Fitness trackers err in measuring calories

By Jennie Dusheck

Millions of people wear some kind of wristband activity tracker and use the device to monitor their own exercise and health, often sharing the data with their physician. But is the data accurate?

Frustrated by the lack of a good study on the accuracy of activity trackers, of these and other conditions in millions of people wear some kind of wristband activity tracker and use the device to monitor their own exercise and health, often sharing the data with their physician. But is the data accurate?

For decades, scientists have relied on mice, fruit flies and worms as genetic models, but despite their success, these organisms routinely fail to mimic many aspects of primate biology, including many human diseases, said Mark Krasnow, MD, PhD, professor of biology, behavior and medicine, at the School of Medicine.

An evaluation of seven devices in a diverse group of 60 volunteers showed that six of the devices measured heart rate with an error rate of less than 5 percent. The best performers were the Apple Watch, Basis Peak, Fitbit Surge, Microsoft Band, Mio Alpha 2, PulseOn and the Samsung Gear S2. Some devices were more accurate than others, and factors such as skin color and body mass index affected the measurements.

In contrast, none of the seven devices measured energy expenditure accurately, the study found. Even the most accurate device was off by an average of 27 percent. And the least accurate was off by 93 percent.

“People are basing life decisions on the data provided by these devices,” said Euan Ashley, DPhil, FRCP, professor of cardiovascular medicine, of genetics and of biomedical data science at Stanford. But consumer devices aren’t held to the same standards as medical-grade devices, and it’s hard for doctors to know what to make of heart-rate data and other data from a patient’s wearable device, he said.

A paper reporting the researchers’ findings was published online May 24 in the Journal of Personalized Medicine. Ashley is the senior author. Lead authorship is shared by graduate student Anna Shcherbina, visiting assistant professor Mikael Marriott, PhD, and senior research scientist Daryl Waggott.

Hard for consumers to know device accuracy

Manufacturers may test the accuracy of activity devices extensively, said Ashley, but it’s hard for consumers to know how accurate such information is or the process that the manufacturers used in testing the devices. So Ashley and his colleagues set out to independently evaluate activity trackers that met criteria such as measuring both heart rate and energy expenditure and being commercially available.

“For a lay user, in a non-medical setting, we want to keep that error under 10 percent,” Shcherbina said.

Sixty volunteers, including 31 women and 29 men, wore the seven devices while walking or running on treadmills or using stationary bicycles. Each volunteer’s heart rate was measured with an electrocardiograph. Metabolic rate was estimated with an instrument for measuring the oxygen and carbon dioxide in breath — a good proxy for metabolism and energy expenditure. Results from the wearable devices were then compared to the measurements from the two “gold standard” instruments.

“The heart rate measurements performed far better than we expected,” said Ashley, “but the energy expenditure measures were way off the mark. The magnitude of just how bad they were surprised me.”

The take-home message, he said, is that the data from these devices aren’t held to the same standards as medical-grade devices, and it’s hard for doctors to know what to make of the data provided by these devices.

By Nicole Feldman

With the abuse of opioids on the rise in the United States, Stanford researchers are concerned that increased HIV transmission from shared needles won’t be far behind.

“There’s an opioid epidemic in our country, and there’s a real public health crisis associated with injecting,” said Cora Bernard, a graduate student in management science and engineering. “We think it’s important to understand what investments give highest value because HIV prevention programs, and especially programs that reduce the prevalence of injection drug use, can have outsized, positive impact on individuals, families and public safety.”

Bernard is the lead author of a study that published online May 24 in PLOS Medicine. The senior author is Margaret Brandeau, PhD, professor of management science and engineering.

In July 2016, Bernard and her co-authors published a different study examining pre-exposure prophylaxis, or PrEP, a pill that reduces a person’s risk of infection when they come into contact with the HIV virus. The researchers found that PrEP was effective, but expensive. The new study examines alternatives that also reduce the risk of HIV infection but are more cost-effective. They created a model to determine how many quality-adjusted life years — a metric that incorporates both life expectancy and quality of life — a person could gain from four HIV prevention methods, and what those years would cost.

“The dynamics of HIV prevention and treatment are complex,” Brandeau said. “Our model allows us to evaluate the costs and benefits of different prevention strategies.”

By Ruthann Richter

The mouse lemur — the world’s smallest primate — has the potential to transform the field of genetics and serve as an ideal model for human disease. Researchers say.

By Euan Ashley and his team conducted a study to determine how accurately fitness trackers measure heart rate and energy expenditure.

Mouse lemurs are primates about twice the size of a mouse and live exclusively in Madagascar.

Working in a Stanford-funded lab on the island country, the scientists report that they have already identified more than 20 individual lemurs with unique genetic traits, including obesity, high cholesterol, high blood sugar, cardiac arrhythmias, progressive eye disease and motor and personality disorders. Their team evaluated the mouse lemur and began biochemistry.

The mouse lemur — the world’s smallest primate — has the potential to transform the field of genetics and serve as an ideal model for human disease. Researchers say. For decades, scientists have relied on mice, fruit flies and worms as genetic models, but despite their success, these organisms routinely fail to mimic many aspects of primate biology, including many human diseases, said Mark Krasnow, MD, PhD, professor of biology, behavior and medicine, at the School of Medicine.

“Mouse lemurs are a great model for human disease,” said Robert Siegel, assistant professor Mikael Mattsson, PhD, and senior research scientist Daryl Waggott.

Cost-effective ways to combat HIV risk among injection-drug users identified

The dynamics of HIV prevention and treatment are complex,” Brandeau said. “Our model allows us to evaluate the costs and benefits of different prevention strategies.”

A new study assesses prevention programs that could head off a resurgence of HIV and perhaps decrease the effects of the opioid crisis.
Inspiring Change Leadership, Spirit award winners announced

By Mandy Erickson

Four staff members have been selected as this year’s winners of the School of Medicine’s Anne G. Crowe Spirit Award or the Inspiring Change Leadership Award.

Spirit Award winners are selected for their outstanding dedication, initiative, motivation, positive attitude and customer service. This year’s recipients are Christine Hendricks, clinical program manager in the Department of Emergency Medicine, and Ana Mezynski, administrative associate for the Stanford-Surgery Policy Improvement Research & Education Center.

The Inspiring Change Leadership Award, which goes to staff members who have implemented processes that improve the school, was given to Kim Walker, learning program manager in the Office of Information Resources & Technology, and Mary Ayers, director of learning spaces for Educational Programs and Services and the Center for Immerse and Simulation-based Learning.

Each winner will receive $3,000.

Christine Hendricks

As the administrative staff for the Department of Emergency Medicine gathers around their award announcement, Hendricks had her camera out, all set to take a photo of the winner. “There I was, ready to take pictures of someone else, and it was me,” she said, laughing. It was typical of Hendricks, whose co-workers say is always ready to assist, always humble, always gracious. “You never feel like you’re interrupting her, though of course you are,” said Stephanie Hendrick, director of finance and administration for surgery and for emergency medicine. “She makes everyone feel that way.”

Hendricks, who has been with Stanford Medicine for 17 years, took on her current role five years ago. As manager of the administrative staff, she’s the glue that binds the team, the jill-of-all-trades who solves problems large and small. Among other tasks, she plans together the department newsletter and organizes meetings, celebrations, faculty and graduate ceremonies. “My job is basically making sure everyone is taken care of,” she said.

Her job exposes her to the work of the faculty, including international programs and other projects outside the walls of the Emergency Medicine Department. “Everyone does so many different things,” she said. “I’m always learning something new.”

The award brought her to tears, she said. “I’ve always appreciated in the department, but they remembered these small details that made a big impact. It was just a great feeling.”

Ana Mezynski

Knowing what her family means to her, Mezynski’s co-workers brought in her youngest child, her 1 ½-year-old daughter, when Mezynski’s award was announced. “I was really moved when I saw her,” Mezynski said, adding that her award is “a legacy for my two children.”

Mezynski plans events for the Stanford-Surgery Policy Improvement Research & Education Center, updates its website — which she developed — and oversees the office’s day-to-day needs, such as ordering supplies and maintaining the directory. She also assists the postdoctoral scholars and visiting scholars in the Division of General Surgery in applying for grants and obtaining visas.

As the support-staff member for a group of researchers, recently she has started collecting data herself. She produces a quarterly report of S-SPIRE’s accomplishments, such as papers published, grants awarded and consultations held with researchers who need help on their projects.

“I face a lot of challenges, and I like that about my job,” Mezynski said. “If I face a lot of challenges, then I do some research and I find the answer.”

The S-SPIRE Center is giving me a lot of opportunities to grow. It was just this sort of enthusiasm for learning that earned her the award. “She keeps it forward,” Edelman said. “She just pushes forward with whatever needs to be done, and comes up with ideas to make the process better. She has a huge work ethic.”

Kim Walker

For the online medical education courses they produce, Walker’s instructional design and production team at UBI goes way beyond training a camera on a professor in front of a whiteboard. Her team of animators, graphic designers and videographers film skills of actors playing physicians, create animated patient scenarios, and incorporate interactive activities such as role-playing. “We are being innovative and learning from every project,” Walker said.

The result, according to Mark Trenchard, director of academic and interactive technology, is “higher quality experiences and more effective content for our learners.”

“From day one, Kim looked above and beyond the way we were building the courses,” Trenchard said. “She inspires and is able to build high-performing and high-morale teams.”

When Walker started 2 ½ years ago, the courses were all continuing medical education for physicians. But her team is now producing courses for undergraduates, residents and health care workers around the globe.

The courses cover all aspects of medicine, including transgender health, opioid addiction and prescribing practices. Walker said the transgender health course “has had an incredibly positive impact on the people who have taken the course, an enlightening on what it means to be born into a life that doesn’t match your body.”

Walker said she’s honored to be part of such life-changing medical education. She’s also inspired by her production team: “I feel very blessed to work with so many wonderful, talented, hardworking, creative individuals, and to be able to touch people’s lives through medical education,” she said.

Mary Ayers

Every year, Ayers and her team face an enormous, Tetris-like task: scheduling the 90 classrooms for the School of Medicine. Policies and priority levels are discussed and the team is asked to find the fact that the number of spaces have doubled since the Center for Immersive and Simulation-based Learning opened in 2011.

This year, Ayers decided to stream-line the system before the schedule- ing began in June using a lean launch initiative. “Working with her “users” — those who ask for classroom space — Ayers’ team addressed the glitches in the system. They redesigned the request form and rewrote the instructions, among other improvements.

Along the way, Ayers tested any changes with the users and tweaked the system to make it even better. Once it was ready to go, she provided training for the new, improved system.

“Now, anyone requesting activities in the center better understands what we need, and we don’t have to go back to ask for more information,” Ayers said. “It makes much more sense.”

Susan Eller, assistant dean for immersive and simulation-based learning, said she believes of Ayers’ improvements, users will know the schedule two weeks earlier, allowing them more time to coordinate faculty and student schedules.

She added that Ayers’ 24 years of building relationships at Stanford were instrumental in the success of the lean launch: “People don’t like change, but so many people know and trust Mary they were willing to go with it.”

Ayers said that the scheduling re-launch has taught her and her colleagues to be more flexible and they’re planning to apply that knowledge to other functions, such as purchasing.

“The huge redesign process like the one we used, people feel like they have a voice,” she said. “It brings people in, which ultimately makes it work.”

Mary and Sash A. Spencer Center for vision research established

By Eileen DiFranco

Stanford University has announced the establishment of the new Mary M. and Sash A. Spencer Center for Vision Research, thanks to a generous gift pledged by Mary Spencer in honor of her late husband, Sash.

The new center, at the renowned Byers Eye Institute, will support innovative vision research and interdisciplinary collaborations across the Stanford campus.

Connecting research to care

The new Mary M. and Sash A. Spencer Center for Vision Research at Stanford is at the heart of an ambitious research program to restore sight, while offering patients new cures and treatments for the most challenging eye diseases, such as macular degeneration and glaucoma, which impact the lives of millions of people — often leaving them partially or wholly without sight.

The center will be at the forefront of the search for new diagnostics and therapies, both to prevent vision loss and to restore sight, while offering patients access to the latest research, technologies, clinical trials and treatments. It will build on the Byers Eye Institute’s reputation for innovation and patient-centered care.

Lloyd Minor, MD, dean of the Stanford School of Medicine, said he is “optimistic that with the establishment of this new center, significant advances in this highly complex science will be translated into improved patient care, transforming the lives of millions suffering from eye disease the world over.” Of Mary Spencer’s gift, he added. See VISION, page 3
Researchers’ technique pinpoints ‘partners in crime’ of cancer genes

By Krista Conger

Bateman and Robin. Sherlock Holmes and Dr. Watson. Fiction is full of dynamic duos that work together to accomplish amazing feats. When one partner is out of commission, the other steps in to make sure the job gets done. But if both are missing in action, the outcome is likely to be dire.

Cancers also often rely on pairs of complementary genes to keep their cells plugging along as they spin increasingly out of the bounds of normal cellular control. If one partner is mutated, the other springs to the rescue like Batman and Robin. Sherlock Holmes and Dr. Watson. Complementing one another between a mutation in a gene called IDH1 that has been known to be associated with leukemia and another gene called ACACA. They validated this synthetic lethal partnership by a variety of tests in laboratory grown cells and human tumor tissue.

“We have just scratched the surface of what we think we can learn with miSIL,” said Majeti. “It’s an incredibly powerful way to analyze large amounts of data to quickly identify relationships of potential interest, and it’s likely to make drug development much more efficient and quick.”

Interestingly, the researchers found that some synthetic lethal pairs predicted by MiSIL were found in multiple human cancers. In particular, the genes tended to be involved in pathways of broad biological significance, including the Krebs cycle, which releases energy stored in carbohydrates, fats and proteins; the DNA repair machinery used by cells to correct genetic mistakes; and the Wnt signaling pathway, which has been shown to be critical in normal development and many human cancers.

The team’s work is an example of Stanford Medicine’s focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Other Stanford co-authors are hematologist Steven Chan, MD; research assistant Damoum Tobabi; post-doctoral scholar Andreas Reinsich, MD, PhD; former CIRM Bridges intern David Cruz; resident Andy Chan, MD; and assistant professor of radiation oncology Erin Rankin, PhD.

Majeti is a member of Stanford’s Bio-X, the Stanford Cancer Institute, the Stanford Institute for Stem Cell Biology and Regenerative Medicine and the Stanford Child Health Research Institute. Dill is a member of Bio-X.

The research was supported by the National Institutes of Health, the New York Stem Cell Foundation, the Leukemia and Lymphoma Society and a CJ Martin Overseas Fellowship. Majeti, Dill, Sinha and Thomas have filed an international patent based on the findings in this paper. Stanford’s departments of Medicine and of Computer Science also supported the work.

Ravi Majeti and his collaborators have developed an algorithm to find new pathways that may help them better target cancer cells.
The key to transforming lives through precision health, experts at the conference said, is the integration of diverse kinds of data sets, including sequencing and imaging data, gene expression data and also behavioral data, such as that from fitness trackers. Finding ways to combine and explore such cross-disciplinary data sets will be key to the focus on prevention, they said.

“Experts draw on prediction and prevention. But that’s all changing today, because of the work being done in this room, Advocating greater focus on prevention”

Eric Topol, MD, a professor of genomics at the Scripps Research Institute, gave a passionate talk in which he criticized U.S. medical care and advocated for a greater focus on prevention. The key, Topol said, is moving “from where we have diabetes can monitor their healthy individuals who don’t have diabetes can monitor their blood pressure through your watch,” said Topol, adding that it’s possible to do so “in real time, that you can watch patients provide blood sugar levels that healthy individuals who don’t have diabetes can monitor their blood glucose as a preventive measure.”

Preventive health at population level

Apply such measurements to 10,000 people, as in the baseline study by Verily, Duke and Stanford, or a million people, as planned for Precision Medicine Initiative, and you can start to see patterns, experts at the meeting said. Both researchers and clinicians can ask and answer specific questions about which factors are associated with which outcomes. Such population-level approaches to preventive health care are inspiring more interest in health care inequity and biases in research, some speakers said. Although about two-thirds of people living in the United States are of European ancestry, participants in medical research trials were 96 percent European-American in 2016; by 2026, it was 81 percent European-American, according to Usha Menon, PhD, RN.

Menon, a professor and associate dean for research and global advances at the University of Arizona, suggested a number of strategies for increasing diversity within biomedical research, including, for example, engaging citizen advisory boards in the design of studies and targeting messages. “We have been telling people to stop smoking — for how long?” she asked. “The key is to target and tailor to culture, to what is most relevant to that individual.”

Topol and cardiologist Robert Harrington, MD, professor and chair of medicine at Stanford, discussed the possibility that letting data streams and algorithms do much of the work of examining, monitoring and diagnosing patients could give practicing physicians a much greater opportunity to form the intimate bond that doctors once had with patients. Harrington brought up Stanford’s Presence, a center whose focus is “trying to bring some of the intimacy and humanity back into medicine,” he said.

Project Baseline

Verily, one of Alphabet’s life sciences units, recently launched Project Baseline with the goal of enrolling 10,000 participants who will share their biomedical data. A long-term goal of the project is to set up scalable and standardized tools for acquiring, organizing and analyzing data, said Jessica Mega, MD, MPH, Verily’s chief medical officer, during a talk at the conference. Formerly called Google Life Sciences, Verily has a variety of projects in development, from wearable sensor devices to big data studies.

“We also want to create a test bed for a number of new tools and devices that are out there,” Mega said. For example, glucose and atrial fibrillation monitoring devices can provide a stream of data that’s valuable to patients and their doctors, valuable to researchers and valuable to whole populations that can eventually benefit from the resulting insights.

“To be sure that’s the known signal,” Mega said. “As each of us is sitting here, in this room, we are preparing our heart rate and our galvanic skin response. That’s digital exhaust all around us that we’re not capturing. Some of it may be actionable, some of it may not be. But until we look we won’t know.”

Project Baseline, Mega said, will serve as a test bed to think about the next generation of tools needed to understand human physiology and variability. The holy grail, she said, is to get in front of disease to know ahead of time that an individual needs help taking preventive measures.

“The job of the scientist is to understand the next generation of tools needed to understand human physiology and variability.”

For example, glucose and atrial fibrillation monitoring devices can provide a stream of data that’s valuable to patients and their doctors, valuable to researchers and valuable to whole populations that can eventually benefit from the resulting insights.
Drug for refractory psoriatic arthritis shows promise in large clinical trial

By Bruce Goldman

In a pivotal phase-3 clinical trial led by a School of Medicine investigator, patients with psoriatic arthritis for whom standard-of-care pharmaceutical treatments have had no lasting effect experienced a significant reduction in symptoms, including joint tenderness and swelling, when they were given a new drug under study.

The randomized, double-blind, placebo-controlled trial was conducted at 109 centers in 10 countries and involved more than 300 adults for whom available biologic drugs — the standard of care for this painful autoimmune condition — had lost their efficacy or lacked it in the first place.

Results of the trial were published online May 24 in The Lancet.

Left untreated or treated unsuccessfully, psoriatic arthritis can progress to induce severe joint and bone damage and functional disability, said Mark Genovese, MD, a professor of immunology and rheumatology at Stanford and the study’s senior author.

In the trial, known as SPIRIT-P2, 314 patients received regular injections of either a biologic drug, ixekizumab, or a placebo for 24 weeks. The trial was sponsored by Eli Lilly & Co., the drug’s manufacturer.

Treatment with ixekizumab resulted in more than 50 percent of the participants having at least a 20 percent reduction in the number of tender and swollen joints, significantly outperforming the placebo, said Genovese. Few serious adverse events were reported for patients receiving the drug, or the placebo, he said.

The search for lasting relief

About one in 200 adults in developed countries lives with psoriatic arthritis. Like the more common rheumatoid arthritis, psoriatic arthritis affects nearly 2 percent of the population. Psoriatic arthritis is an autoimmune disease whose symptoms — including stiffness, pain and swelling of the joints — typically emerge between the ages of 30 and 50.

The two syndromes differ, though, in their constellation of symptoms. For example, psoriatic arthritis manifests most often in the lower extremities and is associated with the autoimmune skin condition called psoriasis, in which raised red, scaly patches appear on the skin. Although psoriatic rashes most often precede the onset of the arthritic stage, the reverse can also be the case.

Three of the 10 top-selling drugs in the United States in dollar sales — adalimumab, etanercept and infliximab — are biologics prescribed for psoriatic arthritis as well as for the more common rheumatoid arthritis.

They block the action of a pro-inflammatory substance called tumor necrosis factor. Secreted by various immune cells, TNF stimulates the immune response and accompanying inflammation.

However, despite the availability of TNF inhibitors, “only about half of psoriatic arthritis patients who are given TNF inhibitors get better,” said Genovese. Although the ultimate cause of the disease remains unknown, there was a good clinical rationale for hoping it might be responsive to ixekizumab. For the last decade or so, Genovese said, another pro-inflammatory substance called IL-17 has been drawing the attention of immunologists focusing on psoriasis and psoriatic arthritis.

Izekizumab works by blocking IL-17. The drug, an injectable monoclonal antibody, is already commercially available for the treatment of psoriasis, for which it has been remarkably effective, said Genovese. And in earlier Lilly-sponsored phase-3 trial, ixekizumab was shown to be effective for psoriatic arthritis patients who had not yet been treated with biologic drugs such as TNF inhibitors.

The Lilly-sponsored trial confirmed the drug’s potential.

Of the 198 patients given ixekizumab and the placebo, 33.2 percent of those getting the drug every four weeks and 23.3 percent of those getting the real drug every four weeks were judged to have met the trial’s specified clinical endpoint — at least a 20 percent reduction in the number of tender and swollen joints — the response rate among those getting the real drug every four weeks was 53.3 percent. Those getting the drug every two weeks didn’t do any better and were slightly more prone to side effects, such as a mild reaction at the injection site.

Although any treatment that works by blocking the immune system’s ability to mount an inflammatory response should be carefully monitored for its potential to render the body vulnerable to infectious disease, there were few observed differences in this category between recipients of placebo versus active drug given every four weeks, Genovese said.

Lilly has filed for approval of the drug by the U.S. Food and Drug Administration. Genovese has served as a consultant to Lilly.

Other co-authors of the study are affiliated with multiple institutions in diverse locations, including the University of Queensland, in Australia; Guy’s & Thomas’ NHS Foundation Trust, in London; St. Luke’s International University, in Tokyo; Memorial University, in Newfoundland; Canada; Lapeyronie Hospital, in Montpellier, France; Charité University Medicine Berlin, in Germany; and Eli Lilly and Company, in Indianapolis.

Stanford’s Department of Medicine also supported the work.

Karl Deisseroth wins 4 million euros Fresenius Research Prize

By Bruce Goldman

Karl Deisseroth, MD, PhD, a Stanford professor of bioengineering and of psychiatry, has won the 2017 Fresenius Research Prize for his pioneering work in two distinct biomedical technologies — optogenetics and hydrogel-tissue chemistry — and for exploring his clinical specialty, depression, at the level of its underlying neural circuitry.

Deisseroth, who holds the D.H. Chen Professorship and is a Howard Hughes Medical Institute investigator, accepted the award May 31 at a ceremony in Berlin. He also gave a talk, followed by a symposium, on June 1.

The prize is presented every four years to a single scientist by the Else Kröner-Fresenius Foundation in Germany. The prize — the world’s most valuable for scientific achievement — comes with a cash award of 4 million euros ($4.47 million). 3.5 million euros for Deisseroth’s laboratory, and 500,000 euros for his personal use.

Deisseroth is only the second scientist to receive the prize, which was launched in 2013 and recognizes achievement in medical research. The 2013 recipient was Yale University immunologist Russel Medzhitov, PhD.

“We are proud that Karl has been recognized for his groundbreaking discoveries,” said Stanford University President Marc Tessier-Lavigne, PhD. “Application of his pioneering technologies by scientists worldwide is accelerating understanding and development of therapies for debilitating neurological and psychiatric disease. His research has provided deep insights into circuit mechanisms of depression. Karl’s work exemplifies how brilliant scientific research can improve lives and move our world forward.”

Many honors to his name

Deisseroth’s scientific achievements have won him many other honors, including the Harvey Prize, to be awarded this June; the Massy Prize (2016); the Dickson Prize (2015); the John H. Florence Breakthrough Prize (2015); the Keio Medical Science Prize (2014); and the Richard Lounsbery Award (2013).

Lloyd Minor, MD, dean of the Stanford School of Medicine, noted that Deisseroth continues to see psychiatric patients on a regular basis. “Karl speaks of the profound impact it’s had on him to know and treat patients with psychiatric disorders and to see firsthand the debilitating nature of these disorders and their effects on patients and their families,” Minor said. “His research promises to one day enable millions of people with mental illness to be treated much more effectively than they are today.”

Pioneered in Deisseroth’s lab between 2004 and 2009, optogenetics is a technology that allows scientists to precisely manipulate nerve-cell activity in freely moving animals. Genes encoding light-sensitive proteins, derived from microorganisms, are inserted into targeted nerve cells. As a result, these cells’ signaling activity can be turned on or off with the flick of a switch by a pulse of laser light, delivered through a hair-thin microelectrode that has been implanted into the animal’s brain. Scientists can deduce the role played by particular nerve cells, relays and circuits by observing the effects of these manipulations on the animal’s behavior.

Making tissue transparent

Hydrogel-tissue chemistry, developed in Deisseroth’s lab between 2009 and 2016, renders intact tissue samples — and even entire organs of small animals — both transparent to light and permeable to bulky molecular probes. It involves replacing the tissue’s fatty substances, which impede transparency, with a hydrogel matrix that not only permits the transmission of light but also permits the transit of large molecules, such as labeled antibodies or oligonucleotides, which can pinpoint the presence of particular proteins or DNA sequences on or in the tissue’s constituent cells.

With the help of the sophisticated methodologies developed in his lab, Deisseroth has co-authored many papers on the underpinnings of depression. He and his team have thus been able to better study neural circuits implicated in different aspects of this multifactorial disorder, such as anhedonia (the failure to experience pleasure) versus hopelessness (the inability to rise to a challenge).

Deisseroth’s lab is now taking advantage of high-powered data-collection, data-storage and data-analysis techniques to explore new questions.

“We’re starting to do whole-brain analysis, collecting information from every cell in the brain and getting insights from not just neurons but glia,” he said.

It’s rare for a researcher to achieve even one breakthrough technology. The development of two such ground-breaking, Nobel Prize-winning cases, is undeniably considered remarkable. Still, he said, “Our primary goal isn’t to develop new methods for their own sake, but to design techniques that help us answer the questions we want to answer. We’re just biologists.”
Margaret Brandeau
data. They welcome others to upload
open to the research community, so they
through proxy calculations.
penditure must be measured indirectly
one's fitness level, height
energy expenditure is
an algorithm that would
clinical measures," she
are making assumptions
expenditure, they said.
measures were so far off.
Heart-rate data reliable
ries your device says you burned is a re-
said, is that a user can pretty much rely

"He was extraordinarily warm and
nonjudgmental," said Gesundheit, who
first met Vosti nearly 40 years ago, when
Geundheit said. "For Vosti, Stanford turned into a fam-
day of the university who not only
'Committed citizen of the university'
He was an extraordinarily commit-
ted citizen of the university not only who
in our hospital but lived on campus." Ge-
said. For Vosti, Stanford turned into a fam-
ty. He earned his bachelor's and
medical degrees from the university, and
and his brother also earned a Stanford
medical degree. His four daughters
stained Stanford as undergraduates, and
two of his grandchildren have earned degrees from
Vosti turned a visual im-
partment — he essentially
became legally blind — to
his advantage. "It's made
us a better listener," he
vearly in a 1984 interview.
In 2013, Vosti was hon-
ored as the first recipient
at the Stanford University
Medical Center Alumni
Association’s Reach, Inspire, Serve
and Engage Award, which recognizes indi-
nuals who have demonstrated excep-
tional dedication to Stanford Medicine
and the alumni community through acts
of leadership, volunteerism, mentoring
and teaching.
In addition, the Division of Infectious
Diseases presents an annual award in
his name: The Kenneth Vosti Teaching
Award for Excellence in Teaching.
"Kenneth Vosti's contribution to Stanford —
as an educator, as a re-
searcher and as a caring assistant —
was immense," said Lloyd Minor, MD,
dean of the School of Medicine. "He ad-
vanced our understanding of infectious
disease and of the medical-training pro-
ceses. He’s one of the very few — if not all miss him."
Modesto native
Born Sept. 15, 1928, in Modesto,
California, Vosti grew up on ranches in
Salida and Modesto. He never outgrew his
boyhood love of wildfowling and outdoor act-
ivities. After two years at Modesto Ju-
nior College, he matriculated at Stanford in 1949, and
graduating in 1950 with a bachelor's degree in medical
science, moved to the Stan-
ford School of Medicine. He
earned an MD in 1953. He
completed an internship, as
well as a fellowship in infec-
tious diseases, at the University
of Illinois Research and Educa-
tion Hospital and a residency
the West Side Veterans Admin-
istration Medical Center in Chicago.
In 1957, Vosti joined the U.S. Army.
Assigned to the Walter Reed Medical
Research Unit, he drove a new, red-and
white Chevrolet Bel Air from Chicago to Fort
Derrict, in Maryland, to report for
duty. The next year, he met and became
engaged to Anne Merrick, a graduating
student at nearby Floyd College. They
married in 1959.
Recruited by Stanford that year, Vosti
joined the medical staff of the Division
of Infectious Diseases as an instructor and
founder member. In 1962, he
became an associate professor, and Lloyd
Minor, MD, was appointed chief of the division,
as well as assistant Stanford Hospital epide-
nemiologist. He was promoted to associ-
ate professor in 1967 and granted a
full professorship and directorship of the
Clinical Microbiology Laboratory in 1972.

effects of the interventions, singly
and in combination, and determine
what programs would be effective and
cost-effective in preventing the spread
of HIV among persons who
inject drugs."

Prevention models studied
Of the prevention programs simulated
in the model, the authors found that
opioid agonist therapy, or OAT, was
the most cost-effective. OAT replaces drugs
like heroin with a prescription that pro-
vides similar effects under safer condi-
tions. Methadone and buprenorphine
maintenance therapies are the most
common.
Needle-syringe exchange programs,
in which people swap their dirty needles
for clean ones, were the next most
cost-effective option. This was
found by test-and-treat programs, which identify
persons with a high risk of contracting
HIV, test them for the virus and treat
them before the disease has much chance
to spread — both within their own
bodies and to others who are exposed.

The study estimated that OAT can
also successfully reduce HIV, but not in
a cost-effective way. The authors write
that the other three combination
strategies cost less than
$50,000 per quality-adjusted life
year (QALY) during 20 years of
care. Mean duration of
life with HIV, based on
those treated, averaged
4.7 years.

"We started out thinking about this as
an HIV problem, but we realized that
the majority of health benefits actually
comes from reducing injection drug use
and improving quality of life for drug us-
ers," said Bernard. "This is why we found
OAT to be the highest-value
investment."

Bernard and her co-authors believe
that employing techniques like OAT
could help reduce the effects of the
opioid crisis. The authors project that expanding OAT
access could decrease the size of the injec-
tion population by up to 23 percent over
20 years for treatment programs and
up to 37 percent over 20 years for more
extensive program expansions.

OAT 'highest-value investment'

"OAT's value is off the charts," said
Bennett. "We should push for
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"It's not just about reducing HIV risk
and improve the quality of life for those
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lemurs have great potential for our understanding of primatology, and also health, because, in a way, the way that fruit flies and mice over the last 50 or 40 years have transformed our understanding of developmental biology and many other areas of biology and medicine, Krasnow said. “Some of the most fascinating and important questions that need to be answered are primate-specific. For those, we really need something besides humans to complete the work that has been done in fruit flies and mice.”

A paper describing the researchers’ findings was published last year in Nature by the Krasnow lab along with other scientists studying lemurs, including those at the Centre ValBio near the Ranomafana National Park in Madagascar, who have been examining lemur biology and ecology for decades. During periodic visits to the island, Krasnow and his colleagues learned how to catch brown mouse lemurs in the rainforest just outside the research station, using a tiny banana slice inside a trap as a lure. The scientists then tagged and photographed each animal, gave them a thorough physical examination, analyzed them for behavioral issues and abnormalities, and removed a drop of blood for detailed genetic and serum studies. The animals then were released back into the wild so the researchers could follow them over time to see how their environments might influence their progress and health. In 2013, Stanford built a sophisticated molecular biology lab within the ValBio complex, where these studies could be carried out.

Distinctive personalities
Lemurs have distinctive personalities, Krasnow said, and the researchers gave each one a name, based on his or her looks or behavior. For instance, one was named Feisty for his unusually aggressive nature; most lemurs are docile.

The work has led to a whole new way of doing genetic studies, said Krasnow, who is also a Howard Hughes Medical Institute investigator. Instead of using the traditional method of introducing genetic mutations into mice to create “knockout” mice — or animals with customized genes — they found they could actually find naturally occurring variants among animals in the wild. Moreover, in working with lemurs in their native habitats, the researchers could better understand how genetic and environmental factors influence the relationship between genes and the environment.

For instance, instead of introducing mutations in mice or fruit flies, we are doing something much more similar to what is done in humans,” he said. “We are looking at all the wonderful genetic variation already existing in nature, since we have millions of lemurs out there. We calculate that most ‘knockout’ mutations are already present in nature, and all we have to do is find them. And burdening the cost of sequencing a genome is rapidly dropping, it’s now possible to sequence the genomes of thousands of mouse lemurs to find mutations of interest.”

In doing so, the researchers could accomplish in a few years for a tiny fraction of the cost what the International Knockout Mouse Consortium accomplished in 10 years, at a cost of nearly $1 billion, he said. But the project could use some additional staff, as the process of capturing the animals and screening them in the laboratory is labor-intensive, he said. And his colleagues have come up with a multipurpose solution that will contribute to the local educational system helping with conservation efforts in Madagascar, whose habitats are threatened by farming, mining and logging interests, he said.

Help from students
The group is developing a science curriculum for use in Malagasy schools in which students learn about biology by exploring the rich environment right outside their school houses. Among the instructors is Manu Prakash, PhD, assistant professor of bioengineering at Stanford and a pioneer in the field of “as- sembly science,” who has brought his powerful $1 paper microscopes to Madagascar and taught students how to explore the microscopic world in which they live, including the lice in their hair, the pathogens in their water and the disease-causing parasites in their environ- ment. The curriculum was first introduced among university students, some of whom now are screening lemurs at the Stanford lab in Madagascar.

“We saw this as an opportunity because we are going over there to study the unique animals and biology and ecology of Madagascar, which is unsurpassed in the world,” Krasnow said. “It is the No. 1 hotspot for biodiversity, but most of the students don’t realize what they have in their backyards because they are being taught from textbooks and from teachers who have learned from Europe.”

He said the researchers hope to expand scientific curricula at all levels of education, helping train the Malagasy scientists of the future and build scientific capacity in the country, all while the creating an appreciation among the local population of the need to understand and preserve lemurs and other species for the future.

“We are trying to do this in a way that is respectful and will help the lemurs and the people of Madagascar, while enlightening many aspects of primate biology and behavior,” Krasnow said.

The researchers plan to make the genetic sequencing and phenotyping information they obtain from the lemurs publicly available so that researchers around the world can take advantage of this trove of knowledge, Albertelli said.

Other Stanford co-authors are graduate students Maya Krasnow and Stephen Chang, former undergraduate student Jason Willick, former research assistant Jingxiang Zhang, and Joseph Pendleton. (Maya Krasnow and Willick are two of the former high school interns who began work on the project in 2009.)

Researchers at the University of Antananarivo and Auburn University also co-authored the study. The research was supported by the Howard Hughes Medical Institute and the Vero Mouton Wall Center of Stanford University.

Stanford’s Department of Biochemistry also sup- ported the work.
Nancy Morioka-Douglas wins professionalism award

Nancy Morioka-Douglas, MD, clinical professor of medicine, was honored with the Dr. Augustus A. White and Family Faculty Professionalism Award.

The award recognizes outstanding work in enhancing the effectiveness of under-represented minorities in the university community through research, education, mentoring or service.

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