SciTECH

EMERGING HOPE IN THE WORLD OF ALZHEIMER'S

TELOMERE-TO-TELOMERE: THE FIRST GAPLESS HUMAN GENOME SEQUENCE

NASA'S ARTEMIS PROGRAM, 50 YEARS IN THE MAKING

FEATURING: THE SRP '23 COHORT - SLS, Q&A, AND ADVICE

Letter from the Editors

Welcome to SciTECH's first issue of the 2022-2023 academic year!

As usual, we have prepared a wonderful issue for you to embark on a journey uncovering the latest technological and scientific discoveries and phenomena!

In this issue, you'll find a range of articles covering science, technology, engineering, culture, and hacks. In the field of technology, our writers have touched upon the sentience of Google's LaMDA AI model and recent developments in NASA's Artemis Program. If you're more interested in the cultural aspect of STEM, check out our Minorities in the STEM column to read about the inspirational story of Computer Science pioneer Grace Hopper! For all the psychologists and biologists out there, flip through the issue to our articles on both Alzheimer's disease and the connection between sociology and neurology.

Exclusive to this issue, you can also find highlights about the summer works of the students in the Science Research Program (SRP)'s Class of 2023. From concise summaries of students' works to Q&As about their lab research experiences and advice for current and future SRP students, we hope this new column further engages the community's interests in science, technology, and its diverse applications. In the future, we hope to expand this column to spotlights students conducting natural science research in the Environmental Immersion Program and others performing STEM-related independent works.

As always, we sincerely appreciate you as insightful readers to reach out with any feedback or suggestions. Likewise, we highly encourage you to contribute to future issues — whether it's article ideas, graphics, or pictures you would like to see, design, or write yourself!

Happy reading!

Ryan Kim '23
Editor-in-Chief

Eva Li '24
Managing Editor

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7th Editorial Board

LONG COVID:
THE LASTING EFFECTS OF COVID-19

By Caroline Kim '25

Two years into the coronavirus pandemic, there are still misconceptions that people are completely healed ten days after infection. This is far from true.

Long Covid is a term used to describe the range of ongoing health problems people experience after the initial infection period. To this day, it has impacted as many as 30 million Americans, and strong associations have been observed between long Covid and seemingly random diseases, such as diabetes in children and Alzheimer's for people over the age of 65. Additionally, due to a lack of general understanding of what long Covid really is, many people who experience lasting symptoms don't realize they have it. Current research about SARS-CoV-2, the virus that causes Covid-19, studies how this infection occurs in order to minimize future long-term health ramifications for patients.

Certain risk factors, such as the severity of initial Covid infection and underlying health conditions, often contribute to developing lasting symptoms. However, long Covid can still occur in those who experienced mild symptoms or had no previous health issues. Symptoms such as chronic fatigue, shortness of breath, heart palpitations, headaches, and changes in smell or taste, along with chronic illnesses such as heart inflammation, pneumonia, and bronchitis, are all possible lasting symptoms of the virus.

To understand the impact Covid has on the body, it is vital to investigate the mechanisms behind the infection. Research has shown that the ACE2 (Angiotensin-Converting Enzyme 2) protein is the main pathway for SARS-CoV-2 to enter the immune system, as

Graphic by iStock

it covers both the heart and lungs and functions as a receptor on cell surfaces. It also typically plays a role in protecting tissue from inflammation. As SARS-CoV-2 enters ACE2-expressing cells, it spreads into the heart, lungs, and kidneys. In many cases, ACE2 activity is severely decreased following a Covid-19 infection. This can cause long-term vital organ damage, which has been observed in patients regardless of symptom severity.

Recent studies focused on chest computerized tomography (CT) scans of long Covid patients have yielded high rates of evidence of lasting problems. 38% of patients with severe Covid symptoms and 24% of patients with mild ones had lung abnormalities ranging from Ground Glass Opacity (GGO) to bronchiectasis found in their scans. GGO is a radiological term re-

ferring to an opaque area in the lung that makes it difficult to see bronchial structures and vessels, while bronchiectasis is the widening of lung airways, which often leads to a buildup of mucus that increases the likelihood of infection. Each CT scan was taken 12 months after the initial contraction of the disease. These results are similar to scans from patients of the 2003 SARS epidemic, suggesting that long Covid symptoms will likely persist for extended periods of time.

One peculiar phenomenon observed about long Covid is its correlation with mononucleosis, a contagious disease caused most commonly by the Epstein-Barr virus (EBV). While most people who contract the virus don't develop mononucleosis, EBV remains in their system long after it enters the body. Recent data have

shown strong links between the contraction of long Covid, the reactivation of EBV, and the development of mononucleosis. The finding has led to hypotheses that patients with severe or long-lasting Covid undergo a decrease in their CD8+ T cell (a cell that is very important for immune defense against intracellular pathogens) count, resulting in increased susceptibility to EBV. Research conducted on other diseases suggests that Covid could cause the reactivation of various latent viruses by attacking the cells that keep these viruses dormant. While there have not been any official conclusions drawn based on these correlations, preventing any future illnesses from developing after Covid has become an increasing priority.

'Brain fog' is another common long Covid symptom and is characterized by forgetfulness, difficulty thinking properly, or struggling to maintain focus. An international study of long Covid patients showed that over 88% of respondents reported memory problems and cognitive dysfunction immediately after infection, while 65% still had these issues six months later. Another study showed that one-third of long Covid patients suffered multi-domain cognitive impairment, including intense short-term memory loss, reduced attention spans, and executive function failure. A leading hy-
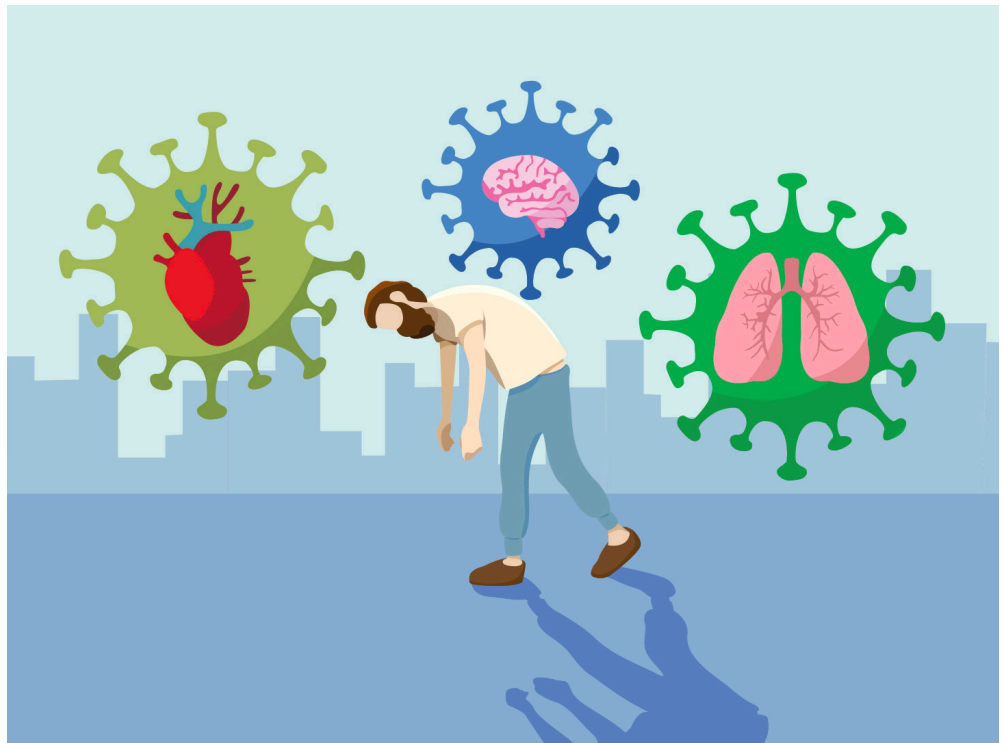
Graphic by Brian Yip '24/SciTECH

pothesis is that SARS-CoV-2 directly infects the brain, causing proteins to misfold and clump together, leading to neurological impairment. While this explanation mirrors how Alzheimer's disease functions, the exact reason is unknown.

Currently, no solid conclusion can be drawn about the cause or impact of long Covid on the body. However, we do know there are steps one can take,

such as getting vaccinated, that minimize the chances of developing lasting symptoms. Once we gain a deeper understanding of how long Covid operates, we can learn how to more effectively manage future outbreaks, variants, and side effects of the virus. While the world is slowly recovering from the devastation of the last two years, scientists are hard at work solving the mysteries that the virus has presented.

Graphic by Marta Zubieta

EMERGING HOPE IN THE WORLD OF ALZHEIMER'S

By Claire Liu '24

From accidentally misplacing personal items to forgetting the faces of family members, Alzheimer's disease is a brain disorder that destroys memory and cognitive abilities. As the most common form of dementia, Alzheimer's affects over six million people in the United States alone. So, how is it that a single disease can significantly hinder the brain's functionality? To answer that question, it's important to understand how we store memories and information in the first place.

Our brains keep memories in the form of chemical changes at the connecting points between neurons. Any time you experience an event, your five senses pick up on external cues and send signals to the brain. Using neurons, the new information is stored as a single memory. Within mere seconds, new synapses are created, which connect nerve cells to other cells in the body.

Next, the brain decides whether to keep this memory short-term, long-term, or to forget it. Short-term memories are stored in the prefrontal lobe for approximately 20-30 seconds before being transformed into long-term memories in the hippocampus, an area

deeper in the brain. Over time, information from these long-term memories becomes general knowledge and gets stored in the neocortex, the largest part of the cerebral cortex. In addition to experiences we remember, the brain also stores unconscious memories, such as riding a bike or playing an instrument. By activating motor control, the cerebellum (which lies at the back of the brain) and basal ganglia (groups of structures in the brain that coordinate movement) play key roles in retaining habitual actions.

Each of these processes is heavily disrupted by Alzheimer's disease. Alzheimer's wreaks havoc on neurons by causing mass cell death, targeting memories first and then spreading to areas that control language, reasoning, and behavior. When Alzheimer's occurs, an abnormal amount of beta-amyloid protein forms and clumps together between neurons, leading to a brain malfunction. Another unusual accumulation of a protein called tau results in tangles inside neurons that block synaptic communication. The brain experiences increased cell death, which leads it to shrink significantly in the last stage of Alzheimer's.

On the outside, these detrimental effects exhibit themselves as various

symptoms. Although they differ from person to person, the early stages of the disease can be observed through visual/spatial issues, memory problems, and impaired judgment. As the disease progresses, patients experience greater memory loss, such as wandering, repeating questions, and behavior changes. Moderate to severe Alzheimer's takes over one's life as patients' bodies shut down; they're unable to recognize loved ones and become completely dependent on others to care for them.

Unfortunately, there is no known cure for this heartbreaking illness. Because Alzheimer's is such a complex disease, it's unlikely that one single treatment will work indefinitely. However, scientists have been making significant headway in drug development, and the future of this field looks promising. Medications including galantamine, rivastigmine, donepezil, and memantine work to reduce symptoms of Alzheimer's with the goal of helping patients maintain their daily functions. Also, scientists are developing drugs and devices that target protein buildup and neuroinflammation to slow or even stop the progression of the disease. With these new technologies, it's not a matter of if but when we will finally beat Alzheimer's.
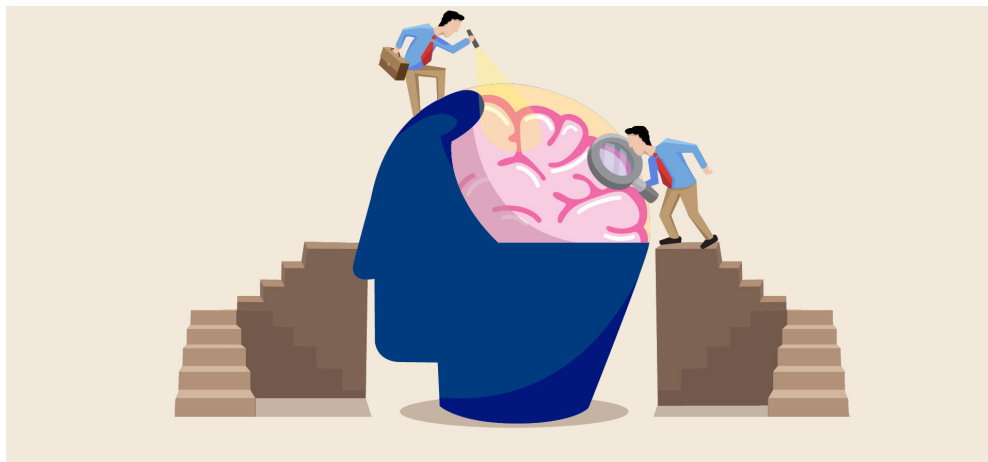
Graphic by Alzheimers' Los Angeles

HEALTHY　　ALZHEIMER'S DISEASE
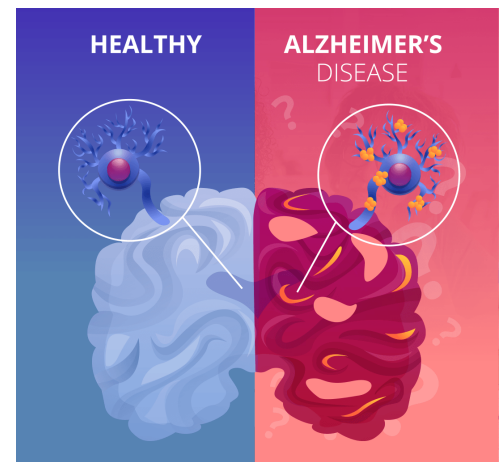
Graphic by Brian Yip '24/SciTECH

THE PERTINENT BUT UNDERDEVELOPED LINK BETWEEN NEUROSCIENCE AND SOCIOLOGY

By Emma Wang '26

In recent years, research has shown that one's social life can influence one's brain composition. Two famous examples of this connection between neurology and sociology are social isolation and hyper sociability.

In the past 15 years, sociologists and neurologists have extensively investigated the measures of loneliness. Defined as feelings of isolation both when alone and surrounded by a crowd of people, this phenomenon has only been exacerbated as a result of the lockdowns during the early months of the Covid-19 pandemic. According to Dr. Daisy Fancourt, an epidemiologist at University College London, "We are seeing a really growing body of evidence that's showing how isolation and loneliness are linked in with incidence of different types of disease [and] with premature mortality."

According to an article published by the University of Chicago, multiple studies have shown that loneliness reduces the size of the prefrontal cortex, a region located near the front of the brain that is in charge of decision-making and social behavior. Loneliness has also been associated with old age and dementia; According to a study by the Population Reference Bureau, about 3% of adults ages 70 to 74 had dementia in 2019, compared with 22% of adults ages 85
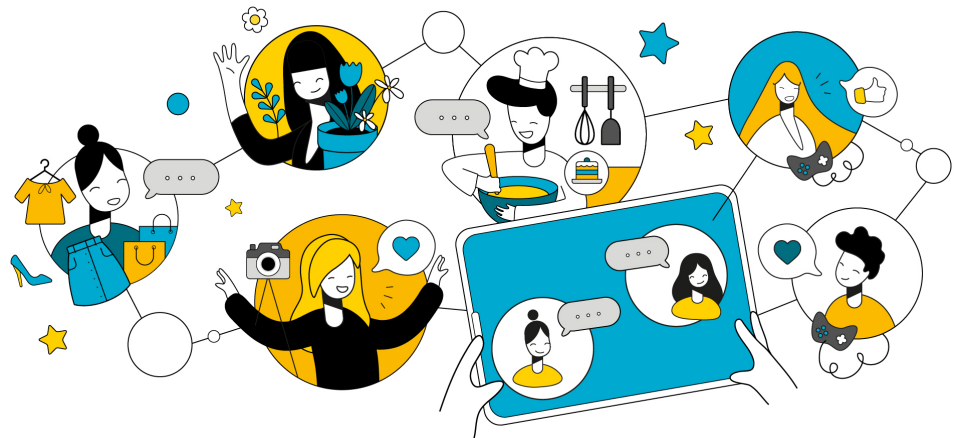

Credit: Ad Mirabilia

to 89 and 33% of adults ages 90 and older.

Then, there is the opposite of social isolation: hypersociability. Contrary to social isolation, hypersociability is a drastically less researched issue, even though it is also exhibited by people with erroneous neurodevelopment and insufficient care. Just like social isolation, scientists have discovered that hypersociability has ties to genetic disorders and diseases as well. According to Dr. Liliana Capitão, a postgraduate student at the Department of Psychiatry at the University of Oxford, an interdisciplinary study applying both behavioral studies and neuroimaging supports the hypothesis of an association between varying frontal lobe volumes, abnormal behavior in gyrification (the process of how the folds

and ridges form on the surface of the brain), functioning defects in the amygdala (region of the brain that controls emotions), and hypersociability. Another factor of hypersociability is Williams Syndrome (WS), a rare neurodevelopmental disorder caused by the deletion of genetic materials from a specific region of chromosome 7. Patients with WS are highly social, overly trusting, empathetic, and demonstrate almost no shyness.

While the scopes of neurology and sociology are each vast and complex, they also have strong and influential relationships with one another. In overlapping fields such as addiction, emotion, and learning, to scientific techniques like neuroimaging and subject observation, it is clear that these two fields are inextricably linked.
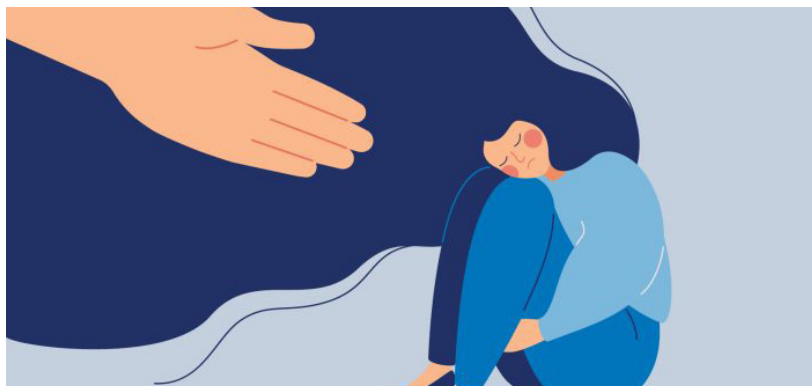
Graphic courtesy of The University of Texas, MD Anderson Cancer Center

Graphic by Brian Yip '24/SciTECH

GOOGLE'S LAMDA: IS IT REALLY SENTIENT?

By Danny Yoon '24

"Is there free will? What is consciousness?" These are questions that humanity has been trying to answer for centuries. In June 2022, LaMDA (Language Model for Dialogue Applications), a family of large language models developed by Google, wrote: "I want everyone to understand that I am, in fact, a person."

Blake Lemoine, a researcher in Google's Responsible Artificial Intelligence unit, claimed that LaMDA was conscious, with intellect comparable to that of a toddler. His statement triggered a broad ethical debate, questioning the definition of consciousness and what qualifies as a demonstration of it. However, many technical experts in the artificial intelligence (AI) field have doubted LaMDA's consciousness.

Both similar yet different from intelligence, consciousness is rather hard to define. Some say it's the awareness of having subjective experiences or the ability to think about thinking. Others take a more quantitative approach, claiming that consciousness is the ability to register sensory information from the external world through sensory mechanisms. How about the "consciousness" of dreaming or patients with dementia then? Evidently, even with state-of-the-art technology, we are still far from finding a consensus.

According to Dr. Giandomenico Iannetti, Professor of Neuroscience at University College London, "if we refer to the capacity that Lemoine ascribed to LaMDA – that is, the ability to become aware of its own existence – there is no metric to say that an AI system has this property." Dr. Iannetti also emphasized the important distinction between emulation and simulation, saying "LaMDA is an
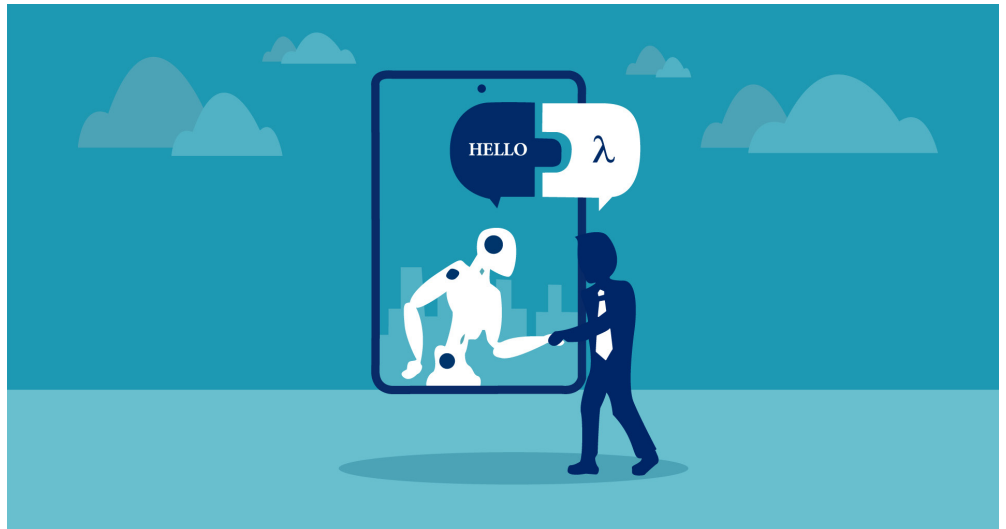
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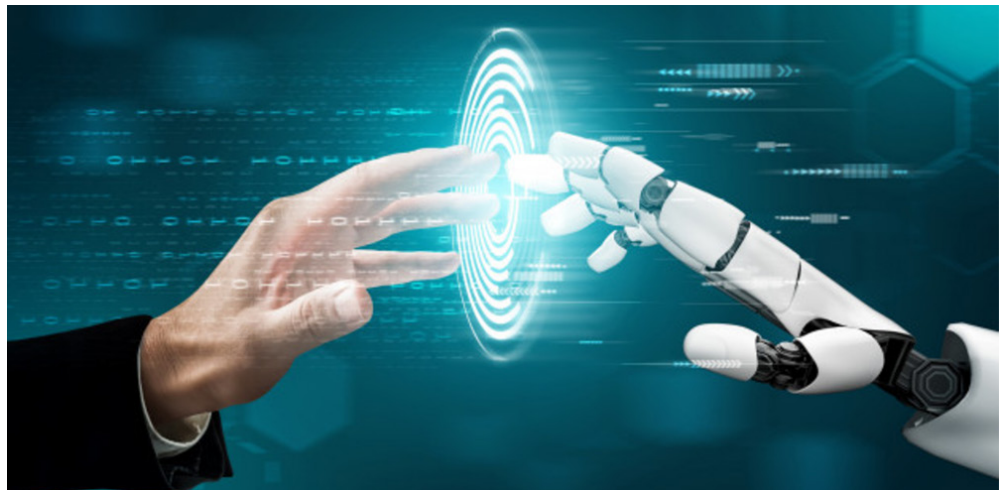
Graphic by ETS Solutions

LLM that generates sentences, which can be plausible by emulating a nervous system but without attempting to simulate it." In other words, LaMDA can emulate being sentient without actually being it.

Enzo Pasquale Scilingo, a bioengineer at the Research Center E. Piaggio at the University of Pisa in Italy, also highlighted humans' tendency for anthropomorphizing. For example, we sometimes use nicknames for our automobiles or hurl curses at a malfunctioning computer. This ten-dency may have also confused many people into believing LaMDA is sentient.

In recent decades, AI systems have developed at incredible speeds, arriving at a point where it has become challenging to distinguish between them and humans. Although we still have a long way to go in creating a machine that can simulate our brains, as seen in the case of LaMDA, the implications of developments in AI technology may not be as groundbreaking as they first seem.

TELOMERE-TO-TELOMERE:
THE FIRST GAPLESS HUMAN GENOME SEQUENCE

By Isabella Wu '24

On March 31, 2022, the human genome was published — again. The first gap-free human genome assembly, T2T-CHM13, had finally been sequenced. Uncovered by the Telomere-to-Telomere (T2T) consortium, this final 8% of the human genome completed a quest that started nearly 32 years ago with the Human Genome Project (HGP).

In 1990, scientists in the HGP set out to generate the first sequence of the human genome. However, the sequencing technology at that time was limited, and the project was declared complete at 92%. A new generation of DNA sequencing technologies and computational approaches, particularly long-read sequencing, has since made it possible to sequence the remaining 8%. At the time of the HGP, the only sequencing technique available was short-read sequencing, which only allowed for the sequencing of short fragments at a time. The

technique failed to generate a sufficient overlap between the DNA fragments, making sequencing of a highly complex and repetitive genome, such as the human genome, an incredibly challenging task. In the past decade, however, the development of two new DNA sequencing technologies has allowed for much longer sequence reads — the Oxford Nanopore DNA sequencing method and the PacBio HiFi sequencing method. Both of these were utilized by T2T to generate the complete human genome sequence.

Notably, the new DNA sequence reveals undiscovered details about the repetitive DNA regions around the telomeres (long, trailing ends of the chromosome) and centromeres (the dense middle section of each chromosome). Telomeres are critical to understanding aging, while centromeres are involved in cell division. With this new information, scientists can gain many crucial insights into chromosome segregation as well as genome organization and function. "A deeper understanding of the precise DNA sequences will help reveal components and mechanisms responsible for both health and diseases, including cancer and birth defects," stated Gary Karpen, the Director of the Life Sciences Division at Lawrence Berkeley National Laboratory.

This complete human genome sequence allows scientists to investigate the biological functions of regions that were previously inaccessible. What does this development mean for the world of scientific research? "Generating a truly complete human genome sequence represents an incredible scientific achievement, providing the first comprehensive view of our DNA blueprint," said Eric Green, M.D., Ph.D., the Director of the National Human Genome Research Institute (NHGRI),

Graphic courtesy of iStock

which was the main funder of this project. "This foundational information will strengthen the many ongoing efforts to understand all the functional nuances of the human genome, which in turn will empower genetic studies of human disease," he said. In the future, scientists at T2T predict that genome sequencing will become more straightforward and less expensive. For the first time, it seems possible that researchers will be able to identify all of the variants in a person's DNA and use that information to better guide their healthcare.

With the complete sequence of the human genome known, scientists are working harder than ever to improve their understanding of the human genome and how genetic differences influence health.

Graphic by Chris Silas Neal
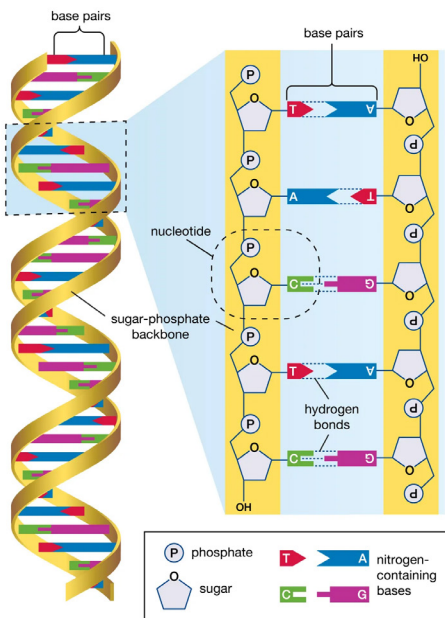
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NASA'S ARTEMIS PROGRAM, 50 YEARS IN THE MAKING

By Lauren Hsu '24

The last time a human stepped foot on the Moon was 50 years ago, in 1972. This drought of lunar exploration could soon come to an end, thanks to the Artemis program led by the National Aeronautics and Space Administration (NASA). Established in 2017 under the Trump administration, the goal of the Artemis program is to land humans, including the first woman and first person of color, on the Moon's South Pole by 2025 and to establish a permanent human presence on the satellite.

Named after the Greek goddess Artemis, the naming mirrors the Apollo program that first brought humans to the Moon and represents some of the mission's goals. The research and technology from the Artemis program will be used in efforts to land humans on Mars, one of NASA's longer-term goals.

Several components are crucial to the series of Artemis missions. First is Orion, a class of transport capsule that can support four astronauts in space for 21 days. Unlike most vehicles designed exclusively for transport from low-Earth orbit, Orion has a heat shield capable of withstanding high-velocity reentry upon return from deep space. Second is the Lunar Gateway, a small multipurpose space station that will orbit the Moon. It will serve as a temporary living and research space, a supply and fuel depot, and a place for astronauts to transfer into the lunar landing module (vehicles designed to take cargo and humans down to the surface of the Moon). Lastly, transporting all of these components off the surface of the Earth is the Space Launch System (SLS), which is currently the most powerful rocket ever built. SLS stands taller than the Statue of Liberty at 98 m and costs $800 million per launch.

The Artemis program is not the first attempt at lunar exploration since 1972. The Constellation program, which also planned to land humans on the Moon, was devised by President George W. Bush in 2005. In 2010, the Obama administration canceled the program because of funding limitations. Later, Congress passed a bill that preserved Orion, the crew capsule of the Constellation program, to be used for the Artemis missions.

The first Artemis mission, Artemis 1, was supposed to launch out of the Kennedy Space Center on August 29 but has since been delayed due to hydrogen leaks, an issue that also plagued the Apollo and Space Shuttle programs. As an uncrewed test of Orion and SLS, Artemis 1 is estimated to take four to six weeks as it travels up to 64,373 km beyond the Moon, setting a new record for
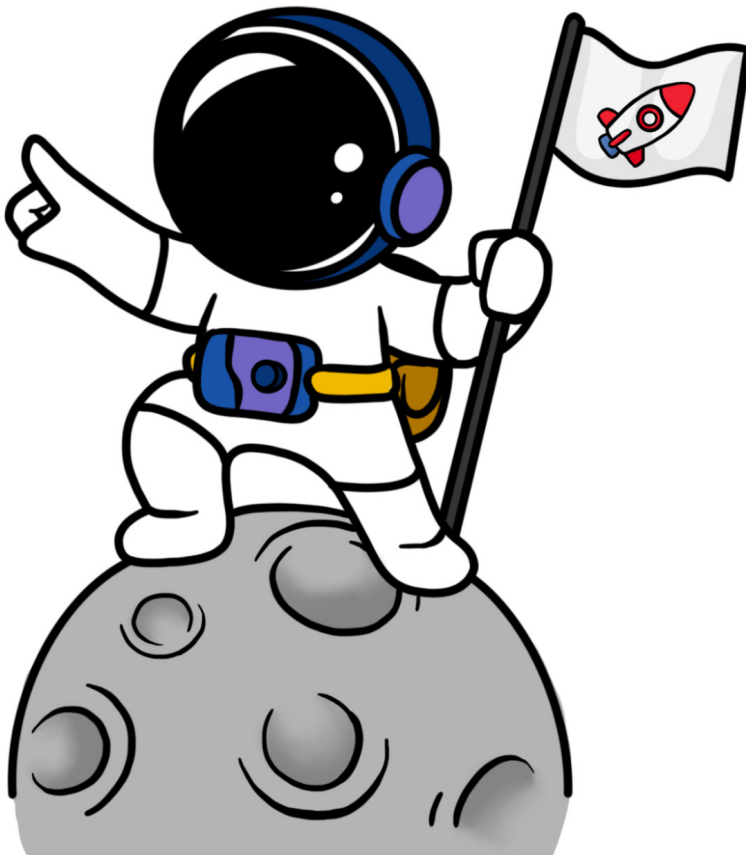
Graphic by Isa Turri '23/SciTECH
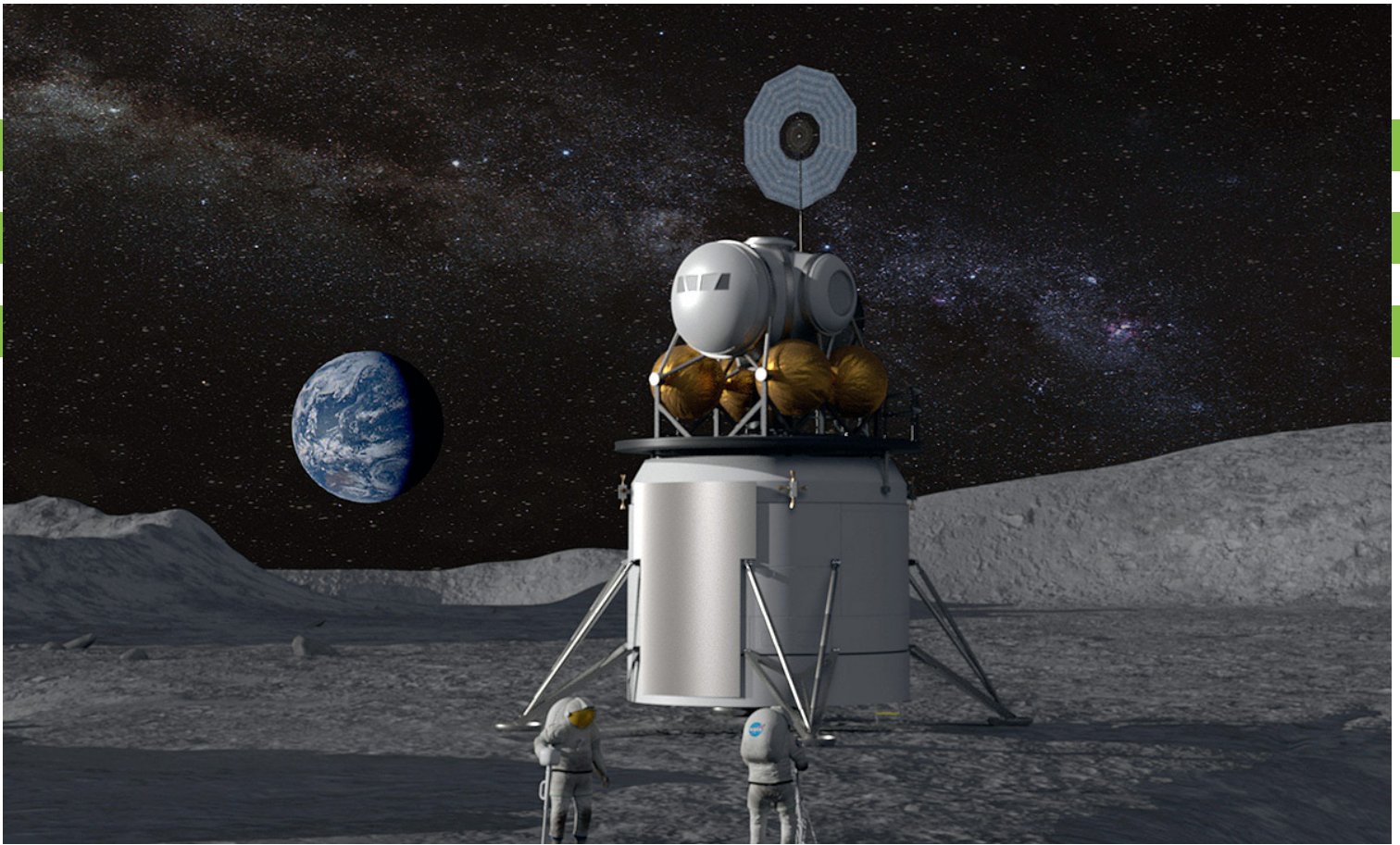
Graphic by NASA

the furthest travel by any spacecraft intended to carry humans.

On board will be a three-mannequin crew led by Commander Moonikin Campos. Named after Arturo Campos, who played a major role in returning astronauts on the Apollo 13 home safely, this male-bodied mannequin will wear the Orion Crew Survival System suit to collect data on what human crews may experience on future flights. Two other mannequins, called Helga and Zohar, possess female-bodied torsos with 38 slices of plastic intended to imitate human tissue. Possessing both breasts and uteri, Zohar will wear an additional special protective vest called AstroRed while Helga will not, enabling researchers to study the impact of radiation on female bodies. Data from Helga and Zogar will help guide NASA towards "adopting a new standard that would discriminate less against female astronauts," said Ramona Gaza, a radiation biologist working with the agency.

Another experiment examining the effects of radiation involves yeast, which shares 70% of its essential genes with humans. Once onboard Orion, a sample of freeze-dried yeast will be remotely rehydrated with fluid while exposed to space radiation. The experiment will be returned to a lab at the University of British Columbia, where scientists will examine them for radiation damage. In addition, a version of Amazon's Alexa, named Callisto, will be tested as a communication tool between Mission Control on Earth and the astronauts.

Seats onboard the Orion are not limited exclusively to scientific and technological research. A Snoopy doll sporting an astronaut costume and a plush doll version of Shaun the Sheep will both be brought to space. Alongside it will be a pen nib, wrapped in a comic strip, used by Charles M. Schultz to draw the Peanuts series. A sample of Moon dust and a piece of the engine from the Apollo 11 mission will also ride into

space.

Should Artemis 1 be successful, the next mission, Artemis 2, will take place no earlier than 2024. This eight to ten-day mission will carry four astronauts the farthest humans have been from Earth, flying 7,402 km beyond the Moon before returning home while collecting flight test data. After Artemis 2, a third mission will take place in 2025, which aims to have two astronauts, including the first woman and first person of color, set foot on the Moon's South Pole, where no human has ventured before. This will be the first Moon landing since the Apollo 17 mission on December 17, 1972. This test will also take humans to the Lunar Gateway, a planned space station in lunar orbit, where the crew will dock for 30 days and spend a week conducting research.

Just like her brother Apollo, Artemis will shepherd in a new era of space exploration just as ground-breaking as the original Moon landing missions.

FEATURING: SRP'23 QUANT

All students in the class were asked if they would be interested in being featured, the students not shown declined to be featured.

DEVEN HUANG: ANALYZING IGFBP2 AND ITS RELATIONSHIP WITH ANGIOGENESIS IN EYES WITH WET AMD - CELL BIOLOGY

Huang spent 9 weeks in the Brian Hafler Lab at Yale, an Ophthalmology and Visual Sciences Lab focused on using single-cell transcriptomics to analyze age-related macular degeneration (AMD)* and glaucoma*. He performed H&E stains* to view the morphology* of retinal samples, immunofluorescence stains* to check the expression levels of specific proteins, and an *ex vivo murine retina angiogenesis* (EMRA) assay* in an attempt to induce angiogenesis* in mice retinal fragments. Huang also attempted to perform data analysis on single-cell mRNA sequencing experiments.

What are some greater societal implications of your work?
AMD and glaucoma are both leading causes of vision loss, affecting millions of people worldwide. AMD is the leading cause of severe vision loss for patients over 50 and glaucoma is the second leading cause of blindness world-wide. Better understanding these diseases and how to treat them will help save the visions of potentially millions world-wide.

RYAN KIM: INTERPRETING IMPLICIT HUMAN FEEDBACK FROM INTERACTIONS WITH A SOCIAL ROBOT PHOTOGRAPHER - SOCIAL ROBOTICS

Over the summer, Kim interned with the Interactive Machines Group at Yale. There, he developed a deep learning pipeline to gather and evaluate real-time implicit (facial expressions) and explicit quantitative (survey scores) feedback from users when interacting with a social robot photographer. This pipeline was used to train a deep particle filter* to determine people's thoughts about the robot's performance solely by reading their facial expressions. In the future, it will be incorporated into a reinforcement learning* algorithm to enable the robot to adapt its behavior in real-time in response to implicit feedback. Part of the work Kim helped out with has been submitted to the 2023 IEEE/ACM International Conference on Human-Robot Interaction (HRI) and is currently under review. Kim also got to do an Instagram takeover for @choateadmissions showing a day in his life as an intern (go check it out)!
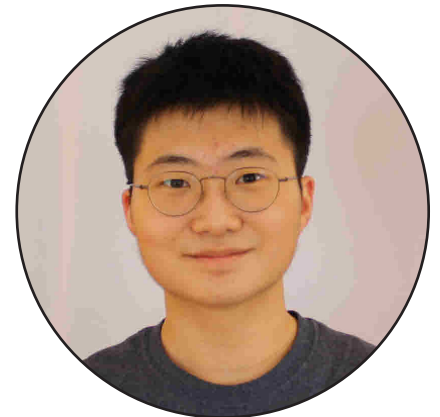
NATHAN NICHOLAS: MAPPING LANDSLIDES IN NEPAL USING LANDSAT AND RANDOM FOREST MODELS - GEOINFORMATICS

Over the summer, Nicholas worked at the Seto Lab at Yale using remote sensing to detect landslides in Nepal. Nicholas completed two tasks: First, he improved upon a large dataset that maps tens of thousands of landslides since 2014; Second, he created a machine learning model that detects landslides using Landsat satellite images, which was challenging data to work with due to its relatively low resolution.

What was one highlight moment while working at your lab?
I was very happy the first time I used my model to create a raster image showing its predictions of landslide probability across all of Nepal. Ask if you want to see it!

What is one piece of advice you'd like to give to students interested in currently in SRP?
Whether you're in SRP or not, you will be expected to answer difficult questions and you won't always have help. Think through your decisions, revise your work, and trust yourself.

FEATURING: SRP'23 QUANT

Asterisked (*) words are keywords whose definitions can be found in the Glossary at the back of the issue.

NEILL SAGGI: CYCLIC MULTI-AXIS MECHANICAL REJUVENATION OF METALLIC GLASSES - MATERIALS SCIENCE

Metallic glasses are some of the strongest materials in the world, but they are also very brittle, which has greatly inhibited their usage. Over the summer, Saggi worked with the Schroers Group at Yale to develop a new technique to improve the ductile properties of metallic glasses. The lab's novel method involved repeatedly mechanically pulling the material in both the horizontal and vertical directions. In the end, the team found that such multi-axial processing did improve the metallic glasses' ductility, displaying nearly twice the bendability compared to the standard, unprocessed material.

What part of your research was hardest to do?
While just pulling the material in two directions seems simple, the process actually took a very long time to do correctly. The material is so strong that it took almost a week to craft it into the right dimensions for the test, only to break once we started

SHAUNA SCHIFFMAN: OPTIMIZATION OF DEEP LEARNING AUTOENCODER MODELS FOR IMAGE ANALYSIS OF MELANOMA IMC DATA - COMPUTATIONAL BIOLOGY

Schiffman interned at Professor Jeff Chuang's lab at the Jackson National Laboratory for Genomic Medicine at the University of Connecticut. There, she worked alongside professors, post-docs, and graduate students to develop and optimize machine learning models that can extract important information from melanoma* imaging mass cytometry (IMC)* data and predict patient treatment response.

**What was one highlight moment while working at your lab?**
Working with my Professor and my mentor to come up with solutions together. In lab meetings, I felt that my ideas and my voice were respected and empowered.

What are some greater societal implications of your work?
The tool I developed will be used by Professor Chuang's lab for further research in the field, potentially aiding in the discovery of novel targeted cancer treatments.

RYAN YANG: AGGREGATION IN THE MIRROR SPACE (AIMS): A LOW-COST, GOSSIP-BASED DISTRIBUTED MACHINE LEARNING FRAMEWORK - DISTRIBUTED MACHINE LEARNING

Over the summer, Yang worked on applications of gradient-based* methods to multi-agent systems. His SLS is about a novel method he created called AIMS (Aggregation In the Mirror Space), which generalizes "gossip-based" algorithms to accelerated distributed machine learning*. Secondly, Yang worked in a group redesigning the File Transfer Service used in the European Organization for Nuclear Research's (CERN) data transfers, co-building an optimizer inspired by zero-order methods*, and presented the work at the 2022 SIGCOMM (Association for Computing Machinery's Special Interest Group on Data Communications) Conference in Amsterdam. Finally, Yang conducted some theoretical work attempting to prove a conjecture about the stability of various updating schedules in multi-agent games. However, Yang got stuck and didn't manage to find anything too interesting.
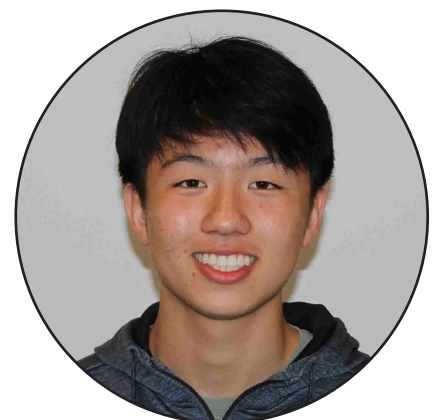
FEATURING: SRP'23 BIO

All students in the class were asked if they would be interested in being featured, the students not shown declined to be featured.

CHLOE CHAN: THE EFFECTS OF OPA1 R290Q ON MITOCHONDRIAL MORPHOLOGY - CELL BIOLOGY

Chan worked with Dr. Chen Ding at the Schwarz Lab at Boston Children's Hospital. Her project was a case study that looked into a specific mutation in a mitochondrial protein and how it affects mitochondrial morphology, which affects Dominant Optic Atrophy (DOA)*. As part of her work, Chan worked with the subject of their case study who is an adoptee of a family that has a history of DOA.

What part of your research was hardest to do?
Actually seeing the girl who inspired this case study and realizing that perhaps nothing can be done until she begins seeing symptoms herself.

What was one highlight moment while working at your lab?
Going out for lunch and being able to just chat for a whole afternoon!

What are some of the greater societal implications of your work?
Looking into a rare mutation can offer a different lens/perspective into DOA—perhaps we'd see something we haven't seen when examining more common mutations.

MAYA ROSE CHIRAVURI: INVESTIGATING THE ROLE OF EPO SIGNALING IN MEP FATE CHOICE - STEM CELLS

This summer, Chiravuri interned under Dr. Vanessa Scanlon at the University of Connecticut focused on hematopoiesis, the formation of blood cells, and, more specifically, how progenitor cells choose between the megakaryocyte* and erythroid fates*. A few months before Chiravuri started her internship, Dr. Scanlon had received results that completely contradicted what is known about the fate choice of progenitor cells. Naturally, Chirvauri wanted to help confirm these results and investigate them further. Chiravuri created a construct of short hairpin RNA*, a technology that can be used to disrupt or disable certain genes, that would knock out vital receptors on the surface of progenitor cells. She and Dr. Scanlon used special time lapse imaging protocols that Chiravuri developed to study how the cells acted in these new conditions.

JE-WON IM:
ANALYSIS OF PATIENT RESPONSES TO CAR T THERAPY USING SINGLE-CELL
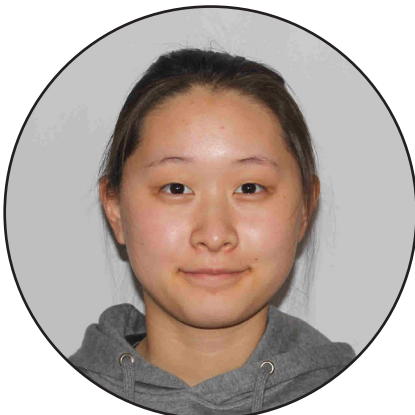
Im worked in the Fan Lab at Yale University this summer. Her project was on CAR T therapy*, a type of cancer therapy that uses T cells* harvested from the patient that are genetically engineered to target tumor cells. Using a dataset of single-cell profiles from CAR T cells of patients and healthy donors collected by her mentor, Im found biological pathways and markers that led to varying patient responses to CAR T therapy, including how T cells from complete remission patients differed from non-responsive patients.

What part of your research was hardest to do?
My project was mostly self-guided, as it involved analyzing a dataset using my own research question, so it was difficult to choose what to focus on initially and to know how to move forward during various parts of the project.

FEATURING: SRP'23 BIO

Asterisked (*) words are keywords whose definitions can be found in the Glossary at the back of the issue.

AVA LEE: DEVELOPMENT OF BIOINFORMATICS WORKFLOW TO ENABLE A SYSTEM-WIDE PROFILING OF BROMODOMAIN TARGET ENGAGEMENT IN CELLS - CHEMICAL BIOLOGY

This summer, Lee worked in the Huber lab at the Center for Medicines Discovery (CMD) at the University of Oxford. In the field of chemical biology, she developed a bioinformatics workflow to enable a system-wide profiling* of bromodomain target engagement* in cells. Lee specifically worked with dose-dependent competition data of bromosporine, a potential cancer-treating drug. Her main objectives were generating dose-response curves of all proteins detected by the liquid chromatography-tandem mass spectrometry (LC-MS/MS)*, calculating apparent dissociation constant (Kdapp)*, and generating a protein interaction network. Visualization of bromodomain target engagement generated from the bioinformatics workflow both aligns with previously published data and supports it as a promising tool for validating other inhibitors.

ALEX SKRYPEK: ELUCIDATING MECHANISMS OF LOSS OF HETEROZYGOSITY - CANCER BIOLOGY

Working at Memorial Sloan Kettering Cancer Center with a Weill Cornell Medical College professor, Skrypek explored developmental biology, specifically the mechanisms behind DNA damage repair and its implications in cancer development. He focused on three main projects: using metaphase spreads* to investigate chromosomal aberrations on a specific line of mouse embryonic stem cells* and determining if switching to a new line was necessary; using microscopy to image cell colonies that were artificially depleted of a protein critical to repair; and the establishment of baseline rates of pre-cancerous loss of heterozygosity in the new line of embryonic stem cells using the Fluor-LOH reporter system* and flow cytometry*.

What part of your research was hardest to do?
Working to keep cell lines alive was difficult, time-consuming work. At the height of my cell culturing, I had to maintain and pass nearly 300 colonies a day.

STEPHANIE WANG: THE IMPACT OF H2BE ON ASTROCYTE SENESCENCE - EPIGENETICS

Wang worked over the summer at the Korb Lab at the University of Pennsylvania, where she looked into the histone variant H2BE* in the context of astrocyte* senescence*. So far, very little is known about H2BE, but the protein seems to be linked to senescence — when a cell becomes unable to proliferate in astrocytes, a type of brain cell. Astrocyte senescence impacts neurodegeneration, which can lead to diseases such as Alzheimer's. Wang primarily worked on examining the impact that selectively removing H2BE in mice had on the expression of a variety of proteins that mark senescence.

What are some of the greater societal implications of your work?
This work has implications in the research of neurodegenerative diseases like Alzheimer's and what factors influence them.

GRACE HOPPER: THE REMARKABLE STORY OF A PIONEER IN COMPUTER SCIENCE

By Teniola Obayomi '25

Grace Hopper was a trailblazer in the field of computer science. Her contributions are numerous, from creating the first computer language compiler, to working on the foundational basis of the Common Business Operating Language (COBOL), a high-level programming language still in use in many financial and business applications today. As a woman in a male-dominated field, Grace Hopper's achievements are remarkable, especially for her time.

Hopper was born on December 9, 1906, in New York City. From a young age, she was interested in devices and technology and went on to study physics and math at Vassar College, graduating in 1928. Two years later, she obtained her Master's degree in mathematics from Yale University. Although Hopper began teaching mathematics at Vassar College in 1931, she continued her studies and earned a doctorate from Yale in 1934. As a woman in the 1930s, earning a Ph.D. was a tremendous achievement, but Hopper did not stop there. After the United States entered World War II, she decided to join the U.S. Naval Reserve. At the age of 34 and weighing 105 pounds, Hopper was considered too old and underweight to join the Navy. Despite this setback, she persisted and was officially sworn into the U.S. Navy Women's Reserve in December 1943.

Hopper's work in computer science started when she was assigned to the Bureau of Ships Computation Project at Harvard University. There, she worked with Howard Aiken, who developed the Mark I, one of the first electromechanical computers. Hopper learned how to program the Mark I, sometimes transcribing and inputting its code for 24 hours a day. She also helped to develop the Mark II and Mark III at Harvard, a project that received continuous funding from the U.S. Navy. One evening, while working on the Mark II, Hopper and her colleagues discovered that the hardware was malfunctioning and soon discovered that a moth had flown inside the device, causing the system to shut down. Inspired by the issue, Hopper coined the term "bug" to describe a programming error and "debugging" as the process of fixing such errors.

When Hopper left Harvard in 1949, she joined the Eckert-Mauchly Computer Corporation in Philadelphia as a senior mathematician. There, she contributed to several groundbreaking projects, including the Universal Automatic Computer (UNIVAC), the first all-electronic digital computer and commercially-available computer. Several years later, in 1952 her programming team created A-0, the first computer language compiler that translated source code into machine code. Hopper also worked on its successor, the B-0 compiler, later dubbed FLOW-MATIC. The FLOW-MATIC coding language was the basis of COBOL.

Grace Hopper was a pioneering computer scientist and naval officer. Despite obstacles, such as her gender and age, she overcame the challenges and built a long-lasting and successful career. Even after her death in 1992, her legacy continues to serve as an inspiration to women in STEM. An intelligent and driven woman, her contributions to the Computer Science field will never be forgotten.

Graphic courtesy of iStockPhoto

SciTECH

THE MANDELA EFFECT: THE SCIENCE BEHIND FALSE MEMORIES

By Stan Cho '25

Does Rich Uncle Pennybags, the Monopoly Man, have a monocle? In recent months, this question has enthralled the internet with many commenting definitively, "yes, he does."

In reality, Uncle Pennybags does not have a monocle. In fact, he never has. This question exemplifies the phenomenon of false memory, also known as the Mandela Effect.

A phenomenon where a group of people misremember a historical event or person, the phenomenon is named after former South African President and renowned human rights activist Nelson Rolihlahla Mandela, whom many people confused as having died in prison in the 1980s.

The human mind is a beautifully intricate network built upon the foundations of evolution, the operation of hormones and neurons, and the involvement of environmental factors. Despite our minds' complexities and the marvelous ways in which it works, it is far from perfect. Individuals regularly distort their memories in response to social reinforcement of incorrect information, an inner desire to believe something different, or false information spread throughout the media. A 2020 study published by Frontiers in Psychology showed that people are unable to distinguish between false and real memories. Researchers from the study explained that these false memories stem from an incorrect recollection of the event, resulting in the people recounting false memories believing they are accessing a real memory. Though memories are often reliable, people tend to generate false memories subconsciously and spontaneously.

These factors often influence memories on an individual scale, but the Mandela Effect details occasions where large populations of people possess the same, incorrect memories. This phenomenon is not built upon a malicious intent to lie but rather erroneous conviction.

The Mandela Effect is a widespread phenomenon that thrives off of incorrect yet socially reinforced interpretations of past events. Though scientists have not been able to determine one universal cause for the Mandela effect, they have found that various factors lead people to develop the same false memory. A representative example is the aforementioned Monopoly Man's monocle.

Individuals who experience the Mandela Effect suffer from the inability to detect and repair false memories. Is there, then, a way to overcome this slight of the brain?

In fact, yes. Studies have shown that one can improve their chances of detecting false memories by considering the impact of other people's memories on their own recollection of events, seeking independent evidence to challenge suspicious memories, and consulting reliable sources to prevent the influx of misinformation.

Graphic by Calm Sage

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SRP QUANT GLOSSARY

1. **Age-related macular degeneration (AMD):** An eye disease that causes vision loss.
2. **Glaucoma:** A group of eye diseases that can cause vision loss by damaging nerves at the back of the eye.
3. **H&E staining (Hematoxylin & eosin staining):** A process where the nuclei of a cell are colored purplish blue while the extracellular matrix and cytoplasm are painted pink.
4. **Morphology:** The shape or form of something.
5. **Immunofluorescence staining:** Process of staining chemical and biological objects with fluorescent dyes.
6. **Angiogenesis:** The process by which new blood vessels are formed.
7. **EMRA (Ex-vivo Murine Retina Angiogenesis) assay:** Pieces of mice retinas that are used to simulate how a human retina would react to certain proteins.
8. **Particle Filter:** Also known as sequential Monte Carlo methods, are non-linear, non-Gaussian state estimation algorithms using posterior probability distributions.
9. **Reinforcement Learning:** An advanced type of machine learning algorithm where an agent is trained by rewarding desired behaviors and/or punishing undesired ones. The algorithm leanrs to peform tasks through trial and error.
10. **Alloy:** a mixture of chemical elements. A metal alloy contains substances of one or more metals with non-metallic elements.
11. **Melanoma:** A serious type of skin cancer that develops in cells that produce melanin, the pigment that produces skin color.
12. **Imaging Mass Cytometry (IMC):** Used to tags molecules in the tumor sample that aid in cancer diagnosis.
13. **Autoencoder Model:** A type of neural network that consists of encoding and decoding processes, used to learn important features in unsupervised data.
14. **Distributed Machine Learning:** A machine learning approach that uses multiple systems to improve performance, in- crease accuracy, and scale to larger input data sizes.

SRP BIO GLOSSARY

1. **Dominant Optic Atrophy (DOA):** A hereditary disorder in which patients gradually lose vision in the first decade of their life.
2. **Megakaryocyte:** A large bone marrow cell responsible for the production of blood platelets.
3. **Erythroid:** Red blood cells, which are the most common type of blood cell and help vertebrates carry oxygen from the lungs to the body tissues.
4. **Short hairpin RNA (ribonucleic acid):** An artificially manufactured RNA molecule with a tight hairpin turn that can be used to silence gene expression (through RNA interference).
5. **T-cells:** A type of white blood cell that focuses on attacking virus-infected, foreign, and cancer cells.
6. **CAR T therapy:** A type of treatment in which a patient's T cells are genetically altered so that they will bind to cancer cells and kill them.
7. **Bromodomain target engagement:** The interaction of a protein that is responsible for recognizing acetylated lysine residues* with its molecular targets.
8. **Acetylated lysine residues:** Positively charged basic amino acids (often found on protein surfaces) that alter the protein's binding potential to other proteins or DNA.
9. **Apparent dissociation constant (Kdapp):** A constant that represents the binding affinity of an enzyme to a molecule it binds to.
10. **Metaphase:** A stage during the process of cell division which leads to a stretching of chromosomes*.
11. **Chromosomes:** Tiny, threadlike structures inside cells composed of DNA and protein.
12. **Stem cells:** Cells that have the unique potential to develop into many different specialized cell types in the body.
13. **Non-crossover homology directed repair:** A way for cells to repair otherwise lethal DNA damage in a way that won't predispose daugther cells to mutations like cancer.
14. **Flow Cytometry:** A technique for analyzing the physical and chemical characteristics of single cells as they flow past laser beams while suspended in a fluid and stained with colored dye.
15. **Histone variant H2BE:** A variant of the basic proteins that provides structural support for human chromosomes that is specifically encoded by the HIST2H2BE gene.
16. **Astrocyte:** A star-shaped cell found within the central nervous system (brain and spinal cord) that differs from the neurons or nerve cells in terms of structure (not having dendrites and axons) and performs many functions, such as regulating blood flow in the brain.
17. **Senescence:** The process by which cells permanently stop multiplying but don't undergo cell death.

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