Helix

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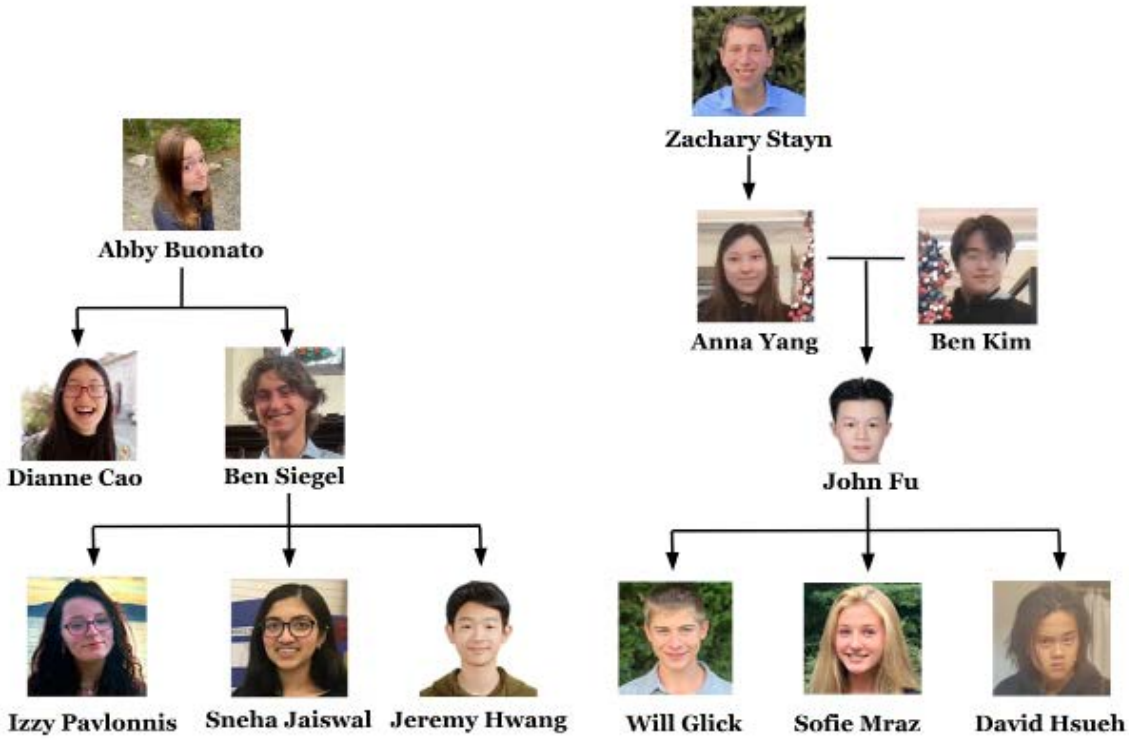

Special thanks to Ms. Lillis and Mr. Carvalho for being the faculty sponsors.

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Mr. Kassatly, Mr. Moore, Mr. Kernohan, and Dr. Richards

"Everything is theoretically impossible, until it is done."
— Robert A. Heinlein

Dianne Cao '24

Helix is Milton Academy's one and only scientific journal, written by and for Milton students on a range of STEM topics. We strive to help students better share their passion for and knowledge of the sciences with the entire Milton community.

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FROM BIOFILMS TO YOUR LIGHT SWITCH: AN INTERVIEW WITH ELECTROCHEMISTRY PROFESSOR HALUK BEYENAL

ANNA YANG '23

Dr. Beyenal is a professor at Washington State University who is widely known for his biofilm engineering expertise in the area of microscale biofilm characterization and electron transfer processes in biofilms. His lab focuses on the fundamental understanding of biofilm processes, their characterization, and applications of biofilm processes.

Q: You study biofilms and the extracellular electron transfer process. Can you tell us a little bit about your research, and the real-world implications?

A: My field of research is biofilm electrochemistry, focusing on understanding how biological systems exchange electrons with an external electron acceptor. To grow, microbes need an electron source. Most of the time, the electron donor is a sugar, such as glucose, and to be metabolized, the cells need an electron acceptor. In nature, the electron acceptor is usually oxygen. With this knowledge, we can learn from microbes by engineering special microbes that can transfer electrons to electrodes instead of oxygen. We are then able to gather the electrons and convert them into electricity. These microbes form biofilms around the electrode, working synchronously to exchange electrons with electrodes and potentially transmit electricity. We have even engineered some biofilm microbes to fix carbon dioxide from the air — in other words, to convert CO2 into organic compounds. These cathodic biofilms take energy from sunlight and electrons from electrodes, and convert atmospheric CO2 into biofuels, such as biodiesel and butanol. They can also produce bioplastics, which are a potential solution for the world's energy and plastic crises.

Q: Why did you decide to pursue engineering, electrochemistry, electronics, and biochemistry? What got you into biofilms specifically?

A: Electronics has always been my hobby. In the summers when I was younger, I would watch an electrical technician fix things in the house and try to learn it myself. During high school, I wanted to make some money in my free time and worked in an electric shop. My interest in electrochemistry emerged through this informal exposure to electronics. For my masters degree, I studied diffusion reactions in heterogeneous catalysis. Even when my mentor left, I remained intrigued by the topic and wanted to continue studying something similar, which was how I landed on biofilms. Biofilms are everywhere! Dental plaque on your teeth are actually dental biofilms, and slippery rocks are actually covered in biofilms as well. It's interesting to see how an everyday biological process has such extensive medical and environmental implications!

Q: I have heard that you were a huge proponent of encouraging women in STEM. What are your thoughts on this topic?

A: I am very passionate about promoting gender equality in STEM fields mostly because of my personal connections with this cause. My sister is really smart but never went to college. Many women like her are very capable, but our culture just doesn't encourage them enough to reach their full potential. We need to teach people at a young age to promote an inclusive culture. Because of my background and my experience watching my sister struggle academically growing up, I always encourage women to delve deep into interesting STEM fields. Resolving this issue of gender equality in STEM could pave the way to create a better future for all of us.

Q: Have you had to work with scientists outside of your field in interdisciplinary studies? What was your experience?

A: I always work with scientists outside of my field; I think it's the best way to advance science. In one of my projects, I worked with a microbiologist and a medical doctor to create an electrochemical bandage (e-bandage) for wound healing. Normal bandages contain hydrogel and antibiotics to help with wound healing, but sometimes biofilm infections can cause chronic wounds that need more advanced solutions. I came up with a technology that can electrochemically produce hydrogen peroxide (H_2O_2) and hypochlorous acid (HOCl) at low concentrations on the wound surface. These compounds (H_2O_2 and HOCl) are biocides, which means that they can eliminate biofilms. However, they need to be supplied continuously in small amounts instead of a large amount at once because large amounts are toxic to the underlying tissue. Our e-bandage design incorporated technology to accomplish this. In this project and many others that I've worked on, interdisciplinary collaboration is necessary. I specialize in electrochemistry, but the medical researchers that I am working with have expertise on antibiotic resistance, biofilms, and animal models; we wouldn't be able to develop such technology without working together. Our e-bandage has been tested on animal models, and so far, it is showing great promise! We hope to continue testing our technology with clinical trials soon.

Q: Do you have any advice for high school students hoping to pursue science as a career?

A: I think high school students should be exposed to many different fields of science before they commit to a field that they are really passionate about in college and beyond. I recommend that students not only communicate with your mentor or whomever you work most closely with, but also reach out to multiple professors. Sometimes a student joins a research lab knowing that they have absolutely no interest in the research topic, but after talking to professors in various fields, they find that the topics they ruled out actually intrigued them a lot! I think high school is too early a time to commit to a path. Explore as broadly as you like, and think of yourself as a potential expert in every field!

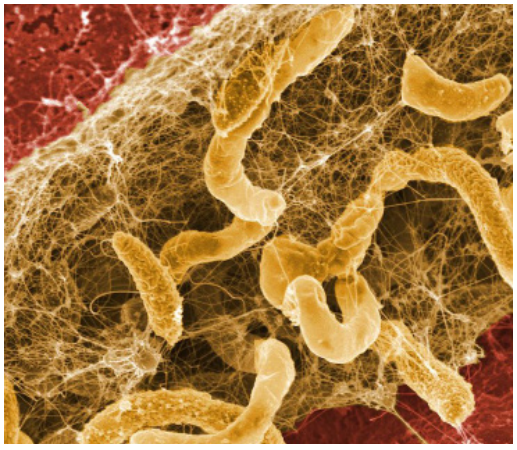

Image Credits: https://theconversation.com/biofilms-the-bacterial-wound-communities-that-protect-themselves-from-attack-42218

MRSA ON HEDGEHOGS CHALLENGES CURRENT BELIEFS ON ANTIBIOTIC RESISTANCE

ALITZA SOIFFER ‘24
Illustrated by Dianne Cao ‘24

From 2000 to 2018, antibiotic use has increased by a dramatic 46% (1). Ideally, increased use could reduce illness; however, CDC studies show that at least 30% of antibiotic prescriptions are unnecessary (2). This overuse has caused antibiotic resistant bacteria to emerge. The dominant belief is that superfluous prescriptions kill most bacteria, but leave resistant organisms to reproduce. However, using lower quantities of antibiotics would not kill the harmful bacteria, thereby rendering the medicine ineffective. Because the risk of underprescribing has more immediate, clear consequences, doctors and vets are more likely to over-prescribe. Human-made drugs likely created antibiotic resistance. However, a new study on the bacterial infection MRSA suggests that natural antibiotics, as opposed to manufactured ones, can have a similar effect of creating resistance. People use penicillin, an antibiotic, to reduce cows’ sickness (3). Therefore, scientists believed that MRSA gained resistance to penicillin due to humans’ excessive use of the drug in cattle. However, a study of MRSA on hedgehogs challenges this belief (4). Scientists discovered that hedgehogs evolved the ability to naturally produce penicillin on their skin (4). As a result, penicillin-resistant MRSA had a genetic advantage over MRSA that had yet to develop resistance (4). MecC-MRSA, a strain of MRSA that is resistant to penicillin, has lived on hedgehogs for around 200 years (5). Therefore, the emergence of MecC-MRSA on hedgehogs likely precedes the discovery of penicillin-resistant MRSA on cattle in the 1970s, suggesting that MecC-MRSA first developed on hedgehogs and spread to cows (6,4). Although some bacteria’s antibiotic resistance may stem from human overuse, naturally occurring chemicals like hedgehogs’ penicillin can be a key factor in producing antibiotic resistant bacteria.

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BIOMIMICRY: FROM ANCIENT INSECTS TO MODERN CAMERAS

BENJAMIN SIEGEL ‘24

Inspired by the Dalmanitina socialis, a 300-million old now-extinct trilobite, scientists have created a new camera lens that can simultaneously focus on objects at different distances (1, 2). Until now, a single lens has been unable to focus on two points simultaneously, but not anymore. This newly created lens has an incredibly high depth of field with its ability to focus on multiple points ranging from 3 cm to 1.7 km away (2). Scientists were able to create such a high depth of field by mimicking the dual focal points in the eyes of the Dalmanitina socialis, the only animal, living or extinct, without a single focal point visual system (2, 3). The eye of this trilobite contains two optically congruent lenses with different refractive indices, or light bending capabilities (2). Similar to bifocal glasses, this new lens has two focal points, allowing the lens to focus on multiple points. But unlike the commonly used bifocal lenses which contain multiple lenses (one for each focal point), these trailblazing new lenses can truly focus on multiple locations at once by precisely bending the light inside the lens (4). To create this dual-focusing lens, researchers created a metalens — a flat lens created from an array of millions of nanopillars — that was arranged in such a way that the lens absorbed light in two different locations (1). Then, through the metalens, the absorbed light would bend in such a way that the near and far objects appear to be focused on a single plane. However, the area in between the two focal point distances remains blurry. To combat this blurriness, the researchers used a neural network to sharpen the mid-range visual information (1, 2). Combining the power of machine learning and the eye structure of an extinct insect, scientists have uncovered the possibility of a revolutionary advancement in photography.

Figure 1: Photo taken with the metalens of 6 dolls arranged at distances of 30 cm to 3.3 meters away from the lens. Notice that all of the dolls are in-focus, no matter their distance away from the lens (2).

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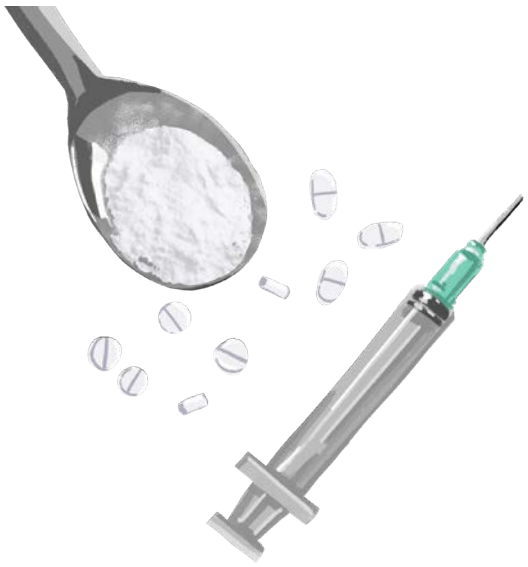
PSYCHOACTIVE DRUGS: GRAPPLING WITH REALITY

CHLOE LI ‘25

Illustrated by Dianne Cao ‘24

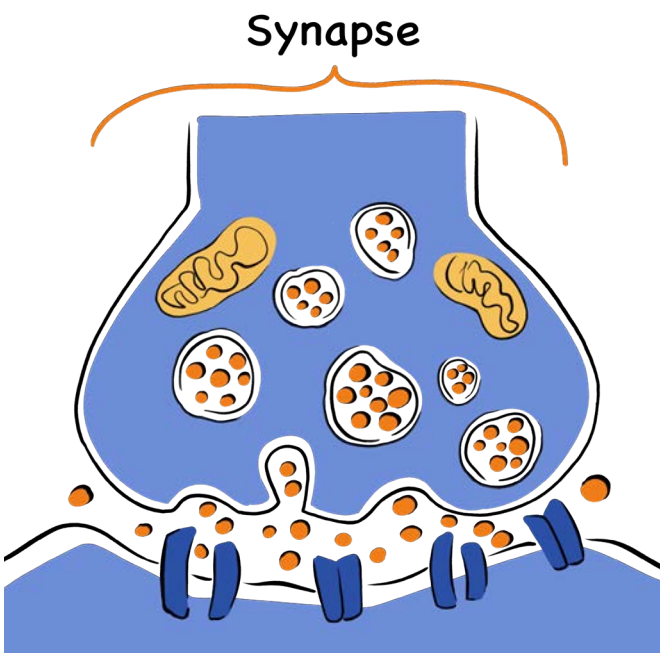
If you were to ask anyone you know, they would almost certainly be able to immediately name one person they know who had dabbled in drugs. But what if you asked them how psychoactive drugs actually work? In the year 2020, approximately 270 million people globally were users of psychoactive drugs, including the estimated 35 million people that are currently victims of drug use disorders (1). Psychoactive drugs are substances that alter an individual's experience of reality and change their behavior, mood, and awareness by affecting their central nervous system (2). The four categories of psychoactive drugs (stimulants, depressants, narcotics, and hallucinogens) each target a different circuit of the brain and have varying effects on an individual's state of mind.

All psychoactive drugs travel through the bloodstream to enter the brain. When present, they dramatically increase or decrease the activity of neurotransmission, affecting the usually stable process. Neurotransmission is the chemical-electrical way in which the brain processes information. Information in the form of a chemical signal is relayed from neuron to neuron until it finally reaches the relevant region in the brain. When crossing the synapse, the miniscule gap separating adjacent neurons, electrical information is converted into the form of a chemical signal. Neurons electrically signal vesicles to bind with the neuron membrane and let the neurotransmitter molecules stored within them go into the synapse after they are opened up. After crossing the synapse, a portion of the neurotransmitters attach to the receptor molecules found on the receiving neuron's surface (3). Psychoactive drugs which target the reward pathway mimic neurotransmitters by binding to sites in the circuit from the ventral tegmental area (VTA) to the nucleus accumbens, areas rich in dopamine synapses (4). While dopamine works as both a stimulatory and inhibitory neurotransmitter, in this interaction, it builds up in the synaptic space and triggers receptors, causing short-term "mood elevating effects" (5).



In the realm of psychoactive drugs, methamphetamine (meth), also known by its nicknames crystal, speed, ice, etc., is a type of stimulant most commonly used for recreation. Stimulants are known to affect the reward system of the brain not only by causing an increase in the release of dopamine, allowing heightened perceptions of pleasure, but also by pretending to be dopamine (2). Sometimes, stimulants are prescribed to people with health disorders such as ADHD, narcolepsy, etc (6).

Meth affects three crucial parts of the brain: the brain stem, which controls life-sustaining functions, the limbic system, which regulates the reward circuitry, and the cerebral cortex, which controls decision making, problem solving, and planning. The high of taking meth lasts up to twelve hours, and during this time, the reward center, composed of the ventral tegmental area (VTA) and nucleus accumbens (NAc), releases high levels of dopamine, creating the intense feeling of pleasure (5, 8). As a response to the sustained usage of the drug and the heightened levels of dopamine released, the brain reduces the availability of dopamine receptors once the high is over (8). While this response ensures that the drug does not overstimulate the dopamine system, it increases the likelihood of an individual's addiction and drug dependency. Nevertheless, this reaction is not the sole contributor to the drug dependency (4). The basal ganglia, composed



of a group of structures found deep within the cerebral hemisphere, contains the dorsal striatum which forms habits and routine (9). The constant release of dopamine changes how the dorsal striatum functions, causing compulsive substance use by "strengthening substance-seeking and substance-taking habits" (9). While tolerance to meth can be built up over time, depending on the individual, it does not always lead to addiction (10). In fact, addiction is worsened by diminished sensitivity of the brain's reward system. As a result, some individuals develop substance use disorders in order to feel the same joy once provided by the reward system through every-day life (9).

Prolonged usage of meth can have detrimental effects towards an individual's body. The effects of meth usage speed up the central nervous system, elevating heart rate, body temperature, and energy levels. The suppression of appetite also leads many individuals to abuse the drug as an easy way to lose weight. When dopamine levels are atypical, the communication of neurons in the brain changes, resulting in the prefrontal cortex and striatum receiving fewer messages of hunger (11). Dopamine's role in addiction is only secondary, but the transmitter plays a large role in reinforcement (12). Due not only to a damaged cerebral cortex but also to significant damage towards the perception pathways and increased neuronal death, patients often struggle with their memory, learning abilities, and movement (13). Reduced cortical, hippocampal, and cingulate gray matter also occurs as a result of excessive meth use (5). As gray matter is a key component in determining how humans function normally, reduction causes a loss in cognitive and motor function (14). Once an individual becomes addicted to meth, quitting becomes extremely difficult due to high dependency and drastic withdrawal symptoms. Patients experience various symptoms such as craving, depression, severe loss of energy, anhedonia (the inability to feel pleasure), and suicidal thoughts (5).

Recently, scientists have been looking at new methods for preventing relapses, which are often triggered by stress, small doses of the drug, or environmental stimuli that remind the individual of the drug, and coping with withdrawal symptoms. One study investigates how using mindfulness and meditation can reduce the cravings of methamphetamine users (15). With a sample of 161 participants, researchers used a hybrid structural equation model to investigate pathways with lower methamphetamine cravings as a result of dispositional mindfulness, a method that requires focused attentiveness towards the present moment. They found that dispositional mindfulness has a positive effect on the path of recovery for individuals with substance use disorders (15). Another study also evaluates the effectiveness of stress-coping strategies with relapse rates, finding that only 29.1% of all subjects were using valuable mechanisms, while the other 70.9% utilized unsuccessful stress-coping strategies and were more likely to go back to methamphetamine use (16). One particular study examines the usage of a virtual reality system to prompt cravings in methamphetamine users. The VR system gauges psychological responses through sensors such as an electrocardiogram (ECG), galvanic skin response (GSR) and eye tracking. Proven to be effective, it may be used in the future as another form of treatment for stimulant drugs (17). Other treatments include the combined usage of the drugs Bupropion and Naltrexone and the usage of agonist replacement medications which bind to receptors in cells and replicate the actions of the drug without inducing the same harms (18, 19, 20).

The recent advancement in technology and a variety of mechanisms to cope with substance use disorders has the potential to revolutionize the journey of recovery, alleviating methamphetamine users from the suffering and considerable stress of withdrawal forever.

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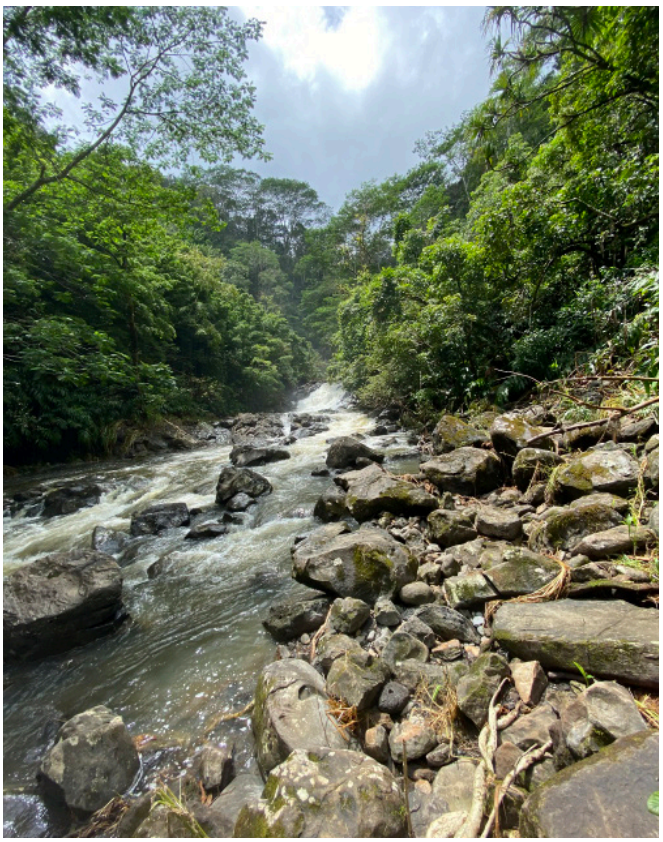
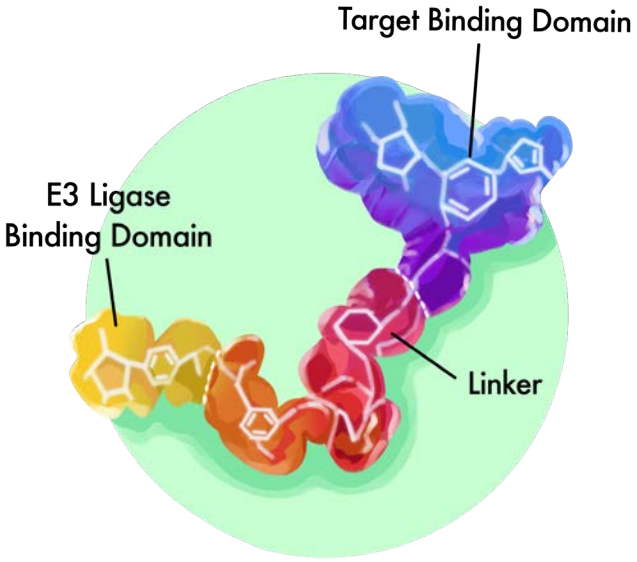


Sebastian Romero ‘24

PROTACS, THE LESS TALKED ABOUT CURE TO CANCER

Zachary Stayn ‘22

Illustrated by Dianne Cao ‘24 and Anna Yang ‘23



We all want there to be a cure for cancer! You’ve probably heard facts such as “10 million people die of cancer each year” and “cancer is the second leading cause of death worldwide” (1). Someone has inevitably told you that advances in CRISPR, RNA interference (RNAi), small molecule inhibitors (SMI’s), monoclonal antibodies, or chemotherapy will cure cancer in the coming years, but is that really true? If we already know what cancer cells look like, where they are in the body, and how each of these cutting-edge technologies work, then why aren’t scientists closer to curing cancer?

It’s a fair question and one that is actually pretty simple to answer. First, cancer is caused by mutations, or genetic changes, in genes responsible for regulating cell division in the human body (2). In most cases, the body is trained to remove or kill these genetically damaged cells through a process of programmed cell death, or apoptosis (3). Cellular DNA repair systems can also normally proofread and repair changes in DNA before the cell becomes permanently damaged. In cancer, though, genetic mutations instruct cells not to die as easily, so abnormal cells continue to divide uncontrollably, forming lumps of tissues called tumors (3). These tumors can spread to organs, nerves, and blood vessels, eventually disturbing the immune system and leading to death (3).

Genetic manipulation through CRISPR-Cas9 (i.e., editing DNA) and RNAi (i.e., using RNA molecules to prevent proper protein synthesis) doesn’t work against cancer yet because these strategies can’t be efficiently delivered to target cells without first being converted by the body into an inactive form. In addition, genetic manipulation through CRISPR and RNAi can cause off-target effects, such as mutations that may even lead to cancer (4).

SMIs, which are molecules that inhibit enzymes responsible for cancer cell development, aren’t effective because they have to be present at very high concentrations to exert a biological effect. In doing so, these SMIs lead to undesired side effects that can cause gene and protein dysfunction, leading to patient death (4). Monoclonal antibodies, engineered proteins that bind to other molecules called antigens on the surface of cancer cells and force parts of the immune system to destroy the cancer cell, don’t work for targets inside the cell (5).

Finally, chemotherapy drugs, medicines that kill rapidly-dividing cells, have severe side effects against healthy cells that divide rapidly, such as cells of the stomach lining, and often don’t work over time as cancer cells acquire drug-resistance mechanisms (6).

So, what is the solution? Will cancer ever be cured?

Luckily, a new method utilizing molecules called proteolysis targeting chimeras (PROTACs) offer a potential solution. PROTACs are an integral part of a cell’s natural, targeted system of protein degradation called the ubiquitin-proteasome system. Natural PROTACs have three chemical parts: a domain that binds to a target protein that is to be degraded, a domain that binds to a protein called E3 ubiquitin ligase, and a linker that connects these two domains together (8). E3 ubiquitin ligase recognizes proteins that need to be degraded, and the PROTAC brings the ligase into close contact with the target protein, allowing E3 ubiquitin ligase

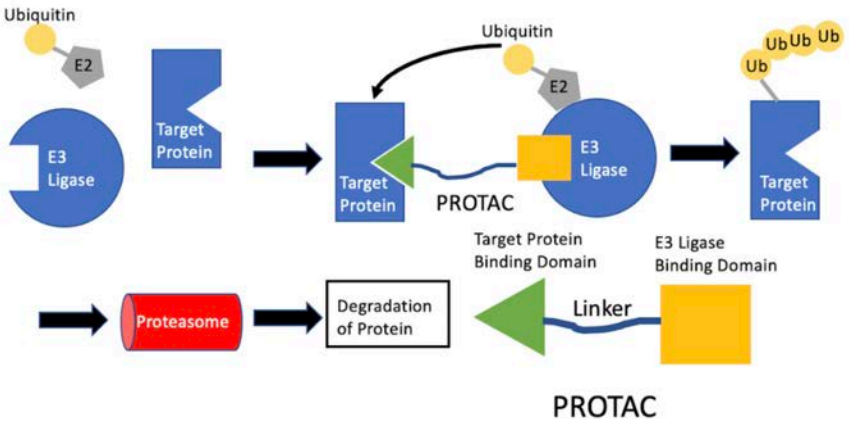


Figure 1: Degradation of the target protein via the ubiquitin-proteasome system. A PROTAC brings the target protein in contact with an E3 ubiquitin ligase, allowing the target protein to to be ubiquitinated and degraded in the proteasome.

to catalyze the chemical labeling of the target enzyme with proteins called ubiquitin tags (8). The presence of ubiquitin tags directs the target protein to the proteasome, an intracellular protein complex that degrades the target protein (Figure 1) (8).

Recognizing their therapeutic potential, pharmaceutical companies such as Pfizer, Bayer, and Arvinas are investing billions of dollars into modifying PROTACs' target protein binding domain and linkage domain to be able to target disease causing proteins, such as ones on cancer cells, that natural PROTACs can't or don't degrade efficiently and effectively (7).

This method solves many of the problems caused by other cancer treatments. Since PROTACs are naturally in the body, they are not converted to an inactive form like CRISPR inserts (4). PROTACs' target protein domain matches one specific protein, so, unlike small interfering RNA (siRNA) molecules used in RNAi, they have a high target specificity (4). Compared to SMI's that must be present in high concentrations to inhibit all enzymes crucial in cancer formation, PROTACs are much more biologically powerful because they catalyze protein degradation without being consumed, meaning lower concentrations are needed and side effects are minimized (9). Unlike monoclonal antibodies, PROTACs naturally target specific proteins inside cells (4). Finally, unlike chemotherapy drugs that target rapidly dividing cells' nuclei at a specific time in the cell division process, PROTACs only loosely bind to the target protein. While the exact location that the PROTAC binds to the target protein depends on the specific target protein and the length of the linker, in all scenarios, the weak binding of the PROTAC to the target protein enables the E3 ligase protein and the target protein to molecularly interact (10). These proteins can then change shape and form a tight bond to the PROTAC regardless of any resistance (i.e., changes in the protein amino acid code) at the initial PROTAC-target protein binding area (9, 10).

Just recently, significant progress was made in PROTAC research. A study published in April 2022 in the Journal of Medicinal Chemistry by researchers at the University of Leicester demonstrated that engineered PROTACs could degrade histone deacetylation enzymes (HDACs), proteins that specifically regulate (i.e., turn on and off) proto-oncogenes, which, when mutated, transform normal cells into cancer cells (11). John Schwabe, director of the Leicester Institute of Structural and Chemical Biology and co-author of the study says that, "the potential of using specific degraders of therapeutic targets is very powerful," though he also admits there is a lot more work to be done (11). "Our next steps," he continues, "will involve optimizing [PROTACs'] chemical structure and biological properties so that one day they could be used to improve the lives of cancer patients" (11).

Nathaneal Gray, Stanford organic chemist and founder of C4 Therapeutics, a PROTAC company, also suggests that PROTACs are not a "slam dunk" yet (7). Just like with most scientific discoveries, more limitations emerge despite research conducted to address them. PROTACs, for instance, don't degrade many types of proteins, their toxicity is still not thoroughly studied, and side effects are largely unknown (7). "The next couple of years will be pivotal," Gray says, but researchers hope that even if PROTACs can't be used alone to treat cancer, they can target specific parts of cancerous cells and work in tandem with new and existing drugs (7, 10).

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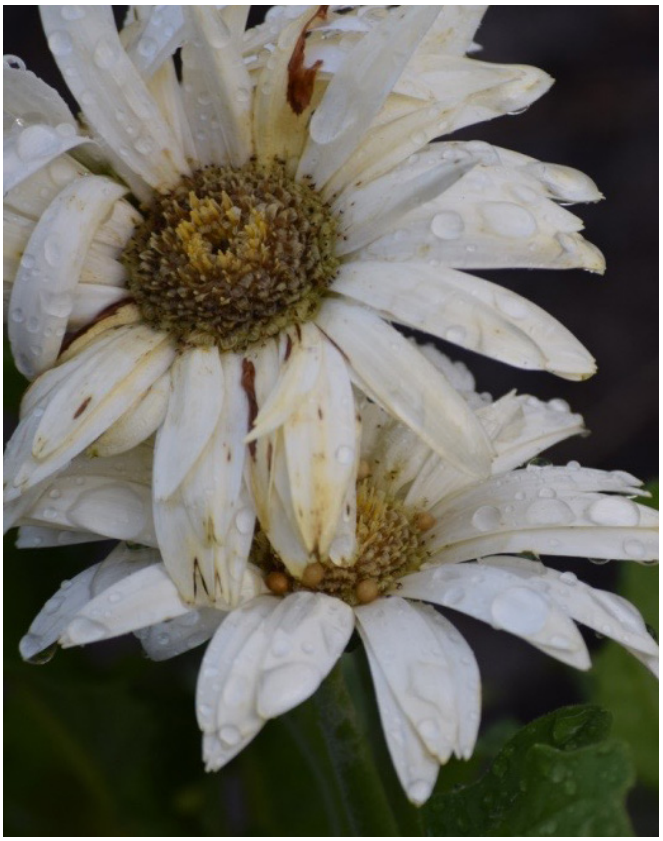
Justin Chen '24

Jillian Taveira ‘22



Benjamin Siegel ‘24

Jillian Taveira ‘22

NEUROSCIENCE AND AI DRIVE EACH OTHER FORWARD

EMMA WANG '23
Illustrated by Emma Wang '23

In 2019, DeepMind's artificial intelligence program, AlphaStar, competed against human players in the e-sport game StarCraft II and was rated at Grandmaster, a level above 99.8% of officially ranked human players (1). To tackle this complex and strategic video game, AlphaStar developed a multi-agent reinforcement learning algorithm, which learns from deep neural networks that represent "data from both human and agent games within a diverse league of continually adapting strategies and counter-strategies" (1). By combining neural networks, deep learning, and general-purpose machine learning, AlphaStar outperformed the best human players in a complex digital environment.

Essentially, AI emulates the human brain to increase the efficiency and sharpen the decision-making of machines and computer programs. The neural network used by AlphaStar are AI networks that model the human nervous system. Humans have around 100 billion neurons that act as the communication agents of our body. These basic units of the nervous system are represented by nodes in a neural network (2). Similar to how neurons communicate through synapses, nodes are interconnected by mathematical weights (3). Like a function, neural networks have several layers of nodes. Data is fed into the input layer, passed through mathematical functions, and finally arrives at a decision represented by nodes in the output layer.

For example, nodes in the input layer represent the different factors that influence one's decision to eat. The brain considers hunger, the appeal of the food, and the health risks. Imagine these nodes, which each correspond to a factor, lighting up when the person makes an affirmative decision. The network then weighs each consideration by multiplying the illuminated nodes by their mathematical weights. If hunger and tastiness have positive weights, allergies would have a negative weight because it decreases one's desire to eat. Finally, by summing the weights, a decision, represented by a node in the output layer, is made (4). This analogy, however, greatly over simplifies neural networks; the numerous, interconnected hidden layers between the input and output layers of neural networks significantly increase their complexity and resemblance to the human brain. Deep neural networks' powerful brain simulations can help neuroscientists predict brain activity and understand brain structure because access to a healthy human brain is very limited. Researchers can only implant electrodes in brain tissues that are to be removed or in animals, though that must still go through an IRB (Institutional Review Board). Hence, using artificial networks to test hypotheses is a great way to address the ethical challenges of neuro-research. Using deep neural networks, researchers can easily modify their AI models to test variables that affect brain performance. For example, in 2014, Daniel Yamins, a computational neuroscientist at the Wu Tsai Neuro

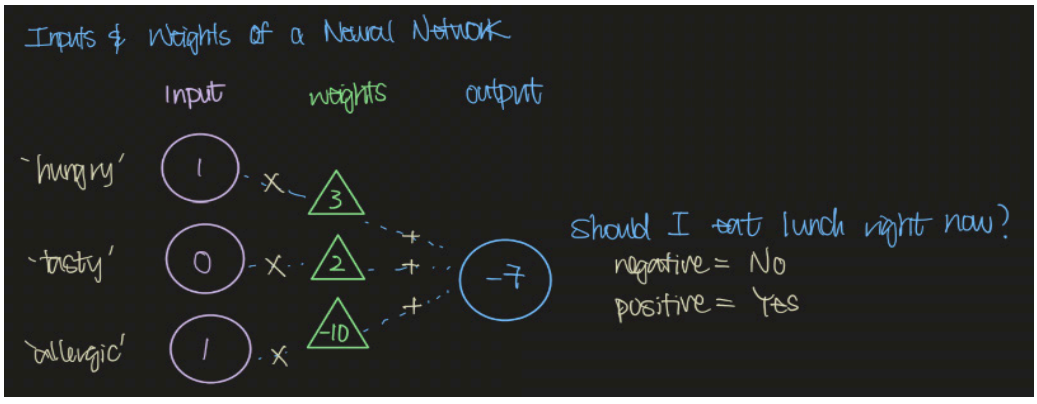


Figure 1: Neural Network: Should I eat lunch?

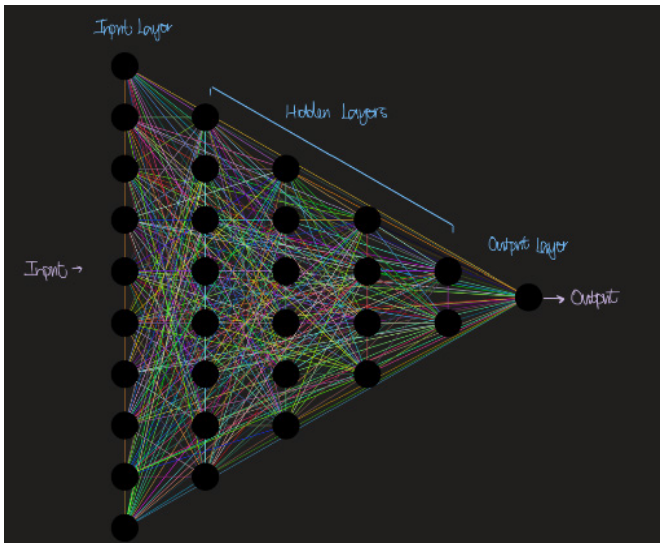


Figure 2: Deep Neural Networks: Hidden layers

sciences Institute at Stanford University in California, created a neural network that emulated a monkey's brain partaking in object recognition (5). "What you find is that the structure of the neurons is mimicked in the structure of the network," Yamins says as their team achieved 70% accuracy when comparing their network patterns with neuron patterns of monkeys. His study proved the relevance of studying the ventral visual stream, the brain system that processes object recognition for many mammalian species (6).

While AI provides many benefits, risks also associate with these increasingly-complex intelligent systems. With the rapid advancement of AI, humans are challenged to understand AI models' potential biases and impacts, especially for deep neural networks, which are mostly data-driven, supervised learning models. Similar to how students learn from homework practice problems and verify our understanding with tests consisting of similar questions, supervised learning models are trained with labeled data then tested for their answers' accuracy to unlabeled data. Then, the individual nodes' mathematical weights, which dictates the importance of each node, are adjusted to increase the accuracy of the output (3). Because neural networks rely on lots of data to repeat this training and testing process to increase their accuracy, the calculations in deep neural networks are heavily reliant on logic and mathematics. The convoluted process of making these calculations is often referred to as a "black box" that AI researchers cannot comprehend (7). According to IBM, "neural networks used in deep learning are some of the hardest for a human to understand. Bias, often based on race, gender, age, or location, has been a long-standing risk in training AI models" (7).

Perhaps XAI (Explainable-Artificial Intelligence) — models that combine theory-driven and data-driven models — is needed to let human users comprehend how the AI model generates its results to prevent bias (8). Some researchers like Tomaso Poggio, a computational neuroscientist at MIT, explore the neuroscience behind human morality (5). "People are afraid of 'evil' machines," Poggio says. "We'd probably better know how our moral behavior arises if we want to build good machines, ethical machines"(5). Hence, developments in neuroscience are needed to provide the biological mechanisms to create XAI that can explain the cognitive aspects of the human brain. With the support of neuroscience, scientists and engineers can keep AI models transparent, moral, and trustworthy, which also complement AI's fundamental purpose: developing advanced, intelligent, and human-like machines.

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(MASTER)PIECE OF MIND

IZZY PAVLONNIS '22
Illustrated by Dianne Cao '24

Whether it is visual arts from painting to photography, performing arts from dance to theater, or music from classical to pop, art has become a huge part of society – but why? Even beyond historical and cultural significance, art is truly ingrained in our lives – our brains are wired to look for, create, and appreciate it.

A large part of why we connect with art so much has to do with how humanity processes beauty. Beauty itself is a confusing concept – scientists have theorized for years about how color, symmetry, and so many other factors play into the idea of "aesthetic." However, every one of us processes images differently, so it is difficult to precisely define beauty. Things we process as "beautiful" invoke stimulation in perceptual, emotional, and reward-processing parts of our brains, primarily the limbic system, which accounts for behavioral and emotional response, and the mesolimbic dopamine pathway that deals with reward. On the contrary, when presented with something we perceive as non-beautiful, only the visual parts of our brains are engaged and less overall stimulation occurs (1, 2). In these "positive" responses, the orbitofrontal cortex is activated, and thus neurological signals indicate a release of dopamine. That is exactly why you'll find that a truly beautiful display of art impacts you more than another piece – the one your brain deemed beautiful activated a much more complex and memorable response through dopamine release; meanwhile, the less beautiful one did not trigger anything that your brain wants to recall. This resultant long term memory encoding from dopamine release is due to the hippocampal-striatal-prefrontal loop that causes the formation of memories. In order for this loop to function, dopamine receptors need to be stimulated; studies found that reactions with higher dopamine release led to more activity in this memory-creation loop (3). These complex and thus memorable reactions are why people often find a piece of art to have "changed their life" – why the truly beautiful and impactful pieces of art stick with us. However, beauty, including in art, remains subjective because each person processes colors, shapes, and images slightly differently, and those differences can lead to vastly different reactions.

Music is slightly different, as it deals with auditory instead of visual stimulants. Similar to visual arts, music that we find enjoyable activates reward-centered parts of our brains. In a 2001 study using magnetic resonance imaging, scientists Anne Blood and Robert Zatorre of McGill University found that good music stimulated the limbic and paralimbic regions of the brain, resulting in the release of dopamine (4). "Good music" is, nonetheless, subjective. Why we deem certain music as enjoyable is a question we don't fully have answers to, despite much speculation. Psychological theories suggest that music draws on the concept of expectation. Throughout our lives, our brains process and retain sounds and patterns we hear, and from that storage we are able to predict the next sequences in sound. When we find that the sounds we hear match up with what we know and expect, our brains process it as meriting reward; through stimuli in the subcortical reward circuits, different amounts of dopamine neurons are released as a reward (4). This response to patterns and prediction is why music often follows similar patterns and why different types of music we consider "good" share common elements – they find a balance between surprise and developing predictability.

Performing arts, such as dance, similarly activate the brain's reward centers but through both visual and au-

ditory signals. As with music, part of the reward from dance comes from prediction. Often, we find ourselves predicting what a dancer would do if we were them. Mirror neurons, situated in the cortex (the brain's central processing unit), are cells whose reactions stay constant between observation versus performance of a particular task or action. Through the studying of these cells, scientists have found the connection between art observation and execution (5). The mirror neurons are pivotal to the inverse nature between action and observation: in order for an action to be completed, informational signals need to flow from the control centers to the limbs carrying out that action, while observation happens inversely, with limbs and sensors (eyes, hands, etc) relaying information back to the brain via the spinal cord (6). According to scientist Christopher Tyler of the Smith-Kettlewell Brain Imaging Center, this "bidirectional flow" bolsters the "aesthetics of art appreciation" (7). If we watch a dancer, our subconscious begins to plan and predict what the dancer may do next. If our prediction lines up with actuality, the inward and outward traveling signals match up, creating a signal for dopamine release. However, if the dancer also performs a move requiring a level of expertise that we did not know and thus could not predict, we are impressed and therefore "happy" (7); according to an Emory University study, surprise is another contributor to dopamine release (8). In addition, music allows us to move in rhythmic ways, thus marking dance with a foundation of regularity. The initial positive auditory sensation from the music lining up with the visual motion allows the brain to process dance as extremely enjoyable and reward-inducing.

As shown by science itself, art truly is good for your mental health. Part of its beauty lies within its subjectivity – the fact that different people can find beauty in different art allows for uniqueness and variation in our human experiences. These differences not only allow our individual, specific tastes to feel special to us but also remind us that each and every person can find beauty in different places in the world around them.

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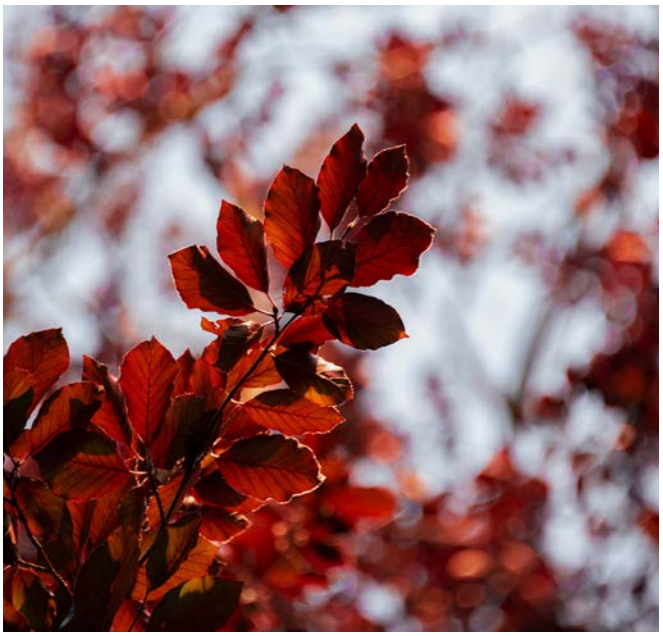

Eliot Hack '24

Senior Interviews

Abby Buonato

Interviewed by Anthony Lee

College/Major/Focus:
Washington University in St. Louis. As a part of the Beyond Boundaries Program and will be studying PNP (Philosophy-Neuroscience-Psychology), Education, and Urban Design.

Q: Why do you like science?
A: I like science because I like the idea of the scientific method, of being able to do background research, form a hypothesis, and experiment to test the hypothesis. Also, I just like to get curious about science and try new experiments to learn more about the world.

Q: What is/are your DYOs this year? Favorite DYO from Milton?
A: From launching arrows to test projectile motion in Freshman Physics to studying temperature's effect on biofilm formation in Advanced Biology, I have done many cool experiments at Milton. My favorite DYO, though, was in Honors Biology when I experimented with Manduca Sexta worms and saw how the worms competed for limited amounts of food and resources.

Victoria Fawcett

Interviewed by John Fu

College/Major/Focus:
I will attend Middlebury College in the fall, and I hope to equally focus on the sciences and humanities through a variety of courses.

Q: How did you first become interested in science and how did you explore your interest in science?
A: My grandfather and uncle in Argentina are both ophthalmologist surgeons, and I've been shadowing them since I was a kid. Since then, I've continuously fallen in love with the operating room and helping patients. Throughout high school, I really delved into Honors Chem, Honors Bio, Advanced Bio, and Organic Chem, and would definitely recommend anyone interested in the sciences to take these courses. For my senior project, I'm interning with a plastic and reconstructive surgeon at Mass. General Hospital to continue exploring my love for the operating room.

Q: Do you have any future plans with your journey in science?
A: Currently, I hope to apply to medical school after college. Then, I look forward to joining a residency program, publishing scientific research, and working towards becoming a surgeon. I am unsure of what branch of surgery I'm interested in yet but I look forward to trying a little of everything in medical school.

Jeremy Hwang

Interviewed by Julie Sullivan

College/Major/Focus:
I will be attending Northeastern University and majoring in Neuroscience.

Q: How did you first become interested in science and how did you explore your interest in science?
A: Growing up, I tried everything. I tried going into the humanities, and I tried going into STEM. I tried to figure out what worked for me, and I landed on science. It just feels like the right thing to do at this point in time, and I'm excited to see how it'll go to pursue it further in college.

Q: What do you like about science, specifically at Milton?
A: I like that they do a really good job with grounding you in the fundamentals at Milton. I know that every highschool curriculum is pretty similar in that everyone takes Biology and Chemistry and Physics, but I loved the creative freedom they give you at Milton with electives and advanced classes. This year I took Neuroscience, and it was great to be able to pursue something that I was curious about and had a strong interest in.

Sneha Jaiswal

Interviewed by Elena Ferrari

College/Major/Focus:
I'm going to Carnegie Mellon College of Computer Science. I haven't decided yet on a specific major, as they have a few different majors in the school of computer science, but I'm interested in the intersection of biology and computer science as well as AI.

Q: What is your DYO this year? Do you have a favorite DYO from Milton?
A: This year, in Advanced Bio, we genotyped one of the genes that affects skin color. We did PCR to replicate our DNA, and then we did gel electrophoresis to try to visualize it. We planned to run a restriction analysis, which is when you use an enzyme to target and cut specific pieces of DNA. We hypothesized that if you had a certain allele, the enzyme would cut the piece of DNA, but if you didn't have that specific allele, it wouldn't make the cut. The allele should have theoretically corresponded with skin color. Unfortunately the PCR didn't work for part of the testing, so we weren't able to come to any conclusions.

Q: What is your senior project?
A: I'm interning at the cancer research center at MGH, where we're investigating what happens to the immune system during chronic illnesses and cancer. My project is more computationally based; I'm doing machine learning analysis on data sets of the epigenetics of these cells.

Ben Kim

Interviewed by Anna Yang

College/Major/Focus:
I am attending Northwestern University's McCormick School of Engineering. I will be majoring in biomedical engineering and integrated sciences, which is basically a math, physics, chemistry, and biology quadruple minor. Plus, a music minor and a business certificate, hopefully in 4 years!

Q: Do you have any science/STEM interests for after college?
A: I would like to go into the biotechnology and pharmaceutical industries focusing on currently incurable diseases such as Alzheimer's and/or certain types of cancer such as lung cancer.

Q: Have you done any internships or held any jobs in the field of science?
A: When COVID struck at the end of my sophomore year, I looked for a science-related activity to keep my mind engaged. So, I held a position as an intern for master's degree students at a lab. I worked with them to model the COVID-19 viral cell using polar lipids and spike proteins. It was a great introduction to university-level lab work!

James Millington

Interviewed by Benjamin Siegel

College/Major/Focus:
I plan to study aerospace engineering at GATech.

Q: What do you like about science specifically at Milton?
A: What I liked about science at Milton was that there were a lot of opportunities to explore topics that I found interesting, especially in my Advanced Physics class. The teachers are pretty supportive of whatever experiment I want to do; I once made a Bass Guitar for a lab. Some of the most important lessons I have learned came through the freedom we were given on the DYOs.

Q: What is your DYO this year?
A: My DYO for Advanced Physics was about self assembling wires. We put metal ball bearings in a pool of castor oil and they formed wires when attached to a generator. We explored the conductivities of different types of metals and saw the effect on how well the ball bearings formed these wires. Before our experiment, people would conduct the experiment and just admire how cool it was. However, nobody had explained what was happening. So, the goal of the experiment was to understand and to explain the concepts behind why these

Izzy Pavlonnis

Interviewed by Christina Gu

College/Major/Focus:
I will attend Connecticut College, and I will double major in Chemistry and English with a focus on sustainability.

Q: Which science/STEM electives did you take?
A: I took Organic Chemistry and Advanced Chemistry this year, Honors Biology last year, Honors Chemistry in sophomore year, and Freshman Physics.

Q: Any teacher/friend/scientist inspired your passion for science?
A: Definitely. I would say that my love for science, specifically chemistry, started in my sophomore year Chemistry class with Mr. Moore, one of my favorite teachers ever. I took Organic Chemistry with him again this year, and I found that I really loved chemistry, not just as a subject but also how it allows us to change the world around us.

Gunner Peterson

Interviewed by Evan Zhang

College/Major/Focus:
I will attend UC San Diego, and I plan to major in cognitive science with an emphasis on computer programming. Philosophy is also interesting to me!

Q: Have you done any internships or held any jobs in the field of science?
A: I've been a computer science tutor for two years at a company called Code Ninjas in Medfield, MA, and I've also had a TA gig doing some teaching on machine learning and AI. This summer, I'm interning at Fidelity, hopefully doing data analysis.

Q: What is your senior project?
A: I actually have two senior projects. In one, I am creating computer science resources for the Computer Science 4 class at Milton. Specifically, I'm making a YouTube series on neural networks. In my other project, I am building an app for the Sustainability Board. The app will pair students who want to carpool, hopefully reducing carbon emissions on campus.

Emma Pottow

Interviewed by Kiera Zhuo

College/Major/Focus:
I'll attend the University of Virginia, and I plan to major in biochemistry with the hope of eventually developing medicines when I get older.

Q: What do you think of science at Milton on a whole?
A: I actually didn't like science at all when I came to Milton. I thought I would go into an English-based career because English was always my favorite subject when I was younger. I started to fall in love with science when I took Chemistry. I especially loved digging into details, because I am a very detail oriented person. After taking Honors Bio, which I loved, I wanted to narrow in on something specific like chem, but also more medical, so that's why I ended up doing neuroscience. The most eye-opening thing about neuroscience was how little we know. I thought that we understood the universe so well but that is just so not true.

Q: Has any science teacher at Milton has made an impact on your perception of what you want to do?
A: Honestly all of them. I want to shout out Mrs. Holman because she was very enthusiastic! She taught me that science could be exciting. I actually struggled a lot early on, and I got a lot of support from her and did very well in her Chemistry class.

Zoe Shleifer

Interviewed by Teddy Wu

College/Major/Focus:
I will attend Harvard College in the fall. My major is undecided, but I will likely study pure math and something in the life sciences, possibly computational biology.

Q: Any teacher/friend/scientist inspired your passion for science?
A: My dad used to read these books, talk about them at dinner and hand them to me. Some of them were the Feynman biography books and the Surely You're Joking, Mr. Feynman! books, which were super accessible. I still read a lot of these books, such as Brave Genius, since they're a lot of fun.

Q: How did you first become interested in science and how did you explore your interest in science?
A: I think I always liked math, probably because of my parents. At Milton, I loved that a lot of science classes involved readings because you could see a biological/physical/chemical system, how a researcher probes the system, the results achieved from probing the system, and the method by which the researcher analyzes the results. Outside of school, I explored my interest in STEM through a neuroscience internship last summer, where I studied neurodes in the brain.

Zachary Stayn

Interviewed by Anna Yang

College/Major/Focus:
I'll be going to Harvard this fall. I'm very interested in how molecules can be used to manipulate biological systems, so I plan to focus on biochemistry or chemical biology.

Q: Do you have any science/STEM interests for after college?
A: Definitely. I am passionate about using organic chemistry and molecular biology to develop pharmaceutical drugs for currently incurable diseases. I find molecular science fascinating; harnessing the world's chemical building blocks can literally save people's lives!

Q: Any teacher/friend/scientist inspired your passion for science?
A: Milton's science department has so many fantastic teachers, and I am grateful to all of them! I am especially grateful to Mr. Moore and to Tyler for helping me realize my passion for chemistry. Entering Honors Chemistry, I didn't know what to expect, but when, on the first day of class, Mr. Moore told us that the entire world boils down to 118 elements and shared stories of medicines he had developed while working in the pharmaceutical industry, I was hooked! Throughout Advanced Chemistry, Tyler's high energy in bringing the molecular world to life was infectious. Both teachers' mentorship, enthusiasm for teaching me new ideas, and willingness to answer my questions have spurred me to continue studying chemistry.

Q: Favorite DYO from Milton?
A: My DYO last year in Advanced Chemistry was my favorite at Milton. Inspired by stomach research I did at Harvard Medical School, I studied the effect of different stomach environments on nasogastric feeding tube biofilm formation and growth. I set up dozens of beakers filled with Tums, vegetable broth, hydrochloric acid, and probiotic tablets, and observed growth of lactobacillus bacteria on the tubes over many days. I loved this experiment because it had practical applications in medicine, taught me important lab skills such as pipetting and bacterial plating, and, more broadly, pushed me to problem solve and to think critically about a procedure that had never been done before.

Q: What is your senior project?
A: For part of my senior project, I am studying the discovery process, the biology, and the organic chemistry of four landmark drugs in the pharmaceutical industry. Each week, I read scientific journal articles, research case studies and current news, and discuss specifics with Mr. Moore. Right now, I am trying to synthesize the cardiac drug Captopril in Pritzker. I love this project because it enables me to explore more deeply the way chemical molecules interact with the body and to learn more about the drug discovery process!

Ian Terell

Interviewed by Devan Agrawal

College/Major/Focus:
I'm going to Occidental college, and I'm planning on majoring in Chemistry with the hope of eventually getting a Ph.D.

Q: What do you like about science?
A: Science, especially biological sciences, fascinates me. I remember going to science museums when I was really young and seeing Rube Goldberg machines and tons of interactive exhibits. With the ability to be hands on, I could discover how stuff works for myself. At Milton, I was able to further discover how things function from the ecological level down to the microscopic level.

Q: Is there any specific teacher, friend, or scientist that has inspired your passion for science?
A: The moment I met Mr. Moore, my organic chemistry teacher, and learned more about who he was and what he did through his educational and professional career, I knew I wanted to be like him. Like him, I want to continue in my educational career, go on to develop medicines and treatments, and, afterwards, pass on my expertise and experience to a new generation by being a teacher or professor.

Q: How did you explore your interest in science in highschool?
A: After taking physics, I took honors chemistry in sophomore year, and I absolutely loved the class! In senior year, I took organic chemistry, and that class unlocked a path in STEM that I really wanted to explore. Organic Chemistry works like a puzzle, and I love puzzles. I want to use organic chemistry and biology in general to develop drugs that cure illnesses and help the world.

Q: What's your favorite DYO that you've done?
A: The DYO I did for Advanced Bio has to be one of my favorites. With one of my best friends, I was able to work in the lab, creating mediums and plating, working with yeast, and generally using techniques that not many high schools can offer. That was one of the reasons that I chose to go to Milton – being able to work in a lab, and have that be a significant portion of our curriculum.

Anthony Zhao

Interviewed by Will Glick

College/Major/Focus:
I plan to attend Duke in the fall! I'm pretty dead-set on doing a Biology major, and I might do a second major which I'm not sure of yet.

Q: How did you first become interested in science and how did you explore your interest in science?
A: Both of my parents are trained scientists, and since I was little, they've always exposed me to lots of science activities, whether it's setting up an experiment for a science fair or signing me up for STEM related summer camps. I only really became interested in biology after taking honors biology here at Milton. Everything that we did in Honors Biology and in Advanced Biology this year was so interesting; we were not just learning these facts but also designing experiments. Linking biological processes, piece to piece, is just so cool.

Q: Have you done any internships or held any jobs in the field of science?
A: The summer before my senior year, I did an internship at a company in San Diego, where I worked on their oncolytic virus project. We think of viruses as bad things, but these genetically engineered viruses actually help you kill the cancer cells in your body and recruit your immune system to help, so the design itself is incredible. I was lucky to get to work on the development of one of these viruses.

Jillian Taveira '22

Memable DYO Moments we've observed in Pritzker

Anna Yang '23 and Ben Kim '22

"We only have one sterile pipette tip left! Let's use it for the (sacred) negative control!"

Calculated the time it takes for an apple to fall, and it's negative. Oh well, guess I have to use g = -9.81 instead of 9.81. Don't know the units anymore (seriously, N/kg or m/s^2??).

"How do we get a stuck centrifuge tube out of the centrifuge?" "Spin it in reverse?" Break Einstein's theory of relativity and think like an engineer.

When the brightness of the light source increases after you've decreased its voltage: blame it on uncertainty!

How to succeed at any microbiology experiment: learn to balance the risk of contamination with the risk of setting your gloves on fire with a bunsen burner.

How to evaluate the quality of any scientific paper: whether the authors use uL or μL.

Every science student ever: "I omit outliers based on a better best-fit-line deviation instead of standard deviation."

How to assign "pseudosignificance" to a nonsignificant p-value: $0.05<p<0.1$, borderline significant. $0.1<p<0.3$, semi-significant. $0.3<p<0.5$, quasi-significant. $0.5<p<1$, not significant. $p>1$, umm...

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