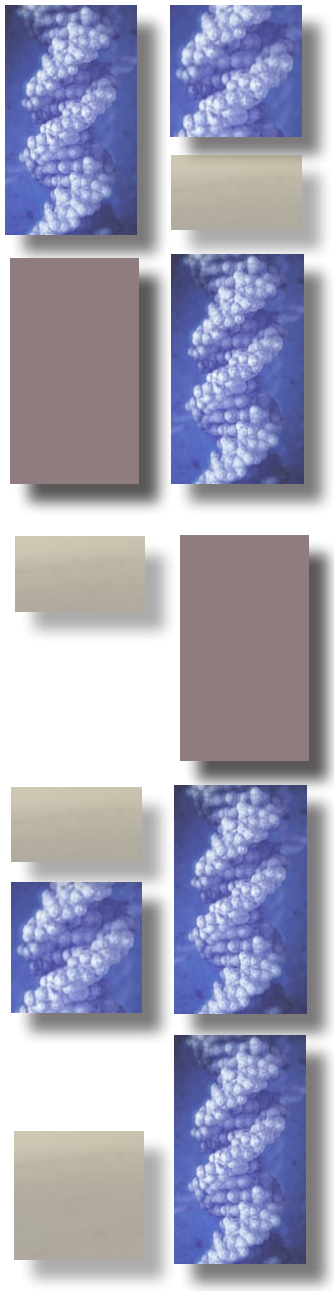
Researchers at the UC San Diego School of Medicine have identified a new possible link between cancer and consumption of red meat and milk products. As a result of consuming red meat, humans produce a type of sugar molecule called Neu5Gc, which tissues can incorporate; anti-Neu5Gc antibodies are then produced as an immune response, potentially leading to chronic inflammation and heightened cancer risk. Tumor tissues have been shown by these researchers to contain a disproportionate amount of Neu5Gc compared to healthy, normal human tissues. -Christine Yeh

The biodiversity of our planet, usually quantified by the number of species, is declining considerably, to a point where biologists have characterized this current time period as a mass extinction event. Coincidence? Not likely. Many ecosystems are responsible for properly handling carbon dioxide, low biodiversitytranslates into less carbon dioxide control. Simply put, the loss of species on our planet - corals and vegetationespecially - is one of the largest contributors to global warming patterns. But it is the most overlooked by the general populace and the most affected by human actions. We derive many benefits from increased biodiversity, such as decreases in pathogens, increased food productivity, and cleaner water. The New York tap water is safe to drink solely because the Catskill Mountains and healthy vegetation in the area work as an effective irrigation system to filter the harmful chemicals out of the water. -Chris Schell



Nippostrongylus brasiliensis (parasitic worm) (40x)
Courtesy of Nikon Small World

A Bioethical Approach to Gene Therapy and its Role in the Future of Mankind



Introduction

Marlee Ickowicz and Larry Geyman

The field of gene therapy has undergone drastic changes in the last decade, growing from a nascent field to a burgeoning science. Gene therapy seeks to cure diseases by fixing problems at their source: genes. The therapy consists of inserting a "healthy" gene into the genome of a patient to replace an "abnormal" gene. This process is typically carried out by an altered virus, called a vector, that is able to deliver human genes into cells. The two types of gene therapy are germ-line gene therapy and somatic gene therapy. In germ-line gene therapy, viruses are used in reproductive cells to alter the genetic composition of preembryos and effectively eliminate their diseased genes. They can also be used in the reproductive cells of adults, eliminating the possibility that their offspring could inherit a disease. Somatic gene therapy, on the other hand, is less invasive, expensive, and controversial because it targets genes in adults' non-reproductive cells.

The current status of gene therapy is both promising and disheartening. Although there have been outstanding improvements in technique and application, there are still numerous procedural difficulties. Because of cell death and cell division, there is no guarantee that the cells into which the genes are inserted will survive long enough for the therapy to have any effect. In addition, the body could attack the virus vector and tag it as a foreign substance. The original virus also might become active and infect the recipient. Although gene therapy is extremely promising, advancements are slow.

The ethical considerations of gene therapy have been debated in political, religious, and scientific circles since 1967. Initially, the controversies presented by each of the aforementioned parties were reflected by lackluster legislation that failed to come to a consensus on how to deal with the issue. In October 1999, the death of 18-year-old Jesse Gelsinger marked the first reported fatality caused by gene therapy. His death, which was followed by six other gene-therapy related deaths, complicated the ethical dilemma. In the years that followed, significant advancements in gene therapy techniques allowed scientists to cure deafness and inherited blindness and re-engineer immune cells to attack cancer cells. These extreme positive and negative reports heightened the ethical debate surrounding gene therapy and pressured political and ethical pundits to play more decisive roles in future research and practice. Currently, the debate about somatic gene therapy has been tabled, but debate regarding germ-line gene therapy continues.

For the Sake of Our Species: An argument in opposition to Germ-line gene therapy

Marlee Ickowicz

Humans have certain essential characteristics that make them distinct from other species. Although gorillas can learn sign language and parrots can repeat sentences, only humans can reason, abstract, form complex language, and display a wide range of emotions. These qualities are fundamentally genetic. There is an organic process of genetic mutation, selection, and permutation that makes the human species unique. In other words, our genes make us human. What if we alter them? With gene therapy, we would have the potential to become healthier and more normal. However, we would also have the power to alter what is essentially human.

Genes are passed on from generation to generation. They give our grandchildren ten fingers, ten toes, and all of the other elements necessary to perpetuate the species. If scientists alter these fundamental units of inheritance, humans have the potential to pass down traits that are artificial or synthetic. Manipulating this process presents the possibility of creating a new species and perhaps permanently impairing our own.

Consider the following analogy regarding the current state of our financial markets. The massive financial failure we are experiencing is a result of artificial and synthetic financial instruments that were created without an understanding of the potential consequences. Political and economic experts have still not agreed on a solution for the broken financial system. Similarly, we have not seriously considered the consequences of germ-line gene therapy and we do not have a solution to mend a potentially "broken" human species.

Although gene therapy currently manipulates genes that carry particular strains of disease, scientists have the potential to alter all diseased genes, and furthermore, to alter genes and human traits not associated with disease. Who draws the line?

On a practical level, scientists and researchers have found that there are uncertainties with germ-line gene therapy, as manifested in the deaths of at least seven people. In addition, researchers have reported unanticipated consequences such as induced leukemia (Kaiser, 2003). A utilitarian approach may consider this justifiable because thousands of people may benefit from germ-line gene therapy. However, because the outcome of gene therapy is unclear, additional deaths are likely to occur during the process of developing effective and safe gene therapy procedures. What if one of the deaths is a future Nobel Peace Prize winner, an accomplished international diplomat, or even your average "Joe the Plumber"? Is any life worth risking for uncertainty, especially when the outcome could possibly be harmful for our species?

Germ-line gene therapy is currently available only to people who can afford the pricey procedure. If this trend continues, affluent people will have the privilege of altering their genes or their children's genes, while the masses will not. This inequity based upon financial stratification has the potential to increase the gap between the wealthy and the poor. Although the possibility of a healthier and wealthier species is appealing, it would have negative consequences because it disrupts the natural order of intermixing and diversity.

Finally, germ-line gene therapy has the potential to accelerate the demise of the human species. If scientists completely eradicated disease, humans would overpopulate at an unnaturally high rate, making the fight over earth's already limited resources a losing battle. Other possible hazards range from bioterrorism to misguided regulation. If gene therapy technology gets into the wrong hands, the ability to manipulate genes could be used as a weapon. Moreover, if scientists and researchers manipulated their own genes, could they be trusted to regulate ours?

A return to the financial analogy seems appropriate. Amidst global economic downturn and fear of recession, lawmakers, businessmen, and politicians have scrambled around Wall Street and Main Street to find a remedy that will hold the fragile economy together. Now imagine scientists frantically struggling to salvage our species after the onslaught of gene therapy's potentially hazardous repercussions. Time is of the essence and, unlike the financial crisis, we do not have the luxury of trial-and-error solutions because the survival of the human species is at stake. If we could go back in time and stop the financial crisis from happening, would we? I would hope so.

It seems clear that the risks are too great and the benefits are too small. Gene manipulation would alter our species, renouncing what is essentially human and accelerating human demise. Tampering with genes-humanity's essential building blocks and the fundamental units of inheritance-threatens human naturalness and calls into question the future of our species.

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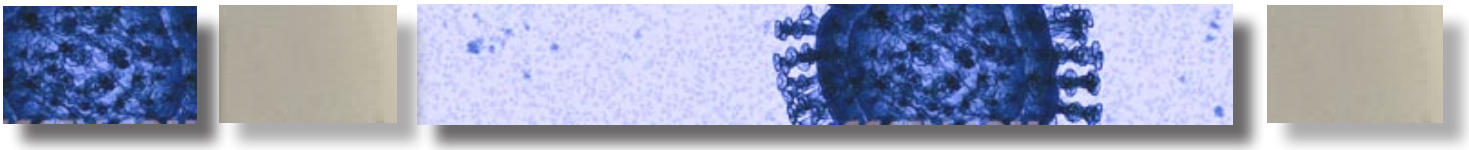
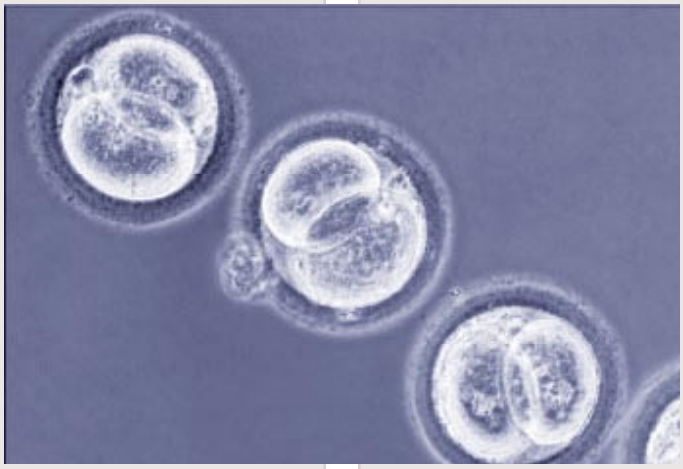
Mastering the Process of Evolution: An Appeal to Increase Gene Therapy Research



Larry Geyman

Just like any scientific field, gene therapy will grow and develop until one day it becomes practical enough to be applied to humans. But what are the justifications for allowing gene therapy to develop to such a level? Gene therapy is, no matter how you look at it, tampering with nature and with DNA, and it will have huge implications in the future. Nonetheless, I claim that gene therapy research should continue at its current pace and I welcome advancements in this exciting new field.

Some argue that gene therapy is tampering with nature. They suggest that by altering our genes, we would lose what is "natural" about us. However, to be human is to be constantly changing, so there is no constant "human" entity in the first place. We are not a static species at all. Genes are "lost" throughout history and are retained in our genome as more-or-less useless pieces of so called "junk" DNA.



In addition, genes themselves are constantly changing. Experiences shape us, but more correctly, they shape our DNA. Through external influences, the body turns on certain genes and turns off others, forming what makes each individual unique. Yet this "uniqueness" is not constant. Think of homo habilis, our ancestor. To these ancient humans, to be human was to be a homo habilis. But to us, to be human is to be a homo sapien. What is deemed human is subject to change. Altering genes synthetically is not unnatural; rather, it is taking control of what nature has been performing for billions of years.

One might also suggest that the costs simply outweigh the benefits. However, every scientific discovery comes with its share of risks. From a utilitarian perspective, one can clearly see that if gene therapy will save more individuals than it will harm in the process of perfecting it, then the research behind its development is worthwhile. However, the risks for the development of gene therapy are higher than the risks for the development of vaccines for diseases because, with gene therapy, humans are tweaking the molecules that define us. If the new, improved gene has but one incorrect nucleotide, the person may die. However, this should not diminish the potential benefits of improved general health, increased longevity, and the eradication of dozens of fatal diseases. In a world in which cancer causes 7.1 million deaths annually (Gene Therapy 2008), and diseases run rampant throughout developing countries, gene therapy offers too many benefits to even consider halting its development.

Thirdly, we must look at future implications of gene therapy, particularly its large-scale effects. If all diseases were eradicated, the human population would skyrocket. However, because of our planet's limited resources, we would be headed for disaster. However, if gene therapy were developed in tandem with renewable energy technology, the planet would be able to support more life.

Evolution takes millions of years to be visible, so try to think of gene therapy as "accelerated evolution." It is no different than traditional natural selection-induced evolution except that now we have become intelligent enough that we are able to select traits without the aid of natural selection. "There is nothing holy about a fragment of DNA," states David King, Director of Genetic News (Bergeson, Ethics of Gene Therapy, The 2008). And there is nothing unnatural about taking evolution into our own hands and guiding it. We have become sufficiently intelligent that we can evaluate the risks and plan ahead for the future to create a society in which all will be able to enjoy the miraculous benefits of gene therapy.

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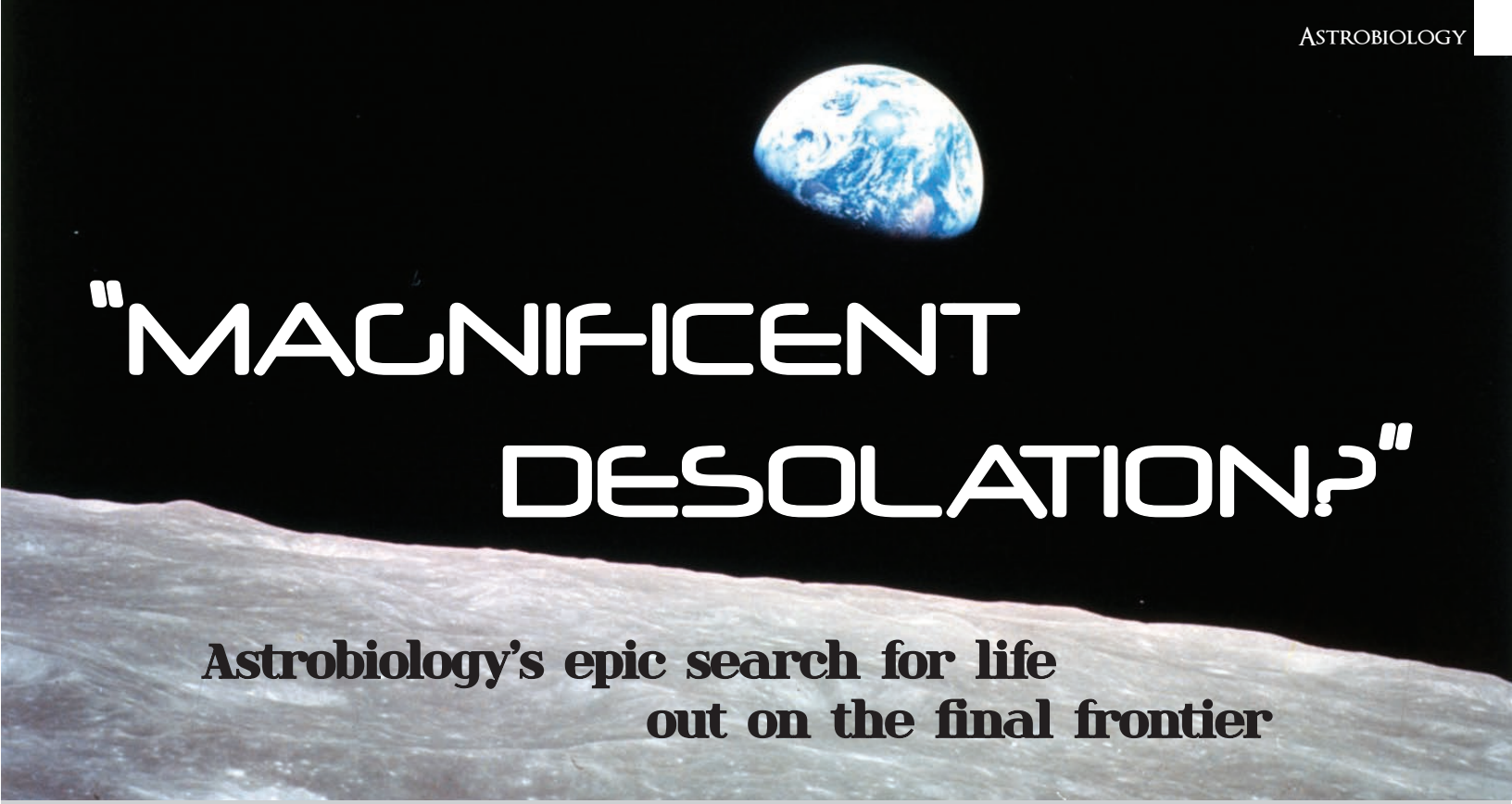

"Magnificent Desolation?"

Astrobiology's epic search for life out on the final frontier

Jonathan Mo

A Pale Blue Dot

When Edwin "Buzz" Aldrin first set foot on the moon in 1969, his words summed up the human experience of outer space: "Beautiful. Beautiful. Magnificent desolation." The stars have always held a unique place in the history of mankind. Millenia ago our ancestors first described the glory of the heavens, lands our race long ago dedicated to the gods and the unknown. Try as we might, despite decades of probes, observations, and incalculable theorizing, the frontier beyond our tiny world ever remains a source of nature's most profound mysteries. Looking up at a night sky often fills young and old alike with wonder, and might cause even the most jaded astronomer to ask the grandest of questions of his unique laboratory: the universe itself.

> "WITHIN THE NEXT 50 YEARS, WE MAY VERY WELL WITNESS THE DISCOVERY OF EXTRA-TERRESTRIAL LIFE."

By demystifying some aspects of outer space, we have answered some of the greatest questions in human history, from the 'Copernican Revolution' concept that humans did not lie at the center of the universe to the realization that our home planet is not some customized construct "irreducibly complex," but rather a natural consequence of the laws of physics. Theology, philosophy, and society at large, in addition to astronomy, all have a great stake in the study of the stars. And yet in the midst of this great confluence of science, faith, and ever expanding humility, perhaps the most profoundly human question has never been answered. Are we indeed alone in the universe?

For all the magnificence of life on earth, we have long considered space to be a lifeless entity, absent evidence to the contrary. Science-fiction writers have long made their living inciting the human imagination about aliens and the possibility of life beyond the earth. The concept of standing alone on what legendary astronomer Carl Sagan called our "pale blue dot" of a planet has fueled many creative attempts to explain the phenomenon of extraterrestrial life.

Yet in the last decade, we have begun to discover hundreds of extra-solar planets, or exoplanets: worlds around other stars. In addition to leading a foundational study of life on earth, we draw nearer to truly searching for life in the cosmos. In fact, we live in one of the most exciting eras of scientific exploration ever.

On 13 November 2008, two independent groups, one using the Keck and Gemini ground telescopes (Marois et al. 2008), and the other using the Hubble Space Telescope (Kalas et al. 2008), announced the first optical and infrared photographs of extrasolar planets orbiting stars other than our own. The first group imaged three exoplanets (Image 1) around the star HR8799, 125 light years from earth. The second group photographed a planet orbiting the nearby star Fomalhaut (Image 2), visible to the naked eye at 25 light years distant. These large gas-planets are known as 'hot Jupiters' because they share several evolutionary and physical characteristics with our eponymous solar system neighbor,

and are still highly energetic, emitting enough light to make their photography possible. As coronagraphs (used to blot out stellar light) improve in the next few years, the optical photography of smaller exoplanets will become possible. With these better imaging techniques and the discovery of more worlds, the actual spectroscopic search for life can begin in earnest.

Within the next 50 years, we may very well witness the discovery of extraterrestrial life. The technology to seek for it exists, the methodologies and mathematical models are ready, and the scientific background to analyze such a discovery is more or less complete. We stand on the brink of what might well be the most jarring discovery in the history of human existence.

What is Astrobiology?

According to astronomer Dr. Jonathan Lunine of the University of Arizona, author of a popular text on astrobiology, "Astrobiology is the multidisciplinary study of the origin, distribution, and evolution (past and future) of life," (Lunine 2005).

Astrobiology could be seen as the ultimate level of abstraction of biology, the most encompassing view of life as a whole. At its highest levels biology presumably reaches beyond the earth into the realm of astronomy, leading the two sciences to find in one another a common ground-our entire universe. The study of life on Earth then, the traditional study of biology, becomes the study of life in the universe as a whole: "astrobiology."

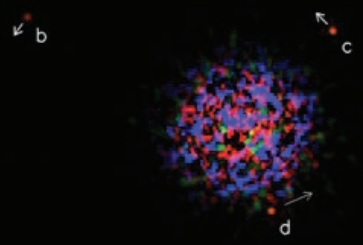

Image 1 (Credit: Christian Marois and Bruce Macintosh)

Of course, astrobiology encompasses so much more than just this grander view of life. It concerns itself with the study of the earth and geology, meteorology, geochemistry, climatology, and environmental and planetary sciences all find great relevance. Likewise, chemistry, physics, medicine, engineering, and of course all fields of biology and astrophysics are united in this great collusion of the sciences.

But ultimately, due to its conglomerate nature, astrobiology has a specific thesis. It seeks to explain the fundamental basis for the development of biochemistry. Is life a natural outcome of physical laws? That is to say, does life emerge in the universe along a basis of rules and fundamental principles, or does it represent some incredible accident here on Earth? This might seem to draw an obvious answer from a chemist or a physicist: life is a product of basic rules of physics and chemistry.

But the claim can be seen as broader and more subtle. Biology has always occupied a special place in the sciences, mainly because of its apparent uniqueness to Earth. But what if, instead, life represents an inevitable and common emergent property of chemistry? The seeming thermodynamic inequilibrium of life processes emerges from a foundation that absolutely follows the laws of physics. Biology, then, is not a separate science, but is rather a subject that occupies the final chapter in a physics or chemistry text. It is the final result, the end product, of a universe which follows some very fundamental laws.

This is different from claiming that biology is based on the other basic sciences. It is instead a claim that the universe actually produces life, as a product of sorts, and that it can be decomposed into its requisite equations that govern its very statistical origin. It can be a profoundly altering concept when taken in the context of theology and faith.

In My Lifetime?

As of print, NASA's Jet Propulsion Laboratory reports that 322 extrasolar planets have been discovered in just a decade of limited searches. We have yet to find a 'terrestrial' type planet like the Earth, but this is likely due to their small size, not necessarily their rarity. Despite heavy budget cuts at the world's space agencies, and with a likely reduction in the overall research and NASA budgets of the United States, the prime leader of this search, we are still poised to find earth-like planets before the end of the next decade.

Missions with names like Darwin, Kepler, and the two-part Terrestrial Planet Finder have long been planned and prepared for execution, but simple funding constraints have grounded them. As soon as these missions, and likely others, launch, we will discover how common such earth-like planets are, which will inform our search for life.

Predictions vary widely, with some of the scientific community siding with the aptly named "rare-Earth hypothesis" that our planet's ability to sustain life, while not unique, is likely an uncommon occurrence. While of course Earth-type planets are not the only worlds we might imagine life to inhabit, they remain our starting point in a search that could well reach beyond the imagination.

Others believe that Earth-type planets are plentiful, and that we will find many hundreds of them nearby in our region of the galaxy. We will not know for sure until surveys of nearby stars are conducted. This is difficult to do for many reasons, including the incredibly small size of planets compared to their parent stars and the light of these stars, which blinds our view.

Once even a single terrestrial world is found, the burning question will be how to determine the presence of

life on this planet. Life fundamentally alters the characteristics of its host planet, and thus produces various signals, called biosignatures, that indicate its existence. Still, they are not easy to read, and a subspecialty has emerged in the field of astrobiology dealing with biosignatures and how to detect and analyze them. While this is certainly still an underdeveloped study, it is rapidly accelerating in anticipation of the impending discovery of terrestrial planets.

Biosignatures include most of the spectral features of a planet that we can obtain from the light we receive from it. A planet covered in vegetation of some kind, even incredibly bizarre by Earth standards, would produce what it is called a vegetative-red-edge. The reflection of light by surface flora would emit a pronounced signature in the infrared spectrum, a particular reflection characteristic of pigments used in photosynthesis.

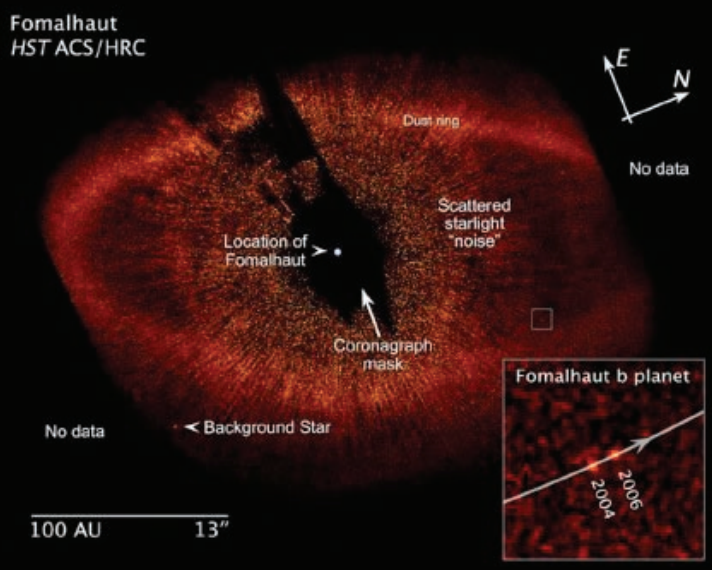

Image 2 (Credit: NASA, ESA, and Z. Levay (STScI))

There are more basic biosignatures, including the presence of ozone, oxygen, and water. Even with the discovery of 'another Earth,' the confirmation of life on the planet could remain contentious, as it might be difficult to make conclusive observations. Life does not announce its presence so readily, and an entirely new field of science will likely emerge dedicated solely to the study of this one, or perhaps many, planets. But in the midst of this scientific cataclysm might well appear evidence that we should not, as the history of science instructs, find surprising.

In my lifetime? Perhaps. We live in the first era during which the technology to even ask these greatest of questions exists. The mission of searching for extraterrestrial life is one that many scientists have considered for much of history, but could never accomplish. It is finally time to make good on these ancient questions and search for answers. If life is common in the universe, or even if we get lucky and find a planet nearby that supports it, it might not be 15 years before every history or science text, and indeed nearly every human conception of our place in the universe and the course of our future, is rewritten forever.

It could well be longer. But it is no longer an extant abstraction or solely a theoretical question for sci-fi authors. We are exploring at last, looking for evidence of something many scientists, at least at some point, have perhaps wanted to believe: that the universe is not some desolate void that we call "outer space," but is rather filled with wonderment, with vibrancy, and with life.

Astrobiology, perhaps more than any other field in science, may yet bring us the final Copernican Revolution - the realization that life, like our position in the cosmos, and the uniqueness of our Earth, is not some great conceit of a divine creator, or an abstraction too complex to reconcile, but is rather an inevitable consequence that lies at the very heart of physics and chemistry; as stars and planets are created by gravity, so too does life represent a fundamental outcome of the laws of the universe.

We would finally say of the cosmos, not even a century after we first walked on the moon, that while magnificent, they are not a desolate wasteland consigned only to the study of astronomy, but are instead a living system of which we are merely specimens on both sides of the lens.

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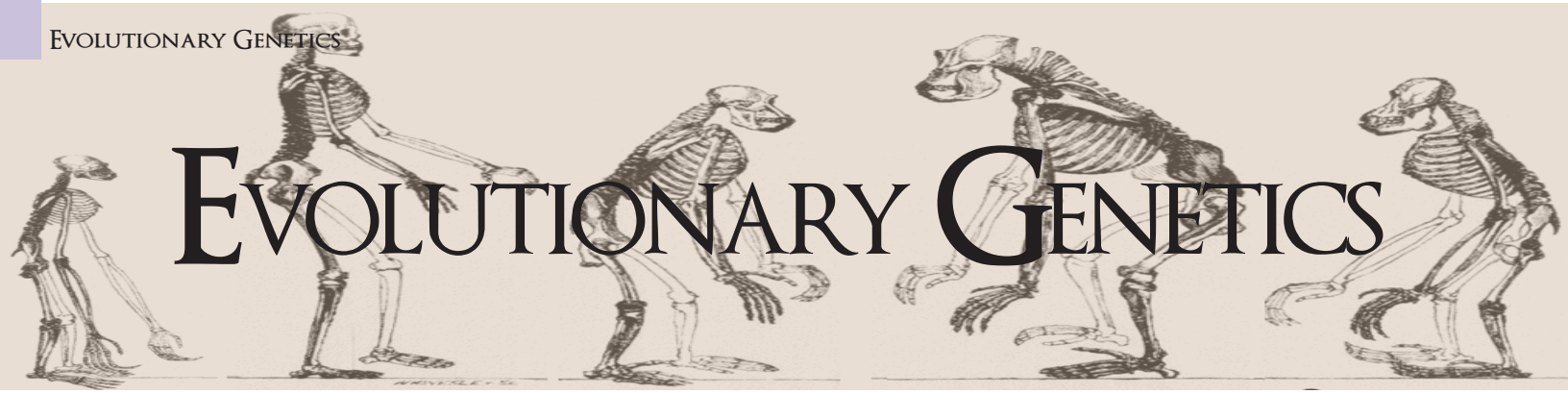


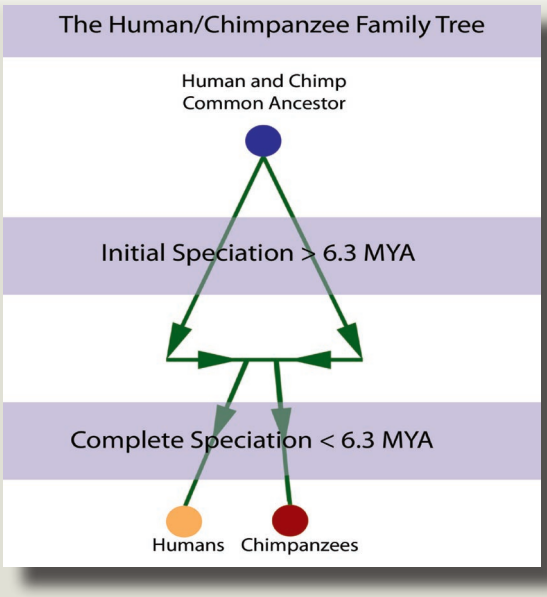
Evolutionary Genetics

Chris Hanks

Approximately six million years ago, a population of approximately 50,000 to 100,000 primates in Africa split into two groups for unknown reasons. Breeding between the groups, and thus the transfer of genetic information, became less common. With this uncoupling, these two populations began to change and differentiate, as each was subjected to separate environmental factors. This was an event of speciation, the process by which one species splits into two. Although it was an unusually complicated and prolonged example of the phenomenon, with the two groups reconnecting and hybridizing before splitting again, ultimately, the differentiation became so pronounced that the split was made complete and permanent. One species of primate had become two.

One of these groups would go on to split again later, and become what we know today as the Common and Pygmy Chimpanzees (Pan troglodytes and Pan paniscus, respectively). The other would become human beings (Homo sapiens).

Historically, this puzzle has been approached through interpretation of the fossil record, but the great advances in recent genetics research, including the release of the sequenced human genome in 2003, and that of the common chimpanzee in 2005, have given us a new looking glass through which we may study our origins. Accordingly, many new techniques in analytical genetics have been developed for the study of evolutionary biology.



Evolution and Mutations

When we say that the pre-humans and pre-chimpanzees differentiated over time, what we really mean is that the overall genetic makeup of each group began to change independently, and there are many factors that can cause this, including natural selection and genetic drift, wherein genes that are less relevant to survival will become more or less common simply by chance. For example, in a given generation, if blue-eyed individuals happen to have a greater number of children than brown-eyed people, blue eyes will become more common in the next generation.

So, where do new genes come from? Every spermatozoa or egg that an individual produces contains a copy of half of their genetic code, in the form of DNA, which will eventually go to contribute to the genetics of their offspring. The cellular machinery responsible for copying this DNA makes mistakes - one "letter" of the code mistakenly replaces another - creating small and novel changes in the genes of their offspring. These are known as "point mutations," and as they affect the genetic code and therefore the biology of the offspring, they will be acted upon by natural selection - if a change is harmful (as the vast majority are), the offspring will be less likely to pass it to the next generation, while a beneficial change is more likely to be passed on, increasing the prevalence of that changed gene over time. Many mutations, however, do nothing - they change the sequence of a gene, but not the actual function of that gene. These are "silent mutations," By contrast, a mutation that does affect the function of a gene, and can be selected for or against, is called a "non-silent mutation."

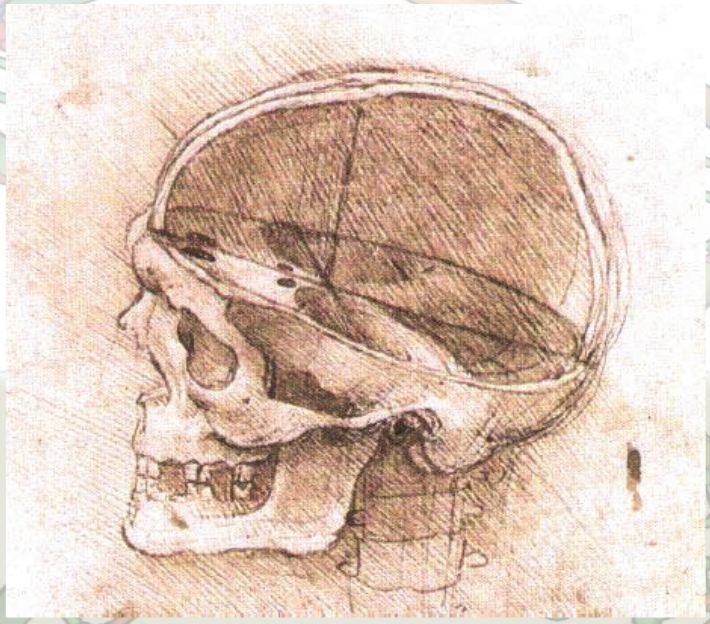
Back to our common ancestor, the primates in Africa six million years ago. They had their own genome, with their own sets of genes, very similar to ours. Because every individual gene from our common ancestor split in two when our species did, the individual genes that make up contemporary humans and Chimpanzees are very similar - they've all changed in the past six million years, but they each come from a common template. Genes that share their own "common ancestors" are called "homologous genes," and by analyzing the mutations that they have collected since our divergence from Chimpanzees, we can learn quite a bit about our evolutionary history.

Molecular Clocks

Let's look first at silent mutations. Since evolution cannot act upon them, they are only subject to genetic drift -

they appear in an individual, start to spread around a population, and become more or less common due to simple chance. As time progresses, one of two things will eventually happen to a silent mutation: it will either become less and less common and die out, or it will become more and more common until it's found in every member of the species. A mutation that does this, and reaches a prevalence of 100%, is called "fixed" and becomes a permanent part of the genome of that species. As time passes, more and more mutations will become fixed in a species.

This means that we can look at homologous genes between two or more species, count up the mutations that differentiate them, and determine which are silent and which are non-silent. The number of silent mutations present will correlate with how much time has passed since these species diverged from one another. For example, if you were to compare the number of differences due to silent mutations between Common and Pygmy Chimpanzees, you would find only about one-sixth as many as you'd find when comparing humans to the Chimpanzee family. Since we know that humans diverged from Chimpanzees about six million years ago, this implies that the two types of Chimpanzee only diverged from one another around one million years ago. This correlation between silent mutation frequencies and time elapsed since a speciation is called the "Molecular Clock."



While we have discussed humans and Chimpanzees so far, this same technique can be applied to divergences between any two species. Looking farther into our own past, we can determine that the lineage that eventually led to Homo sapiens diverged from the genus Gorilla approximately 8.6 million years ago, from the genus Pongo (Orangutans) approximately 18 million years ago, and from the family Cercopithecidae (Baboons, Macaques, Vervet Monkeys) approximately 30 million years ago.

Picturing our ancestral populations

Just like species and populations have genealogical trees, so do individual genes and mutations themselves - they may splinter, propagate in number or die out just as populations do. And although two populations come from one at the time of a speciation event, the mutations and the variants of homologous genes that each population will carry with them will come about well before that time. This means that in a manner similar to estimating the amount of time since two species diverged by analyzing total divergence, we can compare the times of divergence of a variety of individual genes to estimate the population size of a common ancestor at speciation.

First, picture the simple case, that there is a species that is very small in number, and that undergoes a speciation event. Because it is easier for mutations and gene types to reach fixation, or to die out, in a smaller population, there is not very much genetic diversity in this group - genes have comparatively few variants, and not very many mutations reacting to genetic drift are present. After the speciation event, the genetic makeup of each group will start to change and differentiate immediately, and when individual genes are analyzed using the Molecular Clock, they will all appear to have started diverging at approximately the same time.

Now consider a much larger population, where there are many variants present for each gene, and a relatively large proportion of mutations that are varying in prevalence due to genetic drift. After the speciation event occurs, and the two new populations have their own distinct genetic makeup, the diversity they began with will cause them to differentiate more easily and quickly. The gene variants that become common in each population may have diverged from one another long before, and not be the direct result of the speciation event itself. Thus, when the Molecular Clock is used to determine the divergence times of a variety of individual genes in the present day, there will be much more variety in the apparent elapsed time since divergence.

While the Molecular Clock defines a correlation between the total divergence of two species and the time passed since their divergence, a similar correlation exists between the variance of divergence across multiple portions of a genome and the population size of a common ancestor at divergence. This allows an estimate to be made of how large the population of a common ancestor was at the time of speciation.

The Quantification of Natural Selection

While comparing the genes of two related species, examining the proportions of silent and non-silent mutations can also yield useful information. As natural selection hasn't acted on the silent mutations, their number serves as a baseline, and can give us an idea of how common mutations have been in one of our genes over time, regardless of

the forces of evolution. The non-silent mutations, however, have been affected by selection - what can their proportions tell us?

Suppose that a certain gene is vital to human survival, and that any impairment in its functioning will be fatal. Natural selection will work very strongly to protect this gene - because non-silent mutations tend to be harmful, they would be weeded out very effectively, and few would be present. Therefore, we'd expect that the number of fixed non-silent mutations would be very small compared to the number of silent mutations.

But suppose that another gene has no effect on human health, and is completely irrelevant to our survival - for example, it has been rendered obsolete by the presence of another gene. Non-silent mutations, in this case, won't be acted upon by natural selection, and they will accumulate in this gene over time just as silent mutations do - affected only by genetic drift, becoming fixed or dying out due simply to chance. Thus, we'd expect that for an irrelevant gene, the commonality of silent and non-silent mutations would be roughly equal.

Finally, consider a third gene. Suppose that a population's environment has changed such that this gene not only has no benefit, but has become outright detrimental to the survival of any individual that carries it. This is a very rare occurrence, but it is possible that changing circumstances could cause a gene to suddenly become a liability. What would we expect to happen? Since non-silent mutations tend to be harmful to a gene's function, they would be actively selected for, and spread throughout a population quickly. So, we'd expect that this gene would have a greater proportion of non-silent than silent mutations.

> "As natural selection hasn't acted on the silent mutations, their number serves as a baseline, and can give us an idea of how common mutations have been in one of our genes over time, regardless of the forces of evolution."

Let's take a real-world example: a gene named MYH16. First, put a finger to either temple (on the side of your head, just behind your eye), and clench your teeth as though you were a pre-human primate chewing a particularly tough plant. The bulge that you feel is the contraction of the temporalis muscle, which connects your jaw to the side of your head. This is one of the masticatory muscles, which works to close the jaw when you chew your food. You might have noticed that these muscles are very large in gorillas, which need strength to crush plant matter with their flat teeth, but are rather small in humans, who have sharper teeth to pierce their food, and require less biting force.

While all muscles are made up of long strands of proteins that pull against one another to create a contracting force, only the masticatory muscles contain a certain protein, which is formed by the MYH16 (myosin heavy chain 16) gene. This protein is particularly large in size, and a muscle that uses it will be unusually big and strong. However, when we compare the MYH16 gene in humans to that of other primates, we find a moderate number of non-silent mutations - not enough to suggest that the gene is irrelevant, but more than we'd expect to find in the protein of a muscle important to the survival of the species. We also find that one of them is what we call a "loss of function" mutation, meaning that it causes the body to produce only a small part of the complete protein. In fact, when we analyze the human protein itself, we find that some necessary portions of it are completely missing, and that as a whole it's only about one-third the size that it is in other primates. In other words, humans have smaller and weaker masticatory muscles, because one of the major proteins found in those muscles are small and inoperative. This is not a rare condition - it occurs in all humans. So why would a mutation like this survive, and spread throughout the pre-human population?

When we compare the skulls of humans to those of primates with large temporalis muscles, we find major differences in their shape. As bone develops, it is malleable enough that its shape may be formed in part by the muscles exerting forces on it, and while primates with very large temporalis muscles grow, their developing skulls will be constrained and stunted by these muscles. Biologists hypothesize that this loss-of-function mutation, though it resulted in small and weak masticatory muscles, had the benefit of conferring a less constrained and compacted skull, thus allowing for the expansion of the human braincase and the increased brain size that distinguishes Homo sapiens.

Under this hypothesis, we would expect that the masticatory muscles would be preserved by evolution, and non-silent mutations would not develop, until the occurrence of a loss-of-function mutation that would be severe enough to cripple the temporalis muscle and free the brain to develop in size. After that occurred, non-silent mutations would start to appear in the MYH16 gene at the same rate as silent mutations, as the gene had become irrelevant to survival at that point. This finding supports the timeline of braincase development shown by the fossil record - if the gene were rendered inoperative in the human lineage approximately 2.4 million years ago, then a low proportion of non-silent mutations in the human lineage before that event and a higher proportion afterwards would result in the middling proportion of mutations found in the gene.

Next Steps: the Neanderthal Genome

Advances in the field of genetics continue to shed new light on the mystery of human development, and the pace of progress is continuously growing. In 2006, DNA was successfully extracted from the femur of a Neanderthal, estimated to be 38,000 years old, and a new sequencing

project began at the Max Planck Institute for Evolutionary Anthropology in Germany. It's a challenging task - the source material is precious and limited, and the amount of contamination by human DNA, which is at least 99.5% identical, is difficult to determine.

The project is still underway, and only the first bits and pieces of the genome of our closest relative have been put online for all to study. In the meantime, however, if you feel the need to do a little research of your own, you can browse completed genomes hosted by the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/sites/entrez?db=nucleotide) or the University of California, Santa Cruz (http://genome.ucsc.edu/). There's no telling what you'll find.

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EXPANDING THE REACHES OF THE MIND THROUGH ART

■ Niccola Pérez

Professor Dalibor Sames has been a faculty member of Columbia's Department of Chemistry since 1998. His research group's recent research on the neurotransmitter dopamine won the 2008-2009 McKnight Award for Technological Innovations in Neuroscience. Sames and his collaborator, Dr. David Sulzer of the Columbia University Medical School, received the award for their development of Fluorescent False Neurotransmitters (FFNs) that allow dopamine to be visualized at individual synapses. Sames elaborates on the temporal and spatial capability of these FFNs, "the brain works by strengthening or weakening synapses, and now we can optically observe activity of hundreds and thousands of individual synapses at the same time." This technology will enable researchers around the world to further investigate the precise synaptic changes associated with learning and other neurological and psychiatric processes, as well as disorders such as Parkinson's disease and schizophrenia.

But Sames' exploration of the mind does not stop there. After speaking with a good friend in the art magazine industry about his research on dopamine, Sames realized the possibility for a valuable extension of this research into the art world. More than just a neurotransmitter, Sames sees dopamine as an important element of "fundamental subjective forces like reward, emotion and motivation."

Sames and his friend, Nacho Santos y Gugel, creator of mu, a new Spanish art magazine, have put forth the concept for a groundbreaking art exhibition: an artistic conceptualization of the role of dopamine in animal motivation and action. "It is exciting from a scientific point of view," says Sames about his work on dopamine, " but it also opens different perspectives on some philosophical questions, and it is beautiful. I think we have a recipe for an interesting adventure!" The exhibition, currently entitled "A Portrait of the Driving Force of the Animal Universe: The Art and Science of Dopamine," is tentatively set to debut in Madrid in the spring of 2010. Sames hopes to involve artists from around the world, incorporating a variety of media including photography, video, painting, drawing, sculpture, and text.

There are still many decisions to be made, however, each one crucial in shaping the final product. Indeed, one of the largest concerns for Sames is the number of directions he could take the exhibition. Dopamine does, in fact, play a role in many aspects of animal and human life, from motivation and learning to decision-making and cognition, among others, any of which could be emphasized in the exhibition. Nevertheless, whichever direction Sames chooses to take the exhibition, it will be a novel and constructive synthesis between the worlds of art and science, one that will certainly shed new insights in both disciplines.

{Chatting with Chalfie}

Ying Li & Laika Simeon

Martin Chalfie, Chair of the Department of Biological Sciences at Columbia University, shared the 2008 Nobel Prize in Chemistry along with Osamu Shimomura and Roger Y. Tsien "for the discovery and development of the green fluorescent protein, GFP." He has received a great deal of much-deserved attention lately and was one of the 49 American Nobel laureates who wrote to President Obama, urging for an increase in funding for scientific research. We were lucky enough to sit down and talk with him about his life and his education in the sciences. He was funny, warm and incredibly down-to-earth despite the fact that he had just finished another interview and his phone was ringing off the hook. We were all enraptured by his candid account of his time as an undergraduate and his evident passion for scientific research. While gesticulating excitedly, he told us about how he came to be a scientist as well as entertaining anecdotes about his experiences along the way.

Chalfie started out at Harvard in 1965, planning to major in mathematics but after taking an advanced calculus class, discovered he "didn't quite have the aptitude for it." He then turned to biochemistry which was at that time a "sassy topic" with many new and exciting developments. It also allowed his math classes to count towards his major as well as take more science classes including physical chemistry and biology. In his junior year he took a cell biology course that was essential to his decision to go into science. He wrote an essay for the class about experiments involving sodium transport in toad bladders that used the Ussing chamber to measure short circuit current - the current needed to counter the amount of ion transport. And most importantly, it was a mechanism that was activated by the small second messenger molecule cAMP (cyclic adenosine monophosphate). Chalfie enjoyed the class so much that he decided to work in a lab the summer after his junior year. But he was a "complete and utter failure" as he repeated one experiment 10 times and failed miserably every time. The experiment required a great deal of preparation and the experience was very discouraging. By the end of the summer, Chalfie had decided that science was not for him and so during his senior year he finished up his major requirements and took a wide variety of courses in Russian literature, theatre and law.

When asked what the most important thing he learnt from these undergraduate years, Chalfie replied, "the importance of having a bunch of facts and being free to put those together in different ways". Being an undergraduate taught him that there really is no one right answer and that people should feel free to take risks. This sort of thinking definitely influenced his later work as he gained the confidence to take chances and to "think about things in general terms and not be afraid to make strange connections."

Unsure of what to do after graduation, a sentiment many students can identify with, Chalfie worked at a series of short-term jobs and eventually ended up teaching chemistry in a high school outside New Haven. One advantage of the job was that his summers were free to pursue other interests. Before the start of one summer a colleague of his recommended that he work for Jose Zadunaisky, who headed a lab at Yale University. During his meeting with Zadunaisky, Chalfie learnt that the lab was studying chloride transport in the cornea of frogs by using the Ussing chamber. The apparent similarities between the lab he was interviewing to work in and the research he had written about for his undergraduate cell biology class prompted him to ask Zadunaisky whether cyclic AMP was involved. Zadunaisky did not know the answer to his question as no experiments had been conducted before. Chalfie was hired and assigned to do "the world's most boring project to do for a summer project". But his boredom was quickly dissipated when Zadunaisky left for the summer and Chalfie was on his own. He talked to the postdocs and graduate students about the possibility of investigating whether cyclic AMP was involved in the specific pathway the lab was studying. With their help, he managed to set up an experiment in which he proved cyclic AMP did indeed increased chloride transport. When Zadunaisky returned to the lab at the end of the summer and asked to see the data from the experiment he had assigned to Chalfie, he was surprised to see that Chalfie had succeeded in doing an independent experiment. The result of his work that summer was his first scientific publication and the motivation to go on to graduate school to pursue research.

> "Being an undergraduate taught him that there really is no one right answer and that people should feel free to take risks."

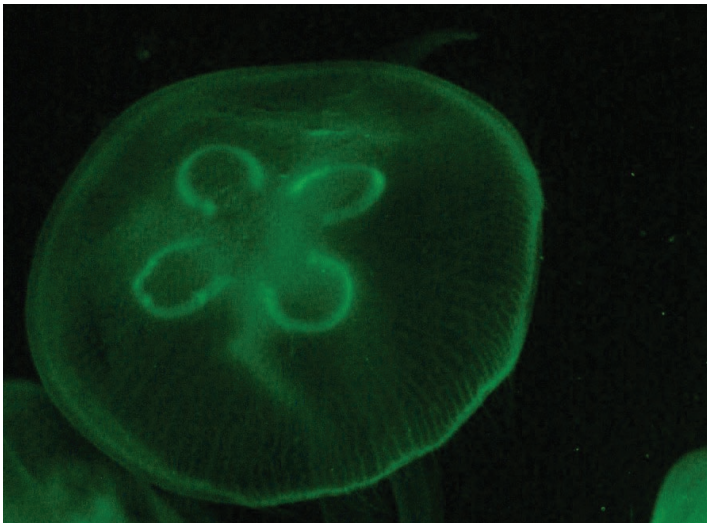
The main difference between what happened in the lab after his junior year and what happened two years later was that he had the help of the other people in the lab. He didn't feel as though he had to do everything on his own. During his first lab experience, he would have felt less discouraged and more inclined to continue in the sciences had someone told him that most experiments never work out and that he shouldn't worry. Instead he felt as though he was failing. However in the Zadunaisky lab he found many people he could talk to and succeeded in doing an experiment. He also credits his undergraduate training for giving him the nerve to ignore what he was assigned to do and do his own experiment.

Photo by Ivy Chen

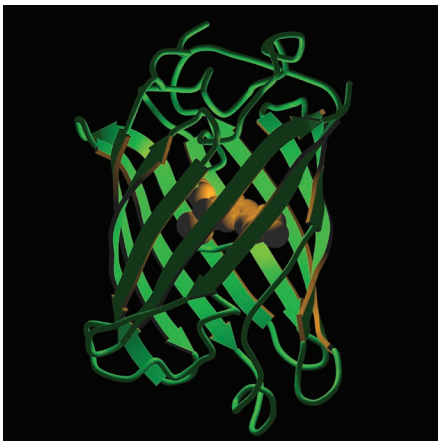
Chalfie continued his studies at Harvard University and enrolled in the physiology department in 1972. He credits his mentor, Robert Perlman, for being a supportive and encouraging figure with whom he could talk "about any idea no matter how silly or stupid it was." During graduate school, Chalfie studied the synthesis and release of adrenaline. When he was looking for postdoctoral positions his high school friend Bob Horowitz, who was a postdoc in Sydney Brenner's lab at the Laboratory for Molecular Biology in Cambridge, United Kingdom, encouraged him to apply for a research position in Brenner's lab. Chalfie liked the research that was going on in Brenner's lab and thought that going off to another country for a few years was a wonderful idea, so he applied and started working there in 1977. Chalfie praises Brenner as being "a dazzling marvel of a scientist" and he believes that his time as a postdoc was "the most formative part of [his] scientific life." He recalls that being a postdoc was "really a wonderful time, you're not taking any courses, you're not taking any exams, you're just doing research. You don't have any obligations that professors have…your time is your own." And the Laboratory of Molecular Biology provided Chalfie with the perfect environment to do research as he was given absolute freedom and all the facilities and supplies for experiments.

When asked what makes a good scientist, Chalfie hesitated before saying that originality, a willingness to do something different and dedication were important. But when asked how one becomes an amazing scientist, he modestly said he has no idea.

A Background on GFP



Green Fluorescent Protein (GFP) is one of the most widely used proteins used in research today. In 1978, Prendergast and Mann at the University of Minnesota isolated GFP from a luminescent jellyfish, Aequorea Victoria. They realized that another protein, aequorin, emits blue light when exposed to calcium ions and GFP absorbs this light and then emits green light. In the 1980s at the Woods Hole Oceanographic Institution, Douglas Prasher first realized that GFP could be used as a tracer and set out to find the genetic sequence for the protein. Columbia University professor, Martin Chalfie continued Prasher's work and was able to incorporate GFP into E. coli bacteria and C. elegans, roundworms.



GFP has since been used in many other organisms. It is very small, doesn't require cofactors, and doesn't harm the structures in which it is expressed. GFP can also be expressed in many different colors besides green. Cyan, red, yellow, and orange fluorescent proteins have been developed. More recently Brainbow, a technique that incorporates many colors to tag hundreds of neurons at the same time, has been developed at Harvard University (the cover of this issue is of these brainbow neurons). GFP has also been used for detecting the activity of a gene promoter. This is possible because GFP and the gene in question are expressed together by the same promoter. Whatever the gene codes for in the cell will then fluoresce. Photoactivatable fluorescent proteins have also been developed. These proteins are able to be hyper fluoresce, which enable researchers to use high energy beams to track individual cell, organelle, or protein movement. Fluorescent proteins also enhance the ability of FRET (Fluorescence Resonance Energy Transfer), a technique to track interaction between proteins. Regardless of the specific technique, GFP has already revolutionized our understanding of molecular and cellular biology, and become a fundamental tool used in many fields of science. It continues to play a crucial role in a great deal of research as it is used more and more creatively, as well as more extensively.

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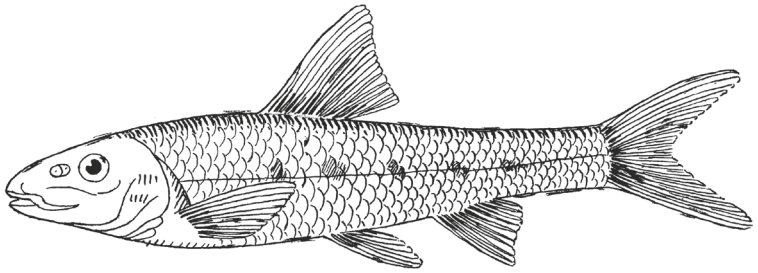
Picture courtesy of the Tsien Lab

The Wonderful World of Sleep

Anna Corke

Imagine you're exhausted after a long night of studying. You stumble to your 9 a.m lecture, eyes hardly open. You try to stay focused as the professor begins to speak. You get the feeling that maybe you're not quite there. But, you're convinced you haven't fallen asleep. Or have you?

Scientists are realizing that one of best way to find out what sleep does is to research the consequences of its absence. Some scientists study the brains and behaviors of sleep-deprived humans. Others are looking at sleep deprivation in animals and are encountering startling disparities in the nature and function of sleep between humans and animals.



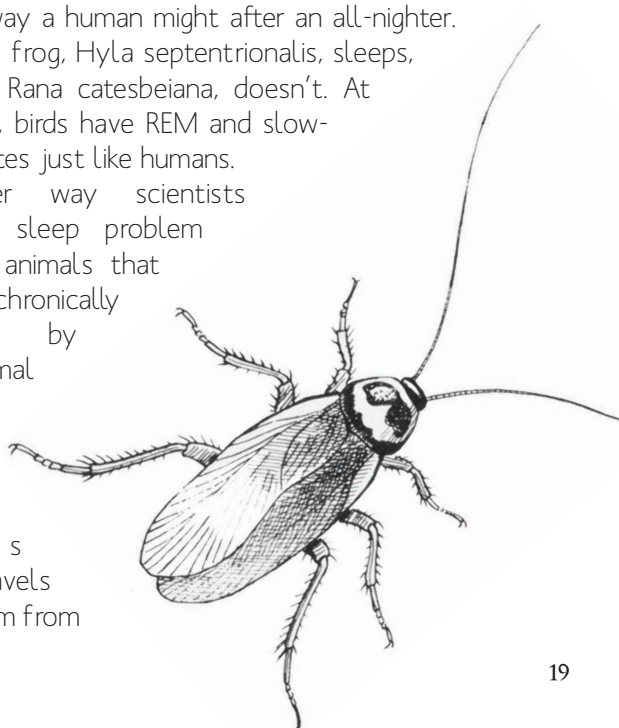
As college students all find out, sleep is vital to maintain health and sanity—in humans at least. In addition to the physical and psychological problems caused by loss of sleep, Dr. Yaakov Stern, Professor of Clinical Neuropsychology at Columbia University's Taub Institute, said that "people who are sleep deprived can have brief bouts of sleep that they are unaware of." With enough sleep-deprivation, we can become unaware of our unconsciousness. Dr. Stern pointed out that this can cause major problems, for instance, "in a situation that requires continuous attention, such as driving."

Scientists who study sleep in animals are finding it more and more difficult to define. Merriam Webster's definition, "the natural periodic suspension of consciousness during which the powers of the body are restored," is simple compared to what the definition would be if it took into account animals' various ways of "sleeping." Now most scientists believe that sleep must be defined at the species-specific level.

For instance, imagine a dog lying on a porch in the sun. His eyes are closed and he is breathing deeply. Is he asleep? In the recent review, "Do all animals sleep?" that appeared in Trends in Neurosciences earlier this year, Jerome M. Siegel, Director of the Center for Sleep Research at UCLA, discusses the problems scientists are having with answering that question. For instance, humans can sit quietly with their eyes closed and not be in the state of reduced sensory awareness that is associated with sleep. Just looking and acting asleep doesn't mean an animal is.

Similarly, looking at brain activity using electroencephalographic recordings, or EEG, during sleep can also complicate things. Scientists know that metabolic activity in the brain is greatly reduced during one type of sleep, called slow-wave sleep. But another type of sleep, Rapid Eye Movement sleep (REM) is associated with an increase in metabolic activity in the brain. Most brain regions look like they're awake in REM. In humans, at least, we know enough about behavior to be able to tell REM sleep from the awake state. But when tapping into the brains of animals, it's difficult to correlate brain activity with specific behaviors since telling whether animals are asleep or not—or whether they need to sleep in the first place—is much more difficult.

In order to explore whether and how animals sleep, scientists are examining what happens when animals are sleep deprived. Since scientists can't tell just by looking whether animals need to sleep, they keep them awake and study the consequences. One study, in which rats were prevented from sleeping for several weeks, found that the rats died after just a few weeks of sleep loss. However, Dr. Siegel reports, some other studies have shown less extreme consequences of sleep deprivation. For instance, keeping pigeons from sleeping doesn't seem to affect them at all. Studies in cockroaches have found that these species have resting states but do not seem to accumulate "sleep debt"—the need to sleep more to make up for lost sleep—in the way a human might after an all-nighter. One species of frog, Hyla septentrionalis, sleeps, while another, Rana catesbeiana, doesn't. At the same time, birds have REM and slow-wave sleep states just like humans.



Another way scientists approach the sleep problem is to look at animals that seem to be chronically sleep-deprived by their normal behavior. For instance, the Swainson's thrush, Catharus ustulatus, travels around 5000 km from

Canada to Mexico or South America and back each year—an exhausting ordeal that leaves little time for sleep. During seasons when they aren't migrating, these birds sleep at night. But a recent study found that during the migration months, Swainson's thrushes fly at night and take short naps during the day to make up for the loss of sleep.

But these are not your average naps. Some birds, including the Swainson's thrush, are able to sleep in just one half of the brain at a time. The phrase, "sleep with one eye open," takes on a whole new meaning for birds: keeping an eye on one's surroundings while taking naps during the day can mean the difference between life and death.

Called "unihemispheric sleep" by scientists, sleeping in one hemisphere of the brain has also been observed in aquatic mammals, such as the fur seal, Callorhinus ursinus. A study found that when fur seals are on land they sleep just like terrestrial mammals. However, when fur seals are in the water, their sleep patterns change: their brains exhibit regular slow-wave sleep in one hemisphere and waking state EEG patterns in the other. Paddling with one fore flipper and floating on one side, they keep one eye open, watching their surroundings and where they are headed, while they sleep in the other half of the body.

Other aquatic mammals, such as dolphins, only sleep with one half of the brain at a time, too. However, they don't exhibit any of the asymmetrical body movements of the fur seal. Dolphins seem to be able to swim while sleeping in one half of the brain just as easily as humans breathe while sleeping.

What would it be like to sleep with just one hemisphere of the brain? Dr. Siegel suggested in an email that "if humans had slow waves in one half of the brain they would presumably be quite impaired, even half-paralyzed." But he went on to say that "dolphin brains have evolved to function at a high level during this behavior, so it is unclear if there is any substantial deficit."

Whether humans could sleep in this way—say, during that 9AM class— is probably "more science fiction [than reality]," Dr. Stern pointed out. But discovering that many animals do not need the kind of sleep that humans do has been changing how scientists think about sleep's purpose in the brain. Knowing that REM sleep has not been observed in dolphins has led some to believe that unihemispheric sleep occurs in lieu of REM. "This suggests that REM sleep is not necessary if half of the brain is always active," Dr. Siegel said. "REM may serve to stimulate the brain in sleep." Exactly why our brains need this stimulation, while other animals' brains do not, is still a mystery. Perhaps further studies of sleep deprivation in animals will help scientists uncover the reasons behind our own sleep patterns.

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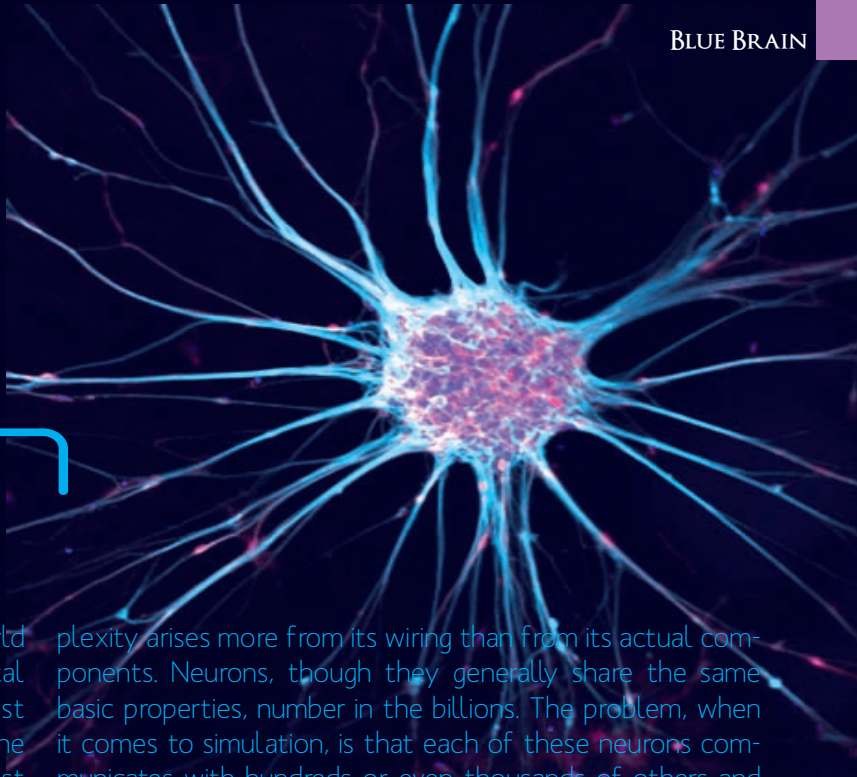
Blue Brain



Elizabeth L. Robinson

In 1997, IBM's Deep Blue supercomputer defeated world chess champion Garry Kasparov. For many, this monumental match up between man and machine was proof that, at least when it comes to calculations, computers had us beat. The likes of Hal from 2001: A Space Odyssey seemed almost inevitable. However, a group of scientists in Switzerland are playing a new game with Deep Blue's progeny, another IBM supercomputer called Blue Gene, and this time humanity has the upper hand.

The project is called Blue Brain. The goal is to build a functional model of the human brain from the ground up. This process of modeling, though common in physics, is an entirely new approach in the field of neuroscience, which generally studies the brain by taking it apart and observing the basic biological processes. The Blue Brain project is using this same biological data to actually put one together. By merging biology, computer science, and design, they hope to open a new window into the brain.

If Blue Brain becomes a reality, scientists will be able to study the brain with unprecedented accuracy and control, repeating and perfecting experiments before performing them in the lab. This technology would also lead to a better understanding of the brain by allowing scientists to simulate brain processes, disorders, and injuries and observe their properties on the neuronal level.

The project uses IBM supercomputers and powerful simulation software to create detailed 3-D representations of neurons that function and communicate just like the real thing. The computer itself is actually designed like a brain in that it consists of thousands of nearly identical, discrete units, like neurons. Also, the components of this computer strengthen their connections the more they communicate. (In a regular computer, the strength and speed of connections is static across the entire system.) The data from Blue Gene is then collected and processed by imaging software that can form navigable pictures of the simulated neurons. In this way, inscrutable data becomes readily comprehensible.

The brain is extremely complex. However, this complexity arises more from its wiring than from its actual components. Neurons, though they generally share the same basic properties, number in the billions. The problem, when it comes to simulation, is that each of these neurons communicates with hundreds or even thousands of others and as of now, there is no computer powerful enough to process all of this information at once. At half speed, it takes a computer the size of several refrigerators to model only .00001% of a human brain. Nevertheless, since the problem is one of volume rather than complexity, it seems likely that technology will eventually catch up.

In as little as two years, the Blue Brain Project expects to be able to create an entire rat brain. They are already working with a robotics company in Japan to design a robotic rat that can embody their model brain. The big question is: what will happen? Will the rat be "alive" and "conscious?"

The stated goal of the project is to create an accurate model of the brain for testing purposes in neurological studies. However, the implications of actually building a brain are vast. If the project is successful, it could answer one of the greatest questions of science and philosophy: what does it mean to be human? If intelligence is entirely biological, a biologically accurate model of the brain should be conscious. Henry Markram, director of the Blue Brain project says, "I think it will be just as interesting, perhaps even more interesting, if we can't create a conscious computer. Then the question will be: 'What are we missing? Why is this not enough?'"(Lehrer). Still, it will take many years and huge technological advances to make this project a reality. At least for now, the human brain is still the most powerful computer around.

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Picture courtesy of Nikon Small World

Tower of Hanoi

So-Eun Park

1. History of the Puzzle

The Tower of Hanoi game is a historically famous mathematical puzzle, which was first invented by the French mathematician Édouard Lucas in 1883. The game consists of three wooden pegs and a certain number of disks, each different in its size and all stacked on a singlepeg initially in order of size with the biggest at the bottom and smallest at the top. The problem is simple, yet interesting size with the biggest at the bottom and smallest at the top. The problem is simple, yet interesting: what is the minimal number of moves needed in order to move all disks to another peg and stack them again in order of size? The players, however, must go by two rules: first, only one disk on top of a peg is moved at a time; second, no disk can be stacked on a smaller one. The puzzle relates its origin to a religious legend about a Vietnamese or Indian temple which contains three posts and 64 golden disks on them. The monks started moving the golden disks at some point in the past, one per second under the rules specified above, and the legend says the world will end when the moving is completed. Now, what would you estimate the lifetime of the world? With only 64 disks, does it seem like it would end sometime soon? Well, the truth is that you don't have to worry about this old myth at all, for roughly the next 555 billion years!

2. Recursive Algorithm

Here comes the logic underlying this puzzle that mathematicians call a "recursive algorithm." Recursive algorithm is a mathematical method used to find solutions to a question by using already given or found solutions to previous questions. An easy example is to calculate the number of bikes one man buys in relation to the number of bikes previous men buy before him. If each man buys twice as many bikes plus one more than the previous man then we could calcuate the number of bikes one man will buy, given an initial purchase. Therefore we can calculate how many bikes the fifth man will buy, when the first man buys only one bike. In order for us to calculate the number of bikes the fifth man will buy, we must know the number of bikes the fourth man will buy (so that we can double it and add one to get the answer); but to get the number for the fourth man, we must again know the number of bikes the third man bought. Recursively, we would have to know the number of bikes each man bought. Of course, those who are mathematically savvy can come up with a simple solution to this sequence problem to save the tedious computations.

The Fibonacci sequence is one example of a famous recursive algorithm. The Italian mathematician Leonardo of Pisa (known as Fibonacci) introduced this sequence in his book written in 1202. The first two terms of the Fibonacci sequence are set to be 1, and starting with the third term, each consecutive term is defined to be the sum of the previous two terms right before it. Therefore, the sequence is1,1,2,3,5,8,13,21,34,55,89,144, and so on and so forth. We can formulate this into a mathematical statement:

$$a_{(n)}=a_{(n-1)}+a_{(n-2)},$$

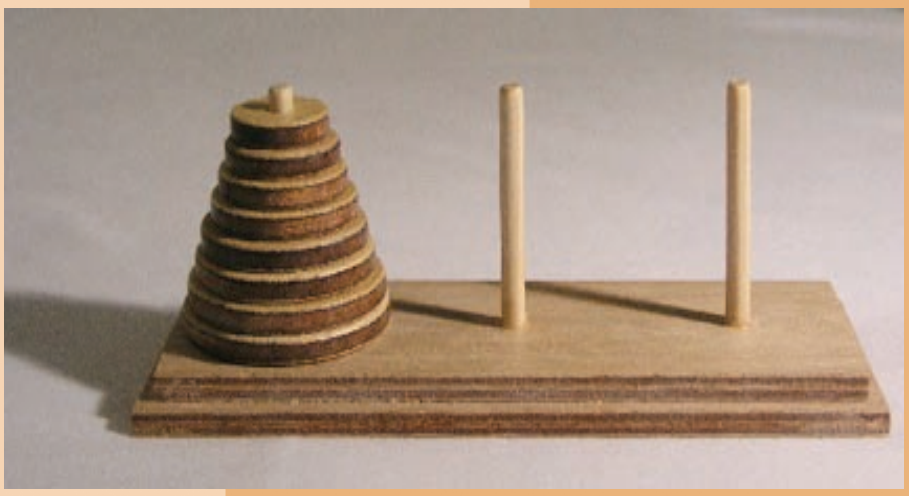
where $a_{(i)}$ indicates the ith term and $a_1 = a_0 = 1$. This implies that we can find the nth term once we know what the n-1st and n-2nd terms are, each of which we can find by calculating the n-3rd and n-4th terms, and recursively the n-5th and n-6th terms, and so on. In short, any particular term can be deduced once we know all previous terms. As in both examples, the characteristic of these mathematical solutions that involve previous steps in finding the answer for the next step is called *recursive*.

3. Solution to the Tower of Hanoi Game for Everyone

Amazingly enough, the solution to the Tower of

Hanoi problem is easy to find with the help of a recursive algorithm and a little bit of modifications. Here, we will define each nth term, a _ n, of the sequence (that is, the nth solution to the Tower of Hanoi game as we defined the nth man and the nth Fibonacci term in section 2) as the solution to the game with exactly n disks. We also want to label each peg: 1, 2, and 3, in order to make this section more readable notation-wise. Then, assume that in all cases, all disks are initially stacked on the peg 1 in size order and we want to move them all to peg 3.

Therefore, a _ 1 will be the minimal number of moves needed to move a single disk from peg 1 to peg 3, and the answer is obviously one! Next, think about a _ 2, the case for 2 disks, which also easy to figure out. First, we will move the smallest disk on top to peg 2, then the largest disk to peg 3 that just became free by the smallest disk moving away. By placing the smallest back on the largest disk on peg 3, we can stack all two disks on peg 3 in order of size as desired by only 3 moves.



From a _ 3, the recursive algorithm will finally begin to be used and lead us to find the answer in the simplest way possible. For us to move all disks to peg 3, we need to at some point in the middle move the largest disk to peg 3. This indicates that at the moment the other 2 disks will be stacked on peg 2. This is because, by the rules of the game, only the top disk on each peg can be moved and any disk cannot sit on a smaller one. On top of that, the other 2 disks will have to be stacked on peg 2 in order of size.

Now, let's look at this procedure backward from this point on. The largest disk is on peg 1, peg 3 is empty to receive a visit from the largest disk, and the other 2 disks are stacked on peg 2. How can this stage be reached from the initial state in a minimal number of moves? Yes, only by repeating exactly what we did to get a _ 2. The 2 smallest disks were initially on peg 1 on top of the largest disk, but now they moved their peg and are sitting on peg 2 (Moving them to peg 3, as in the a _ 2 procedure, or to peg 2 require the same number of minimal moves because they are symmetric). Hence, up to this point, the moves require a _ 2 number of moves. Then, we move the largest disk to peg 3, which adds one more move (it is a _ 2 + 1 now). What we have to in the next step is to move the smallest 2 disks on peg 2 back to the top of the largest disk on peg 3. This again requires a _ 2 number of moves by the symmetry of pegs. If these final moves are done, all three disks will be all stacked on peg 3 as we wished. This piecewise understanding of the problem will give us a recursive equation:

$$a\_3 = 2 * a\_2 + 1$$

which can be extended to general cases for any number of disks:

$$a\_n = 2 * a\_n - 1 + 1$$

By a simple mathematical computation, we get the answer:

$$a\_n = 2^n - 1$$

Therefore, the answer to the original question about the world's lifetime is 2^64-1 seconds, which is approximately 600 billion years.

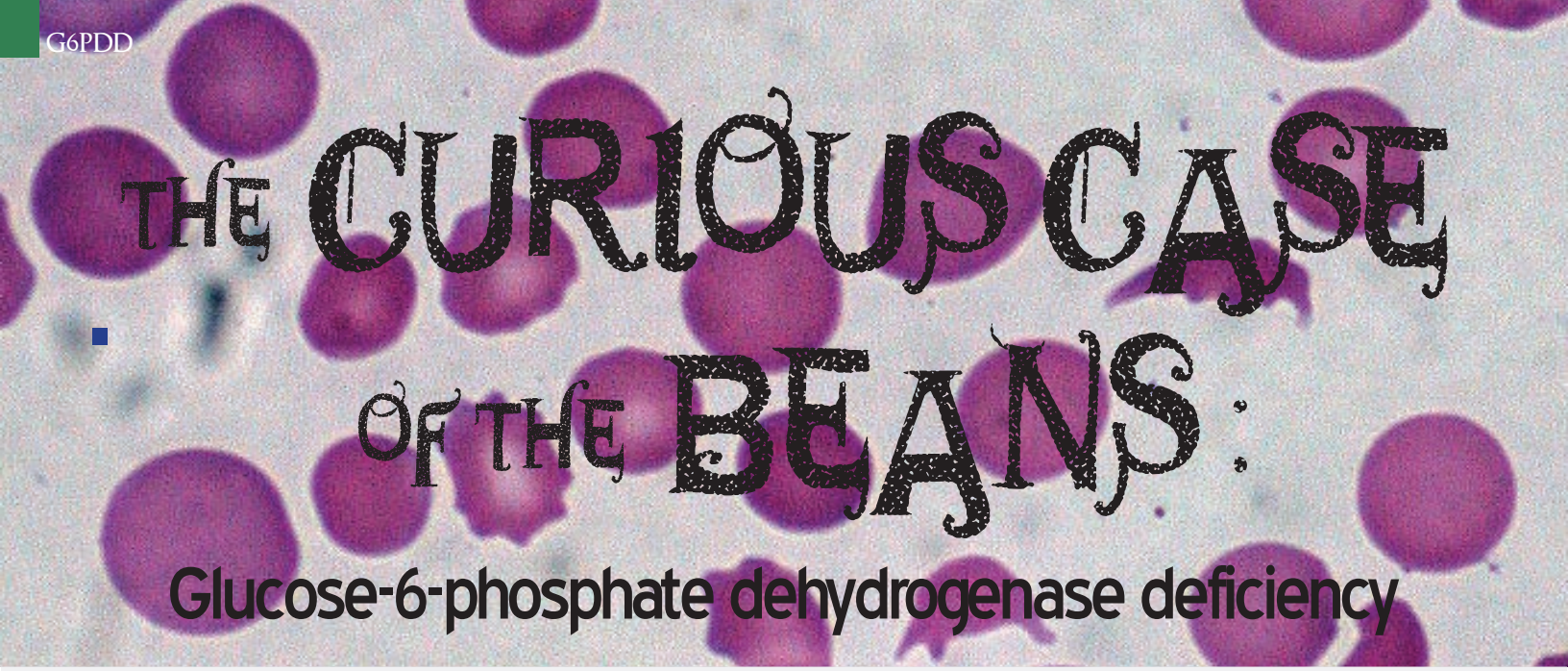
4. Unanswered Variations

In fact, the Tower of Hanoi problem with 3 pegs is an easy problem to solve for all of those who are interested in mathematics or mathematical puzzles .

Then why is the Tower of Hanoi game called the "long unsolved mystery"? Amazingly enough, once the number of pegs goes over three, the solution to the problem becomes unbelievably complicated and the only discovered "algorithm" (not a solution) that is most likely to be the answer, which is called the Frame-Stewart Algorithm, is the closest we have gotten so far to the general solution.

Moreover, there are interesting variations to this question as more restrictions on the moves can be added (ex: labeling disks with numbers and not allowing odd numbered disks to sit on odd numbered disks; only allowing disks to be moved to the right) to looking at this problem from more mathematical angles (ex: defining a graph of the game, applying graph properties to the game) to extending the minimal number of moves (shortest path) concept to between any states of disks on pegs (ex: we don't have to begin with all disks on a single peg, what is the minimal number of moves needed to stack all back to a single peg if they were initially all spread out?).

We can all name many different kinds of restrictions off the top of our heads and make our own Tower of Hanoi variation problem. If it is challenging enough, you will have an open problem known to the world, like Fermat's last theorem, named after you!



The Curious Case of the Beans:

Glucose-6-phosphate dehydrogenase deficiency

Amy Huang

A 44 year old Ashkenazi Jewish woman with "a five day history of feeling tired and unwell" and "bouts of vomiting" is rushed to the emergency room. She denies any drug use, foreign travel, or previous cases similar to the one she is presenting. She displays hypertension and jaundice, a condition in which bilirubin builds up to produce a yellowing of the skin, sclera and the whites of the eye, and dark urine. She denies a family history of anemia and neonatal jaundice. However, she states that she had eaten a whole pound of broad beans shortly before her symptoms started. A case of the food allergies? Not quite. Her blood smear shows extensive red blood cell damage and irregularly-shaped cells, atypical results for a mere allergy. What was in those beans that made her display these severe symptoms within such a short period of time?

Beans, aspirin, and liver problems?

Broad beans contain a toxic chemical called vicine, which oxidizes red blood cells, causing hemolytic anemia, a condition in which red blood cells burst. Nevertheless, most people who consume broad beans do not display such symptoms, except for those who lack the enzyme to protect their erythrocytes from oxidative damage. This enzyme is glucose-6-phosphate dehydrogenase, and those who have a deficiency of it have glucose-6-phosphate dehydrogenase deficiency (G6PDD). Though it seems severe, this condition is surprisingly common. G6PDD, or favism, is one of the most common enzyme deficiency disorders in the world. It affects more than 400 million people, with higher prevalence in Africa, Asia, Southern Europe, and Oceania. Although it is a commonly inherited disorder that dates back to 5th century BC, G6PDD was not widely studied until the early 1950's, when the US Army conducted research on the etiology of the high rates of drug-related sensitivity in black soldiers. It was found that the antimalarial drug, primaquine, was responsible for up to 15% of the cases, while later studies identified other factors such as the intake of various antimalarial agents, sulfonamides, acetaminophen, anthelmintics, non-steroidal anti-inflammatory drugs (NSAIDs), naphthalene, quinine, Thiazide diuretics, nitrofurantoin, and the fava beans that give the disorder its characteristic name.

Glucose-6-phosphate dehydrogenase, a polypeptide of 515 amino acids, is crucial for the production of NADH, a cellular coenzyme, in the hexose monophosphate shunt, an important metabolic pathway. D-glucose-6-phosphate must be dehydrogenized by D-glucose-6-phosphate dehydrogenase into 6-phosphogluconolacton and NADH. The NADH produced maintains the level of glutathione in the cells, which protects erythrocytes from oxidative damage. A deficiency in glucose-6-phosphate dehydrogenase severely limits the level of glutathione and NADH, creating a high risk for hemolytic anemia. The consumption of foods rich in oxidants such as the vicine, divicine, convicine and isouramil chemicals in broad beans, can bring about oxidative stress and hemolysis in patients.

Other biological elements like proteins are damaged in oxidative stress, as all glutathione are consumed during the pathway. The oxidation of proteins causes electrolyte imbalance and hemolysis, leading to acute renal failure, hemoglobinuria, hemolytic anemia, and jaundice from the metabolism of hemoglobin into bilirubin. Clinical manifestations include splenomegaly, hepatomegaly, confusion, fever, fatigue, pallor, dark urine from the filtering of lysed erythrocytes, tachycardia, dyspnea, and palpitations. Some symptoms of G6PDD are present after birth, with persistent neonatal jaundice being the most prevalent. The low levels and inefficient activity of G6PD in the liver result in the yellow discoloration of the mucous membranes, skin, and the whites of the eyes. If left untreated, there can be death or permanent neurological damage. In G6PDD individuals, a hemolytic crisis ensues from the intake of certain medications and foods rich in oxidants. The buildup of oxygen

chemicals in erythrocytes destroys the cells by lysis, causing anemia.

Diagnostic Techniques

Many diagnostic tests are available for the testing of G6PDD, such as the methylene blue test and the methemoglobin reduction test. In the methylene blue test, a catheter is placed into a vein and methylene blue, a dark green powder, is placed into the catheter. The health care provider will observe how the powder will turn methemoglobin into hemoglobin in order to determine the type of methemoglobinemia, in which several types of such have genetic causes. The methemoglobin reduction test is a blood test determines the ratio of normal hemoglobin versus hemoglobin derivatives (methemoglobin, carboxyhemoglobin, and sulfhemoglobin). Abnormal values of hemoglobin derivative levels may indicate inefficient transport of oxygen to cells, as the derivatives are unable to carry oxygen. Another test, the Beutler fluorescent spot test, looks at G6PD enzyme activity under UV light at 30°C. Elevated bilirubin and serum LDH levels, low serum haptoglobin and hemoglobin count, hemoglobinuria, elevated absolute reticulocyte count, and the presence of Heinz bodies in a blood smear can also indicate G6PDD.

Treatments and Prevention

Although there is no known cure for G6PDD, various treatments alleviate symptoms of the patient. For infants with neonatal jaundice, special lamps called bili-lights help relieve the jaundice by breaking down the bilirubin accumulated in the skin and mucous membranes (since bilirubin is readily decomposed by light). However, this treatment does not cure the underlying condition of jaundice.

In the case of acute hemolytic anemia, a blood transfusion may be necessary. However, the simplest procedure is to treat the patient with nasal oxygen and adequate bed rest to alleviate symptoms. Folic acid supplements and treatment with human haptoglobin products can also be administered. In severe cases, patients can undergo a splenectomy to lessen the symptoms of anemia, as the spleen is the main organ in erythrocyte destruction. Nonetheless, the best way to prevent a hemolytic crisis is to avoid eating broad beans and taking certain medications. Patients should consult their physicians before they attempt to take medications and supplements. It is noted that some patients can tolerate small amounts of certain drugs, depending on the severity of the disorder. For patients with acute renal failure, dialysis offers a temporary solution to a severe problem.

Infections can also precipitate into a hemolytic crisis, and patients are advised that many medications that are normally safe to administer may lead to hemolysis. In a study done in Algeria, it has been discovered that even the ingestion of low doses (400mg) of acetaminophen in G6PDD patients can lead to hemolysis in two cases out of forty. Although there is controversy over the validity of the data, G6PDD patients should limit or avoid the intake of aspirin.

Epidemiological Significance

G6DD is of epidemiological significance, in that it offers some resistance to Blackwater fever, or malaria caused by Plasmodium falciparum. This relationship is similar to that of sickle cell anemia, in which erythrocytes take on a distinct crescent form. The mechanism of action for this resistance is that the spleen rapidly clears out the malaria parasite for G6PDD patients, offering them an evolutionary advantage against a virulent disease. Since the erythrocytes are abnormal, the malaria parasite has a difficult time attacking them.

Researchers have also found that G6PDD may be linked to cataractogenesis, Fulminant Rocky Mountain spotted fever (RMSF), cancer, and possibly cystic fibrosis and diabetes. A study among Saudi-Arabian patients found that G6PD activity in diabetics is much lower than in non-diabetics. Another study illustrated how insulin deficiency was proportional to decreased G6PD activity.

The Genetics of G6PDD

G6PDD is an X-linked recessive disorder resulting from a single-point mutation of a substitution of an amino acid coding for the G6PD structural gene at the Xq28 region located on the tip of the long arm of the X- chromosome. It is inherited from heterozygote females who carry the gene on one X chromosome, who then passes it to her offspring, in which the sons who carry one copy of the gene is affected, and the daughter who also carries one copy is a carrier. Thus, males are more likely to be affected than females. The severity of the disorder is affected by race, as Africans who carry the disorder exhibit a milder form of hemolysis than do Caucasians. People with G6PDD should consult genetic counselors to assess their disorder and to determine the risk of passing it on to their children.

Potential Cures

Future treatments of G6PDD are limited, but can involve genetic engineering of certain food items containing high amounts of oxidative chemicals in order to prevent the onset of hemolytic anemia in people who consume these staple foods, especially for people in Middle Eastern and African countries. Scientists are attempting to produce genetically engineered fava beans that lack oxidative agents, a move that can benefit Saudi Arabians, whose rates of favism are high even though fava beans remain a food staple.

A potential treatment proposal may be the introduction of potent antioxidants into the bodies of G6PDD patients. Although it is difficult to always maintain an adequate level of glutathione in the cells, it might be possible

to put these antioxidants in slow-release capsules to help prevent oxidative stress and hemolysis when consuming foods. One method is to encapsulate them in kelp derivatives for slow release, a technique some researchers found useful for the delivery of certain drugs. One solution can be to use potent antioxidants to reduce drug dosage and lessen intake frequency. Research from the Salk Institute of Biological Studies and Columbia University shows that nanoparticles, particles composed of yttrium and cerium oxides, can potentially become the most potent antioxidant used to counteract severe oxidative stress. However, the cytotoxicity of such particles is undetermined and the chemicals are possibly dangerous to humans. If discovered to be safe for use, they can help improve the lives of thousands of G6PDD patients. Although these treatments may not prove feasible, they are only ideas that can perpetuate the study for the finding of better treatments for G6PDD.

One potential cure may be to find a chemical alternative to glutathione and infuse it into the body of the G6PDD patient, or to find a chemical to help maintain glutathione levels. Pharmaceutical research helps advance the search for such a drug that can replace NADH as the chemical that balances glutathione levels. These drugs should target the liver and enhance the activity of G6PD there, as G6PD activity is lowest in that organ in patients, accounting for the jaundice and hepatomegaly.

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The Delian Problem

Atanas Atanasov

1. Introduction

During a rigorous geometry course in middle school or high school one often encounters various construction problems. We are customarily asked to construct or extend a chart using straight edge and compass alone. For example, it is useful to build the median or the altitude of a triangle and other such. Most of these problems bear their roots in the ancient world. By no means we will attempt a complete historic assessment of such constructive geometric problems, but only give the flavor of the general picture.

All problems previously mentioned may be resolved by elementary means - most people should have no trouble constructing a solution in a very short timespan. Mathematicians, on the other hand, take equal pleasure in asking questions of existence and inexistence. It is natural to try identifying ob jects which we cannot construct. A well-known legend tells the story of a plague in Athens during the 5th BCE. After consulting the oracle of Apollo at Delos, a decision has been taken to double the size of the altar devoted to Athens, which was roughly the shaped of a cube. Initially, the sidelength of the altar was doubled, however the plague did not cease - it even spread further. It was later realized the omen was interpreted incorrectly. The volume of the cube had to be doubled, not its sidelength. Such an attempt, would involve the construction of the ratios between the sides of the older altar and the doubled one, namely $\sqrt[3]{2}$. Namely, the construction of a line segment with this given length is famously referred as the Delian problem, after Delos where the mystical oracle of Apollo was situated.

There are a large supply of other ob jects one might find difficult to construct with straight edge and compass. Two famous ones are "trisecting an angle" (given an arbitrary angle, construct angles that split it in three equal parts) and "squaring the circle" (given a circle, construct a square with the same ares). Both of these are impossible to achieve using straight edge and compass. We need to make the rules more precise since the allowed moves greatly impacts our constructive powers.

We are allowed to use an unruled edge and a compass. The term "edge" is adopted instead of "ruler", in order to indicate an idealized nature, namely that it has only one side and extends infinitely. What is often omitted from the description is the availability of a marking device, say a pencil, using which we can draw lines along the edge (we use draw as a synonym for construct). Similarly, the compass is a device such that given two points, we can construct a circle having the former as a center and the latter lying on the circumference of the circle. It is important to note, once lifted the compass collapses. In other words, we cannot use it to transport lengths as one would often use such a device in real life. If this were allowed, then trisecting the angle is possible. It is by no means apparent why these are the set of construction axioms we abide by. This set of rules turns out to correspond to a tractable algebraic model.

If we are asked to construct a line segment with a prescribed length, only given a straight edge and compass, there is no indication of scale. That is, a segment is of length two, if and only if it is twice a segment of length one. For this purpose of scaling, we assume there exists a coordinate system in the plane all constructions take place. Simpler put, there is a marking on the edge that indicates the unit length (this enables us to construct segments of unit length, but not to record lengths, as it is equivalent to leaving the compass uncollapsed).

We proceed to demonstrate a few of the simplest and most useful constructions that often come up.

- Given a positive integer n, we can always construct the segment of length n by imposing the unit segment n times (see Figure 1).
- Actually, given any positive rational number p/q we can construct a segment with the prescribed length as shown below (see Figure 2).
- Given a segment of length x, we can find a segment with length $\sqrt{x}$ as demonstrated below. Notice, the Delian problem lies in the difficulty of generalizing this to cube roots (see Figure 3).

For a long time scholars have been aware of the aforementioned constructions. There were many figures we could construct, however nobody knew how to prove cer-

tain figures are not constructible. There was the call for a more elaborate tool, a concept that would break tradition.

How do you show something is impossible? The fact it is possible to prove such a statement took people a while to wrap their minds around. One simple trick is to establish an invariant or indicator. For example, we are presented with a very complicated object - a figure. We would like to associate a much simpler ob ject with it, for example a number. Then we study the way this number varies as we extend the figure. If we can conclude that some numbers are unattainable in such a fashion, then we would know that the figures corresponding to them would not be constructible either. This is precisely the point of view we are going to take in the rest of the article.

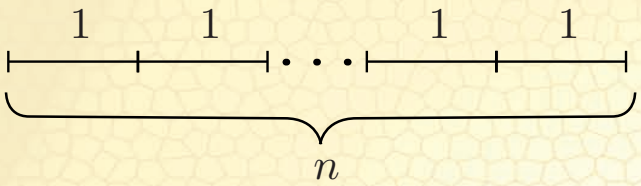

Figure 1. Constructing a segment of integer length.

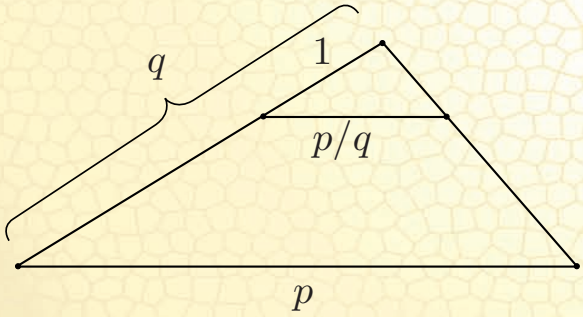

Figure 2. Constructing a segment of rational length.

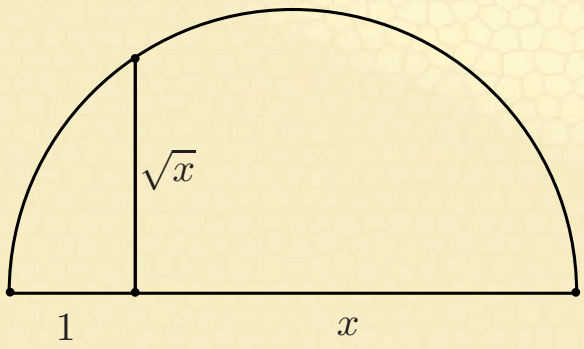

Figure 3. Constructing a segment of square root length.

2. Algebra

Evariste Galois (1811-1832) was a brilliant young mathematician and a fierce political proponent. Today he is best known for his work on Galois groups in the theory of fields. While studying field extensions, he was also able to come to a simple solution of the Delian and other similar problems. Before we can describe the heart of his method, we need to introduce what a field is.

Think of one's mathematical education. For the most of it, we study certain sets of numbers and operations on them. By the fifth or sixth grade, we learn all about the rational numbers $\mathbb{Q}$. A bit later, we encounter π and e which do not fit the old scheme. They are both irrational and form part of the bigger set of real numbers $\mathbb{R}$. Later, we come to realize one cannot compute the square root of -1. Then, we are forced to extend our horizon to the set of complex numbers $\mathbb{C}$.

In reality, all three sets $\mathbb{Q}$, $\mathbb{R}$, $\mathbb{C}$ look alike. They contain 0 and 1. Addition, negation, multiplication and division by non-zero values are all well-defined. Furthermore, multiplication is distributive over addition. Despite the fact all three sets vary enormously in their size, they bear the same stricture - what we call a field. These objects together with a few more form the front line of (abstract) algebra. They are so important nowadays one can hardly imagine any branch of mathematics without them.

There exists a notion called field extension. We know that $\mathbb{Q} \subset \mathbb{R} \subset \mathbb{C}$. In other words, the rational numbers are contained in the real numbers, which in turn are contained in the complex numbers. If one field is contained in another, we call the latter a (field) extension of the former. For example $\mathbb{C}$ is an extension of $\mathbb{R}$ and so is $\mathbb{R}$ of $\mathbb{Q}$. If E is an extension of F , the question we are interested is "How much bigger is E than F ?" What do we mean by "bigger"? We refer to the degree of E over F , often denoted [E : F], which is the dimension of E as a vector space over F . We will not try to describe this in full but elaborate on an example. Think of the complex plane. We call it a plane because it is two dimensional as a space where by one dimension we refer to the real line. And indeed, $[\mathbb{C} : \mathbb{R}] = 2$ where the generators of the complex numbers are 1 and i. On the other hand, the real numbers are of infinite degree over the reals - we cannot find a finite number of generators as above. In the rest of this article, we will use finite extensions, that is extensions of finite degree.

Fields allow the action of adjoining elements. The ra-

tional numbers are a very convenient field for many reasons. However, it is a very restrictive one too. For example, the square root of 2 has famously been proved to be irrational. Adjoining (adding) $\sqrt{2}$ to $\mathbb{Q}$, we obtain a new field denoted $(\sqrt{2})$. Please note the new field is not all rationals with one extra element $\sqrt{2}$. In order to preserve the structure of a field we need to make sure adding, subtracting, multiplying and dividing are well-defined on elements on the new field, hence we take all possible combinations with these operations including rational numbers and $\sqrt{2}$. This field naturally extends the rationals and is of degree two (not the 2 in $\sqrt{2}$). An extension of degree two is called a quadratic extension. It turns out we can construct $\mathbb{Q}(\sqrt{2})$ as all numbers of the form $a + b\sqrt{2}$ as a and b vary over the rationals. Similarly, adjoining any irrational square root (not that of a perfect square e.g. 4) would lead to a quadratic extension. Similarly, adjoining an irrational cube root would lead to a cubic extension, or one of degree 3. For example, $\mathbb{Q}(\sqrt[3]{2})$ is the set of all numbers of the form $a+b2^{1/3}+c2^{2/3}$ where a, b, c are rationals. Several adjoinings may be performed in sequence. For example, if we take we may first enlarge to $\mathbb{Q}(\sqrt{2})$ and then further to $\mathbb{Q}(\sqrt{2}, \sqrt{3})$. Suppose F is a field, E a finite extension of it and L a finite extension of E. Then [L : F] = [L : E][E : F]. This demonstrates the degree acts in a predictable way upon multiple extension (adjoining).

3. The Solution

At this point, we have provided enough background on field theory to prove $\sqrt[3]{2}$ is not constructible solving the Delian problem.

If F if a field, by the F -plane we mean F^2, that is all points (x, y) such that both x and y are elements of F. Can we construct all points on the $\mathbb{Q}$-place (the rational plane)? We have discussed a segment of any rational length may be constructed. If we have to construct a point in the rational plane, we may start with segments of length corresponding to each of its coordinates and then use the coordinate axes to obtain the desired point.

Could we construct points outside the rational plane? That is impossible using only the straight edge alone. However, we have not used the compass so far. It is time to formally asses adding new points to a chart. This may occur only under the following circumstances (provided intersections do occur).

(1) Adding an intersection point of two lines.
(2) Adding an intersection point of a line and a circle.
(3) Adding an intersection points of two circles.

Computing the intersection point of two lines involves the solution of two simultaneous linear equations which can be done by the elementary operations a field allows (addition, subtraction, multiplication and division) without taking square roots or anything fancier. On the other hand, the latter two constructions may involve taking square roots (since circles are given by quadratic equations), but nothing else. Hence, we may only adjoin square roots to $\mathbb{Q}$. Similarly, if we are working in the F -plane, one may only adjoin square roots. That is, if x is an element of F and the F -plane is constructible, so is the F $(\sqrt{x})$-plane. Careful inspection of the construction rules demonstrates there are no further possibilities. Notice that [F $(\sqrt{x})$: F] = 1 or 2 (depending whether x is a square in F). If we start with the $\mathbb{Q}$, we may only achieve extensions F such that there exists a positive integer n and a chain of intermediate extensions

$$\mathbb{Q} = F_0 \subset F_1 \subset \cdots F_{n-1} \subset F_n = F,$$

such that for each $1 \leq i \leq n$, F_i is a degree two extension of F_{i-1} (formally $[F_i : F_{i-1}] = 2$). By multiplicativity of degrees we conclude

$$[F : Q] = [F_n : F_0] = [F_n : F_{n-1}] \cdots [F_1 : F_0] = 2^n.$$

If $\mathbb{Q}(\sqrt[3]{2})$ were constructible, this would imply $[\mathbb{Q}(\sqrt[3]{2}) : \mathbb{Q}]$ = 3 is a power of 2 which is clearly false. This yields a contradiction and we have solved the Delian problem. It all boils down to the fact 3 is not a power of 2! That is why we cannot construct $\sqrt[3]{2}$.

Once we established the necessary background material, the reader may be surprised with the ease this result slipped out. Furthermore, the other two construction problems we mentioned, namely trisecting an angle and squaring the circle, are resolved by analogous arguments. Abstract algebra is such a powerful tool in modern mathematics, one should not be taken by surprise with these results. In this particular case we used the dry and abstract language of field theory to answer a practical question in constructive geometry.

We have demonstrated a very important trend in the historical development of mathematics - the interplay among seemingly unrelated branches. Upon second thought, the distinctions among the various branches of mathematics are entirely man-made. We are not trully connecting sub jects, but simply uniting what should have been one in the first place. Terms such as algebraic geometry, algebraic topology and algebraic number theory have a central place in the palate of the modern mathematician. The twentieth century has marked applications of alebraic techniques to almost all other parts of mathematics, even the most obscure ones such as constructive geometry.

Mirror, Mirror

Elizabeth L. Robinson

Entertainment, in spite of its great variety across time and culture, is really just about one thing: watching. From movies to sports to trapeze artists, there is something about watching other people that we just can't get enough of. But shouldn't we prefer doing to watching? The study of a new class of brain cells, called "mirror neurons," may offer some insight. Although these cells were discovered in 1996, it is only now that we are beginning to understand their significance.

It was a day like any other in Giacomo Rizzolati's neuroscience lab in Parma, Italy. Rizzolati and his team were busy collecting data for a study on the brain areas that control hand movements in monkeys. They had implanted wires in certain brain cells so that whenever the monkey reached for a peanut, the brain cells involved would make a buzzing sound signaling that they were active. The study was proceeding as expected until, one day, there was a buzz from a monkey sitting perfectly still when a researcher reached for a peanut. Somehow, the monkey's motor neurons were responding as if the monkey was doing exactly what it saw the researcher doing. This finding was so unexpected that, initially, the researchers suspected their equipment was faulty. However, their observations were confirmed repeatedly in a number of different contexts. The scientists were baffled and, according to Rizzolatti, "it took several years for us to believe what we were seeing"(Blakeslee). He rather poetically named the cells "mirror neurons" and continues to study them today.

Initially (and more aptly) known as "monkey-see monkey-do neurons," these cells allow us to understand what other people are doing by, essentially, mirroring them. Our minds actually act out what we see others doing. Although this capacity may seem trivial when talking about peanuts, the ability to "mirror" is extremely important because it is the mechanism by which we make sense of other's actions and intentions. Without this ability, social behaviors including communication, cooperation, and imitation learning would be much more difficult.

"These cells allow us to understand what other people are doing by, essentially, mirroring them."

Although they are called "mirror neurons," the cells themselves do not actually represent actions; they remember and recreate patterns. You can, for example, imagine your brain as a grid of thousands of tiny light bulbs: the lights are meaningless when lit individually, but certain groups of them turned on at the same time can make letters, pictures, and patterns. These patterns, rather than the individual brain cells, represent information. A mirror cell functions by activating the specific group of neurons that creates the action when you perform it. In fact, the only reason you don't literally "ape" the person you are watching is that cells in your spinal cord stop these motor signals from reaching your limbs.

From studies using functional magnetic resonance imaging (fMRI), an imaging technique that records brain activity by monitoring blood flow, Oxford neuroscientist J. Grezes and others have shown that mirror neurons are also present in humans. Although fMRI is less precise than direct-cell recording (as was used in the primate research referenced earlier), there is evidence that human neurons are actually far more advanced than those found in other species. Our mirror cells respond to the individual sub-movements that make up an action rather than only to the action as a whole. Also, our mirror cells respond to people's movements regardless of whether or not they have a definite purpose, unlike monkey mirror neurons, which only respond to directed actions. This seemingly trivial difference is significant from an evolutionary perspective because it allows for the formation of new movement sequences and, as a result, complex learning and creative innovation. This in turn enables individuals to recreate an action through observation and, subsequently, to pass it on to the next generation. It is clear that this ability to parse actions into smaller units offers a huge evolutionary advantage. Imagine trading in your paper airplane for a box of legos: suddenly the possibilities are endless.

According to neuroscientist V. S. Ra-

machandran, the existence of mirror cells may solve an abiding mystery of human evolution known as "the great leap forward" in which, 40 thousand years ago, sophisticated technology, art, clothing, and culture emerged suddenly and without apparent cause. If mirror neurons began parsing information at this time, it would explain how individuals were suddenly able to learn so much faster.

Interestingly, the mirror system also encompasses aspects of emotion. According to Marco Iacoboni of UCLA, the mirror system is the mechanism that underlies our ability to empathize. Mirror neurons allow us to respond to another's experiences as if they were our own: we cringe when we see someone get hurt and cheer when an athlete scores. We, quite literally, feel each other's pain. This ability to make sense of other people's actions also facilitates the creation of social groups by allowing individuals to understand others' efforts at communication and cooperation.

Beyond this, a study by Lisa Aziz-Zadel at the University of Southern California shows that our mirror cells can also be activated by descriptions of actions, both heard and read. Based on these findings, some speculate that mirror cells played a crucial role in the emergence and evolution of language, as well as in language learning. One could speculate that mirror cells are part of the reason why even the rowdiest of teenagers can spend hours on end glued to a Harry Potter book. They may be sitting still, but in their brains they are catching golden snitches and dueling with evil wizards.

We may only be scratching the surface of the potential of mirror neurons; for instance, they may have important applications in the study of autism. Autism is characterized by impaired language and social skills, both of which are, as we have seen, associated with mirror neurons. A study by Ramachandran and Lindsay Oberman at UCLA monitored the brains of ten autistic children while they watched videos of other people's hands moving and while they watched their own hands moving. They discovered that these children's mirror systems were only activated by watching their own hands, suggesting that they are unable to internalize other people's actions. Hopefully, further studies will lead to a better understanding of autism, which according to the Center for Disease Control and Prevention currently afflicts one out of every one hundred fifty children in the United States.

Since their discovery, mirror neurons have been implicated in discussions of a broad range of topics including sports fandom, physical therapy, altruism, and even pornography. However, it is important to acknowledge that these ideas are still speculative and more research is needed before the role of mirror cells can be completely defined. In neuroscience, as in many other areas of study, it is rarely accurate to explain a problem as the direct result of a single cause. The human brain is made up of billions of neurons that are constantly sending signals and changing their connections. They are always influencing each other and none ever acts alone. Mirror cells are, however, distinctive in one significant way: they only function in a social context. That is, they are part of the biological mechanism that underlies our ability to understand other people. The fact that we have neurons such as these proves that we are hard-wired to be together.

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