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I found myself hooked by Dr. Sandra Chapman's video about undersea medicine for Navy divers. While Dr. Chapman takes advantage of technology for innovative projects like Diver Augmented Vision Display, she focuses on biology to fulfill her vision of seamless diver transitions between sea and land, like Aquaman. In her video, she said that technological solutions, like wetsuits and drysuits, are "inherently flawed, because you're depending on engineered solutions." Chapman hopes to "figure out how to adapt the human because biology is always the smartest solution… that [will] make the human most independent."

Currently, Chapman and her department, the Office of Naval Research (ONR), are following biology through study of the Bajau Sea Nomads. The Bajau are a group of people in waters off of Indonesia, Malaysia, and the Philippines, who, for over 1,000 years, have lived a hunter-gathering lifestyle at sea. Researcher Melissa Ilardo, who spent the summer of 2015 with the Bajau people, said of their abilities: "Underwater, the Bajau are as comfortable as most people are on land. They walk on the seafloor. They have complete control of their breath and body." Ilardo wondered how they could do this, and whether it was genetic.

The spleen is one adaptation she found that allows the Bajau people to stay underwater for so long. The spleen "acts as a warehouse for oxygen-carrying red blood cells," which can be released into the blood stream as needed. When mammals hold their breath, the amount of oxygenated red blood cells (RBCs) in the bloodstream goes down. In response, the spleen contracts, pushing oxygenated RBCs into the bloodstream, which can "boost oxygen levels by up to 10 percent" in humans. Ilardo used an ultrasound for organ scans of 59 Bajau villagers. For a control measurement, she took body scans of the Saluan, a neighboring group, who don't dive. The spleens in the Bajau people were about 50 percent bigger. Even Bajau villagers who don't dive had enlarged spleens, indicating that the spleen size was a genetic adaptation.

After collecting blood samples from the 59 Bajau and 34 Saluan participants, Ilardo looked for genetic differences. Based on her observations and prior studies, lower expression of the PDE10A gene seems to be behind the enlarged spleens. Located on chromosome six, PDE10A regulates the release of hormones from the thyroid gland. One thyroid hormone, T4, increases spleen size. In 2019, Navy ONR researchers injected mice with a "selective PDE10A inhibitor, MP-10," and found that the spleen was "significantly larger" in the MP-10 treated mice. Because PDE10A slows the release of T4, it makes the spleen smaller; inhibiting PDE10A increases the release of T4, making it bigger. Further, studies show that direct injection of T4 hormones into mice increased the size of the spleen.

As of 2019, in addition to studying PDE10A and spleen size in mice, the Navy "collect[ed] physiological measurements and "performing[ed] whole genome sequencing" on samples of DNA collected from divers in Malaysia, Korea, and the Philippines. Using these, the Navy will soon have biological ways to adapt divers to the water.

Another way Chapman and ONR hope to transition from technological solutions to biological ones seems more like science fiction. In the future, they hope to use engineered bacteria in the human microbiome to control diver temperature. According to Chapman, "temperature control is a real issue for the divers because water conducts thermal energy 25 times faster than air, so divers will get cold in water… faster than on land." The current solutions are wetsuits and drysuits, which are "inherently flawed, because you're depending on engineered solutions." For example, "anytime that [a] dry suit has a rip… you've lost your thermal protection completely." Military divers are often near sharp objects and

in tight spaces, so they are especially prone to rips. To solve the issue of temperature control biologically, Chapman hopes to make the "human body's own thermostat" by modifying the bacteria of the microbiome "to sense and respond to thermal changes."

The microbiome refers to the ecosystem of microbes, including bacteria, viruses, and fungi, that live on or in human tissue. In many ways, 'our' bodies aren't really ours: the "ratio of microbial to human cells for the average man [is] 1.3:1," which equates to about 57% of cells in the body being microbes, while the other 43% are human cells. Our microbiome is mostly bacteria, and our skin is, literally, covered in bacteria: "~1 billion bacteria inhabit a typical square centimeter of skin." "We live in a symbiotic relationship with our microbes, and our human cells closely interact and communicate with bacteria… cells." The bacteria "act like a shield that protects the body from external aggressors," trap moisture in, and control skin immunity. Our immune system produces antimicrobial peptides (AMPs), which target prokaryotic (single-celled) organisms and protect us from pathogens. Contrary to what the name suggests, AMPs "are important communication signals between the host immune system and the microbiota." For example, Staphylococcus epidermis boosts immunity to Staphylococcus aureus, an often pathogenic bacteria species, by activating skin AMP production.

Engineering bacteria to respond to temperature changes is already underway. In 2016, Mikhail Shapiro and his team at Caltech engineered bacteria to respond to certain temperatures. First, they selected the switches: "proteins that bind to DNA to turn a genetic circuit on or off in response to temperature." One switch, TlpA, is a protein from Salmonella typhimurium bacteria, and the second, TcI, originated in bacteriophages. Both have "sharp switching" - a change of just a few degrees Celsius takes them "from completely off to very strongly on in terms of gene expression." Shapiro and his team were able to "tune these thermal bioswitches so that they operate exactly at the temperature" needed for human applications. For example, TlpA was "originally activated by temperatures ranging between 42 and 44 degrees Celsius." Using a protein engineering technique called directed evolution, "the scientists generated versions with activations temperatures between 36 and 39 degrees Celsius."

By 2040, this technology could revolutionize medicine. Studies in microbial therapeutics have shown that engineered bacteria "can be directed to release a medicine onto tumors, such as the tumor-destroying drug hemolysin." While amazing, this technique "lack[s] spatial precision." In the case of treating a tumor, for example, the bacteria often spread beyond the target site, and damage surrounding healthy tissue. Shapiro hopes to solve this with temperature responsive bacteria and ultrasound technology, which can apply heat to tissue at millimeter precision. Imagine, bacteria are engineered to release tumor-killing drugs when activated at an elevated temperature. With ultrasound technology, heat can be applied to the precise area of the tumor, minimizing damage to nearby healthy cells.

Another future application for this technology is to help Navy divers stay warm underwater. While the "microbial metabolism in the human gut… produces approximately 70% of the total heat of an average person at rest," heat production will be harder on the skin. During digestion, the bacteria in our gut help to break down the food we eat. They extract calories when breaking down the food, creating heat. Our skin microbiome doesn't have the same access to food energy that can be converted to heat. Another challenge is to maintain the balance of the skin microbiome, which prevents skin disorders. In addition, different bacteria species thrive on different parts of the skin, so it could take many species of

engineered bacteria to cover every part of the diver. I believe the Navy will rise to these challenges to help keep divers healthy.

Dr. Chapman's career inspires me for two reasons: her belief in biological solutions and her foresight. Biology and evolution have shown themselves smarter than humans. CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), the revolutionary gene-editing technology that won Jennifer Doudna and Emmanuelle Charpentier a Nobel Prize in 2020, was adapted from bacteria. Bacteria evolved CRISPR as an immune defense against bacteriophages. In computer coding, a topic I am interested in, many artificial intelligence programs use neural networks, which are based on the human brain. In the brain, each neuron is either activated or inhibited, depending on whether the energy potential it receives is above or below a threshold. Imitating this, computer neural networks use layers of "neurons". Computers use a binary 1 and 0 system; the computer states 1 and 0 are the equivalent of the biological states activated or inhibited. Shapiro, mentioned above, also relied on biology. He used the temperature-activated proteins already existing in bacteria, and fine-tuned them to activate at a different temperature. Dan Piraner, co-author of Shapiro's study, commented, "It all started with what nature gave us, and engineering took us the rest of the way."