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MURJ

Massachusetts Institute of Technology Undergraduate Research Journal

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MURJ Staff
MIT Undergraduate Research Journal

Massachusetts Institute of Technology

December 2022

Dear MIT Community,

We are delighted to present to you the 44th issue of the MIT Undergraduate Research Journal (MURJ). MURJ is a biannual student-run publication that has featured diverse and groundbreaking undergraduate research happening across campus for over 20 years.

In publishing this issue, we would like to emphasize the importance of collaborative science toward improving ourselves and each other as a global community, while being mindful of the role of science in both building unity and tempering division. At a time that is witnessing the convergence of critical milestones for pressing issues such as climate change, the open sharing of research and strengthening of public engagement with science are absolutely necessary. We are proud to showcase the hard work and creativity of MIT students to the world, and we are grateful to passionate students and mentors at MIT who continue to dedicate themselves to making the world a better place through the relentless pursuit of knowledge, its ethical application, and communication. We hope that you, too, are inspired and find reassurance in reading the work of these amazing students and scientists.

In this issue, we feature original student work on a wide range of subjects, including the development of SeaPerch II as an extension of the classically successful SeaPerch program for ocean robotics, GAN-based data augmentation for analysis of defects in metal manufacturing, the creation of a real-time air quality map, and a study of trends and challenges presented by digital health in the U.S.

Massachusetts Institute of Technology

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MIT Undergraduate Research Journal

This issue additionally highlights exciting scientific topics and recent happenings around the Institute, surveying the development of synthetic mucus and commenting on the interplay between theoretical and experimental physics. Other featured reporting spotlights the Spanish department at MIT with Professor Javier Barroso and the seminal role of Professor Robert A. Weinberg, head of the Weinberg Lab which discovered the first human oncogene, about his eighty years as one of century's foremost educators.

Biannual publication of this journal is the product of dedicated collaboration and commitment by MURJ staff members and undergraduate researchers. We would like to thank our Editorial Board and contributors for their time and hard work, as well as the greater MIT community for its continued support of our publication.

For previous issues of MURJ, please visit our website murj.mit.edu. If you are interested in contributing to future issues of the MIT Undergraduate Research Journal, we invite you to join our team of authors and editors or submit your research for our Spring 2023 issue. Please contact murj-officers@mit.edu if you have any questions or comments.

Sincerely,

Gabrielle Kaili-May Liu
Editor-in-Chief

Massachusetts Institute of Technology

UNDERGRADUATE RESEARCH JOURNAL
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BIOCHEMISTRY

The Study of Mucins in Biology and Chemistry Labs

Dr. Alty and Carolyn Barnes work with the Ribbeck Lab to develop synthetic mucus analogues.

Have you ever stared in horror at your snot in a Kleenex, perplexed by the fluorescent color or the never-ending abundance?

Mucus' color-changing properties are actually a direct result of one of the many vital functions of mucus, the unsung hero of our immune-defense system.

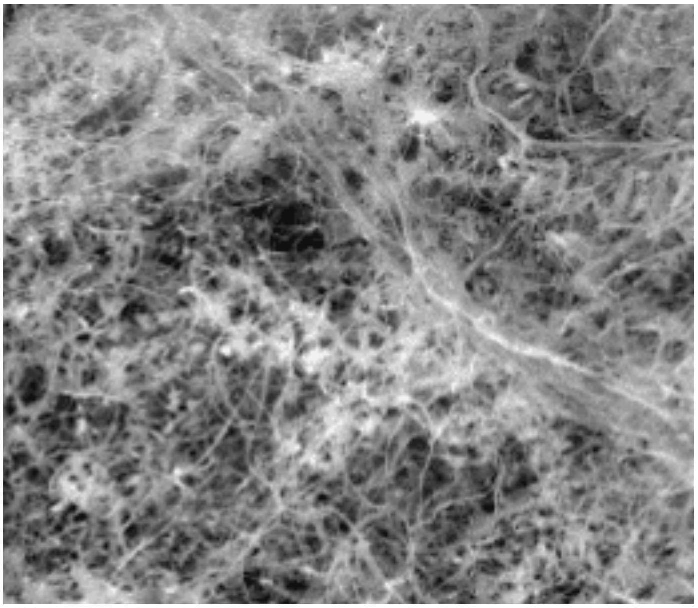
Goblet cells are cup-like cells that line the epithelia of various structures in the body like the respiratory and reproductive tracts. Goblet cells continuously produce mucins- a set of heavily-glycosylated, long chain proteins. Mucins are great at linking with each other and because of all the sugar groups on the chain, they are great at absorbing water. Mucins are the primary component of mucus.

Almost ½ cup of mucus is produced daily by an average healthy human. The structure of mucins as well as its collaboration with the other components of mucus makes mucus very good at its various jobs in the body. In the eyes, mucus serves as a lubricant so we can blink. In the stomach, mucus forms a thick barrier, coating the inside of the stomach and protecting the underlying epithelial cells from the ultra-acidic hydrochloric acid and the host of bacteria introduced into the stomach via food. Throughout the body, mucus prevents delicate tissues from drying and cracking, which would make them susceptible to infection.

Mucus contains mucins, antibodies, antimicrobial peptides and bacteriophages that work together to protect the body against invaders. However, sometimes viruses evade this slippery booby trap and cause an infection. The body ramps up production of mucus in response to flush out the invaders as soon as possible. This extra mucus contains extra white blood cells to assist in defense. Interestingly, that yellow-green color mucus becomes when we are sick is as a result of an enzyme produced by the white blood cells.

Mucus is not only found in animals. In fact, many animals and living things produce mucus for a variety of different uses. In fact, even coral reefs secrete a layer of mucus that protects the reef from the surrounding seawater and harmful bacteria.

With the uptick in cases of chronic and perplexing diseases on campus such as the "Frat Flu" and "Baker Bronchitis", the demand for mucus is at an all-time high. To find a solution to this problem, I reached out to Dr. Jill Alty and Carolyn Barnes from the Kiessling lab. The Kiessling lab, led by Novartis Professor of Chemistry Laura L. Kiessling, has been studying and creating glycopolymers that have biological activity since 1994. Specifically, Dr. Alty and Carolyn are working on a team hoping to develop a synthetic analogue to mucus.



Mucin polymers like those show under high magnification above make up mucus gel (Photo: The Ribbeck Lab).

Carolyn is a third year graduate student in the Kiessling lab who studied chemistry in her undergrad at the University of Tennessee. Dr. Alty is a postdoctoral fellow who studied chemistry at the College of William and Mary in Virginia before working on synthetic polymer chemistry for her PhD at the University of North Carolina at Chapel Hill.

For Carolyn and Dr. Alty, most of their day to day involves setting up reactions and trying to characterize what they're making. More specifically, Carolyn has been working on synthesizing mucin mimetic polymers and the sugars to decorate the protein chains. Dr. Alty focuses a lot on creating assays to characterize the biological activity of the polymers.

Mucus' dynamic structure and size makes it difficult to understand and synthesize. The various mechanisms by which mucus protects us are still not entirely understood. As a result, the Kiessling lab is taking a step-wise approach to making their synthetic mucin polymer that can mimic the mucins found in mucus. A very valuable part of their research is their partnership with the Ribbeck lab.

The Ribbeck lab, led by Hyman Career Development Professor at MIT, Katharina Ribbeck, is a world leader in mucin research. The Kiessling lab uses data from the Ribbeck lab and other groups within the Kiessling lab about the behavior of mucins and other similarly-behaving substances, such as leptins, to model the behavior of their synthetic mucins.

Before Jill and Carolyn joined the group a year ago, previous researchers on this project managed to synthesize cis-stereo controlled glycopolymers which are very soluble in water and therefore much more biologically significant than their trans analogues.

Right now, the group is focused on synthesizing galactose, one of the main sugars found in mucus but they are hoping to expand their library of sugars and look at different proteins that have different sugar specificity.

"In many, many years it would be cool to have a synthetic mucus on a CVS shelf. There are eye drops, there are dry mouth electrolytes, it would be really cool if they had a polymer matrix that you could add water to and administer topically.", Dr. Alty smiles as she sips her coffee. "That is very far from where we are. But we have had progress to maybe suggest that is possible."

An over-the-counter dehydrated mucus could be used for a variety of uses from wound-dressing to disease prevention. Maybe it could even be used to help protect coral reefs! The possibilities for usage are endless and as the world becomes more and more connected and more and more sick, such a product could potentially save lives and maybe even slow the next pandemic.

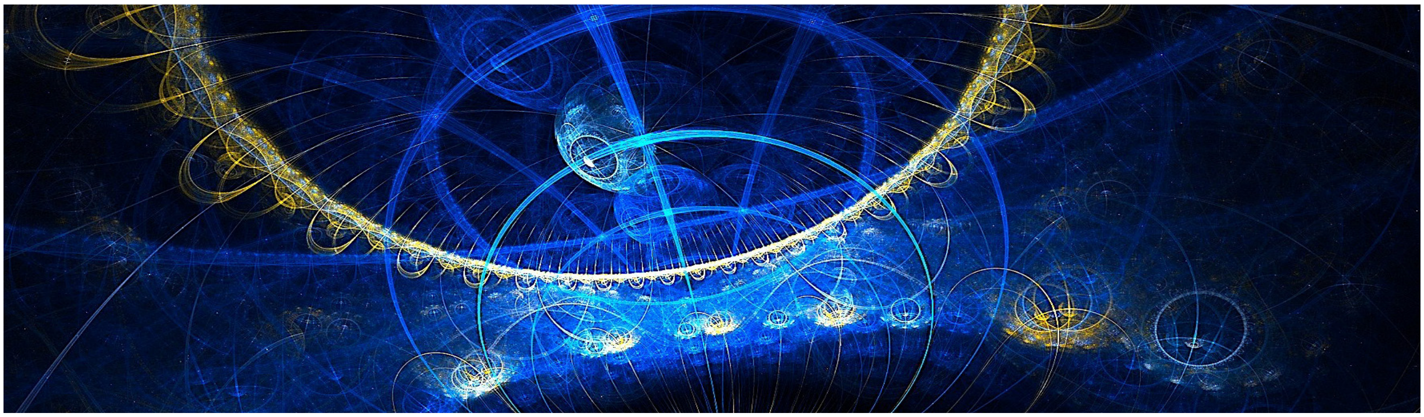
"Such a product could potentially save lives and maybe even slow the next pandemic."

So the next time you curse your runny nose, remember: Mucus? Snot all bad.

PHYSICS

Progress Drives Progress

Self-propelling preocess create paths to new knowledge in physics.



You find yourself in a strange new land. You look back to a comfortable and familiar world. Ahead lies a shrouded terrain of untold discovery or peril. Some enter this land with a destination in mind or possibly know which direction to begin. Worst of all, some might have no thought of where to begin the journey.

Progress in science is much like the exploration of a new land. We may have clues about where to examine or none at all. Exploring and studying the modern world has led to great leaps in human understanding. In just the last 120 years, we have seen an explosion of physics progress unparalleled in human history. At the start of the 20th century, Einstein introduced special relativity and a short ten years later he generalized his results to what is now our current theory of gravity. One that intertwines space and time into one inseparable medium, spacetime.

In the mid-1920s, Schrödinger, Heisenberg, and Dirac (among others) had set the foundation for quantum mechanics. Over the next fifty years, quantum mechanics developed into what we now call quantum field theory. With the foundation built by relativity and quantum mechanics, physicists could now understand the universe at the atomic scale and galactic scale.

From black holes to the Higgs boson, there are countless momentous achievements that I've skipped and many Nobel prizes left unmentioned. Just listing discoveries doesn't show the process of real physics done every day across the world. This short summary of modern physics is more of a victory lap.

"Just listing discoveries doesn't show the process of real physics done every day across the world."

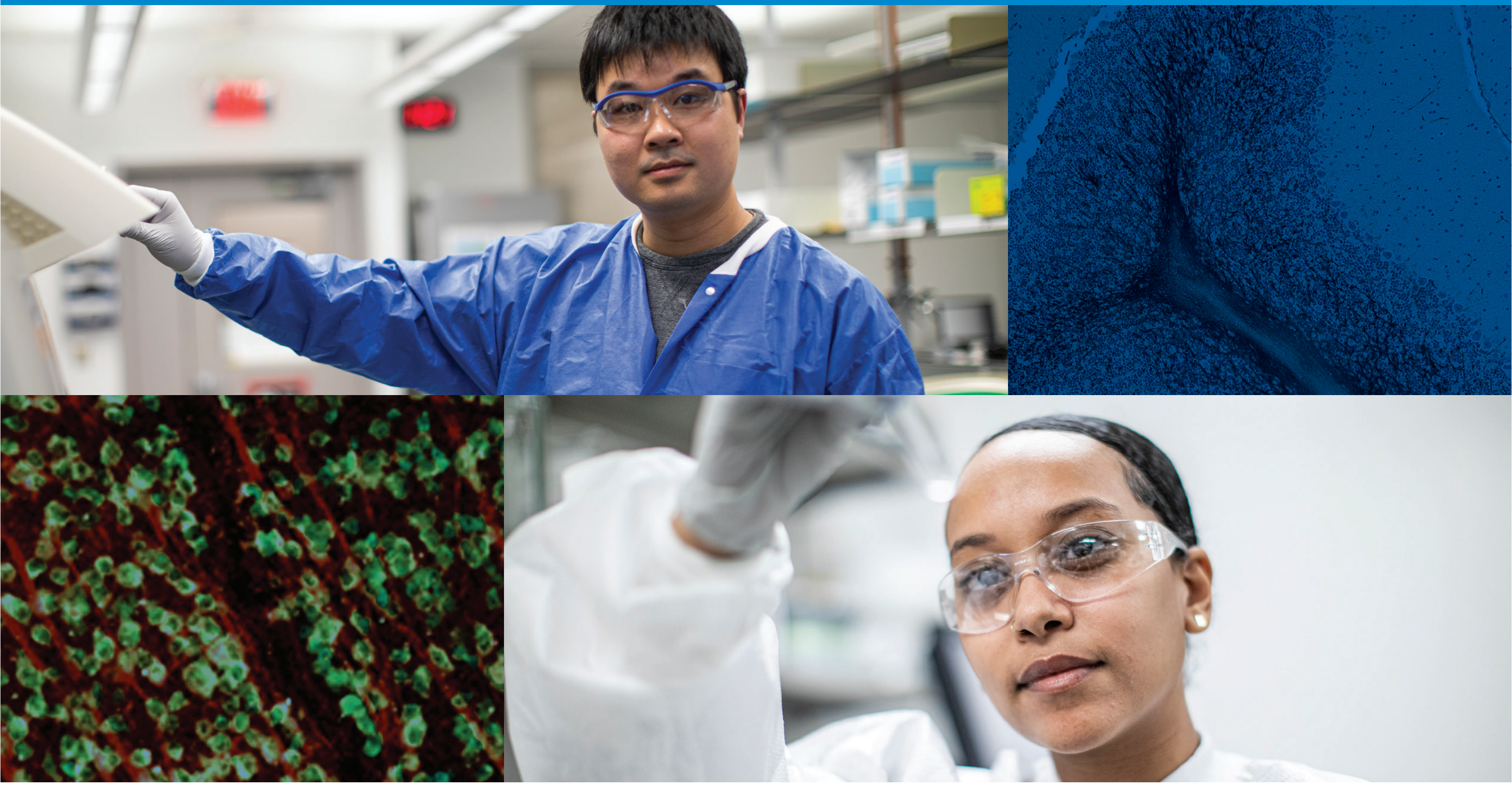
Physics can be largely divided into theoretical physics and experimental physics. Experimental physicists quantify phenomena we see across the physical world through experimentation. Theoretical physicists aim to develop the mathematical foundations for these phenomena or possibly predict new phenomena. The interplay between theory and experiment is everpresent.

To discover new physics we need to step into the shrouded landscape we faced at the start. Experimental physics and theoretical physics can both guide us along the way, albeit in different ways.

Experimentation shows us the destination we must work towards. Physics must match the world we observe. Experimentation gives us these crucial phenomena that we are required to explain through new or modified physical laws. Exactly how we arrive at this expanded theory is a job for theoretical physicists. Theorists construct mathematical paths through our unknown landscape and, hopefully, can arrive out our destination.

While experimentation can often motivate theory, theoretical work can as well serve as the motivator. When theorists develop promising new physics, it directs where new experimentation should occur. New theory gives us a heading entering the shrouded land. We don't know our destination, but the theorists have provided a direction to start our search.

Theory and experimentation are necessarily intertwined. They motivate each other and propel one another forward.



MURJ Features

Español at MIT: A Highlight of Spanish and its Department at MIT with Prof. Javier Barroso

By Lia Bu

"Nunca es tarde para aprender." This Spanish proverb translates to "it is never late for learning, or never too late to learn." Perfectly encapsulating the spirit of MIT, the Spanish department shifts to complement the societal trends and changes in its student body to better serve its students. It has gone through recent transformations through its faculty, especially through Javier Barroso, one of MIT's current Spanish faculty.

Javier Barroso, originally from Mexico, started his Spanish career in the United States as a college student. While originally intending to study business, he switched over to Spanish Literature and Communications out of a love of Spanish literature born from his childhood experiences spending a lot of time in a home library surrounded by Spanish books. Upon graduation, he worked as a journalist in South Texas before completing a Master's and Ph.D. in Spanish at the University of Kansas. There, he experienced a love of teaching Spanish with his doctoral program, and decided to pursue teaching full-time. From there, in his last semester at the University of Kansas, he applied to a position on MIT's Spanish faculty, where he currently remains.

To discuss the changes the Spanish department has recently pursued, especially with the heritage classes, we must start at the beginning. To clarify, heritage classes are uniquely designed for students with Spanish backgrounds, whether that be with speaking, writing, reading, or hearing. At MIT, this constitutes a different track of learning separate from the traditional Spanish I, II, III, and IV.

At MIT, Professor Barroso began teaching Heritage Spanish for the first time. There, he states that he felt an instant connection with the students. For heritage students especially, the Spanish language is an important part of their identity. Not having a full grasp of it can lead to anxiety in some students. As a result, the heritage class can sometimes be emotional but extremely rewarding as students are able to explore aspects of their identity they originally did not realize. However, MIT used to only teach this class once every two years. For the student completing their degree in four years, that meant only two chances to take this class. With a cap of 18 students for language classes at MIT, Professor Barroso found himself cutting the class in half (as 35 or more students would sign up). Through time, he discovered that these students especially would have excellent oral and listening skills, but lacked confidence with writing and speaking. As a result, 21G.700, Introduction to Spanish for Heritage Learners, was developed as a springboard to help prepare heritage students for 21G.714, Spanish for Heritage Learners, in which Spanish texts are explored and more of an emphasis is placed on writing and reading skills.

Through time, Professor Barroso additionally discovered that exams would cause stress for heritage learners to a much greater extent than regular Spanish learners. Exams caused validity fears. It is important to recognize that Spanish is not a universal language. Each country and district can have a unique dialect that other parts simply do not have. Professor Barroso felt that giving a grade to a person's Spanish was not fully fair, as the Spanish reflected their culture and background. However, students were still able to accomplish the same learning goals through projects, graded notebooks, and knowledge activity checks. With much lower stress, they were able to still achieve high standards of learning.

Just as Spanish is not a universal language, it is also an adapting language, especially in the United States. Professor Barroso has found that over the years, the heritage class was having an increase in students for two reasons: MIT was recruiting more minority students to create a more robust, diverse class, and the United States population itself was changing, with an increasing number of Hispanic families. Not only has the number of Hispanic families increased, however, but the origin of the Hispanic family has also changed. At the start of the heritage class, ½ to ⅔ of the class was of Mexican descent. However, in the current and past semesters of 21G.700, the class has been composed of Peru, Paraguay, Puerto Rico, Honduras, Cuba, El Salvador, and Colombia. The class content has therefore also been altered to reflect these changes - more material is covered to reflect the new regions.

"Professor Barroso discovered that exams caused stress for heritage learners to a much greater extent than regular Spanish learners."

And as for Spain Spanish? MIT's curriculum rarely delves into the language characteristics of Spain Spanish, as students will have little interaction with Spain Spanish in the United States. However, Professor Barroso acknowledges this incongruity. For example, most textbooks include the vosotros form of address, usually only used in Spain. It's not particularly used in Latin America. Additionally, the vocabulary provided by textbooks often used vocabulary from Spain, and so Professor Barrosos and others often bridge the gap between the "neutral Spanish" of the textbook and the Spanish students will encounter in their lives. (Professor Barroso actually argues that there is no neutral or commercial Spanish, even though textbooks and publishing houses try to accomplish this to increase accessibility to their content).

As MIT is a leading research institution, the university has the potential to reach and create deep impacts with a lot of communities. While MIT currently does not do a lasting collaboration between global languages and other departments (such as teaching or creating projects in other languages), in classes such as 21G.714, students complete a final project in which they present about an academic topic of their interest in Spanish to either their peers or to friends and family (encouraging a more colloquial style of speaking). Through their courses, MIT offers the tools for students to keep exploring and learning the language jargon specific to their field so that they may reach larger audiences.

For anyone nervous starting Spanish at MIT, Professor Barroso offers sage advice: simply talk to the Spanish professors. With a simple conversation, the professors will be able to gauge your foundation in the subject and place you in a proper class. While this placement is not taken lightly, especially for heritage learners, MIT's Spanish constantly updating program ensures that a student's confidence and skills grow in the language before they graduate. It is a wonderful program, and I would definitely encourage any student even slightly interested to explore their opportunities. After all, nunca es tarde para aprender.

Español en MIT: como la universidad enseña el español, con Prof. Javier Barroso

Por Lia Bu

Como el proverbio en español nunca es tarde para aprender, también el tema de MIT motiva a los estudiantes para explorar cosas nuevas, especialmente para mejorar la vida de la sociedad. El departamento de español también cambia para servir mejor a sus estudiantes. Javier Barroso, uno de los profesores de la facultad de MIT, cambia su currículo para reflejar los cambios de la sociedad, estudiantes, y más.

Javier Barroso, originalmente de México, empezó su carrera en español en los Estados Unidos como un estudiante de universidad. Cuando entró a la universidad, tenía la idea de que iba a estudiar administración de empresas. Sin embargo cambió a literatura de español y comunicación porque cuando era niño, él pasaba mucho tiempo en la biblioteca de su casa que tenía muchos libros de literatura de español. Después de su graduación, trabajó como periodista en Tejas. Regresó a la Universidad para completar un máster y un Ph.D. Allí, él se daba cuenta que le gusta enseñar el español. En el último año de su programa, aplicó para trabajar como profesor en MIT.

Para describir los cambios en el departamento de español en MIT, especialmente con las clases de herencia, necesitamos empezar al principio. Para aclarar, las clases de herencia están diseñadas para los estudiantes que tienen experiencia con español, a veces hablado, escrito, leído, o escuchado. En MIT, estas clases son diferentes que las clases tradicionales de español I, II, III, y IV.

En MIT, Profesor Barroso empezó enseñando con el español de herencia por primera vez. El dice que hay una conexión inmediata con los estudiantes. Para los estudiantes con herencia especialmente, la lengua de español es una parte importante de sus identidades. Para aprender en una clase por primera vez, puede crear ansiedad. Por eso, las clases de herencia pueden ser un tiempo emotivo pero gratificante. Sin embargo, MIT sólo tenía esta clase una vez cada dos años al principio. Para un estudiante completando su carrera en cuatro años, sólo tenía la oportunidad para tomar esta clase dos veces. Las clases de lenguaje en MIT también tienen un límite de 18 estudiantes en cada clase. Profesor Barroso encontraba que muchas veces necesitaba reducir el número de estudiantes por clase por la mitad (como 35 estudiantes querían tomar la clase). A lo largo del tiempo, él encontraba que los estudiantes desarollaban habilidades buenas en habla y escucha, pero no en lectura o escritura. Por eso, Profesor Barroso formó 21G.700, Introducción a Español para preparar los estudiantes de herencia para la clase 21G.714, Español para Los Estudiantes de Herencia, con la cual los estudiantes exploran los textos de español, y hay un énfasis en las habilidades de la lectura y escritura.

A lo largo del tiempo, Profesor Barroso también encontró que los exámenes eran una fuente de estrés para los estudiantes de herencia que para los estudiantes de español regulares. Los exámenes eran una causa de los miedos de validez. Es importante reconocer que español no es una lengua universal. Todos los países tienen diferentes dialectos únicos que las otras partes no tienen. Profesor Barroso sintió que una nota de español de un estudiante no era muy justo, porque el español es un reflejo de su cultura y experiencia con español. Sin embargo, los estudiantes logran las mismas metas con los proyectos, los cuadernos, y otras actividades. Con menos estrés, los estudiantes también logran niveles altos de aprendizaje.

Como el español no es una lengua universal, también es una lengua que se adapta. Después de muchos años, Profesor Barroso encontraba que la clase de herencia tenía más estudiantes cada año por dos razones: MIT estaba reclutando más estudiantes de minoría, y que la población de los Estados Unidos también estaba cambiando. Al principio de la clase de herencia, ½ o ⅔ de la clase era Mexicana. Pero ahora, en el semestre actual y pasados, la clase ha tenido estudiantes de Perú, Paraguay, Puerto Rico, Honduras, Cuba, El Salvador, y Colombia. El contenido de la clase se altera y adapta para reflejar estas cambios - más material con información de estos regiones.

¿Y el español de España? El currículo de MIT no enfoca las características del español de España. Los estudiantes en los Estados Unidos no van a encontrar mucho este tipo de español. Sin embargo, Profesor Barroso reconoce este incongruencia. Por ejemplo, los textos de español tiene el vosotros, usualmente se usa solamente en España. Además, el vocabulario de este textos también es de España, que un estudiante aprendendiendo el español de latinoamerica no va a usar. Profesor Barroso y otros profesores necesitan conectar este espacio con el "español neutro" y el español que los estudiantes van a encontrar en sus vidas. (Profesor Barroso de verdad habla que no hay un "español neutro," pero las compañías y casas editorials quieren eso para crecer la audiencia para sus libros).

MIT es una universidad muy grande en el mundo y tiene la posibilidad para hacer un impacto grande con muchas comunidades. Ahora MIT no tiene una colaboración entre las lenguas globales y otro departamentos, pero en clases como 21G.714, los estudiantes completan un proyecto final en que ellos hablan de un aspecto académico que les gusta mucho para su familia (para motivar un estilo coloquial), y para traducir la jerga de la ciencas en español. Con sus clases, MIT ofrece las habilidades a los estudiantes para continuar explorando y aprendiendo la lengua jerga especialmente para su carrera.

Para los estudiantes que están nerviosos para empezar su español en MIT, Profesor Barroso tiene un buen consejo: hablen con los profesores de español. Con una conversación, los profesores pueden poner un estudiante en la clase correcta. Esta disposición es un punto importante, especialmente para los estudiantes de herencia. El departamento de Idioma de Español de MIT actualiza mucho el español y asegura que los estudiantes crecen en su confianza y habilidades en español antes de su graduación. Es un programa excelente, y yo motivo a cualquier estudiante a empezar sus estudios en español y explorar las oportunidades de español que MIT tiene. Después de todo, nunca es tarde para aprender.

MURJ Spotlight

Robert A. Weinberg

Forty years ago, the Weinberg lab at MIT discovered the first human oncogene, showing the world that some human genes are able to cause cancer by acquiring mutations. This issue's spotlight celebrates the pioneering works of Daniel K. Ludwig Professor Robert A. Weinberg and his eighty years as one of century's foremost educators.

By Hanjun Lee

INTRODUCTION

In striking contrast to its pivotal role in modern biology, cancer research half a century ago was in an entirely different place in the minds of scientists and clinicians. On one side, the entire field of cancer research was held in contempt by many biologists who regarded cancer cells as poor model systems. On the other side, the molecular biological view on the field was often derided as being simplistic, if not simple-minded. The astonishing transformation of cancer research over the past decades as one of the main pillars of modern biology cannot be discussed without citing the works of Daniel K. Ludwig Professor Robert A. Weinberg at the Institute. His work enlightened the world that it is mutations, not tumor viruses, which are the primary cause of cancer, and opened the door for targeted cancer therapies which are saving the lives of millions every year. Celebrating his 80th birthday, the MURJ reflects on his lifelong journey as world's foremost educator in biology and on his 58 years at MIT.

Dr. Robert A. Weinberg is the Daniel K. Ludwig Professor for Cancer Research at MIT, the director of the Ludwig Center, and the founding member of the Whitehead Institute. (Photo: Gretchen Ertl, Whitehead Institute)

BECOMING A COURSE 7

Weinberg was born in Pittsburgh, PA, on November 11th, 1942, to a family of refugees who escaped from Nazi persecution four years prior. When he became a freshman at the Institute in 1960, the field of biology was experiencing one of the most dramatic metamorphosis in millennia. The central dogma of molecular biology—the revolutionary notion that the transfer of information in biology occurs from nucleic acids to nucleic acids and proteins—was proposed by Francis Crick in 1957. The first codon was then deciphered by Marshall Nirenberg and Heinrich J. Matthaei four years later. During this era of great molecular biological transformation, Professor Maurice S. Fox at the Institute extensively revised and modernized 7.03 (Genetics), a course that later attracted Weinberg to the field of molecular biology.

Q. What was the class that influenced you the most at the Institute?

A. Ultimately, the most influential was the course in genetics (7.03 as it is called in MIT) that was taught by Professor Maurice S. Fox. He was describing what was then the rapidly expanding discoveries of the triplet code and of the paradigm of DNA, RNA, and proteins. Then I came to realize that this model—the molecular biology of a cell—was applicable to all forms of life in the biosphere and that through a simple set of rules, one could really understand the infinite variety of life on the planet. So that was what really excited me. In contrast, I was not so excited about studying different species, taxonomy, or evolution, but really was interested in trying to understand a small number of basic principles, and that is what molecular biology offered at that time.

Q. So do you think you also had a natural affinity for reductionist approach at that time?

A. Yes, the fact of the matter is that I am and was a product of MIT education. Obviously, very influential were things like physics in which the complexity of the physical world could be reduced to a small number of fundamental principles, starting with the laws of Newton. So again, rather than describing phenomena without any end—thousands of species and each of their idiosyncrasies—it seemed to be much more satisfying to understand and reduce their behavior to a small number of underlying principles.

CIVIL RIGHTS MOVEMENT

After graduating from MIT, Weinberg spent another five years at the Institute as a PhD student. However, after his first year at the graduate school, he took a leave of absence and instead headed to Stillman College, what was then a traditionally black college in Tuscaloosa, AL. Weinberg believes that this experience has helped him learn how to teach.

Q. When you got into the PhD program in MIT Biology, you took a leave of absence for Stillman as an instructor. Can you detail on this experience?

A. After a year at MIT in graduate school, I said to myself, I had already been there in total five years, and it was good time for me to see a little bit of the world—it was one of the last chances, so I would have to do so. This was at the height of the civil rights movement, so I, like many other young people in the north, took on teaching positions in small, traditionally black colleges in the south. I interviewed in several of them and was ultimately accepted to teach in the biology department of Stillman College in Tuscaloosa, AL, which I did for a year. I taught four courses each semester, which meant that at the end of each teaching day, I was totally exhausted, but it was a useful experience because it really taught me the essence of how to teach things.

Q. Do you think your experience at Stillman has translated into your later life as a professor at MIT?

A. Yes, I do indeed think so, because teaching is a wonderful way of purifying the mind while being forced to express in ways that are understandable by the people in the audience. Some people present science, and they hope that the essence of what they are presenting already explains itself and does not require very much clarity because it is so self-evident. But the fact is that I was teaching in a place where the students were from culturally deprived backgrounds—many of them were the children of the sharecroppers—so this drove me to begin to explain things in simple and intuitively accessible ways, and I think that turned out to be very useful subsequently when I came back to MIT.

TUMOR VIRUSES TO MUTATIONS

When President Richard Nixon declared the war on cancer through the enactment of the National Cancer Act of 1971, the field was fueled by the conviction that cancer was ultimately a disease of infectious tumor viruses, not of mutations. The bandwagon for the war was Howard Temin and David Baltimore's discovery of the reverse transcriptase enzyme in 1970, but it had been for the wrong reason, since cancer-causing human retroviruses were never found with the exception of rare leukemias in the Caribbean and southern Japan. Weinberg's lab at the MIT Cancer Center was key in elucidating that it is mutations that is responsible for the majority of human cancers, not tumor viruses. His lab discovered the first functionally validated human oncogene in 1982 and showed that cancer-causing mutations affect the structure of the encoded protein. Six years later, his lab also isolated the first human tumor suppressor gene.

Q. What made you to delve into mutations as opposed to tumor viruses?

A. By 1975 or 1976, it had become apparent that this dream that retroviruses could be assigned of culprits in triggering significant numbers of human cancers—the whole dream was going up in smoke. There were people who were still pursuing the idea aggressively, but sooner or later they stopped because they were failing time after time in demonstrating the presence of retroviruses in human cancers. Obviously, that suggested an alternative scenario, fueled in part by the work of Bruce Ames, that in fact carcinogens are mutagenic, which led to the speculation that cancer cells, including human cancer cells, were somatically mutated cells. This led in turn to the further speculation that mutant alleles, found in cancer cells that had been created by mutagenic carcinogens, were in turn responsible for directing or orchestrating phenotypes of a cancer cell.

Q. What you are describing here is your seminal discovery from 1979 to 1982 that mutant genes arising from chemical mutagenesis could transform mouse fibroblasts into cancer cells.

A. You have correctly described it. There was extensive work in Wisconsin by a man named Charles Heidelberger, that he could use methylcholanthrene, which was a well-known carcinogen, to induce transformed mouse cells—ostensibly the methylcholanthrene was working through its mutagenic powers. When he gave us those cells, we speculated that within the DNA of those cells, there lay genetic information that was causing the cells to behave like cancer cells. At that time, there was no direct proof that the abnormal behavior of cancer cells could in fact directly be traced back to mutant alleles carried in the genomes of those cells. So attacking that—what was for us clearly a very important question—seemed to motivate our work, and so in 1975, I had a graduate student whose name was David Smotkin, and he brought into the laboratory the technique of DNA transfection—the technique that allows one to take naked DNA from one cell and introduce it into a second recipient cell and then to observe thereafter the biology of the responses of the recipient cell to the DNA. In 1977 or 1978, I got a new graduate student, Chiaho Shih, and he began the experiments of taking the DNA from chemically transformed cells and introducing it to normal cells—mouse cells in both cases with no indication of the involvement of any viruses—suggesting of obviously focusing on more intensively the existence of non-viral mechanisms of cell transformation. So, by late 1978 or early 1979, it had been evident that DNA of certain chemically transformed cells carried a non-viral cellular transforming information that the DNA of normal cells did not carry. This was the definitive proof that within the DNA of cancer cells, there lay the genetic information that was responsible for the transformation of cells which was in the end the most important thing that was done in my career, obviously some years ago—more than forty.

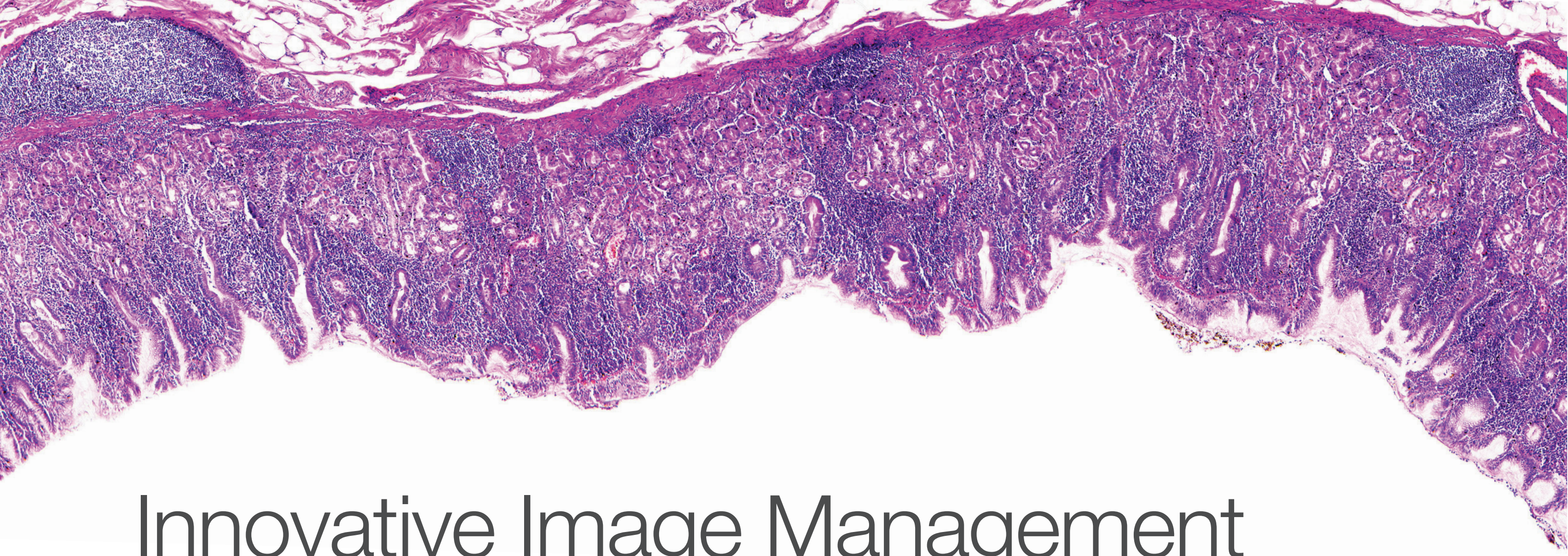
TO FUTURE BIOLOGISTS

Finally, the MURJ asked Professor Weinberg for some advice for future biologists at MIT.

Q. For students at MIT who might be having their midterms, for instance for 7.01, when the Spotlight is published, what would be your words of advice?

A. I am hard pressed for words of wisdom. I do not know who it has been taught by—clearly it is taught by different people than when Eric S. Lander and I taught it—we were mostly interested in teaching the students whether they could understand conceptually the logical take-home lessons we were trying to teach them. As Eric and I said explicitly to the students, we were not really interested in your supping up and absorbing all kinds of facts, rather in your becoming more intelligent in the way you can reason through the complexity of biology and figure out the logic of science. That was our emphasis at that time—using the teachings of 7.01 as a way of sharpening minds, rather than trying to test them for how much they have memorized in terms of facts, which by the way was very threatening for some students who had done brilliantly in high school biology where they were tested on their ability to learn and memorize facts and not so much on their ability to reason through complex scientific logic.

Professor Robert A. Weinberg will be celebrating his 80th birthday and his lab's 40th anniversary for the discovery of the first functionally validated human oncogene on November 11th, 2022.



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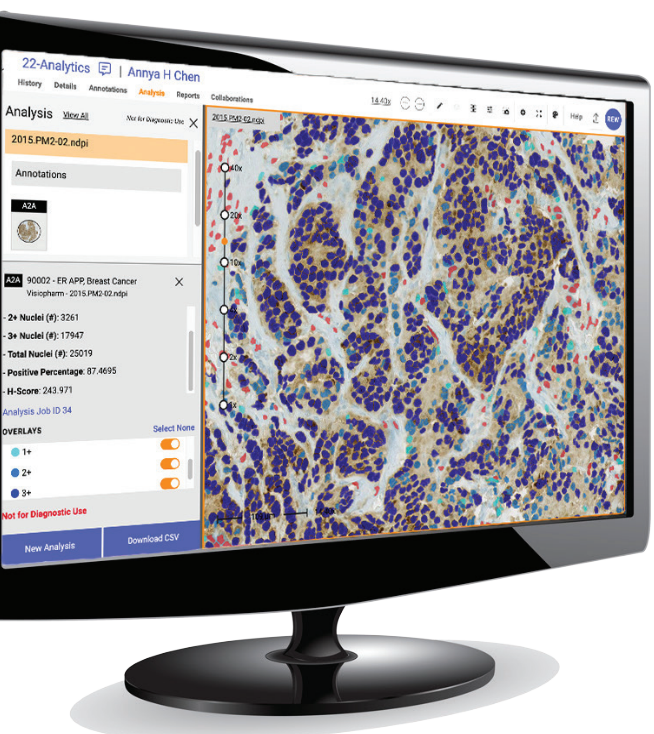

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MURJ UROP Summaries

A Machine Learning Approach to Create a Hyperlocal Real-time Air Quality Map

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Air pollution has many negative consequences, including increasing the rate of global warming. More directly, however, poor air quality can damage our health, leading to respiratory illnesses and allergy aggravation. To this end, private and government agencies have measured and calculated AQI (air quality index) to give residents in every city an idea of the air quality on that day. While this number is very useful for general purposes, it does not directly show how the air directly nearby is affected by hyperlocal factors (ex: smoke from a nearby car).

Several researchers have worked on the problem of predicting air quality. There have been many insights into this field, such as that "the previous two days [should be] considered due to the memory effect" for air quality prediction [1] and that "pollutants show a strong diurnal pattern" [4]. However, they mostly focus on air quality in general for a city [1] or in one very specific location [4, 5]. Some papers have worked on predicting hyperlocal through mobile sensing, but they are limited in data. In other words, they do not have access to data that is spatially and temporally changing, so they cannot create a full air quality map of a city.

Hyperlocal data from various locations and times within a small region was obtained from the City Scanner project. This dataset was then augmented with measurements from stationary sensors that collect hyperlocal data at various times in the same location, which will function as a 'ground truth' to inform my model. With these two datasets, the aim is to predict air quality readings across the Bronx borough in New York City, such that the air quality at any specific time and location will be reasonably accurate.

September 2021 – December 2021 data from the City Scanner deployment in New York City (nyc3_data.csv), which included values for PM1, PM10, PM25, raw values from the particulate matter sensor, nitrogen oxides, carbon monoxide, humidity, temperature, latitude, longitude, time, and other measurements for debugging (such as the number of glitches in the particulate matter sensor) was used for this project. There were close to 800,000 rows of data because the device was collecting data once every few seconds, and this was later cleaned and adjusted to average data every minute.

Data was obtained from 2 Purple Air Sensors, dubbed CUNY-1 and W36stNYC2, from September 2021 through December 2021, which had measurements of PM2.5, latitude, and longitude. These sensors were located outside along streets, and provided stationary data that is available year round. These two sensors were used to provide a sense of the air quality in various locations throughout the Bronx area using the air quality measurements from two fixed locations within this area.

After a brief literature review, gradient boost [1], XGBoost [2, 3], neural networks [2, 5], support vector machine [5], random forest [5, 6], stacking ensemble [5, 6], and Adaboost [5] were the most referenced models and best fit the project. These models with various different hyperpermaters were then tested on the training data (calibrated CityScanner data + local meteorological data). The RMSE and R2 of each were evaluated in order to decide which technique was best to use.

The results of four highest-performing regression models are summarized below. The final model chosen was a gradient boosting algorithm with 100 boosting stages, a max depth of 3 for each regression estimator, a min samples split of 5, a learning rate of 0.01, and a loss of mean squared error (the square root of which is RMSE, root mean squared error). A min samples split describes the minimum number of nodes needed to have a split in the tree.

	RMSE	R^2
Decision Trees	2.240	-0.585
Neural Network	3.704	-0.780
Gradient Boost	0.213	0.045
XGBoost	3.243	0.139

Table 1. A summary of the RMSE and R2 of four key algorithms.

The work accomplished through this UROP is an addition to work in detecting air quality to improve quality of life. There are limitations to this approach, such as considering air quality over only three months and the small number of stationary sensors from which data was available. With a dataset spanning a full year, it would be feasible to learn more about the effect of tourism on air quality readings, the effect of temperature causing urban heat islands, and how humidity and pressure interact with the data. With more hyperlocal stationary sensors, they could help check the CityScanner data and be used for future predictions through this project.

An ongoing goal of this project is to create a real-time air quality map, which would help people plan the healthiest route when walking outside. As of now, a machine learning model has been programmed to predict the air quality values to, essentially, fill in the gaps of data from the City Scanner project. Currently, creating and publishing a real time map on a website that will

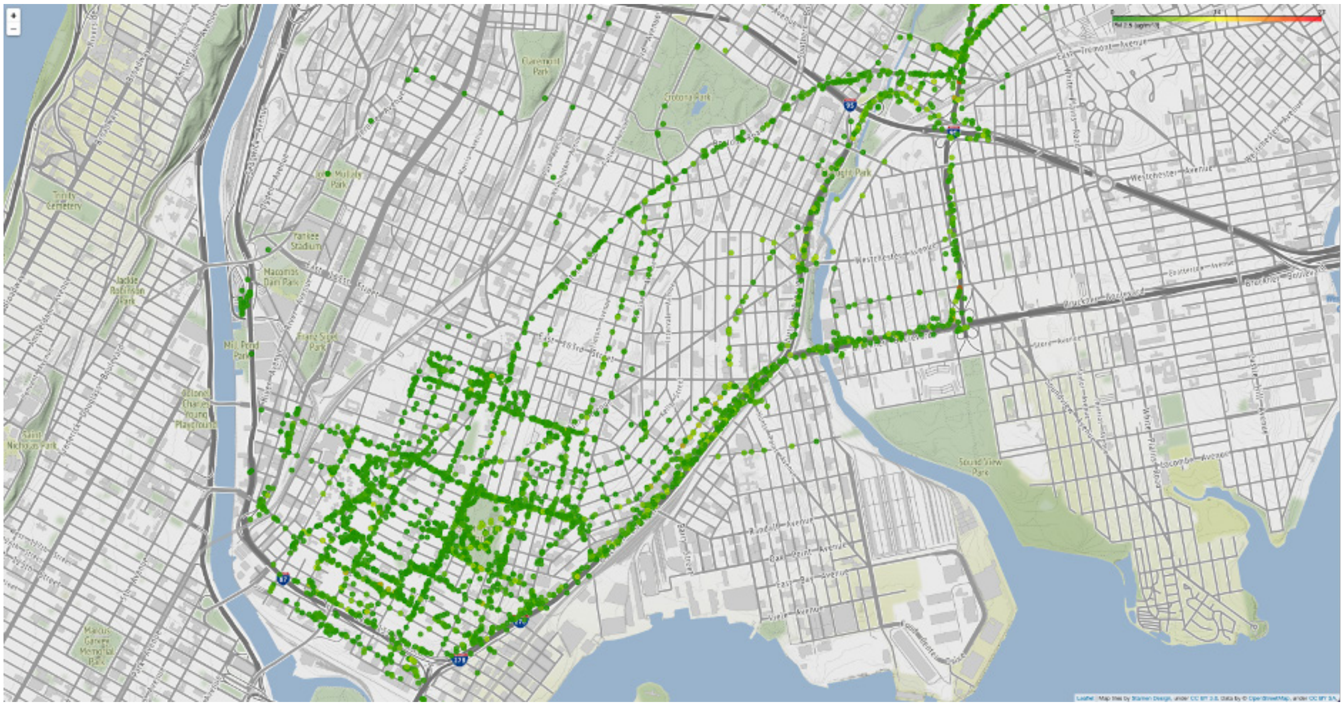

Figure 2: A draft of the real-time air quality map.

display these predictions are next steps for this project, and an image of the work in progress is shown in Figure 2.

References

[1] Lee, M., Lin, L., Chen, CY. et al. Forecasting Air Quality in Taiwan by Using Machine Learning. Sci Rep 10, 4153 (2020). https://doi.org/10.1038/s41598-020-61151-7

[2] Wang, A., Xu, J., Tu, R. et al. Potential of machine learning for prediction of traffic related air pollution, Transportation Research Part D: Transport and Environment, Volume 88, 2020, 102599, ISSN 1361-9209, https://doi.org/10.1016/j.trd.2020.102599.

[3] Gordon, M., Staebler, R., Liggio, J. et al. Measured and modeled variation in pollutant concentration near roadways, Atmospheric Environment, Volume 57, 2012, Pages 138-145, ISSN 1352-2310, https://doi.org/10.1016/j.atmosenv.2012.04.022.

[4] Liang Y-C, Maimury Y, Chen AH-L, Juarez JRC. Machine Learning-Based Prediction of Air Quality. Applied Sciences. 2020; 10(24):9151. https://doi.org/10.3390/app10249151

[5] Lim, C., Kim, H., Vilcassim, M.J. et al. Mapping urban air quality using mobile sampling with low-cost sensors and machine learning in Seoul, South Korea, Environment International, Volume 131, 2019, 105022, ISSN 0160-4120, https://doi.org/10.1016/j.envint.2019.105022.

[6] Song, J., Han, K., Stettler, M. E. J. (2021, May 1). Deep-MAPS: Machine-Learning-Based Mobile Air Pollution Sensing.

[7] "Real-Time Air Quality Map." PurpleAir, map.purpleair.com/1/mAQI/a10/p604800/cC0#10.7/40.9084/-73.7077.

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MURJ Reports

Analysis of Defects in Metal Additive Manufacturing with Augmented Data Generation

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Laser powder bed fusion (LPBF) is a method of additive manufacturing (AM) that selectively melts and fuses together microscopic metallic powder. LPBF offers the benefit of producing custom structures out of high strength metals that can be difficult to fabricate with conventional methods. The challenge of LPBF is that 3D printed structures often have internal pores due to process flaws. Pulsed thermal tomography (PTT) is a method for reconstructing the depth profile of materials, allowing the visualization of internal voids in solids. In prior work, we developed a convolutional neural network (CNN) which, having been trained on simulated 2D PTT images of subsurface elliptical defects, was able to classify the semi-major radii, semi-minor radii, and angular orientation of the best-fit ellipses in previously unseen PTT images. The unseen PTT images contained subsurface irregular defect shapes imported from scanning electron microscopy (SEM) images of metallic LPBF-printed specimens. Training the CNN on irregular defect shapes instead of on elliptical shapes would make the resulting classifications more descriptive of actual defect shapes. However, this requires a much higher volume of SEM images of material defects, which are difficult to obtain because of random occurrence of defects in LPBF. To address this challenge, we developed a generative adversarial network (GAN) to augment the existing dataset of SEM defect images. The GAN model is demonstrated to create novel yet realistic defect shapes that can be used as input for simulated PTT images to train CNN.

1. Introduction

Laser powder bed fusion (LPBF) is a method of additive manufacturing (AM) that selectively melts and fuses together microscopic metallic powder (Khairallah et. al., 2016). LPBF offers the benefit of producing custom structures out of high strength metals that can be difficult to fabricate with conventional methods. The challenge of LPBF is that 3D printed structures often have internal pores due to process flaws caused by either insufficient or excessive laser power (Zhang et. al., 2020, 2021, 2022). Quality control of metallic LPBF structures can be performed with Pulsed thermal tomography (PTT) nondestructive imaging. PTT method allows for reconstructing the depth profile of materials, which provides visualization of internal voids in solids (Ankel et. al., 2021, 2022; Heifetz et. al., 2019, 2020). However, resolution of PTT images decreases with defects depth due to blur inherent in diffusion-based imaging. This can be compensated with machine learning-based classification of PTT images.

In prior work, we developed a deep learning convolutional neural network (CNN) to automatically extract features of thermal effusivity from PTT images (Ankel et. al., 2022). The CNN was trained on simulated PTT images of 5 mm x 5 mm metallic plates with elliptical subsurface air voids. The images were created with MATLAB PDE Toolbox heat transfer calculations for 2D structures. The elliptical subsurface voids were parametrized by their semi-major radii, semi-minor radii, and angular orientations. The CNN was then applied to PTT images with irregularly shaped subsurface defects that were extracted from SEM images of stainless-steel sections. These PTT images were simulated by creating MATLAB polyshape data structures that follow the contours of the SEM images, using them to model irregularly-shaped subsurface air voids on the metallic plate, and similarly running heat transfer calculations. Upon comparison to a given irregular defect's ellipse of best fit, the CNN is capable of classifying irregular defects with area error (AE) and area orientation error (AOE) metrics that were smaller than 0.62 and 0.55, respectively. This indicates that the CNN has good predictive ability.

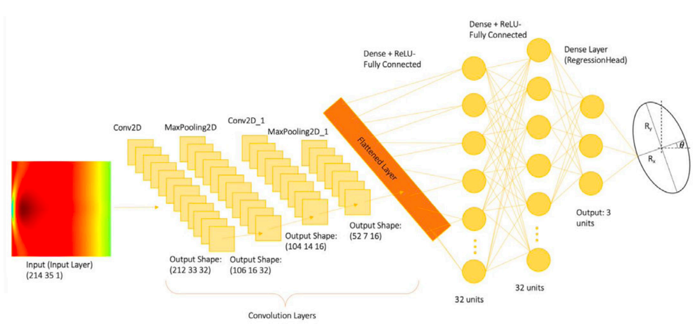

Figure 1: Flowchart of CNN algorithm for classifying defects in PTT thermal effusivity images (Ankel et. al., 2022).

The elliptical model is easily parameterizable and performs well in the CNN; however, it does not encompass all characteristics of an irregularly-shaped defect. Information about certain sharp points and concaves is lost when we use the equivalent elliptical model of these defects. It would be more advantageous to extend the CNN to classify irregular shape defects, because this would enhance the ability to estimate the risk of material failure.

2. Analysis of Gaussian Random Circle for Classification of Irregular Defects

Training the CNN on irregular defect shapes instead of on elliptical shapes would make the resulting classifications more descriptive of actual defect shapes. To transition from elliptical shape model approximation to irregular shape model, we considered a Gaussian random circle (GRC) model as a better fit for the irregular shapes of realistic defects (Muinonen et. al., 1996; Peltoniemi et. al., 1989). The GRC model refers to a log-normally distributed random field that is defined on the unit circle. The irregular shape can be reproduced by stochastically deforming a circle, such that the probability density of the distance from the center of the shape to the surface has a lognormal distribution. A dataset has a lognormal distribution if applying a log function to it creates a normal distribution. With this model, the irregular shape can be parametrized by the mean radius, the standard deviation of radial distance, and the power-law index of the covariance function. Because the random shapes are parametrized with GRC model, this approach is advantageous for generating a large database for training the CNN.

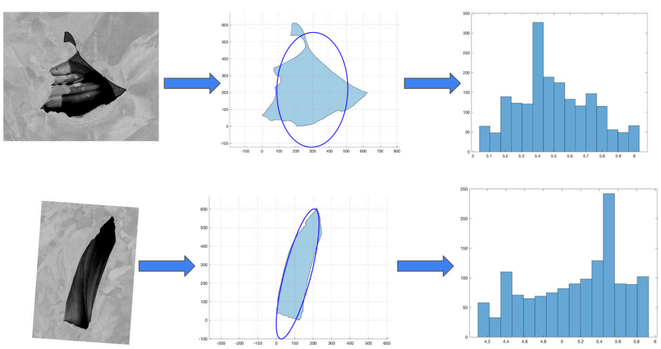

Figure 2: Examples of the radial distribution analysis of two real defect shapes. Although some shapes had lognormal distributions (such as the first defect shape above), many of the longer, less circular shapes did not have a lognormal distribution (such as the second defect shape above). Note that the histograms are plotted on the output of the log function of the distances. For a lognormal distribution, the histograms are expected to have a normal distribution.

To determine the feasibility of GRC model in representing material defect shapes, we analyzed the radial distribution of defects in several SEM images. As seen in Figure 2, the SEM images of each defect were transformed into the MATLAB polyshape data structure to extract the coordinates of the perimeter. The distances from each coordinate to the center of the shape (defined by the center of the best-fit ellipse). The natural logarithm of the distances was then calculated and plotted in a histogram to determine whether the radial distribution was lognormal. We found that not all of the defect shapes have a lognormal radial distribution.

3. Development of a Generative Adversarial Network (GAN) for Data Augmentation

3.1. Background

A generative adversarial network (GAN) is a deep learning architecture that has been popular method in recent literature for synthesizing robust, novel images from a limited amount of training data (Goodfellow et. al., 2014). GANs use two neural networks, a generator model and a discriminator model, that train simultaneously to outperform each other. The training dataset is the original set of images that is expected to be augmented, which gives the target domain. The objective of the generator model is to produce high quality images that are novel, but similar enough to the training images such that the two datasets are indistinguishable. Working in opposition, the objective of the discriminator model is to accurately distinguish whether that image is from the original training dataset or a synthesized image from the generator. An ideal GAN model will stabilize to a point of equilibrium between the generator and the discriminator.

3.2. Architecture of the GAN Model

The generator developed in this work is a sequential model, built using the Keras library in Python. It has three Dense layers with dimensions of 256, 512, and 1024, respectively. In between each layer, there is a Leaky ReLU activation function with an alpha value of 0.2, as well as Batch Normalization. There is a final Dense layer with a tanh activation function. When running the generator, a latent vector (or randomly generated 1D vector on a Gaussian distribution that can be thought of as noise) is input into the network, and a fake 2D image is generated with a size of 425 x 425 pixels.

The discriminator is also a sequential model built using Keras in Python. It has three Dense layers with a Leaky ReLU activation function in between each, but the third dense layer has a Sigmoid activation function. The input is the image we supply, and the output is the decision of of image validity (whether the image is real or fake).

During GAN training, the discriminator is trained first. Then, as the generator trains, it is important to note that the discriminator is not trained at the same time. For each epoch, given the batch size n, we create a matrix with size n 100 noise vectors, and input vectors that into the generator to produce n fake images. The discriminator is then trained on the real images. A set of real images (all labeled as 1 to signify that they are real) is input into the discriminator to learn to classify whether they are real or fake. Then the same operation is performed with the fake images, which are labeled as 0 instead to signify that they are fake. From this procedure, we obtain two loss values of the discriminator: one for the real images and one for the fake images. The overall loss of the discriminator is the average of the two losses values. Next, the generator is trained using the combined model. Another set of noise vectors is input into the combined model, but they are labeled as 1 to trick the model that the fake images are real. The combined model uses both the generator and discriminator, but the discriminator is not actively being trained, only the generator is being trained based on the feedback of the discriminator's output. The loss of the generator is calculated by the loss of this combined model.

The flowchart of the GAN model is depicted in Figure 3. The model was trained on images of MATLAB polyshapes (extracted from the original SEM images) with a black background and

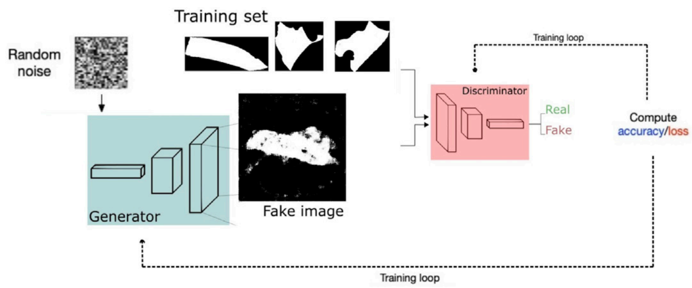

Figure 3: The flowchart of the GAN model. The input training set is the real shapes, shown on top, which the discriminator is trained on. The output is the fake image produced by the generator, which improves upon training.

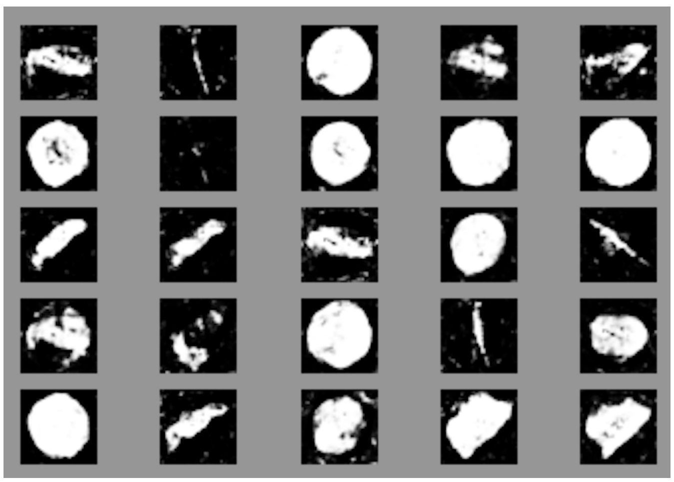

Figure 4: An example output of the GAN model with mode collapse. Number the images from left to right, top to bottom. Images 3, 6, 8-10, 14, 18, and 21 are all almost identical shapes. Similarly, images 11, 12, and 22 are also almost identical. These outputs do not have the same variability as the training dataset.

white filling. We determined that this approach produced the best quality images, each with a clear shape that had distinct enough boundaries. The defect shape images can be used as input for MATLAB to generate thermal effusivity images.

3.3. Troubleshooting Mode Collapse and Convergence Failure

Mode collapse occurs when the model generates only a single or small subset of the different possible outcomes (Brownlee, 2019). This is identifiable by the output images lacking the same variability as the training dataset. As seen in Figure 4, we observed that many of the output defect shapes were identical to each other, so they had very low diversity.

Convergence failure occurs when the generator and the discriminator are unable to settle down to a point of equilibrium. Figure 5 shows the loss of the discriminator in blue and the loss of the generator in orange over the course of 50,000 epochs in training. The loss of the discriminator falls to zero and stays extremely low, while the loss of the generator continues to rise. The

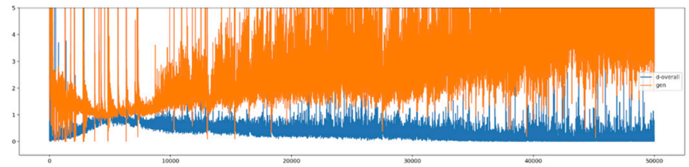

Figure 5: The loss function of the GAN model when convergence failure is observed.

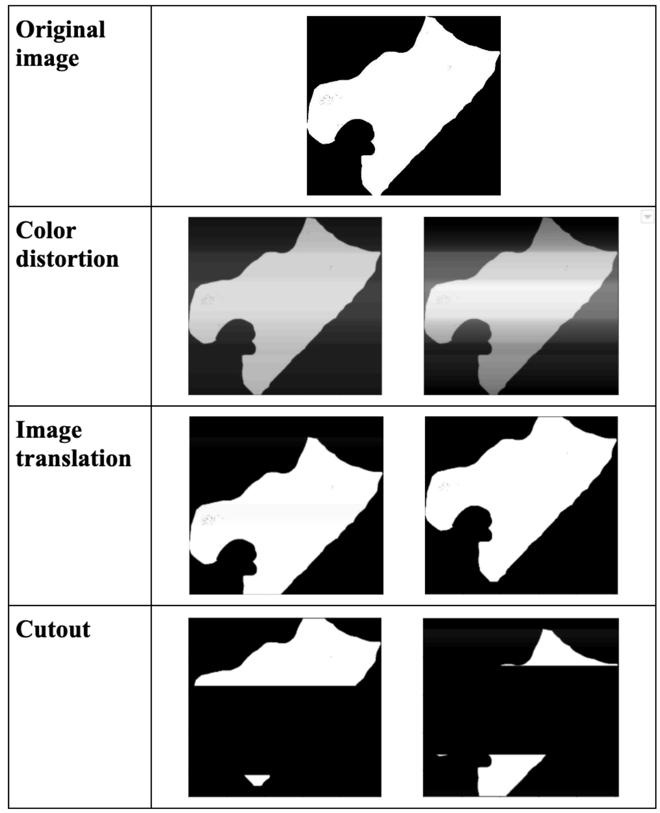

Figure 6: Examples of the image transformations used for differentiable augmentation, applied to one of the defect shapes used as training input data.

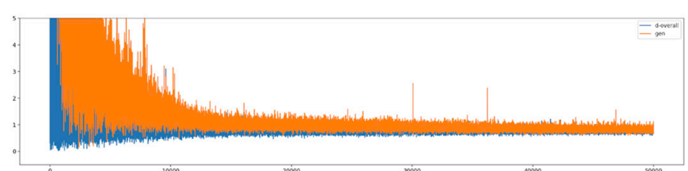

Figure 7: The loss function of the GAN model after implementing differentiable augmentation.

discriminator having a very low loss means it is performing well, so it is able to easily identify whether a given image is real or fake. However, note that in the GAN model, the discriminator should not be performing that well because that means that the generator is producing very poor images that are easy to distinguish from the original training dataset. The likely cause for both mode collapse and convergence failure is the small number of SEM images in our training dataset. Because the amount of real SEM images of internal defects is limited, there were only 31 images to train our model on.

Some GAN models already exist to address this problem, such as "Few-Shot-GAN," which requires 5-100 images in the target domain to train, and even "One-Shot-GAN," which requires only one image (Robb et. al., 2020; Sushko et. al., 2021). Both of these models utilize data augmentation to create more robust training sets. We implemented differentiable augmentation, a specific type of data augmentation, which applies image transformations to both the real and the fake images for both generator and discriminator training (Zhao et. al., 2020). More specifically, the image transformations used were color distortion, image translation (with padding of zeros), and cutouts (masking the image with rectangles of variable sizes). Examples of these augmentations can be seen in Figure 6.

Implementing differentiable augmentation corrected mode collapse by introducing more variability, and corrected convergence failure by preventing the discriminator from simply memorizing the training data. By applying the augmentations to both real and fake images for both models (as opposed to just the original training dataset), the model also stayed balanced so that it did not produce images that were skewed by the image transformations. The resulting outputs did not show any signs of the scaling, unnatural color, or other augmentations that were applied. As seen in Figure 6, which was also produced during a 50,000 epoch training, the losses of the two models converge and stay balanced. For the generator, it stays between 0.5 to 2.0; while for the discriminator, it is slightly lower, around 0.5. These values are much closer to what we are looking for in the loss plot of a successful.

The shapes created with GAN can then be used for training the CNN. Similar to images of actual material defects, the shapes output by the GAN can be transformed into a MATLAB polyshape data structure, consisting of a 5 mm x 5 mm plate containing a hole with the contours of the shape. MATLAB PDE Toolbox 2D heat transfer calculations are then performed on this computational mesh, which results in the simulated PTT images that can then be used as inputs into the CNN, as shown in Figure 8.

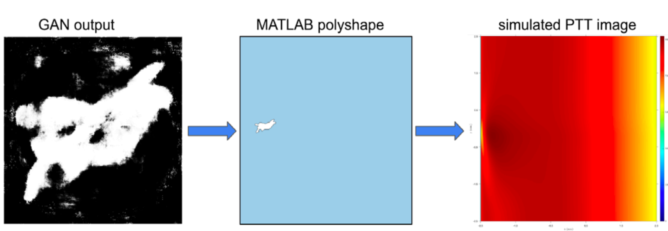

Figure 8: An example of the simulated shapes generated by the GAN is transformed into a MATLAB polyshape data structure, which is then transformed into a PTT image that can be used as training data for the CNN.

4. Conclusions

To more realistically classify the shape of material defects in PTT, one has to train the CNN to identify irregular shapes. To accomplish this goal, a more robust augmented dataset of SEM images of internal defects is needed. The GAN model was trained on only 31 inputs of different real-life defects from SEM imaging, yet it produced a much larger, novel dataset with similar characteristics and variability of shapes. The model can continue to output new images without being retrained. These shapes can then be used for training the CNN. Similar to images of actual material defects, the shapes output by the GAN can be transformed into a MATLAB polyshape data structure, consisting of a 5 mm x 5 mm plate containing a hole with the contours of the shape. MATLAB PDE Toolbox 2D heat transfer calculations are then performed on this computational mesh, which results in the simulated PTT images that can then be used as inputs into the CNN.

Using GAN, we have developed a capability to create robust dataset to train CNN. In future work, we will continue modifying the CNN to better parameterize irregular shapes, similar to the radii and angular orientation of ellipses. For the identification of shapes at the end of the CNN structure, the GRC model still shows promise because of its parametrizability. After creating a CNN that can identify characteristics of irregular defects from PTT images, we will implement the COMSOL Multiphysics software to extract information on the likelihood of crack initiation and material failure as well. Additionally, this CNN-based classification approach will be extended to the analysis of simulated 3D thermography data to gain more comprehensive information about the internal defects.

References

1. Ankel, V. / Shribak, D. / Chen, W.-Y. / Heifetz, A. (2022). "Classification of computed thermal tomography images with deep learning convolutional neural network," J. Appl. Phys. 131, 244901.

2. Ankel, V. / Shribak, D. / Heifetz, A. (2021). "Defect Classification in Simulated Pulsed Thermal Tomography Images using Deep Learning Convolutional Neural Network," Trans. Am. Nucl. Soc. 125(1), 102-105.

3. Brownlee, J. (2019). "How to identify unstable models when training generative adversarial networks," https://machinelearningmastery.com/practical-guide-to-gan-failure-modes/.

4. Goodfellow, I. / Pouget-Abadie, J. / Mirza, M. / Xu, B. / Warde-Farley, D. / Ozair, S. / Courville, A. / Bengio, Y. (2014). "GenerativeAdversarial Nets," Proceedings of the International Conference on Neural Information Processing Systems (NIPS 2014), 2672– 2680.

5. Heifetz, A. /Ankel, V. / Chen, W.-Y. (2022). "Convolutional Neural Network for Classification of Material Defects in Pulsed Thermal Tomography Images," Bulletin of the American Physical Society.

6. Heifetz, A. / Shribak, D. / Zhang, X. / Saniie, J. / Fisher, Z. L. / Liu, T. / Sun, J. G. / Elmer, T. / Bakhtiari, S. / Cleary, W. (2020). "Thermal tomography 3D imaging of additively manufactured metallic structures,"AIP Adv.10, 105318.

7. Heifetz, A. / Sun, J.G. / Shribak, D. / Liu, T. / Elmer, T.W. / Kozak, P. / Bakhtiari, S. / Khaykovich, B. / Cleary, W. (2019).

"Pulsed Thermal Tomography Nondestructive Evaluation of Additively Manufactured Reactor Structural Materials," Trans. Am. Nucl. Soc. 121(1), 589-591.

8. Heifetz, A. / Zhang, X. / Saniie, J. / Bakhtiari, S. (2022). "Pulsed Infrared Thermography with Unsupervised Machine Learning for Imaging of Microscopic Subsurface Defects in Metals," Bulletin of the American Physical Society.

9. Khairallah, S. A. /Anderson, A. T. / Rubenchik, A. / King, W. E. (2016). "Laser powder-bed fusion additive manufacturing: Physics of complex melt flow and formation mechanisms of pores, spatter, and denudation zones,"Acta Mater.108, 36–45.

10. Muinonen, K. / Nousiainen, T. / Fast, P. / Lumme, K. / Peltoniemi, J. I. (1996). "Light Scattering by Gaussian Random Particles: Ray OpticsApproximation," J. Quant. Spectrosc. Radiat. Transf. 55(5), 577-601.

11. Peltoniemi, J. / Lumme, K. / Muinonen, K. / Irvine, W. M. (1989). "Scattering of light by stochastically rough particles," Appl. Opt. 28(19), 4088-4095.

12. Robb, E. / Chu, W.-S. / Kumar, A. / Huang, J.-B. (2020). "Few-ShotAdaptation of GenerativeAdversarial Networks," arXiv:2010.11943.

13. Sushko, V. / Gall J. / Khoreva, A. (2021) "One-Shot GAN: Learning to Generate Samples from Single Images and Videos," 2021 IEEE/CVF Conference on Computer Vision and Pattern Recognition Workshops (CVPRW), 2596-2600.

14. Zhang, X. / Saniie, J. / Bakhtiari, S. / Heifetz, A. (2022)."Compression of Pulsed Infrared Thermography Data with Unsupervised Learning for Nondestructive Evaluation of Additively Manufactured Metals,"IEEE Access 10, 9094-9107.

15. Zhang, X. / Saniie, J. / Bakhtiari, S. / Heifetz, A. (2022). "Unsupervised Learning for Detection of Defects in Pulsed Infrared Thermography of Metals," 2022 IEEE International Conference on Electro Information Technology (EIT), 330-334.

16. Zhang, X. / Saniie, J. / Cleary, W. / Heifetz, A. (2020). "Quality control of additively manufactured metallic structures with machine learning of thermography images,"JOM 72(12), 4682–4694 (2020).

17. Zhang, X. / Saniie, J. / Heifetz, A. (2020). "Detection of defects in additively manufactured stainless steel 316L with compact infrared camera and machine learning algorithms,"JOM 72(12), 4244–4253.

18. Zhang, X. / Saniie, J. / Heifetz, A. (2020). "Neural learning based blind source separation for detection of material defects in pulsed thermography images,"2020 IEEE International Conference on Electro Information Technology (EIT), 112-116.

19. Zhang, X. / Saniie, J. / Heifetz, A. (2021). "Spatial Temporal Denoised Thermal Source Separation in Images of Compact Pulsed Thermography System for Qualification of Additively Manufactured Metals,"2021 IEEE International Conference on Electro-Information Technology (EIT), 209-214.

20. Zhao, S. / Liu, Z. / Lin, J. / Zhu, J.-Y. / Han, S. (2020). "DifferentiableAugmentation for Data-Efficient GAN Training," 34th Conference on Neural Information Processing Systems (NeurIPS 2020), Vancouver, Canada.

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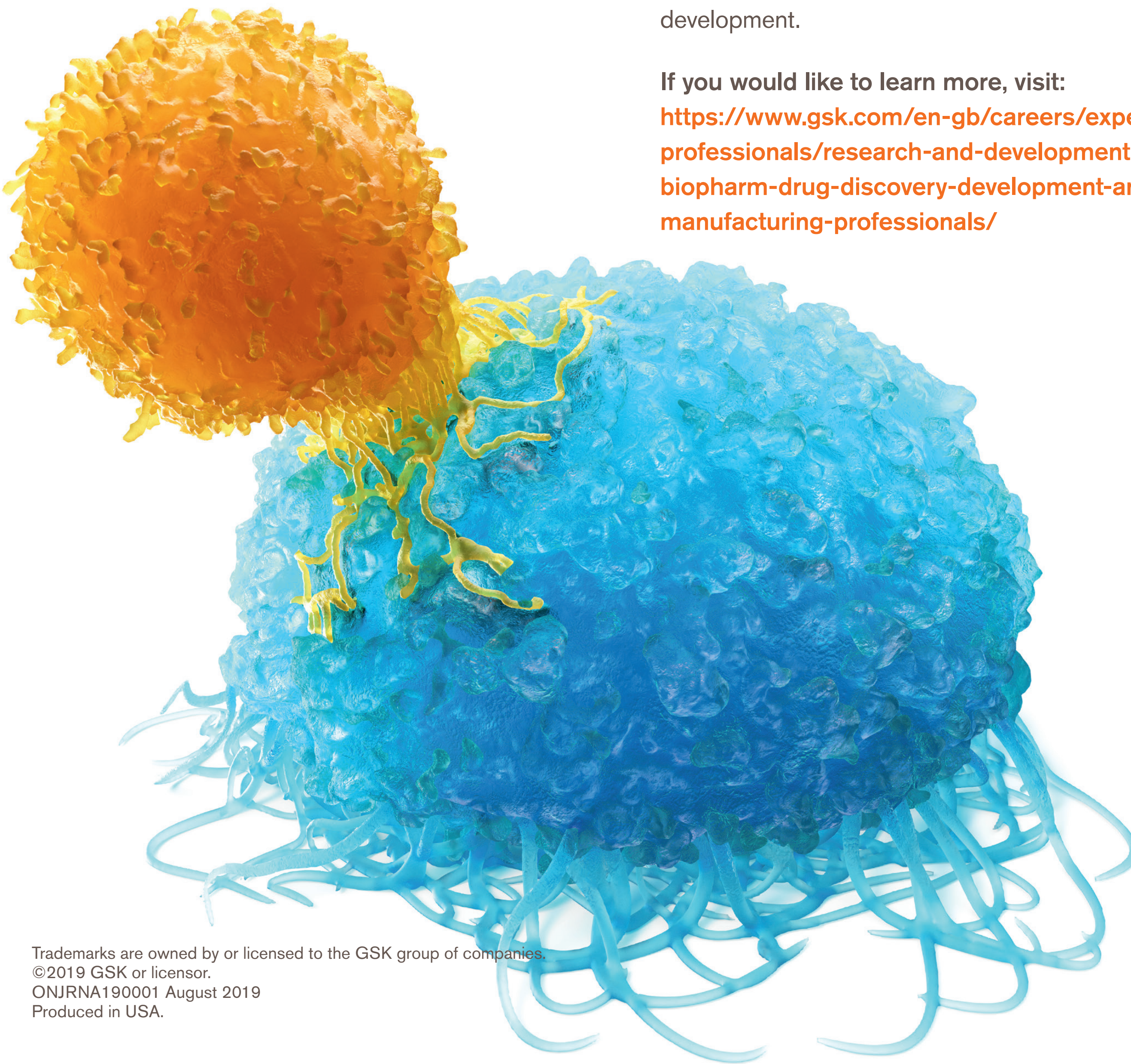

T-cell attacking cancer tumour

Digital Health at the NIH: Trends, Challenges, and Opportunities

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1. Introduction

Over the past decade, digital health has increasingly pushed to the forefront of biomedical research. From clinical artificial intelligence to telehealth and health informatics, stakeholders in the public and private sector tout the digitization of health data and new applications of technology in medicine for increased efficiency, access, and personalization.

Yet digital health also poses new challenges. In a 2019 Nature article, Mathews et al. write about the "cultural clash" between the fast-moving pace of technology companies and the bureaucracy of healthcare regulation.[1] Likewise, the translation and application of software, artificial intelligence, and other technologies—developed first in non-clinical contexts—

in healthcare settings now rubs up against what Mathews et al. describe as "the risk-averse clinical principle of 'first, do no harm.'" The digital health technology development lifecycle, their article argues, disrupts traditional ceilings and checkpoints in the medical device industry such as manufacturing, standards testing, and validation. The longstanding question of public-private partnerships in biomedical research takes on a new meaning in this light.

Given the rapid pace of evolution and growth in the field, it is worth taking a step back to examine the current state of digital health as well as the big picture trends at the National Institutes of Health (NIH). Such efforts can help to inform future investments, strategic plans, and/or frameworks regarding digital health at the NIH. This report aims to tackle these goals through a review of current topics of discussion at federal agencies and independent organizations, as well as through a search of publicly available NIH grant information.

2. What is Digital Health?

The COVID-19 pandemic propelled interest in digital health to a greater degree and wider audience. In response to the U.S. state of public health emergency and the social distancing requirements imposed by it, the Center for Medicare and Medicaid Services temporarily waived certain telehealth policies concerning patient location, the modality of care delivery, and other factors to expand healthcare access.[2] Similarly, the Food and Drug Administration (FDA) exempted digital therapeutics for behavioral health from certain regulatory requirements for the duration of the public health emergency in attempts to

increase efficiency and access to mental health care that complied with social distancing restrictions.[3] Yet even before COVID-19, digital health had been the subject of heated discussion. Attempts to develop, regulate, or define digital health technologies have been frustrated by the ever-shifting and still emerging nature of the field, as well as the multiplicity of its applications—a fact documented by media outlets as well as healthcare organizations.[4]

Various federal agencies have been involved in digital health efforts. The Office of the National Coordinator for Healthcare Information (ONC) has spearheaded efforts on health information technology; ONC has also created a Global Digital Health Partnership initiative, intended to promote best practices for healthcare data internationally.[5] The Agency for Healthcare Research and Quality (AHRQ) Digital Healthcare Research Program has also contributed insight at a systems level of health services, in areas such as clinical decision support, patient-generated health data, telehealth, and health information exchange.[6] At the White House, the Office of Science and Technology Policy's Community Connected Health initiative is exploring the relationships between digital health technology, community engagement, and health equity.[7] The FDA, in addition to its digital health center described later in this report, has also published a Technology Modernization Action Plan and a Data Modernization Action Plan relating to the usage of technology in the agency itself.[8]

Given their overlapping responsibilities and the wide variation in digital health technologies and applications, cross-cutting collaborations between different agencies—both inside and outside of HHS—have also proved crucial, particularly in clarifying the regulatory landscape and implementation process for digital health technologies. For example, health information technologies such as mobile health and wireless have been considered under the jurisdiction of just the FDA, but also the independent Federal Communications Commission (FCC) agency and the Office of the National Coordinator for Health Information Technology.[9] Accordingly, the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) directed the three agencies to collaborate on a "Health IT Regulatory Framework" working group.[10] The resulting report is displayed on FDA's Digital Health Center of Excellence website.[11]

The NIH has also undertaken various digital health efforts. For example, the NIH Strategic Plan for Data Science outlines how the Health Level Seven (HL7) Fast Healthcare Interoperability Resources (FHIR) standard are being integrated into existing initiatives in the National Library of Medicine (NLM), the National Human Genome Research Institute (NHGRI), and the National Institute of Diabetes and Digestive and Kidney Diseases

(NIDDK).[12] Different institutes and centers such as the National Heart, Lung, and Blood Institute (NHLBI), the National Institute for Biomedical Imaging and Bioengineering (NIBIB), and the National Institute on Aging (NIA) have their own digital health programs targeted towards their areas of focus.[13-15] In recent years, the NIH has also hosted a number of workshops and webinars on digital health data and interventions.[16-18] Moreover, notices of special interest, such as a 2022 Notice of Special Interest (NOSI) focused on validation of digital health and artificial intelligence tools, have spurred trans-institute discussion on the subject.[19] The Smart and Connected Health Initiative, an interagency funding opportunity between the NIH and the National Science Foundation (NSF), has also helped to catalyze collaboration across a wide range of internal stakeholders on digital health.[20] Yet to date, a comprehensive, external-facing NIH digital health strategy has not yet been published.

3.1 Digital Health Definitions

With regards to public-facing information, the FDA Digital Health Center of Excellence (DHCoE), established in September 2020, had previously published digital criteria on their website that outlines ten separate categories: Software as a Medical Device (SaMD), Advanced Analytics, Artificial Intelligence, Cloud, Cybersecurity, Interoperability, Medical Device Data System (MDDS), Mobile Medical App (MMA), Wireless, and Novel Digital Health.[21] Although the DHCoE has since moved away from these criteria to a more generalized description[22], their 2018 criteria still provide context into categories of digital health that have been identified and are currently being studied.

In June 2022, the National Academy of Medicine (NAM) published a discussion paper titled "The Promise of Digital Health: Then, Now, and the Future." The report uses two different axes to categorize digital health: its applications, and its infrastructure. Their figure on digital health applications, details 12 broad areas of healthcare: health information, knowledge generation, knowledge integrators, personal health devices, telemedicine, diagnostics, imaging, pharmaceuticals, implantable devices, surgical, personalized therapeutics, and geospatial & environmental. A second diagram lays out 12 infrastructure requirements: individual access and

engagement, equity and ethics, privacy and identifier protocols, cybersecurity, data quality and reliability, data storage and stewardship, interoperability, virtual health data trusts governance, data science, AI/ML, and workforce.[23]

In another vein, the Healthcare Information and Management Systems Society (HIMSS) published a white paper on digital health frameworks in early 2020.[24] Their scoping analysis of existing digital health definitions yields three broad themes: one category "defined in terms of type and use of digital technologies," another "focused on improvement of healthcare delivery," and lastly one that portrayed "digital health as a strategy for health system transformation."[25] The report also identifies four main themes of Governance and Leadership, Data Infrastructure and Interoperability, Analytics, and Person-Enabled Healthcare.

These varied attempts at defining digital health exemplify the difficulties of said task. While the FDA focused on providing examples of products for regulation, the NAM paper concerned itself more with the broader implications of digital health across all stakeholders, in line with its mission as an independent advisory organization. Conversely, the HIMSS white paper takes a generalized, sweeping approach that brands digital health as information technology—a much narrower view than the other groups. The contrast between the FDA, HIMSS, and NAM approaches reveals how the definition of digital health depends, in part, on the goal of the group in question. This conclusion, then, raises several questions: what are the impacts of defining digital health in any given context? What would such a task look like at the NIH?

3. Methods and Approaches

For the purposes of this report, which aims to survey digital health at the NIH, digital health was defined according to the FDA criteria from 2018. These terms, despite being several years old, still reflect the broad areas of interest in which the Digital Health Center of Excellence has invested and provide the most comprehensive set of keywords to use in a manual search. The report also examines three Research, Condition, and Disease Category (RCDC) terms from NIH related to digital health to provide further context across the two agencies' terminologies.

The NIH Research Portfolio Online Reporting Tools (RePORT) website contains a publicly electronic tool, RePORTER, that allows users to search a repository of NIH-funded research projects and access publications and patents resulting from this funding.[26] This report utilizes the RePORT database to examine big-picture trends in NIH-funded digital health research. It focuses specifically on extramurally funded and investigator initiated research projects under the R01 and SBIR/STTR activity codes from the last ten fiscal years, FY 2013- 2022. Furthermore, the search was limited to Type 1 (New) projects. Although these search criteria helped limit the project to a manageable scope, it also limited the data collected to a portion of all projects in the NIH and NHLBI portfolios relating to digital health. Further, more in-depth studies could supplement this limitation.

RePORTER was first used to filter search results by RCDC category. A manual search for more detailed digital health keywords was conducted using the aforementioned filters on activity code, award type, and fiscal year. Searching by exact keywords in advanced search further reduced the total number of results. The number of projects by category thus includes some duplicate search results due to overlap between different criteria (for example, "cloud" and "wireless").

Figures 1 through 5, on projects in each RCDC category, were created directly from data exported from RePORTER, which was only available through FY 2021 at the time. For the "ML/AI" and "Telehealth categories," data was drawn from the years of creation to present: 2019 and 2021, respectively. When visualizing projects awarded over time for the manual search in Figures 10 and 12, FY 2022 was excluded from the graphs as RePORTER was still updating and did not yet reflect the total number of projects, leading to a dip in numbers across the board.

4. RCDC Terms: Broad Trends at NIH

The broad definitions of digital health make it challenging to quantify the scope of research that NIH funds on it across different agencies. Within the NIH, a portfolio analysis of extramural grants at the National Heart, Lung, and Blood Institute (NHLBI) from FY 2008- 2017 found that areas of opportunity for increased data science funding include precision medicine, clinical informatics, clinical decision support, imaging informatics, and computational tools. Digital health, related to data science in some aspects, is a rapidly evolving target; moreover, the COVID-19 pandemic's effects on digital health during the past three years must also be taken into consideration. This report aims to supplement previous analyses with a big-picture examination of recent trends in different forms of digital health technology.

Table 1 summarizes the information obtained from the manual search. Figure 1 below shows the trend in projects awarded per year over time from FY 2013 to 2021 (FY 2022 was unavailable for this particular function in RePORTER). Figures 2–4 also visualize the number of projects funded in each RCDC category across the twelve Institutes and Centers (I/C) with the greatest number of total projects over the time period—with NHLBI highlighted.

Table 1. RCDC Manual Search, FY 2013-2022

RCDC Category	R01	SBIR/ STTR	All Projects
Networking and Information Technology Research and Development	1182	711	3655
Machine Learning and Artificial Intelligence (FY 2019 – present)	592	192	1606
Telehealth (FY 2019 – present)	72	34	234

4.1 Networking and Information Technology Research and Development (NITRD)

Much of the digital health research funded by NIH fall under the older spending category of "NITRD," referring to the Networking and Information Technology Research and Development program. NITRD had served as the primary source of federal research and development funding for advanced informational technologies for several decades. Thus, the RCDC term provides some context on NIH funding of digital health—one of NITRD's coordination areas— especially in a historical context. As seen in Figure 1, the number of projects awarded in NITRD as a whole has increased significantly since 2013. Digital health comprises only a portion of these total projects; unfortunately, the functionality of RePORTER does not allow RCDC subcategories to be separated. NHLBI has been one of the five agencies that funded the most projects in this category in the last ten years.

4.2 Machine Learning and Artificial Intelligence

The "Machine Learning and Artificial Intelligence" (ML/AI) spending category, despite only being created a few years ago, has already amassed a number of search results. Similar to the NITRD category, it is not clear whether all of these projects fall under the umbrella of digital health; however, the steep upward trend in projects funded per fiscal year (Figure 1) helps illustrate the growing interest.

4.3 Telehealth

Telehealth, which gained more widespread attention during the COVID-19 pandemic, is the newest of the three categories, created in FY 2021. For both ML/AI and telehealth, the institutes with the greatest numbers of total projects, in decreasing order, were the National Institute of Mental Health (NIMH), NIA, National Cancer Institute (NCI), and NHLBI. Given the prominent and continuing usage of telehealth for mental health care in particularly, this data is not surprising. It also helps to illustrate the potential of digital health for care management in the fast-growing aging population in the U.S., in cancer diagnostics and treatment, and in the tracking and management of heart, lung, blood, and sleep conditions.

Although looking at RCDC terms provides a starting point in capturing digital health trends, they do not capture all recent developments in digital health. NITRD's current efforts, in renaming their Health Information Technology Research and Development Interagency Working Group (IWG) to the Digital Health Research and Development IWG, reflect attempts to keep up with the rapidly expanding forms of technology that digital health encompasses.[27] However, such efforts have likely not yet percolated down into the classification of NIH-funded grants in RePORTER under the RCDC term. As the field matures, classification of digital health research projects will likely continue to adapt and evolve across different agencies and groups.

5. Adopting FDA Digital Health Terms

A manual search in RePORTER using some of the aforementioned FDA terms revealed—even in the slice of the overall portfolio collected with the project limitations—a wide range of digital-health-related projects being conducted across the NIH. An upward trend in grant funding over the past 10 years was also observed in almost every category. A summary of the data obtained is presented below. Figure 7 displays a breakdown of overall distribution of project numbers across the

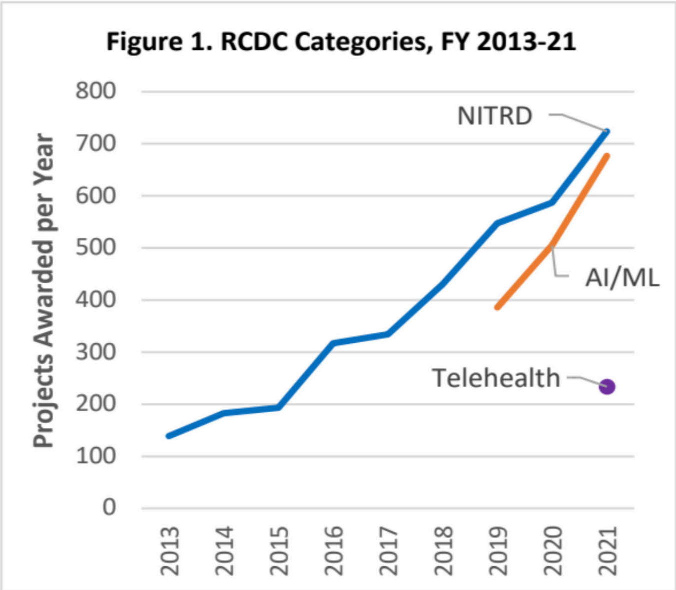


Figure 2. "NITRD" by I/C, FY 2013-21

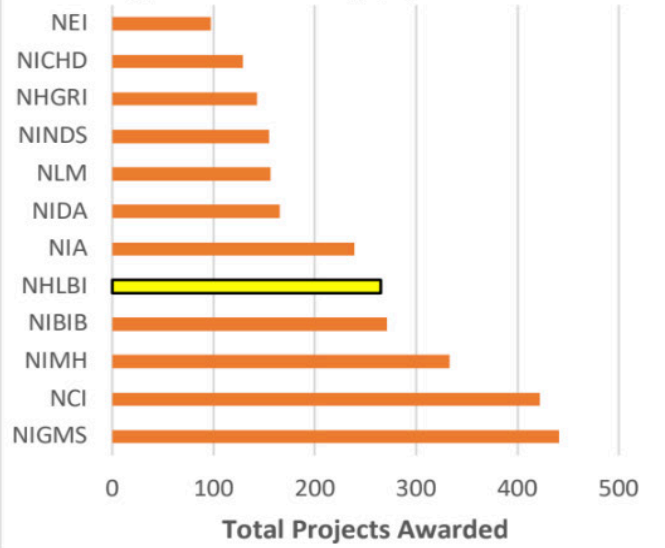


Figure 3. "ML/AI" by I/C, FY 2019-21

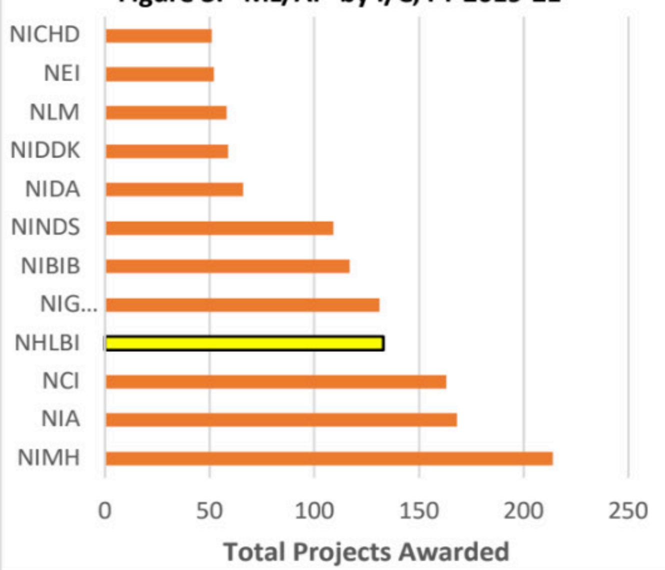
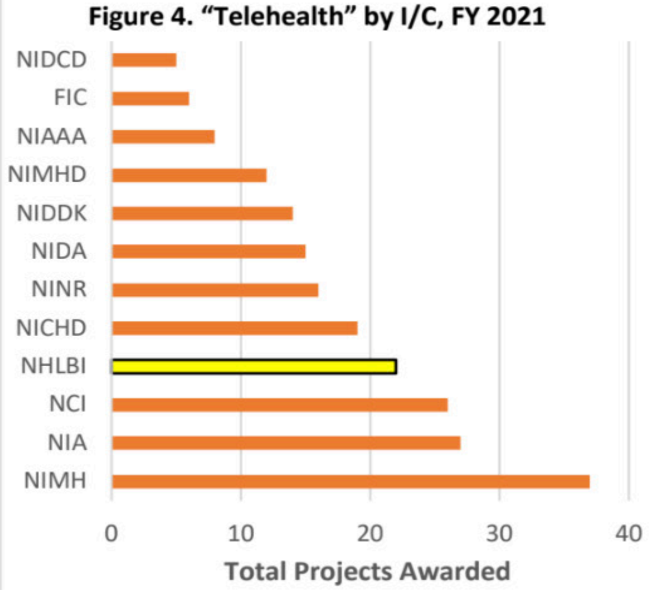


Figure 4. "Telehealth" by I/C, FY 2021



different keywords, and Figure 8 displays trends over time for the 5 categories that had more than 10 search results. 9 of the 10 categories from the 2018 FDA criteria are surveyed below.

5.1 Software as a Medical Device (SaMD)

Drawing on work from the independent International Medical Devices Forum, the DHCoE defines SaMD as "software intended to be used for one or more medical purposes" independent of hardware.[28] This standalone quality distinguishes SaMD from software that is part of a medical device or used in manufacturing/maintenance of one.[29] In RePORTER, only 5 search results came up for the terms "software as a medical device" or "SaMD"—a reflection on how the NIH does not currently track research on SaMD.

5.2 Advanced Analytics

The DHCoE criteria include statistical modeling and big data analysis in this category. The need for data analytics reflects the growing quantities of healthcare data from sources such as Electronic Health Records or advanced imaging technologies. According to the DHCoE, analytics can be used to "discover new patterns in data" beyond human capability and as a result, supply new "insights, predictions, and recommendations."[30] 36 projects in RePORTER contained the "advanced analytics" keyword in their abstract.

5.3 Artificial Intelligence

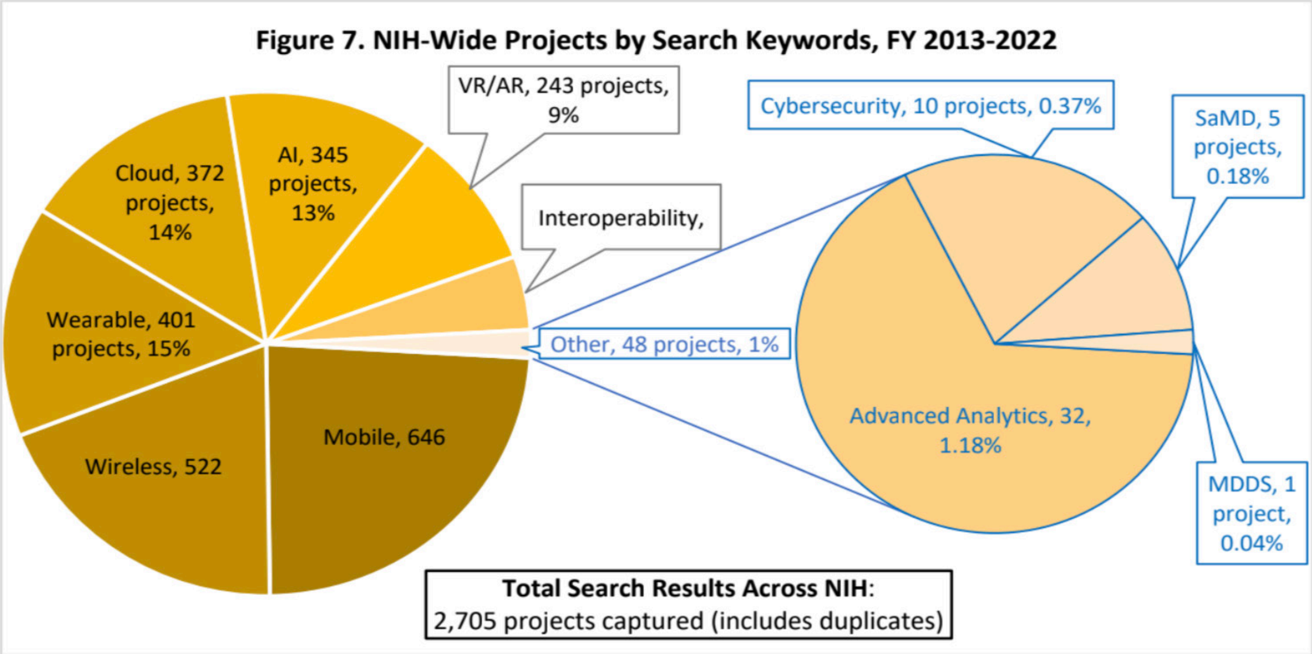
Much has been written on AI in healthcare outside the scope of this report, yet an important point to reiterate is the computational power that poses both new opportunities and challenges for advanced analytics, AI, and machine learning in digital health. As applications of AI and ML in healthcare continue to expand, new practices have been touted, such as continuous learning systems that allow for incremental learning and training in models. The manual search found 332 projects that contain "artificial intelligence" in their title or abstract from FY 2013-2022. This is a noticeably smaller portion of search results than the earlier results for the ML/AI RCDC category, especially given the fact that the RCDC term was only created in 2019. This discrepancy may, unfortunately, be a function of the search functions used in RePORTER.

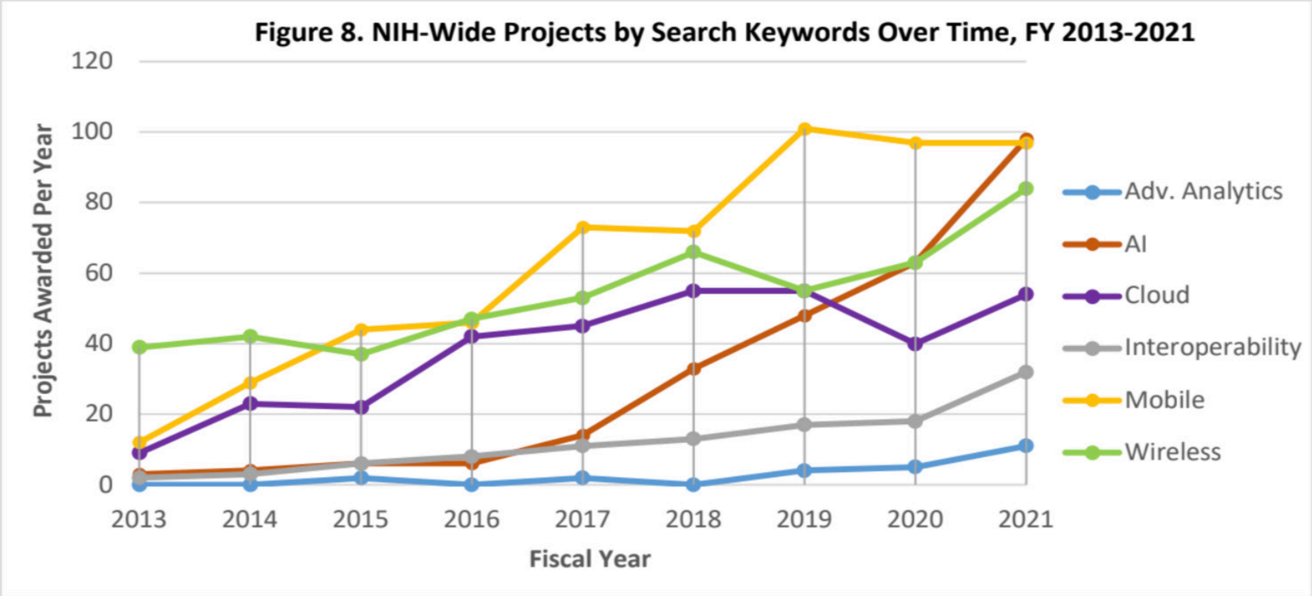
5.4 Cloud

The DHCoE defines the cloud as "internet based computing that provides computer processing resources and data on demand."[31] Its goals of connectivity and efficient storage connects cloud technology with digital health categories such as interoperability and wireless health. The search returned 367 projects over the past 10 years.

5.5 Cybersecurity

With increased data storage in electronic forms such as the cloud, sensors, or wireless devices, cybersecurity proves to be another cross-cutting concern in digital health. The FDA Center for Devices and Radiological Health—which houses the DHCoE—has provided draft guidances, playbooks, and a fact sheet on their role in on bolstering cybersecurity in medical devices.[32] However, the NIH's role in these efforts may require further consideration (see the section below on ethical and social implications) 10 projects turned up in a search for "cybersecurity."





5.6 Interoperability

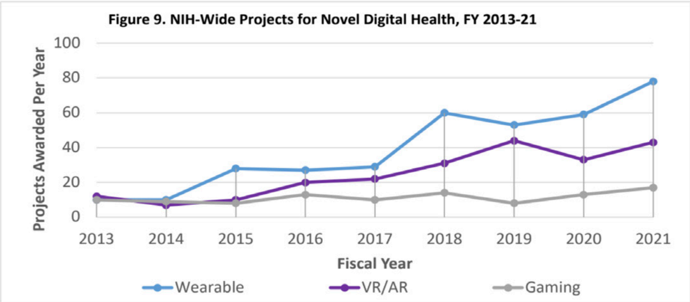
Interoperability stems from the Internet of Things concept, which imagines the Internet as a resource that facilitates connection among, and the exchange of data between, not just computers and smartphones—so-called "traditional computing devices"—but all electronic devices such as sensors and appliances.[33] Particularly in medical devices, interoperability provides both opportunities to increase efficiency among researchers, providers, and patients alike. However, as with cloud, it poses increased risks of cybersecurity, and the FDA has been actively involved in defining, shaping, and regulating this space.[34] 122 projects were found with this keyword, summarized in the chart above.

5.7 Medical Data Device System (MDDS)

A medical data device system is by these criteria as hardware or software for the storage and conversion of healthcare data for later usage; it forms one component of a larger system.[35] Only 1 search result was found for this keyword.

5.8 Mobile Medical App (MMA)

Mobile health, or mHealth, has become increasingly relevant alongside the expansion of telehealth during the COVID-19 pandemic. mHealth and audio-only telemedicine have been touted by some for its potential to further increase access to remote care, as a greater percentage of the U.S. population owns a smartphone compared to a personal computer.[36] Yet others point out aspects of the digital divide in underserved populations that persist with telehealth.[37] RePORTER returned 618 projects with a "mobile health" OR "mHealth" OR "mobile application" OR "mobile medical application" advanced search. However, the wide-ranging terminology used to describe mHealth may obscure some relevant search results.



5.9 Wireless

As previously mentioned, wireless health technologies cut across the regulatory duties of the FDA, ONC, and FCC. With wireless devices, one particular benefit is patient mobility and a provider's ability to gather and monitor data remotely. Such opportunities have led to growth in the area of "real world evidence," especially after the passing of the 21st Century Cures Act in 2016, which led the FDA to release guidance and frameworks in this area as well.[38] 514 projects were found with this search keyword, as summarized above.

6. A Comment on Novel Digital Health

At the end of their 2018 criteria, the Digital Health Center of Excellence tacks this category on as a "catch-all." Despite the catch-all definition, "novel" digital health technologies share some common traits: they tend to be emerging; situated in fields that are rapidly evolving or not yet well defined; and rapidly growing in terms of research interest. Thus, the concept of "novel digital health" exacerbates many of the challenges with classifying digital health in general. The DHCoE had defined novel digital health as "new, unfamiliar, or unseen digital health technology never submitted, cleared, or approved by FDA" and gave three examples: virtual reality, gaming, and Medical Body Area Network (MBAN) devices.[39] These examples of "novel digital health" technologies, along with other search terms sourced through research and conversations, are summarized in Figure 9, and several are surveyed below.

6.1 Medical Body Area Networks (MBANs)

Researchers have defined Body Area Networks (BANs) as a collection of wireless sensors designed to monitor the human body and surrounding environment.[40,41] Interest in healthcare applications of BANs, specifically, emerges from their lightweight, low power, and wearable nature. In 2012, the FCC published guidelines on Medical Body Area Network bandwidths to ensure patient protection during technology usage.[42] Similar to wireless technology, MBAN technology has been touted for its potential to increase real-world evidence gathering and remote monitoring capabilities. However, as mentioned with other types of devices, cybersecurity presents a large concern. Although no search results in RePORTER come up for "medical body area network" or "embedded device," 4 projects contained "implanted wireless" in their abstracts or titles.

6.2 Wearable Devices

Wearable devices hold the potential to monitor a wide range of physiological symptoms. While commercialized technologies such as smart watches are already being used to track heart rate, sleep, and other common markers, digital health also encompasses the various types of biosensors that are being developed to monitor more specialized substance levels and biomarkers.[43] 389 projects were found in RePORTER for the search terms "wearable" OR "wearable device" OR "wearable devices" in the past 10 years, with growth in numbers over time.

6.3 Digital Twins

Digital twin technology, which has been applied in the technology industry, refers to the virtual representation of a physical object. This nascent area, which does not yet have any search results in RePORTER, may present opportunities in healthcare and precision medicine in the future; however, the creation of human digital twin still poses challenges of the kind addressed in the section of ethical and social implications below.[44]

7. Ethical and Social Implications

Digital health has created important shifts in the dynamics of healthcare and biomedical research for patients, providers, regulators, researchers, and developers alike. Given the rapid expansion and increasing relevance of the field, it is beneficial to take a closer look at these implications and their ultimate impact on digital medicine users.[45] The NIH published a funding opportunity announcement in 2021 to address Ethical, Legal and Social Implications (ELSI) Research, which mentioned concerns around data use, privacy, and protection as well as community decision-making and the inclusion of traditionally underserved populations in biomedical research.[46] To date, ELSI efforts at the NIH has been focused on genomics and genomic data science, including the ELSI Research Program at the NHGRI[47]; however, similar approaches and values may prove useful in examining digital health. Digital health has been implicated in the growing interest around real-world evidence (RWE) and decentralized clinical trials. In addition to their RWE Program, the FDA has also published two articles on the subject. The 2021 FDA Draft Guidance on Digital Health Technologies for Remote Data Acquisition in Clinical Investigations makes recommendations on digital health technology selection, validation, and risk management.[48] RWE and decentralized clinical trials have also been cited as opportunities to increase equitable access in clinical trials for underserved populations and as components of a patient-centered approach to clinical research.[49]

Data privacy and patient protection are other often-cited areas where attention is needed, especially with the expansion of RWE and remote data collection. Digital health expands the breadth and scope of healthcare data beyond the healthcare settings covered by Health Insurance Portability and Accountability Act (HIPAA) privacy protections, such as third-party consumer apps and devices.[50] With wearable devices and apps, information about data ownership is currently buried in lengthy documents. Data governance has thus been a topic of interest for ELSI experts.[51] For artificial intelligence and machine learning, decentralized federated learning approaches may present one avenue for addressing privacy concerns, and further research on this topic may be of interest.[52]

Cybersecurity presents a related privacy concern. The FDA has mentioned collaborations with the Department of Homeland Security (DHS) and external stakeholders on the subject.[53] Additionally, the Defense Advanced Research Projects

Agency (DARPA) has a Guaranteeing AI Robustness Against Deception (GARD) program that aims to promote a theoretical understanding of vulnerabilities in machine learning models and to strengthen systems against potential adversarial AI attacks.[54] The NIH does not currently have a program similar to DARPA's. However, given the increasing complexity of AI and ML models in healthcare—and the recent creation of the Advanced Research Projects Agency for Health (ARPA-H) initiative modelled off of DARPA[55]—establishing such an initiative to bolster cybersecurity efforts may be a consideration for NIH. Given the small number of search results on cybersecurity in RePORTER (possibly due to the search limitations), future biomedical research may be needed in this area.

This section has laid out some of the key issues raised by digital health experts with regards to ethical and social implications in the field. Although a detailed examination of any of these issues is beyond the scope of this report, the information above can serve as a starting point for future efforts and discussions.

8. Discussion

This report surveyed broad trends in digital health funding using publicly available NIH data, with many limitations. Although only two grant activity codes were examined here to make the scope of the report more manageable, many projects in other R01 Equivalent categories such as U01, R21, etc. grants and career development categories were missed. RePORTER also does not capture certain mechanisms such as supplements or other transactions (OTs) that may have been used to fund digital health related projects. With regards to COVID-19, projects in the Rapid Acceleration of Diagnostics (RADx) initiative, for example, are a significant oversight in the report given the constraints in its methodology.

Another issue is that some digital health technologies cut across several of these categories— such as telehealth, which could be considered a wireless technology by the criteria above but which also shares challenges with mobile health as well as raising new issues of its own. As digital health technology continues to grow and evolve, further efforts to study and monitor the digital health portfolio across and within institutes and centers in NIH will prove worthwhile.

With regards to NHLBI and especially blood disease areas, consideration could be given to the distribution of projects across different types of digital health technologies among heart, lung, and blood diseases to identify future funding opportunities. Areas such as wireless, wearable, advanced analytics, and AI were especially prominent in the search results, but the emergence of new technologies and so-called "novel digital health" may be a gap to investigate in the current portfolio. Projects administered by other agencies may also be relevant for treating symptoms of diseases. For example, research mobile health and gaming interventions from the National Institute of Nursing Research (NINR) and the National Institute on Minority Health and Health Disparities (NIMHD), respectively, have addressed stress and pain management for sickle cell patients.[56,57]

To compare the digital health typology between different federal agencies, Table 3 maps the similarities between FDA and NIH terminology. At the federal level, the FDA has had the largest amount of public-facing engagement with digital health regulation, with its draft guidances, webinars, and digital health center. Part of this has been motivated by requirements in policies from Congress, such as the 21st Century Cures Act and the aforementioned FDA Safety and Innovation Act. However, how could the NIH, as a steward of scientific research standards, continue to contribute to this developing area of research? Moreover, as digital health at the NIH continues to develop, how can various programs, working groups, and initiatives across different institutes and centers

Table 3. Inter-Agency Comparison of Digital Health Terminology Over Time

FDA DHCoE Criteria (last updated Mar. 2018)	DHCoE Definition Page (last updated Sep. 2020)	NIH RCDC Terms
Artificial Intelligence	AI/ML in Software as a Medical Device	Machine Learning and Artificial Intelligence (FY 2019 – present)
Advanced Analytics	Health Information Technology	Data Science (FY 2019 – present)
Cloud		Networking and Information Technology Research and Development (NITRD)
Cybersecurity		
Interoperability		
Software as a Medical Device (SaMD)	Software as a Medical Device (SaMD)	
Medical Data Device Systems (MDDS)	Medical Data Device Systems (MDDS)	
Mobile Medical App (MMA)	Mobile Health (mHealth)	
Novel Digital Health	Wearable Devices	
Wireless		
	Telehealth and telemedicine	Telehealth (FY 2021 – present)

integrate the ethical, legal, and social implications of digital health into their work? Such questions should be considered in future discussions on digital health across the NIH.

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References

1 Mathews SC, McShea MJ, Hanley CL, Ravitz A, Labrique AB, Cohen AB. Digital health: a path to validation. NPJ Digital Med. 2019;2:38. doi: 10.1038/s41746-019-0111-3.

2 Health Resources and Services Administration (US) [Internet]. Medicare and Medicaid Policies. Rockville (MD): Health Resources and Services Administration; [modified 2021 Mar 9; cited 2022 Aug 17]. Available from: https://telehealth.hhs.gov/providers/policy-changes-during-the-covid-19-public-health-emergency.

3 Food and Drug Administration (US) [Internet]. Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the COVID-19 Public Health Emergency. Silver Spring (MD): Food and Drug Administration; [modified 2020 Apr 14; cited 2022 Aug 17]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement policy-digital-health-devices-treating-psychiatric-disorders-during-coronavirus-disease.

4 Muoio D. What exactly is a 'digital health IPO'? MobiHealthNews. 2019 Jul 25 [cited 2022 Aug 17]. Available from: https://www.mobihealthnews.com/news/north-america/what-exactly-digital-health-ipo.

5 Office of the National Coordinator for Health Information Technology (US) [Internet]. The Global Digital Health Partnership. Washington, DC (DC): Office of the National Coordinator for Health Information Technology; [cited 2022 Aug 17]. Available from: https://www.healthit.gov/topic/global-digital-health-partnership.

6 Digital Healthcare Research: Agency for Healthcare Research and Quality (US) [Internet]. Current Priorities. Rockville (MD): Agency for Healthcare Research and Quality; [cited 2022 Aug 17]. Available from: https://digital.ahrq.gov/program overview/directors-corner#current.

7 Wolinetz C, Ward J. Community Connected Health: We Need to Hear From You. 2022 Mar 16 [cited 2022 Aug 17]. In: Office of Science and Technology Blog [Internet]. Washington, DC (DC): The White House. Available from: https://www.whitehouse.gov/ostp/news-updates/2022/03/16/community-connected-health-we-need-to-hear-from-you/.

8 Food and Drug Administration (US) [Internet]. Modernization in Action 2022. Silver Spring (MD): Food and Drug Administration; [modified 2022 Mar 30; cited 2022 Aug 17]. Available from: https://www.fda.gov/about fda/reports/modernization-action-2022.

9 Gunawardhana SP, Delacourt S, Rein W. An Introduction To FDA And FCC Regulations Impacting mHealth. Med Device Online. 2015 Aug 24 [cited 2022 Aug 17]. Available from: https://www.meddeviceonline.com/doc/an-introduction-to-fda-and-fcc regulations-impacting-mhealth-0001.

10 Food and Drug Administration (US) [Internet]. Food and Drug Administration Safety and Innovation Act (FDASIA). Silver Spring (MD): Food and Drug Administration; [modified 2018 Mar 28; cited 2022 Aug 17]. Available from: https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-administration-safety-and innovation-act-fdasia.

11 Center for Devices and Radiological Health (US) [Internet]. FDASIA Health IT Report. Silver Spring (MD): Food and Drug Administration; [modified 2020 Nov 18; cited 2022 Aug 17]. Available from: https://www.fda.gov/about-fda/cdrh reports/fdasia-health-it-report.

12 Office of Data Science and Strategy (US) [Internet]. NIH Fast Healthcare Interoperability Resources Initiatives. Bethesda (MD): National Institutes of Health; [reviewed 2021 Apr 9; cited 2022 Aug 17]. Available from: https://datascience.nih.gov/fhir initiatives.

13 National Heart, Lung, and Blood Institute (US) [Internet]. Digital Health and Informatics Technologies Program. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 17]. Available from: https://www.nhlbi.nih.gov/node/92109.

14 National Institute of Biomedical Imaging and Bioengineering (US) [Internet]. Digital Health – Mobile Health and Telehealth. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 17]. Available from: https://www.nibib.nih.gov/research funding/digital-health.

15 National Institute on Aging (US) [Internet]. Digital Health and Sensing Technologies. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 17]. Available from: https://www.nia.nih.gov/research/sbir/nia-small-business-showcase/digital-health sensing-technologies.

16 National Institutes of Health: All of Us Research Program (US) [Internet]. Digital Health Data in a Million-Person Precision Medicine Initiative Cohort. Bethesda (MD): National Institutes of Health; [reviewed 2016 Nov 16; cited 2022 Aug 17]. Available from: https://www.nih.gov/allofus-research-program/digital-health-data-million-person-precision-medicine-initiative-cohort.

17 National Heart, Lung, and Blood Institute (US) [Internet]. Harnessing Novel Data Sources and Technologies for the Study of Social Determinants of Health in Heart, Lung, Blood, and Sleep disorders. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 17]. Available from: https://www.nhlbi.nih.gov/events/2020/harnessing-novel-data-sources-and-technologies-study social-determinants-health-heart.

18 National Institute on Drug Abuse (US) [Internet]. NIH Digital Health Interventions Workshop. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 17]. Available from: https://nida.nih.gov/news-events/meetings-events/2022/07/nih digital-health-interventions-workshop.

19 Grants and Funding: Office of Extramural Research (US) [Internet]. NOT-CA-22-037 Notice of Special Interest (NOSI): Validation of Digital Health and Artificial Intelligence Tools for Improved Assessment in Epidemiological, Clinical, and Intervention Research. Bethesda (MD): National Institutes of Health; [released 2022 Jan 28; cited 2022 Aug 17]. Available from: https://grants.nih.gov/grants/guide/notice-files/NOT-CA-22-037.html.

20 Grants and Funding: Office of Extramural Research (US) [Internet]. NOT-OD-21-011 Notice of NIH Participation in Smart Health and Biomedical Research in the Era of Artificial Intelligence and Advanced Data Science. Bethesda (MD): National Institutes of Health; [released 2020 Nov 24; cited 2022 Aug 17]. Available from: https://grants.nih.gov/grants/guide/notice files/NOT-OD-21-011.html.

21 Digital Health Center of Excellence (US) [Internet]. Digital Health Criteria. Silver Spring (MD): Food and Drug Administration; [modified 2018 Mar 23; cited 2022 Aug 17]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/digital-health-criteria.

22 Digital Health Center of Excellence (US) [Internet]. What is Digital Health? Silver Spring (MD): Food and Drug Administration; [modified 2020 Sep 22; cited 2022 Aug 17]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/what-digital-health.

23 Abernethy A, Adams L, Barrett M, Bechtel C, Brennan P, Butte A, et al. The Promise of Digital Health: Then, Now, and the Future. National Academy of Medicine Perspectives. 2022. doi: 10.31478/202206e. Available from: https://nam.edu/the promise-of-digital-health-then-now-and-the-future/.

24 Snowdon A. HIMSS Defines Digital Health for the Global Healthcare Industry. 2020 Mar 2 [cited 2022 Aug 18]. In: HIMSS News [Internet]. Chicago (IL): Healthcare Information and Management Systems Society, Inc. Available from: https://www.himss.org/news/himss-defines-digital-health-global-healthcare-industry.

25 Snowdon A. Digital Health: A Framework For Healthcare Transformation. Healthcare Information and Management Systems Society, Inc. 2020. Available from: https://www.himss.org/news/himss-defines-digital-health-global-healthcare-industry.

26 Research Portfolio Online Reporting Tools [Internet]. Frequently Asked Questions. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 18]. Available from: https://report.nih.gov/faqs.

27 The Digital Health R&D (DHRD) Interagency Working Group. In: News [Internet]. Washington, DC (DC): Networking and Information Technology Research and Development (NITRD) Program; [modified 2022 May 2; cited 2022 Aug 18]. Available from: https://www.nitrd.gov/the-digital-health-rd-dhrd-interagency-working-group/.

28 CDRH International Programs (US) [Internet]. International Medical Device Regulators Forum (IMDRF). Silver Spring (MD): Food and Drug Administration; [modified 2019 Aug 27; cited 2022 Aug 18]. Available from: https://www.fda.gov/medical devices/cdrh-international-programs/international-medical-device-regulators-forum-imdrf.

29 Digital Health Center of Excellence (US) [Internet] Software as a Medical Device (SaMD). Silver Spring (MD): Food and Drug Administration; [modified 2018 Dec 4; cited 2022 Aug 18]. Available from: https://www.fda.gov/medical-devices/digital-health center-excellence/software-medical-device-samd.

30 Digital Health Center of Excellence (US) [Internet]. Digital Health Criteria. Silver Spring (MD): Food and Drug Administration; [modified 2018 Mar 23; cited 2022 Aug 17]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/digital-health-criteria.

31 Digital Health Center of Excellence (US) [Internet]. Digital Health Criteria. Silver Spring (MD): Food and Drug Administration; [modified 2018 Mar 23; cited 2022 Aug 17]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/digital-health-criteria.

32 Digital Health Center of Excellence (US) [Internet]. Cybersecurity. Silver Spring (MD): Food and Drug Administration; [modified 2022 Jun 2; cited 2022 Aug 18]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/cybersecurity.

33 Fruhlinger J. What is IoT? The internet of things explained. Network World. 2022 Aug 7 [cited 2022 Aug 18]. Available from: https://www.networkworld.com/article/3207535/what-is-iot-the-internet-of-things-explained.html.

34 Digital Health Center of Excellence (US) [Internet]. Medical Device Interoperability. Silver Spring (MD): Food and Drug Administration; [modified 2022 Apr 5; cited 2022 Aug 18]. Available from: https://www.fda.gov/medical-devices/digital-health center-excellence/medical-device-interoperability.

35 Digital Health Center of Excellence (US) [Internet]. Digital Health Criteria. Silver Spring (MD): Food and Drug Administration; [modified 2018 Mar 23; cited 2022 Aug 17]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/digital-health-criteria.

36 Shah S, Alkureishi L, Lee WW. Seizing The Moment For Telehealth Policy And Equity. Health Affairs Forefront. 2021 Sep 13 [cited 2022 Aug 18]. doi: 10.1377/forefront.20210909.961330. Available from: https://www.healthaffairs.org/do/10.1377/forefront.20210909.961330/full/.

37 Weiner S. What happens to telemedicine after COVID-19? 2021 Oct 21 [cited 2022 Aug 18]. In: AAMC News [Internet]. Washington, DC (DC): Association of American Medical Colleges. Available from: https://www.aamc.org/news-insights/what happens-telemedicine-after-covid-19.

38 Food and Drug Administration (US) [Internet]. Real-World Evidence. Silver Spring (MD): Food and Drug Administration; [modified 2022 May 20; cited 2022 Aug 18]. Available from: https://www.fda.gov/science-research/science-and-research special-topics/real-world-evidence.

39 Digital Health Center of Excellence (US) [Internet]. Digital Health Criteria. Silver Spring (MD): Food and Drug Administration; [modified 2018 Mar 23; cited 2022 Aug 17]. Available from: https://www.fda.gov/medical-devices/digital-health-center excellence/digital-health-criteria.

40 Chen M, Gonzalez S, Vasilakos A, Cao H, Leung VC. Body Area Networks: A Survey. Mob Netw Appl. 2011;16(2):171–93. doi: 10.1007/s11036-010-0260-8.

41 Ullah S, Higgins H, Braem B, Latre B, Blondia C, Moerman I, et al. A Comprehensive Survey of Wireless Body Area Networks. J Med Syst. 2012;36:1065–1094. doi: 10.1007/s10916-010-9571-3.

42 Federal Communications Commission (US). Medical Area Body Network. Fed Regist. 2012;77:55715–55735.

43 Tu J, Torrente-Rodríguez RM, Wang M, Gao W. The Era of Digital Health: A Review of Portable and Wearable Affinity Biosensors. Adv Funct Mater. 2019;30(29):1906713. doi: 10.1002/adfm.201906713.

44 Kamel Boulos MN, Zhang P. Digital Twins: From Personalised Medicine to Precision Public Health. Journal of Personalized Medicine. 2021;11(8):745. doi: 10.3390/jpm11080745.

45 Gordon WJ, Coravos, A.R. & Stern, A.D. Ushering in safe, effective, secure, and ethical medicine in the digital era. NPJ Digital Medicine. 2021;4:56. doi: 10.1038/s41746-021-00424-5.

46 Grants and Funding: Office of Extramural Research (US) [Internet]. PAR-20-254 Ethical, Legal and Social Implications (ELSI) Research (R01 Clinical Trial Optional). Bethesda (MD): National Institutes of Health; [posted 2020 Jul 28; cited 2022 Aug 18]. Available from: https://grants.nih.gov/grants/guide/pa-files/par-20-254.html.

47 National Human Genome Research Institute (US) [Internet]. Ethical, Legal, and Social Implications Research Program. Bethesda (MD): National Institutes of Health; [updated 2022 Jun 10; cited 2022 Aug 18]. Available from: https://www.genome.gov/Funded-Programs-Projects/ELSI-Research-Program-ethical-legal-social-implications.

48 Food and Drug Administration (US) [Internet]. Digital Health Technologies for Remote Data Acquisition in Clinical Investigations. Silver Spring (MD): Food and Drug Administration; [modified 2021 Dec 22; cited 2022 Aug 18]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/digital-health-technologies-remote-data acquisition-clinical-investigations.

49 Khozin S, Coravos A. Decentralized Trials in the Age of Real-World Evidence and Inclusivity in Clinical Investigations. Clinical pharmacology and therapeutics. 2019;106(1):25–27. doi: 10.1002/cpt.1441.

50 McGraw D, Mandl KD. Privacy protections to encourage use of health-relevant digital data in a learning health system. NPJ Digital Medicine. 2021;4:2. doi: 10.1038/s41746-020-00362-8.

51 Suver C, Thorogood A, Doerr M, Wilbanks J, Knoppers B. Bringing Code to Data: Do Not Forget Governance. J Med Internet Res. 2020;22(7):e18087. doi: 10.2196/18087.

52 Nguyen, T.V., Dakka, M.A., Diakiw, S.M. et al. A novel decentralized federated learning approach to train on globally distributed, poor quality, and protected private medical data. Sci Rep. 2022;12:8888. doi: 10.1038/s41598-022-12833-x.

53 Food and Drug Adminsitration (US) [Internet]. FDA Fact Sheet: The FDA's Role in Medical Device Cybersecurity: Dispelling Myths and Understanding. Silver Spring (MD): Food and Drug Administration; [cited 2022 Aug 18]. Available from: https://www.fda.gov/medical-devices/digital-health-center-excellence/cybersecurity.

54 Defense Advanced Research Projects Agency (US) [Internet]. Guaranteeing AI Robustness Against Deception (GARD). Arlington (VA): Defense Advanced Research Projects Agency; [cited 2022 Aug 18]. Available from: https://www.darpa.mil/program/guaranteeing-ai-robustness-against-deception.

55 Advanced Research Projects Agency for Health (ARPA-H) (US) [Internet]. Bethesda (MD): National Institutes of Health; [cited 2022 Aug 18]. Available from: https://www.nih.gov/arpa-h.

56 Research Portfolio Online Reporting Tools [Internet]. Bethesda (MD): National Institutes of Health. [1985] - . A Stress and Pain Self-management m-Health App for Adult Outpatients with Sickle Cell Disease; [cited 2022 Aug 18]. Available from: https://reporter.nih.gov/project-details/10050181.

57 Research Portfolio Online Reporting Tools [Internet]. Bethesda (MD): National Institutes of Health. [1985] - . PINPOINT: Gaming technology to engage adolescent sickle cell patients in precision pain management; [cited 2022 Aug 18]. Available from: https://reporter.nih.gov/project-details/90459621.

Development of Educational Marine Soft Robotics STEM Platform as New Iteration of SeaPerch K-12 National Outreach Program

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In the past thirty years, educational programs like the Massachusetts Institute of Technology/Office of Naval Research's SeaPerch have been effective at introducing students to robotics, science and engineering concepts through low-cost, hands-on curricula (Nelson et al., 2015; Giver & Michetti, 2008). These programs have been integral in preparing students to pursue degrees and careers in STEM that meet the needs of a 21st century global economy (Committee on STEM Ed, 2018). In order to address rapid technological growth and our dynamic digital climate, such vital STEM educational opportunities must continuously evolve to provide students the tools necessary for meaningful engagement within a future global workforce.

First developed at MIT Sea Grant three decades ago, the SeaPerch program was a novel approach at hands-on project based learning with a STEM curriculum for K-12 audiences. Students built their own remotely operated vehicle (ROV) unit with low-budget materials and learned about concepts such as buoyancy and circuits while being given the opportunity to compete in design challenges that built off of the base SeaPerch unit (Wang et al., 2020).

Returning to the roots of the program, MIT Sea Grant is again investing in the fundamental ideas behind SeaPerch by developing SeaPerch II in order to keep up with emerging and since-established advances in technology. We found soft robotics and Arduino microcontrollers to be the most suitable areas of focus, which further increase exposure to STEM topics at the K-12 level. The redesign will include the implementation of tiers in the curriculum, which will help cater to different ages and experience levels. SeaPerch II will emphasize the iterative model of design engineering with opportunities for students to take creative direction by exploring these universal and utile technologies.

SeaPerch II will bridge the gap between the previous educational modules of SeaPerch and advances in emerging technologies. Introducing innovative science to students at an earlier age in an accessible, low-cost manner will increase the diversity of STEM programs and will reinforce interest and awareness in pursuing careers in STEM. SeaPerch II serves to inspire the next generation as well as contribute to the decentralization of robotic systems and their dissemination into the public domain.

1. Introduction and Background

Incorporating modern developments in technology into education is necessarily at the forefront of scientific progress. Therefore, it is critical to update successful educational programs to include currently relevant technology and subjects. The SeaPerch program consists of an underwater robotics kit with supporting educational materials which guides educators and students to build their own underwater remotely operated vehicle (ROV). The program's main function is to "reduce traditional barriers to participation in robotics programs and promote…inquiry-based learning with real-world applications" (About SeaPerch, n.d.). Since it was first conceived in the 1990's, SeaPerch has been picked up and adapted by groups like the Association for

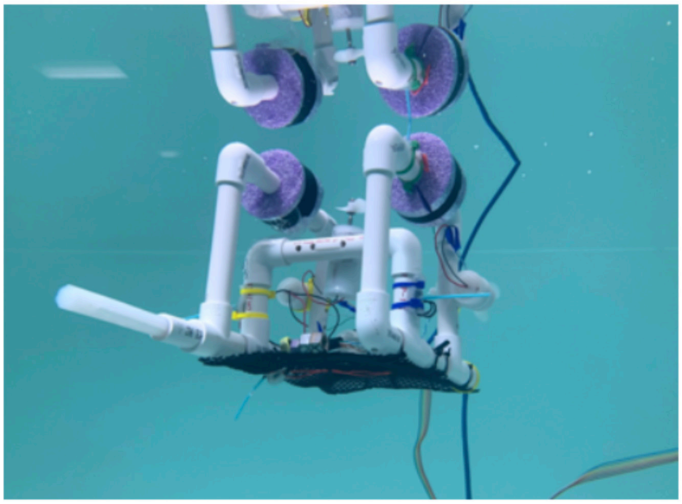

Figure 1: SeaPerch II ROV Unit.

Figure 2: Students participating in a SeaPerch challenge (Pike, 2018).

Unmanned Vehicle Systems International Foundation (AUVSI) for a widespread national and international audience. SeaPerch has reached thousands over the span of decades and has become a rich community of students and educators with an established infrastructure (Groark et al., 2019).

However, technological capabilities have greatly increased since SeaPerch's initial design. Including new modules with these capabilities would inspire even more student growth and preparedness for future careers. The two areas of technological advancement we found to be most relevant to SeaPerch's vision are soft robotics and Arduino microcontrollers (El-Abd, 2017; Nurzaman et al., 2020). As such, SeaPerch II includes modules that build on these ideas.

In an effort to increase the breadth of program engagement, we have developed SeaPerch II to enable young scientists to take their creations to the field and make discoveries in their communities using a modular set of instruments. The program's core learning values are laid out in several modules which are designed to accommodate students of different experience levels and will be disseminated with educators in mind. The modules will include Arduino-enabled sensors for the higher levels and soft robotic actuators throughout all levels.

In response to the increasing importance of computer science since SeaPerch's early development in the 1980s and '90s, we are establishing a roadmap towards autonomy by creating a series of modules which build on each other and utilize the capabilities of Arduino microcontrollers. Since the design of SeaPerch's curriculum, there have been major advances in microprocessing capabilities, lowering barriers of entry. Sea Perch II will use the user-friendly, open-source interactive Arduino hardware and software to help students understand the construction of circuits and basic programming principles. Much like SeaPerch's well-established community infrastructure, Arduino has a rich volume of resources that students can reference to help them innovate with their ROV designs. The Arduino module will provide an introduction to feedback control and sensor integration that gives students a solid foundation for electromechanical systems.

SeaPerch II will also allow students to experiment with state-of-the-art soft robotic technology which has far-reaching applications, especially piquing the interest of the marine sector (Office of Naval Research, 2022). We are developing silicone-based soft robotic modules for gripping actuation that aim to introduce students to this emerging paradigm in robotics. The most accessible versions of the soft robotics module will only require standard classroom supplies along with easily obtained castable silicone. More complex implementations of the module are also available, which require 3D printed molds for casting the silicone. By covering the fundamentals of soft robotics, we hope to encourage students to design, prototype, and test their own soft robotic actuators. The modules will prepare students for soft robotics' increasing prevalence as a technology.

SeaPerch II will expand accessibility and relevance of ocean robotics to classrooms while enriching the existing community of the original SeaPerch program. The following sections describe the design, roadmap, and development of the new SeaPerch II modules, as well as our findings and areas for future improvement.

2. Program Design and Roadmap

The SeaPerch program was successful in part due to its simplicity and effectiveness (Nelson et al., 2015). With SeaPerch II, we strive to maintain these two facets of the original program while simultaneously adapting to how the world has evolved since SeaPerch's initial inception. We want to provide a path to higher levels of technology without compromising the original SeaPerch mission. Through a series of quarterly incremental improvements to the existing SeaPerch platform, the SeaPerch II modules will be made available to teachers starting with update and additive modules, then integrating the modules into basic feedback control and eventually an integrated system that gives the SeaPerch ROV a level of autonomy.

A continued focus of the updated modules is for learners of all ages to have the opportunity to engage with their environments in ways that optimize their potential for discovery. All of SeaPerch II's modules strive towards this goal and are thoroughly backed by support materials that we continue to test, adapt, and improve as the community embraces these new capabilities.

One of the most critical components of SeaPerch II are the supporting materials that have been synthesized in order to walk students and educators through the implementation of any of the new modules. These materials should ensure that students are given freedom and encouragement to explore the design approach of the SeaPerch II modules from a critical perspective while aid is provided wherever necessary.

SeaPerch II is designed with educators and students in mind, ensuring it works with existing SeaPerch programs in the field today. For example, if an educator teaches different grade levels and doesn't want to detract from what they are already doing, we provide a structure that allows for gradual additive implementation. The first level is the entirely new sensors or soft actuator modules one can add to the SeaPerch with which they are familiar. Then if the educator decides they want a more complex project for more advanced students, they can move forward with our forthcoming high level modules which will include the autonomous depth maintenance and obstacle detection.

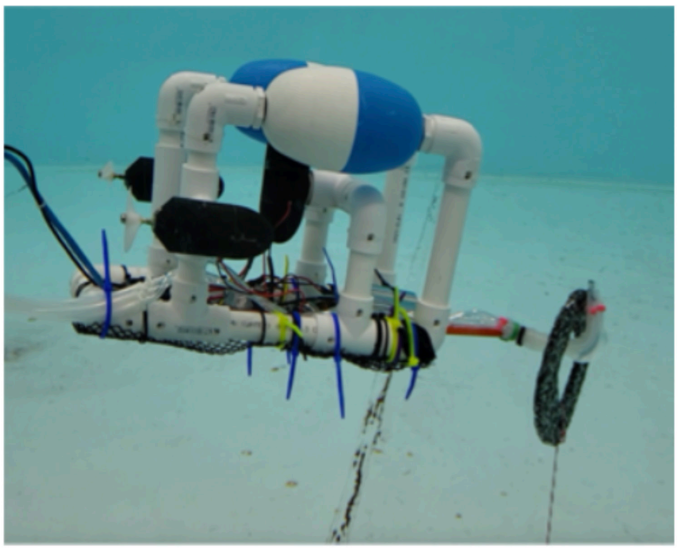

Figure 3: Image of SeaPerch vehicle with soft robotic three-chambered pen gripper module testing.

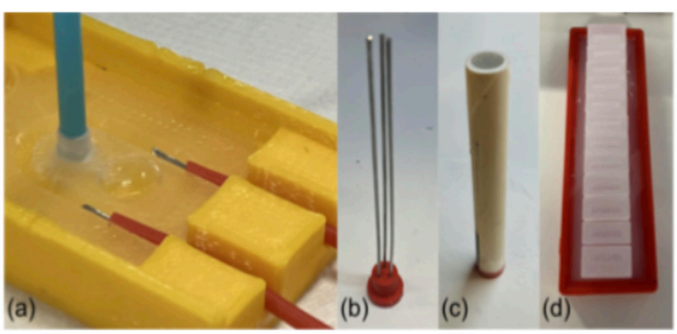

Figure 4: A-D. Various uses of silicone in Sea Perch II modules: (a) whisker sensor mold, (b) PVC pipe gripper mold, (c) PVC gripper casting, (d) chambered network gripper casting.

The modules will be continuously developed and released on the MIT Sea Grant website every quarter. These quarterly releases will consist of new modules as well as associated educational materials, videos, documentation and more. In some cases these may be entirely new modules like the soft robotic actuators, or in others they may be updated versions of a pre-existing module.

We hope that seeing the different alternatives to the same modules will help students feel capable and comfortable as they take the design of these components into their own creative hands. Once learners have attained familiarity with the fundamentals of soft robotics and electronic systems that SeaPerch II provides, they can use these concepts to construct ROV units that are uniquely their own using an iterative model of design in the same way that students currently do for SeaPerch, except now with more tools under their belt.

Introducing students to these new technologies produces benefits far beyond their applications in SeaPerch II. Bringing soft robotics, casting silicone, and Arduino into classrooms is part of a larger shift occurring in STEM as a whole (El-Abd, 2017; Nurzaman et al., 2020). SeaPerch II is meant to serve as a lens which concentrates a wave of novel engineering materials and methods into an accessible and digestible platform.

3. Modules

I. Overview

This update aims to increase the functionality of a SeaPerch ROV while remaining true to the core principles of SeaPerch. We have taken new technologies and adapted them to the platform which allows students to interact with objects using soft actuators, record data with sensors not previously accessible, and explore marine environments using their SeaPerch ROV.

A fundamental update made to the SeaPerch curriculum is the castable silicone material that is utilized for sensors and soft robotic actuators. We have selected the Smooth-On Ecoflex 00-30 castable silicone due to its availability and versatility. This flexible and extensible material has been used for soft robotics in the past and creates a low barrier of entry into the field of soft robotic actuation due to its ease of use (Shepherd et al., 2011).

The soft robotic actuators are another core component of the program update. SeaPerch's three configurations of soft actuators allow students to interact with objects in classroom challenges or marine environments by pairing the actuators to the motion of the chassis.

Additionally, Sea Perch II electronics include specially repurposed sensors. SeaPerch II takes generic, inexpensive, open-air sensors that are commonly used in introductory surface autonomous systems and adapts them with economical waterproofing methods enabling an underwater autonomous learning experience.

The updated program also required development of waterproofing methods for a cost-effective, open-air pressure sensor that works with Sharp IR Sensors in underwater environments. The pressure sensor is waterproofed using some common materials like a balloon and a pill bottle as its case, whereas we developed two

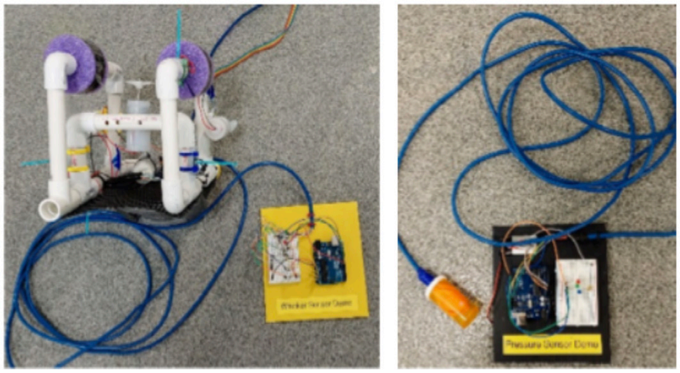

Figure 5: SeaPerch II ROV outfitted with whisker sensors (left). Educational Demo for pressure sensor (right).

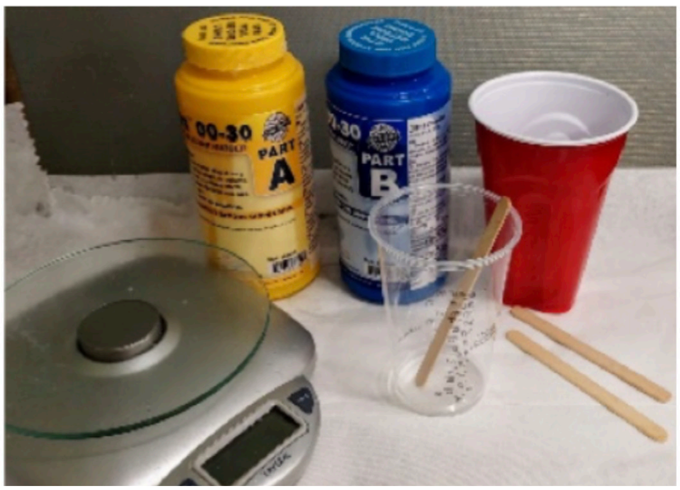

Figure 6: Materials necessary for casting with EcoFlex silicone rubber (right).

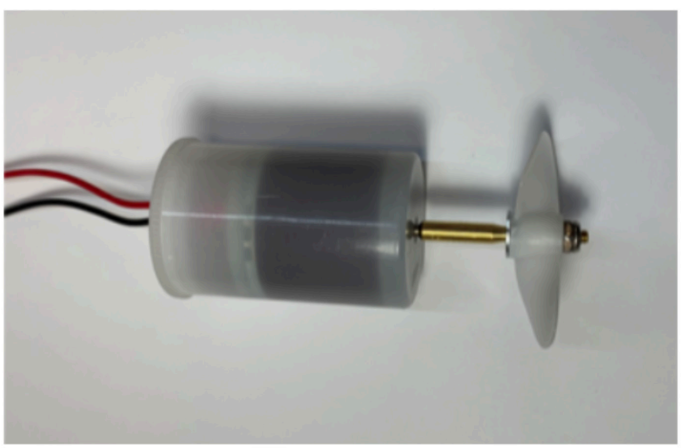

Figure 7: Updated Waterproof Motor in a film canister using the Ecoflex 00-30 Silicone as a sealant.

ways to waterproof the IR sensor: one using an acrylic box, and the other using plastic wrap.

SeaPerch II notably utilizes a new sensor which was developed entirely in-house with the casting silicone. The whisker sensor is a touch sensor that detects distortions on SeaPerch; students can easily build it by combining everyday materials, a 3D printed mold, and the Ecoflex 00-30 silicone rubber. Particular consideration was given to ensuring these sensors are effective for SeaPerch yet not costly to students.

Another important consideration with this update was the growing accessibility of 3D printing technologies, with an estimated 871,000 3D-printing devices in use worldwide in 2021 (Alsop 2022). This increasingly ubiquitous technology is incorporated into SeaPerch II modules to ensure there are generally methods that do not require 3D printer access, but included are other methods which take advantage of this revolutionary fabrication process.

All of these different components come together to impart fundamental concepts and experience to our entire learner base, providing the room necessary for students to expand upon those concepts.

II. Waterproof Motors

The largest change to the core SeaPerch modules is the motor waterproofing methodology. All new methods to seal the motors utilize the same Smooth-On Ecoflex 00-30 Silicone. Additionally, 3D printing is incorporated into SeaPerch II motors as an alternative but not primary method for fabrication so as not to limit students without a 3D printer.

There are three main methods of waterproofing the motors. The first uses the original SeaPerch film canister and the silicone to seal in the classic SeaPerch 12V DC motor without wax. Similarly, the second method uses a pill bottle and the silicone to seal the motors. The third method uses a 3D printed mold to cast the motor in a silicone encasing so that it can move freely with a soft exterior. By supporting these different methods, we hope to cater to students' experience level and on-hand materials as much as possible to increase accessibility of the program.

III. Soft Robotic Grippers

An entirely new item on the SeaPerch roster is the soft robotic actuators. The fundamental concern of soft robotics is the construction of physically flexible systems (Iida & Laschi, 2011) . Working with alternate materials can shift the paradigm of what students consider to be robotics, and it opens doors to unique biomimicry applications. However, there are very limited soft robotic educational materials which are accessible to classrooms and tailored towards a large range of age groups. Due to these factors, we developed three separate actuators as part of the Sea Perch II soft robotics modules. The construction of the two main actuators (a PVC pipe gripper and a chamber innetwork gripper) require basic 3D printing capabilities and some materials that are already being used in SeaPerch II. The third actuator mold (a three-chambered pen gripper) only requires common classroom materials and is more simply assembled and customized.

a) PVC Pipe Gripper: The simplest soft actuator that we developed is a PVC pipe gripper. It uses a PVC pipe for its structure and three small metal rods for the chambers, which are used for actuation. Two 3D printed end caps go on each end of the PVC pipe to position the rod chamber-molds accordingly. This actuator

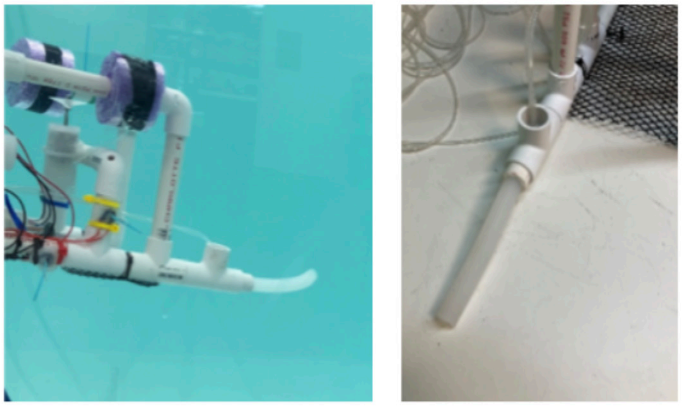

Figure 8: PVC Pipe Gripper mounted on SeaPerch ROV.

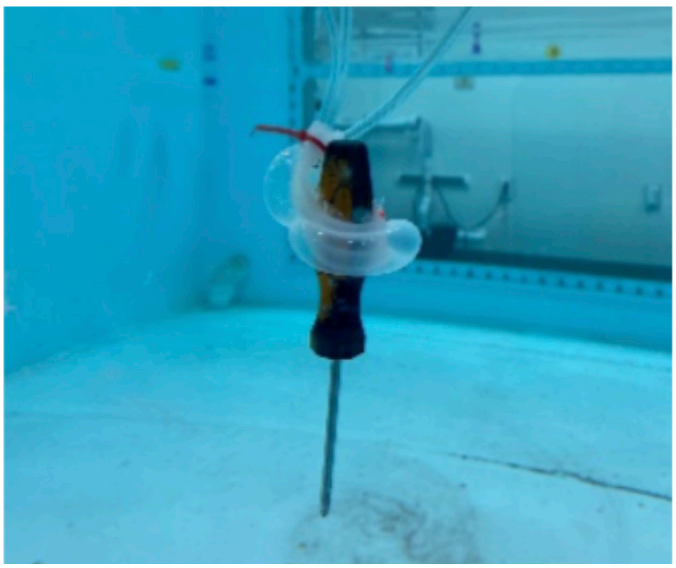

Figure 9: A functional three-chambered pen gripper prototype successfully using hydraulic actuation to holding a screwdriver underwater.

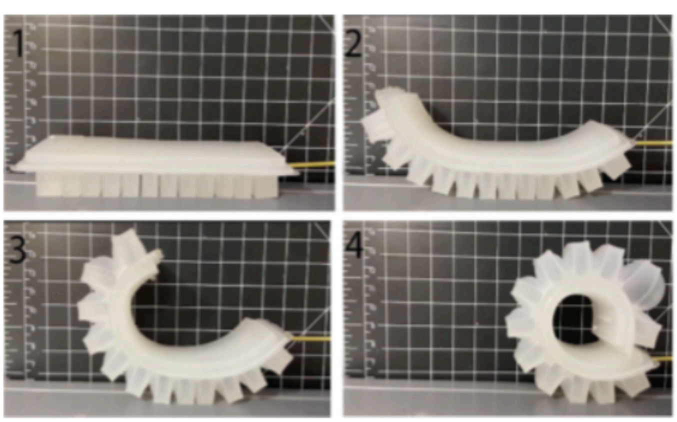

Figure 10: Stages of pneumatic actuation for chamber network gripper prototype cast out of silicone using a custom designed, 3D printed mold.

has three separate chambers which can all be inflated to operate the tentacle using vinyl tubing (which is inserted and zip tied off) and controlled by three craft syringes. Its three degrees of freedom make this actuator the ideal choice for a multipurpose SeaPerch II ROV seeing as it can curl in nearly any direction.

b) Three-Chambered Pen Gripper: The most accessible soft robot included in the new module is the three-chambered pen actuator, cast using parts from common pens, which can grasp small objects. This design is based off of Instructables and YouTube content developed by Harrison Young (2016). It shares similar capabilities with SeaPerch II's other three-chambered actuator. Each individual chamber is cast using standard BIC ballpoint pens or similar pen models, with the inkwell forming the interior chamber. The three chambers are then joined with more silicone to create the final product. A flexible tube is placed within each chamber, zip-tied to create a seal, and then controlled using three separate craft syringes. Since each individual chamber is manufactured separately, students can creatively configure the chambers to make compound actuators with more degrees of freedom.

c) Chamber Network Gripper: The most complex, yet most dextrous actuator, is the chamber network gripper, which is made up of a series of smaller chambers which are all connected through a central channel. This actuator is inspired by the PneuNets (pneumatic network) Bending Actuators developed by Harvard's Whitesides Research Group (Mosadegh et al., 2014). Due to its complexity, this actuator can only be reliably made using 3D printed molds. The actuator is composed of two parts, made with three total 3D printed pieces. A rectangular piece of fabric is surrounded by silicone to serve as the base of the actuator. The component with the chambers and channel is cast using a two part 3D printed mold. Both pieces are allowed to fully cure, and then assembled through a final casting process to create a single, airtight robotic actuator. A tube is then inserted to inflate the robot, and the fabric constrains the flexible body which forces the actuator to curl. Although this actuator has several small chambers, they are all connected by a central channel into one large chamber network, resulting in one degree of freedom actuated by a single craft syringe. However, the layout of the small chambers leads to efficient and reliable actuation, which surpasses the capability of SeaPerch II's other three-chambered grippers in one direction.

All of these actuators are documented with in-depth, step-by-step instructions on construction and use which include visual aids for students and educators. If an educational department has access to 3D printers, then all of the SeaPerch II actuators are castable and they can use the three-dimensional models included in the instructions and support materials to print the soft robot molds.

IV. Sensors

One aspect of SeaPerch that was notably missing when it was first developed was sensor packages. While certain SeaPerch-mounted sensors were explored during development, they were not available at scale nor affordable prices for the program's education-based audience. Since SeaPerch was first released, sensor technology has come a long way. Many sensor types downsized significantly, and open-air, small, affordable sensors of all kinds are now developed and produced en masse. However, lacking the widespread applications at scale, cheap and small underwater sensors have not quite kept up.

Through new ways of combining unconventional materials that are easily accessible, we have developed methods of adapting the small and affordable open-air sensors already used in education to suit underwater applications at the SeaPerch level. Three of the specific sensors we worked with are IR short distance range sensors, pressure-depth sensors, and whiskers touch sensors.

a) IR Sensors: The IR sensor uses two different techniques to seal the sensor from the water as shown in Fig. 11. The first method involves an acrylic box casing that is put together using silicone sealant and butyl tape. The second method involves wrapping the sensor with saran wrap and taping off the end with butyl tape. Both configurations work, however we explored multiple options in order to best suit students' available resources. This Sharp IR range sensor allows students to program automated guidance functionalities. Some program examples include an autonomous virtual bumper which automatically stops the ROV a short distance before hitting a wall or a bottom-following function where the SeaPerch unit maintains a certain height from the floor of its underwater environment. After being introduced to the basics of the sensor, we hope that students can come up with their own expanded uses for the device.

b) Pressure Sensors: The second type of sensor that was adapted to fit SeaPerch II's underwater environment are open-air pressure sensors. Using common materials such as a balloon, a pill bottle, and butyl tape, SeaPerch II is equipped with a fully functional depth sensor up to 12 meters. This opens up the possibility of both providing depth feedback to students (which is a key element in exploring new terrains or simply operating an underwater ROV in general) and having the ROV autonomously maintain a certain depth at any level.

c) Whisker Sensors: The whisker sensor is a physical touch sensor that functions using soft robotics. Originally developed to mimic seal/cat whiskers, this iteration consists of a layer of conductive grease connected to wires in between two layers of Ecoflex 00-30 silicone, with a cotton swab protruding from the silicone acting as the "whisker." Fundamentally, the whisker is a variable resistor that increases resistance when the cotton swab is struck due to stretching of the silicone and grease. When set up in a specific circuit, this increase in resistance can be constantly monitored using an Arduino board, turning the whisker into a waterproof touch sensor. The steps to make the whisker are easy and repeatable for students. It is constructed with reusable 3D-printed parts and other everyday items.

To detect the distortions (changes in resistance) of the whisker, the whisker is set up in a voltage divider circuit, which places the whisker in series with a resistor that has a similar neutral resistance to that of the whisker. A 5-volt power supply is then applied to this series of resistors. The voltage after the normal (first) resistor is constantly being reported, along with a simple moving average that constantly averages those twenty most recent voltage readings. When the whisker is touched and the resistance of it increases, the voltage reading will increase proportionally, allowing students to track and sense these distortions.

The learning points for the whisker sensors are extremely valuable. Students will be introduced to the concepts of electrical physics such as Ohm's Law, resistance, voltage, current, and circuit design. At the same time, they will learn the basics of programming in C and data filtering through the moving average code provided.

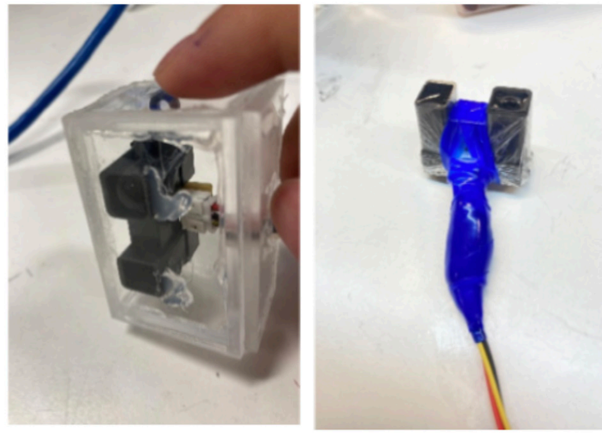

Figure 11: Sharp IR range sensor waterproofed with acrylic box (left) and plastic wrap (right).

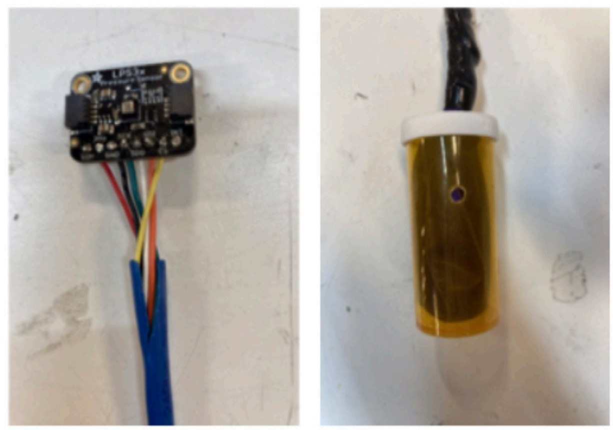

Figure 12: Pressure sensor without waterproof casing (left) and with the pill bottle, balloon and butyl tape enclosure (right).

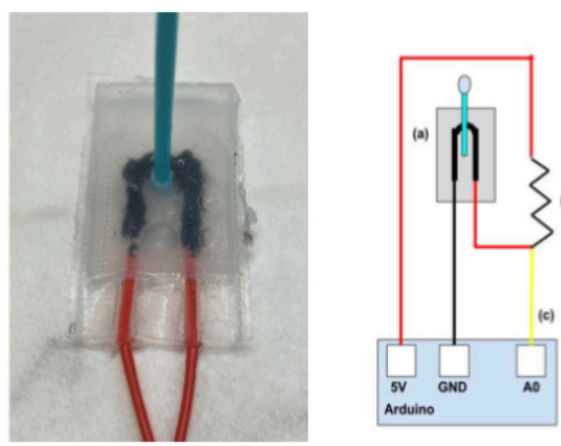

Figure 13: Whisker (left) and Whisker Sensor Circuit (right): (a) Whisker sensor, (b) Resistor of approximately 5 kΩ, (c) Analog Read Wire.

After being introduced to the concepts of the whisker sensors, we hope that students will come up with their own unique uses for the device to explore deeper into the world of physics, programming, and engineering.

4. Conclusion

The key principle of the first SeaPerch program iteration was making marine robotics simple and accessible for younger, beginner audiences in an unprecedented manner. From a development perspective, the current SeaPerch II program includes more modules than initially planned while keeping components low-cost and accessible at an introductory level. Our current sensor and gripper modules are so far performing to the standard we require, making the planned quarterly development and release roadmap appear very promising.

The three current sensor modules offer interesting data collection capabilities, but their potential is greatly amplified by utilizing Arduino microcontrollers. Using the Arduino UNO, students are able to learn valuable skills in programming. Students are able to engage with SeaPerch II's data focused systems by calibrating their sensors to use provided code in the support materials or even by programming entire automated guidance systems on their own (the automated guidance modules are currently still in development). The range of difficulty levels allows students to choose elements which they find appropriately challenging.

Another educational opportunity is the introduction of Arduino microcontrollers in general to SeaPerch students. The ability to integrate and program these microcontrollers is a huge stepping stone in empowering students to create any form of electronic system that they can imagine. Furthermore, students will have gained hands-on experience with sensors through Arduino, which is a powerful tool to support young scientists as they explore their own environments and test to their curiosity's limit.

SeaPerch II's soft actuators have also performed surprisingly well. While we are still working on methods to increase the viability of the pneumatic and hydraulic actuation within SeaPerch's tethered format, the grippers themselves are proving to be versatile and simple to make with a fairly high effectiveness with regards to manipulation. They will prove to be a solid introduction of soft robotics to the SeaPerch community.

On top of the grippers themselves, real world use cases for casting silicone expand far past soft robotics (Block 1995). So, no matter where students end up, having experience with the material opens up new possibilities for anything from crafts and hobbies to home maintenance. On top of that, silicone and other rubbers are being used for more and more applications in robotics and engineering at large (Shiitake et al., 2018). It opens up an entirely new perspective for many on how to think about robotics.

All in all, SeaPerch II provides students with the tools and materials necessary to enable significant learning achievement in fundamental STEM concepts as well as transformative discovery opportunities to foster critical inquisitive development.

5. Next Steps

I. Improvements on Current Designs

There are several key technical improvements that we are considering going forward. A few of our current modules require some additional development. Namely, we need to further test and refine our waterproofing methods to ensure that they are fully reliable, write and test example code for the automated guidance systems so it can build on the existing sensor modules, and improve the system for actuating the soft actuators as they can currently require a lot of tubing to operate at the full tether distance of the standard SeaPerch ROV.

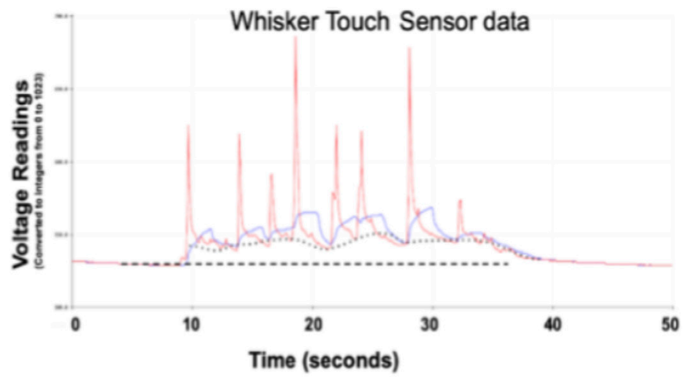

Figure 14: Example Whisker Data Plot: The red line represents the value read from the whisker sensor; the spikes in the red line indicate a distortion of the whisker. The blue line represents a moving average of the twenty most recent values read from the whisker sensor. The dashed bottom line represents the neutral reading of the whisker before any distortions. Meanwhile, the dotted line tracks the neutral reading of the whisker after distortions. Notice how the dotted line is different from the dashed; the whisker's neutral reading changes after being distorted and doesn't return to the dashed (no distortion) neutral reading.

SeaPerch II will learn from student and teacher testing for each module released and work to update the existing modules accordingly and incorporate that community feedback. The program will feature several more general accessibility, reliability, and ease of use updates which will be released with the quarterly modules. We want these modules to grow with the community and remain as relevant as possible for new learners. Along similar lines, as we find more accessible versions of these modules (any instances that may not require 3D printed or specific parts) we will be supplementing our modules with the additional build materials in the hopes that as many users as possible will be able to incorporate SeaPerch II into their SeaPerch experience as possible.

II. Future Design Work

SeaPerch II engages students in numerous key areas, but more exploration is needed to optimize educational impact. Some avenues include integration of alternative chassis models, more soft robotics, and increased autonomous capabilities.

SeaPerch II's inclusion of soft actuators could open the door for those who are up to the challenge of designing entirely soft robotic ROV units. While they will likely lack the versatile and modular structure of the classic SeaPerch ROV, the design and construction of an entirely soft-robotic unit poses several engineering challenges to students which build on what they learned with soft actuators in SeaPerch II and will demonstrate a more advanced level of understanding for this revolutionary technology.

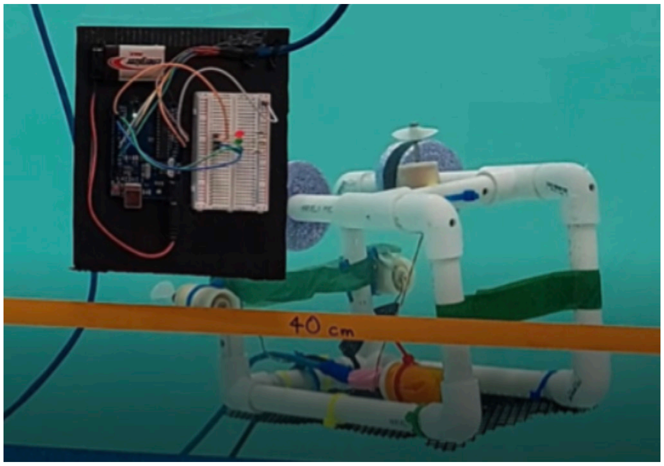

Figure 15: Development for proof of concept depth holding capabilities using SeaPerch II's pressure sensor module.

Another potential step for SeaPerch II would be the development of a guide to serve as a base platform for students wishing to creatively design their own soft robotic actuators. A more in-depth guide would enable students to take their knowledge from the original modules and expand upon these principles themselves. Further guidance can then enable learners to design and construct their own soft robotic actuators to fit any situation or task.

One of the big promises of SeaPerch II is that of automated guidance systems. With the addition of the SeaPerch II sensor suite, students will be constructing SeaPerch units that have the capacity to integrate certain autonomous navigation functions such as obstacle detection and avoidance, depth holding, ground following, and automatic surfacing. With much of the hardware modules developed, adding autonomous functionality to SeaPerch II seems like a logical next step.

All things considered, SeaPerch II is prepared to build upon the incredibly successful classic SeaPerch program and incorporate several 21st century technologies in order to meet the needs of any learner. With the current and future modules, we hope SeaPerch II is able to encourage a new influx of learners to foster their own passion for growing STEM fields with ever-changing problems, projects, and paradigms.

References

"About SeaPerch." SeaPerch.org. Retrieved on August 31, 2022 from https://seaperch.org/about/

Alsop, T. (2022, March 18). 3D Printing & Additive Manufacturing Devices 2030. Statista. Retrieved November 14, 2022, from https://www.statista.com/statistics/1259618/3d-printing-and-additive-manufacturing-devices-worldwide/

Block, S. R. (1995). A silicone toolbox: Engineering materials for today and the future. Retrieved August 31, 2022 from https://www.osti.gov/etdeweb/biblio/125137

Committee on STEM Education of the National Science and Technology Council. (2018). Charting a Course for Success: America's Strategy for STEM Education. Retrieved on August 31, 2022 from https://www.energy.gov/sites/default/files/2019/05/f62/STEM-Education-Strategic-Plan-2018.pdf

El-Abd, M. (2017). A Review of Embedded Systems Education in the Arduino Age: Lessons Learned and Future Directions. International Journal of Engineering Pedagogy (IJEP), 7(2), 79. Retrieved August 31, 2022 from https://doi.org/10.3991/ijep.v7i2.6845

Giver, S., & Michetti, S. (2008). The Sea Perch Challenge Generating Interest In Marine Engineering, Ocean Engineering, Naval Engineering And Naval Architecture Through Hands On Activities. 2008 Annual Conference & Exposition Proceedings, 13.1264.1-13.1264.13. Retrieved August 31, 2022 from https://doi.org/10.18260/1-2--3496

Groark, L., Cooper, K., & Davidson, D. (2019). The SeaPerch Evolution: From Grassroots to a Global Community. 2019 IEEE Integrated STEM Education Conference (ISEC), 274–280. Retrieved August 31, 2022 from https://doi.org/10.1109/ISECon.2019.8882075

Iida, F., & Laschi, C. (2011). Soft robotics: Challenges and perspectives. Procedia Computer Science, 7, 99–102. https://doi.org/10.1016/j.procs.2011.12.030

Mosadegh, B., Polygerinos, P., Keplinger, C., Wennstedt, S., Shepherd, R. F., Gupta, U., Shim, J., Bertoldi, K., Walsh, C. J., & Whitesides, G. M. (2014). Pneumatic Networks for Soft Robotics that Actuate Rapidly. Advanced Functional Materials, 24(15), 2163–2170. Retrieved August 31, 2022 from https://doi.org/10.1002/adfm.201303288

Nelson, S. G., Cooper, K. B., & Djapic, V. (2015). SeaPerch: How a start-up hands-on robotics activity grew into a national program. OCEANS 2015 - Genova, 1–3. Retrieved August 31, 2022 from https://doi.org/10.1109/OCEANS-Genova.2015.7271419

Nurzaman, S. G., Sadati, S. M. H., Eldiwiny, M., & Iida, F. (2020). Soft Robotics: The Journey Thus Far and the Challenges Ahead [TC Spotlight]. IEEE Robotics & Automation Magazine, 27(4), 75–77. Retrieved August 31, 2022 from https://doi.org/10.1109/MRA.2020.3028676

Office of Naval Research. (2022). Aquatic Soft Robotic STEM Education Kit. Retrieved August 31, 2022 from https://www.navysbir.com/n22_A/N22A-T023.htm

Pike, D. (2018). Robot makes its way through one of the challenges. UTRGV. Retrieved on August 31, 2022 from https://www.utrgv.edu/newsroom/2018/10/05-seaperch-challenge-tests-the-stem-minds-of-students-through-underwater-robot-challenge.htm

Shepherd, R. F., Ilievski, F., Choi, W., Morin, S. A., Stokes, A. A., Mazzeo, A. D., Chen, X., Wang, M., & Whitesides, G. M. (2011). Multigait soft robot. Proceedings of the National Academy of Sciences, 108(51), 20400–20403. Retrieved on August 31, 2022 from https://doi.org/10.1073/pnas.1116564108

Shintake, J., Cacucciolo, V., Floreano, D., & Shea, H. (2018). Soft Robotic Grippers. Advanced Materials, 30(29), 1707035. Retrieved on August 31, 2022 from https://doi.org/10.1002/adma.201707035

Wang, S., Andrei, S., Urbina, O., & Sisk, D. A. (2020). Introducing STEM to 7 th Grade Girls using SeaPerch and Scratch. 2020 IEEE Frontiers in Education Conference (FIE), 1–8. Retrieved on August 31, 2022 from https://doi.org/10.1109/FIE44824.2020.9273984

Young, H. (2016). DIY Soft Robotic Tentacle. Instructables. Retrieved on August 31, 2022 from https://www.instructables.com/DIY-Soft-Robotic-Tentacle/