BLUE MOON

ANDOVER'S STEM-BASED MAGAZINE

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ISSUE I.

Blue Moon was created as a platform for STEM research, as a means by which students can exercise the final step of the scientific method: communication. It aims to foster curiosity and cooperation in both its writers and its readers. Bi-annual print publications are made possible by a grant from the Abbot Academy Association, continuing Abbot's tradition of boldness, innovation, and caring. Issue I of Blue Moon spotlights the diversity of student interests within the sciences, topics ranging from immunotherapy to gender discrimination to prosthetics.

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SCIENCE

NANOPARTICLES for DRUG DELIVERY

DAVID MOON

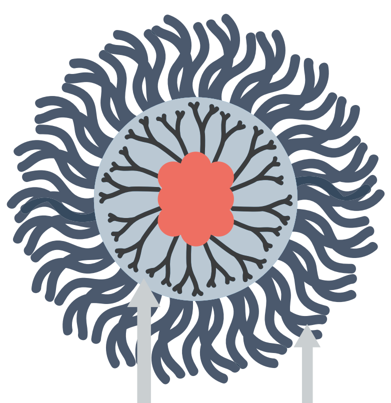
Targeted nanoparticles have gained considerable attention as an efficient drug and gene delivery system, especially for cancer therapy. In some cases, such as hepatocellular carcinoma (most types of liver cancers), these nanoparticles have achieved the highest accumulation of cytotoxic agents in tumor tissue, modifiable drug pharmacokinetic- and bio-distribution, improved effectiveness of treatment and limited side effects (Varshosaz et al., 2015).

Nanoparticulate (NP) drug delivery systems are solid particles with size of 10 to 1000 nm; in nanomedicine, they often refer to size < 200 nm (Athar et al., 2014). There are two types of NPs: nanocapsules and nanospheres. Nanocapsules are vesicular systems in which a drug is confined to a cavity surrounded by a polymeric membrane, whereas nanospheres are matrix systems in which the drug is physically and uniformly dispersed (Singh et al., 2009). NPs can contain encapsulated, dispersed, absorbed or conjugated drugs, a unique characteristic that can lead to enhanced performance in a variety of dosage forms. The vast majority of molecules in NPs reside at the surface, which maximizes the loading and delivery of therapeutic drugs to targeted cells and tissues (Arzt et al., 2001). Highly efficient drug delivery based on NPs could potentially reduce the drug dose needed to achieve therapeutic benefit, which, in turn, would lower the cost and reduce the side effects associated with certain drugs (Bamrungsap et al., 2012).

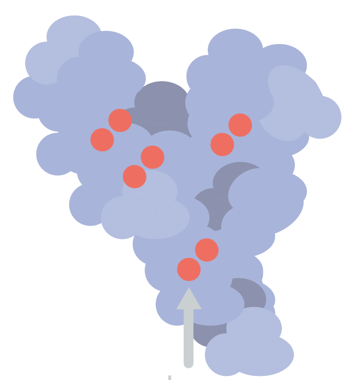
One of the major challenges in drug delivery is to correctly transport the drug to the precise body part, thereby avoiding potential side effects to non-diseased organs (De Jong et al., 2008). This is especially challenging in cancer treatment where the tumor may be localized as distinct metastases in various organs. The toxicity of chemotherapeutics thus limits the full use of their therapeutic potential (De Jong et al., 2008). Local drug delivery or drug targeting results in increased local drug concentrations and provides strategies for more specific therapy. Nanoparticles have specific particulate markers as tools to enable these strategies. These include benefits such as their small size allowing penetration of cell membranes, binding and stabilization of proteins, and lysosomal escape after endocytosis (Moghimi et al., 2001).

Targeted delivery may be achieved passively or actively. In the passive targeting, no ligand is used and targeting is achieved by incorporating the therapeutic agent into NPs that passively reaches the target organ (Varshosaz et al., 2015). In this strategy, the leaky nature of vessels in cancer tissue and lack of well-defined

POLYMERIC MICELLE



PROTEIN-BASED NP



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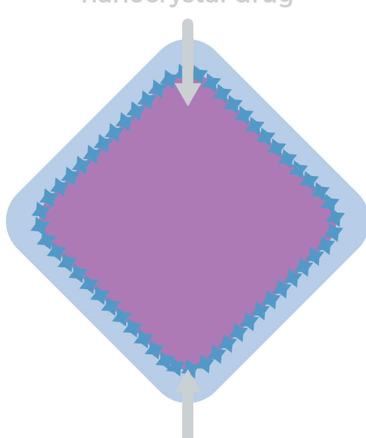

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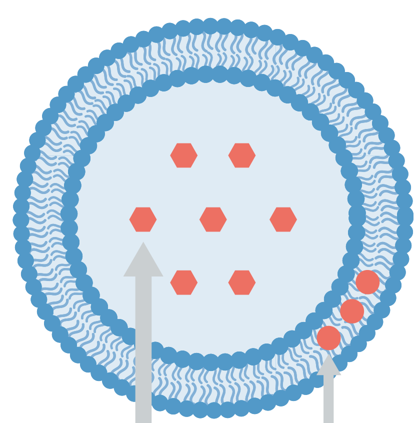


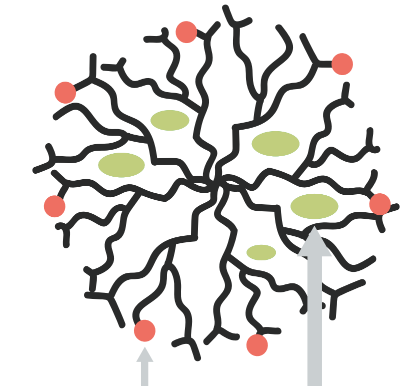
lymphatic system can enhance the permeation and retention of NPs, which is called the enhanced permeation and retention (EPR) effect (Kobayashi et al., 2013). Moreover, the EPR effect, which characterizes the microenvironment surrounding tumor tissue, is different from that of healthy cells, a physiological phenomenon that also supports passive targeting. These fast-growing tumor cells require more oxygen and nutrients due to high metabolic rate, resulting in an acidic environment. Taking advantage of this, pH-sensitive liposomes have been designed to degrade and release drug molecules at a specific acidic pH range (Liu et al., 2013). Although passive targeting approaches form the basis of clinical therapy, they suffer from several limitations. Ubiquitously targeting cells within a tumor is not always feasible because the random nature of the approach makes it difficult to control the process and because some drugs cannot efficiently diffuse (Peer et al., 2007).

On the other hand, the therapeutic agent or carrier system in active targeting is conjugated to a tissue or cell specific receptor over-expressed specifically in tumor cells. Antibodies, peptides, aptamer or other ligands can be incorporated onto NPs surface, which would allow them to specifically target certain cells (Peer et al., 2007). In order to achieve high specificity, those receptors should be highly expressed on tumor cells, but not on normal cells. This also poses some limitations, as it is often difficult to find those specific markers.

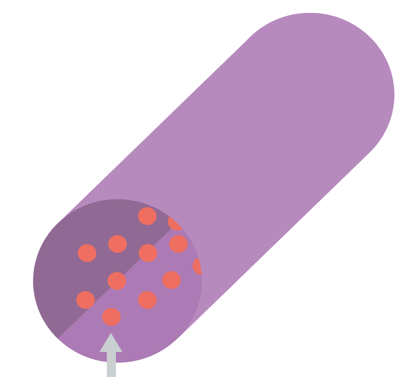
While there are still many limitations and risks to the cancer patients, the field of using nanoparticles to delivery cancer drugs is rapidly growing to overcome those challenges. Overall, nanoparticles are a very effective and efficient way of delivering drugs.

See Appendix 1.1 for references.

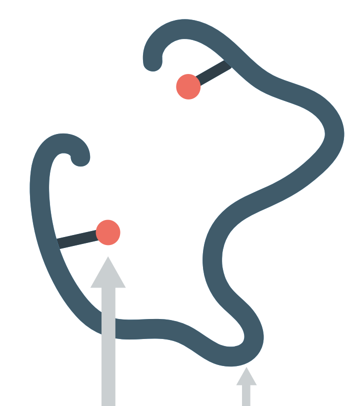
DENDRIMER



CARBON NANOTUBE



POLYMER-DRUG CONJUGATE



THE **HISTORY** OF THE COSMIC MICROWAVE BACKGROUND

ANDREW WANG

When you go outside on a clear night and look up at the sky, you might find yourself fascinated by the stars overhead. Even though they are light-years away, the stars seem to glimmer brightly against the dark background of the Universe. Interestingly, the stars that we see are not actually the current stars themselves—they are the stars from an earlier time. When the stars emit light, the light takes many years to travel across space and reach the Earth, so the light we see were emitted by the stars a long time ago. In a way, our short backyard excursion to see the stars is actually a trip back in time.

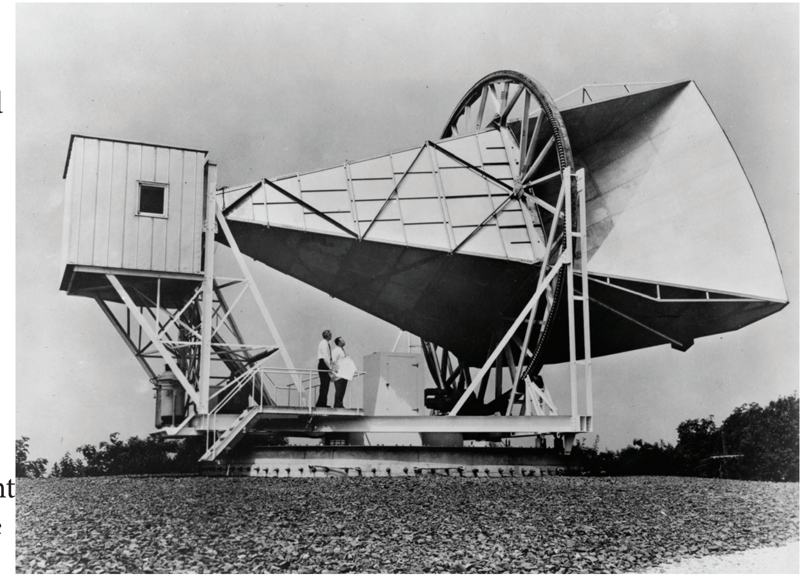


Figure SEQ Figure * ARABIC 1: The Holmdel Horn Antenna that Penzias and Wilson used to detect the cosmic microwave background radiation.

But there is actually an even older piece in the history of the Universe that you cannot see with your naked eye when you look up at the sky: the cosmic microwave background, or the CMB. The CMB is a relic of the oldest light in the Universe from just 380,000 years after the Big Bang. Given that we currently live 13.8 billion years after the Big Bang, 380,000 years is extremely close to the time of the origin of the Universe by comparison (Tate, 2013). The CMB, in turn, shows us a glimpse of the Universe in its earliest observable moments.

The CMB is made up of microwave radiation that was scattered across the sky after light particles, or photons, began moving freely through the expanding Universe. Since these photons existed nearly uniformly during the period after the Big Bang, they spread across the Universe in a similarly consistent manner throughout the growth of the Universe, even until the present day. The CMB is therefore virtually isotropic, meaning that its radiation has the same intensity no matter in what direction it is examined. Even so, however, we cannot see this uniform CMB relic when we look up at the sky because the microwave radiation travels with a wavelength outside the spectrum of visible light. Many scientific experiments, however, have confirmed the existence and intensity of the CMB.

The discovery of the CMB was, in many ways, a complete accident that eventually revolutionized the field of cosmology. In the mid-20th century, scientists considered two theories about the state of the Universe: the steady-state theory which claimed that the Universe had always existed and will always

continue to exist, and the Big Bang theory which maintained that the Universe was created in a massive Big Bang billions of years ago (Tate, 2013). In 1964, when American radio astronomers Arno Penzias and Robert Wilson were experimenting with the Holmdel Horn Antenna (Fig. 1), a radio telescope intended to detect radio waves from balloon satellites, they found that the telescope detected an unexplained and constant signal with ~3K of radiation. Several theoretical cosmologists who supported the Big Bang theory had predicted that there would be microwave background radiation left over from the Big Bang, but Penzias and Wilson did not know about this research, so they worked desperately to find a source of the signal, even cleaning out the pigeon droppings in the telescope to try to remove the signal (Evans, 2015). Ultimately, after being informed about the predictions of CMB, they realized that they had discovered it. They won a Noble Prize for this discovery in 1978.

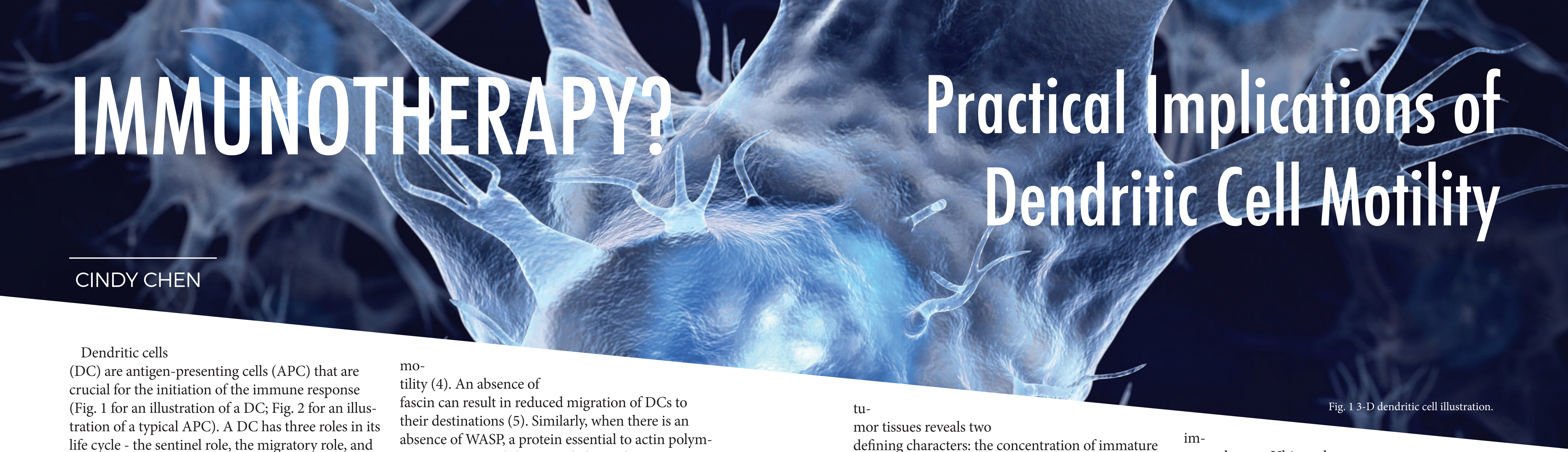
The discovery of the CMB provided strong scientific evidence for the Big Bang, and other scientists began developing further experiments to measure the properties of the CMB and thus the initial state of the Universe. Radio astronomers across the globe confirmed that the signal was always ~2.7K above absolute zero, no matter where they pointed their telescopes. Today, even amateur radio astronomy groups can build their own horn antennas and detect the microwave relics of the Universe in its earliest observable moments ("John Kovac," 2013). All of these observations provide strong evidence for the isotropy of the CMB.

Despite the near-perfect isotropy of the CMB, however, there are some very subtle anisotropies, or irregularities in the intensity of the radiation, that give astrophysicists even more clues as to how the early Universe developed. These anisotropies provided the earliest variation in the Universe that eventually led to the formation of galaxies and stars and everything else in the Universe (Evans, 2015).

Many experimental cosmology groups are also hoping that the CMB will provide evidence for predictions about inflation, gravitational waves, dark matter, dark energy, and other interesting properties of the Universe. Several telescopes have been set up to measure the polarization of the CMB radiation—this means that they detect the orientation of the incoming light perpendicular to the direction of propagation (Bischoff, n.d.). Gravitational waves from immediately after the Big Bang are thought to have affected early microwave signals and sourced them as B-mode polarization (a specific type of polarization). If these telescopes are able to detect this extremely tiny B-mode polarization of the CMB, it will be a "smoking gun" for the theory of inflation. As of yet, nobody has found a truly significant signal, but there is lots of hope for the discovery. This is just one of many studies taking place today to study the signals from the earliest moments of our Universe.

So next time you look up at the stars, remember that the seemingly empty sky around you is actually filled with radiation from the earliest moments of the Universe. It's a blast to the past.

See Appendix 1.2 for references.



IMMUNOTHERAPY? Practical Implications of Dendritic Cell Motility

CINDY CHEN

Dendritic cells (DC) are antigen-presenting cells (APC) that are crucial for the initiation of the immune response (Fig. 1 for an illustration of a DC; Fig. 2 for an illustration of a typical APC). A DC has three roles in its life cycle - the sentinel role, the migratory role, and the adjuvant and activation role. During the sentinel role, the immature DC surveys the surroundings for pathogens. When the cell recognizes an antigen, it matures, uptakes and processes an antigen, and then uses a major histocompatibility complex (MHC) to present the antigen on the cell surface. Subsequently, during the migratory phase, the mature DC moves through the bloodstream to T-cell rich areas, such as the lymph nodes. During the adjuvant and activation role, the T-cell recognizes the antigen that is presented by the mature DC. This causes the T-cell to activate and proliferate, initiating an immune response. Although various impairments to the migratory role have been recognized, much of this role is currently unknown.

A detailed motor complex composed of actin filaments, myosin motor proteins, and actin regulatory proteins assists in DC migration. Known proteins include hematopoietic lineage cell-specific protein 1 (HS1), fascin, Wiskott-Aldrich Syndrome Protein (WASP), and a protein complex Arp2/3, though their specific interactions with each other have yet to be clarified (1-3).

Significantly, fascin is an actin filament bundling protein that forms bundles around membrane protrusions caused by actin congregation to assist motility (4). An absence of fascin can result in reduced migration of DCs to their destinations (5). Similarly, when there is an absence of WASP, a protein essential to actin polymerization, DCs exhibit severely limited movement to T-cell rich areas during their migratory roles, causing reduction in T-cell activation and low initiation of the immune response (6, 7).

While deficiency of actin regulatory proteins like fascin and WASP have been shown to cause autoimmune diseases, such as Wiskott-Aldrich Syndrome, severe congenital neutropenia, and X-linked thrombocytopenia (8). These relevant autoimmune diseases, however, although severe and result in extremely shortened life expectancy, usually affect very little portions of the population (9). On the other hand, DCs are believed to play a central role in the immune system's potential to eliminate neoplastic cells, commonly known as tumor cells, as malignant tumor still takes 7.6 million lives per year (10).

The ability of the immune system to combat tumor growth has been evidenced by the occasional spontaneous remissions of renal cell carcinomas and melanomas (11, 12, 13). While these documented cases are clinical and unpredictable, a study of paraneoplastic neurological disorders discovered onconeural Ags, a group of tumor-targeting antibodies, in this case specifically linked to breast and ovarian cancer (14).

Analysis of DC distribution in breast carcinoma tumor tissues reveals two defining characters: the concentration of immature DCs in tumor bed while the mature DCs are confined to peritumoral areas (15). DC's unique ability to initiate primary immune responses makes it invaluable to vaccination protocols in cancer, while the aforementioned locational distinction requires for the targeted enhancement of DC motility in tumorous areas (12, 16, 17).

DCs loaded with tumor-associated antigens (TAAs) have already shown the ability to induce protective/rejection-immune responses in animal models and promising preliminary data in human; however, current research is looking for ways to mobilize endogenous DCs to perform the same function (18). In the next few years, the current clinical trials with ex vivo–generated DCs will undoubtedly unveil important information of DCs' quality as vectors of immunotherapy. Ultimately, enhanced DC motility is expected to be combined with viral vectors with ligands of interest that incorporate onco antibodies and can either bind nonspecifically or specifically to targeted DCs.

See Appendix 1.3 for references.

Fig. 1 3-D dendritic cell illustration.

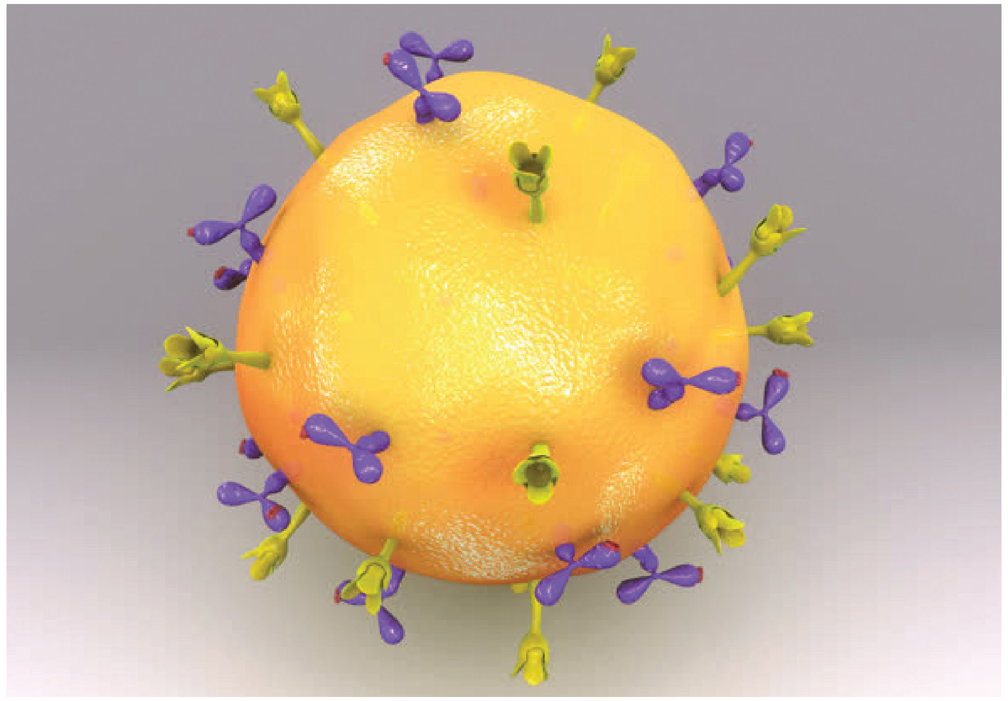


Fig. 2 3-D illustration of an antigen-presenting cell with purple and yellow molecules representing different markers on the surface of the cell.

Carbon on Carbon Action:
GROWING GRAPHENE ON DIAMONDS

ERIC YOU

Graphene, a single layer of carbon atoms, has been one of the most hyped materials these past few years, and for good reason, too. It has demonstrated extraordinary electrical conductivity, thermal conductivity, as well as electron mobility, an essential property of a good semiconductor material . Its super strength and flexibility also arise to applications in flexible touch screens and circuits, as well as energy storage and solar cells. However, since its discovery in 2004, graphene has always been a long way from mass production, because it is still extremely hard to create.

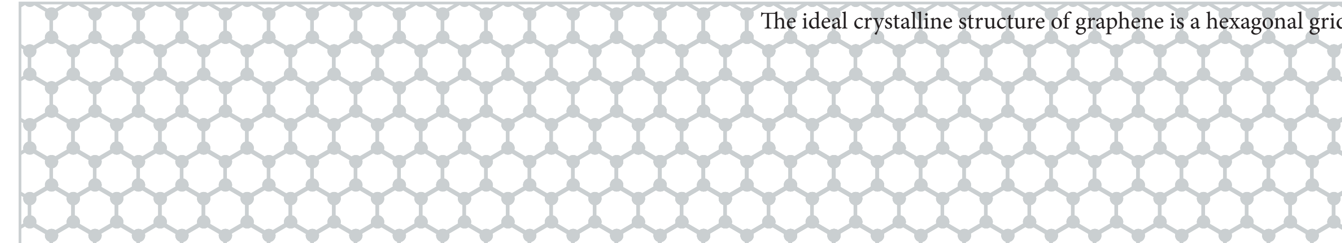
When it was first discovered, researchers used tape to peel layers off of graphite until they isolated a single layer of graphite. This process was known as mechanical exfoliation, and it was extraordinarily laborious. As time went on, however, researchers developed more efficient methods, such as chemical vapor deposition (CVD), which uses metal catalysts as substrates on which graphene grows. This method could quickly create graphene in much larger quantities than before. One method invented was even as simple as applying a layer of graphite oxide onto a DVD, and then burning it with a DVD writer. Yet these processes all lacked the ability to produce large domains (that is, large, continuous sheets) of single layer graphene with relatively few impurities, once transferred onto a usable surface. Furthermore, what they lacked in time efficiency, they did not always make up in cost-effectiveness.

Recently, however, a team led by Materials Scientist Anirudha Sumant with the U.S. Department of Energy's (DOE) Argonne National Laboratory's Center for Nanoscale Materials (CNM) and Materials Science Division, along with collaborators at the University of California-Riverside, has developed a new method to grow graphene that solves just those issues.

Their new process is based off of the rapid thermal annealing (that is, rapid heating and then slow cooling) of ultrananocrystalline diamond (UNCD) in the presence of a Nickel catalyst. UNCD, like in CVD, serves as a substrate, or surface on which graphene grows, as well as the source for the carbon that makes up the graphene sheet (Berman et al., 2016). In addition, UNCD, a synthetic diamond, is the result of years of work by Argonne researchers.

To actually grow the graphene, researchers deposit a 50 nm nickel (Ni) film onto a UNCD surface, which itself is on silicon (Si) (Berman et al., 2016). Once they begin to ramp up the temperatures to 800o to 1000o C, most of the nickel quickly diffuses through the boundaries of between grains of UNCD, and sits at the bottom of the UNCD/Si boundary (Berman et al., 2016). The remaining nickel, described as lone islands, serves as a site of nucleation, or a location where the graphene can begin to grow from, before it also diffuses in diamond (Berman et al., 2016). Sumant describes the Nickel's wondrous role "…like meeting a good Samaritan at an unknown place who helps you, does his job and leaves quietly without a trace" (Grant, 2016). In addition, this process occurs extremely rapidly, or at least compared to conventional methods, because the UNCD beneath is constantly supplying carbon (Berman et al., 2016).

Using this process, the team found that graphene can be grown over micron-size (that is, 10-6 meters, and for comparison our hair is 40-50 microns in diameter) holes laterally, making them completely free-standing (that is, detached from the underlying substrate) (Berman et al., 2016). As a result, it is finally possible to harness the powerful properties of graphene, so long as devices are created directly over the free-standing graphene.



The ideal crystalline structure of graphene is a hexagonal grid

Moreover, this new process is also much more cost-effective than conventional methods where silicon carbide is used as a substrate. Sumant says that these growth methods typically use 3- to 4-inch silicon carbide wafers that cost about $1,200, while UNCD films on silicon wafers cost less than $500 to make (Grant, 2016). Of course, compared to popular methods like CVD, this is still much more expensive, and will require some fine-tuning. On the other hand, though, this new method cuts the amount of time from hours to minutes (Grant, 2016).

Once created, the high quality of graphene was confirmed by the UC Riverside co-authors Zhong Yan and Alexander Balandin, who found the sheet resistance of the graphene films varied from 0.09 ohms per square to 3.1 ohms (Grant, 2016). These are the lowest values of sheet resistance reported so far for multilayer, bilayer, and free standing, single layer graphene, and they solely attribute to the high quality of their graphene (Berman et al., 2016).

Diana Berman, the first author of the study and former postdoctoral research associate who worked with Sumant, similarly remarked "I'd been dealing with all these different techniques of growing graphene, and you never see such a uniform, smooth surface" (Grant, 2016).

Still, the hard work is not yet over, as the Argonne researchers are now refining the process—varying the temperature used to catalyze the reaction, as well as adjusting the thickness of the diamond substrate and the composition of the metal film that facilitates the graphene growth—to not only improve their reaction, but also better study the physics at the graphene-diamond boundary (Grant, 2016). As Berman explains "We're trying to tune this more carefully to have a better understanding of which conditions lead to what quality of graphene we're seeing" (Grant, 2016).

Looking ahead, the researchers have already struck a collaboration with Swedish Institute of Space Physics involving the European Space Agency for their Jupiter Icy Moons Explorer (JUICE) program to develop graphene-coated probes that may help exploratory vehicles sense the properties of plasma surrounding the moons of Jupiter.

Other authors involved in the study were Subramian Sankaranarayanan and postdoctoral students Badri Narayanan and Sanket Deshmukh, as well as Alexander Zinovev and Daniel Rosenmann. Finally, you can find their new paper, "Metal-induced rapid transformation of diamond into single and multilayer graphene on wafer scale," in the online Nature Communications journal.

See Appendix 1.4 for references.

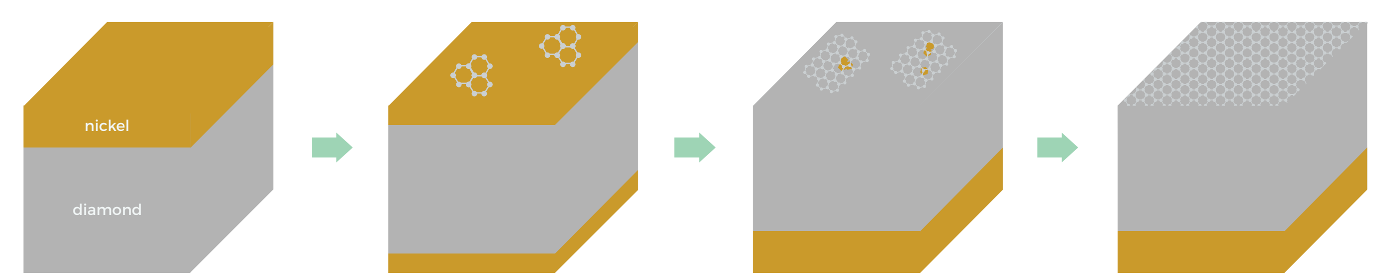


Figure 1: 1. Ni film is deposited onto a UNCD surface. 2. Ni begins to diffuse through UNCD, and graphene begins to grow. 3. Remaining Ni serve as site of nucleation, as more graphene grows. 4.Graphene covers UNCD surface.

TRUST ME, THE PROBLEM ISN'T ROOTED IN THE SOIL!

DAN TRAN

Recently, in August of 2015, our neighbors up North published a paper entitled "Temporal dynamics of plant-soil feedback and root-associated fungal communities over 100 years of invasion by a non-native plant." The authors, Nicola Day, Kari Dunfield, and Pedro Antunes all hail from Canadian universities. In this paper, Day et al. set out to assess whether soil that had been invaded by *V. rossicum* for a longer period of time would negatively affect the growth of new *V. rossicum* in the same soil. They also set out to determine whether the roots of *V. rossicum* coming from older invasion periods would have a greater diversity of fungi that are known to be plant pathogens.

Vincetoxicum rossicum, more widely known as European shallowwort, originated from Western Europe, in the Ukraine and Western Russia (Anon 2016). In the 1800's, *V. rossicum* was introduced to North America, where it settled mainly in Ontario, Canada around the Great Lakes regions (Cappuccino 2004).

Because *V. rossicum*'s native range is in Europe, it is therefore considered an invasive species in North America. By the National Invasive Species Council, which was established in a USDA library, an invasive species is "a species that is non-native to the ecosystem under consideration and whose introduction causes or is likely to cause economic or environmental harm or harm to human health" (ISAC 2006). Invasive species can be of particular interest because of the ways in which they can drastically alter an ecosystem by outcompeting the native organisms for resources. Invasive species often also do not have as many natural enemies in the newly introduced environment, allowing them to flourish.

In the experiment, two things were accounted for: the effect of invasion period on plant growth and the effect of invasion period on pathogen diversity. The authors hypothesized that plants grown in soil that had been invaded by *V. rossicum* for a longer period of time would not grow as much as plants grown in more recently invaded soil. The assumption here as that the plants in older invaded soils would have a larger build up of pathogens, thus negatively impacting the growth of plants. By this logic, they also hypothesized that plant roots taken from soil that had been invaded for a longer period of time would have a greater diversity and amount of pathogens.

So what effect does the invasion time of soil have on *V. rossicum*, one might ask? After a painstaking experimental process, the answer, to put it quite bluntly, was none. The only thing that can be determined for sure from the results was that *V. rossicum* does not grow as well in soil deplete of microbiota compared to soil with biotic factors in it. The plants grown in sterile soil consistently had lower biomasses than the other plants and also generally had a much higher root-shoot ratio, which makes sense because plants struggling to get nutrients from the soil will likely allocate energy to doing so, hurting shoot development and thus having a higher ratio. The plants grown in the soils distinguished by invasion time with microbiota in them did not show any correlation between invasion time and growth.

So if nothing happened for plant growth, then the diversity of root pathogens must have gone up, because otherwise, the experiment would have been worthless, right? Well, unfortunately, there was no correlation found between the roots of different invasion periods and the diversity and amount of root pathogens. Although plenty of fungal, pathogenic DNA sequences were found, there was not any correlation between invasion time and the diversity and amount of pathogens found. Therefore, both hypotheses were proven to be untrue. Something to keep in mind, however, was that the methods never really specified what Day et al. were looking for in terms of root pathogens. In the methods, "A potential pathogen on *V. rossicum* was defined as an OTU in a genus that contained at least one species identified as a plant pathogen on any plant species in the literature" (Day et al. 2015). That is, to say the least, a very broad categorization for what constitutes a pathogen. But, as little research has been done on soil pathogens on invasive plant growth, the method is somewhat acceptable for the technology available.

V. rossicum

One thing of note, however, was that there were plenty of mycorrhizal fungi (AM fungi) found in the roots of *V. rossicum*. Mycorrhizal fungi have a mutualistic relationship with plants, a symbiotic relationship where both members benefit. The fungi benefit the plant by attaching to its roots, extending the roots' surface area and improving their ability to take in water and nutrients. In exchange, the AM fungi receive sugars from the plants (Bonfante 2010). It is a win-win relationship, and perhaps helps explain why the *V. rossicum* in sterile soil did not perform as well as the ones in live soil.

So what about this experiment made it scientifically significant? Well, in other previous studies on invasive plants and pathogens, not much attention had been given to the temporal effect of pathogen accumulation on plants. In other words, not much effort had been directed to actually determining whether or not more pathogens on invasive plants would cause negatively affect their growth. While studies have found correlations between invasion time and pathogen richness, studies have not actually found if more pathogens actually affect the plants over time (Hawkes 2007). By testing the affect of the different soils on the growth of the plants, Day et al. were able to incorporate a new temporal aspect of pathogen invasion into their experiment.

Another component that Day et al. investigated that was rather unique was that they looked exclusively at pathogens found underground in the soil. In a review written by Flory and Clay, they identified pathogens that accumulated above ground, on the shoot part of the plant. These were pathogens such as *Bipolaris*, *pseudonmonas syringae*, and *Erysiphe cruciferarum* (Flory and Clay 2013). *Bipolaris* is a fungus, *P. syringae* is a bacterium, and *E. cruciferarum* is a mildew. All of these types of pathogens infect plants by penetrating their cell walls from above ground, rather than by infecting via the roots. (Domiciano 2013, Kim et al. 2013, Ichinose 2013). Although never fully explicated in the methods section, examples of root pathogens are *Fusarium oxysporum* and *Rhizoctonia solani*. These pathogens are also both fungi (Lichtenzveig et al. 2006). By focusing on the invasion period of the soil, Day et al. were mostly limited to checking plant pathogens in the soil, rather than on the plants. However, the fact that they focused on underground plant pathogens was a novel technique that had not been repeated by earlier experiments of the same nature.

The results of Day et al.'s study compels us to look towards other factors that may impact the growth of these often pesky plants. Of course, since it has been shown that pathogens in the *soil* do not do much in terms of limiting growth, it does not necessarily mean that other pathogens that infect the plant *above* ground would have the same effect. A study that should be performed in the near future should somehow relate above-ground pathogens with the temporal dimension that was utilized in this experiment. Perhaps above ground pathogens tend to have more detrimental effects than soil pathogens to invasive plant growth. As mentioned above, many of the fungi identified in the experiment were the beneficial AM fungi, so by looking to above ground pathogens, an entire group of beneficial fungi can be overlooked.

So, in the end, why should we even care about invasive plants and how they interact with the environment? Well, unless your money tree is immune to fungal pathogens, then there is a good chance you could be affected by the monetary costs of invasive plants. Because invasive plants often come into their new environments with little competition, they can outcompete with native plants and cause massive damage to ecosystems. According to data compiled in 2005, invasive plants, including weeds, cost Americans 34 billion dollars annually! That is in 2005 dollars, the number today must be much higher to account for inflation (Pimental et al. 2004). By learning what positively and what negatively affects the spread and growth of these plants, we can find better (and cheaper!) ways of controlling them.

By keeping in mind that underground pathogens, at least according to Day et al.'s data, do not seem to affect invasive plants, we should make sure that herbicides are made to be directly applied to the plant and not in the soil to try and affect the roots. Most herbicides affect necessary processes of the plant, from inhibiting photosynthesis, synthesis of amino acids, and lipid synthesis among other things (Duke 1990). Herbicides should continue to focus on affecting the above ground parts of plants, not the roots. Besides, by putting herbicide in soil, it can create a harmful environment for other organisms living in the soil.

In terms of regulating invasive plants, another factor to take into account is competition. According to the enemy release hypothesis, invasive plants do so well in their new habitats because they no longer have to worry about the enemies that may have lived in their native habitats. If the plants go to a new habitat without these enemies, then they are "released" from predation by them (Keane and Crawley 2002). Thus, a potential, yet eccentric, way of dealing with invasive plants could be to introduce organisms that are natural enemies to them. Surprisingly, goats and sheep do an incredible job of eating undesirable weeds and leaving grasses intact (Hogue 2014, Adams 2010, Edwards 2011, Latshaw 2009)! Rather than try waiting for pathogen accumulation underground to take care of invasive plants, which if we are to take the conclusion of Day et. al seriously, will never happen, a better idea would be to employ these natural enemies if they do not disturb the rest of the ecosystem. So, feel free to put in your orders for goats and sheep!

Also, if invasive plants enter ecosystems without any competition, they can multiply without bound, crowding out native species and making it difficult for them to live in their natural habitats. By better understanding how to control invasive plant growth, we can take better steps in protecting ecosystems from being damaged.

As for growing plants in general, the study makes it clear that it is always a better idea to grow plants in soil with living matter in it than sterile soil. Biotic factors in the soil like AM fungi can really assist in plant growth while plants growing in biota-less soil have a significantly more miserable time growing.

Overall, more studies should be done on how other plants might collect pathogens underground. The idea of using the invasion time to distinguish soil adds a valuable temporal component to these types of studies, and more experiments of this type should be done to further ascertain the relationship between soil pathogens and invasive plant growth. Although Day et al.'s experiment did not confirm its hypotheses, their results leave us with valuable information that helps us better understand the nature of invasive plants.

See Appendix 1.5 for references.

MATH

GIRLS IN STEM

ELIZABETH TSO

In thirty-five years, only three of the 224 USA national team members sent to the International Mathematics Olympiad (IMO) have been female. That's equivalent to 1.3 percent. You might ask why this astounding gender gap exists in the realm of high level mathematics -- I most certainly hope that you do. But, in the frank words of IMO gold medalist Evan Chen, we've got pretty much "no clue whatsoever."

So, instead, this article is going to be about the hugely important resultant topic: how this deplorable imbalance has impacted the self-worth and achievements of many young women today and what that in turn has done to the STEM community.

As mentioned above, high level science is highly male dominated. Many institutions have tried to remedy this; for example, MIT PRIMES, a competitive research opportunity for high school students, specifically urges females to apply. However, despite the best intentions of these programs, one pretty devastating consequence of this increased desire for female participants is that many people assume accepted females aren't nearly as qualified as their male peers.

A female PA student (who wishes to remain unnamed) recently attended a prestigious STEM summer program. When she placed first on a camp-wide assessment, the counselors so strongly doubted her ability that some wished to reweight the data to create a different winner. Many males at her same demonstrated level of accomplishment had also finished in top spots, and yet no authorities questioned any of their results. Commenting on this, she said, "They thought I got in to fill quotas and not on my brains."

Although this young woman "still absolutely [wants] to get a Ph.D and become a professor one day," it's pretty clear that this level of sexism deters many girls from STEM. Dr. Jeremy Copeland, acclaimed instructor and administrator at the online mathematical academy Art of Problem Solving, explained that some women at UChicago, where he attended, "felt frustrated by others assuming they're not qualified." Furthermore, Evan Chen commented that one factor into high level competition-math performance is “whether you signed up” or not. Though this may seem self evident, it’s pretty easy to see the consequences on the gender gap. Doubted and disrespected, women are more likely to pursue other, non-STEM paths; this then reinforces the stereotype that women are not as good at STEM and therefore that those actually in the field are only there to fill quotas. The vicious cycle perpetuates itself.

But there is hope. In recent years, there have been many programs encouraging more women to pursue math, such as the annual Math Prize for Girls, which was founded in 2009. The Technovation Challenge and the NCWIT Aspirations in Computing are all-girls competitions that provide opportunities in technology and computer science respectively. And here in our own Andover community, according to Michael Ren ’18, in STEM classes, “Everyone trusts each other, and never is the ability of any girl doubted.”

See Appendix 2.1 for references.

SPOTLIGHT ON A SCIENTIST: Ambika M. Krishnamachar

REPORTING BY SHREYA PATEL

Ambika Krishnamachar graduated from Andover in 2011. She then pursued a degree in computer science at MIT. She now works as a Product manager at Uber where she works with teams of software engineers, designers, and data scientists to create new products.

What is the hardest part of your job?

There are two hard things about being a product manager. Firstly, you can’t get as deep with all facets of your project as you want. Secondly, you interact with many people, and issues can pop up, sometimes it is tough to motivate people. You have to figure out how to motivate a group around one vision.

How has your gender shaped your experience as a computer science?

It can be really tough to be a woman in computer science. It can be intimidating and not very inclusive. In college I felt like I didn’t belong. There were very few other girls in my classes. I am a lot more comfortable now, but I still notice that only about 10% of software engineers ware female. I think girls in computer science, and in STEM in general need to receive more support and mentorship. It is really important to remember that you are definitely good enough. Be confident and you will do great.

What has been your greatest failure? What did you learn from it?

At MIT I got started with a project with a professor. I set myself up in a situation where I could not succeed. I did not give myself the time, or the ability to collaborate, or the resources. I ended up dropping out halfway through the term. I learned that to be successful, I had to make sure that I had to put myself it in a situation where I could succeed.

What did your time at Andover teach you?

Andover taught me how to work with people, and live independently. The academic rigor that it provided has been the foundation for everything I’m doing. Andover really inspired me to love learning, and encouraged me to pursue STEM.

AN OVERVIEW OF FINITE GEOMETRY

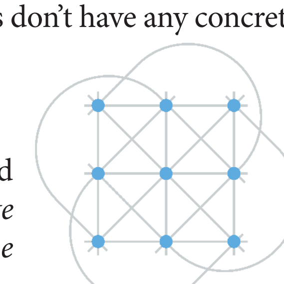
Somehow, geometry with finitely many points is even harder than geometry with infinitely many points

MICHAEL REN

What is finite geometry?

Everyone who graduates from Andover has taken at least one geometry course in their time here or before. Most people struggle with it, but the few people who find it enjoyable soon realize that it is a beautiful subject with many fascinating problems. But just like algebra, once you get to college, everyone makes it really complicated and abstract, because why not? High schoolers do geometry in *Euclidean space*, where everything is nice and flat and square.Other geometries include *spherical geometry*, where your points and lines and circles are now on the surface of a sphere, *projective geometry*, where the ratios of distances between points matter much more than the distances themselves, and *finite geometry*, geometry in a space with finitely many points.

Now, you might be thinking, ”Don’t I already do geometry with finitely many points? If I do a problem about a pentagon and a circle, then I only have a few points that I actually care about and will use.” This geometry is even more finite than that. In your regular geometry, though you only use finitely many points on any problem, you will always have an infinite number of points in your space. In a finite geometry, the universe only consists of N points, where N is some positive integer. Lines are now subsets of these points such that there is a unique line that goes through every two points in our universe and there is a unique point that lies on every two lines in our universe, unless they are ”parallel”, which we will define later. The tricky part here is that most finite geometries don’t have any concrete representations where all lines look like lines. As an example, here is a finite geometry with 9 points and 12 lines, known as the *finite affine plane of order 3 or the Hesse configuration*:



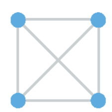
All black paths in this diagram represent lines in the geometry. You can indeed see that every two points lie on a unique line and that every two lines intersect at one point (unless they are parallel). This may be hard to grasp at first, but once people understood this, they were able to extend other concepts such as circles and are now researching how to generalize projective properties.

Axioms of finite geometry and finite projective geometry

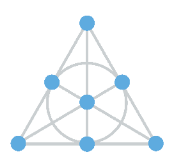
Now that we have a general sense of what a finite geometry is, let’s go over the rigorous definition of it from the basic axioms:

1. Every two points lie on exactly one line.
2. Given a line and a point not on it, there is at most one line through that point that does not intersect the line. If two lines don’t intersect, then they are parallel. (This is known as *Playfair’s Axiom* and is a property of our regular old Euclidean geometry as well as finite geometry.)
3. There are four points, no three of which lie on a line. This is to ensure that the geometry doesn’t just consist of a bunch of points all on a line, which is pretty boring. While this does not necessarily need to be an axiom, it elimi- nates trivial spaces so that results like the Bruck-Ryser theorem (There do not exist finite geometries with N points if $N \equiv 1, 2 \pmod 4$ and N is not the sum of two perfect squares.) hold in general. There is also an analogue of projective geometry in finite geometry. Projective geometry has the property that every two lines intersect, along with all of the other properties of Euclidean geometry. To account for parallel lines, points at infinity are added to our set of points. Each point at infinity corresponds with one value of the slope of a line, and every line with that slope passes through it. All parallel lines with one slope then all pass through that infinity point. Finite geometries like this exist too, but we don’t need points at infinity because there are only a finite number of points. However, when connecting projective finite geome-

tries to things we can understand, it might be helpful to think of some points as the "point at infinity", even though it's just another point in the geometry. The axioms of finite projective geometry are the same, except the condition in the second one is that any two lines intersect instead. Here is the simplest example of a projective finite geometry, known as the *projective plane of order 2* or the *Fano plane*.



This geometry has 7 points 7 lines. The circle in the middle there is actu- ally a line. It is shown like that because there is no good way to draw it. You might have a hard time with finite geometry if you think of lines as lines instead of subsets of the points. We can actually think of the circle there as the line at infinity containing all of the points at infinity. The finite affine plane of order 2 looks like this:



Note that every two lines intersect, except for the pairs of parallel lines AB || CD, AC || BD, and AD || BC. When we extend an affine plane to a projective plane, we add in the points at infinity and put them all on the line at infinity. Of course, we can think of any of those lines as the line at infinity, but because of symmetry the circle is preferred.

Affine?

I'm throwing around a lot of terms like "affine". Before moving on, let's go over what this means and unpack the term "finite affine plane of order 3." An informal definition of an affine space is just a plane or space without an origin. Now, the idea is that operations with vectors and linear transformations (and a translation) in this space are still preserved and are independent of where the origin is. More formally, it has to be a vector space over a field. (A field is just a set of numbers with the property that you can add, subtract, multiply, divide by nonzero numbers like usual.) In finite geometries we will consider finite fields rather than infinite ones like the set of rational numbers or the set of real numbers. For those that know modular arithmetic, the most basic finite fields are those that consist of the residues modulo a prime *p*, denoted by $\mathbb{F}_p$ or the finite field of order 3. Sound familiar? To get the finite affine plane of order 3, we simply take a 2-dimensional vector space of $\mathbb{F}_3$. What we end up with is the Hesse configuration. Now, we define the slope of the line through points (x_1, y_1) and (x_2, y_2) as $\frac{x_1-x_2}{y_1-y_2}$, where this fraction may be undefined. In our configuration below, all points have 4 lines passing through them that consist of all possible slopes, and all lines contain 3 points. This is equivalent to taking $\mathbb{Z}^2$ mod 3, component-wise. Now, projective planes can be constructed similarly. You can also make finite affine spaces, where you take $\mathbb{F}_p^3$ instead of $\mathbb{F}_p^2$. If you know about field extensions, affine and projective spaces consisting of vector spaces of $\mathbb{F}_{p^k}$ can be constructed as well, though they get exponentially more complex.

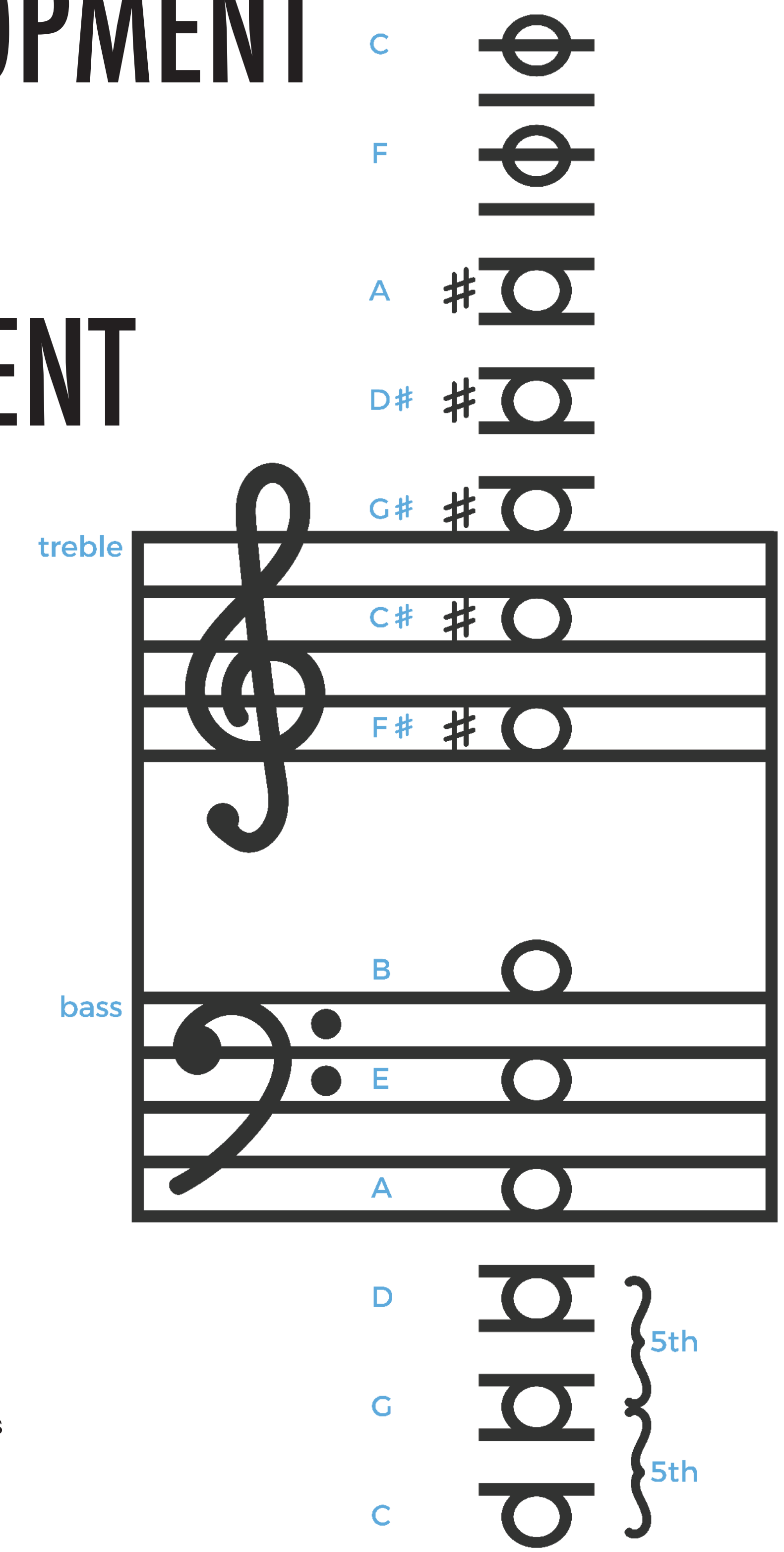
Finite geometry is unsolved

Any regular geometry problem can be put into a coordinate system and 'bashed' out. This is why mathematicians consider Euclidean geometry to be solved, because a computer can do any problem, given enough time and computation. However, this can't be done with nite geometry. For example, one of the simplest yet unsolved questions is: For what *n* does there exist a geometry containing *n* points? The best guess right now is all prime powers that are not primes, and we can show this with our results above. But showing that nonprime-powers can't be the number of points in a nite geometry is extremely dicult. A computer search gets too complicated even for small numbers like $n = 12$, which is still unsolved to this day. Partial results like the aforementioned Bruck-Ryser theorem have been proven, but a full proof becomes dicult without further research in the eld. It is surprising how geometry and number theory, two seemingly unrelated mathematical topics, can be connected through this branch of study. Perhaps this is why people are fascinated with finite geometry.

MATHEMATICS IN MUSIC:

THE DEVELOPMENT OF EQUAL TEMPERAMENT

JP TANG



In the Stone Age, cavemen sang chants in unison or octaves, as other harmonic intervals had not been discovered yet. Then one fateful day, the fifth was discovered by accident, perhaps because someone was singing out of tune and found that this new interval sounded "good". Using a reference pitch and the interval of a fifth, one can derive the entire twelve-note chromatic scale. For example, if we use C as our base pitch and move upwards in fifths, we get the sequence:

C – G – D – A – E – B – F# - C# - G# - D# - A# - F – C

These are the twelve distinct notes of the modern chromatic scale, which almost all Western music uses today. The prehistoric humans soon learned to arrange them such that each note was as possible from its neighbor: C- C# - D – D# etc. The distance between a pair of adjacent notes is called a semitone.

However, a standard system of tuning had yet to be developed. One important thing to note about tuning is human perception: we perceive pitches in terms of logarithms, meaning the distance between a pitch of frequency *k* and another pitch *2k* is perceived to be the same as the distance between pitch *2k* and pitch *4k*. This is because the ratio of pitch frequencies is the same. Therefore, if the distance between every pair of notes in the chromatic scale is to sound the same, the ratio of frequencies between each pair (C: C#), (C#: D) etc. must be equal.

If ratio frequency between any pitch and the pitch an octave above it is *r*, the ratio frequency between any pitch and the pitch a semitone above it is *s*, the frequency of the base reference pitch is f_1, and the frequency of the pitch an octave above the base pitch is f_2, we intuitively get the following relationship:

$$f_2 = f_1 \times s^{12}$$

Because $f_2 = r \times f_1$, we have:

$$r = s^{12}$$

In the time of Bach, musical theorists decided to define *r* to be equal to 2. Then,

$$s = \sqrt[12]{2} \approx 1.0595 \approx \frac{18}{17}$$

The frequency of a pitch is generally measured in terms of Hz (periods/second). With a reference pitch A as 440 Hz, we can calculate the pitch (P_n) of any note based on how many semitones (*n*) it is from A:

$$P_n = 440 * (\sqrt[12]{2})^n$$

n can be negative if the frequency of the pitch is lower than that of A.

We can also calculate the frequency ratio of any musical interval. For example, a perfect fifth is equal to 7 semitones, so we have

$$P_{P5} = (\sqrt[12]{2})^7 \approx 1.498 \approx \frac{3}{2}$$

Similarly,

$$P_{P4} = (\sqrt[12]{2})^5 \approx 1.33 \approx \frac{4}{3}$$

$$P_{M3} = (\sqrt[12]{2})^4 \approx 1.26 \approx \frac{5}{4}$$

$$P_{M7} = (\sqrt[12]{2})^{11} \approx 1.89 \approx \frac{15}{8}$$

If one calculates the frequency ratios of all the intervals, it can be seen that there is a clear relationship between the complexity of the ratio and the perceived consonance (pleasantness) of the harmonic interval. Nominally dissonant intervals have more complex frequency ratios (e.g. M7 has a frequency ratio of 15/8), whereas nominally consonant intervals have more simple frequency ratios (P5 has a frequency ratio of 3/2).

However, there is no proof that such a perception of consonance is universal. For example, in one study, psychologist Tom Fritz lived amongst the Mafa people of Cameroon for some time. The Mafa people had some very strange-sounding music rituals, including "a flute ritual that's extremely disturbing to the Western ear." When played somewhat dissonant 20th century Western music, they did not have as negative a reaction as most Westerners, and they even thought of it as interesting.[1] In addition, scientific explanations for the relationship between complexity of a frequency ratio and its dissonance are often hazy, in the likes of: "More complex ratios are harder for our brains to make sense of," which is clearly a tautology. Perhaps, as 20th-century musical hero A. Schoenberg argues in his Theory of Harmony, consonance and dissonance is merely a social construct set up by musical theorists over time: "These theories … always serve to block the evolution of art!"[2]

See Appendix 2.2 for references.

COUNTING TO INFINITY

SIYE ZHU

Introduction

What is the size of infinity? We have all been taught since a young age that there are infinitely many natural numbers, integers, rationals, and reals. But are they all really the same size? Are there about twice as many integers as positive integers, and are there more rationals than integers? What about reals?

What is Countability?

Our questions can be answered in the realm of real analysis. We must first notice that infinity does not imply uncountability. In fact, with the definitions of infinity and countability in definition 2.2, all countable sets are infinite.

Definition 2.1. A mapping f : A → B is a **bijection** if each element of A is paired with exactly one element of B. See fig. 1 for a visualization.

Definition 2.2. Let $J_n = \{1, 2, \cdots, n\}$, *n* be the set of all integers between 1 and *n* inclusive.

- A set *A* is finite if there is a bijection between J_n and *A* for some positive integer n; *A* is **infinite** otherwise.
- A set *A* is countable if there is a bijection between $\mathbb{N}$ and *A*; *A* is **uncountable** if it is neither countable nor finite.

Intuitively, such a definition of countability is equivalent to enumerating the elements of a set in a specific order while making sure that all elements of the set is accounted for. We may use this definition to approach some of the most common sets, and obtain the following obvious results:

Example 2.1. $\{1, 2, 3\}$ *is finite.*

Example 2.2. $\mathbb{N}$ *is infinite and countable.*

We now move on to some less obvious examples.

Example 2.3. *The set of all positive even numbers is countable.*

Proof. Let the set of all positive even numbers be *E*. We may define $f : \mathbb{N} \to E$, such that $f(x) = 2x$, and we obtain a bijection. This can be seen in fig. 2a

Example 2.4. $\mathbb{Z}$*, the set of all integers, is countable.*

At first glance, this seems impossible. Our intuition tells us that there are twice as many integers as natural numbers. After all, don't integers exist in pairs symmetric around 0? Not quite so. To prove this seemingly counterintui-

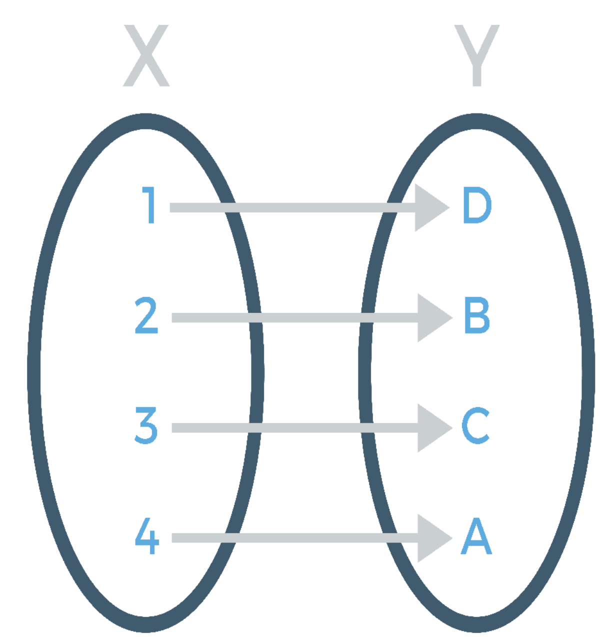


Figure 1: Bijection

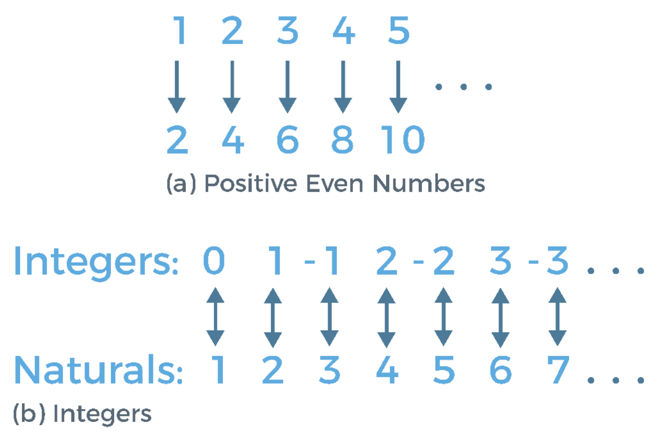


Figure 2: Examples of Countable Sets

tive result, it suffices to find a correspondence between the two infinite sets, and here is how.

Proof. Define $f : \mathbb{N} \to \mathbb{Z}$ as

$$f(n) = \begin{cases} 0 & \text{if } n = 0, \\ k & \text{if } n = 2k \text{ for } k \in \mathbb{N}, \\ -k & \text{if } n = 2k - 1 \text{ for } k \in \mathbb{N}. \end{cases}$$

Visually, we start from 0 and we count by jumping to the left and to the right of the origin alternately.

Therefore, the set of integers is also countable.

Filling in the (W)holes

So far, we have looked at a few example of sets of integers, and concluded that they are all countable. In fact, all subsets of countable sets are countable; it suffices to skip the numbers that we have left out in our subset when we are counting! That said, all subsets of $\mathbb{Z}$, i.e. all sets that consist entirely of integers and integers only, must be countable because we have already showed in example 2.4 that $\mathbb{Z}$ is countable.

However, if we look at the real number line, integers are only a very "small" subset of all the values that we encounter in our math and science classes. Between two neighboring integers, there are infinitely many rationals and real numbers. Therefore, the question arises: are there really more rational numbers than integers? What about reals?

Example 3.1. *$\mathbb{Q}$, the set of all rational numbers, are countable.*

Proof. It suffices to limit ourselves to the set of all positive rational numbers, $\mathbb{Q}^+$. If $\mathbb{Q}^+$ is countable, than we may extend our argument to $\mathbb{Q}$ similar to our trick in example 2.4. See if you can convince yourself that this is true.

We now show that $\mathbb{Q}^+$ is countable. Note that all elements of $\mathbb{Q}^+$ can be expressed as the fraction $\frac{p}{q}, p, q \in \mathbb{N}$. We make an infinite table of rational numbers, such that the n-th row consists entirely of rational numbers with numerator n, and the m-th row consists entirely of rational numbers with denominator m. We now start from the top left corner and count in the order indicated by the pink arrows in fig. 3, skipping over the reducible fractions (crossed out in the figure).

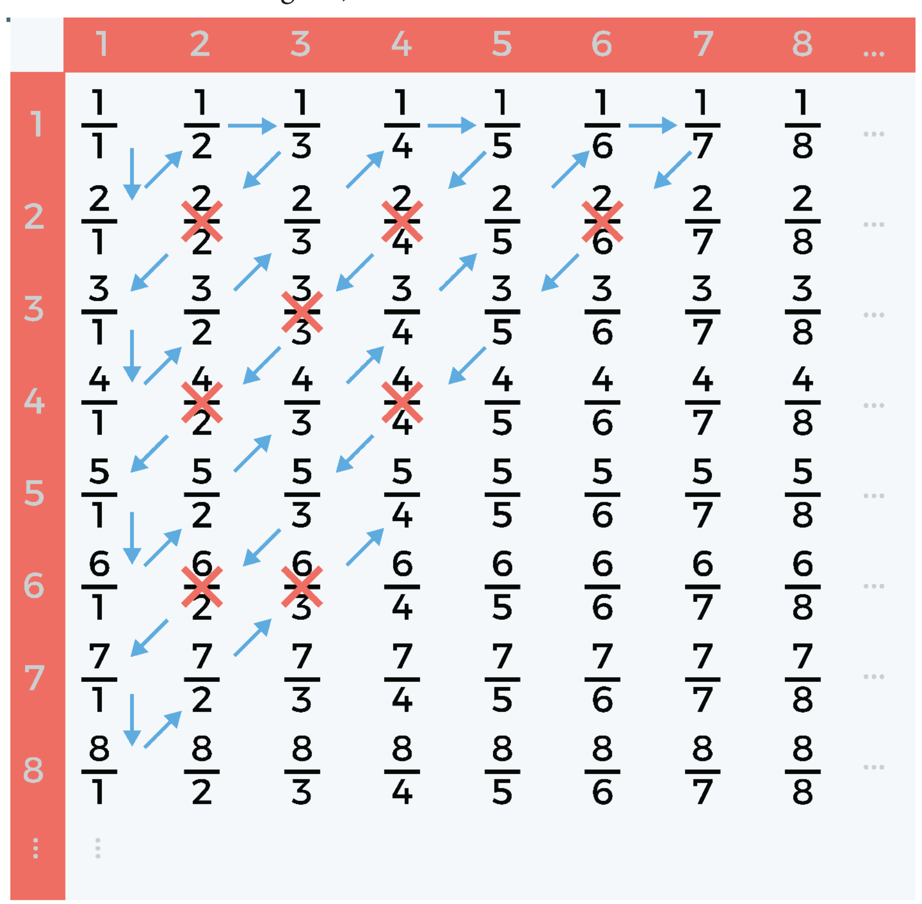


Figure 3: Rational Numbers

Therefore, $\mathbb{Q}^+$ is countable, and $\mathbb{Q}$ is countable.

Example 3.2. *$\mathbb{R}$, the set of all real numbers, is uncountable.*

Proof. Assume for the sake of contradiction that these real numbers are countable. We may find a bijection f from $\mathbb{N}$ to these numbers, say, as follows:

$$f(1) = 6.\boxed{4}78563487\ldots$$
$$f(2) = 1.2\boxed{9}76523\ldots$$
$$f(3) = 0.43\boxed{7}565674\ldots$$
$$f(4) = 9.487\boxed{5}65648\ldots$$
$$f(5) = 3.5489\boxed{1}5747\ldots$$
$$\vdots$$

We take the n-th decimal place of $f(n)$, and we obtain the following value:

$$n = 0.49751...$$

We then increase each of the decimal places by 1, wrapping 9 back to 0, and we obtain the following real number:

$$n' = 0.50862...$$

Note that for all $m \in \mathbb{N}$, this value differs from $f(m)$ on the m-th decimal place. Therefore, $n' \in \mathbb{R}$, but there does not exist a natural number m such that $f(m) = n'$, contradiction. Hence, the bijection cannot exist, and real numbers cannot be countable.

You may wonder why we cannot use the same argument to show that $\mathbb{Q}$ is "uncountable." This is because n' that we obtain through this mechanism is definitely a real number, but we have no guarantee that it is rational.

The above proof is widely known as Cantor's diagonal argument, first published by the mathematician Georg Cantor in 1891. We will revisit this idea later on.

The Sizes of Infinity

We may conclude from example 3.1 and example 3.2 that infinity comes in different sizes. While the sets $\mathbb{N}$, $\mathbb{Z}$, $\mathbb{Q}$ and their subsets are all countable and therefore of the same size, $\mathbb{R}$ is uncountable and of a bigger size.

What are other sets that may not be countable? A good example would be the power set.

Definition 4.1. *The* **power set** *of set S is the set of all subsets of S.*

Example 4.1. *The power set of* {1,2,3} *is* {{1, 2, 3}, {2, 3}, {1, 3}, {1, 2}, {1}, {2}, {3}, ∅}

Example 4.2. *The power set of $\mathbb{Z}$ is uncountable.*

Proof. Let the power set of $\mathbb{Z}$ be P. Assume for the sake of contradiction that there exists $f : \mathbb{N} \to P$. Let $M = x | x \in \mathbb{N}, x \notin f(x)$, so $M \in P$. Note that this denition of M revisits the idea behind Cantor's diagonal argument.

We now show that there does not exist natural number m such that $f(m) = N$. To prove this, we consider whether m is in M:

- If $m \in M$, then by definition of M, $m \in f(m) \Rightarrow m \notin M$, which is a contradiction.
- If $m \notin M$, then by definition of M, $m \notin f(m) \Rightarrow m \in M$, which is a contradiction.

Therefore, there does not exist $m \in N$ such that $f(m) = M$.

We may expand our argument above and show that there does not exist a bijection from any set to its power set. In other words, the power set of S is always bigger than S itself. The details of the proof are left to the readers.

Our proof of example 4.2 reaffirms that there are different sizes of infinity. However, are these the only levels of infinity, or are there other infinite sets that are bigger than P or that have sizes between P and $\mathbb{N}$? Such questions are beyond the scope of our discussion, and we encourage the readers to find the answer through their exploration of set theory.

See Appendix 2.3 for references.

TECH + ENG

GENETICALLY MODIFIED ORGANISMS: SINISTER OR SAVIOR?

ANDIE PINGA

CONTAINS GENETICALLY MODIFIED ORGANISMS.

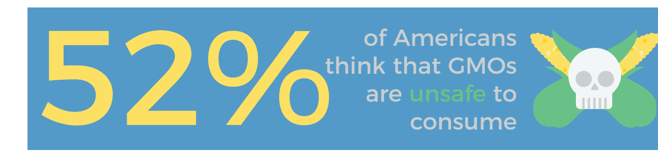
These four words incite fear and recoil among the population of grocery-goers and concerned families in the United States. Genetically modified organisms (GMOs), have become a widespread controversial topic among food scientists, farmers, government law-makers, and the general public for the last 50 years (Ben-Shahar, 2016).

A genetically modified plant or animal contains genes that had not inherently occurred in their DNA. Their DNA is modified by transferring individual genes from a "source organism" to a "target organism." GMO plants are the only type of genetic modification legal in the United States, so these practices are largely targeted to produce crops that are resistant to insect damage and herbicide usage (Abou-Gabal, 2015).

The first FDA-approved GMO product appeared in markets in 1982. Since then, the use of GMOs has become a relatively common practice among major crops in the United States. 90% of all soybean, cotton, and corn acreage is used to grow genetically engineered (GE) crops. Other common GMO foods include sugar beets, alfalfa, canola, papaya, and summer squash. Apples that don't brown and bruise-free potatoes have also been recently FDA-approved. Furthermore, most of the feed consumed by animals contain genetically modified crops (Johnson and O'Connor, 2015).

Although it's an integral component in food consumption in the United States, there is large backlash and splitting controversy regarding the safety and consequences of using GMOs. The arguments against GMO usage mostly cite its potentially harmful effects on humans, the environment, and on the agricultural economy. The Non-GMO Project states that GMOs are "unstable combinations of plant, animal, bacterial and viral genes that did not occur in nature or through traditional crossbreeding methods" (The Non-GMO Project, 2016). There is high concern that these GMO products will lead to health complications such as cancer, obesity, gastrointestinal tract illnesses, kidney disease, disorders such as autism spectrum, and allergies (Committee on Genetically Engineered Crops: Past Experience and Future Prospects, 2016).

In addition to possible disastrous outcomes in regard to human health, the Non-GMO Project cites that the farming economy and environment will be led into disarray if GMOs are implemented. Farmers who practice organic methods can have their fields contaminated with GMO crops that are transmitted through the wind. This reduces seed purity and value, and also leaves the farmer vulnerable to lawsuits because GMOs are patented products. In addition to farmers, the environment is harmed due to the evolution of "super weeds" and "super bugs" as toxic herbicides are used more often against stronger



GMO crops. Furthermore, organisms are feared to go extinct once they are replaced by stronger species (The Non-GMO Project, 2016).

These arguments are used consistently against the use of GMOs. However, there is no scientific evidence that supports these claims – in fact, the data supports the opposite. These myths about the negative impacts of using genetically modified foods have been completely invalidated by the scientific community (Norris, 2015).

The study conducted by the National Academy of Science (NAS) was considered to be "the long-awaited, mother-of-all-studies on the science of GMOs," according to Forbes magazine (Ben-Shahar, 2016). The NAS is known for their careful and meticulous methods and overall credibility. Issued in May 2016, the study examined over 400 pages of evidence and studied 20 years of data to confirm that "while recognizing the inherent difficulty of detecting subtle or long-term effect in health or the environment, the study committee found no substantial evidence of a difference in risks to human health between currently commercialized genetically engineered (GE) crops and conventionally bred crops, nor did it find conclusive cause-and-effect evidence of environmental problems from the GE crops" (Committee on Genetically Engineered Crops: Past Experience and

Future Prospects, 2016).

Contrary to claims by the Non-GMO Project, the NAS found favorable economic outcomes for farmers using GMO crops, mostly depending on the institutional support and access to profitable local and global markets, especially for resource-poor farmers. In addition, crops that contained insect resistance from the soil bacterium Bacillus thuringiensis (Bt) resulted in reduced crop losses, higher insect biodiversity, and lower usage of insecticide. In regard to the concern of "super bugs," the NAS found that the insects were slow to evolve, and implementing resistance management strategies addressed this issue. These outcomes were similar in regard to herbicide usage. The NAS acknowledged that it was difficult to make definite conclusions because of the complexity when dealing with the environment, they had found no conclusive evidence of consequential environmental problems (Committee on Genetically Engineered Crops: Past Experience and Future Prospects, 2016).

A 2015 paper by Stefaan Blancke, a philosopher at Ghent University and co-editor of Creationism in Europe, argues that the public opposes genetically modified organisms so fervently due to a psychological element. "Psychological essentialism" is a mindset where DNA is believed to be an organism's "essence," and tampering with the immutable core would deform the organism's identity. In addition, Blancke argued that religion is a factor in observing GMO practices as "unnatural," as biochemists are "playing God." The assumption that GMOs contaminate the world's natural pool of species simply leads to disgust (Blancke, 2015).

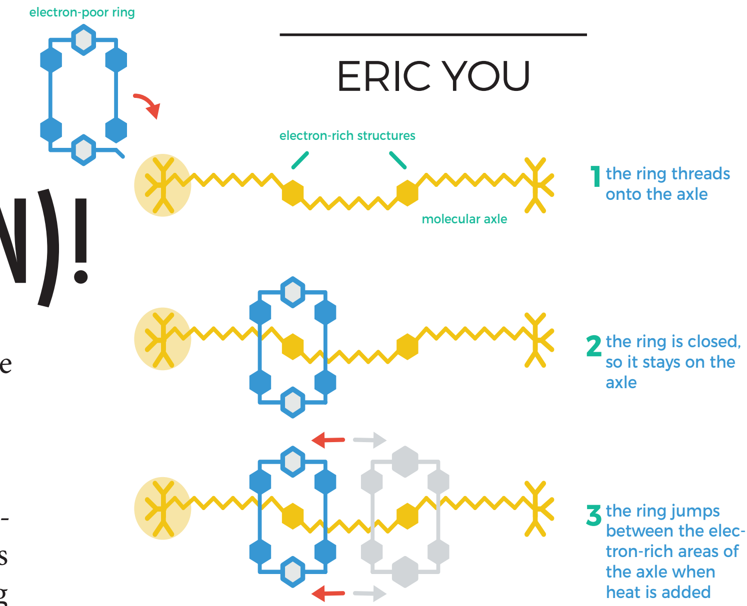
The resistance against GMOs can lead to severe consequences. The United Nations predicts that the world population wile reach 8.5 billion by 2030, and 9.7 billion by 2050 (UN News Centre, 2015). Modern processes aren't even enough to sustain today's population. Breeding missing nutrients into staple crops is cost-effective and is able to reach remote rural populations. Furthermore, malnutrition is directly linked to poverty. The elimination of malnutrition is a massive step towards the elimination of poverty (Lynas, 2013).

Using GMO crops doesn't eradicate organic and non-GMO farming. Organic practices are only sustainable on a small-scale, and will fail to feed the 8.5 billion people expected to arrive in the next 14 years (Abou-Gabal, 2015). A mixture of organic and GMO farming is required. Traditional practices have already proven to be effective in growing healthy food, but it is important to realize that progressive, innovative processes are crucial for a rapidly expanding world. Solving the massive problem of food insecurity may seem impossible, but creating a mindset open to change is the first step.

See Appendix 3.1 for references.

SLOW AND STEADY WINS THE RACE (FOR INNOVATION)!

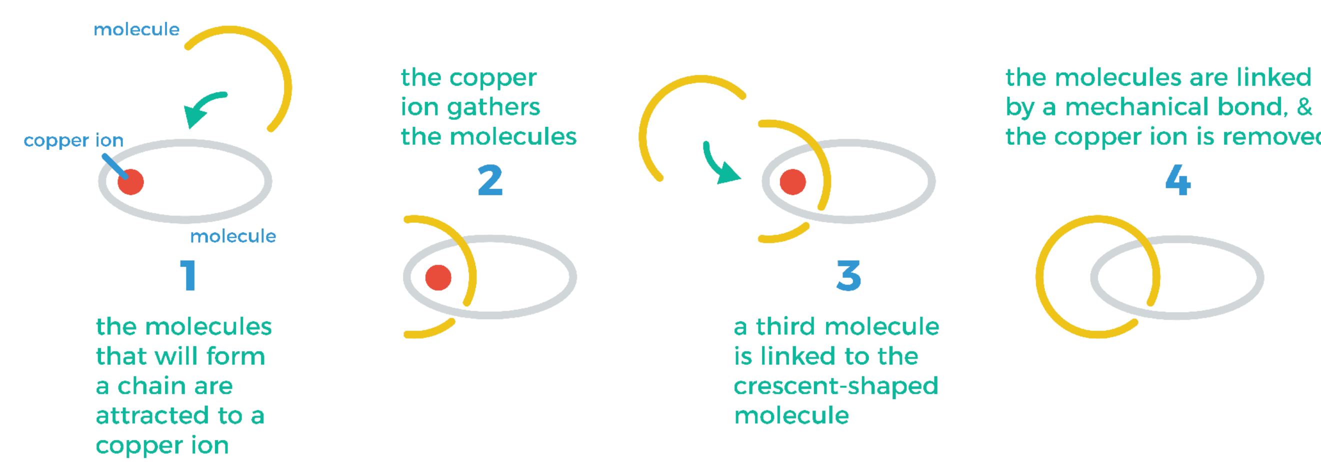
ERIC YOU



Vroom, vroom! The cars rev up and begin the race, racing along the gold floor. in Toulouse, France in 2017. At subzero temperatures of -268oC, surrounded in an ultra-high vacuum, these cars are more than special—they're nanocars. Powered by molecular "engines", nanocars represent more than 30 years of efforts creating molecular machines, by Jean-Pierre Sauvage, Sir J. Fraser Stoddart, Bernard L. Feringa, and countless others. Even more recently, these three scientists were the recipients of the 2016 Nobel Prize in Chemistry "for the design and synthesis of molecular machines."

It all started in 1983, when Jean-Pierre Sauvage, now a Professor Emeritus at the University of Strasbourg in France, created a new method for synthesizing catenanes which are two or more ring-shaped molecules linked together. His method, the metal template synthesis allowed for much greater yields than before, revolutionizing the production of catenanes, and reviving the field of research. In the process, Sauvage used metal coordination to thread a crescent into another ring, before closing the crescent structure into a ring. As a result, they were able to create quite exotic structures much more easily using their template synthesis. Furthermore, the linking found in a catenane chain created a new type of bond: a mechanical bond. A mechanical bond is physically freer than the covalent bonds that typically join molecules—paving the way for rotational motion, as well as the synthesis of future molecules such as rotaxane.

The next step was made by Sir James Fraser Stoddart, currently a Professor of Chemistry at Northwestern University, when he created the rotaxane

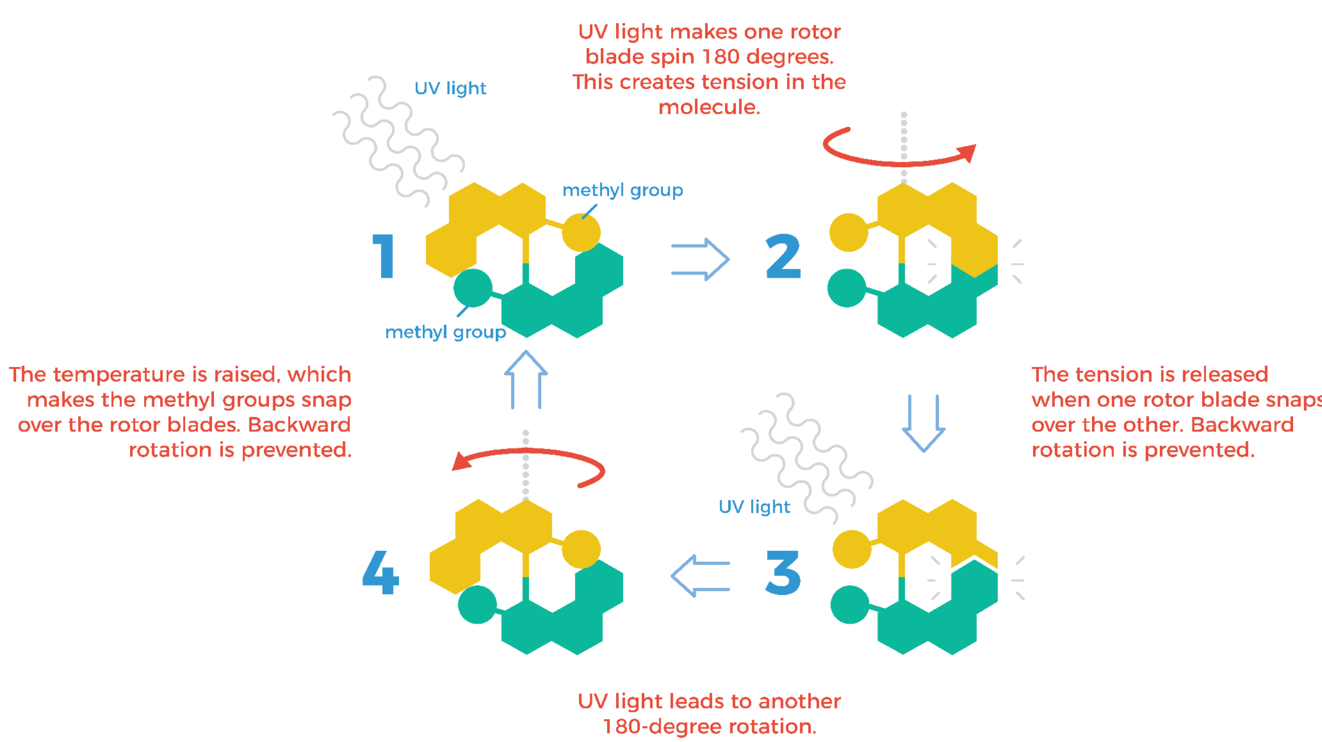


in 1991. The rotaxane is a ring-shaped molecule free to move about on a molecular thread—the molecular analog of a wheel and axle. Specifically, Stoddart's work showed the creation of a molecular shuttle, in which the ring could move left and right along special molecular "stations" on the thread. Although simple in its design, Stoddart's research paved the way for the creation of molecular machines, as by changing the types of stations, Stoddart's team envisioned that as it becomes "possible to control the movement of one molecular component with respect to the other in rotaxane, the technology for building "molecular machines" will emerge."

The final step came in 1999, when Bernard L. Feringa, a professor in Organic Chemistry at the University of Groningen in the Netherlands, created the first example of controlled unidirectional rotation—a necessary feature to any rotational motor. At the time, he used UV light to drive two rotors, and used the structural geometry of the locked, double bond in the molecule to prevent backwards rotation. In this process, known as photochemical E-Z isomerization, UV light provides the necessary energy for one rotor to rotate 180o, transitioning into a state of high tension. The tension is then relieved when the energy's light provides the necessary energy to move the opposite rotor, in the opposite direction, relieving the tension, and restoring the molecule back to its original state. Feringa later devised an even more promising method of rotary, unidirectional motion using chemical energy in 2005. Of course, with the successful demonstration of a molecular motor, the path to new technology was complete.

Now, the field of nanotechnology has expanded enormously, all due to the profound innovations of these three scientists. Molecular switches have been created out of rotaxane, Molecular pumps have also been made out of rotaxane-like structures, and of course, nanocars have been created by Feringa and others, such as James Tour, of Northwestern University. The first nanocar race has even been scheduled for 2017 in Toulouse, France, featuring 6 teams in total, all with their own unique design. With these molecular machines finally finding applications, the future looks quite promising. Perhaps, one day, we'll be able to look back, and trace the development of nanotechnology, like we can now with the impact of the electric motor. Until then, as Feynman duly noted: "there's plenty of room at the bottom" for more innovation.

See Appendix 3.2 for references.



GENETIC ENGINEERING: YAY OR NAY?

KAITLIN LIM

Cloudy grey eyes? Check. Jet black hair? Check. Laser vision and superhuman strength? Check and check.

Of course, this is far from the truth regarding modern genetic engineering. Technology has yet to enable people to design their own babies. However, current technology has already proven to have benefits for many—especially embryos harboring fatal congenital diseases, but some theorize that genetic engineering can wreak havoc upon humankind. By inspecting the history and impact of genetic engineering, one can see that this field epitomizes modern scientific breakthroughs regardless of possible advantages and disadvantages. But it is hard to believe that one of the greatest topics of contention first rose to prominence after two professors experimented with strains of bacteria.

The year is 1973. One man, residing in his laboratory at the University of California in San Francisco, is working with restriction enzymes, which are produced by bacteria to counter sieges from bacteriophages. Another man is working in his research laboratory at Stanford University, experimenting with plasmids, or circular units of DNA exchanged by bacteria.1 These men are Herbert Boyer and Stanley Cohen respectively, and they are the fathers of modern genetic engineering. Through their collaboration, the two researchers found a way to replicate an E. coli bacterium that is resistant to the antibiotic tetracycline. They even proved the feasibility of interspecies gene swaps when they took the DNA from the bacteria *Staphylococcus* (which causes staph infections) and successfully combined it with the DNA of *E. coli*.2

Boyer and Cohen's work with genetic engineering in small organisms soon kickstarted the biotechnology industry. Now, with technology improving at a rapid pace, genetic engineering is having a wider and wider reach. Many geneticists and molecular biologists have also been spurred into action by CRISPR-Cas9, which is DNA taken from bacteria that can act as a word processor, can snip and modify genes—even those of a human embryo—to the heart's content.[3] How did such a thing come about? To put it simply, CRISPR, which stands for Clustered Regularly Interspaced Short Palindromic Repeats, are repeating sequences of genetic code with "spacers." These spacers can be transcribed into genetic code that can match another portion of the DNA. From then on, Cas9, which is one of the enzymes that CRISPR creates, can either shut down or activate the targeted DNA.[4]

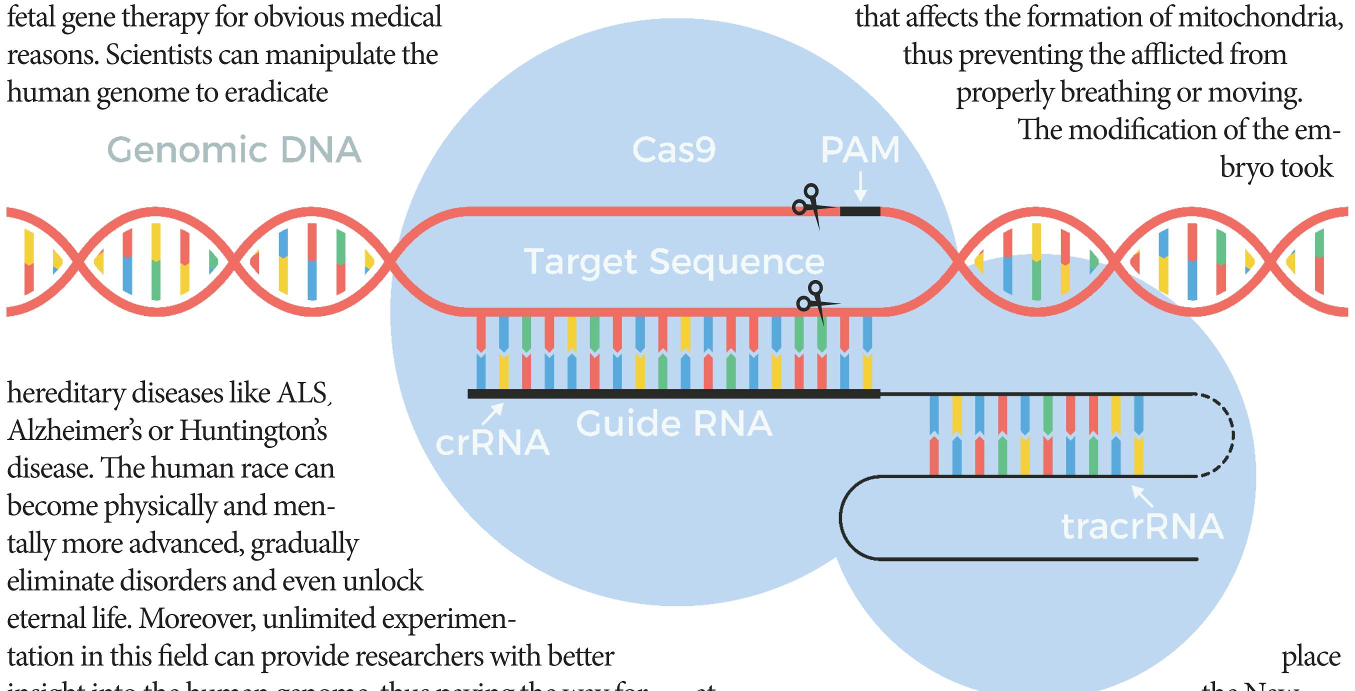
There has obviously been a considerable amount of backlash accompanying discoveries such as CRISPR. Scientists are debating the ethical, social and political implications of possessing such a life-changing tool. One of the longest-occurring debates were about the safety of genetically modified organisms, or GMOs. As a result of the way their genes have been edited, a few scientists are skeptical about "synthetic" organisms, citing allergic reactions, sick livestock and even damaged organs within the animals that have been genetically modified. On the opposing side, researchers have conducted studies that, when inspecting plants/animals that have been properly genetically modified, there are no following health ramifications.[5]

Concerning human genetic engineering, there are many potential benefits and consequences that geneticists have been juggling back and forth. Some advocate fetal gene therapy for obvious medical reasons. Scientists can manipulate the human genome to eradicate hereditary diseases like ALS, Alzheimer's or Huntington's disease. The human race can become physically and mentally more advanced, gradually eliminate disorders and even unlock eternal life. Moreover, unlimited experimentation in this field can provide researchers with better insight into the human genome, thus paving the way for possible medical/technological advancements.

Those against genetic engineering cite potential class divisions and trial errors as reasons to curb research in this field. When experiments go wrong, scientists are scrapping fetuses. That is identical to abortion to some. Many are also tentative about successfully genetically modified humans. If they are not "engineered" correctly, society will have to deal with new cases of physical/mental illnesses regarding erroneously created babies. Bioethicists also allude to the plausible threat of decreasing genetic diversity. If many people are created with one specific image in mind, humankind will be more prone to natural forces. Additionally, genetic engineering is rather pricey, making it a privilege that only the wealthier classes can obtain. Therefore, if it became the norm to customize a fetus to be superhuman, the lower classes would be stuck being genetically inferior as the upper classes lead elite, sickness-free lives. This would immediately tip the scales in favor of the upper class. Genetically modified humans would assume higher positions in social and economic structure whilst the lower classes are stuck scrambling up the ladders. *Gattaca*, anyone?

Nonetheless, genetic engineering, either in animals or humans, has already begun to make significant change. For example, after a fertility procedure at a Mexican clinic, a baby was born in New York to not two, but three parents. The baby was the couple's third attempt at having a child. The two preceding it had died shortly after birth from Leigh syndrome, which is a congenital disease that affects the formation of mitochondria, thus preventing the afflicted from properly breathing or moving. The modification of the embryo took place at the New Hope Fertility Center clinic in Mexico, as the United States federal government issued a ban on attempting such procedures. The technique itself, supervised by Dr. John Zhang, was to move the DNA from the egg of the mother to the egg of a donor with healthy mitochondria. Now, with the baby being healthy at five months, many scientists have found this medical breakthrough as an opportunity to advocate the benefits of gene therapy.[6]

Genetic engineering, with its revolutionary benefits and potentially terrifying consequences, typifies the modern scientific breakthrough. It can solve medical conundrums save millions, but can also act as the great divide between classes, or worse, exacerbate genetic problems by creating a new category of disorders. Is genetic engineering worth the risk, or is it better to nip it in the bud while it is still possible?



See Appendix 3.3 for references.

DRONES IN PRECISION AGRICULTURE

ALEX KARIM EL ADL

Before we tackle the uses and importance of drones employed in agriculture we must first understand the concept of precision agriculture. Precision agriculture is a farming management method based on observing, measuring, and responding to minute variations in crops within a field or between fields. These variations could be the moisture level of plants or the ground, amount of chlorophyll in leaves, mineral levels in the soil, or pests on the crop. These factors are monitored by sensors and allow farmers to act accordingly in order to increase their farm's efficiency. For example, if collected data indicates that a certain type of bug is feeding on plants in one patch of a field, a farmer would spray a specific pesticide in exact amounts on only that area of the field.

Precision agriculture is superior to old school farming methods because as farms have become larger and more industrialized they must also become more efficient to limit crop losses and their impact on the environment. In our previous pesticide example, precision farming helped the farmer save the crop while reducing the amount of pesticide used, which saved money and did not damage the environment as much through chemicals that poison the groundwater. Farmers that do not employ precision agriculture must spray multiple types of pesticides on their entire crop each season, fertilize the whole field, and guess when and where water is needed. This lack of specific data reduces the efficiency and profitability of the farm immensely through wasted resources and lower crop turnout.

The advancement of the agricultural industry is becoming increasingly important because of the increasing population and consequences of traditional farming methods. We have been using the same techniques for more than 10,000 years, after all, and we cannot keep guessing on how to best grow our food. Farming is becoming more and more industrialized and large scale. In 2014 agriculture was estimated to be a 3.348 trillion-dollar industry ("Agriculture, Value," 2016). The problem with this is that farms today contribute 24% of greenhouse gas emissions, account for 70% of water withdrawal from bodies of water, take up 37% of Earth's landmass, and chemicals used to grow crops pollute the groundwater and poison livestock (Ranganathon, 2013). Furthermore, by 2050 there will be 2 billion more people on Earth that must be fed. This will require an estimated 69% increase in food production through agriculture (Ranganathon, 2013). Precision agriculture does not only save tons of money by increasing crop turnout but is the key to solving this food crisis. Among other things, precision farming reduces water used, chemicals sprayed, fertilizer wasted, and allows more food to be grown in a smaller area. To achieve food sustainability without surrendering anymore land or natural resources to farming, we must revolutionize the agricultural industry and bring it into the twenty-first century by implementing high tech drone crop monitoring and data

analysis systems.

The leading precision agriculture solution, currently, is to employ drones to monitor large swaths of farm land and notify farmers what variables they must adjust for each section of plants to ensure maximum efficiency. These fixed wing or multirotor drones in agriculture are specially outfitted with sensors to analyze specific values as they fly over the crops. They are sometimes paired with sensors in the ground and the data collected will then be sent back to the farmer to adjust farming strategies. This allows farmers to analyze crop turnout and efficiency over many years and lets them grow more crops, make more money, and be more sustainable. The use of drones in precision agriculture is currently surging and many different solutions and products have been created and new, innovative products are being worked on today.

An example of an agricultural drone I will be using is the solution created right here at Phillips Academy by students: Ruide Wang ’18, Kunal Vaisnavi ’18, Vish Dhar ’19, and Alex El Adl ’19 (myself) in the 2016 Real World Design Challenge. Our current solution consists of a commercial foam airframe with a 1.8-meter wingspan that carries a video camera for surveying land and a multispectral sensor that collects all of the crop data necessary for the farmer. A multispectral sensor collects image data at multiple frequencies across the electromagnetic spectrum, including light from frequencies beyond the visible light range. It works by emitting light and then measuring reflected rays. We used a sensor with five filters to separate bands of light. The frequencies detected are: red, green, blue, red edge, and NiR (near infrared). As our drone autonomously flies over the farmer’s crops our sensor collects raw data which is later processed by a computer to determine moisture content of surfaces, chlorophyll within leaves to determine overall plant health, egg clusters of pests on the crop, and much other useful information. This drone covers a 1 mile by 2 mile farm in only 31 minutes at 74 miles per hour and can scan stay in the air for up to 2 hours for larger area of land. It is operated by two employees that execute each sensing mission and analyze the resulting data so farmers must not be trained or waste time. Our bi-weekly crop monitoring service is sold as a subscription and is currently priced at only a few hundred dollars per month to be affordable to farms of different calibers. This product pays for itself and even increases profits of the farm after just one harvest season so it will be a worthy investment for farmers. Our product is only one example of drones being applied in precision agriculture and while this specific drone is barely past its preliminary design stages there are hundreds of other companies operating today that offer similar services.

Drone solutions like ours will definitely revolutionize the agricultural industry by impacting the way farms operate and the way we think of farms. Farms are no longer dirty and unsophisticated but high tech, incredibly complex, and essential to the survival of the expanding population. Drones monitor moisture level in plants, chlorophyll in leaves, moisture level, and minerals in the soil to help farmers adjust levels and types of fertilizer, pesticide, and change watering techniques or the crop. This increases crop turnout to feed the exploding population, raises profit for the farmer, and decreases harmful effects of farming practices on the environment. In the future these types of efficiency boosting farming solutions will be imperative and the use of drones is emerging as the leader on this front.

See Appendix 3.4 for references.

BIOMECHANICS:
AN OVERVIEW OF ANKLE-FOOT PROSTHETICS

JOCELYN SHEN

The foot functions as a shock absorber, stabilizer, and mechanism of progression. These functions are observable in the bipedal gait cycle, which is the sequence of events during locomotion. When the foot first makes contact with a surface, it absorbs the force on the muscles by using ankle motion. In prosthetic foot designs, springs and other elastic mechanisms are commonly used to mimic the ankle’s motion. The human ankle efficiently provides energy return from the contact motion and body weight further propels a person forward. Lower-limb amputees with varying requirements have varying prosthetic foot designs. Runners, who have high energy return demands, typically require designs with stronger springs, allowing them to “bounce.” Hikers, who travel through uneven terrain, require more ankle flexibility so they can balance more easily. During midstance, the foot, particularly the arch and ankle, provides weight-bearing stability by adapting to uneven surfaces. At the end of the gait cycle, during progression, dorsiflexion creates tension within the foot, locking the foot and ankle to create a sort of lever for the foot to rock through.

Our understanding of the gait cycle and how the foot works is essential to the process of designing a suitable prosthetic foot. In some active prosthetics, the ankle adjusts to changes in the ground condition based on sensor readings that measure the forces on the device. These sensors measure changes in gait phase in order to create more comfortable, natural, and precise motion. One way to study this cycle and the effectiveness of a design is to study the mechanics of the ankle-foot system during stair ambulation. Many lower-limb amputees experience kinematic asymmetries when climbing up and down stairs and by studying the differences in motion during stair ascent, descent, and walking on level ground, prosthetists can generate data to help design feet with wider ranges of motion. Adaptable ankle-foot prostheses are available to best mimic the human foot during stair ascent and descent, however there are still limitations to current designs.

As important as mobility is in designing a prosthetic ankle-foot system, it is equally as important to minimize load on the residual limb. While increasing the elastic response of the foot increases the energy returned to the limb during late stance of the gait cycle, this increased energy return puts pressure on the residual limb, which can often result in discomfort. This is why the middle and late stance of the gait cycle is equally as important as energy return in the foot design. Prosthetic ankle-foot systems are typically stiffer than the anatomical ankle-foot system, which can induce moments onto the residual limb and contribute to skin breakdown. Prosthetic foot prototypes have been designed to mitigate the pain associated with the amputee’s movement. By collecting data from patients using these prototypes, biomechanical engineers have concluded that ankle stiffness of the prosthetic is extremely important in making an ankle-foot system more natural and comfortable. Engineers have also determined that between stiff, compliant, and inter-

Fig. 1 Single-axis prosthetic foot design

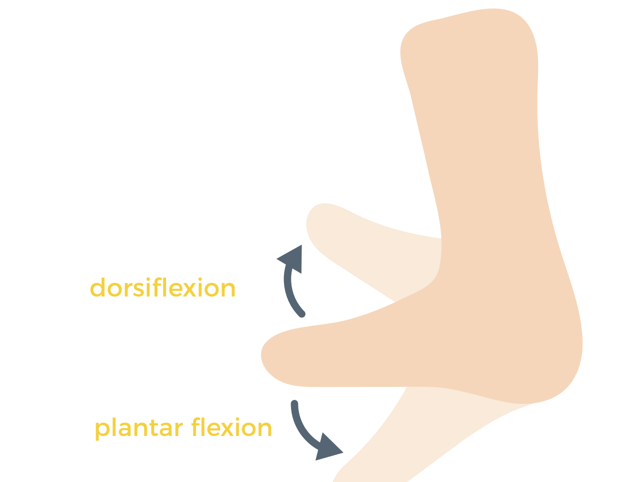


Fig. 2 Dorsiflexion and Plantarflexion of the anatomical foot

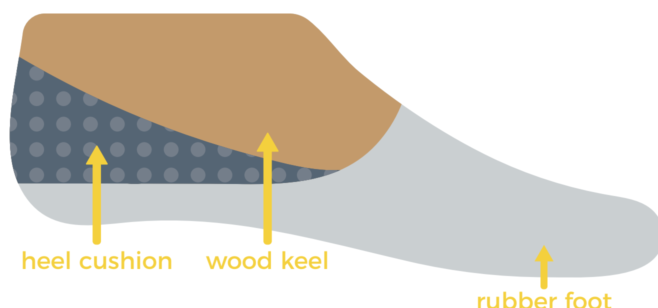


Fig 3. The SACH design

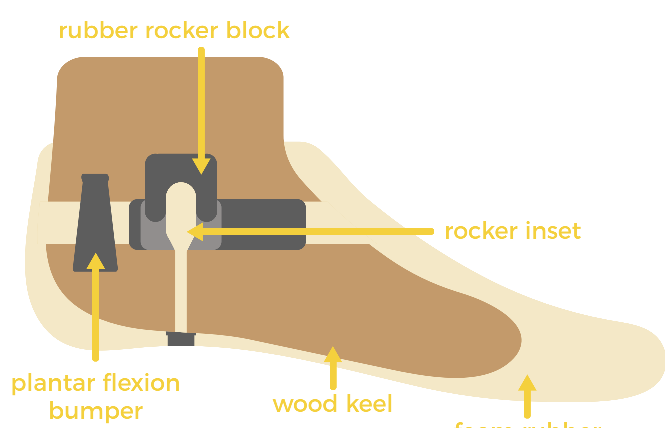


Fig. 4 Multi-axial design

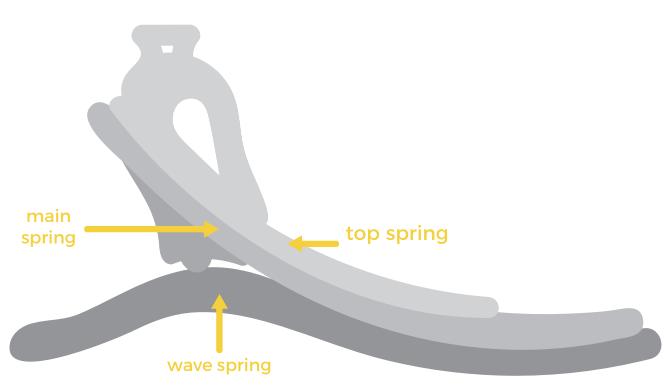


Fig. 5 Dynamic response design

mediate prosthetics, amputees prefer compliant and intermediate feet over stiff feet.

Some of the most common ankle-foot prosthetic designs include single-axis, SACH, multi-axis, and dynamic response prosthetics. Single-axis foot designs (Fig. 1) actively mimic the motion of the sagittal plane (running from heel to toe), and passively control plantarflexion and dorsiflexion (Fig. 2) by using bumpers of variable-stiffness, which determine the range of motion of the foot.

The SACH foot (Fig. 3) effectively promotes knee flexion by using a cushioned heel that compresses under load to simulate plantarflexion and dorsiflexion. The SACH foot incorporates the functions of the single-axis foot into an integrated design, and simulates stiffening of the ankle during late stance with a rigid keel, often made of wood.

Multi-axial foot designs (Fig. 4) give amputees the ability to walk on uneven terrain by taking inversion and eversion of the anatomical foot into account. The mechanism often contains a split keel made of carbon-fiber that acts as two levers complying to the underlying surface. The carbon plates are flexible and allow the foot to comply to the unevenness of the ground.

Lastly, the dynamic response foot (Fig. 5) uses a stiff anterior keel or "leaf spring" to store spring potential energy during deformation and return this energy during progression. These designs provide foot stability and more support compared to other foot designs. Reportedly, the dynamic response foot feels more natural during ambulation.

By using automatic feedback control, biomechanical engineers are finding ways to iteratively control neuroprosthetics. This field is important in patients who suffer motor impairment from strokes. By facilitating small electrical signals to muscles, neuroprosthetic feet can treat impairment by inducing contraction of the leg muscles. This technology is known as functional electrical stimulation (FES) and is promising in treating foot drop, but poses risks in triggering action potentials of surrounding nerves. As technology advances, the complexity of prosthesis increases as well and the future promise of neuroprosthetic ankle-foot systems could help amputees move more naturally in their prosthetics.

See Appendix 3.5 for references.

APPENDIX

Appendix 1.1

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