



letters from the

dear reader

dear reader

Well, I sure didn't see this coming back when I was a freshman. I first joined Saltman Quarterly as a member of the Review Board; I participated in biweekly journal clubs and edited a few online articles or research manuscripts here and there. I honestly didn't expect to get to be so involved in this journal or this coalition of biology students, all of us striving to set the highest standard for undergraduate biology journalism.

If you're reading this, you're living in the peak age of misinformation. It's such a basic thing, isn't it! When I speak, I want what I say to be true, and I want whoever is listening to understand. To me, Saltman Quarterly is very much a product of my generation that grew up among the rise of anti-vaxxes, political resistance to climate science, and—worst of all—the harsh treatment of foods previously shunned by pervasive health fads, like full-fat yogurt and (dark) chocolate. Saltman Quarterly is as much for our readers as it is for the writers and editors we train. We are the incoming generation of scientists and science communicators: read on!

Sincerely.

Salma Sheriff Editor-in-Chief 2020-2021 2020. A year beyond anything anyone could have ever imagined. This was not how I envisioned my last year of college to look like—a sentiment I'm sure many other UCSD students share. Having to transition almost every aspect of our lives to a virtual platform this year has been detrimentally isolating.

Even Saltman Quarterly, a publication holding a legacy of over ten years, felt the effects of it. However, this new normal presented us with an opportunity to take a moment, appreciate the beauty of the world we live in, and experience our humanity within it. I am so incredibly proud to see how the SQ family came together and created outstanding content representative of today's world experiences.

The kindness and empathy we showed each other as a team while so many of our members went through life-altering circumstances was humbling. No amount of experience from the past could have prepared us for the situations we faced, but the individual and organizational growth we have gained will stay with us forever.

Warmly.

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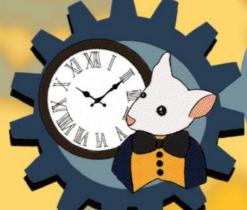
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SHOCKINGLY MOVING

Understanding the processes of refined limb movement and developing devices that harness our neural circuits

Annika So & PHOTO BY
Emily White Sam Zilberman

CIRCUITS in Yichen Wang NEUROBIOLOGY and ENGINEERING

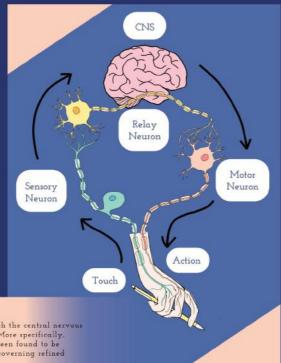
magine yourself reaching for a pencil, walking to your morning class, or even flipping a page of this publication. Do these actions require your focus, or do you hardly think about them at all? While these simple motions may seem like second nature, they are actually quite complex when considering the millions of neurons and hundreds of muscles necessary for movement. Scientists have barely scratched the surface of characterizing the neuroscience behind motion, but two laboratories at UC San Diego are currently delving deeper into this topic. By looking into different aspects of the neurobiology behind motion, these researchers can gain a better understanding of these intricate processes that could allow for great strides in biological devices, prosthetics, and other movement technologies.



THE NEUROBIOLOGY BEHIND MOTION

At the lab of Dr. Eiman Azim, researchers are exploring the neurobiology of movement by analyzing neural circuits in the brain. Nick Baltar is a first-year medical student who worked in the Azim Lab for over three years, first as an undergraduate research assistant and later as a lab technician. The premise of the lab includes observing motor feedback loops, which are the neural pathways between muscles and the brain that control refined limb movement. One type of feedback loop they found was faster than a classical neural circuit going through the cortex of the brain would be. However, it was more complex than spinal cord reflexes, in which neural circuits remain within the vertebrae for quick reactions and do not extend to the brain.

Researchers hypothesized that this motor feedback loop was correlated to a section of the brain known as the lateral reticular nucleus (LRN), located near the base of the brain. Baltar's work involved putting this hypothesis to the test. To understand the structure of the LRN better, gene sequences from single cells in the LRN were analysed in order to identify gene candidates where expression rates diverged across different regions of the nucleus. From this pool, he used a fluorescence in-situ hybridization protocol to establish the location of the possible genes that could be influencing these feedback loops in the chromosome. Additionally, Baltar utilized a method of manipulating genes in mice cells called cre-lox recombination in order to better understand the function of different parts of the LRN. After repeating these procedures for ten different candidate genes, he found genes



HTR2C and PCP4 had specific expression beneath and to the side of the LRN, the portion of the brain the Azim Lab originally thought to be involved in motor feedback loops. He compared the movement of mice with manipulated DNA to the movement of mice with unaltered DNA in order to observe the effect of the altered DNA on the mice's movement. The Azim Lab continues to develop on Baltar's finding, investigating these gene's involvement with motor feedback loops and complex movement.

BRIDGING THE GAP

I Baltar's research now aims to characterize the structure and function of the complicated neural circuits that allow us to perform movements we hardly think about on a daily basis. However, just like any complicated machine, our bodies can malfunction. What happens when things go wrong? Amputations and spinal cord injuries are examples of incidents that cause people to lose their normal motor functions. Neurobiological research is now paving the way for engineering of devices that can address such situations.

In the Nanoengineering Department at UC San Diego, one group is aiming to bridge the gap between theory and application. In 2018, Dr. Sheng Xu's lab made the cover of Nature Electronics for developing a small, multilayer, flexible electrical circuit that stretches and distorts without any damage. This design allows the circuit to stick to fabric or skin. Thanks to their novel framework, these non-invasive circuits are now being developed for many different applications in healthcare such as a blood pressure monitoring system.

TURNING NATURE INTO

One of the developing applications of this technology in the field of neurobiology is the use of the electromyography (EMG) sensor, which takes advantage of the electrical signals involved in movement. A tiny chip three centimeters wide and two millimeters thick can

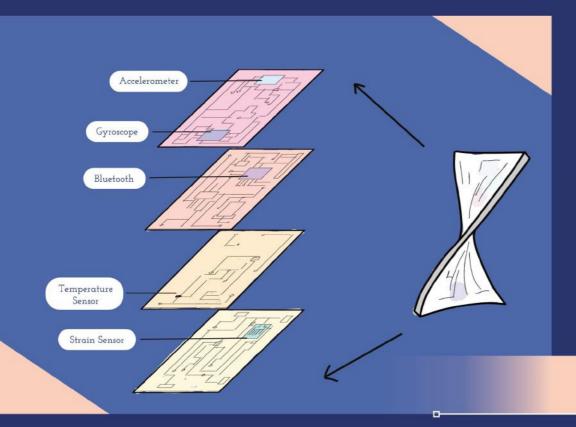
be stuck onto skin and transform human movement into robot movement. EMG sensors utilize the electrical signals our brain sends to our muscles via motor neurons; these motor neurons then stimulate muscle fibers, causing them to twitch and elicit contraction of the whole muscle. During contraction, muscles emit electrical signals known as EMG waves. As muscles can conduct electricity in a manner similar to neurons, sensors placed on the skin near muscle are able to measure the amplitude and frequency of these waves. Then, these signals can be gathered and interpreted, before being translated into code and relayed to machines such as a robotic arm, opening the door to many possibilities, such as prosthetics for amputees and those with spinal cord injury, and remote-control robots capable of performing work.

At the Xu lab, two UC San Diego seniors, Amer Yaghi and Geoffrey Hand, are working to bring a small, wearable EMG sensor to life. The circuit they built contains a gyroscope (which can measure orientation), an accelerometer (which can measure acceleration), an EMG sensor, and a Bluetooth transmitter, which all work together to control a robotic arm. Thanks to their labs novel 3D approach to stretchable electronics, the team is able to fit a large amount of information into one small patch. In the past, engineers were limited to single-layer circuits, but by fabricating multiple layers of this flexible circuitry and joining them vertically through soldering, it is now possible to layer circuits on top of each other and accommodate many more components. The self-contained system can then wirelessly transmit to a robotic arm through Bluetooth, controlling movements with almost no delay. This technology has implications for prosthetics for amputees and controlling remote work in the future.

When asked how the EMG sensor can translate electric waves into a specific movement to control a robotic arm, Hand says there is not a way for humans to recognize the patterns based on EMG readings by eye. The lab is currently using artificial intelligence guided by deep learning algorithms to determine the meaning of EMG signals. Their program is trained to recognize specific EMG wave patterns associated with certain movements such as grabbing or releasing.

MOTOR FEEDBACK LOOPS

The body and brain communicate through the central nervous system (CNS) to dictate our movement. More specifically, the lateral reticular nucleus (LRN) has been found to be involved in some motor feedback loops, governing refined limb movement.



Another potential application of this technology is to detect fatigue in muscles. Fatigue is sometimes identified by calculating the mean and median frequencies of the EMG waves, with a decrease in these frequencies indicating muscle fatigue. However, this theory is not well established, and Hand is exploring novel metrics and statistical methods which may allow him to better quantify fatigue through more complex analyses of wave frequency.

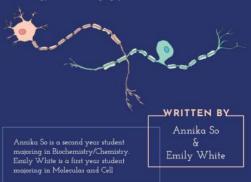
Although these flexible biosensors are innovative pieces of technology, this project has not come without its difficulties. Yaghi explains that the electronics are delicate and fragile, requiring the handler to be very careful; in fact, they are so tiny that he had to learn how to weld under a microscope. In developing software used to program these types of sensors, the devil is in the details, as Yaghi once spent four weeks debugging a single circuit. Hand agrees that there is always lots of debugging to do, as it is difficult to smoothly connect code to the device. Using flexible silicone rubber instead of a rigid circuit board also opens the door to more obstacles than would be encountered in traditional electronics. Much like Hand and Yaghi's coding and circuits, motion is a very complicated subject. This developing technology will become useful in the future, as those with limb deficiencies can wear similar devices to control a prosthetic limb that mimics their movements.

LOOKING FORWARD

Unlike the Azim lab, which characterizes specific neural pathways and the structure of the nervous system, researchers in the Xu lab do not have to understand the specific route electricity takes to cause particular maneuvers. Instead, artificial intelligence can be trained to

STRETCHABLE ELECTRONICS

New breakthroughs in nanoengineering allow multiple circuits to be layered on top of each other, increasing the amount of functionalities the small, flexible device can hold. fill this gap and to translate electricity into movement. This is a stark contrast to Baltar's work in the Azim lab, where he is working to piece together the minute details of how electrical signals are processed and transmitted to perform motions. Baltar admits that the interface between neurobiology and engineering still has a long way to go before being viable for use in robust neural prosthetics, especially when considering the intricate neural circuits he is studying. Since there is some disconnect between the frontiers of engineering and biology, a greater collaboration between the two sides is required to reach a common ground, and both theoretical understanding and its applications are vital in reaching these advanced goals. Those involved in research of motion and neural circuits will always be searching for further understanding. However, new technologies and protocols, such as circuit components and genetic engineering, are constantly allowing for breakthroughs in the field. Through collaborative research between biology and engineering, we can come to better understand how electricity directs motion and work towards solutions for neurobiology's most challenging questions.



THE ROAD TO EQUITY

The healthcare system regularly fails women of African ancestry, transgender patients, and HIV+ individuals, calling for reform in access to treatment, a restructuring of the healthcare referral process, and an increase in awareness of patient needs.

or years, Amira Lewally had lost the ability to hear in one of her ears. As an African American woman, she was wary of doctors and was always frightened that they would not take her seriously. Her primary care physician diagnosed her with allergies, yet her worsening symptoms and her continued doubt led her to take matters into her own hands. She went to several medical professionals, yet specialist after specialist continued to insist that her symptoms were simply allergies. Lewally eventually stumbled across an article that matched her symptoms, and finally found an ear, nose and throat doctor (the third one she had been to) who diagnosed her with a cerebrospinal fluid leak.

Lewally's testimony, published in the LA Times, is not unique, and reveals a grim reality about Western medicine—it caters primarily to white, cisgender men. However, all patients deserve a clinical experience in which doctors are unbiased: aware of their patient needs and takes patients seriously.

Researchers at UC San Diego have begun to tackle this issue, focusing specifically on women of African ancestry with breast cancer, transgender individuals, and HIV positive patients with cancer. These researchers are exposing age-old biases, identifying core issues in the current system, and providing feasible solutions to improve medical care for minority groups. Healthcare prides itself on its ability to care for all, and it's time to make that claim a reality.

IMPROVING the MEDICAL LANDSCAPE

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AT A CROSSROADS

What path would you take if you felt like you couldn't trust your own doctor? Many historically marginalized groups often face bias from medical professionals, resulting in inadequate treatment and even fatal outcomes



BREAST CANCER SURVIVAL

According to breastcancer.org, breast cancer is a common form of cancer among women, affecting around 1 in 8 women in the United States, particularly women of African ancestry (WAA), Although breast cancer has been well-researched over the past few decades, disparities among rates of diagnosis and survival for the disease still exist.

Yilin Xu, a Biochemistry/Chemistry major at UC San Diego, delved deeper into this topic through her research on the correlation between BRCA mutations and survival disparities among women of African descent

Mutations in the BRCA genes are the main causes of hereditary breast cancer in women, according to the Illinois Department of Public Health. When there is a mutation in the DNA coding for BRCA proteins, the resulting proteins cannot repair DNA or suppress tumors as they normally would, resulting in the development of cancer. Women with African ancestry are more likely to have the BRCA mutation and are at higher risk of developing triple-negative breast cancer, a highly aggressive form of breast cancer that is difficult to treat.

To quantify the obstacles faced by WAA with regard to breast cancer risk and diagnosis, Xu drew comparisons between these women and non-Hispanic white women by compiling data from various research papers. In doing so, she was able to draw several conclusions about the correlation between the BRCA mutations and survival rates of breast cancer for WAA

Primarily, she found that WAA are diagnosed with breast cancer less frequently, even though they face a higher mortality rate. Women of African ancestry have a ten-year survival rate of 64% compared to 81% for non-Hispanic white women.

How might we address these disparities in survival rates? Xu proposes multiple avenues for improving the situation. For starters, she states that health education is a necessity. Informing women, specifically those with African ancestry, about breast cancer-related issues shows potential in dramatically decreasing the gap in survival rates. Additionally, Xu says providing cancer diagnostic resources such as free mammograms would allow many women to discover breast cancer at an earlier stage. She also emphasizes that genetic testing is a useful tool for preemptive diagnosis and treatment, as 69% of those who carry the BRCA mutation receive a triple-negative breast cancer diagnosis.

Eliminating systemic biases from society is arduous, as they are often ingrained in our subconscious. But by promoting awareness of these issues, we come one step closer to making the medical world a better place for women of African ancestry.

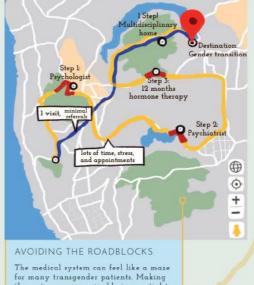
GENDER TRANSITION PROCESS

Transgender ('trans') patients are another marginalized group in the medical field. Trans individuals are those who identify with a different gender than the one they were assigned at birth. They have the option to go through medical treatment in order to transition; this process often involves hormone therapy and gender-affirming surgeries in order to achieve the physical and hormonal makeup of the gender with which they identify

Unfortunately, these procedures are complicated, as trans patients usually deal with unsafe medical environments. 85% of trans patients are misgendered in clinical settings because many professionals are unaware of the social etiquette and medical needs of these individuals. Furthermore, there is a systemic lack of patient autonomy for trans patients and no clear route through the transition process.

David Everly, a Public Health major at UC San Diego, addresses these disparities through his research on specific medical practices that can improve both the transition process and general medical care for transgender patients. Through a systematic review, Everly identified papers containing the "best practices" that address parts of the trans clinical experience.

Currently, to be eligible for gender transition services, clients must meet criteria for a diagnosis of "gender dysphoria." This is known as the gatekeeper model, and involves a meeting with a psychiatrist, approval by a psychologist, and a year of hormone therapy before eventually beginning the transitioning procedures. By placing roadblocks in the transition process, this model limits the autonomy of transgender people and is therefore viewed as unethical by many in



the system more navigable is essential to ensuring patient wellbeing.

the trans community. Instead, Everly proposes the informed consent model. This model involves a general practitioner providing adequate information to a person before allowing the individual to make an informed decision regarding gender-affirming medical treatment, providing medical equity and autonomy for trans patients.

Everly's next suggested practice is the multidisciplinary medical home, a team based health care delivery model where specialties collaborate to provide their patients with the best care. Trans patients are often overwhelmed with referral processes as a patient sometimes requires multiple referrals for only one of the many procedures they undergo. Therefore, a "medical home" in the form of a vetted referral system would be effective. This system greatly lowers the risk of unfavorable experiences with providers due to a lack of education or a lack of cultural competency training. The healthcare company Kaiser Permanente has already been implementing this model through the opening of a Multi-Specialty Transition Department at several locations.

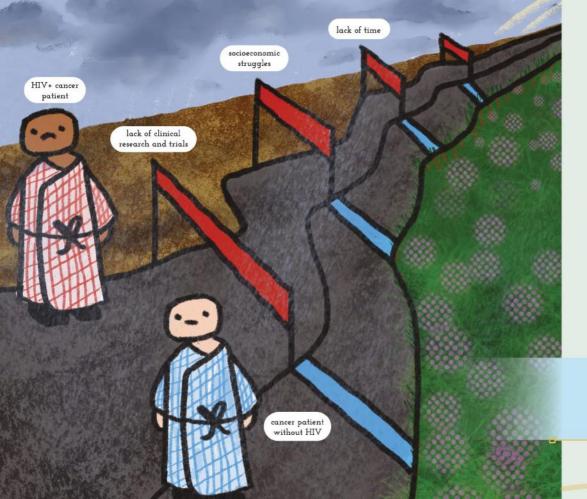
Medical professionals' awareness of these disparities—and how to alleviate them-is a must. Without the types of changes highlighted by Everly, trans patients will continue to experience the repercussions of a system not tailored to suit their needs.

CREATING TOOLS TO HELP V

To this day, human immunodeficiency virus (HIV) is a major global health issue. According to the Kaiser Family Foundation, over 38 million people worldwide were HIV+ in 2019. HIV attacks the immune system and increases patients' susceptibility to other diseases, including cancer. Unfortunately, HIV+ patients with cancer face disparities in healthcare treatment compared to other cancer patients.

Rowan Ustoy, a UC San Diego General Biology major, conducted a literature review to look into the barriers that HIV+ cancer patients face. Based on Ustoy's research, HIV+ patients suffer from higher rates of cancer but lower rates of adequate treatment. Why? Like the cases of women of African ancestry and trans individuals, the answer stems from a lack of awareness of patient needs.

Alarmingly, many physicians lack knowledge about the treatment



of cancer patients with HIV. Part of this may be due to the fact that 45% of oncologists (cancer specialists) do not discuss treatment with a patient's HIV specialist. Furthermore, HIV patients have been, and continue to be, excluded from cancer clinical trials.

This lack of inclusion has resulted in a scarcity of data regarding the needs of such patients. Consequently, a shocking 75% of physicians report lacking confidence in cancer treatment approaches for their HIV+ patients. This can be life-threatening, as antiretroviral therapy (ART) drugs, the primary treatment for HIV, are known to often clash with cancer treatments.

In addition to the factors mentioned above, many HIV patients face socio-economic struggles. HIV is a lifelong disease and requires daily medication, and cancer requires intense treatment involving multiple hospital stays. Treating these diseases demands both time and money, and many of those afflicted lack the funds necessary for these treatments. Furthermore, HIV+ patients are more likely to be non-Hispanic Black or Hispanic. These are groups that are disproportionately less likely to receive treatment, as they lack insurance and therefore access to healthcare.

Is there a way to overcome these challenges? Yes, and one may look to the promising advancement in anal cancer treatment as proof. Anal cancer has been well-documented in clinical guidelines, allowing HIV+ patients to obtain quicker diagnoses and more specific treatment options. Knowing this, we can be confident that it is indeed possible to lessen the disparities between HIV- and HIV+ cancer patients.

In order to extend the same chances of survival to HIV+ patients

with other forms of cancer, Ustoy emphasizes the necessity of promoting clinical trials that include HIV+ patients and those that focus on the link between HIV and cancer.

ADVOCATING FOR HEALTH EQUITY



Medicine, just like the rest of society, is biased. Society's racism, transphobia, and HIV stigma are rampant, and solving these issues is complicated. In 2020, America faced a wake-up call to the inequalities and injustices carried out against its historically marginalized populations. The murder of George Floyd shed light on police brutality against African Americans. The Trump administration proposed a new rule that would allow sex-segregated shelters to refuse service to transgender people. Eight in 10 people in the US with HIV continue to feel internalized stigma while receiving treatment, a direct result of the discrimination they face.

Under these circumstances, it is more important than ever for medical professionals to take the appropriate steps to tackle these injustices. Providing healthcare resources to underserved communities, furthering inclusion of minorities in clinical trials, and providing quality care that respects patient autonomy are some of the first steps to providing a more inclusive healthcare system.

By acknowledging these disparities and spreading awareness that they exist, we as a society can take the first steps towards closing the gaps in healthcare equality.

A SKEWED RACE

From lack of research to high-cost treatment that many cannot afford, HIV+ patients with cancer face many hurdles in getting any access to help.



MEDICATION OR MEDITIATION

A SYNERGISTIC MIND

and BODY

In the landscape of mental health, scientists are researching how upholding mental well-being can impede or even cure disease. Varsha Mathew

PHOTO BY

Sam Zilberman

Varsha Madrigal

his fall, 16,700,000 students began another term of their undergraduate degrees. In October 2020, 31,842 Tritons began an intense online quarter filled with midterms, assignments, projects, final exams, and extracurriculars—all of which can combine to form an alarming recipe for stress and potentially poor mental health. This precarious balance between academics and mental health is often difficult for students to manage, as reflected in the popularity of on-campus resources such as Counseling and Psychological Services (CAPS).

That said, what happens after an individual is diagnosed with anx-

iety or depression? Upon receiving a diagnosis, many may initially hesitate before asking their physician if there is a "pill for that." In fact, according to a report released in March 2020 by the National Center for Health Statistics, the rate of antidepressant use in the United States increased by 400% between 1988-1992 and 2005-2008 in people ages 12 years and over. This alarming increase in the number of people turning to prescriptions to improve their mental well-being leads us to the following question: what does a healthy balance between prescribed and self-initiated care look like?



GOT BIOLOGY?

Over the last several decades, researchers have slowly uncovered a number of biological pathways that directly tie into our mental well-being. From the development of selective serotonin reuptake inhibitors (SSRIs) for treating depression to the role of lithium in the treatment of bipolar disorder, the success researchers have had in utilizing these pathways to treat mental illnesses has somewhat reinforced our culture's enthrallment with prescriptions. After all, prescriptions initially seem to offer the most direct way of changing our mind's biological and chemical landscape. The power of the pill is nothing short of immense—so much so that it has influenced our society's understanding of what recovery looks like.

Here at UC San Diego, researchers across campus are working in a variety of ways to better understand this biochemical aspect of mental wellbeing and how, if at all, we can influence it. One such group is the Spitzer lab, where integral research is being done to identify a biological pathway implicated in PTSD.

THE SPITZER LAB

Under the guidance of Dr. Huiquan Li, UC San Diego alumnus Wuji Jiang worked in the Spitzer Lab and conducted research on the possible connection between neurotransmitter switching, or when one neurotransmitter is replaced with another, and harmful outcomes such as PTSD result. By associating a specific neurotransmitter change with the onset of PTSD in mice, Jiang and the Spitzer Lab hoped to develop a biological explanation for PTSD in humans.

In order to induce PTSD, the mice were placed into a box which periodically delivered shocks, stressing them to the point of traumatization. Jiang then tested mice for "freezing behavior," characterized by the mice's inability to move during re-exposure to a trigger, as an indicator of PTSD. Once this behavior was confirmed in all the mice, the researchers analyzed each mouse's brain for a neurotransmitter change by measuring neurotransmitter levels. To measure the neurotransmitter levels, Jiang used an antibody targeting the neurotransmitter.

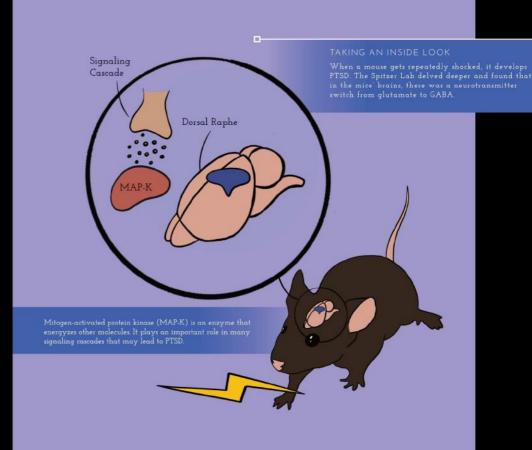
producing enzymes and measured its growth via a process called immunohistochemistry (IHC). The researchers reasoned that detecting an increase in these enzymes via IHC suggested that more of a particular neurotransmitter was being made, indicating a neurotransmitter switch had occurred.

It turned out that Jiang did find a switch: from glutamate, an excitatory neurotransmitter, to GABA, an inhibitory one. Despite successfully investigating one notable hypothesis, the lab has yet to find an explanation for why this switch occurred. In spite of this frustrating aspect of science, Jiang believes that the Spitzer lab should persist in their search for this molecular explanation in order to gain a stronger biological understanding of mental well-being. By finding a biological response to PTSD with the neurotransmitter switch, the Spitzer lab's work reinforces the validity of the connection between mental health and the brain's biochemistry, a connection which prescriptions successfully utilize.

Therefore, Jiang's research highlights the importance of prescribed care, or the care prescriptions provide for our mental health, as a potential tool for undergraduate students. Although inconclusive, Jiang's work shows us that an assortment of neurotransmitters and molecules play a key role in determining our mental well-being, as seen in conditions like PTSD. While the most obvious takeaway from this research might be the direct approach of prescriptive care, this study's insight leaves another potential research question on the table: can self-initiated care, through practices such as meditation, positively impact our mental health? Can we self-initiate and activate the influence of these molecular pathways through practices such as meditation, and thus move away from prescribed care as a primary form of treatment?

SELF-SUPPORTING MENTAL HEALTH

Through mindfulness exercises such as prayer, yoga, and tai chi, humans have consistently utilized methods to alleviate distressing



emotions, from angst to anger. This leads one to wonder: can we improve our society's rapidly declining mental health by incorporating these centuries-old practices?

While mindfulness cannot remedy all mental health conditions, the benefits of prioritizing mindfulness in our daily lives are becoming increasingly clear, as it provides a level of autonomy beyond the effects of any pill. Located on UC San Diego's campus, Debra Lindsay, a graduate student under Dr. Karen Dobkins' mentorship, is looking at the effect of self-confidence on overall mental wellbeing.

HUMAN EXPERIENCE LAB

In September of 2018, Lindsay and her team recruited 338 UC San Diego undergraduates to participate in a study researching the relationship between positive self-reinforcement on overall mental wellbeing. Lindsay first had the participants take an initial personality test that identified their "top strength," such as being funny, and "bottom strength," such as being empathetic. Lindsay also measured the participants' baseline wellbeing through self-reported surveys and established measures of happiness and self-esteem using the Centers for Disease Control and Prevention (CDC) symptomology for depression.

Lindsay then divided the participants into two groups: the first group would be told the truth about what their top

A BALANCING ACT

A young woman practices yoga while holding a prescription bottle. The Spitzer Lab and Human Experience Lab show that mental health is a multifaceted entity that can be maintained in a well-rounded way. strength was, and the second group who would be lied to and told that their bottom strength was their top strength. Lindsay instructed all participants to deliberately use their "top strength" over the course of a week and be aware of how this affected their mental well-being. Lindsay predicted both groups of participants would experience a positive increase in their wellbeing as a result of exercising their "strength." She hypothesized that a participant's resulting belief in themself would have a positive effect on their mental health.

A week later, the participants returned to the lab and filled out another self-reported survey to re-assess their mental wellbeing. The results were intriguing—Lindsay found that most of the participants who reported an improved mental wellbeing believed that their incorrectly assigned character strength was their true top strength. Lindsay's results suggest that we do have some degree of autonomy over our mental health, as we can fortify our mental well-being just by increasing self-empowering behaviors such as working on positive aspects of ourselves.

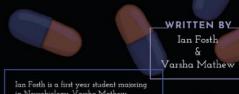
This leads us to ask a final unanswered question: do we have enough autonomous control over our mental well-being to consciously protect it from mental illnesses, or must we still depend on directly influencing our biological pathways via medications and external care?

A SYNERGISTIC APPROACH

As seen by these questions about the prevention and development of mental health illnesses, there is still much to be answered regarding the level of control we have over our mental well-being. The conclusions drawn by both the Spitzer Lab and The Human Experience Lab suggest a partial answer to these questions, showing that both prescribed and self-initiated factors should be considered when developing a well-rounded regimen for effectively maintaining a positive wellbeing. This being said, how does this research apply to the mental well-being of the average college undergraduate?

The Spitzer Lab shows us that basic emotions like stress are rooted in an intricate system of biological pathways we have traditionally addressed with medicine. While it might be impossible for us to control the outcome of these pathways once activated, can we attempt to mitigate the initiation of these pathways by reducing our stress levels? Yes! The Human Experience Lab suggests that simple actions like self-empowerment can have a significant positive impact on overall mental well being. In other words, although we may not have complete control over how a biological pathway proceeds, we might have some control over when these pathways are activated simply by treating ourselves with kindness.

Unlike molecular pathways, self-care doesn't need to be complex and can be as simple as going for a walk, drinking enough water, calling a friend, reading a book, or stepping outside for a breath of fresh air. The Spitzer and Human Experience Labs' projects show that both prescriptions and self-care practices can help our mental well-being, suggesting that our mental health is optimized through a combination of approaches rather than a singular investment. Midterms, projects, finals, and interviews may come and go, but our mental health is important for life. Ultimately, if you are contemplating between taking the medication or doing the meditation—why not consider both?



Ian Fosth is a first year student majorin in Neurobiology. Varsha Mathew is a second year student majoring in Molecular and Cell Biology.

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CURIOUSER AND CURIOUSER

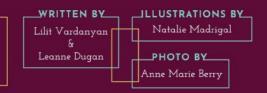
Our model organism (mouse) runs on a clock, our circadian rhythm stand-in.



CIRCADIAN CYCLES

CURIOUSER and CURIOUSER RESEARCH

Down the rabbit hole of circadian rhythms, these daily cycles are involved in cancer, digestion, and reproduction.



'm late! I'm late! For a very important date! We've all got a schedule to keep, and the maintenance of these schedules is what allows for the cohesive and smooth operation of one's plans. Just like the white rabbit's clock in Lewis Carroll's Alice in Wonderland, our bodies schedule all of our biological processes on a 24-hour cycle, referred to as a "circadian rhythm." This rhythm lets our bodies know when to perform certain processes and when to cease others. To maintain this biological rhythm, our bodies have a strict schedule to follow throughout the day, and our everyday actions have a strong impact on this schedule. However, some of these actions can lead to major changes in this rhythm and disrupt bodily

functions, producing disastrous effects. But exactly why is this? Let's jump down the rabbit hole and find out.

UC San Diego has a whole wonderland of research opportunities for undergraduates in various departments and programs like the Center for Circadian Biology. As we explore this wonderland of information, we will meet four undergraduate researcherswho are focusing on groundbreaking circadian research during their undergraduate careers. As they help us navigate this new, undiscovered territory, you will more easily be able to understand for yourself the discoveries that lie ahead and see this new world through a scientist's eyes.

NAVIGATING THROUGH CANCER

Our first navigator is Sabrina Major, an undergraduate researcher in Dr. Gabriele Sulli's lab who studies the circadian rhythms of various cancer cell lines. Cancer cells maintain their own circadian rhythms which are distinct from those of healthy tissue cells. Therefore, understanding the pathways by which cancer cell circadian rhythms are formed and maintained is critical to the development of new therapeutic treatments. Because circadian rhythms are an integral part of cell maintenance, disrupting these cycles can lead to cell death which, in the case of cancer cells, is the desired outcome of treatment. Major and other researchers in the Sulli lab are testing various drugs which can disrupt circadian rhythms in cancer cells while leaving the more robust rhythms in non-cancerous cells intact. While current cancer treatments such as chemotherapy are very successful in destroying cancer cells, they also destroy healthy tissue in the process. So, new treatments which solely target cancer cells, like the ones being explored by Major and her colleagues, are extremely necessary. It is evident that Dr. Sulli's lab is undertaking a very significant project in the field of circadian biology and cancer, and Sabrina Major is there to experience it all.

THE SCHEDULE OF FEEDING

Alexis Oberg will now show us a puzzlingly complex area of circadian study: the circadian rhythms of cancer. Studying circadian rhythms in the context of cancer development and treatment discovery by rhythm disruption continues to be an important topic in the field of circadian biology. Alexis Oberg is spending her post-graduation year in Dr. Nick Webster's lab studying the effects of time-restricted feeding on breast cancer development in obese and post-menopausal mice. Time-restricted feeding involves designated time frames during which one either eats or fasts on a daily basis. In her project, Oberg studies mouse models that are not only on time-restricted diets, but are also only allowed to eat during a distinct eight-hour period of time. According to Oberg, previous studies have shown a correlation between disrupted



PILOTING OUR PACE

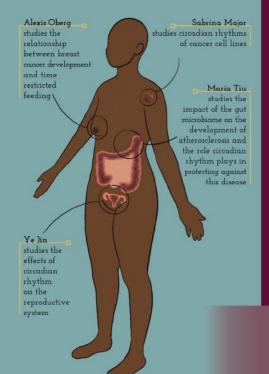
Meet the student researchers who are guiding us through the mysteries of markings of circadian rhythms.

circadian rhythms in the context of time-restricted feeding and various types of cancers in post-menopausal individuals. Through the work being done in Dr. Webster's lab, it is evident that time-restricted feeding and possible disruptions of circadian rhythms do reduce cancer growth in their mouse models; however, the exact association between disrupted circadian rhythms and cancer development is not yet clear. Alexis Oberg and her colleagues are continuing the search for a specific mechanism of action behind their findings.

THE CYCLES OF MICROBIOME

Our next stop is the human digestive tract. Maria Tiu, a fourthyear human biology undergraduate, is conducting circadian research by delving into the world of the gut microbiome in Dr. Amir Zarrinpar's lab. The gut microbiome encompasses the microbes located in the digestive tract that play a major role in the way food is digested. In Dr. Zarrinpar's lab, researchers are working with mice models to understand the effect of the microbiome on the development of atherosclerosis and whether the circadian rhythm protects against this disease. Atherosclerosis is a disease in which the arteries become clogged with the build-up of plaque, blocking blood flow of oxygenrich blood to vital organs, according to the NIH National Heart, Lung, and Blood Institute.

The Zarrinpar lab used mice models to observe circadian rhythms due to the similarities between mice and humans. Two groups of mice were observed: those that were free to eat all day and those that were on a timed feeding schedule (intermittent fasting). However, all "mice were fed an atherogenic diet," or a diet that leads to plaque build-up



in the arteries, and all the mice used were 'Apoe -/- and Ldlr -/- mice', or mice that are prone to atherosclerosis. Throughout the day, the gut microbiome composition changes," Tiu notes, and when the mice are placed on the timed feeding schedule, this "induces a circadian cycling of the microbiome." Tiu defines the circadian rhythm to be "any biological process that has a 24-hour cycle." However, circadian rhythms have been primarily studied during certain isolated time frames. What makes their research unique, Tiu explains, is that their data is collected during the entire 24-hour cycle.

In each group of mice, stool is collected every four hours and analyzed using 16s rRNA sequencing. According to CD genomics, 16s rRNA is a gene found ubiquitously in bacterial genomes; due to its abundance in bacterial DNA, gene sequencing can readily detect 16s rRNA. According to LC Sciences, the 16s gene differs between various species of bacteria, allowing for the sequencing of bacterial samples composed of many different species-such as in a gut microbiome. Therefore, this provides data about the microbes that are present at various points of the gut circadian cycle. After they complete the two week data collection period, the Zarrinpar lab stains the lesions found in mice hearts in order to determine the severity of the atherosclerosis. Looking at their heart lesions, they have noticed that mice placed on the time-restricted diet "exhibited a significant change in gut microbiome composition," and "developed significantly less aortic lesions and significantly improved cholesterol profiles." Overall, their findings suggest the strong role that the gut microbiome plays in the development of atherosclerosis and the effects it has on overall health.

RHYTHMS AND REPRODUCTION

Leading you through the reproductive system is Ye Jin, a third-year undergraduate researcher in Dr. Karen Tonsfeldt's lab who is looking at the effects of circadian rhythms on the reproductive system of mice. Jin notes that the brain controls circadian rhythms, which the Tonsfeldt lab hypothesizes are controlled by certain genes, Jin defines circadians rhythms as "any 'inner clock' in the body which is on a 24-hour cycle." This applies not only to something such as feeding at the same time every day, but also to the timing of the reproductive cycle, which is the focus of the Tonsfeldt Lab's research. During the menstrual cycles of both mice and humans, body temperature rises. By taking the temperature of the mice periodically, the Tonsfeldt lab hopes to garner a correlation between this temperature and circadian rhythms as a way of measuring the menstrual cycle. Every six minutes for three weeks, they take the mice's temperatures. Due to the large amount of information this method generates, the lab uses wavelet analysis to sort the data. According to Associate Professor Lachezar Filchev, wavelet analysis is a mathematical tool that is used to find patterns that lie hidden in large data sets, depicting the data as a graph, and allowing for a deeper understanding of this data. In the study, which uses about 100 different mice, the gene Bmall was knocked out so the lab could determine its effect on circadian rhythms. This gene "is a very important 'cog' of the molecular clock," says Jin. It is important to the functioning of the suprachiasmatic nucleus, a region of the brain that is responsible for "coordinat[ing]

the rest of the body," essentially functioning as the body's clock. Ultimately, the lab hopes to see the effect this knockout gene has on the mice's circadian rhythms, as it is an integral part of the timing of many of the body's functions.

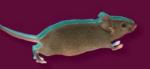
Circadian rhythms are an exciting and relatively new area of research, the surface of which has barely been scratched by scientists. This rhythm plays a large role in many important biological processes. From eating to sleeping and even to the development of pathological diseases, circadian rhythms are a crucial background player in their cycle and perpetuation. Without circadian rhythms, our bodies would be fundamentally different. Though not much is known about circadian rhythms currently, this means there is an entire wonderland of discoveries waiting to be uncovered and explored.



Lilit Vardanyan is a fourth year student majoring in Human Biology. Leanne Dugan is a second year student majoring in General Biology.

THE WHOLE PICTURE

Circadian rhythms exist everywhere in our body! Her are some tissues and organs that operate on rhythms







BEYOND THE GUT

The incredibly diverse human microbiome plays a vital role across its host's many organ environments, carrying enormous implications for treating diseases and preserving humankind's well-being.

he human body is composed of tens of trillions of cells, with almost as many cells as all of the stars in the Milky Way. Operating together as a wonder of evolution, the body's organ systems work constantly to maintain a living balance. So, what would it mean for the human body to harbor more microbial life than bodily cells themselves?

Meet the human microbiota, the miniscule zoo inside each one of us, inhabiting a vast landscape of surfaces across the human body. The microbiota, collectively known as the microbiome, reflects this diversity, together sporting over three million unique protein-coding genes.

This adaptability of microbes to the unique niches of the human body allows them to forge a symbiotic relationship with their hosts. The benefits are many, ranging from keeping their locale in homeostasis by ensuring metabolic balance, to synthesizing valuable compounds such as vitamins, to contributing to a more robust immune system. Conversely, without the help of these microbes, symptoms of disease begin to emerge. Microbiota changes have been associated with weight fluctuations, states of mood, and even the growth of cancer.

What makes the microbiome so uniquely fascinating? Since the beginning of time, humans have gravitated toward "big picture" interpretations that explain every nuance of the natural world, even when these were a stretch. Galen, the father of ancient medicine and Hippocrates's most prominent student, believed the body to be composed of four fluids that could explain all human function. We now know, of course, the errors of Galenic theory, but besides DNA, the language of all living organisms, very few discoveries with all-encompassing ramifications have surfaced.

Although the field is extremely novel, the microbiome already unveils an expanded view of human life. Its origin in each person is brewed in the habits of their predecessors and molded by the qualities of that person's diet, stress levels, and related ailments. The microbiome's presence across the diverse environments of any one human body is difficult to fully describe, a biochemically intricate display with many nuanced effects on its human host and mysterious behaviors yet to be deciphered. As the microbiome's full story becomes clearer, there remains little doubt as to how integral it has been in the evolution and wellbeing of humanity, a realization that would tickle even the likes of Galen and Plato.



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CHASING CANCER'S TRACKS



The ancient Greeks may have found their idol in Dr. Rob Knight. An expert in microscopic organisms, he is the Director of the Center for Microbiome Innovation at UC San Diego. His development of the computational tool Unifrac, allowing measurements of differences among microbial genomes, has propelled a career in microbiota and inspired auxiliary projects among his cohort of graduate students. Greg Poore, an MD/PhD candidate in close collaboration with Dr. Knight, elaborated on his own research.

Previous papers had shown the ways in which bacteria were often associated with a variety of cancer cells and metastases. Using the Microbe Genome Atlas, which is a vast catalogue of microbial DNA sequences, Knight and Poore applied machine learning methods to diagnose cancer types solely by identifying the types of microbial DNA found in blood samples from cancer patients.

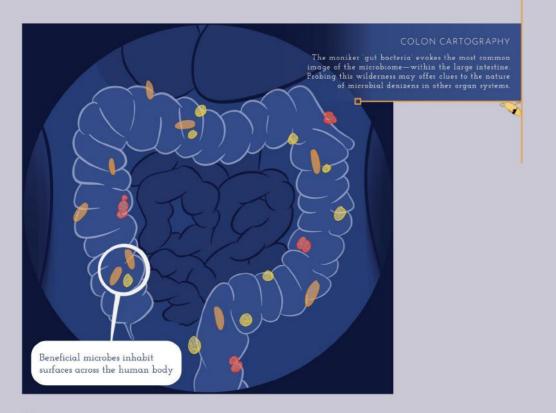
Decades of literature showed that patients suffering from certain bacteremias, or bacterial infections of the blood, were later diagnosed with colon cancer-even asymptomatically. "We wanted to see if we could selectively diagnose colon cancer versus other types," said Poore. "The results were phenomenal." He used the Atlas's reserve of 2000 whole genome sequences from blood across twenty cancer types to produce correlation curves between microbial DNA and colon cancer characteristics. The area readings for these curves were 0.98 or 0.99. For reference, the maximum possible value for a correlation coefficient that has perfect overlap is 1. To further test the validity of their analyses, blood plasma samples from patients at the UCSD Moores Cancer Center were compared, both between cancer types and between patients with and without cancer. These are the most controversial sample types, as they were conventionally thought to be sterile and devoid of microbial DNA. In terms of these validity studies, the best results were seen with lung and prostate cancer. Supported by extensive data analyses and validation studies, their data indicated an ability to locate and diagnose many kinds of cancer across the body in their initial stages (Stage 1 or 2). In other words, malignancies could be identified early on, all thanks to the presence of specific microbial genomic residues serving as beacons for the presence of cancer prior to the onset of conventionally detected symptoms.

MICROSCOPIC, MERCURIAL MESSENGERS

At UC San Diego's School of Medicine, the Weg Ongkeko Lab explores another facet of the microbiome's connection to pathology. Harrison Li, a recipient of the Churchill Scholarship and recent UC San Diego graduate, studied the microbiome in a host of diseases and organs in order to understand its greater implications in fomenting states of disease. For example, the analysis of microbes present in patients' joints yielded results that potentially implicated certain microbes' role in the development of arthritis. An abundance of recent papers have similarly found microbes contributing to tumor formation in numerous ways. Their metabolic interactions with healthy tissue cells promote normal cell growth, but this may spin out of control, disrupting cell cycle controls that can then domino into tumor development. To worsen matters, microbes can also damage cell DNA, jumpstarting the route to cancer. Moreover, microbes may stimulate the growth factors that nurture tumor cells, while hindering the immune system's ability to detect these abnormalities early on.

Given the many unknowns of the physiological jungle within us, therapeutic applications of the microbiome appear unlimited. Cancerous cells could be screened for biomarkers that indicate the presence or activity of microbial species, especially those that work synergistically with the disease. The microbiome could also be manipulated using probiotics, i.e. healthy bacterial species. Probiotics might thus be used to alleviate disease conditions. Alternatively, they might serve as a drug delivery tool through genetic engineering, capable of transporting a treatment to a microscopic bodily point of interest. "If you were able to take a probiotic supplement," claimed Li, "there would be no need for poisonous chemicals." Further research is taking place to make Li's vision of therapeutic probiotics a reality.





RUMBLE IN THE JUNGLE

The microbiota's ubiquitous role in the jungle of human organ systems relies just as much on the bacterial populations' interactions with one another as it does on these populations' interactions with the human body. Dr. Karsten Zengler's lab in the Pediatrics and Engineering Departments at UCSD focuses on the microbiomes of community systems, which encompass ecosystems, animals, and the people that interact with them. Dr. Cristal Zuniga, a former postdoctoral researcher in the lab, studied the metabolic workings of bacteria on human skin, a "savannah"-like environment where conditions are not as dark and damp as some of these microbes would prefer.

The helpful Staphylococcus epidermidis bacteria and the infectious S. aureus bacteria are two related species in perpetual competition for resources. The "goodness" of each is relative to the bodily region they inhabit; S. epidermidis has a commensal relationship with its human skin environment, where it benefits by obtaining nutrients while the human host is unaffected. It outcompetes the more virulent S. aureus on human skin, thus maintaining healthy nutrient cycling across this surface. However, S. epidermidis may also become an opportunistic pathogen, hitching a ride on a host's medical devices or implants and turning infectious or "bad" once it enters the body. Zuniga's work centered on designing community models, computer simulations that incorporated all elements of the bacteria's surroundings in order to predict their interactions with the body — and tentatively, each other.

"There is very little known about modeling microbe interactions," Zuniga said. "The skin is a very interesting organ. On the surface, you have a lot of exposure to oxygen, but you can go deep enough that it is almost anaerobic [doesn't rely on oxygen]." Using computational systems, community skin models can predict how specific mixtures of oxygen-associated metabolites, or molecules produced as a result of reactions sparked by oxygen, may contribute to skin health. In fact, the varied bacterial populations themselves were associated with these molecular findings.

Such modeling, called constraint-based modeling, said Zuniga, "changes constraints ... and gives you results that contextualize things. We look at the problems in a very mathematical way," S. epi-

dermidis's helpful qualities on the harshly exposed skin surface shifts to harmful, parasitic goals in the host's bountiful insides, as access to resources increases. Therefore, we see that a bacterial species' utility to the host can vary widely. It was observed that S. aureus could consume almost any metabolite, even in deep layers of the skin where there is little oxygen. Overall, while S. epidermidis changes its relationship to the host based on its location, S. aureus acts as a pathogen in both environments. Indeed, both bodily geography and responsiveness to resource ratios are central to this microbial tug-of-war. Ultimately, such models have the potential to serve as powerful predictors of the species' contribution to other localized infections, such as pneumonia.

FOR THE FUTURE



The cutting edge of microbiome research today is especially sharp. Venturing beyond the bacteria of the gut, current efforts sample the composition, behavior, and effects of bacterial communities throughout the body, which together rival the Amazon rainforest in sheer biological wealth. In the blood, microbial genomic elements serve as red flags for the more insidious threat of early cancer, while on the skin and in the lungs, the open ground promotes a wild arena for microbial competition. The frontier of microbiome research is advancing on an almost monthly basis, spurred forward by gene-editing technologies such as CRISPR, which allows for microbial manipulation. Likewise, the medical field is beginning to realize the gargantuan therapeutic potential of the human microbiota, with personalized treatments forging a possible revolution in the battle against infectious disease. As the scientific community expands its sights, the microbial ecosphere of our bodies may well become the next frontier in healthcare.



QUOTES FROM

COVID-19 BUBBLES ACROSS the GL BE



Anna Hakimi Santa Cruz. California,

Nicole Adamson St. George's, Bermuda 3,000 mi away



Emily Beckman Junior, Bioengineering San Diego, California, U.S.A.



Madeline Brown Sophomore, Molecular & Cell Biology Texas, U.S.A | 1,000 mi away I was the only student available at my work due to the pandemic. This led to me taking on a heavy work schedule and my grades suffering. Due to financial circumstances, I have to

graduate a year early. For a few months in summer, I lived alone, making

Andre Lovola Senior, Bioengineering: Biotechnology Curitiba, Paraná, Brazil 6,000 mi away

QUARANTINE



Francesca Falzon Young Sliema, Malta | 6,800 mi away



Changzhou, Jiangsu, China 6,600 mi away

Courtesy of Interviewees

Salma Sheriff Andra Thomas



That we have the option to switch our grading option to P/NP reduces the stress of those classes,

Yashaswat Singh

New Delhi, India. 8,000 mi away

Malhotra Senior, Cell Biology



Shanghai, China 6,600 mi away

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Anna Hakimi Sophomore, Neurobiology Santa Cruz, California, USA 450 mi away

Even though I loved strolling into Galbraith or York for a lecture, seeing my professor struggle with the projector, or meeting new people around campus, asynchronous lectures have made my life much more organized and my education more balanced—quite the unexpected result! I took extremely heavy science course loads and was able to succeed largely due to the very efficient online format. So, in a way the pandemic has improved my chances for achieving my goal of graduating in three years! Sometimes, it is much easier for me to hop onto a Zoom call with a professor, as it feels less scary to stare just at their image rather than walk into their empty office all alone.

Nicole Adamson Sophomore, Marine Biology St. George's, Bermuda 3000 mi away

Bermuda is a beautiful place, and thanks to travel restrictions and strict testing protocols, there was no local transmission of COVID-19 on the island when I was there during the fall quarter. It was an amazing and bizarre bubble where life seemed virtually normal. Indoor dining and public transit felt safe, and I was incredibly lucky to explore the island with the other NSF research interns! In general, people in Bermuda were worried about tourists accidentally importing COVID-19. They were especially wary of Americans tourists because Bermudians had seen America's uncoordinated response and the prevalence of disproven hoax conspiracy theories in the news. Earlier, in the summer of 2020, Bermuda completely banned travel, going so far as completely shutting down the airport. As far as I could tell, Bermudians were generally weary of repeating that experience, so compliance with basic preventative measures like masks was high.



The hardest aspect for me was definitely the 9-hour time difference. I would be completing all of my classes and quizzes at night, which was very hard on my sleeping schedule and my swimming schedule.... An unexpected benefit from attending UCSD from Malta was actually being back home with most of my distant family close by. Since I usually only see them in summer, it was lovely to be close to them



In pretty much all public places, [wearing a] mask has been a mandate since January 2020. Any positive cases discovered result in a community lockdown, mass testing, contact tracing, and travel restrictions. Any foreign arrivals require two negative tests (nucleic acid test + IgM antibody serum test) pre-boarding and a mandatory 14-day hotel quarantine + 7-day stay-at-home quarantine + 7-day health monitoring. That's why our country can have this pandemic under control. Our life has been basically back to pre-pandemic normality since April 2020. I have more time to spend with my family [and] my friends from home and do what I always wanted (ex. badminton class). I have gotten to know traditional Chinese culture and the country of China much better by experiencing different festivals and traveling to difference places. I think I love my country even more after COVID. Many people think of this pandemic as an obstacle of their lives which created so much catastrophe, devastation, and forced them off their well-worn path. And I don't blame people for thinking of it that way. For me, yes, it ruined my summer lab internship; it ruined my trip to Costa Rica over spring break; it cost me \$8,000 to fly back, but more importantly, it created so many opportunities that would otherwise be impossible. Detours can be scary, but we can



I have not even lived at home for this long since high school because I went abroad. I think this long stay really got me and my little sister closer. She's 10 years younger than me, and we had very little interactions because I was always away. ... Some of my sections are [starting at] midnight [or] super early morning. Sometimes I can barely open my eyes during sections, and I feel bad about it. Also, when I am working on my homework during the day, it's my friends' midnight, and I can't really discuss with them like I usually do. Education is really a luxury. There are so many things in life that can go wrong, and we should cherish every moment that we are able to learn. I just wanna say it is really a tough time for everyone, and please don't be too harsh on yourself. We are living through a once-in-a-lifetime pandemic after all

