Sense of Health

Caltech engineers are developing wearable sensing technologies and materials that could transform the practice of medicine.

By Emily Velasco

Illustrations by Jason Holley

While modern medicine has advanced in ways that would seem miraculous to our ancestors, one key characteristic has remained almost unchanged: The practice of medicine is largely reactive. People book an appointment with their doctor when they feel unwell. They visit urgent care when that nagging pain in their abdomen finally becomes too painful to handle, and they end up in the emergency room when they have trouble breathing.

Studies have shown that preventive medicine—the act of detecting and trying to avert potential health conditions before they begin—vastly improves patient outcomes. Now, several Caltech researchers are working to make preventive medicine more accessible through the development of wearable sensors—small, unobtrusive devices that can provide continuous real-time monitoring of biomarkers related to diabetes, stress, inflammation, heart disease, gout, fertility, and more. The goal: to bring medical care to the patient instead of bringing the patient to the medical care. While a visit to a doctor's office requires an appointment and is just a moment in time, a wearable sensor can monitor the health of a patient as long as it is worn, whether the patient is at home or at work, asleep or awake.

Body parts, clockwise from top: Pituitary gland, female reproductive system, pancreas, toe joint, adrenal glands, heart.

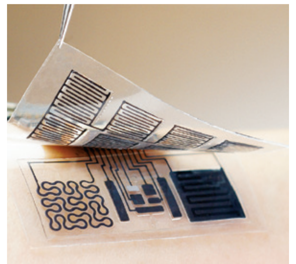
Much of this effort has taken place in the labs of medical engineer Wei Gao, whose sensors detect compounds in sweat that can signify illness; electrical and medical engineer Azita Emami, who uses machine learning and neural networks to detect heart problems; and mechanical engineer Chiara Daraio, who looks to the natural world for inspiration when designing materials with sensing properties.

Sweaty Signals

Gao's noninvasive sensors can be worn almost anywhere on the body and make use of sweat to provide clues about a person's health: If someone's blood sugar is too high, for instance, that can be reflected in their sweat. In addition, when someone experiences stress, their body secretes increased levels of the hormone cortisol, in part through sweat. Also found in perspiration are proteins linked to inflammation, and other biomarkers such as a hormone linked to women's reproductive health, and uric acid, which causes gout.

But because sweat contains lower concentrations of these compounds than are found in blood, Gao and his colleagues have had to invent specialized technologies to detect them. As Gao discussed in his 2023 Watson Lecture, "Wearable Biosensors and the Future of

Personalized Medicine," these new and innovative tools include gold nanoparticles, graphene impregnated with antibodies, and even artificial DNA. Using these technologies, which are precisely tuned to bind to a specific molecule such as cortisol and then generate a small electrical current that can be measured on the skin, the sensors can detect even minute levels of important biomarkers linked to health conditions.



"Wearable sensors give us an opportunity to identify health problems at an early phase, allowing for timely intervention," Gao explains. In addition, he says, "they could play a very important role in monitoring disease treatment. For example, we could monitor therapeutic drug levels in our body."

Machine Learning

Gao's team collaborated with Emami's lab on one of his newer sensors, utilizing her expertise in semiconductor and circuit design to build a chip that can simultaneously measure multiple conditions and biomarkers—a process known as multimodal sensing—and can fit in a compact package measuring only 2 millimeters square. Emami and Gao are also working on sensors that require such a small amount of power they could use the lactic acid found in sweat as a power source, eliminating the need for an external power source such as a battery, or recharging.

Emami and her team have also developed a wearable sensor to detect heart arrhythmias, which are irregular heartbeats that can presage more serious heart conditions. People at risk of arrhythmia are typically sent to a clinic where they undergo an electrocardiogram and have their heartbeat monitored by medical professionals. But since arrhythmias can be unpredictable, they might not occur while the patient is at the clinic. Emami aims to fill this diagnostic gap.

While many people monitor their heartbeat with an Apple Watch or Fitbit, Emami's sensor—which is worn on the chest—does something more complex. In addition to monitoring heart rate, it also detects the heart's electrical activity using a neural network that was trained on a set of heartbeat patterns to look for abnormalities. (Neural networks are AI systems inspired by biological systems such as the brain.)

Left: A sweat sensor developed by Wei Gao's lab. **Below, left to right:** Azita Emami, Chiara Daraio, and Wei Gao, whose labs are developing different types of wearable sensors.

The idea, Emami says, is that doctors could prescribe the sensor for people at high risk for arrhythmia to wear over the course of a week. This interval of time would allow the sensor, which is smaller and consumes less power than current models, to collect data on rare events that might not occur in a clinic, while also alerting the patient to the onset of a dangerous arrhythmia that requires immediate medical attention. "Arrhythmia can happen randomly at different times," Emami says. "If you go to the clinic, everything may look good. Secondly, there are some arrhythmias that are very dangerous, and you immediately have to go to a hospital or an emergency room. This sensor would help to selectively send people either to a clinic or to an ER."

Biomimicry

Daraio has taken another approach to wearable sensors, looking to nature for inspiration. In her 2023 Watson Lecture at Caltech, "Making Wearable Materials Smarter," she discussed how the properties of pectin, a complex sugar found in plants and fruits, led her lab to develop a new polymer that detects changes in temperature and humidity. This polymer, Daraio says, can be woven into fabric that could be fashioned into clothing or directly integrated into wearable sensors that could monitor a person's body temperature for fever, potentially signaling an illness.

Pectin, the molecule responsible for making jams and jellies "set," is so sensitive to temperature changes that a piece of dried mango can be used as a makeshift thermometer, Daraio said in her lecture. She and her colleagues examined the structure and behavior of pectin, particularly its ionic conductivity, to develop the synthetic polymer, which possesses a similar molecular backbone. Yet the polymer represents an improvement on pectin, possessing stronger physical properties and more precise temperature-sensing capabilities. "Pectin as a natural molecule is 300 times more responsive and more accurate than the best temperature sensors available today," Daraio says. "Our synthetic polymer, which is very cost-effective and can be produced in large batches, is even more responsive and more accurate than pectin."

Pectin also tears easily when not dissolved in water. The polymer, however, can be made stretchy and resilient, making it well suited for use in devices that move with the wearer. "Many current wearable sensors are made with rigid electronic components that do not easily interface with soft and conformable fabrics," Daraio says. "However, for all-day wearability,

Wearable Sensors: Looking Ahead

Viviana Gradinaru, the Lois and Victor Troendle Professor of Neuroscience and Biological Engineering, director of the Center for Molecular and Cellular Neuroscience, and the director and Allen V. C. Davis and Lenabelle Davis Leadership Chair of the Richard N. Merkin Institute for Translational Research, discusses the potential role of wearable sensors in preventive medicine.

What is the state of translational research regarding preventive medicine?

For preventive medicine, early diagnosis is critical. Right now, there's a shortage of basic biological understanding of vital health and disease biomarkers, particularly biomarkers that could be accessed easily and frequently. It's difficult to do these kinds of periodic measurements if they're expensive, invasive, or painful, or if they stress you out. Post COVID, there's also been a backlog of access to health care.

Do you believe wearable sensors will play a key part in preventive medicine going forward?

Absolutely. There's a quote that originates with [management consultant] Peter Drucker: "You can't manage what you can't measure." Wearable sensors can play a crucial role because they would allow frequent measurement of factors that can educate healthy humans about what's still to come when changes in course are still possible. There's a lot of talk about lifespan, but wearables could change the conversation from lifespan to "health span." There is absolute value for healthy people to have these frequent measurements, to have a time course and, depending on that time course, to intervene with actionable, helpful behaviors to extend their health span.

What is unique about the wearable sensors being developed at Caltech?

An effective wearable sensor needs to integrate multiple, sometimes complex technologies, and you also need everything to work seamlessly to increase user compliance. Caltech is uniquely good at this type of cross-fertilization due to its small size and pillars of excellence across biology, chemistry, engineering, and data science. And with the Merkin Institute at Caltech, we are excited to connect technology with end users and, as needed, clinicians to inform the best path toward increased health span for all.

sensors should be imperceptible, resilient to washing, and compatible with humid environments because natural fibers like cotton and wool tend to absorb moisture. The new polymers we are developing use changes in ionic conductivity to respond to temperature variations. Such ionic conductors can be integrated in smart threads, for example, that can be embroidered into electronic textiles with new functionalities using conventional manufacturing methods."

The Future

Because the pursuit of wearable sensors benefits from expertise in disciplines such as biology, medical engineering, electrical engineering, computer science, materials engineering, and chemistry, Caltech's focus on interdisciplinary faculty collaboration makes the Institute well suited to be a hub for this kind of research. Though wearable sensors are still relatively new, and their future somewhat unclear, these products may become more commonplace in our lives as computing technology becomes ever smaller, faster, and cheaper, and the novel materials used to make the sensors themselves become more practical and efficient.

"In the future, I think we will have wearable devices that can simultaneously collect a broader range of information from our body," Gao says. "With more comprehensive information, such as physical and chemical information detected with sweat sensors, we could know a lot more about our bodies and our health."

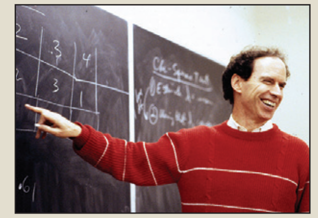
Azita Emami is the Andrew and Peggy Cherng Professor of Electrical Engineering and Medical Engineering; executive officer for electrical engineering; and director of the Center for Sensing to Intelligence, which funds her work along with the Carver Mead New Adventure Fund, Office of Naval Research, and Heritage Medical Research Institute (HMRI).

Chiara Daraio is the G. Bradford Jones Professor of Mechanical Engineering and Applied Physics, and a Heritage Medical Research Institute Investigator. She is the Caltech director of the National Science Foundation's IUCRC Center to Stream Healthcare in Place, which funds her work.

Wei Gao is an assistant professor of medical engineering; a Heritage Medical Research Institute Investigator; and a Ronald and JoAnne Willens Scholar. His work is funded in part by the National Institutes of Health, National Science Foundation, Office of Naval Research, and HMRI.

In Memoriam

To learn more about their lives and work, visit **magazine.caltech.edu/post/in-memoriam**.



Gary Lorden
(1941–2023)

Gary A. Lorden (BS '62), a Caltech professor of mathematics, emeritus, passed away on October 25, 2023, at age 82. A statistics researcher, Lorden focused on applications to real-world problems and served as an expert witness in trials. He also worked as a technical advisor to the TV show *NUMB3RS*. Lorden was Caltech's dean of students from 1984–88, vice president for student affairs from 1989–98, and acting vice president for student affairs in 2002. He was also executive officer for mathematics from 2003–06.

Frank Borman (1928–2023)

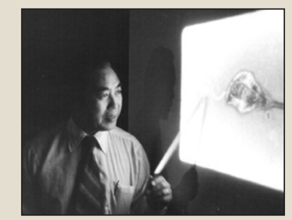
Frank Borman (MS '57), a NASA astronaut who, in 1968, commanded Apollo 8, the first crewed mission to orbit the Moon and return safely to Earth, passed away on November 7, 2023, at age 95. Borman was the first person to be named a distinguished alumnus by GALCIT. A veteran of Gemini 7 and Apollo 8, Borman was a fighter pilot and experimental test pilot in the Air Force, and he served as an assistant professor of thermodynamics and fluid mechanics at the United States Military Academy at West Point. Borman was inducted into the U.S. Astronaut Hall of Fame in 1993.

Fred E. Culick
(1933–2023)

Fred E. Culick, the Richard L. and Dorothy M. Hayman Professor of Mechanical Engineering and Professor of Jet Propulsion, Emeritus, passed away on December 11, 2023, at age 90. He joined Caltech as a research fellow in jet propulsion in 1961. Two years later, he joined the faculty as an assistant professor. He was named associate professor in 1966, full professor in 1971, professor of applied physics and jet propulsion in 1978, professor of mechanical engineering and jet propulsion in 1988, and Hayman Professor in 1997. He retired in 2004. Culick's research focused on the dynamics of combustion chambers.

Betty I. Moore
(1928–2023)

Betty I. Moore, co-founder of the Gordon and Betty Moore Foundation and honorary life member of the Caltech community, passed away on December 12, 2023, at age 95. Moore (born Whitaker) became affiliated with Caltech in 1950 after marrying Gordon E. Moore (PhD '54) and moving to Pasadena. (Gordon passed away in 2023.) The Moores, two of the Institute's most significant philanthropists, donated $300 million to Caltech in 2001 alongside a contribution of $300 million from the Gordon and Betty Moore Foundation. The resources supported health and medicine, alternative energy development, information systems, seismology, nanotechnology, and astronomy, among other areas. The Moores also provided two unrestricted gifts during Caltech's *Break Through* campaign: $100 million that the Institute used to match graduate fellowships and $37 million for student scholarships.



Theodore Y. Wu
(1924–2023)

Theodore Y. Wu (PhD '52), a Caltech professor of engineering science, emeritus, passed away on December 16, 2023, at age 99. Wu was hired as a research fellow at Caltech in 1952 and became an assistant professor of applied mechanics in 1955. He was made full professor in 1961 and retired in 1996. Wu's interdisciplinary research combined aeronautics, mathematics, and fluid physics, covering topics such as the physics of jets and wakes, the energy of ocean currents and wind, ocean waves, the flight of birds and insects, how fish swim, and the locomotion of microorganisms.