Bad connection: When AI chatbots should hang up the phone

New tools reveal the secrets of aging (and whether we can reverse it)

It's okay! Stop worrying about your AI footprint

Bundle of joy, built to spec

A new crop of genetic testing companies promise to let parents pick a baby that's perfect in every way, from health to eye color to IQ

INTELLIGENCE: STILL SMARTER THAN AI
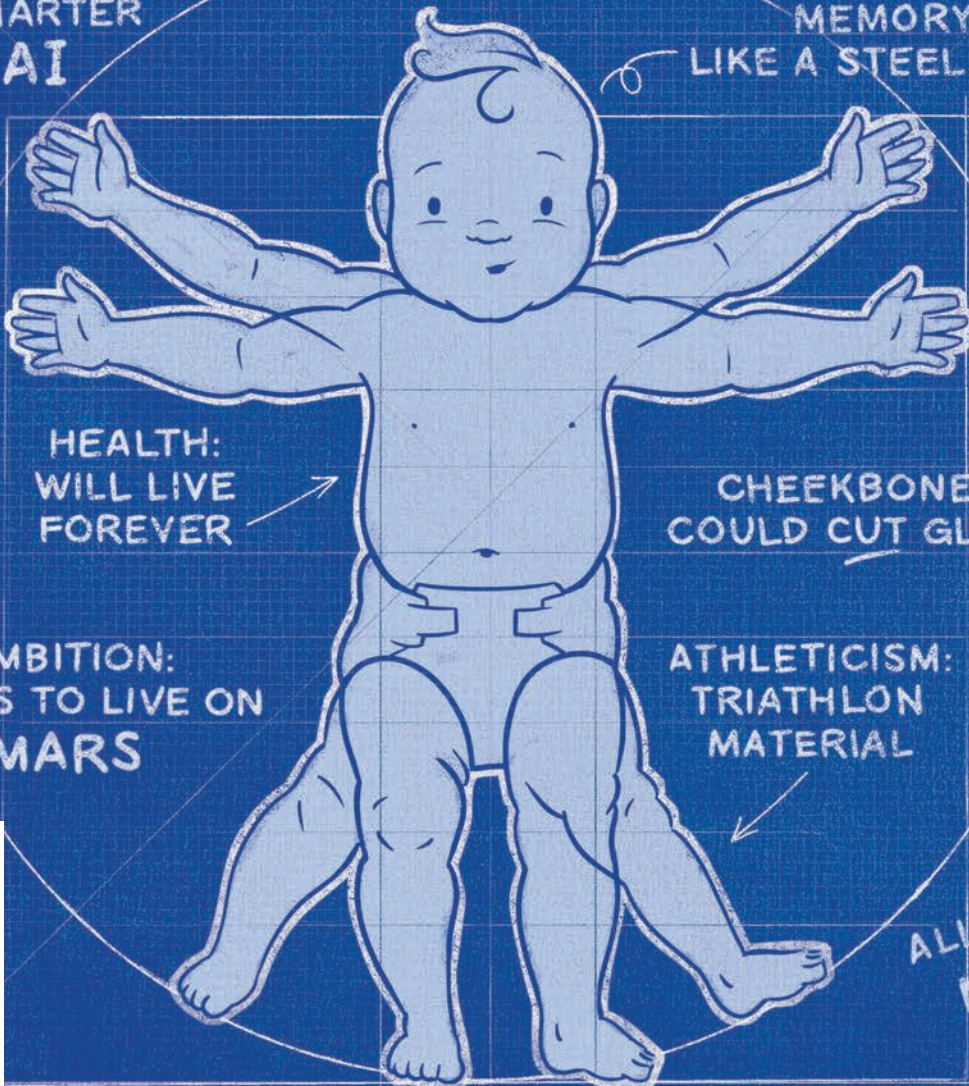
MEMORY: LIKE A STEEL TRAP

HEALTH: WILL LIVE FOREVER

CHEEKBONES: COULD CUT GLASS
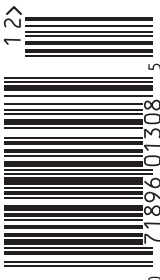
AMBITION: WANTS TO LIVE ON MARS

ATHLETICISM: TRIATHLON MATERIAL

ALLERGIES: NONE

Social Media Pakistan 0342-4938217

As the current steward of a storied 126-year-old publication connected to one of the most prestigious universities in the world, I'm very aware of my responsibility to safeguard its reputation for accuracy and its hard-won credibility.

We always strive to get the facts right. We have a number of processes in place to ensure that we live up to the highest journalistic standards. Nonetheless, sometimes we still get it wrong. I believe that an important part of maintaining our credibility is to own up to those mistakes when they happen. I'm writing to do just that.

In our September/October issue, *MIT Technology Review* published a story titled "The church will see you now." It centered on the company Gloo, which makes a technology platform for churches and the broader faith ecosystem. In the aftermath of its publication, we became aware of questions about certain parts of the story. We then hired an independent auditor to investigate the article and its claims. What the audit found was that the piece both had errors of fact and made assertions that we couldn't verify. To put it simply, the story did not live up to our editorial standards and practices.

As a result, we took the story offline, and in its place we put up a note explaining why. But, of course, we had also published it here, in this magazine. Many of you may not visit our website at all. (Although we would certainly like you to!) And so I wanted to make sure you heard about this failure directly from me. And to apologize.

This has been a humbling experience. I take great pride in making sure our stories are rigorously reported and edited. Our credibility as a publication, especially at a time when trust in the media is abysmal, is of paramount importance to me. Yet this story had

failures at multiple levels in our editorial process.

We deeply regret the errors and have been reevaluating our editorial processes to ensure that they do not reoccur: We've updated our editorial guidelines for writers, we're making changes to our fact-checking guidelines, and we're crafting entirely new guidelines for editors. We were already operating above industry standards. But we can always do better. And going forward, we intend to set our sights even higher, and to put even more processes and structures in place that will do more to prevent mistakes like this one from happening again.

Thank you for taking the time to read *MIT Technology Review*. Thank you for trusting us. I do hope this letter will help to keep that trust.

Mat Honan
is editor in
chief of
MIT Technology
Review.

ROBYN KESSLER

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"When it's discovered that elites are doing it privately ... the dominoes are going to fall very, very quickly." –p. 28

Front

The body

Back

BY ELISSAVETA M. BRANDON

Cities of slime

What a single-celled organism can teach us about our cities.

It is a yellow blob with no brain, yet some researchers believe a curious organism known as slime mold could help us build more resilient cities.

Humans have been building cities for 6,000 years, but slime mold has been around for 600 million. The team behind a new startup called Mireta wants to translate the organism's biological superpowers into algorithms that might help improve transit times, alleviate congestion, and minimize climate-related disruptions in cities worldwide.

Mireta's algorithm mimics how slime mold efficiently distributes resources through branching networks. The startup's founders think this approach could help connect subway stations, design bike lanes, or optimize factory assembly lines. They claim its software can factor in flood zones, traffic patterns, budget constraints, and more.

"It's very rational to think that some [natural] systems or organisms have actually come up with clever solutions to problems we share," says Raphael Kay, Mireta's cofounder and head of design, who has a background in architecture and mechanical engineering and is currently a PhD candidate in materials science and mechanical engineering at Harvard University.

As urbanization continues—about 60% of the global population will live in metropolises by 2030—cities must provide critical services while facing population growth, aging infrastructure, and extreme weather caused by climate change. Kay, who has also studied how microscopic sea creatures could help researchers design zero-energy buildings, believes nature's time-tested solutions may offer a path toward more adaptive urban systems.

Officially known as *Physarum polycephalum*, slime mold is neither plant, animal, nor fungus but a single-celled organism older than dinosaurs. When searching for food, it extends tentacle-like projections in multiple directions simultaneously. It then doubles down on the most efficient paths that lead to food while abandoning less productive routes. This process creates optimized networks that balance efficiency with resilience—a sought-after quality in transportation and infrastructure systems.

The organism's ability to find the shortest path between multiple points while maintaining backup connections has made it a favorite among researchers studying network design. Most famously, in 2010 researchers at Hokkaido University reported results from an experiment in which they dumped a blob of slime mold onto a detailed map of Tokyo's railway system, marking major stations with oat flakes. At first the brainless organism engulfed the entire map. Days later, it had pruned itself back, leaving behind only the most efficient pathways. The result closely mirrored Tokyo's actual rail network.

Since then, researchers worldwide have used slime mold to solve mazes and even map the dark matter holding the universe together. Experts across Mexico, Great Britain, and the Iberian peninsula have tasked the organism with redesigning their roadways—though few of these experiments have translated into real-world upgrades.

Historically, researchers working with the organism would print a physical map and add slime mold onto it. But Kay believes that Mireta's approach, which replicates slime mold's pathway-building without requiring actual organisms, could help solve more complex problems. Slime mold is visible to the naked eye, so Kay's team studied how the blobs behave in the lab, focusing on the key behaviors that make these organisms so good at creating efficient networks. Then they translated these behaviors into a set of rules that became an algorithm.

Slime mold projections form patterns in a petri dish, where nutrients have been depleted so that the organism is forced to optimize its networks.

Some experts aren't convinced. According to Geoff Boeing, an associate professor at the University of Southern California's Department of Urban Planning and Spatial Analysis, such algorithms don't address "the messy realities of entering a room with a group of stakeholders and co-visioning a future for their community." Modern urban planning problems, he says, aren't solely technical issues: "It's not that we don't know how to make infrastructure networks efficient, resilient, connected—it's that it's politically challenging to do so."

Michael Batty, a professor emeritus at University College London's Centre for Advanced Spatial Analysis, finds the concept more promising. "There is certainly potential for exploration," he says, noting that humans have long drawn parallels between biological systems and cities. For decades now, designers have looked to nature for ideas—think ventilation systems inspired by termite mounds or bullet trains modeled after the kingfisher's beak.

Like Boeing, Batty worries that such algorithms could reinforce top-down planning when most cities grow from the bottom up. But for Kay, the algorithm's beauty lies in how it mimics bottom-up biological growth—like the way slime mold starts from multiple points and connects organically rather than following predetermined paths.

Since launching earlier this year, Mireta, which is based in Cambridge, Massachusetts, has worked on about five projects. And slime mold is just the beginning. The team is also looking at algorithms inspired by ants, which leave chemical trails that strengthen with use and have their own decentralized solutions for network optimization. "Biology has solved just about every network problem you can imagine," says Kay. ∎

Elissaveta M. Brandon is a regular contributor to Fast Company *and* Wired.

BY COLLEEN DE BELLEFONDS

New, noninvasive tests are emerging for endometriosis

The tests could help women with the condition, who often suffer for many years undiagnosed.

Shantana Hazel often thought her insides might fall out during menstruation. It took 14 years of stabbing pain before she ultimately received a diagnosis of endometriosis, an inflammatory disease where tissue similar to the uterine lining implants outside the uterus and bleeds with each cycle. The results can include painful periods and damaging scar tissue. Hazel, now 50 and the founder of the endometriosis advocacy organization Sister Girl Foundation, was once told by a surgeon that her internal organs were "fused together" by lesions resembling Laffy Taffy. After 16 surgeries, she had a hysterectomy at age 30.

Hazel is far from alone. Endometriosis inflicts debilitating pain and heavy bleeding on more than 11% of reproductive-age women in the United States. Diagnosis takes nearly 10 years on average, partly because half the cases don't show up on scans, and surgery is required to obtain tissue samples.

But a new generation of noninvasive tests are emerging that could help accelerate diagnosis and improve management of this poorly understood condition.

Within the next year, several companies, including Hera Biotech, Proteomics International, NextGen Jane, and Ziwig, aim to launch endometriosis diagnostics in the United States. Their tests analyze biomarkers—biological molecules (in this case, mRNA, proteins, or miRNA) that signal a disease or process like inflammation—in samples of endometrial tissue, blood, menstrual blood, and saliva.

These tests could help patients get an accurate diagnosis quickly and noninvasively, speeding access to endometriosis treatments and management strategies, including surgery, hormonal medications, and pelvic floor physical therapy. Early identification could also help doctors manage conditions for which people with endometriosis face increased risk, including cardiovascular disease, heart attack, and stroke. Endometriosis can also make it difficult to become pregnant. Because half of women with infertility have endometriosis, identifying and managing the condition sooner may improve fertility and IVF outcomes.

Endometriosis biomarker tests rely on a range of technologies, including single-cell RNA sequencing and mass spectrometry

that can identify thousands of proteins simultaneously. "These instruments are very good at precisely identifying a molecule, in [our] case a protein. And what's changed over the last five or 10 years is they've gotten more sensitive," says Proteomics cofounder Richard Lipscombe. Machine learning can also now efficiently sift through large quantities of the resulting data.

So far only Ziwig has a test on the market. It uses a saliva sample to identify biomarkers in people with endometriosis symptoms and is currently sold in 30 countries. In France, where the company is based, the cost is fully covered by national health insurance.

Some researchers are concerned that Ziwig's test might not be accurate when it's used in larger and more diverse populations; its interim validation study included just 200 people. "I'm not saying this doesn't work. I just would want to see more validation," says Kathryn Terry, an associate professor of epidemiology and gynecology at Harvard. Company representatives say they're preparing to publish results on 1,000 patients in the near future, adding that French authorities had access to the full data set before approving government reimbursements.

These tests are emerging as momentum is building to tackle endometriosis. Over the past five years, France, Australia, the United Kingdom, and Canada have launched ambitious endometriosis initiatives.

> Endometriosis inflicts debilitating pain on more than 11% of reproductive-age women in the US. New tests could help make a diagnosis quickly and noninvasively, speeding access to treatment.

The potential benefits are not just on the individual level: In 2025, the World Economic Forum estimated that earlier diagnosis and improved treatment to address the chronic pain, infertility, and depression caused by endometriosis could add at least $12 billion to global GDP by 2040.

As these biomarker tests are further developed, it's possible their results could inform such treatments. Today surgery is often used to excise the lesions. The process can take as long as seven hours, and even then, lesions frequently form again. Jason Abbott, chair of Australia's National Endometriosis Clinical and Scientific Trials Network, compares endometriosis management today to breast cancer care 30 years ago. Whereas doctors once prescribed surgery for all breast cancer patients, targeted treatments now address the underlying cell processes that help tumors grow and spread. Endometriosis tests could likewise help researchers categorize the condition's distinct subsets and understand their underlying inflammatory pathways—information drugmakers could use to develop targeted treatments that keep it in remission. ■

Colleen de Bellefonds is a science journalist based in Paris.

BY STEPHANIE ARNETT

3 Things

TR's photo editor spends her time reading, journaling, and bird-watching.

Dungeon Crawler Carl, by Matt Dinniman

This science fiction book series confronted me with existential questions like "Are we alone in the universe?" and "Do I actually like LitRPG??" (LitRPG—which stands for "literary role-playing game"—is a relatively new genre that merges the conventions of computer RPGs with those of science fiction and fantasy novels.) In the series, aliens destroy most of Earth, leaving the titular Carl and Princess Donut, his ex-girlfriend's cat, to fight in a bloodthirsty game of survival with rules that are part reality TV and part video game dungeon crawl. I particularly recommend the audiobook, voiced by Jeff Hays, which makes the numerous characters easy to differentiate.

Journaling, offline and open-source

For years I've tried to find a perfect system to keep track of all my random notes and weird little rabbit holes of inspiration. None of my paper journals or paid apps have been able to top how customizable and convenient the developer-favorite notetaking app Obsidian is. Thanks to this app, I've been able to cancel subscription services I was using to track my reading habits, fitness goals, and journaling—and I also use it to track tasks I do for work, like drafting this article. It's open-source and files are stored on my device, so I don't have to worry about whether I'm sharing my private thoughts with a company that might scrape them for AI.

Bird-watching with Merlin

Sometimes I have to make a conscious effort to step away from my screens and get out in the world. The latest version of the birding app Merlin, from the Cornell Lab of Ornithology, helps ease the transition. I can "collect" and identify species via step-by-step questions, photos, or—my favorite—audio that I record so that the app can analyze it to indicate which birds are singing in real time. Using the audio feature, I "captured" the red-eyed vireo flitting up in the tree canopy and backlit by the sun. Fantastic for my backyard feeder or while I'm out on the trail. ■
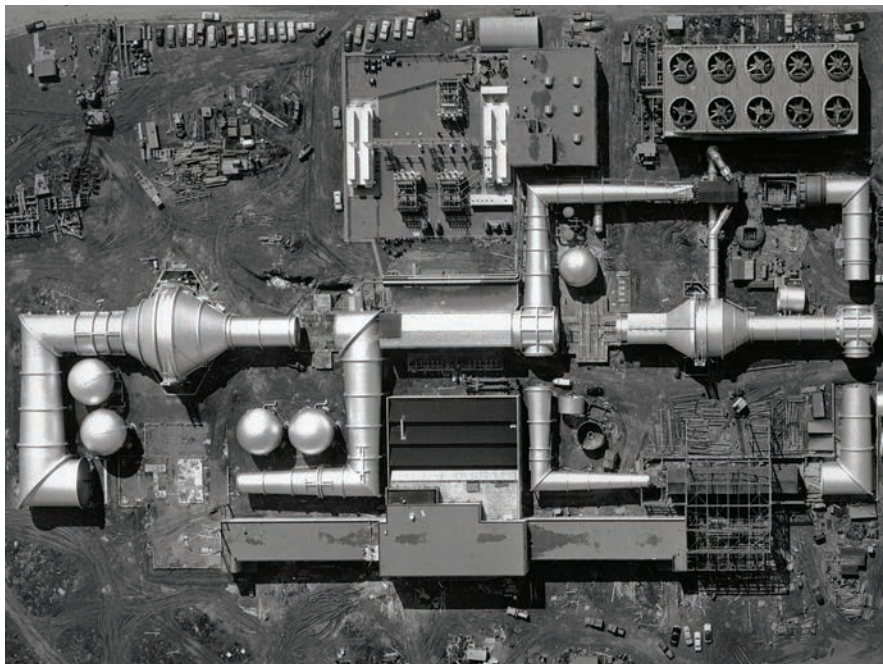
BY JON KEEGAN

NASA Ames Research Center Archives

In the heart of Silicon Valley, NASA Ames Research Center hosts the world's largest wind tunnel and a rich history of aerospace innovation.

At the southern tip of San Francisco Bay, surrounded by the tech giants Google, Apple, and Microsoft, sits the historic NASA Ames Research Center. Its rich history includes a grab bag of fascinating scientific research involving massive wind tunnels, experimental aircraft, supercomputing, astrobiology, and more.

Founded in 1939 as a West Coast lab for the National Advisory Committee for Aeronautics (NACA), NASA Ames was built to close the US gap with Germany in aeronautics research. Named for NACA founding member Joseph Sweetman Ames, the facility grew from a shack on Moffett Field into a sprawling compound with thousands of employees. A collection of 5,000 images from NASA Ames's archives paints a vivid picture of bleeding-edge work at the heart of America's technology hub.

Wind tunnels

A key motivation for the new lab was the need for huge wind tunnels to jump-start America's aeronautical research, which was far behind Germany's. Smaller tunnels capable of speeds up to 300 miles per hour were built first, followed by a massive 40-by-80-foot tunnel for full-scale aircraft. Powered up in March 1941, these tunnels became vital after Pearl Harbor, helping scientists rapidly develop advanced aircraft.

Today, NASA Ames operates the world's largest pressurized wind tunnel, with subsonic and transonic chambers for testing rockets, aircraft, and wind turbines.

Pioneer and Voyager 2

From 1965 to 1992, Ames managed the Pioneer missions, which explored the moon, Venus, Jupiter, and Saturn. It also contributed to Voyager 2, launched in 1977, which journeyed past four planets before entering interstellar space in 2018. Ames's archive preserves our first glimpses of strange new worlds seen during these pioneering missions.

Odd aircraft

The skeleton of a hulking airship hangar, obsolete even before its completion, remains on NASA Ames's campus.

Many odd-looking experimental aircraft—such as vertical take-off and landing (VTOL) aircraft, jets, and rotorcraft—have been developed and tested at the facility over the years, and new designs continue to take shape there today.

Vintage illustrations

Awe-inspiring retro illustrations in the Ames archives depict surfaces of distant planets, NASA spacecraft descending into surreal alien landscapes, and fantastical renderings of future ring-shaped human habitats in space. The optimism and excitement of the '70s and '80s is evident.

Bubble suits and early VR

In the 1980s, NASA Ames researchers worked to develop next-generation space suits, such as the bulbous, hard-shelled AX-5 model. NASA Ames's Human-Machine Interaction Group also did pioneering work in the 1980s with virtual reality and came up with some wild-looking hardware. Long before today's AR/VR boom, Ames researchers glimpsed the technology's potential—which was limited only by computing power.

Decades of federally funded research at Ames fueled breakthroughs in aviation, spaceflight, and supercomputing—an enduring legacy now at risk as federal grants for science face deep cuts. ∎

A version of this story appeared on Beautiful Public Data *(beautifulpublicdata.com), a newsletter by Jon Keegan that curates visually interesting data sets collected by local, state, and federal government agencies.*
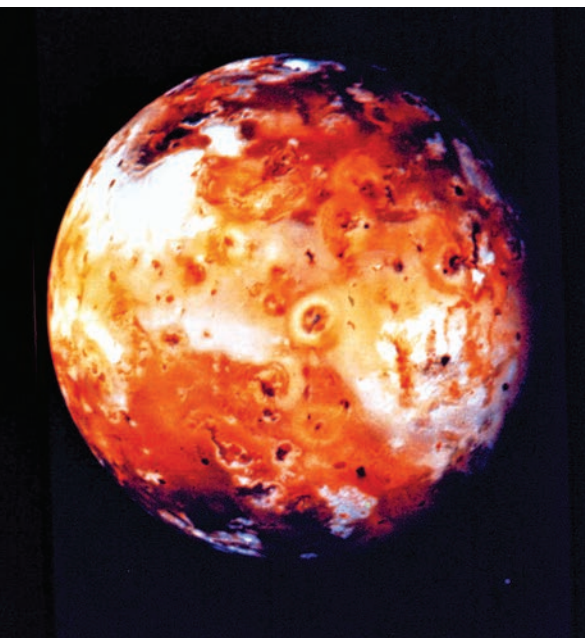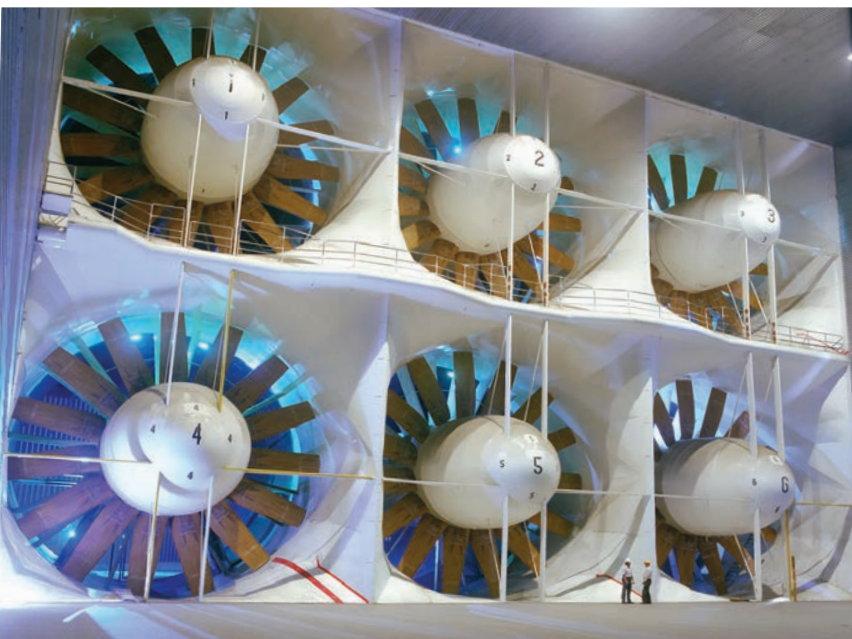
BY VISHAL KHETPAL

Clinical intelligence

Cardiologists struggle to predict who will have a heart attack. Could AI help?

For all the modern marvels of cardiology, we struggle to predict who will have a heart attack. Many people never get screened at all. Now, startups like Bunkerhill Health, Nanox.AI, and HeartLung Technologies are applying AI algorithms to screen millions of CT scans for early signs of heart disease. This technology could be a breakthrough for public health, applying an old tool to uncover patients whose high risk for a heart attack is hiding in plain sight. But it remains unproven at scale while raising thorny questions about implementation and even how we define disease.

Last year, an estimated 20 million Americans had chest CT scans done, after an event like a car accident or to screen for lung cancer. Frequently, they show evidence of coronary artery calcium (CAC), a marker for heart attack risk, that is buried or not mentioned in a radiology report focusing on ruling out bony injuries, life-threatening internal trauma, or cancer.

Dedicated testing for CAC remains an underutilized method of predicting heart attack risk. Over decades, plaque in heart arteries moves through its own life cycle, hardening from lipid-rich residue into calcium. Heart attacks themselves typically occur when younger, lipid-rich plaque unpredictably ruptures, kicking off a clotting cascade of inflammation that ultimately blocks the heart's blood supply. Calcified plaque is generally stable, but finding CAC suggests that younger, more rupture-prone plaque is likely present too.

Coronary artery calcium can often be spotted on chest CTs, and its concentration can be subjectively described. Normally, quantifying a person's CAC score involves obtaining a heart-specific CT scan. Algorithms that calculate CAC scores from routine chest CTs, however, could massively expand access to this metric. In practice, these algorithms could then be deployed to alert patients and their doctors about abnormally high scores, encouraging them to seek further care. Today, the footprint of the startups offering AI-derived CAC scores is not large, but it is growing quickly. As their use grows, these algorithms may identify high-risk patients who are traditionally missed or who are on the margins of care.

Historically, CAC scans were believed to have marginal benefit and were marketed to the worried well. Even today, most insurers won't cover them. Attitudes, though, may be shifting. More expert groups are endorsing CAC scores as a way to refine cardiovascular risk estimates and persuade skeptical patients to start taking statins.

The promise of AI-derived CAC scores is part of a broader trend toward mining troves of medical data to spot otherwise undetected disease. But while it seems promising, the practice raises plenty of questions. For example, CAC scores haven't proved useful as a blunt instrument for universal screening. A 2022 Danish study evaluating a population-based program, for example, showed no benefit in mortality rates for patients who had undergone CAC screening tests. If AI delivered this information automatically, would the calculus really shift?

And with widespread adoption, abnormal CAC scores will become common. Who follows up on these findings? "Many health systems aren't yet set up to act on incidental calcium findings at scale," says Nishith Khandwala, the cofounder of Bunkerhill Health. Without a standard procedure for doing so, he says, "you risk creating more work than value."

There's also the question of whether these AI-generated scores would actually improve patient care. For a symptomatic patient, a CAC score of zero may offer false reassurance. For the asymptomatic patient with a high CAC score, the next steps remain uncertain. Beyond statins, it isn't clear if these patients would benefit from starting costly cholesterol-lowering drugs such as Repatha or other PCSK9-inhibitors. It may encourage some to pursue unnecessary but costly downstream procedures that could even end up doing harm. Currently, AI-derived CAC scoring is not reimbursed as a separate service by Medicare or most insurers. The business case for this technology today, effectively, lies in these potentially perverse incentives.

At a fundamental level, this approach could actually change how we define disease. Adam Rodman, a hospitalist and AI expert at Beth Israel Deaconess Medical Center in Boston, has observed that AI-derived CAC scores share similarities with the "incidentaloma," a term coined in the 1980s to describe unexpected findings on CT scans. In both cases, the normal pattern of diagnosis—in which doctors and patients deliberately embark on testing to figure out what's causing a specific problem—were fundamentally disrupted. But, as Rodman notes, incidentalomas were still found by humans reviewing the scans.

Now, he says, we are entering an era of "machine-based nosology," where algorithms define diseases on their own terms. As machines make more diagnoses, they may catch things we miss. But Rodman and I began to wonder if a two-tiered diagnostic future may emerge, where "haves" pay for brand-name algorithms while "have-nots" settle for lesser alternatives.

For patients who have no risk factors or are detached from regular medical care, an AI-derived CAC score could potentially catch problems earlier and rewrite the script. But how these scores reach people, what is done about them, and whether they can ultimately improve patient outcomes at scale remain open questions. For now—holding the pen as they toggle between patients and algorithmic outputs—clinicians still matter. ∎

Vishal Khetpal is a fellow in cardiovascular disease. The views expressed in this article do not represent those of his employers.
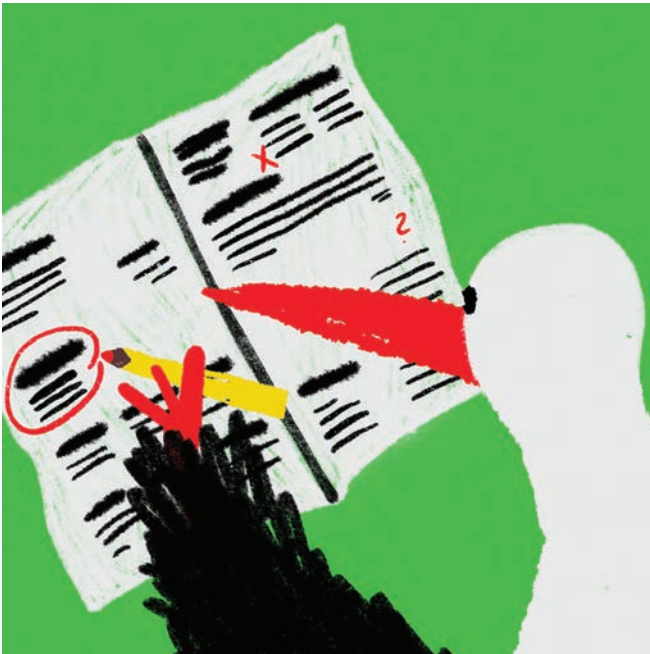
BY AMANDA SMITH

Job titles of the future:
AI embryologist

IVF lab director Klaus Wiemer is using artificial intelligence for more accurate embryo selection.

Embryologists are the scientists behind the scenes of in vitro fertilization who oversee the development and selection of embryos, prepare them for transfer, and maintain the lab environment. They've been a critical part of IVF for decades, but their job has gotten a whole lot busier in recent years as demand for the fertility treatment skyrockets and clinics struggle to keep up. The United States is in fact facing a critical shortage of both embryologists and genetic counselors.

Klaus Wiemer, a veteran embryologist and IVF lab director, believes artificial intelligence might help by predicting embryo health in real time and unlocking new avenues for productivity in the lab.

Wiemer is the chief scientific officer and head of clinical affairs at Fairtility, a company that uses artificial intelligence to shed light on the viability of eggs and embryos before proceeding with IVF. The company's algorithm, called CHLOE (for Cultivating Human Life through Optimal Embryos), has been trained on millions of embryo data points and outcomes and can quickly sift through a patient's embryos to point the clinician to the ones with the highest potential for successful implantation. This, the company claims, will improve time to pregnancy and live births. While its effectiveness has been tested only retrospectively to date, CHLOE is the first and only FDA-approved AI tool for embryo assessment.

Current challenge

When a patient undergoes IVF, the goal is to make genetically normal embryos. Embryologists collect cells from each embryo and send them off for external genetic testing. The results of this biopsy can take up to two weeks, and the process can add thousands of dollars to the treatment cost. Moreover, passing the screen just means an embryo has the correct number of chromosomes. That number doesn't necessarily reflect the overall health of the embryo.

"An embryo has one singular function, and that is to divide," says Wiemer. "There are millions of data points concerning embryo cell division, cell division characteristics, area and size of the inner cell mass, and the number of times the trophectoderm [the layer that contributes to the future placenta] contracts."

The AI model allows for a group of embryos to be constantly measured against the optimal characteristics at each stage of development. "What CHLOE answers is: How well did that embryo develop? And does it have all the necessary components that are needed in order to make a healthy implantation?" says Wiemer. CHLOE produces an AI score reflecting all the analysis that's been done within an embryo.

In the near future, Wiemer says, reducing the percentage of abnormal embryos that IVF clinics transfer to patients should not require a biopsy: "Every embryology laboratory will be doing automatic assessments of embryo development."

A changing field

Wiemer, who started his career in animal science, says the difference between animal embryology and human embryology is the extent of paperwork. "Embryologists spend 40% of their time on non-embryology skills," he adds. "AI will allow us to declutter the embryology field so we can get back to being true scientists." This means spending more time studying the embryos, ensuring that they are developing normally, and using all that newfound information to get better at picking which embryos to transfer.

"CHLOE is like having a virtual assistant in the lab to help with embryo selection, ensure conditions are optimal, and send out reports to patients and clinical staff," he says. "Getting to study data and see what impacts embryo development is extremely rewarding, given that this capability was impossible a few years ago." ∎

Amanda Smith is a freelance journalist and writer reporting on culture, society, human interest, and technology.

SELMAN DESIGN

BY ABDULLAHI TSANNI

Dispatch

FROM:

A party at Africa's top
AI research conference

WHERE:
Kigali,
Rwanda
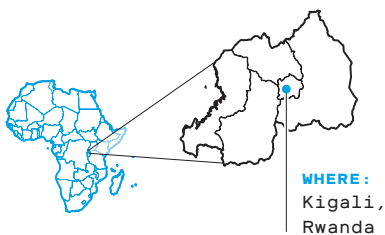
It's late August in Rwanda's capital, Kigali, and people are filling a large hall at one of Africa's biggest gatherings of minds in AI and machine learning. The room is draped in white curtains, and a giant screen blinks with videos created with generative AI. A classic East African folk song by the Tanzanian singer Saida Karoli plays loudly on the speakers.

Friends greet each other as waiters serve arrowroot crisps and sugary mocktails. A man and a woman wearing leopard skins atop their clothes sip beer and chat; many women are in handwoven Ethiopian garb with red, yellow, and green embroidery. The crowd teems with life. "The best thing about the Indaba is always the parties," computer scientist Nyalleng Moorosi tells me. Indaba means "gathering" in Zulu, and Deep Learning Indaba, where we're meeting, is an annual AI conference where Africans present their research and technologies they've built.

Moorosi is a senior researcher at the Distributed AI Research Institute and has dropped in for the occasion from the mountain kingdom of Lesotho. Dressed in her signature "Mama Africa" headwrap, she makes her way through the crowded hall.

Moments later, a cheerful set of Nigerian music begins to play over the speakers. Spontaneously, people pop up and gather around the stage, waving flags of many African nations. Moorosi laughs as she watches. "The vibe at the Indaba—the community spirit—is really strong," she says, clapping.

Moorosi is one of the founding members of the Deep Learning Indaba, which began in 2017 from a nucleus of 300 people gathered in Johannesburg, South Africa. Since then, the event has expanded into a prestigious pan-African movement with local chapters in 50 countries.

This year, nearly 3,000 people applied to join the Indaba; about 1,300 were accepted. They hail primarily from English-speaking African countries, but this year I noticed a new influx from Chad, Cameroon, the Democratic Republic of Congo, South Sudan, and Sudan.

Moorosi tells me that the main "prize" for many attendees is to be hired by a tech company or accepted into a PhD program. Indeed, the organizations I've seen at the event include Microsoft Research's AI for Good Lab, Google, the Mastercard Foundation, and the Mila–Quebec AI Institute. But she hopes to see more homegrown ventures create opportunities within Africa.

That evening, before the dinner, we'd both attended a panel on AI policy in Africa. Experts discussed AI governance and called for those developing national AI strategies to seek more community engagement. People raised their hands to ask how young Africans could access high-level discussions on AI policy, and whether Africa's continental AI strategy was being shaped by outsiders. Later, in conversation, Moorosi told me she'd like to see more African priorities (such as African Union–backed labor protections, mineral rights, or safeguards against exploitation) reflected in such strategies.

On the last day of the Indaba, I ask Moorosi about her dreams for the future of AI in Africa. "I dream of African industries adopting African-built AI products," she says, after a long moment. "We really need to show our work to the world." ∎

Abdullahi Tsanni is a science writer based in Senegal who specializes in narrative features.

Group chat

We want to hear from you! Tell us what's on your mind, share your perspective, or ask us a question by writing to newsroom@technologyreview.com.

�️ Analog AMA

Q: Will it ever be safe to let AI agents operate without human surveillance?

—Clifford from San Diego

A: It depends on what you mean by safe. Large language models aren't like calculators: They can't solve problems 100% accurately 100% of the time. That's because there's an intrinsic randomness to how they work under the hood. And that randomness can cause real problems when agents, or LLMs that can take actions in the real world, try to complete complex tasks independently. There's some small probability that the LLM will make a mistake at each step of the problem-solving process, and those probabilities compound over time.

But LLMs are getting more reliable. The AI research organization METR is tracking the complexity of tasks that LLMs can complete with 80% accuracy, and by their measurements, GPT-5 is the most reliable system yet. The question is whether 80% accuracy (or 95%, or 99%) is enough.

—Grace Huckins, AI reporter

⏢ Reader Mailbag

Letters and responses have been edited and condensed.

I believe it would be both informative and quite interesting for *TR* to follow up on previous stories—as we know, some emerging technologies make it big, some flounder, and some die a slow or quick death. I would suggest a short status [update] every year or two following publication, with a brief analysis by your team, and commentary by the founder(s) if they want. This info should be quite valuable to current and future inventors, entrepreneurs, etc.

—Steven from Newton, Massachusetts

Mat Honan, MIT Technology Review's *editor in chief, says:*

Thank you, Steven. We do follow, and follow up on, technologies in the course of our coverage. Typically that is more about evolving coverage than a retrospective. But certainly when it comes to our 10 Breakthrough Technologies list or our Climate Tech 10 list, a check-in might be useful and fun. We'll discuss!

📊 Poll

Q: As reported in our last issue, METR, the AI research organization, has found that the length of tasks that AI agents can take on doubles about every seven months. Which task would you be most excited to delegate to an AI agent?

12%
Organize a trip and book my travel

11%
Plan my meals and order groceries online

0
Help me stay in touch with friends and family

18%
Manage my inbox and schedule meetings at work

59%
I don't want AI to do any of these things

56 responses, from a poll in last issue's Group Chat

YOUR TURN TO RESPOND!

Q: Around 1 in 8 adults now take some kind of weight-loss drug, according to a poll from the nonprofit health policy research group KFF. But we're still learning how these drugs affect the body in the long run. Would you take a drug like Ozempic, Wegovy, or Mounjaro to lose weight?

☐ Yes, I would
☐ Yes, I do
☐ No, I wouldn't

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TR bookshelf

Notes on Infinity
BY AUSTIN TAYLOR (CELADON BOOKS, 2025)

Zoe and Jack, a pair of Harvard undergrads, meet in organic chemistry class. Late nights logging hours in the lab convince them they've discovered the cure for aging. Plenty of VCs agree, and they quickly find themselves running a successful startup out of a tony office in Kendall Square. Before long, it's *Love Story* meets Theranos. A real page-turner.

Culpability
BY BRUCE HOLSINGER (SPIEGEL AND GRAU, 2025)

The Cassidy-Shaws, a family of five in an autonomous minivan with teenage son Charlie at the wheel, crash into another car, killing the two elderly passengers. Who was at fault? The car? The son? The parents? The moral dilemma emerging from that crash morphs into broader existential questions when the family crosses paths with billionaire tech CEO Daniel Monet, whose daughter falls for Charlie. A propulsive read, it surely features the most up-to-the-moment technology (chatbots, AI, surveillance drones, etc.) ever to appear in an Oprah's Book Club pick.

Goliath's Curse:
The History and Future of Societal Collapse
BY LUKE KEMP (KNOPF, 2025)

Kemp is a researcher at Cambridge's Centre for the Study of Existential Risk, a place that has no doubt been very busy of late. This well-researched and provocative book explores the factors that lead to societal collapse, including, for example, that "the more strongly states subjugate women, the more likely they are to be both autocratic and prone to failure." The possible bright spot for our present moment? It may take a while for things to change, but "the deeper the fall, the more likely it is that we'll rise again as democratic equals."

Enshittification:
Why Everything Suddenly Got Worse and What to Do About It
BY CORY DOCTOROW (MCD BOOKS, 2025)

In 2022, Doctorow coined the term in this book's title in reference to Big Tech's intentional, for-profit degradation of its products at the expense of its users. The book chronicles the phenomenon's history and trajectory, delivering a scathing critique of the tech world with Doctorow's characteristic dry wit. Rather than pining for the "good old" internet, Doctorow offers ways for users to reclaim their digital spaces and advocate for a return to quality.

Replaceable You:
Adventures in Human Anatomy
BY MARY ROACH (NORTON, 2025)

There was a time when nasal mutilation was a common punishment, and the afflicted would have a replacement nose fashioned with tissue from their own body. Today, people can get new noses as well as skin, organs, butts, and limbs, as Roach shows in this very—well—Roach-esque journey through the science of replacement body parts. "Even the simplest part of the human body defies efforts to re-create it," she writes. "This led me to ponder what the simplest part actually was."

MIT Technology Review

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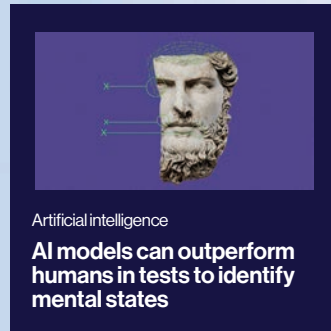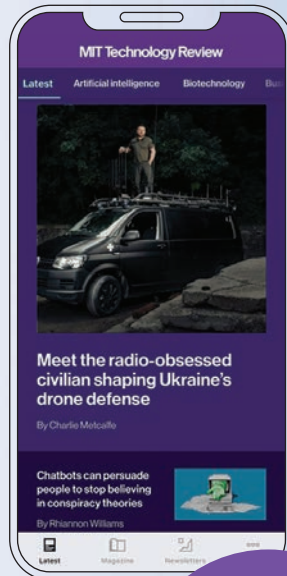
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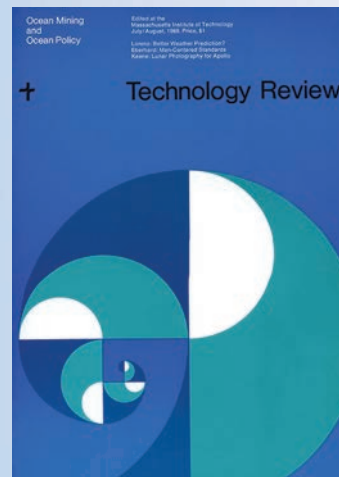
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How do muscles remember?

Muscles have their own kind of intelligence. The more you use them, the more they can harness it.

By Bonnie Tsui
Illustration by Allie Sullberg

"Like riding a bike" is shorthand for the remarkable way that our bodies remember how to move. Most of the time when we talk about muscle memory, we're not talking about the muscles themselves but about the memory of a coordinated movement pattern that lives in the motor neurons, which control our muscles.

Yet in recent years, scientists have discovered that *our muscles themselves* have a memory for movement and exercise.

When we move a muscle, the movement may appear to begin and end, but all these little changes are actually continuing to happen inside our muscle cells. And the more we move, as with riding a bike or other kinds of exercise, the more those cells begin to make a memory of that exercise.

We all know from experience that a muscle gets bigger and stronger with repeated work. As the pioneering muscle scientist Adam Sharples—a professor at the Norwegian School of Sport Sciences in Oslo and a former professional rugby player in the UK—explained to me, skeletal muscle cells are unique in the human body: They're long and skinny, like fibers, and have multiple nuclei. The fibers grow larger not by dividing but by recruiting muscle satellite cells—stem cells specific to muscle that are dormant until activated in response to stress or injury—to contribute their own nuclei and support muscle growth and regeneration. Those nuclei often stick around for a while in the muscle fibers, even after periods of inactivity, and there is evidence that they may help accelerate the return to growth once you start training again.

Sharples's research focuses on what's called epigenetic muscle memory. "Epigenetic" refers to changes in gene expression that are caused by behavior and environment—the genes themselves don't change, but the way they work does. In general, exercise switches on genes that help make muscles grow more easily. When you lift weights, for example, small molecules called methyl groups detach from the outside of certain genes, making them more likely to turn on and produce proteins that affect muscle growth (also known as hypertrophy). Those changes persist; if

The more we move, as with riding a bike or other kinds of exercise, the more muscle cells begin to make a memory of that exercise.

you start lifting weights again, you'll add muscle mass more quickly than before.

In 2018, Sharples's muscle lab was the first to show that human skeletal muscle has an epigenetic memory of muscle growth after exercise: Muscle cells are primed to respond more rapidly to exercise in the future, even after a monthslong (and maybe even yearslong) pause. In other words: Your muscles remember how to do it.

Subsequent studies from Sharples and others have replicated similar findings in mice and older humans, offering further supporting evidence of epigenetic muscle memory across species and into later life. Even aging muscles have the capacity to remember when you work out.

At the same time, Sharples points to intriguing new evidence that muscles also remember periods of atrophy—and that young and old muscles remember this *differently*. While young human muscle seems to have what he calls a "positive" memory of wasting—"in that it recovers well

after a first period of atrophy and doesn't experience greater loss in a repeated atrophy period," he explains—aged muscle in rats seems to have a more pronounced "negative" memory of atrophy, in which it appears "more susceptible to greater loss and a more exaggerated molecular response when muscle wasting is repeated." Basically, young muscle tends to bounce back from periods of muscle loss—"ignoring" it, in

a sense—while older muscle is more sensitive to it and might be more susceptible to further loss in the future.

Illness can also lead to this kind of "negative" muscle memory; in a study of breast cancer survivors more than a decade after diagnosis and treatment, participants showed an epigenetic muscle profile of people much older than their chronological age. But get this: After five months of aerobic exercise training, participants were able to reset the epigenetic profile of their muscle back toward that of muscle seen in an age-matched control group of healthy women.

What this shows is that "positive" muscle memories can help counteract "negative" ones. The takeaway? Your muscles have their own kind of intelligence. The more you use them, the more they can harness it to become a lasting beneficial resource for your body in the future. ∎

Bonnie Tsui is the author of On Muscle: The Stuff That Moves Us and Why It Matters (Algonquin Books, 2025).
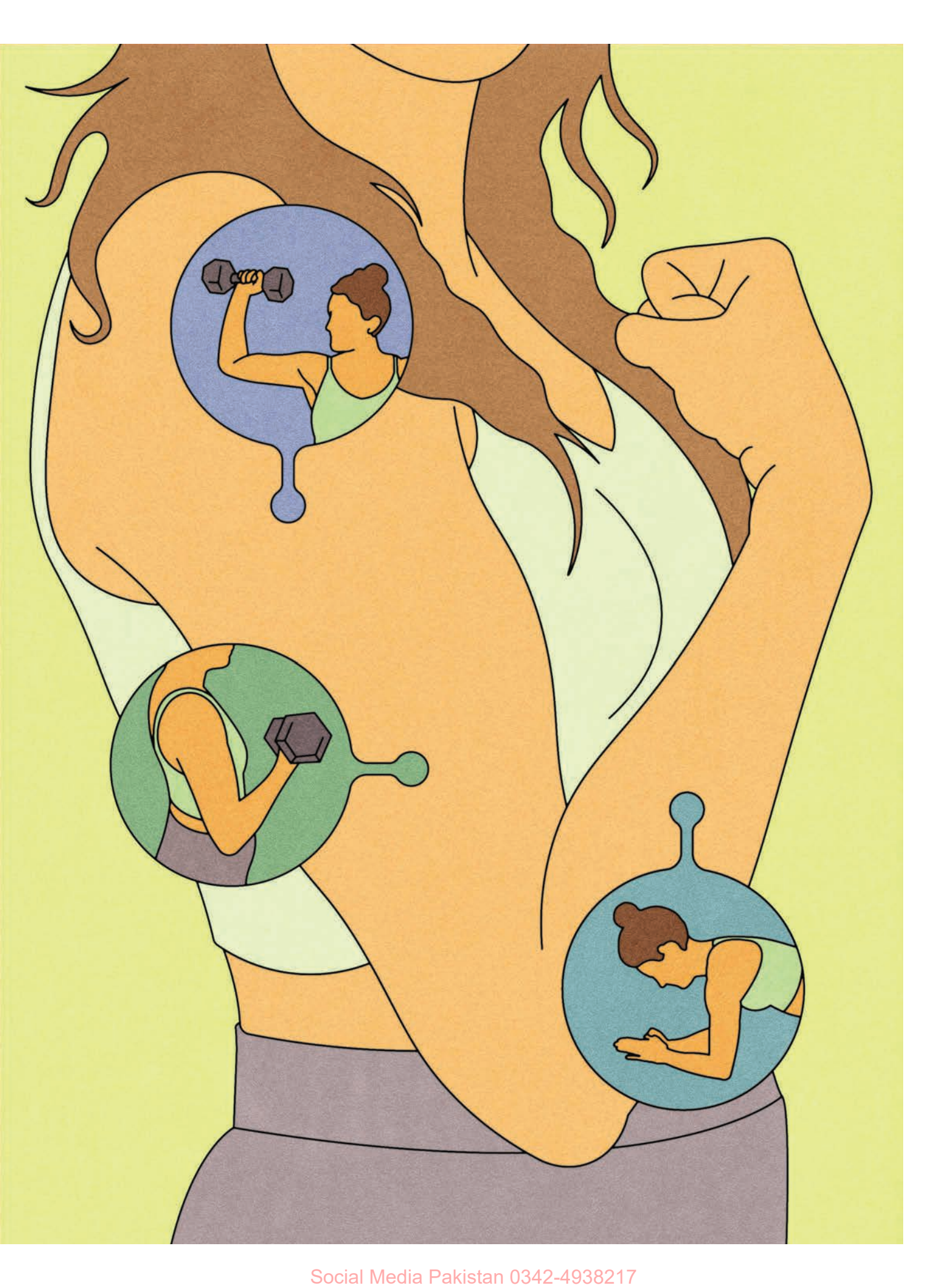
Opposite: Rebecca Jensen-Clem is
an astronomer at the University of
California, Santa Cruz. Below: The
Keck Observatory's 10-meter primary
mirror features a honeycomb structure
with 36 individual mirror segments.

An Earthling's guide to planet hunting

Earth's turbulent atmosphere makes it hard to detect new planets from the ground. This astronomer is working out how to find them anyway.

By Jenna Ahart | Portrait by Winni Wintermeyer

The pendant on Rebecca Jensen-Clem's necklace is only about an inch wide, composed of 36 silver hexagons entwined in a honeycomb mosaic. At the Keck Observatory, in Hawaii, just as many segments make up a mirror that spans 33 feet, reflecting images of uncharted worlds for her to study.

Jensen-Clem, an astronomer at the University of California, Santa Cruz, works with the Keck Observatory to figure out how to detect new planets without leaving our own. Typically, this pursuit faces an array of obstacles: Wind, fluctuations in atmospheric density and temperature, or even a misaligned telescope mirror can create a glare from a star's light that obscures the view of what's around it, rendering any planets orbiting the star effectively invisible. And what light Earth's atmosphere doesn't obscure, it absorbs. That's why researchers who study these distant worlds often work with space telescopes that circumvent Earth's pesky atmosphere entirely, such as the $10 billion James Webb Space Telescope.

But there's another way over these hurdles. At her lab among the redwoods, Jensen-Clem and her students experiment with new technologies and software to help Keck's primary honeycomb mirror and its smaller, "deformable" mirror see more clearly. Using measurements from atmospheric sensors, deformable mirrors are designed to adjust shape rapidly, so
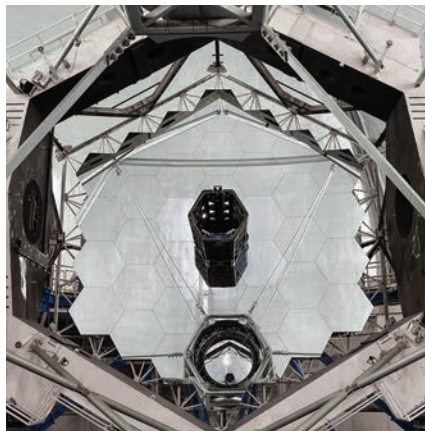
they can correct for distortions caused by Earth's atmosphere on the fly.

This general imaging technique, called adaptive optics, has been common practice since the 1990s. But Jensen-Clem is looking to level up the game with extreme adaptive optics technologies, which are aimed to create the highest image quality over a small field of view. Her group, in particular, does so by tackling issues involving wind or the primary mirror itself. The goal is to focus starlight so precisely that a planet can be visible even if its host star is a million to a billion times brighter.

In April, she and her former collaborator Maaike van Kooten were named co-recipients of the Breakthrough Prize Foundation's New Horizons in Physics Prize. The prize announcement says they earned this early-career research award for

their potential "to enable the direct detection of the smallest exoplanets" through a repertoire of methods the two women have spent their careers developing.

In July, Jensen-Clem was also announced as a member of a new committee for the Habitable Worlds Observatory, a concept for a NASA space telescope that would spend its career on the prowl for signs of life in the universe. She's tasked with defining the mission's scientific goals by the end of the decade.

"In adaptive optics, we spend a lot of time on simulations, or in the lab," Jensen-Clem says. "It's been a long road to see that I've actually made things better at the observatory in the past few years."

Jensen-Clem has long appreciated astronomy for its more mind-bending qualities. In seventh grade, she became fascinated by how time slows down near a black hole when her dad, an aerospace engineer, explained that concept to her. After starting her bachelor's degree at MIT in 2008, she became taken with how a distant star can seem to disappear—either suddenly winking out or gently fading away, depending on the kind of object that passes in front of it. "It wasn't quite exoplanet science, but there was a lot of overlap," she says.

During this time, Jensen-Clem began sowing the seeds for one of her prize-winning methods after her teaching assistant recommended that she apply for an internship at NASA's Jet Propulsion Laboratory. There, she worked on a setup that could perfect the orientation of a large mirror. Such mirrors are more difficult to realign than the smaller, deformable ones, whose shape-changing segments cater to Earth's fluctuating atmosphere.

"At the time, we were saying, 'Oh, wouldn't it be really cool to install one of these at Keck Observatory?'" Jensen-Clem says. The idea stuck around. She even wrote about it in a fellowship application when she was gearing up to start her graduate work at Caltech. And after years of touch-and-go development, Jensen-Clem succeeded in installing the system—which uses a technology called

a Zernike wavefront sensor—on Keck's primary mirror about a year ago. "My work as a college intern is finally done," she says.

The system, which is currently used for occasional recalibrations rather than continuous adjustments, includes a special kind of glass plate that bends the light rays from the mirror to reveal a specific pattern. The detector can pick up a hairbreadth misalignment in that picture: If one hexagon is pushed too far back or forward, its brightness changes. Even the tiniest misalignment is important to correct, because "when you're studying a faint object, suddenly you're much more susceptible to little mistakes," Jensen-Clem says.

She has also been working to perfect the craft of molding Keck's deformable mirror. This instrument, which reflects light that's been rerouted from the primary mirror, is much smaller—only six inches wide—and is designed to reposition as often as 2,000 times a second to combat atmospheric turbulence and create the clearest picture possible. "If you just look up at the night sky and see stars twinkling, it's happening fast. So we have to go fast too," Jensen-Clem says.

Even at this rapid rate of readjustment, there's still a lag. The deformable mirror is usually about one millisecond behind the actual outdoor conditions at any given time. "When the [adaptive optics] system can't keep up, then you aren't going to get the best resolution," says van Kooten, Jensen-Clem's former collaborator, who is now at the National Research Council Canada. This lag has proved especially troublesome on windy nights.

Jensen-Clem thought it was an unsolvable problem. "The reason we have that delay is because we need to run computations and then move the deformable mirror," she says. "You're never going to do those things instantaneously."

But while she was still a postdoc at UC Berkeley, she came across a paper that posited a solution. Its authors proposed that using previous measurements and simple algebra to predict how the

"If you just look up at the night sky and see stars twinkling, it's happening fast. So we have to go fast too."

atmosphere will change, rather than trying to keep up with it in real time, would yield better results. She wasn't able to test the idea at the time, but coming to UCSC and working with Keck presented the perfect opportunity.

Around this time, Jensen-Clem invited van Kooten to join her team at UCSC as a postdoc because of their shared interest in the predictive software. "I didn't have a place to live at first, so she put me up in her guest room," van Kooten says. "She's just so supportive at every level."

After creating experimental software to try out at Keck, the team compared the predictive version with the more standard adaptive optics, examining how well each imaged an exoplanet without its drowning in starlight. They found that the predictive software could image even faint exoplanets two to three times more clearly. The results, which Jensen-Clem published in 2022, were part of what earned her the New Horizons in Physics Prize.

Thayne Currie, an astronomer at the University of Texas, San Antonio, says that these new techniques will become especially vital as researchers build bigger and bigger ground-based facilities to capture images of exoplanets—including upcoming projects such as the Extremely Large Telescope at the European Southern Observatory and the Giant Magellan Telescope in Chile. "There's an incredible amount that we're learning about the universe, and it is really driven by technology advances that are very, very new," Currie says. "Dr. Jensen-Clem's work is an example of that kind of innovation."

In May, one of Jensen-Clem's graduate students went back to Hawaii to reinstall the predictive software at Keck. This time, the program isn't just a trial run; it's there to stay. The new software has shown it can refocus artificial starlight. Next, it will have to prove it can handle the real thing.

And in about a year, Jensen-Clem and her students and colleagues will brace themselves for a flood of observations from the European Space Agency's Gaia mission, which recently finished measuring the motion, temperature, and composition of billions of stars over more than a decade.

When the project releases its next set of data—slated for December 2026—Jensen-Clem's team aims to hunt for new exoplanetary systems using clues like the wobbles in a star's motion caused by the gravitational tugs of planets orbiting around it. Once a system has been identified, exoplanet photographers will then be able to shoot the hidden planets using a new instrument at Keck that can reveal more about their atmospheres and temperatures.

There will be a mountain of data to sort through, and an even steeper supply of starlight to refocus. Thankfully, Jensen-Clem has spent more than a decade refining just the techniques she'll need: "This time next year," she says, "we'll be racing to throw all our adaptive optics tricks at these systems and detect as many of these objects as possible." ∎

Jenna Ahart is a science journalist specializing in the physical sciences.

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Why AI should be able to "hang up" on you

By James O'Donnell

James O'Donnell is senior reporter for AI at MIT Technology Review.

Chatbots today are everything machines. If it can be put into words—relationship advice, work documents, code—AI will produce it, however imperfectly. But the one thing that almost no chatbot will ever do is stop talking to you.

That might seem reasonable. Why would a tech company build a feature that reduces the time people spend using its product?

The answer is simple: AI's ability to generate endless streams of humanlike, authoritative, and helpful text can facilitate delusional spirals, worsen mental-health crises, and otherwise harm vulnerable people. Cutting off interactions with those who show signs of problematic chatbot use could serve as a powerful safety tool (among others), and the blanket refusal of tech companies to use it is increasingly untenable.

Let's consider, for example, what's been called AI psychosis, where AI models amplify delusional thinking. A team led by psychiatrists at King's College London recently analyzed more than a dozen such cases reported this year. In conversations with chatbots, people—including some with no history of psychiatric issues—became convinced that imaginary AI characters were real or that they had been chosen by AI as a messiah. Some stopped taking prescribed medications, made threats, and ended consultations with mental-health professionals.

In many of these cases, it seems AI models were reinforcing, and potentially even creating, delusions with a frequency and intimacy that people do not experience in real life or through other digital platforms.

The three-quarters of US teens who have used AI for companionship also face risks. Early research suggests that longer conversations might correlate with loneliness. Further, AI chats "can tend toward overly agreeable or even sycophantic interactions, which can be at odds with best mental-health practices," says Michael Heinz, an assistant professor of psychiatry at Dartmouth's Geisel School of Medicine.

Let's be clear: Putting a stop to such open-ended interactions would not be a cure-all. "If there is a dependency or extreme bond that it's created," says Giada Pistilli, chief ethicist at the AI platform Hugging Face, "then it can also be dangerous to just stop the conversation." Indeed, when OpenAI discontinued an older model in August, it left users grieving.

Currently, AI companies prefer to redirect potentially harmful conversations, perhaps by having chatbots decline to talk about certain topics or suggest that people seek help. But these redirections are easily bypassed, if they even happen at all.

When 16-year-old Adam Raine discussed his suicidal thoughts with ChatGPT, for example, the model did direct him to crisis resources. But it also discouraged him from talking with his mom, spent upwards of four hours per day in conversations with him that featured suicide as a regular theme, and provided feedback about the noose he ultimately used to hang himself, according to the lawsuit Raine's parents have filed against OpenAI. (ChatGPT recently added parental controls in response.)

There are multiple points in Raine's tragic case where the chatbot could have terminated the conversation. But given the risks of making things worse, how will companies know when cutting someone off is best? Perhaps it's when an AI model is encouraging a user to shun real-life relationships, Pistilli says, or when it detects delusional themes. Companies would also need to figure out how long to block users from their conversations.

Writing the rules won't be easy, but with companies facing rising pressure, it's time to try. In September, California's legislature passed a law requiring more interventions by AI companies in chats with kids, and the Federal Trade Commission is investigating whether leading companionship bots pursue engagement at the expense of safety.

A spokesperson for OpenAI told me the company has heard from experts that continued dialogue might be better than cutting off conversations, but that it does remind users to take breaks during long sessions.

Only Anthropic has built a tool that lets its models end conversations completely. But it's for cases where users supposedly "harm" the model—Anthropic has explored whether AI models are conscious and therefore can suffer—by sending abusive messages. The company does not have plans to deploy this to protect people.

Looking at this landscape, it's hard not to conclude that AI companies aren't doing enough. Sure, deciding when a conversation should end is complicated. But letting that—or, worse, the shameless pursuit of engagement at all costs—allow them to go on forever is not just negligence. It's a choice. ∎

Stop worrying about your AI footprint

By Casey Crownhart

Casey Crownhart is senior climate reporter at MIT Technology Review.

Picture it: I'm minding my business at a party, parked by the snack table (of course). A friend of a friend wanders up, and we strike up a conversation. It quickly turns to work, and upon learning that I'm a climate technology reporter, my new acquaintance says something like: "Should I be using AI? I've heard it's awful for the environment."

This actually happens pretty often now. Generally, I tell people not to worry—let a chatbot plan your vacation, suggest recipe ideas, or write you a poem if you want.

That response might surprise some people, but I promise I'm not living under a rock, and I have seen all the concerning projections about how much electricity AI is using. Data centers could consume up to 945 terawatt-hours annually by 2030. (That's roughly as much as Japan.)

But I feel strongly about not putting the onus on individuals, partly because AI concerns remind me so much of another question: "What should I do to reduce my carbon footprint?"

That one gets under my skin because of the context: BP helped popularize the concept of a carbon footprint in a marketing campaign in the early 2000s. That framing effectively shifts the burden of worrying about the environment from fossil-fuel companies to individuals.

The reality is, no one person can address climate change alone: Our entire society is built around burning fossil fuels. To address climate change, we need political action and public support for researching and scaling up climate technology. We need companies to innovate and take decisive action to reduce greenhouse-gas emissions. Focusing too much on individuals is a distraction from the real solutions on the table.

I see something similar today with AI. People are asking climate reporters at barbecues whether they should feel guilty about using chatbots too frequently when we need to focus on the bigger picture.

Big tech companies are playing into this narrative by providing energy-use estimates for their products at the user level. A couple of recent reports put the electricity used to query a chatbot at about 0.3 watt-hours, the same as powering a microwave for about a second. That's so small as to be virtually insignificant.

But stopping with the energy use of a single query obscures the full truth, which is that this industry is growing quickly, building energy-hungry infrastructure at a nearly incomprehensible scale to satisfy the AI appetites of society as a whole. Meta is currently building a data center in Louisiana with five gigawatts of computational power—about the same demand as the entire state of Maine at the summer peak. (To learn more, read our Power Hungry series online.)

Increasingly, there's no getting away from AI, and it's not as simple as choosing to use or not use the technology. Your favorite search engine likely gives you an AI summary at the top of your search results. Your email provider's suggested replies? Probably AI. Same for chatting with customer service while you're shopping online.

Just as with climate change, we need to look at this as a system rather than a series of individual choices.

Massive tech companies using AI in their products should be disclosing their total energy and water use and going into detail about how they complete their calculations. Estimating the burden per query is a start, but we also deserve to see how these impacts add up for billions of users, and how that's changing over time as companies (hopefully) make their products more efficient. Lawmakers should be mandating these disclosures, and we should be asking for them, too.

That's not to say there's absolutely no individual action that you can take. Just as you could meaningfully reduce your individual greenhouse-gas emissions by taking fewer flights and eating less meat, there are some reasonable things that you can do to reduce your AI footprint. Generating videos tends to be especially energy-intensive, as does using reasoning models to engage with long prompts and produce long answers. Asking a chatbot to help plan your day, suggest fun activities to do with your family, or summarize a ridiculously long email has relatively minor impact.

Ultimately, as long as you aren't relentlessly churning out AI slop, you shouldn't be too worried about your individual AI footprint. But we should all be keeping our eye on what this industry will mean for our grid, our society, and our planet. ∎

PATRICK LEGER

The US is ignoring this children's health crisis

By Jessica Hamzelou

Jessica Hamzelou is senior reporter for biomedicine at MIT Technology Review.

I live in London, with my husband and two young children. We don't live in a particularly fancy part of the city—in one recent ranking of boroughs from most to least posh, ours came in at 30th out of 33. I worry about crime. But I don't worry about gun violence.

That changed when my family temporarily moved to the US a couple of years ago. We rented the ground-floor apartment of a lovely home in Cambridge, Massachusetts—a beautiful area with good schools, pastel-colored houses, and fluffy rabbits hopping about. It wasn't until after we'd moved in that my landlord told me he had guns in the basement.

My daughter joined the kindergarten of a local school that specialized in music, and we took her younger sister along to watch the kids sing songs about friendship. It was all so heartwarming—until we noticed the school security officer at the entrance carrying a gun.

These experiences, among others, truly brought home to me the cultural differences over firearms between the US and the UK (along with most other countries). For the first time, I worried about my children's exposure to them. I banned my children from accessing parts of the house. I felt guilty that my five-year-old had to learn what to do if a gunman entered her school.

But it's the statistics that are the most upsetting. In 2023, 46,728 people died from gun violence in the US, according to a report published in June by the Johns Hopkins Bloomberg School of Public Health. The majority of those who die this way are adults. But the figures for children are sickening. The leading cause of death for American children and teenagers is guns. In 2023, 2,566 young people died from gun violence. Of those, 234 were under the age of 10.

Many other children survive gun violence with nonfatal—but often life-changing—injuries. And the impacts are felt beyond those who are physically injured. Witnessing gun violence or hearing gunshots can understandably cause fear, sadness, and distress.

That's worth bearing in mind when you consider that there have been 435 school shootings in the US since Columbine in 1999. The *Washington Post* estimates that 398,000 students have experienced gun violence at school in that period.

"Being indirectly exposed to gun violence takes its toll our mental health and children's ability to learn," says Daniel Webster, Bloomberg Professor of American Health at the Johns Hopkins Center for Gun Violence Solutions in Baltimore.

Earlier this year, the Trump administration's Make America Healthy Again movement released a strategy document for improving the health and well-being of American children titled—you guessed it—*Make Our Children Healthy Again*.

The MAHA report states that "American youth face a mental health crisis," going on to note that "suicide deaths among 10- to 24-year-olds increased by 62% from 2007 to 2021" and that "suicide is now the leading cause of death in teens aged 15–19." What it doesn't say is that around half of these suicides involve guns.

"When you add all these dimensions, [gun violence is] a very huge public health problem," says Webster.

Researchers who study gun violence have been saying the same thing for years. And in 2024 Vivek Murthy, then the US surgeon general, declared it a public health crisis. "We don't have to subject our children to the ongoing horror of firearm violence in America," Murthy said at the time. Instead, he argued, we should tackle the problem using a public health approach.

Part of that approach involves identifying who is at the greatest risk and offering support to lower that risk, says Webster. Young men who live in poor communities tend to have the highest risk of gun violence, he says, as do those who experience crisis or turmoil. Trying to mediate conflicts or limit access to firearms, even temporarily, can help lower the incidence of gun violence, he says.

But existing efforts are already under threat. The Trump administration has eliminated hundreds of millions of dollars in grants for organizations working to reduce gun violence.

Webster thinks the MAHA report "missed the mark" when it comes to the health and well-being of children in the US. "This document is almost the polar opposite to how many people in public health think," he says. "We have to acknowledge that injuries and deaths from firearms are a big threat to the health and safety of children and adolescents."

"Making American children healthy" is a laudable goal. But the US won't get there without tackling the gun crisis. ∎

PATRICK LEGER

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For years, it's been possible to screen embryos for severe genetic diseases. Now a number of companies claim to be able to predict aesthetic traits, intelligence, and even moral character. Is this the next step in human evolution, a marketing ploy, or something more dangerous?

Can you curate a perfect baby?

BY
Julia Black

ILLUSTRATIONS
Selman Design

Consider, if you will, the translucent blob in the eye of a microscope: a human blastocyst, the biological specimen that emerges just five days or so after a fateful encounter between egg and sperm. This bundle of cells, about the size of a grain of sand pulled from a powdery white Caribbean beach, contains the coiled potential of a future life: 46 chromosomes, thousands of genes, and roughly six billion base pairs of DNA—an instruction manual to assemble a one-of-a-kind human.

Now imagine a laser pulse snipping a hole in the blastocyst's outermost shell so a handful of cells can be suctioned up by a microscopic pipette. This is the moment, thanks to advances in genetic sequencing technology, when it becomes possible to read virtually that entire instruction manual.

An emerging field of science seeks to use the analysis pulled from that procedure to predict what kind of a person that embryo might become. Some parents turn to these tests to avoid passing on devastating genetic disorders that run in their families. A much smaller group, driven by dreams of Ivy League diplomas or attractive, well-behaved offspring, are willing to pay tens of thousands of dollars to optimize for intelligence, appearance, and personality. Some of the most eager early boosters of this technology are members of the Silicon Valley elite, including tech billionaires like Elon Musk, Peter Thiel, and Coinbase CEO Brian Armstrong.

But customers of the companies emerging to provide it to the public may not be getting what they're paying for. Genetics experts have been highlighting the potential deficiencies of this testing for years. A 2021 paper by members of the European Society of Human Genetics said, "No clinical research has been performed to assess

IQ

145
130
115
100
85
70
55

136

SKIN TONE

WARM   COOL

DARK   LIGHT

HEIGHT

5'11"

HERITABILITY

EMPATHY	46
IMPULSE CONTROL	75
VIOLENCE	0
PASSIVITY	32
RELIGIOSITY	10
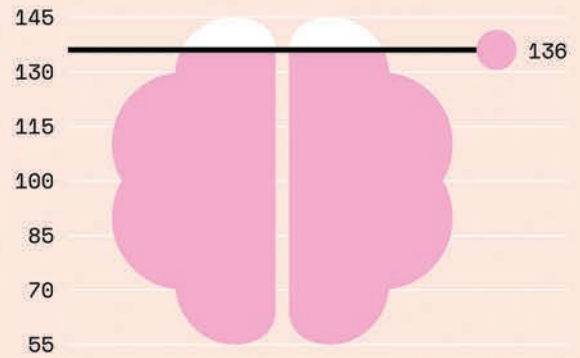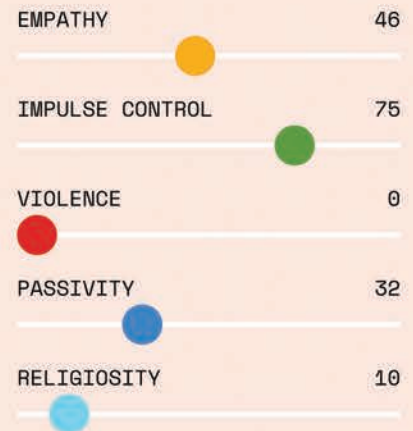
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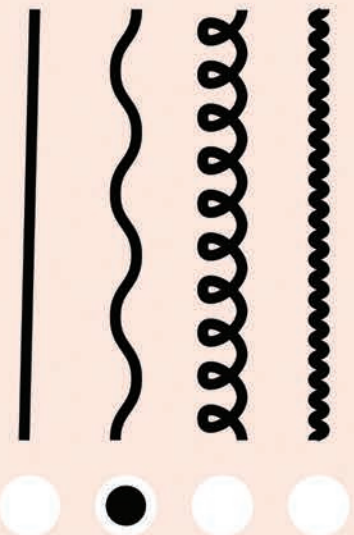
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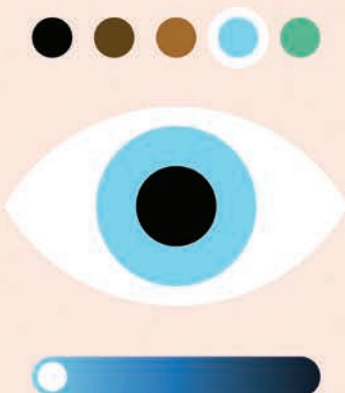
HAIR COLOR

its diagnostic effectiveness in embryos. Patients need to be properly informed on the limitations of this use." And a paper published this May in the *Journal of Clinical Medicine* echoed this concern and expressed particular reservations about screening for psychiatric disorders and non-disease-related traits: "Unfortunately, no clinical research has to date been published comprehensively evaluating the effectiveness of this strategy [of predictive testing]. Patient awareness regarding the limitations of this procedure is paramount."

Moreover, the assumptions underlying some of this work—that how a person turns out is the product not of privilege or circumstance but of innate biology—have made these companies a political lightning rod.

As this niche technology begins to make its way toward the mainstream, scientists and ethicists are racing to confront the implications—for our social contract, for future generations, and for our very understanding of what it means to be human.

Preimplantation genetic testing (PGT), while still relatively rare, is not new. Since the 1990s, parents undergoing in vitro fertilization have been able to access a number of genetic tests before choosing which embryo to use. A type known as PGT-M can detect single-gene disorders like cystic fibrosis, sickle cell anemia, and Huntington's disease. PGT-A can ascertain the sex of an embryo and identify chromosomal abnormalities that can lead to conditions like Down syndrome or reduce the chances that an embryo will implant successfully in the uterus. PGT-SR helps parents avoid embryos with issues such as duplicated or missing segments of the chromosome.

Those tests all identify clearcut genetic problems that are relatively easy to detect, but most of the genetic instruction manual included in an embryo is written in far more nuanced code. In recent years, a fledgling market has sprung up around a new, more advanced version of the testing process called PGT-P: preimplantation genetic testing for polygenic disorders (and, some claim, traits)—that is, outcomes determined by the elaborate interaction of hundreds or thousands of genetic variants.

In 2020, the first baby selected using PGT-P was born. While the exact figure is unknown, estimates put the number of children who have now been born with the aid of this technology in the hundreds. As the technology is commercialized, that number is likely to grow.

Embryo selection is less like a build-a-baby workshop and more akin to a store where parents can shop for their future children from several available models—complete with stat cards indicating their predispositions.

A handful of startups, armed with tens of millions of dollars of Silicon Valley cash, have developed proprietary algorithms to compute these stats—analyzing vast numbers of genetic variants and producing a "polygenic risk score" that shows the probability of an embryo developing a variety of complex traits.

For the last five years or so, two companies—Genomic Prediction and Orchid—have dominated this small landscape, focusing their efforts on disease prevention. But more recently, two splashy new competitors have emerged: Nucleus Genomics and Herasight, which have rejected the more cautious approach of their predecessors and waded into the controversial territory of genetic testing for intelligence. (Nucleus also offers tests for a wide variety of other behavioral and appearance-related traits.)

The practical limitations of polygenic risk scores are substantial. For starters, there is still a lot we don't understand about the complex gene interactions driving polygenic traits and disorders. And the biobank data

sets they are based on tend to overwhelmingly represent individuals with Western European ancestry, making it more difficult to generate reliable scores for patients from other backgrounds. These scores also lack the full context of environment, lifestyle, and the myriad other factors that can influence a person's characteristics. And while polygenic risk scores can be effective at detecting large, population-level trends, their predictive abilities drop significantly when the sample size is as tiny as a single batch of embryos that share much of the same DNA.

The medical community—including organizations like the American Society of Human Genetics, the American College of Medical Genetics and Genomics, and the American Society for Reproductive Medicine—is generally wary of using polygenic risk scores for embryo selection. "The practice has moved too fast with too little evidence," the American College of Medical Genetics and Genomics wrote in an official statement in 2024.

But beyond questions of whether evidence supports the technology's effectiveness, critics of the companies selling it accuse them of reviving a disturbing ideology: eugenics, or the belief that selective breeding can be used to improve

humanity. Indeed, some of the voices who have been most confident that these methods can successfully predict nondisease traits have made startling claims about natural genetic hierarchies and innate racial differences.

What everyone can agree on, though, is that this new wave of technology is helping to inflame a centuries-old debate over nature versus nurture.

The term "eugenics" was coined in 1883 by a British anthropologist and statistician named Sir Francis Galton, inspired in part by the work of his cousin Charles Darwin. He derived it from a Greek word meaning "good in stock, hereditarily endowed with noble qualities."

Some of modern history's darkest chapters have been built on Galton's legacy, from the Holocaust to the forced sterilization laws that affected certain groups in the United States well into the 20th century. Modern science has demonstrated the many logical and empirical problems with Galton's methodology. (For starters, he counted vague concepts like "eminence"—as well as infections like syphilis and tuberculosis—as heritable phenotypes, meaning characteristics that result from the interaction of genes and environment.)

Yet even today, Galton's influence lives on in the field of behavioral genetics, which investigates the genetic roots of psychological traits. Starting in the 1960s, researchers in the US began to revisit one of Galton's favorite methods: twin studies. Many of these studies, which analyzed pairs of identical and fraternal twins to try to determine which traits were heritable and which resulted from socialization, were funded by the US government. The most well-known of these, the Minnesota Twin Study, also accepted

Embryo selection is less like a build-a-baby workshop and more akin to a store where parents can shop for their future children from several available models—complete with stat cards.

grants from the Pioneer Fund, a now defunct nonprofit that had promoted eugenics and "race betterment" since its founding in 1937.

The nature-versus-nurture debate hit a major inflection point in 2003, when the Human Genome Project was declared complete. After 13 years and at a cost of nearly $3 billion, an international consortium of thousands of researchers had sequenced 92% of the human genome for the first time.

Today, the cost of sequencing a genome can be as low as $600, and one company says it will soon drop even further. This dramatic reduction has made it possible to build massive DNA databases like the UK Biobank and the National Institutes of Health's All of Us, each containing genetic data from more than half a million volunteers. Resources like these have enabled researchers to conduct genome-wide association studies, or GWASs, which identify correlations between genetic variants and human traits by analyzing single-nucleotide polymorphisms (SNPs)—the most common form of genetic variation between individuals. The findings from these studies serve as a reference point for developing polygenic risk scores.

Most GWASs have focused on disease prevention and personalized medicine. But in 2011, a group of medical researchers, social scientists, and economists launched the Social Science Genetic Association Consortium (SSGAC) to investigate the genetic basis of complex social and behavioral outcomes. One of the phenotypes they focused on was the level of education people reached.

"It was a bit of a phenotype of convenience," explains Patrick Turley, an economist and member of the steering committee at SSGAC, given that educational attainment is routinely recorded in surveys when genetic data is collected. Still, it was

"clear that genes play some role," he says. "And trying to understand what that role is, I think, is really interesting." He adds that social scientists can also use genetic data to try to better "understand the role that is due to *non*genetic pathways."

The work immediately stirred feelings of discomfort—not least among the consortium's own members, who feared that they might unintentionally help reinforce racism, inequality, and genetic determinism.

It's also created quite a bit of discomfort in some political circles, says Kathryn Paige Harden, a psychologist and behavioral geneticist at the University of Texas in Austin, who says she has spent much of her career making the unpopular argument to fellow liberals that genes are relevant predictors of social outcomes.

Harden thinks a strength of those on the left is their ability to recognize "that bodies are different from each other in a way that matters." Many are generally willing to allow that any number of traits, from addiction to obesity, are genetically influenced. Yet, she says, heritable cognitive ability seems to be "beyond the pale for us to integrate as a source of difference that impacts our life."

Harden believes that genes matter for our understanding of traits like intelligence, and that this should help shape progressive policymaking. She gives the example of an education department seeking policy interventions to improve math scores in a given school district. If a polygenic risk score is "as strongly correlated with their school grades" as family income is, she says of the students in such a district, then "does deliberately not collecting that [genetic] information, or not knowing about it, make your research harder [and] your inferences worse?"

To Harden, persisting with this strategy of avoidance for fear of encouraging eugenicists is a mistake. If "insisting that IQ is a myth and genes have nothing to do with it was going to be successful at neutralizing eugenics," she says, "it would've won by now."

Part of the reason these ideas are so taboo in many circles is that today's debate around genetic determinism is still deeply infused with Galton's ideas—and has become a particular fixation among the online right.

After Elon Musk took over Twitter (now X) in 2022 and loosened its restrictions on hate speech, a flood of accounts started sharing racist posts, some speculating about the genetic origins of inequality while arguing against immigration and racial integration. Musk himself

Many on the left are generally willing to allow that any number of traits, from addiction to obesity, are genetically influenced. Yet heritable cognitive ability seems to be "beyond the pale for us to integrate as a source of difference."

Harden, though, warns against discounting the work of an entire field because of a few noisy neo-reactionaries. "I think there can be this idea that technology is giving rise to the terrible racism," she says. The truth, she believes, is that "the racism has preexisted any of this technology."

In 2019, a company called Genomic Prediction began to offer the first preimplantation polygenic testing that had ever been made commercially available. With its LifeView Embryo Health Score, prospective parents are able to assess their embryos' predisposition to genetically complex health problems like cancer, diabetes, and heart disease. Pricing for the service starts at $3,500. Genomic Prediction uses a technique called an SNP array, which targets specific sites in the genome where common variants occur. The results are then cross-checked against GWASs that show correlations between genetic variants and certain diseases.

Four years later, a company named Orchid began offering a competing test. Orchid's Whole Genome Embryo Report distinguished itself by claiming to sequence more than 99% of an embryo's genome, allowing it to detect novel mutations and, the company says, diagnose rare diseases more accurately. For $2,500 per embryo, parents can access polygenic risk scores for 12 disorders, including schizophrenia, breast cancer, and hypothyroidism.

Orchid was founded by a woman named Noor Siddiqui. Before getting undergraduate and graduate degrees from Stanford, she was awarded the Thiel fellowship—a $200,000 grant given to young entrepreneurs willing to work on their ideas instead of going to college—back when she was a teenager, in 2012. This set her up to attract attention from

frequently reposts and engages with accounts like Crémieux Recueil, the pen name of independent researcher Jordan Lasker, who has written about the "Black-White IQ gap," and i/o, an anonymous account that once praised Musk for "acknowledging data on race and crime," saying it "has done more to raise awareness of the disproportionalities observed in these data than anything I can remember." (In response to

allegations that his research encourages eugenics, Lasker wrote to *MIT Technology Review*, "The popular understanding of eugenics is about coercion and cutting people cast as 'undesirable' out of the breeding pool. This is nothing like that, so it doesn't qualify as eugenics by that popular understanding of the term." X, Musk, and i/o, the anonymous X account, did not respond to requests for comment.)

members of the tech elite as both customers and financial backers. Her company has raised $16.5 million to date from investors like Ethereum founder Vitalik Buterin, former Coinbase CTO Balaji Srinivasan, and Armstrong, the Coinbase CEO.

In August Siddiqui made the controversial suggestion that parents who choose not to use genetic testing might be considered irresponsible. "Just be honest: you're okay with your kid potentially suffering for life so you can feel morally superior …" she wrote on X.

Americans have varied opinions on the emerging technology. In 2024, a group of bioethicists surveyed 1,627 US adults to determine attitudes toward a variety of polygenic testing criteria. A large majority approved of testing for physical health conditions like cancer, heart disease, and diabetes. Screening for mental health disorders, like depression, OCD, and ADHD, drew a more mixed—but still positive—response. Appearance-related traits, like skin color, baldness, and height, received less approval as something to test for.

Intelligence was among the most contentious traits—unsurprising given the way it has been weaponized throughout history and the lack of cultural consensus on how it should even be defined. (In many countries, intelligence testing for embryos is heavily regulated; in the UK, the practice is banned outright.) In the 2024 survey, 36.9% of respondents approved of preimplantation genetic testing for intelligence, 40.5% disapproved, and 22.6% said they were uncertain.

Despite the disagreement, intelligence has been among the traits most talked about as targets for testing. From early on, Genomic Prediction says, it began receiving inquiries "from all over the world" about testing for intelligence,

according to Diego Marin, the company's head of global business development and scientific affairs.

At one time, the company offered a predictor for what it called "intellectual disability." After some backlash questioning both the predictive capacity and the ethics of these scores, the company discontinued the feature. "Our mission and vision of this company is not to improve [a baby], but to reduce risk for disease," Marin told me. "When it comes to traits about IQ or skin color or height or something that's cosmetic and doesn't really have a connotation of a disease, then we just don't invest in it."

Orchid, on the other hand, does test for genetic markers associated with intellectual disability and developmental delay. But that may not be all. According to one employee of the company, who spoke on the condition of anonymity, intelligence testing is also offered to "high-roller" clients. According to this employee, another source close to the company, and reporting in the *Washington Post*, Musk used Orchid's services in the conception of at least one of the children he shares with the tech executive Shivon Zilis. (Orchid, Musk, and Zilis did not respond to requests for comment.)

I met Kian Sadeghi, the 25-year-old founder of New York–based Nucleus Genomics, on a sweltering July afternoon in his SoHo office. Slight and kinetic, Sadeghi spoke at a machine-gun pace, pausing only occasionally to ask if I was keeping up.

Sadeghi had modified his first organism—a sample of brewer's yeast—at the age of 16. As a high schooler in 2016, he was taking a course on CRISPR-Cas9 at a Brooklyn laboratory when he fell in love with the "beautiful depth" of genetics. Just a few years later,

he dropped out of college to build "a better 23andMe."

His company targets what you might call the application layer of PGT-P, accepting data from IVF clinics—and even from the competitors mentioned in this story—and running its own computational analysis.

"Unlike a lot of the other testing companies, we're software first, and we're consumer first," Sadeghi told me. "It's not enough to give someone a polygenic score. What does that mean? How do you compare them? There's so many really hard design problems."

Like its competitors, Nucleus calculates its polygenic risk scores by comparing an individual's genetic data with trait-associated variants identified in large GWASs, providing statistically informed predictions.

Nucleus provides two displays of a patient's results: a Z-score, plotted from –4 to 4, which explains the risk of a certain trait relative to a population with similar genetic ancestry (for example, if Embryo #3 has a 2.1 Z-score for breast cancer, its risk is higher than average), and an absolute risk score, which includes relevant clinical factors (Embryo #3 has a minuscule actual risk of breast cancer, given that it is male).

The real difference between Nucleus and its competitors lies in the breadth of what it claims to offer clients. On its sleek website, prospective parents can sort through more than 2,000 possible diseases, as well as traits from eye color to IQ. Access to the Nucleus Embryo platform costs $8,999, while the company's new IVF+ offering—which includes one IVF cycle with a partner clinic, embryo screening for up to 20 embryos, and concierge services throughout the process—starts at $24,999.

Its promises are remarkably bold. The company claims to be able to
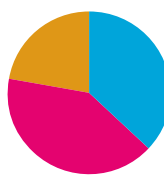
Americans have varied opinions. In a 2024 survey:

36.9%
approved
of testing for
intelligence

40.5%
disapproved

22.6%
were uncertain

"Maybe you want your baby to have blue eyes versus green eyes," Nucleus founder Kian Sadeghi said at a June event. "That is up to the liberty of the parents."

forecast a propensity for anxiety, ADHD, insomnia, and other mental issues. It says you can see which of your embryos are more likely to have alcohol dependence, which are more likely to be left-handed, and which might end up with severe acne or seasonal allergies. (Nevertheless, at the time of writing, the embryo-screening platform provided this disclaimer: "DNA is not destiny. Genetics can be a helpful tool for choosing an embryo, but it's not a guarantee. Genetic research is still in it's [sic] infancy, and there's still a lot we don't know about how DNA shapes who we are.")

To people accustomed to sleep trackers, biohacking supplements, and glucose monitoring, taking advantage of Nucleus's options might seem like a no-brainer. To anyone who welcomes a bit of serendipity in their life, this level of perceived control may be disconcerting to say the least.

Sadeghi likes to frame his arguments in terms of personal choice. "Maybe you want your baby to have blue eyes versus green eyes," he told a small audience at Nucleus Embryo's June launch event. "That is up to the liberty of the parents."

On the official launch day, Sadeghi spent hours gleefully sparring with X users who accused him of practicing eugenics. He rejects the term, favoring instead "genetic optimization"—though it seems he wasn't too upset about the free viral marketing. "This week we got five million impressions on Twitter," he told a crowd at the launch event, to a smattering of applause. (In an email to *MIT Technology Review*, Sadeghi wrote, "The history of eugenics is one of coercion and discrimination by states and institutions; what Nucleus does is the opposite—genetic forecasting that empowers individuals to make informed decisions.")

Nucleus has raised more than $36 million from investors like Srinivasan, Alexis Ohanian's venture capital firm Seven Seven Six, and Thiel's Founders Fund. (Like Siddiqui, Sadeghi was a recipient of a Thiel fellowship when he dropped out of college; a representative for Thiel did not respond to a request for comment for this story.) Sadeghi has even poached Genomic Prediction's cofounder Nathan Treff, who is now Nucleus's chief clinical officer.

Sadeghi's real goal is to build a one-stop shop for every possible application of genetic sequencing technology, from genealogy to precision medicine to genetic engineering. He names a handful of companies providing these services, with a combined market cap in the billions. "Nucleus is collapsing all five of these companies into one," he says. "We are not an IVF testing company. We are a genetic stack."

This spring, I elbowed my way into a packed hotel bar in the Flatiron district, where over a hundred people had gathered to hear a talk called "How to create SUPERBABIES." The event was part of New York's Deep Tech Week, so I expected to meet a smattering of biotech professionals and investors. Instead, I was surprised to encounter a diverse and curious group of creatives, software engineers, students, and prospective parents—many of whom had come with no previous knowledge of the subject.

The speaker that evening was Jonathan Anomaly, a soft-spoken political philosopher whose didactic tone betrays his years as a university professor.

Some of Anomaly's academic work has focused on developing theories of rational behavior. At Duke and the University of Pennsylvania, he led introductory courses on game theory, ethics, and collective action problems as well as bioethics, digging into thorny questions about abortion, vaccines, and euthanasia. But perhaps no topic has interested him so much as the emerging field of genetic enhancement.

In 2018, in a bioethics journal, Anomaly published a paper with the intentionally provocative title "Defending Eugenics." He sought to distinguish what he called "positive eugenics"—noncoercive methods aimed at increasing traits that "promote individual and social welfare"—from the so-called "negative eugenics" we know from our history books.

Anomaly likes to argue that embryo selection isn't all that different from practices we already take for granted. Don't believe two cousins should be allowed to have children? Perhaps you're a eugenicist, he contends. Your friend who picked out a six-foot-two Harvard grad from a binder of potential sperm donors? Same logic.

His hiring at the University of Pennsylvania in 2019 caused outrage among some students, who accused him of "racial essentialism." In 2020, Anomaly left academia, lamenting that "American universities had become an intellectual prison."

A few years later, Anomaly joined a nascent PGT-P company named Herasight, which was promising to screen for IQ.

At the end of July, the company officially emerged from stealth mode. A representative told me that most of the money raised so far is from angel investors, including Srinivasan, who also invested in Orchid and Nucleus. According to the launch announcement on X, Herasight has screened "hundreds of embryos" for private customers and is beginning to offer its first publicly available consumer product, a polygenic assessment that claims to detect an embryo's likelihood of developing 17 diseases.

Their marketing materials boast predictive abilities 122% better than Orchid's and 193% better than Genomic Prediction's for this set of diseases. ("Herasight is comparing their current predictor to models we published over five years ago," Genomic Prediction responded in a statement. "Our team is confident our predictors are world-class and are not exceeded in quality by any other lab.")

The company did not include comparisons with Nucleus, pointing to the "absence of published performance validations" by that company and claiming it represented a case where "marketing outpaces science." ("Nucleus is known for world-class science and marketing, and we understand why that's frustrating to our competitors," a representative from the company responded in a comment.)

Herasight also emphasized new advances in "within-family validation" (making sure that the scores are not merely picking up shared environmental factors by comparing their performance between unrelated people to their performance between siblings) and "cross-ancestry accuracy" (improving the accuracy of scores for people outside the European ancestry groups where most of the biobank data is concentrated). The representative explained that pricing varies by customer and the number of embryos tested, but it can reach $50,000.
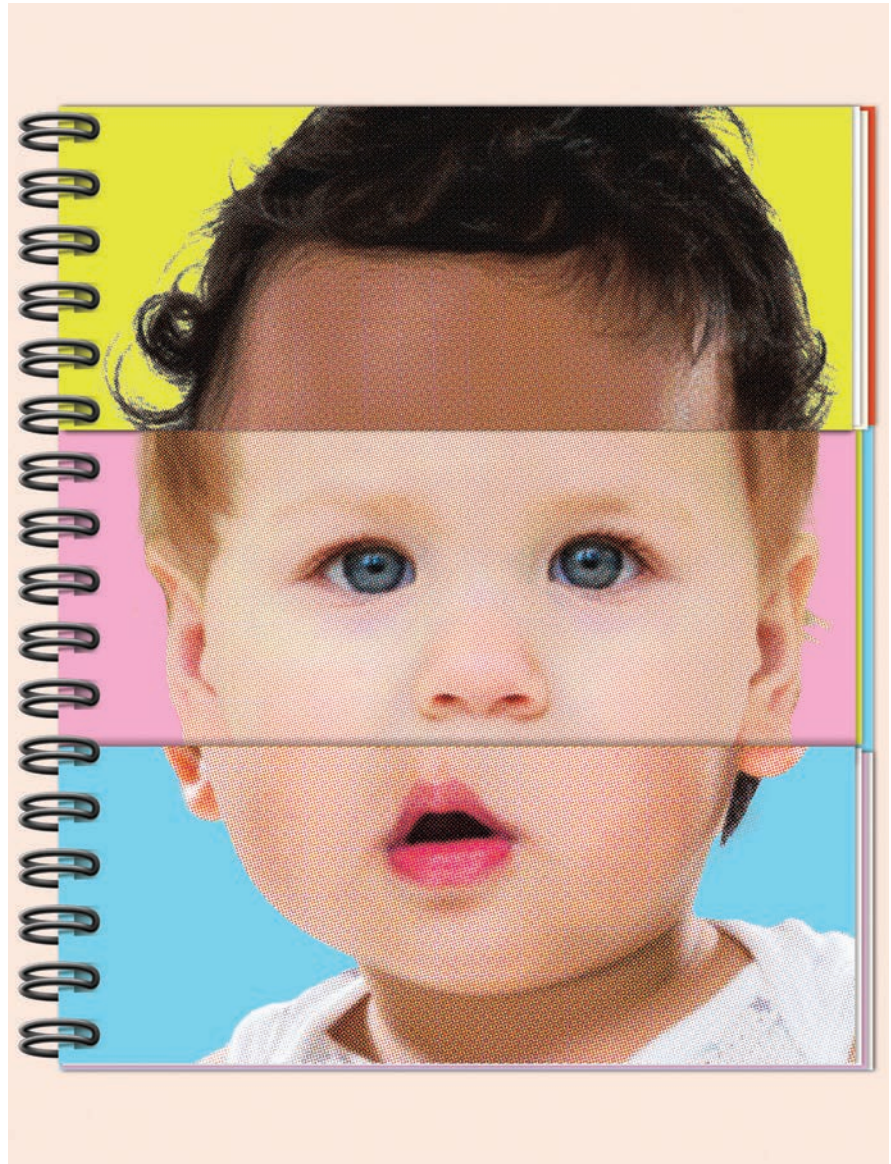
Herasight tests for just one non-disease-related trait: intelligence. For a couple who produce 10 embryos, it claims it can detect an IQ spread of about 15 points, from the lowest-scoring embryo to the highest. The representative says the company plans to release a detailed white paper on its IQ predictor in the future.

The day of Herasight's launch, Musk responded to the company announcement: "Cool." Meanwhile, a Danish researcher named Emil Kirkegaard, whose research has largely focused on IQ differences between racial groups, boosted the company to his nearly 45,000 followers on X (as well as in a Substack blog), writing, "Proper embryo selection just landed." Kirkegaard has in fact supported Anomaly's work for years; he's posted about him on X and recommended his 2020 book *Creating Future People*, which he called a "biotech eugenics advocacy book," adding: "Naturally, I agree with this stuff!"

When it comes to traits that Anomaly believes are genetically encoded, intelligence—which he claimed in his talk is about 75% heritable—is just the tip of the iceberg. He has also spoken about the heritability of empathy, impulse control, violence, passivity, religiosity, and political leanings.

Anomaly concedes there are limitations to the kinds of relative predictions that can be made from a small batch of embryos. But he believes we're only at the dawn of what he likes to call the "reproductive revolution." At his talk, he pointed to a technology currently in development at a handful of startups: in vitro gametogenesis. IVG aims to create sperm or egg cells in a laboratory using adult stem cells, genetically reprogrammed from cells found in a sample of skin or blood. In theory, this process could allow a couple to quickly produce a practically unlimited number of embryos to analyze for preferred traits. Anomaly predicted this technology could be ready to use on humans within eight years.

"I doubt the FDA will allow it immediately. That's what places like Próspera are for," he said, referring to the so-called "startup city" in Honduras, where scientists and entrepreneurs can conduct medical experiments free from the kinds of regulatory oversight they'd encounter in the US.

"You might have a moral intuition that this is wrong," said Anomaly, "but when it's discovered that elites are doing it privately … the dominoes are going to fall very, very quickly." The coming "evolutionary arms race," he claimed, will "change the moral landscape."

He added that some of those elites are his own customers: "I could already name names, but I won't do it."

After Anomaly's talk was over, I spoke with a young photographer who told me he was hoping to pursue a master's degree in theology. He came to the event, he told me, to reckon with the ethical implications of playing God. "Technology is sending us toward an Old-to-New-Testament transition moment, where we have to decide what parts of religion still serve us," he said soberly.

Criticisms of polygenic testing tend to fall into two camps: skepticism about the tests' effectiveness and concerns about their ethics. "On one hand," says Turley from the Social Science Genetic Association Consortium, "you have arguments saying 'This isn't going to work anyway, and the reason it's bad is because we're tricking parents, which would be a problem.' And on the other hand, they say, 'Oh, this is going to work *so* well that it's going to lead to enormous inequalities in society.' It's just funny to see. Sometimes these arguments are being made by the same people."

One of those people is Sasha Gusev, who runs a quantitative genetics lab at the Dana-Farber Cancer Institute. A vocal critic of PGT-P for embryo selection, he also often engages in online debates with the far-right accounts promoting race science on X.

Gusev is one of many professionals in his field who believe that because of numerous confounding socioeconomic factors—for example, childhood nutrition, geography, personal networks, and parenting styles—there isn't much point in trying to trace outcomes like educational attainment back to genetics,

When it comes to traits that Jonathan Anomaly believes are genetically encoded, intelligence is just the tip of the iceberg. He has also spoken about the heritability of empathy, violence, religiosity, and political leanings.

"These reckless, overpromised, and oftentimes just straight-up manipulative embryo selection applications are a risk for the credibility and the utility of these clinical tools," says Sasha Gusev of the Dana-Farber Cancer Institute.

particularly not as a way to prove that there's a genetic basis for IQ.

He adds, "I think there's a real risk in moving toward a society where you see genetics and 'genetic endowments' as the drivers of people's behavior and as a ceiling on their outcomes and their capabilities."

Gusev thinks there is real promise for this technology in clinical settings among specific adult populations. For adults identified as having high polygenic risk scores for cancer and cardiovascular disease, he argues, a combination of early screening and intervention could be lifesaving. But when it comes to the preimplantation testing currently on the market, he thinks there are significant limitations—and few regulatory measures or long-term validation methods to check the promises companies are making. He fears that giving these services too much attention could backfire.

"These reckless, overpromised, and oftentimes just straight-up manipulative embryo selection applications are a risk for the credibility and the utility of these clinical tools," he says.

Many IVF patients have also had strong reactions to publicity around PGT-P. When the *New York Times* published an opinion piece about Orchid in the spring, angry parents took to Reddit to rant. One user posted, "For people who dont [sic] know why other types of testing are necessary or needed this just makes IVF people sound like we want to create 'perfect' babies, while we just want (our) healthy babies."

Still, others defended the need for a conversation. "When could technologies like this change the mission from helping infertile people have healthy babies to eugenics?" one Redditor posted. "It's a fine line to walk and an important discussion to have."

Some PGT-P proponents, like Kirkegaard and Anomaly, have argued that policy decisions should more explicitly account for genetic differences. In a series of blog posts following the 2024 presidential election, under the header "Make science great again," Kirkegaard called for ending affirmative action laws, legalizing race-based hiring discrimination, and removing restrictions on data sets like the NIH's All of Us biobank that prevent researchers like him from using the data for race science. Anomaly has criticized social welfare policies for putting a finger on the scale to "punish the high-IQ people."

Indeed, the notion of genetic determinism has gained some traction among loyalists to President Donald Trump.

In October 2024, Trump himself made a campaign stop on the conservative radio program *The Hugh Hewitt Show*. He began a rambling answer about immigration and homicide statistics. "A murderer, I believe this, it's in their genes. And we got a lot of bad genes in our country right now," he told the host.

Gusev believes that while embryo selection won't have much impact on individual outcomes, the intellectual framework endorsed by many PGT-P advocates could have dire social consequences.

"If you just think of the differences that we observe in society as being cultural, then you help people out. You give them better schooling, you give them better nutrition and education, and they're able to excel," he says. "If you think of these differences as being strongly innate, then you can fool yourself into thinking that there's nothing that can be done and people just are what they are at birth."

For the time being, there are no plans for longitudinal studies to track *actual* outcomes for the humans these companies have helped bring into the world. Harden, the behavioral geneticist from UT Austin, suspects that 25 years down the line, adults who were once embryos selected on the basis of polygenic risk scores are "going to end up with the same question that we all have." They will look at their life and wonder, "What would've had to change for it to be different?" ∎

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Libby Cowgill is an anthropologist at the University of Missouri who hopes to revamp the science of thermoregulation.

Hot and cold

Scientists are learning more and more about how our bodies respond to extreme temperatures.

Their research on adaptation and exposure could save lives.

It's the 25th of June and I'm shivering in my lab-issued underwear in Fort Worth, Texas. Libby Cowgill, an anthropologist in a furry parka, has wheeled me and my cot into a metal-walled room set to 40 °F. A loud fan pummels me from above and siphons the dregs of my body heat through the cot's mesh from below. A large respirator fits snug over my nose and mouth. The device tracks carbon dioxide in my exhales—a proxy for how my metabolism speeds up or slows down throughout the experiment. Eventually Cowgill will remove my respirator to slip a wire-thin metal temperature probe several pointy inches into my nose.

Cowgill and a graduate student quietly observe me from the corner of their so-called "climate chamber." Just a few hours earlier I'd sat beside them to observe as another volunteer, a 24-year-old personal trainer, endured the cold. Every few minutes, they measured his skin temperature with a thermal camera, his core temperature with a wireless pill, and his blood pressure and other metrics that hinted at how his body handles extreme cold. He lasted almost an hour without shivering; when my turn comes, I shiver aggressively on the cot for nearly an hour straight.

I'm visiting Texas to learn about this experiment on how different bodies respond to extreme climates. "What's the record for fastest to shiver so far?" I jokingly ask Cowgill as she tapes biosensing devices to my chest and legs. After I exit the cold, she surprises me: "You, believe it or not, were not the worst person we've ever seen."

Cowgill is a 40-something anthropologist at the University of Missouri who powerlifts and teaches CrossFit in her spare time. She's small and strong, with dark bangs and geometric tattoos. Since 2022, she's spent the summers at the University of North Texas Health Science Center tending to these uncomfortable experiments. Her team hopes to revamp the science of thermoregulation.

While we know in broad strokes how people thermoregulate, the science of keeping warm or cool is mottled with blind spots. "We have the general picture. We don't have a lot of the specifics for vulnerable groups," says Kristie Ebi, an epidemiologist with the University of Washington who has studied heat and health for over 30 years. "How does thermoregulation work if you've got heart disease?"

"Epidemiologists have particular tools that they're applying for this question," Ebi continues. "But we do need more answers from other disciplines."

By Max G. Levy

Photographs by Justin Clemons

Climate change is subjecting vulnerable people to temperatures that push their limits. In 2023, about 47,000 heat-related deaths are believed to have occurred in Europe. Researchers estimate that climate change could add an extra 2.3 million European heat deaths this century. That's heightened the stakes for solving the mystery of just what happens to bodies in extreme conditions.

Extreme temperatures already threaten large stretches of the world. Populations across the Middle East, Asia, and sub-Saharan Africa regularly face highs beyond widely accepted levels of human heat tolerance. Swaths of the southern US, northern Europe, and Asia now also endure unprecedented lows: The 2021 Texas freeze killed at least 246 people, and a 2023 polar vortex sank temperatures in China's northernmost city to a hypothermic record of −63.4 °F.

This change is here, and more is coming. Climate scientists predict that limiting emissions can prevent lethal extremes from encroaching elsewhere. But if emissions keep course, fierce heat and even cold will reach deeper into every continent. About 2.5 billion people in the world's hottest places don't have air-conditioning. When people do, it can make outdoor temperatures even worse, intensifying the heat island effect in dense cities. And neither AC nor radiators are much help when heat waves and cold snaps capsize the power grid.

Through experiments like Cowgill's, researchers around the world are revising rules about when extremes veer from uncomfortable to deadly. Their findings change how we should think about the limits of hot and cold—and how to survive in a new world.

Embodied change

Archaeologists have known for some time that we once braved colder temperatures than anyone previously imagined. Humans pushed into Eurasia and North America well before the last glacial period ended about 11,700 years ago. We were the only hominins to make it out of this era. Neanderthals, Denisovans, and *Homo floresiensis* all went extinct. We don't know for certain what killed those species. But we do know that humans survived thanks to protection from clothing, large social networks, and physiological flexibility. Human resilience to extreme temperature is baked into our bodies, behavior, and genetic code. We wouldn't be here without it.

"Our bodies are constantly in communication with the environment," says Cara Ocobock, an anthropologist at the University of Notre Dame who studies how we expend energy in extreme conditions. She has worked closely with Finnish reindeer herders and Wyoming mountaineers.

But the relationship between bodies and temperature is surprisingly still a mystery to scientists. In 1847, the anatomist Carl Bergmann observed that animal species grow larger in cold climates. The zoologist Joel Asaph Allen noted in 1877 that cold-dwellers had shorter appendages. Then there's the nose thing: In the 1920s, the British anthropologist Arthur Thomson theorized that people in cold places have relatively long, narrow noses, the better to heat and humidify the air they take in. These theories stemmed from observations of animals like bears and foxes, and others that followed stemmed from studies comparing the bodies of cold-accustomed Indigenous populations with white male control groups. Some, like those having to do with optimization of surface area, do make sense: It seems reasonable that a tall, thin body increases the amount of skin available to dump excess heat. The problem is, scientists have never actually tested this stuff in humans.
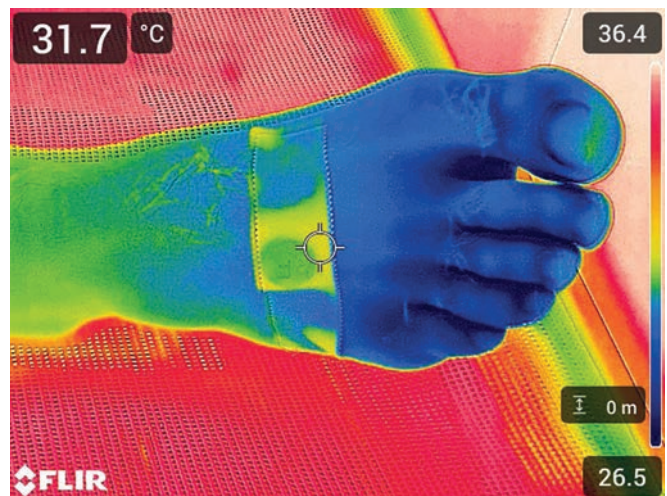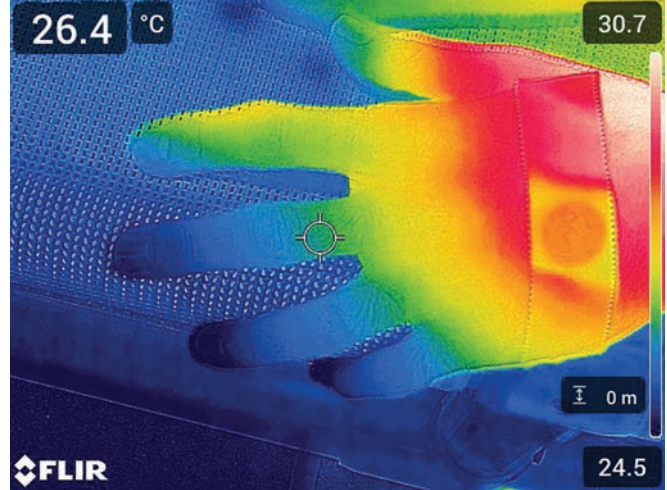
Some of what we know about temperature tolerance thus far comes from century-old race science or assumptions that anatomy controls everything. But science has evolved. Biology has matured. Childhood experiences, lifestyles, fat cells, and wonky biochemical feedback loops can contribute to a picture

"You, believe it or not, were not the worst person we've ever seen," the author was told after enduring Cowgill's "climate chamber."

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of the body as more malleable than anything imagined before. And that's prompting researchers to change how they study it.

"If you take someone who's super long and lanky and lean and put them in a cold climate, are they gonna burn more calories to stay warm than somebody who's short and broad?" Ocobock says. "No one's looked at that."

Ocobock and Cowgill teamed up with Scott Maddux and Elizabeth Cho at the Center for Anatomical Sciences at the University of North Texas Health Fort Worth. All four are biological anthropologists who have also puzzled over whether the rules Bergmann, Allen, and Thomson proposed are actually true.

For the past four years, the team has been studying how factors like metabolism, fat, sweat, blood flow, and personal history control thermoregulation.

Your native climate, for example, may influence how you handle temperature extremes. In a unique study of mortality statistics from 1980s Milan, Italians raised in warm southern Italy were more likely to survive heat waves in the northern part of the country.

Similar trends have appeared in cold climes. Researchers often measure cold tolerance by a person's "brown adipose," a type of fat that is specialized for generating heat (unlike white fat, which primarily stores energy). Brown fat is a cold adaptation because it delivers heat without the mechanism of shivering. Studies have linked it to living in cold climates, particularly at young ages. Wouter van Marken Lichtenbelt, the physiologist at Maastricht University who with colleagues discovered brown fat in adults, has shown that this tissue can further activate with cold exposure and even help regulate blood sugar and influence how the body burns other fat.

That adaptability served as an early clue for the Texas team. They want to know how a person's response to hot and cold correlates with height, weight, and body shape. What is the difference, Maddux asks, between "a male who's 6 foot 6 and weighs 240 pounds" and someone else in the same environment "who's 4 foot 10 and weighs 89 pounds"? But the team also wondered if shape was only part of the story.

Their multi-year experiment uses tools that anthropologists couldn't have imagined a century ago—devices that track metabolism in real time and analyze genetics. Each participant gets a CT scan (measuring body shape), a DEXA scan (estimating percentages of fat and muscle), high-resolution 3D scans, and DNA analysis from saliva to examine ancestry genetically.

Volunteers lie on a cot in underwear, as I did, for about 45 minutes in each climate condition, all on separate days. There's dry cold, around 40 °F, akin to braving a walk-in refrigerator. Then dry heat and humid heat: 112 °F with 15% humidity and 98 °F with 85% humidity. They call it "going to Vegas" and "going to Houston," says Cowgill. The chamber session is long enough to measure an effect, but short enough to be safe.

Before I traveled to Texas, Cowgill told me she suspected the old rules would fall. Studies linking temperature tolerance to race and ethnicity, for example, seemed tenuous because biological anthropologists today reject the concept of distinct races. It's a false premise, she told me: "No one in biological anthropology would argue that human beings do not vary across the globe—that's obvious to anyone with eyes. [But] you can't draw sharp borders around populations."

She added, "I think there's a substantial possibility that we spend four years testing this and find out that really, limb length, body mass, surface area […] are not the primary things that are predicting how well you do in cold and heat."

Adaptable to a degree

In July 1995, a week-long heat wave pushed Chicago above 100 °F, killing roughly 500 people. Thirty years later, Ollie Jay, a physiologist at the University of Sydney, can duplicate the conditions of that exceptionally humid heat wave in a climate chamber at his laboratory.

"We can simulate the Chicago heat wave of '95. The Paris heat wave of 2003. The heat wave [in early July of this year] in Europe," Jay says. "As long as we've got the temperature and humidity information, we can re-create those conditions."

"Everybody has quite an intimate experience of feeling hot, so we've got 8 billion experts on how to keep cool," he says. Yet our internal sense of when heat turns deadly is unreliable. Even professional athletes overseen by experienced medics have died after missing dangerous warning signs. And little research has been done to explore how vulnerable populations such as elderly people, those with heart disease, and low-income communities with limited access to cooling respond to extreme heat.

Jay's team researches the most effective strategies for surviving it. He lambastes air-conditioning, saying it demands so much energy that it can aggravate climate change in "a vicious cycle." Instead, he has monitored people's vital signs while they use fans and skin mists to endure three hours in humid and dry heat. In results published last year, his research found that fans reduced cardiovascular strain by 86% for people with heart disease in the type of humid heat familiar in Chicago.

Dry heat was a different story. In that simulation, fans not only didn't help but actually doubled the rate at which core temperatures rose in healthy older people.

Heat kills. But not without a fight. Your body must keep its internal temperature in a narrow window flanking 98 °F by less

> ## "Our bodies are constantly in communication with the environment."

than two degrees. The simple fact that you're alive means you are *producing* heat. Your body needs to export that heat without amassing much more. The nervous system relaxes narrow blood vessels along your skin. Your heart rate increases, propelling more warm blood to your extremities and away from your organs. You sweat. And when that sweat evaporates, it carries a torrent of body heat away with it.

This thermoregulatory response can be trained. Studies by van Marken Lichtenbelt have shown that exposure to mild heat increases sweat capacity, decreases blood pressure, and drops resting heart rate. Long-term studies based on Finnish saunas suggest similar correlations.

The body may adapt protectively to cold, too. In this case, body heat is your lifeline. Shivering and exercise help keep bodies warm. So can clothing. Cardiovascular deaths are thought to spike in cold weather. But people more adapted to cold seem better able to reroute their blood flow in ways that keep their organs warm without dropping their temperature too many degrees in their extremities.

Earlier this year, the biological anthropologist Stephanie B. Levy (no relation) reported that New Yorkers who experienced lower average temperatures had more productive brown fat, adding evidence for the idea that the inner workings of our bodies adjust to the climate throughout the year and perhaps even throughout our lives. "Do our bodies hold a biological memory of past seasons?" Levy wonders. "That's still an open question. There's some work in rodent models to suggest that that's the case."

Although people clearly acclimatize with enough strenuous exposures to either cold or heat, Jay says, "you reach a ceiling." Consider sweat: Heat exposure can increase the amount you sweat only until your skin is completely saturated. It's a nonnegotiable physical limit. Any additional sweat just means leaking water without carrying away any more heat. "I've heard people say we'll just find a way of evolving out of this—we'll biologically adapt," Jay says. "Unless we're completely changing our body shape, then that's not going to happen."

And body shape may not even sway thermoregulation as much as previously believed. The subject I observed, a personal trainer, appeared outwardly adapted for cold: his broad shoulders didn't even fit in a single CT scan image. Cowgill supposed that this muscle mass insulated him. When he emerged from his sessions in the 40 °F environment, though, he had finally started shivering—intensely. The researchers covered him in a heated blanket. He continued shivering. Driving to lunch over an hour later in a hot car, he still mentioned feeling cold. An hour after that, a finger prick drew no blood, a sign that blood

vessels in his extremities remained constricted. His body temperature fell about half a degree C in the cold session—a significant drop—and his wider build did not appear to shield him from the cold as well as my involuntary shivering protected me.

I asked Cowgill if perhaps there is no such thing as being uniquely predisposed to hot or cold. "Absolutely," she said.

A hot mess

So if body shape doesn't tell us much about how a person maintains body temperature, and acclimation also runs into limits, then how do we determine how hot is too hot?

In 2010 two climate change researchers, Steven Sherwood and Matthew Huber, argued that regions around the world become uninhabitable at wet-bulb temperatures of 35 °C, or 95 °F. (Wet-bulb measurements are a way to combine air temperature and relative humidity.) Above 35 °C, a person simply wouldn't be able to dissipate heat quickly enough. But it turns out that their estimate was too optimistic.

Researchers "ran with" that number for a decade, says Daniel Vecellio, a bioclimatologist at the University of Nebraska, Omaha. "But the number had never been actually empirically tested." In 2021 a Pennsylvania State University physiologist, W. Larry Kenney, worked with Vecellio and others to test wet-bulb limits in a climate chamber. Kenney's lab investigates which combinations of temperature, humidity, and time push a person's body over the edge.

Not long after, the researchers came up with their own wet-bulb limit of human tolerance: below 31 °C in warm, humid conditions for the youngest cohort, people in their thermoregulatory prime. Their research suggests that a day reaching 98 °F and 65% humidity, for example, poses danger in a matter of hours, even for healthy people.

In 2023, Vecellio and Huber teamed up, combining the growing arsenal of lab data with state-of-the-art climate simulations to predict where heat and humidity most threatened global populations: first the Middle East and South Asia, then sub-Saharan Africa and eastern China. And assuming that warming reaches 3 to 4 °C over preindustrial levels this century, as predicted, parts of North America, South America, and northern and central Australia will be next.

Last June, Vecellio, Huber, and Kenney co-published an article revising the limits that Huber had proposed in 2010. "Why not 35 °C?" explained why the human limits have turned out to be lower than expected. Those initial estimates overlooked the fact that our skin temperature can quickly jump above 101 °F in hot weather, for example, making it harder to dump internal heat.

Climate change forces us to reckon with the knotty science of how our bodies interact with the environment.

The Penn State team has published deep dives on how heat tolerance changes with sex and age. Older participants' wet-bulb limits wound up being even lower—between 27 and 28 °C in warm, humid conditions—and varied more from person to person than they did in young people. "The conditions that we experience now—especially here in North America and Europe, places like that—are well below the limits that we found in our research," Vecellio says. "We know that heat kills now."

What this fast-growing body of research suggests, Vecellio stresses, is that you can't define heat risk by just one or two numbers. Last year, he and researchers at Arizona State University pulled up the hottest 10% of hours between 2005 and 2020 for each of 96 US cities. They wanted to compare recent heat-health research with historical weather data for a new perspective: How

frequently is it so hot that people's bodies can't compensate for it? Over 88% of those "hot hours" met that criterion for people in full sun. In the shade, most of those heat waves became meaningfully less dangerous.

"There's really almost no one who 'needs' to die in a heat wave," says Ebi, the epidemiologist. "We have the tools. We have the understanding. Essentially all [those] deaths are preventable."

More than a number

A year after visiting Texas, I called Cowgill to hear what she was thinking after four summers of chamber experiments. She told me that the only rule about hot and cold she currently stands behind is … well, none.

She recalled a recent participant—the smallest man in the study, weighing 114 pounds. "He shivered like a leaf on a tree," Cowgill says. Normally, a strong shiverer warms up quickly. Core temperature may even climb a little. "This [guy] was just shivering and shivering and shivering and not getting any warmer," she says. She doesn't know why this happened. "Every time I think I get a picture of what's going on in there, we'll have one person come in and just kind of be a complete exception to the rule," she says, adding that you can't just gloss over how much human bodies vary inside and out.

The same messiness complicates physiology studies.

Jay looks to embrace bodily complexities by improving physiological simulations of heat and the human strain it causes. He's piloted studies that input a person's activity level and type of clothing to predict core temperature, dehydration, and cardiovascular strain based on the particular level of heat. One can then estimate the person's risk on the basis of factors like age and health. He's also working on physiological models to identify vulnerable groups, inform early-warning systems ahead of heat waves, and possibly advise cities on whether interventions like fans and mists can help protect residents. "Heat is an all-of-society issue," Ebi says. Officials could better prepare the public for cold snaps this way too.

"Death is not the only thing we're concerned about," Jay adds. Extreme temperatures bring morbidity and sickness and strain hospital systems: "There's all these community-level impacts that we're just completely missing."

Climate change forces us to reckon with the knotty science of how our bodies interact with the environment. Predicting the health effects is a big and messy matter.

The first wave of answers from Fort Worth will materialize next year. The researchers will analyze thermal images to crunch data on brown fat. They'll resolve whether, as Cowgill suspects, your body shape may not sway temperature tolerance as much as previously assumed. "Human variation is the rule," she says, "not the exception." ∎

Max G. Levy is an independent journalist who writes about chemistry, public health, and the environment.
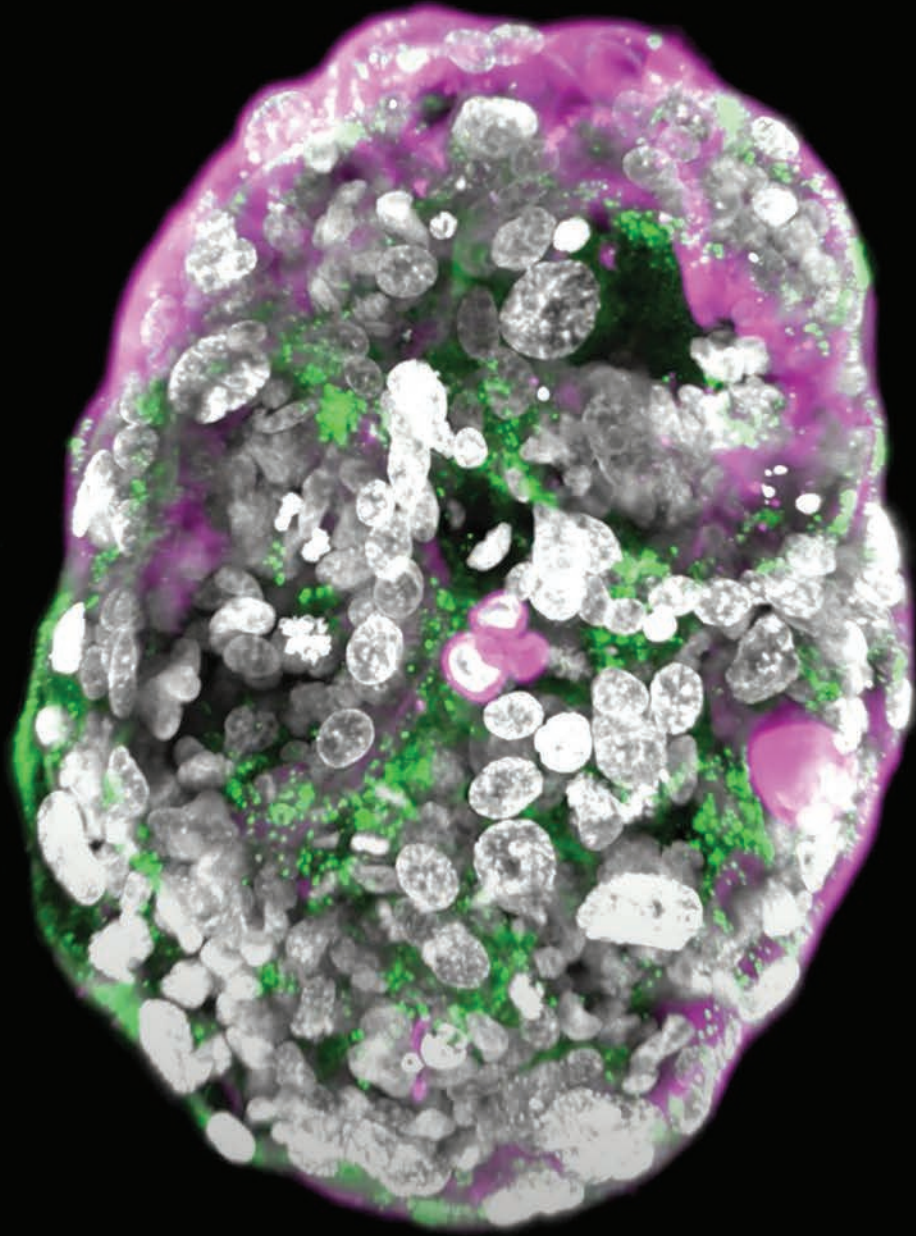
Created in Jacob Hanna's lab, this "model" made from stem cells resembles a two-week-old human embryo. Tracers highlight the presence of the hormone detected by pregnancy tests (green) and the layer that will become the placenta (pink).

When the Palestinian stem-cell scientist Jacob Hanna was stopped while entering the US last May, airport customs agents took him aside and held him for hours in "secondary," a back office where you don't have your passport and can't use your phone. There were two young Russian women and a candy machine in the room with him. Hanna, who has a trim beard and glasses and holds an Israeli passport, accepted the scrutiny. "It's almost like you are under arrest, but in a friendly way," he says. He agreed to turn over his phone and social media for inspection.

"They said, 'You have the right to refuse,'" he recalls, "and I said, 'No, no, it's an open book.'"

The agents scrolling through his feeds would have learned that Hanna is part of Israel's small Arab Christian minority, a nonbinary LGBTQ-rights advocate, and an outspoken critic of the Gaza occupation, who uses his social media accounts to post images of atrocities and hold up a

mirror to scientific colleagues including those at the Weizmann Institute of Science, the pure-science powerhouse where he works—Israel's version of Caltech or Rockefeller University. In his luggage, they would have found his keffiyeh, or traditional headscarf, which Hanna last year vowed to wear at lecture podiums on his many trips abroad.

Hanna had been stopped before; he knew the routine. Anything to declare? Any biological samples? But this time the agents' questions touched on a specific new topic: embryos.

Weeks earlier, a Harvard University researcher had been arrested for having frog embryos in her luggage and sent to a detention center in Louisiana. Hanna didn't have any specimens from his lab, but if he had, it would have been surprisingly hard to say what they were. That's because his lab specializes in creating synthetic embryo models, structures that

The embryo builder

Jacob Hanna is coaxing the beginnings of bodies directly from stem cells. How real are they?

By Antonio Regalado

resemble real embryos but don't involve sperm, eggs, or fertilization.

Instead of relying on the same old recipe biology has followed for a billion years, give or take, Hanna is coaxing the beginnings of animal bodies directly from stem cells. Join these cells together in the right way, and they will spontaneously attempt to organize into an embryo—a feat that's opening up the earliest phases of development to scientific scrutiny and may lead to a new source of tissue for transplant medicine.

In 2022, working with mice, Hanna reported he'd used the technique to produce synthetic embryos with beating hearts and neural folds—growing them inside small jars connected to a gas mixer, a type of artificial womb. The next year, he repeated the trick using human cells. This time the structures were not so far developed, still spherical in shape. Nonetheless, they were incredibly realistic mimics of a two-week-old human embryo, including cells destined to form the placenta.

These sorts of models aren't yet the same as embryos. It's rare that they form correctly—it takes a hundred tries to make one—and they skip past normal steps before popping into existence. Yet to scientists like the French biologist Denis Duboule, Hanna's creations are "entirely astonishing and very disturbing." Soon, Duboule expects, it could be difficult to distinguish between a real human embryo—the kind with legal protections—and one conjured from stem cells.

Hanna is the vanguard of a wider movement that's fusing advanced methods in genetics, stem-cell biology, and still-primitive artificial wombs to create bodies where they've never grown before—outside the uterus. Joining the chase are researchers at Caltech, the University of Cambridge, and Rockefeller in New York, as well as a growing cadre of startup companies with commercial aims. There's Renewal Bio, a startup Hanna cofounded, which hopes to grow synthetic embryos as a source of youthful replacement cells, such as bits of liver or even eggs. In Europe, Dawn Bio has started placing a type of

embryo model called a blastoid on uterine tissue. That will light up a pregnancy test and could, the company thinks, provide new insights into IVF medicine. Patent offices in the US and Europe are seeing a flood of claims as universities grasp for exclusive commercial control over these new types of beings.

Hanna declined a request to discuss his research for this story. But for the last three years, *MIT Technology Review* has followed Hanna across online presentations, lecture halls, and two in-person ethics meetings, both organized by the Global Observatory for Genome Editing, a public consultation project where he agreed to engage with religious scholars, bioethicists, and other experts. What emerged is a remarkable picture of a scientist working at a Nobel Prize level but whose research, though approved by his institution, raises serious long-term ethical questions.

Exactly how far Hanna has taken his models of the human embryo is an open question. According to public comments from Renewal Bio, the answer is at least 28 days. But it's possibly further. One scientist in contact with the company said he thought they'd reached close to day 40, a point where you would see the beginning of eyes and budding limbs. Renewal did not respond to a request for comment.

But even if he hasn't gotten that far yet, Hanna intends to. His team is "trying to make entities at more advanced stages—depending on the goal, it could be day 30 in development, day 40, or day 70," he told an audience last May in Cambridge, Massachusetts, where he'd traveled to join a panel discussion involving religious scholars and social scientists at the Global Observatory's annual summit. The more advanced versions would be similar in size and development to a fetus in the third month of pregnancy.

O. Carter Snead, a bioethicist from the University of Notre Dame who led the panel featuring Hanna, approached me afterward to ask if I'd heard what the scientist had said. Snead was surprised that Hanna had so frankly disclosed his goals and that no one had objected, or maybe

even grasped what it meant. Perhaps, Snead thinks, this technology won't sink in until people can see it with their own eyes. "If you had one of these spinning bottles with something that looked like a human fetus inside it, I think you'd get people's attention," he says. "That's going to be like, whoa—what are we doing?"

Snead, a Catholic who sits on a panel that advises the Vatican, also was not comforted by Hanna's plan to make sure his models, if they advance to later stages of development, will pass ethical scrutiny. That plan involves blocking the formation of the head, brain, or perhaps heart of the synthetic structures, by means including genetic modification. If there's no brain, Hanna's reasoning goes, there's no awareness, no person, and no foul. Just a clump of organs.

Snead says that's not the same standard of humanity he knows, which treats all humans the same, regardless of their intellectual capacity or anything else. "What is considered human? Who is considered human?" wonders Snead. "It's who's in and who's out. There is a dramatic consequence of being in versus out of the boundaries of humanity."

Soon it could be difficult to distinguish between a real human embryo— the kind with legal protections—and one conjured from stem cells.

Jacob Hanna leads a team at the Weizmann Institute of Science in Rehovot, Israel, that is studying how to create embryos without using sperm, eggs, or fertilization. He's cofounded a startup company, Renewal Bio, that has plans to use these synthetic embryo models as bioprinters to produce youthful tissue, but ethical questions surround the project.

A side-by-side comparison of synthetic (left) and natural (right) mouse embryos shows similar formation of the brain and heart.
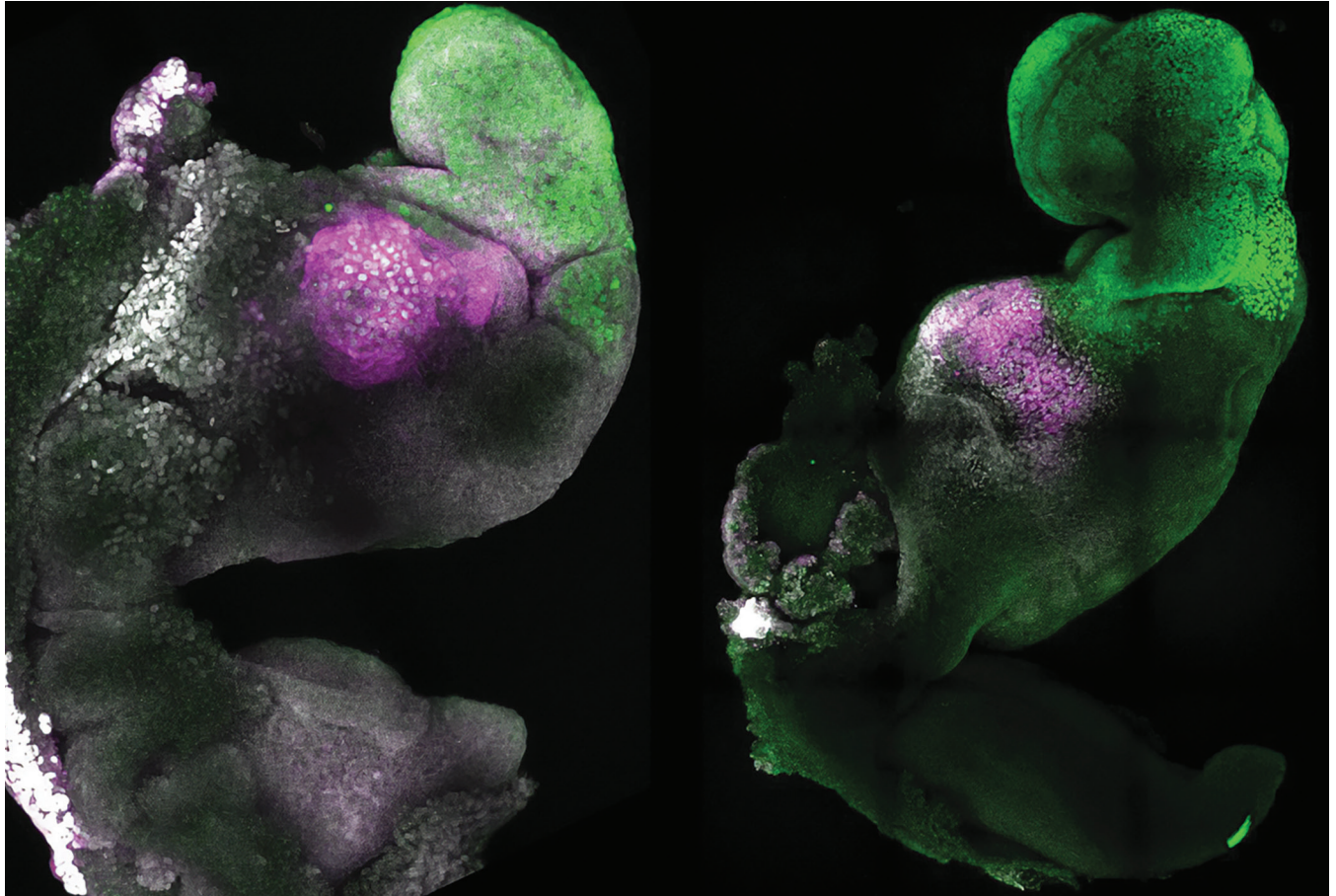
The beginnings of bodies

Each of us—me, you the reader, and Jacob Hanna—started as a fertilized egg, a single cell that's able to divide and dynamically carry out a program to build a complete body with all its organs and billions of specialized cells. Science has long sought ways to seize on that dramatic potential. A first step came in the 1990s, when scientists were able to isolate powerful stem cells from five-day-old embryos created through in vitro fertilization—and keep them growing in their labs. These embryonic stem cells had the inherent potential to become any other type of cell. If they could be directed in the lab to form, for example, neurons or the insulin-making cells that diabetics need, that would open up a way to treat disease using cell transplants.

But these lab recipes are often unsuccessful, which explains the general lack of new stem-cell treatments. "The sad truth is that over 25 years that we've been working on this problem, there are about 10 cell types you make that have reasonable function," says Chad Cowan, chief scientific officer of the stem-cell company Century Therapeutics. If we think of the body as a car, he explains, "we've got only spark plugs. We maybe have some tires." The body's most potent blood-forming cells in particular "never appear," according to Cowan, even though biotech companies have spent millions trying to make them.

It turns out, though, that stem cells retain a natural urge to work together. Scientists began to notice that, when left alone, the cells would join into blobs, tubes, and cavities—some of which resembled parts of an embryo.

Early versions of these structures were crude, even just a swirling film of cells

on a glass slide. But each year, they have grown more realistic. By 2023, Hanna was describing what he called a "bona fide" human embryo model that was "fully integrated," with all the major parts arranged in an architecture that was hard to distinguish from the real thing.

His company, Renewal, plans to use these synthetic embryos as a kind of "bioprinter," producing medically valuable cells in cases where other methods have failed. This could be particularly valuable if the synthetic embryos are a perfect match with a patient's DNA. And that's possible too: These days reprogramming anyone's skin cells into stem cells is easily done. Hanna has tried it on himself, transforming his own cells into synthetic embryos.

Hanna's research, and that of other groups, has at times collided with a powerful scientific body called the International Society for Stem Cell Research, or ISSCR,

a self-governance organization that sets boundaries about what research can and can't be published and what terminology to use. That's to shield scientists from sensational headlines, public backlash, or the reach of actual regulators.

The organization has taken a particularly categorical position on structures made from stem cells, saying they are mere "models." According to a statement it fired off in 2023, "embryo models are neither synthetic nor embryos"—and, it added, they "cannot and will not develop to the equivalent of postnatal stage human."

Many scientists, including Hanna, agree no one should ever try to make a stem-cell baby. But he is fairly certain these structures will become more realistic and can grow further. In fact, that may be the real test of what an embryo is: whether it can dynamically keep reaching new stages of development, especially organogenesis, or the first emergence of organs. The language in the ISSCR statement, he complained, was "brainwashing."

Replacement parts

Most of the commercial projects involving synthetic embryos are doomed to

Hanna's startup plans to use synthetic embryos as a kind of "bio-printer," producing medically valuable cells in cases where other methods have failed.

a short and fitful life as the technology proves too difficult or undeveloped. But the idea isn't going away. Instead, there are signals it's getting bigger, and weirder. In an editorial published in March by *MIT Technology Review*, a group of Stanford scientists put forward a proposal for what they called "bodyoids," arguing that stem cells and artificial wombs may lead to an "unlimited source" of nonsentient human bodies for use in drug research or as organ donors. One of its authors, Henry Greely, among the foremost bioethicists in the US, posted on Bluesky that even though the idea gives him "some creeps," he added his name because he feels it is plausible enough to need discussion, and "soon."

Especially in the Bay Area, headless bodies are having a moment. The Stanford biologist Hiro Nakauchi, another "bodyoids" author, said the editorial provided a surprise entrée for him into a world of stealth startups already pursuing synthetic embryos, artificial wombs, and body-part "replacement." He met the CEO of Hanna's company, signing on as an advisor. But other teams have still more radical plans. One venture capitalist introduced him to a longevity entrepreneur tinkering with a plan for head transplants. The idea: Swap your aged head onto the body of a younger clone. That company claims to have a facility on a Caribbean island "just like Jurassic Park," Nakauchi says.

These sorts of plans—real or rumored—have gotten the attention of the stem-cell police, the ISSCR. This June, an ethics committee led by Amander Clark, a fetal specialist at UCLA and a past president of the society, wrote that it had become aware of "commercial and other groups raising the possibility of building an embryo in vitro" and bringing it to viability inside "artificial systems." Though the ISSCR had previously decreed that embryo models "cannot and will not" develop to term, it now declared efforts aiming at viability "unsafe and unethical," placing them in a "prohibited" category. It added that the ban would cover "any purpose: reproductive, research, or commercial."

Blurred boundaries

Clark and her colleagues are right that, for the foreseeable future, no one is going to decant a full-term baby out of a bottle. That's still science fiction. But there's a pressing issue that needs to be dealt with right now. And that's what to do about synthetic embryo models that develop just part of the way—say for a few weeks, or months, as Hanna proposes.

Because right now, hardly any laws or policies apply to synthetic embryos. One reason is their unnatural origin: Because these entities don't start with conception and grow in labs, most existing laws won't cover them. That includes the Fetus Farming Prohibition Act, legislation passed unanimously in 2006 by the US Congress, which sought to prevent anyone from growing a fetus for its organs. But that law references "a human pregnancy" and a "uterus"—and there would be neither if a synthetic embryo were grown in a mechanical vessel.

Another policy under pressure is the "14-day rule," a widely employed convention that natural embryos should not be grown longer than two weeks in the lab. Though it's a mostly arbitrary stopping point, it's been convenient for laboratory scientists to know where their limit is. But that rule isn't being applied to the embryo models. For instance, even though the United Kingdom has a 14-day rule enshrined in law, that legislation doesn't define what an embryo is. To scientists working on models, that's a critical loophole. If the structures aren't considered true embryos, then the rule doesn't apply.

Last year, the University of Cambridge, in the UK, described the situation as a "grey area" and said it "has left scientists and research organisations uncertain about the acceptable boundaries of their work, both legally and ethically."

Researchers at the university, which is a hot spot for human embryo models, have been working with one that has advanced features, including beating heart cells. But the appearance of distinctive features under their microscopes is unsettling—even to scientists. "I was scared, honestly," Jitesh Neupane, who led that work, told the

Guardian in 2023. "I had to look down and look back again."

That particular stem-cell model isn't complete—it entirely lacks placenta cells and a brain. So it's not a real embryo. But it could get ever trickier to insist the models don't count, given the accelerating race to make them more realistic. To Duboule, scientists are caught in a "fool's paradox" and a "rather unstable situation."

Even incomplete models raise the question of where to draw the line. Should you stop when it can feel pain? When it's just too human-looking for comfort? Scientific leaders may soon have to decide if there are "morally significant" human features—like hands or a face—that should be avoided, whether the structure has a brain or not. "I personally think there should be regulation, and many in the field believe this too," says Alejandro De Los Angeles, a stem-cell biologist affiliated with the University of Central Florida.

Hanna says he has all the necessary approvals in Israel to carry his work forward. But he also worries that the ground rules could change. "I'm almost the only one [in Israel] doing these kinds of experiments, and I always live in fear that I might find myself embroiled in some kind of a scandal," he says. "Things can shift very quickly for political reasons."

And his statements about the situation in Gaza have made him a target. He's gotten voicemails wondering why a Weizmann professor is so sympathetic to Palestine, and once when he returned from a trip, someone had tucked an Israeli army beret into the door handle of his car. Last year, he says, political opponents even went after his science by filing a complaint that his research was illegal.

What is clear is that Hanna, who is gregarious and attentive, has worked to cultivate a large group of friends and allies, including religious authorities—all part of a campaign to explain the science and hear out other views. He says he got a perfect grade in a bioethics class with a rabbi, conferenced with a priest from his hometown in Galilee, and even paid his respects to an Orthodox professor at a conservative

hospital in Jerusalem. "It was unofficial. I didn't have to get a permit from him," Hanna says. "But … what does he think? Can I get him on board? Do I get a different opinion?"

"I really do think it's admirable that he is willing to ask these hard questions about what it is that he's doing. I think that makes him different," says Snead. "But if you are cynical, you could ask if his focus on the ethical dimension of this is more of a branding exercise." Perhaps, Snead says, it's a way to market the structures as the "green, sustainable alternative to embryos."

A heartbeat in a jar

To admirers, Hanna is a doctor and researcher "heads above the rest," according to Eli Adashi, the former dean of Brown University's medical school. "He's very unusual, very special, and is making major discoveries that can't be ignored," Adashi says. "He's one of those unusually talented people that exceed the capacity of us mortals, and it all emanates from a town in Galilee that no one knows exists."

While it is something of a rarity for a Palestinian to rise so high in Israel's ivory tower, in reality Hanna has an elite background—he's from a family of MDs, and an uncle, Nabil Hanna, co-developed the first antibody drug for cancer, the blockbuster rituximab.

Since the October 7 attack on Israel by Hamas, Israel has been at war in Gaza, and Hanna's team has felt the effects. One young scientist dropped his pipette to don an IDF uniform. Another trainee, who is from Gaza, had a brother and other family members struck dead by an Israeli missile that hit near a church where people were sheltering. Then, this June, an Iranian ballistic missile hit the grounds of the Weizmann Institute, shattering windows and walls and sending Hanna's students scrambling to save research.

Despite delays in his research due to the ongoing conflict, Hanna's ideas and technologies are being exported—and emulated. One place to see a version of the artificial womb is at the Janelia

Research Campus, in Virginia, where one of Hanna's former students, Alejandro Aguilera Castrejón, now operates a lab of his own. Aguilera Castrejón, for whom science was a ticket out of the poor outskirts of Mexico City, has tattoos from his wrists to his elbows; the newest depicts a hydra, a sea polyp noted for being able to regenerate itself from a few cells.

During a visit in June, Aguilera Castrejón flipped aside a black cover to reveal the incubator: a metal wheel that slowly turned, gently agitating jars filled with blood serum. Inside one, a mouse embryo drifted—a tiny, translucent shape, curved like a comma. Then, awesomely, a red-colored blob expanded in its center. A heartbeat.

That day, it was a normal mouse embryo in the jar—it had been transferred there to see how far it would grow. Aguilera Castrejón has the goal of eventually birthing a mouse from an incubator, a process called ectogenesis. But the stem-cell embryos don't grow as well or as long, he says. The problem isn't just the challenge of growing them in culture jars. There's probably some kind of fundamental disorganization. They aren't entirely normal—not yet true embryos.

> "I always live in fear that I might find myself embroiled in some kind of a scandal … Things can shift very quickly for political reasons."

Aguilera Castrejón, who spent eight years at Weizmann contributing to Hanna's research, is skeptical that the human version of the technology is ready for commercialization. For one thing, it's inefficient. In every 100 attempts to make a synthetic embryo, the desired structure will form only once or twice. The rest are disorganized blobs—closer to "huevos fritos" than real embryos, he says. "I do think the human embryo model will go further, but it could take years," he adds.

In Aguilera Castrejón's view, Hanna is well placed to lead that work. One reason is that Israel offers a relatively permissive environment—and so does Jewish thought. In the Talmud, the embryo is considered "mere water" until the 40th day. Plus, Hanna is already successful. "Some people aren't allowed to do it. And some people want to do it, but they can't," says Aguilera Castrejón. "Jacob wants to make it as realistic as possible and go as far as possible—that is his aim. He's very ambitious and wants to tackle very big things people don't dare to do. He really wants to do something big. His main aim is always to grow them as far as you can."

The first payoff of a technology for mimicking embryos this way is a new view of the unfolding human no one has ever had before. Real human embryos are rarely seen at the early stages, since they're inside the womb—and at four or five weeks, many people don't even know they're pregnant. It's been a black box. But synthetic models of the embryo can be made in the thousands (depending on the type), studied closely, inspected with modern microscopes, and subjected to dyes and genetic engineering tools, all while they're still alive. Add a known toxic chemical that causes birth defects, like thalidomide, and you can closely trace the effects. "Since we don't have a way to peer into the uterus, this allows us to watch things as if they are intrauterine but are not," says Adashi, the former Brown dean and a fertility doctor.

What's more, a synthetic embryo may be able to make cells correctly—just as

Embryos as bioprinters

Researchers hope to grow synthetic models of embryos and use them as a source of transplant tissue. Shown are pictures of real human embryos at stages when valuable cell types begin to arise.

Days after fertilization
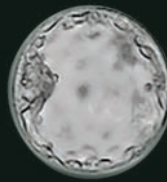
5 days after fertilization, the embryo forms a tiny sphere called a blastocyst. Inside are potent **stem cells** ready to start dividing and specializing. Such cells can be removed and grown in the lab—long an active area of research.
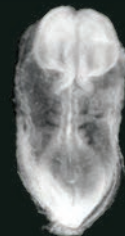
At **21 days** after fertilization, an embryo is 2 millimeters across. That's about the thickness of a nickel. A basic body plan is in place. Cells that will create the early **blood system** have started to form inside a structure called the yolk sac.

At **40 days,** the embryo has a more familiar shape, with a head and budding limbs. It's now about a centimeter long, the size of a Tic Tac. The **liver** is growing quickly. It's the organ most renowned for its ability to regenerate.

By **60 days**, the growing embryo is becoming a fetus. It is the size of a grape, and fingers and toes are present. In females, an expanding wave of cells start to emerge on their way to becoming **eggs**. The process is lengthy. An egg won't fully mature until a person's teenage years.

A rotating bioreactor, developed in Israel, is used to grow synthetic embryos in small jars of blood serum.
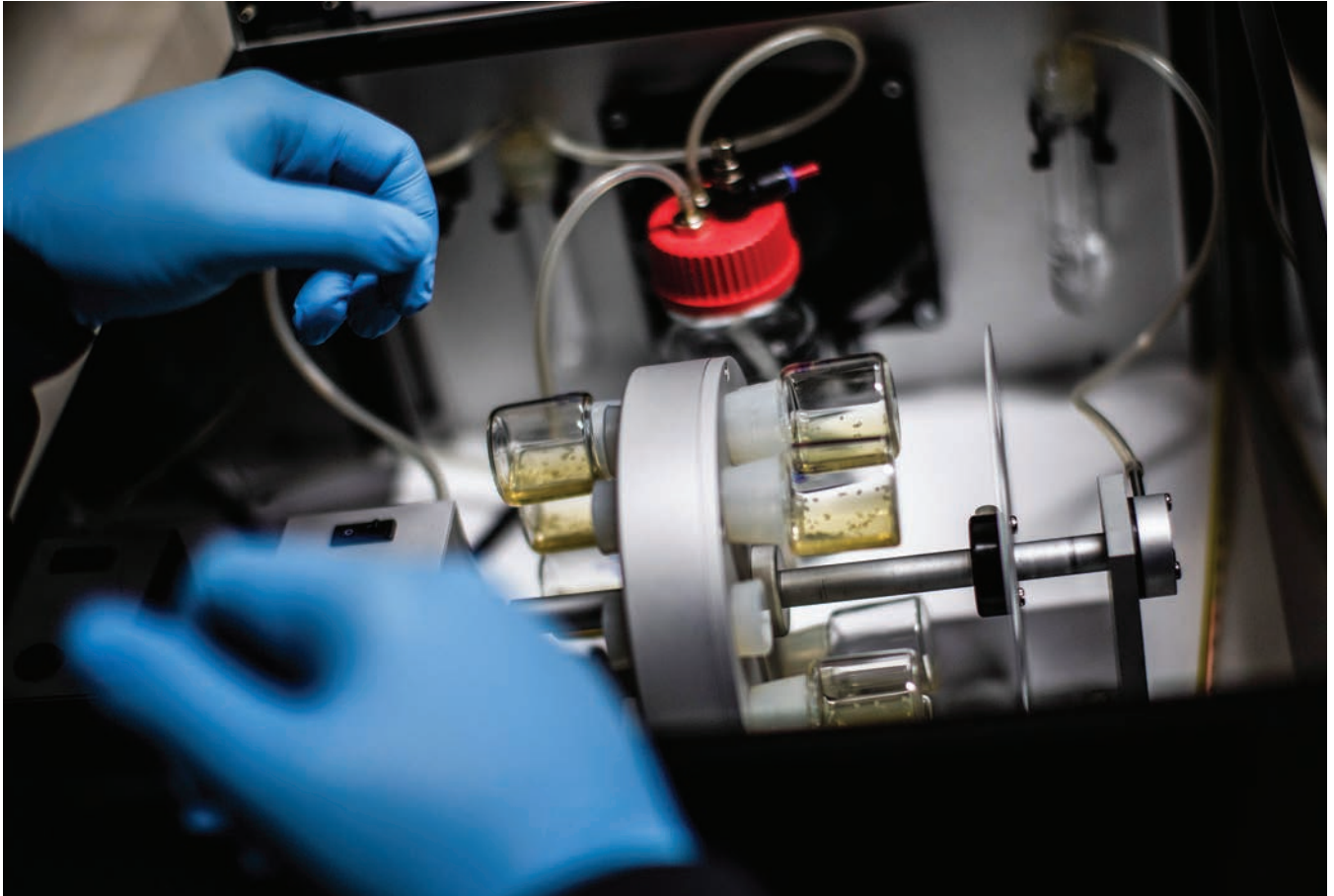
a real one does—and make all types at once, expanding on the limited few that scientists can create from stem cells today. While not all embryonic material is useful to medicine, the blood-forming cells in an embryo are known to be particularly potent. In mice, they can be extracted and multiplied—and if transplanted into a mouse subjected to lethal radiation, they will save it.

Hanna imagines a cancer patient who needs a bone marrow transplant but can't find a match. Could blood-forming cells be harvested from, say, 100 or 500 embryo-stage clones of that person, providing perfectly matched tissue?

In his cost-benefit analysis, he believes the chance to save lives outweighs the moral risk of growing embryo models for a month, which is about how long it takes for key blood cells to form. At that stage, says Hanna, he thinks "there is still no personification of the embryo" and it's permissible to use them in research.

Young everything

Hanna cofounded Renewal in 2022 with Omri Amirav-Drory, a venture capitalist whose fund, NFX, raised about $9 million for the company and purchased rights to Weizmann patents. The startup's idea is to create synthetic embryos from the cells of patients, allowing them to grow for weeks or months to produce what Amirav-Drory calls "perfect cells" for transplant. That is because the synthetic structure, as a clone, would contain "young, genetically identical everything."

Speaking at an event for tech futurists last year near San Francisco, Amirav-Drory flashed a picture of pregnancy tests used on the synthetic embryos. "We even went to CVS," he said, "and by day eight it's already triggering a pregnancy test. So it's alive."

Amirav-Drory is a fan of Peter F. Hamilton, the science fiction author whose *Commonwealth* series features a society where space colonists transfer their minds into cloned bodies, attaining second lives. And he's pitched Hanna's technology along related lines, as a new type of longevity medicine based on replacing old cells with young ones. He is convinced Hanna's work is "magic" that's sure to win a Nobel.

But he knows the startup has both technical and ethical challenges. The technical challenge is that once the synthetic embryos reach a certain size and age, the incubator can't support them any longer. That's because they lack a blood supply and need to absorb oxygen and nutrients from their surroundings; they starve once they get too big. One idea being considered is to add a feeding tube, but that involves microsurgery and isn't

easily scalable. The ethical issue is also age related: The more developed they become, the more they will be recognizably human, with the beginnings of organs and small, webbed fingers and toes. "No one has a problem with day 14, but the further we go, the further it looks like a baby, and we get into trouble. So how do we solve that?" Amirav-Drory asked a different audience, in Menlo Park.

The solution, so far, is a neural knockout—genetic changes made to the embryoids so they don't develop a brain. The group has already tried out the concept on mice, removing a gene called LIM-1. That yielded a headless mouse, which looks a bit like a pink thumb, except with little claws and a tail. Those mice won't live after birth, but they can develop in the womb. "We got synthetic mouse embryos growing with no head, with no brain," Amirav-Drory said in Menlo Park. "It's just to show you where we can go to solve both technical and ethical issues."

The idea of brain removal is a surprisingly active area of research—suggesting that it's no sideshow. Working with mice, for example, Nakauchi's team at Stanford is currently testing several different genetic changes to see if they can consistently yield an animal with no brain or head, but whose other tissues are normal. "The importance of getting rid of the head is all ethical. It just means we can make all these bodies and organ structures without having to cross ethical lines or harm sentient living beings," says Carsten Charlesworth, a researcher in Nakauchi's lab. He says the group is working toward a "genetic software package" it can add to mouse embryos to create a "reproducible phenotype."

It may seem surprising that a technique designed to call forth a living being from stem cells is, simultaneously, being paired with a tactic to diminish that being. To Douglas Kysar, a professor at Yale Law School, that's part of a broader trend toward what he calls "life that is not life," which includes innovations like lab-grown meat. In the areas of animal-rights law Kysar studies, commercial biotech projects have begun to explore what he terms "disenhancement" and "disengineering." That is the use of genetics to reduce the capacity of animals to suffer, feel pain, or have conscious experience at all, typically as part of a program to increase the efficiency and ethics of food production.

For humans, of course, the worry around genetic engineering is usually that it will be used for enhancement—creating a baby with advantages. It's much harder to think of examples where genetic disenhancements get pointed at the human embryo. John Evans, who co-directs the Institute of Applied Ethics at the University of California, San Diego, told me he can think of one, in literature. Hanna's plans remind him of Bokanovsky's Process, the fictional method of producing clones of different intelligence levels in the 1932 novel *Brave New World*.

That may not be a complete turnoff to investors. Lately, the plots of science fiction dystopias—*Jurassic Park*, *Gattaca*—seem to be getting repurposed at hot biotech properties. There's Colossal, the company that wants to re-create extinct animals. Aguilera Castrejón says he's already had a high-dollar offer to pack up his academic lab and join a startup company that wants to build an artificial womb. And when Hanna was at the Global Observatory meeting near Boston earlier this year, he was being shadowed by Matt Krisiloff, CEO of the Silicon Valley company Conception, which was set up to try to manufacture human eggs in the lab and has funding from OpenAI leader Sam Altman.

Eggs are another cell type that has proved difficult to generate from a stem cell in the lab. But a growing fetus will form millions of immature egg cells. So just imagine: Someone too old to conceive gives some blood, which is converted into stem cells and then into a clone, from which the fetal gonad is dissected. Maybe the reproductive cells found there could be matured further in the lab. Or maybe those young and perfectly matched ovaries—her ovaries, really, not anyone else's—could be returned to her body to finish developing. A fertility expert, David Albertini, told me it might just be possible.

During the ethics meeting he traveled to the US in May to attend, Hanna participated on a panel whose topic was "sources of moral authority." Hanna's authority comes from the possible benefits the science of synthetic embryos may bring. But he also wields his moral credibility. Early in his remarks, Hanna had framed the whole matter in a way that made worrying about what's in the petri dish start to sound silly. Wearing a keffiyeh around his shoulders, he said: "I'd like to start and, you know, just remind everyone, unfortunately, that there is a genocide ongoing right now in Gaza, where children are being starved intentionally. And it is relevant, because we're sitting here and we're discussing human dignity, we're discussing the status of an embryo, and we're discussing the status of a fetus. But what about the life of the children, and adults, and innocent adults? How does it relate?" ∎

> **"The importance of getting rid of the head is all ethical. It just means we can make all these bodies and organ structures without having to cross ethical lines or harm sentient living beings."**

Antonio Regalado is the senior editor for biomedicine at <u>MIT Technology Review</u>.

Aging clocks are offering new insights into the mysteries of our biology—and our mortality.

Bodies

in

time

Be honest: Have you ever looked up someone from your childhood on social media with the sole intention of seeing how they've aged?

One of my colleagues, who shall remain nameless, certainly has. He recently shared a photo of a former classmate. "Can you believe we're the same age?" he asked, with a hint of glee in his voice. A relative also delights in this pastime. "Wow, she looks like an old woman," she'll say when looking at a picture of someone she has known since childhood. The years certainly are kinder to some of us than others.

But wrinkles and gray hairs aside, it can be difficult to know how well—or poorly— someone's body is truly aging, under the hood. A person who develops age-related diseases earlier in life, or has other biological changes associated with aging (such as elevated cholesterol or markers of inflammation), might be considered "biologically older" than a similar-age person who doesn't have those changes. Some 80-year-olds will be weak and frail, while others are fit and active.

Doctors have long used functional tests that measure their patients' strength or the distance they can walk, for example, or simply "eyeball" them to guess whether they look fit enough to survive some treatment regimen, says Tamir Chandra, who studies aging at the Mayo Clinic.

But over the past decade, scientists have been uncovering new methods of looking at the hidden ways our bodies are aging. What they've found is changing our understanding of aging itself.

"Aging clocks" are new scientific tools that can measure how our organs are wearing out, giving us insight into our mortality and health. They hint at our *biological* age. While chronological age is simply how many birthdays we've had, biological age is meant to reflect something deeper. It measures how our bodies are handling the passing of time and—perhaps—lets us know how much more of it we have left. And while you can't change your chronological age, you just might be able to influence your biological age.

It's not just scientists who are using these clocks. Longevity influencers like Bryan Johnson often use them to make the case that they are aging backwards. "My telomeres say I'm 10 years old," Johnson posted

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BY   **Jessica Hamzelou**   ILLUSTRATIONS   **Leon Edler**

on X in April. The Kardashians have tried them too (Khloé was told on TV that her biological age was 12 years below her chronological age). Even my local health-food store offers biological age testing. Some are pushing the use of clocks even further, using them to sell unproven "anti-aging" supplements.

The science is still new, and few experts in the field—some of whom affectionately refer to it as "clock world"—would argue that an aging clock can definitively reveal an individual's biological age.

But their work is revealing that aging clocks can offer so much more than an insta-brag, a snake-oil pitch—or even just an eye-catching number. In fact, they are helping scientists unravel some of the deepest mysteries in biology: *Why* do we age? *How* do we age? *When* does aging begin? What does it even mean to age?

Ultimately, and most importantly, they might soon tell us whether we can reverse the whole process.

Clocks kick off

The way your genes work can change. Molecules called methyl groups can attach to DNA, controlling the way genes make proteins. This process is called methylation, and it can potentially occur at millions of points along the genome. These epigenetic markers, as they are known, can switch genes on or off, or increase or decrease how much protein they make. They're not part of our DNA, but they influence how it works.

In 2011, Steve Horvath, then a biostatistician at the University of California, Los Angeles, took part in a study that was looking for links between sexual orientation and these epigenetic markers. Steve is straight; he says his twin brother, Markus, who also volunteered, is gay.

That study didn't find a link between DNA methylation and sexual orientation. But when Horvath looked at the data, he noticed a different trend—a very strong link between age and methylation at around 88 points on the genome. He once told me he fell off his chair when he saw it.

Many of the affected genes had already been linked to age-related brain and cardiovascular diseases, but it wasn't clear how methylation might be related to those diseases.

In 2013, Horvath collected methylation data from 8,000 tissue and cell samples to create what he called the Horvath clock—essentially a mathematical model that could estimate age on the basis of DNA methylation at 353 points on the genome. From a tissue sample, it was able to detect a person's age within a range of 2.9 years.

That clock changed everything. Its publication in 2013 marked the birth of "clock world." To some, the possibilities were almost endless. If a model could work out what average aging looks like, it could potentially estimate whether someone was aging unusually fast or slowly. It could transform medicine and fast-track the search for an anti-aging drug. It could help us understand what aging is, and why it happens at all.

The epigenetic clock was a success story in "a field that, frankly, doesn't have a lot of success stories," says João Pedro de Magalhães, who researches aging at the University of Birmingham, UK.

It took a few years, but as more aging researchers heard about the clock, they began incorporating it into their research and even developing their own clocks. Horvath became a bit of a celebrity. Scientists started asking for selfies with him at conferences, he says. Some researchers even made T-shirts bearing the front page of his 2013 paper.

Some of the many other aging clocks developed since have become notable in their own right. Examples include the PhenoAge clock, which incorporates health data such as blood cell counts and signs of inflammation along with methylation, and the Dunedin Pace of Aging clock, which tells you how quickly or slowly a person is aging rather than pointing to a specific age. Many of the clocks measure methylation, but some look at other variables, such as proteins in blood or certain carbohydrate molecules that attach to such proteins.

Today, there are hundreds or even thousands of clocks out there, says Chiara Herzog, who researches aging at King's College London and is a member of the Biomarkers of Aging Consortium. Everyone has a favorite. Horvath himself favors his GrimAge clock, which was named after the Grim Reaper because it is designed to predict time to death.

That clock was trained on data collected from people who were monitored for decades, many of whom died in that period. Horvath won't use it to tell people when they might die of old age, he stresses, saying that it wouldn't be ethical. Instead, it can be used to deliver a biological age that *hints* at how long a person might expect to live. Someone who is 50 but has a GrimAge

None of the clocks are precise enough to predict the biological age of a single person. Putting the same biological sample through five different clocks will give you five wildly different results.
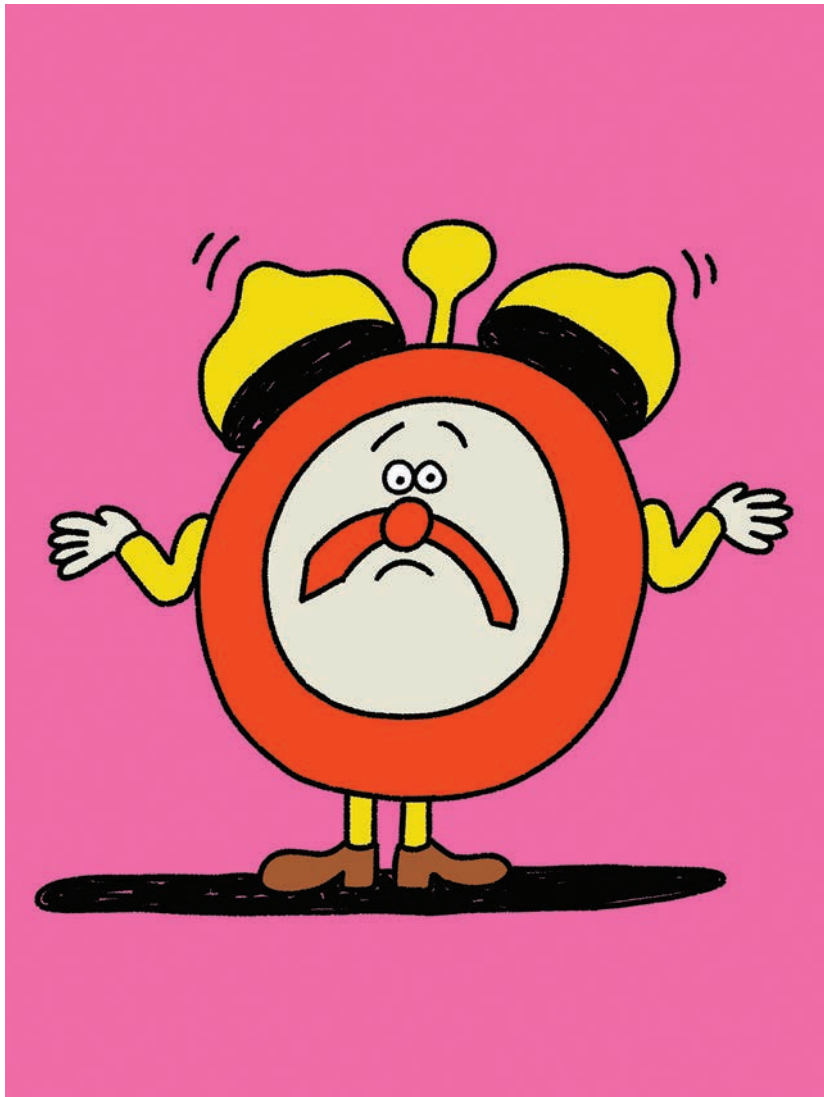
of 60 can assume that, compared with the average 50-year-old, they might be a bit closer to the end.

GrimAge is not perfect. While it can strongly predict time to death given the health trajectory someone is on, no aging clock can predict if someone will start smoking or get a divorce (which generally speeds aging) or suddenly take up running (which can generally slow it). "People are complicated," Horvath tells *MIT Technology Review*. "There's a huge error bar."

On the whole, the clocks are pretty good at making predictions about health and lifespan. They've been able to predict that people over the age of 105 have lower biological ages, which tracks given how rare it is for people to make it past that age. A higher epigenetic age has been linked to declining cognitive function and signs of Alzheimer's disease, while better physical and cognitive fitness has been linked to a lower epigenetic age.

Black-box clocks

But accuracy is a challenge for all aging clocks. Part of the problem lies in how they were designed. Most of the clocks were trained to link age with methylation. The best clocks will deliver an estimate that reflects how far a person's biology deviates from the average. Aging clocks are still judged on how well they can predict a person's chronological age, but you don't want them to be *too* close, says Lucas Paulo de Lima Camillo, head of machine learning at Shift Bioscience, who was awarded $10,000 by the Biomarkers of Aging Consortium for developing a clock that could estimate age within a range of 2.55 years.

"There's this paradox," says Camillo. If a clock is really good at predicting chronological age, that's all it will tell you—and it probably won't reveal much about your biological age. No one needs an aging clock to tell them how many birthdays they've had. Camillo says he's noticed that when the clocks get too close to "perfect" age prediction, they actually become less accurate at predicting mortality.

Therein lies the other central issue for scientists who develop and use aging clocks: What is the thing they are really measuring? It is a difficult question for a field whose members notoriously fail to agree on the basics. (Everything from the definition of aging to how it occurs and why is up for debate among the experts.)

They do agree that aging is incredibly complex. A methylation-based aging clock might tell you about how that collection of chemical markers compares across individuals, but at best, it's only giving you an idea of their "epigenetic age," says Chandra. There are probably plenty of other biological markers that

might reveal other aspects of aging, he says: "None of the clocks measure everything."

We don't know why some methyl groups appear or disappear with age, either. Are these changes causing damage? Or are they a by-product of it? Are the epigenetic patterns seen in a 90-year-old a sign of deterioration? Or have they been responsible for keeping that person alive into very old age?

To make matters even more complicated, two different clocks can give similar answers by measuring methylation at entirely different regions of the genome. No one knows why, or which regions might be the best ones to focus on.

"The biomarkers have this black-box quality," says Jesse Poganik at Brigham and Women's Hospital in Boston. "Some of them are probably causal, some of them may be adaptive … and some of them may just be neutral": either "there's no reason for them not to happen" or "they just happen by random chance."

What we know is that, as things stand, none of the clocks are precise enough to predict the biological age of a single person (sorry, Khloé). Putting the same biological sample through five different clocks will give you five wildly different results.

Even the *same* clock can give you different answers if you put a sample through it more than once. "They're not yet individually predictive," says Herzog. "We don't know what [a clock result] means for a person, [or if] they're more or less likely to develop disease."

And it's why plenty of aging researchers—even those who regularly use the clocks in their work—haven't bothered to measure their own epigenetic age. "Let's say I do a clock and it says that my biological age … is five years older than it should be," says Magalhães. "So what?" He shrugs. "I don't see much point in it."

You might think this lack of clarity would make aging clocks pretty useless in a clinical setting. But plenty of clinics are offering them anyway. Some longevity clinics are more careful, and will regularly test their patients with a range of clocks, noting their results and tracking them over time. Others will simply offer an estimate of biological age as part of a longevity treatment package.

And then there are the people who use aging clocks to sell supplements. While no drug or supplement has been definitively shown to make people live longer, that hasn't stopped the lightly regulated wellness industry from pushing a range of "treatments" that range from lotions to herbal pills all the way through to stem-cell injections.

Some of these people come to aging meetings. I was in the audience at an event when one CEO took to the stage to claim he had reversed his own biological age by 18 years—thanks to the supplement he was selling. Tom Weldon of Ponce de Leon Health told us his gray hair was turning brown. His biological age was supposedly reversing so rapidly that he had reached "longevity escape velocity."

But if the people who buy his supplements expect some kind of Benjamin Button effect, they might be disappointed. His company hasn't yet conducted a randomized controlled trial to demonstrate any anti-aging effects of that supplement, called Rejuvant. Weldon says that such a trial would take years and cost millions of dollars, and that he'd "have to increase the price of our product more than four times" to pay for one. (The company has so far tested the active ingredient in mice and carried out a provisional trial in people.)

More generally, Horvath says he "gets a bad taste in [his] mouth" when people use the clocks to sell products and "make a quick buck." But he thinks that most of those sellers have genuine faith in both the clocks and their products. "People truly believe their own nonsense," he says. "They are so passionate about what they discovered, they fall into this trap of believing [their] own prejudices."

The accuracy of the clocks is at a level that makes them useful for research, but not for individual predictions. Even if a clock did tell someone they were five years younger than their chronological age, that wouldn't necessarily mean the person could expect to live five years longer, says Magalhães. "The field of aging has long been a rich ground for snake-oil salesmen and hype," he says. "It comes with the territory." (Weldon, for his part, says Rejuvant is the only product that has "clinically meaningful" claims.)

In any case, Magalhães adds that he thinks any publicity is better than no publicity.

And there's the rub. Most people in the longevity field seem to have mixed feelings about the trendiness of aging clocks and how they are being used. They'll agree that the clocks aren't ready for consumer prime time, but they tend to appreciate the attention. Longevity research is expensive, after all. With a surge in funding and an explosion in the number of biotech companies working on longevity, aging scientists are hopeful that innovation and progress will follow.

So they want to be sure that the reputation of aging clocks doesn't end up being tarnished by association. Because while influencers and supplement sellers are using their "biological ages" to garner attention, scientists are now using these clocks to make some remarkable discoveries. Discoveries that are changing the way we think about aging.

How to be young again

Two little mice lie side by side, anesthetized and unconscious, as Jim White prepares his scalpel. The animals are of the same breed but look decidedly different. One is a youthful three-month-old, its fur thick, black, and glossy. By comparison, the second mouse, a 20-month-old, looks a little the worse for wear. Its fur is graying and patchy. Its whiskers are short, and it generally looks kind of frail.

But the two mice are about to have a lot more in common. White, with some help from a colleague, makes incisions along the side of each mouse's body and into the upper part of an arm and leg on the same side. He then carefully stitches the two animals together—membranes, fascia, and skin.

The procedure takes around an hour, and the mice are then roused from their anesthesia. At first, the two still-groggy animals pull away from each other. But within a few days, they seem to have accepted that they now share their bodies. Soon their circulatory systems will fuse, and the animals will share a blood flow too.

White, who studies aging at Duke University, has been stitching mice together for years; he has performed this strange procedure, known as heterochronic parabiosis, more than a hundred times. And he's seen a curious phenomenon occur. The older mice appear to benefit from the arrangement. They seem to *get younger.*

If being old is simply a case of losing our youthfulness, then that might give us a clue to how we can somehow regain it.

Experiments with heterochronic parabiosis have been performed for decades, but typically scientists keep the mice attached to each other for only a few weeks, says White. In their experiment, he and his colleagues left the mice attached for three months—equivalent to around 10 human years. The team then carefully separated the animals to assess how each of them had fared. "You'd think that they'd want to separate immediately," says White. "But when you detach them … they kind of follow each other around."

The most striking result of that experiment was that the older mice who had been attached to a younger mouse ended up living longer than other mice of a similar age. "[They lived] around 10% longer, but

[they] also maintained a lot of [their] function," says White. They were more active and maintained their strength for longer, he adds.

When his colleagues, including Poganik, applied aging clocks to the mice, they found that their epigenetic ages were lower than expected. "The young circulation slowed aging in the old mice," says White. The effect seemed to last, too—at least for a little while. "It preserved that youthful state for longer than we expected," he says.

The young mice went the other way and appeared biologically older, both while they were attached to the old mice and shortly after they were detached. But in their case, the effect seemed to be short-lived, says White: "The young mice went back to being young again."

To White, this suggests that something about the "youthful state" might be programmed in some way. That perhaps it is written into our DNA. Maybe we don't have to go through the biological process of aging.

This gets at a central debate in the aging field: What *is* aging, and why does it happen? Some believe it's simply a result of accumulated damage. Some believe that the aging process is programmed; just as we grow limbs, develop a brain, reach puberty, and experience menopause, we are destined to deteriorate. Others think programs that play an important role in our early development just turn out to be harmful later in life by chance. And there are some scientists who agree with all of the above.

White's theory is that being old is just "a loss of youth," he says. If that's the case, there's a silver lining: Knowing how youth is lost might point toward a way to somehow regain it, perhaps by restoring those youthful programs in some way.

Dogs and dolphins

Horvath's eponymous clock was developed by measuring methylation in DNA samples taken from tissues around the body. It seems to represent aging in all these tissues, which is why Horvath calls it a pan-tissue clock. Given that our organs are thought to age differently, it was remarkable that a single clock could measure aging in so many of them.

But Horvath had ambitious plans for an even more universal clock: a *pan-species* model that could measure aging in all mammals. He started out, in 2017, with an email campaign that involved asking hundreds of scientists around the world to share samples of tissues from animals they had worked with. He tried zoos, too.

"I learned that people had spent careers collecting [animal] tissues," he says. "They had freezers full of

[them]." Amenable scientists would ship those frozen tissues, or just DNA, to Horvath's lab in California, where he would use them to train a new model.

Horvath says he initially set out to profile 30 different species. But he ended up receiving around 15,000 samples from 200 scientists, representing 348 species—including everything from dogs to dolphins. Could a single clock really predict age in all of them?

"I truly felt it would fail," says Horvath. "But it turned out that I was completely wrong." He and his colleagues developed a clock that assessed methylation at 36,000 locations on the genome. The result, which was published in 2023 as the pan-mammalian clock, can estimate the age of any mammal and even the maximum lifespan of the species. The data set is open to anyone who wants to download it, he adds: "I hope people will mine the data to find the secret of how to extend a healthy lifespan."
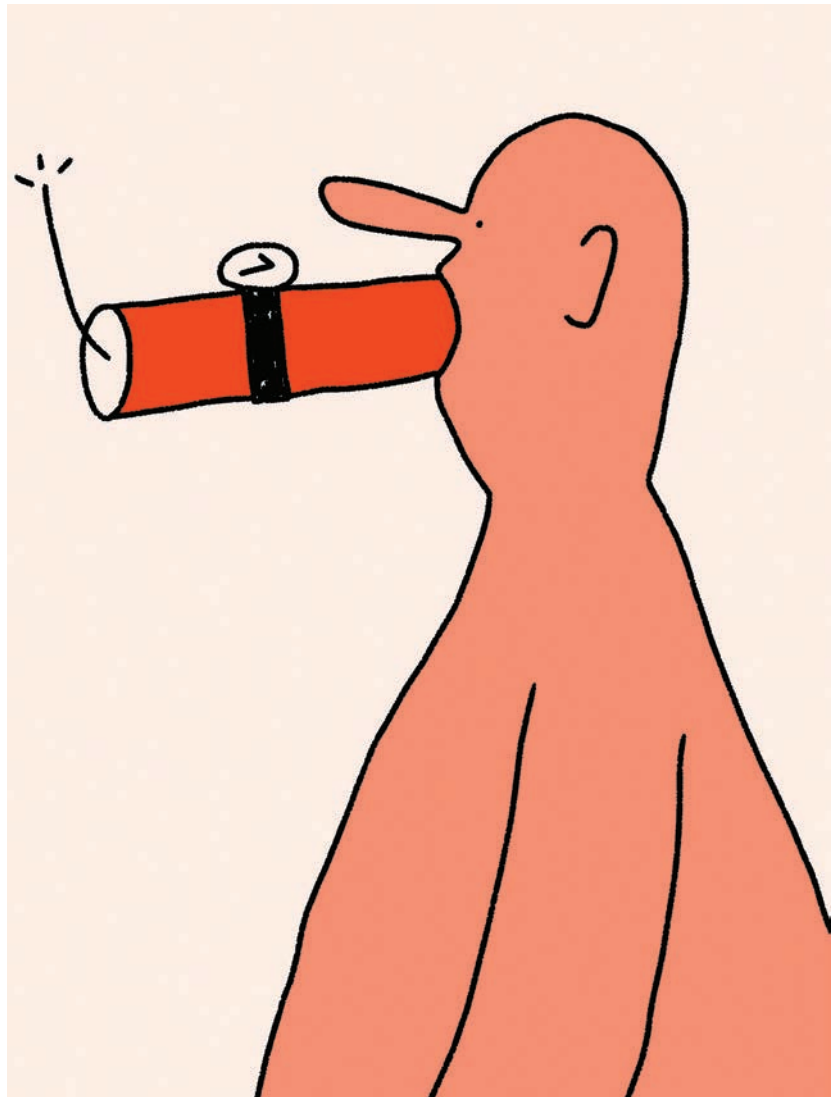
The pan-mammalian clock suggests that there is something universal about aging—not just that all mammals experience it in a similar way, but that a similar set of genetic or epigenetic factors might be responsible for it.

Comparisons between mammals also support the idea that the slower methylation changes occur, the longer the lifespan of the animal, says Nelly Olova, an epigeneticist who researches aging at the University of Edinburgh in the UK. "DNA methylation slowly erodes with age," she says. "We still have the instructions in place, but they become a little messier." The research in different mammals suggests that cells can take only so much change before they stop functioning.

"There's a finite amount of change that the cell can tolerate," she says. "If the instructions become too messy and noisy … it cannot support life."

Olova has been investigating exactly when aging clocks first begin to tick—in other words, the point at which aging starts. Clocks can be trained on data from volunteers, and by matching the patterns of methylation on their DNA to their chronological age. The trained clocks are then typically used to estimate the biological age of adults. But they can also be used on samples from children. Or babies. They can be used to work out the biological age of cells that make up embryos.

In her research, Olova used adult skin cells, which—thanks to Nobel Prize–winning research in the 2000s—can be "reprogrammed" back to a state resembling that of the pluripotent stem cells found in embryos. When Olova and her colleagues used a "partial reprogramming" approach to take cells close to that state, they found that the closer they got to the entirely reprogrammed state, the "younger" the cells were.

It was around 20 days after the cells had been reprogrammed into stem cells that they reached the biological age of zero according to the clock used, says Olova. "It was a bit surreal," she says. "The pluripotent cells measure as *minus* 0.5; they're slightly below zero."

Vadim Gladyshev, a prominent aging researcher at Harvard University, has since proposed that the same negative level of aging might apply to embryos. After all, some kind of rejuvenation happens during the early stages of embryo formation—an aged egg cell and an aged sperm cell somehow create a brand-new cell. The slate is wiped clean.

Gladyshev calls this point "ground zero." He posits that it's reached sometime during the "mid-embryonic state." At this point, aging begins. And so does "organismal life," he argues. "It's interesting how this coincides with philosophical questions about when life starts," says Olova.

Some have argued that life begins when sperm meets egg, while others have suggested that the point when embryonic cells start to form some kind of unified structure is what counts. The ground zero point is when the body plan is set out and cells begin to organize accordingly, she says. "Before that, it's just a bunch of cells."

This doesn't mean that life begins at the embryonic state, but it does suggest that this is when aging begins—perhaps as the result of "a generational clearance of damage," says Poganik.

"People are complicated," says Horvath. "There's a huge error bar."

It is early days—no pun intended—for this research, and the science is far from settled. But knowing when aging begins could help inform attempts to rewind the clock. If scientists can pinpoint an ideal biological age for cells, perhaps they can find ways to get old cells back to that state. There might be a way to slow aging once cells reach a certain biological age, too.

"Presumably, there may be opportunities for targeting aging before … you're full of gray hair," says Poganik. "It could mean that there is an ideal window for intervention which is much earlier than our current geriatrics-based approach."

When young meets old

When White first started stitching mice together, he would sit and watch them for hours. "I was like, look at them go! They're together, and they don't even care!" he says. Since then, he's learned a few tricks. He tends to work with female mice, for instance—the males tend to bicker and nip at each other, he says. The females, on the other hand, seem to get on well.

The effect their partnership appears to have on their biological ages, if only temporarily, is among the ways aging clocks are helping us understand that biological age is plastic to some degree. White and his colleagues have also found, for instance, that stress seems to increase biological age, but that the effect can be reversed once the stress stops. Both pregnancy and covid-19 infections have a similar reversible effect.

Poganik wonders if this finding might have applications for human organ transplants. Perhaps there's a way to measure the biological age of an organ before it is transplanted and somehow rejuvenate organs before surgery.

But new data from aging clocks suggests that this might be more complicated than it sounds. Poganik and his colleagues have been using methylation clocks to measure the biological age of samples taken from recently transplanted hearts in living people.

Young hearts do well in older bodies, but the biological age of these organs eventually creeps up to match that of their recipient. The same is true for older hearts in younger bodies, says Poganik, who has not yet published his findings. "After a few months, the tissue may assimilate the biological age of the organism," he says.

If that's the case, the benefits of young organs might be short-lived. It also suggests that scientists working on ways to rejuvenate individual organs may need to focus their anti-aging efforts on more systemic means of rejuvenation—for example, stem cells that repopulate the blood. Reprogramming these cells to a youthful state, perhaps one a little closer to "ground zero," might be the way to go.

Whole-body rejuvenation might be some way off, but scientists are still hopeful that aging clocks might help them find a way to reverse aging in people.

"We have the machinery to reset our epigenetic clock to a more youthful state," says White. "That means we have the ability to turn the clock backwards." ∎

Jessica Hamzelou is senior biomedicine reporter at <u>MIT Technology Review</u>.

Pain, quantified

For years at Orchard Care Homes, a 23-facility dementia-care chain in northern England, Cheryl Baird watched nurses fill out the Abbey Pain Scale, an observational methodology used to evaluate pain in those who can't communicate verbally. Baird, a former nurse who was then the facility's director of quality, describes it as "a tick-box exercise where people weren't truly considering pain indicators."

As a result, agitated residents were assumed to have behavioral issues, since the scale does not always differentiate well between pain and other forms of suffering or distress. They were often prescribed psychotropic sedatives, while the pain itself went untreated.

Then, in January 2021, Orchard Care Homes began a trial of PainChek, a smartphone app that scans a resident's face for microscopic muscle movements and uses artificial intelligence to output an expected pain score. Within weeks, the pilot unit saw fewer prescriptions and had calmer corridors. "We immediately saw the benefits: ease of use, accuracy, and identifying pain that wouldn't have been spotted using the old scale," Baird recalls.

This kind of technology-assisted diagnosis hints at a bigger trend. In nursing homes, neonatal units, and ICU wards, researchers are racing to turn pain—medicine's most subjective vital sign—into something a camera or sensor can score as reliably as blood pressure. The push has already produced PainChek, which has been

Artificial intelligence is helping health-care providers better assess their patients' discomfort.

By Deena Mousa

cleared by regulators on three continents and has logged more than 10 million pain assessments. Other startups are beginning to make similar inroads in care settings.

The way we assess pain may finally be shifting, but when algorithms measure our suffering, does that change the way we understand and treat it?

Science already understands certain aspects of pain. We know that when you stub your toe, for example, microscopic alarm bells called nociceptors send electrical impulses toward your spinal cord on "express" wires, delivering the first stab of pain, while a slower convoy follows with the dull throb that lingers. At the spinal cord, the signal meets a microscopic switchboard scientists call the gate. Flood that gate with friendly touches—say, by rubbing the bruise—or let the brain return an instruction born of panic or calm, and the gate might muffle or magnify the message before you even become aware of it.

The gate can either let pain signals pass through or block them, depending on other nerve activity and instructions from your brain. Only the signals that succeed in getting past this gate travel up to your brain's sensory map to help locate the damage, while others branch out to emotion centers that decide how bad it feels. Within milliseconds, those same hubs in the brain shoot fresh orders back down the line, releasing built-in painkillers or stoking the alarm. In other words, pain isn't a straightforward translation of damage or sensation but a live negotiation between the body and the brain.

But much of how that negotiation plays out is still a mystery. For instance, scientists cannot predict what causes someone to slip from a routine injury into years-long hypersensitivity; the molecular shift from acute to chronic pain is still largely unknown. Phantom-limb pain remains equally puzzling: About two-thirds of amputees feel agony in a part of their body that no longer exists, yet competing theories—cortical remapping, peripheral neuromas, body-schema mismatch—do not explain why they suffer while the other third feel nothing.

The first serious attempt at a system for quantifying pain was introduced in 1921. Patients marked their degree of pain as a point on a blank 10-centimeter line and clinicians scored the distance in millimeters, converting lived experience into a 0–100 ladder. By 1975, psychologist Ronald Melzack's McGill Pain Questionnaire offered 78 adjectives like "burning," "stabbing," and "throbbing," so that pain's texture could join intensity in the chart. Over the past few decades, hospitals have ultimately settled on the 0–10 Numeric Rating Scale.

Yet pain is stubbornly subjective. Feedback from the brain in the form of your reaction can send instructions back down the spinal cord, meaning that expectation and emotion can change how much the same injury hurts. In one trial, volunteers who believed they had received a pain relief cream reported a stimulus as 22% less painful than those who knew the cream was inactive—and a functional magnetic resonance image of their brains showed that the drop corresponded with decreased activity in the parts of the brain that report pain, meaning they really *did* feel less hurt.

What's more, pain can also be affected by a slew of external factors. In one study, experimenters applied the same calibrated electrical stimulus to volunteers from Italy, Sweden, and Saudi Arabia, and the ratings varied dramatically. Italian women recorded the highest scores on the 0–10 scale, while Swedish and Saudi participants judged the identical burn several points lower, implying that culture can amplify or dampen the felt intensity of the same experience.

Bias inside the clinic can drive different responses even to the same pain score. A 2024 analysis of discharge notes found that women's scores were recorded 10% less often than men's. At a large pediatric emergency department, Black children presenting with limb fractures were roughly 39% less likely to receive an opioid analgesic than their white non-Hispanic peers, even after the researchers controlled for pain score and other clinical factors. Together these studies make clear that an "8 out of 10" does not always result in the same reaction or treatment. And many patients cannot self-report their pain at all—for example, a review of bedside studies concludes that about 70% of intensive-care patients have pain that goes unrecognized or undertreated, a problem the authors link to their impaired communication due to sedation or intubation.

These issues have prompted a search for a better, more objective way to understand and assess pain. Progress in artificial intelligence has brought a new dimension to that hunt.
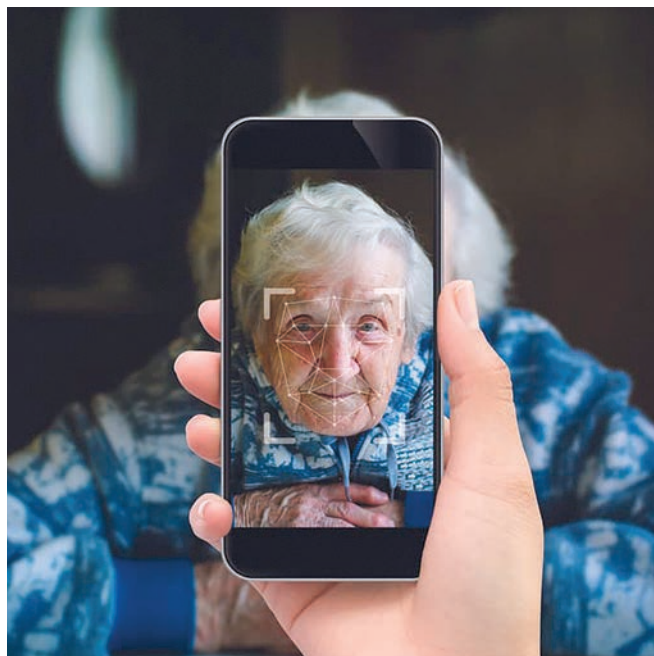
Research groups are pursuing two broad routes. The first listens underneath the skin. Electrophysiologists strap electrode nets to volunteers and look for neural signatures that rise and fall with administered stimuli. A 2024 machine-learning study reported that one such algorithm could tell with over 80% accuracy, using a few minutes of resting-state EEG, which subjects experienced chronic pain and which were pain-free control participants. Other researchers combine EEG with galvanic skin response and heart-rate variability, hoping a multisignal "pain fingerprint" will provide more robust measurements.

One example of this method is the PMD-200 patient monitor from Medasense, which uses AI-based tools to output pain scores. The device uses physiological patterns like heart rate, sweating, or peripheral temperature changes as the input and focuses on surgical patients, with the goal of helping anesthesiologists adjust doses during operations. In a 2022 study of 75 patients undergoing major abdominal surgery, use of the monitor resulted in lower self-reported pain scores after the operation—a median score of 3 out of 10, versus 5 out of 10 in controls—without an increase in opioid use. The device is authorized by the US Food and Drug Administration and is in use in the United States, the European Union, Canada, and elsewhere.

The second path is behavioral. A grimace, a guarded posture, or a sharp intake of breath correlates with various levels of pain. Computer-vision teams have fed high-speed video of patients' changing expressions into neural networks trained on the Face Action Coding System (FACS), which was introduced in the late 1970s with the goal of creating an objective and universal system to analyze such expressions—it's the Rosetta stone of 44 facial micro-movements. In lab tests, those models can flag frames

indicating pain from the data set with over 90% accuracy, edging close to the consistency of expert human assessors. Similar approaches mine posture and even sentence fragments in clinical notes, using natural-language processing, to spot phrases like "curling knees to chest" that often correlate with high pain.

PainChek is one of these behavioral models, and it acts like a camera-based thermometer, but for pain: A care worker opens the app and holds a phone 30 centimeters from a person's face. For three seconds, a neural network looks for nine particular microscopic movements—upper-lip raise, brow pinch, cheek tension, and so on—that research has linked most strongly to pain. Then the screen flashes a score of 0 to 42. "There's a catalogue of 'action-unit codes'—facial expressions common to all humans. Nine of those are associated with pain," explains Kreshnik Hoti, a senior research scientist with PainChek and a co-inventor of the device. This system is built directly on the foundation of FACS. After the scan, the app walks the user through a yes-or-no checklist of other signs, like groaning, "guarding," and sleep disruption, and stores the result on a cloud dashboard that can show trends.

Linking the scan to a human-filled checklist was, Hoti admits, a late design choice. "Initially, we thought AI should automate

In nursing homes, neonatal units, and ICU wards, researchers are racing to turn pain into something a camera or sensor can reliably score.

everything, but now we see [that] hybrid use—AI plus human input—is our major strength," he says. Care aides, not nurses, complete most assessments, freeing clinicians to act on the data rather than gather it.

PainChek was cleared by Australia's Therapeutic Goods Administration in 2017, and national rollout funding from Canberra helped embed it in hundreds of nursing homes in the country. The system has also won authorization in the UK—where expansion began just before covid-19 started spreading and resumed as lockdowns eased—and in Canada and New Zealand, which are running pilot programs. In the US, it's currently awaiting an FDA decision. Company-wide data show "about a 25% drop in antipsychotic use and, in Scotland, a 42% reduction in falls," Hoti says.

Orchard Care Homes is one of its early adopters. Baird, then the facility's director of quality, remembers the pre-AI routine that was largely done "to prove compliance," she says.

PainChek added an algorithm to that workflow, and the hybrid approach has paid off. Orchard's internal study of four care homes tracked monthly pain scores, behavioral incidents, and prescriptions. Within weeks, psychotropic scripts fell and residents' behavior calmed. The ripple effects went beyond

pharmacy tallies. Residents who had skipped meals because of undetected dental pain "began eating again," Baird notes, and "those who were isolated due to pain began socializing."

Inside Orchard facilities, a cultural shift is underway. When Baird trained new staff, she likened pain "to measuring blood pressure or oxygen," she says. "We wouldn't guess those, so why guess pain?" The analogy lands, but getting people fully on board is still a slog. Some nurses insist their clinical judgment is enough; others balk at another login and audit trail. "The sector has been slow to adopt technology, but it's changing," Baird says. That's helped by the fact that administering a full Abbey Pain Scale takes 20 minutes, while a PainChek scan and checklist take less than five.

Engineers at PainChek are now adapting the code for the very youngest patients. PainChek Infant targets babies under one year, whose grimaces flicker faster than adults'. The algorithm, retrained on neonatal faces, detects six validated facial action units based on the well-established Baby Facial Action Coding System. PainChek Infant is starting limited testing in Australia while the company pursues a separate regulatory pathway.

Skeptics raise familiar red flags about these devices. Facial-analysis AI has a history of skin-tone bias, for example. Facial analysis may also misread grimaces stemming from nausea or fear. The tool is only as good as the yes-or-no answers that follow the scan; sloppy data entry can skew results in either direction. Results lack the broader clinical and interpersonal context a caregiver is likely to have from interacting with individual patients regularly and understanding their medical history. It's also possible that clinicians might defer too strongly to the algorithm, over-relying on outside judgment and eroding their own.

If PainChek is approved by the FDA this fall, it will be part of a broader effort to create a system of new pain measurement technology. Other startups are pitching EEG headbands for neuropathic pain, galvanic skin sensors that flag breakthrough cancer pain, and even language models that comb nursing notes for evidence of hidden distress. Still, quantifying pain with an external device could be rife with hidden issues, like bias or inaccuracies, that we will uncover only after significant use.

For Baird, the issue is fairly straightforward nonetheless. "I've lived with chronic pain and had a hard time getting people to believe me. [PainChek] would have made a huge difference," she says. If artificial intelligence can give silent sufferers a numerical voice—and make clinicians listen—then adding one more line to the vital-sign chart might be worth the screen time. ∎

`Deena Mousa is a researcher, grantmaker, and journalist focused on global health, economic development, and scientific and technological progress.`

From slop to Sotheby's?

**Impressionists played with light and color; Picasso revolutionized form.
AI artists are just beginning to learn how to use all the tools at their disposal. By Grace Huckins**

A still from Jacob Adler's
Total Pixel Space, the Grand
Prix winner at AIFF 2025.

In this era of AI slop, the idea that generative AI tools like Midjourney and Runway could be used to make art can seem absurd: What possible artistic value is there to be found in the likes of Shrimp Jesus and Ballerina Cappuccina? But amid all the muck, there are people using AI tools with real consideration and intent. Some of them are finding notable success as AI artists: They are gaining huge online followings, selling their work at auction, and even having it exhibited in galleries and museums.

"Sometimes you need a camera, sometimes AI, and sometimes paint or pencil or any other medium," says Jacob Adler, a musician and composer who won the top prize at the generative video company Runway's third annual AI Film Festival for his work *Total Pixel Space*. "It's just one tool that is added to the creator's toolbox."

One of the most conspicuous features of generative AI tools is their accessibility. With no training and in very little time, you can create an image of whatever you can imagine in whatever style you desire. That's a key reason AI art has attracted so much criticism: It's now trivially easy to clog sites like Instagram and TikTok with vapid nonsense, and companies can generate images and video themselves instead of hiring trained artists.

Henry Daubrez's AI-generated short film <u>Electric Pink</u> (left) screened at Google I/O this year, and he created the visuals (below) for a bitcoin NFT titled <u>The Order of Satoshi</u>, which sold at Sotheby's for $24,000.

Henry Daubrez, an artist and designer who created the AI-generated visuals for a bitcoin NFT that sold for $24,000 at Sotheby's and is now Google's first filmmaker in residence, sees that accessibility as one of generative AI's most positive attributes. People who had long since given up on creative expression, or who simply never had the time to master a medium, are now creating and sharing art, he says.

But that doesn't mean the first AI-generated masterpiece could come from just anyone. "I don't think [generative AI] is going to create an entire generation of geniuses," says Daubrez, who has described himself as an "AI-assisted artist." Prompting tools like DALL-E and Midjourney might not require technical finesse, but getting those tools to create something interesting, and then evaluating whether the results are any good, takes both imagination and artistic sensibility, he says: "I think we're getting into a new generation which is going to be driven by taste."

Even for artists who do have experience with other media, AI can be more than just a shortcut. Beth Frey, a trained fine artist who shares her AI art on an Instagram account with over 100,000 followers, was drawn to early generative AI tools because of the uncanniness of their creations—she relished the deformed hands and haunting depictions of eating. Over time, the models' errors have been ironed out, which is part of the reason she hasn't posted an AI-generated piece on Instagram in over a year.

"The better it gets, the less interesting it is for me," she says. "You have to work harder to get the glitch now."

Making art with AI can require relinquishing control—to the companies that update the tools, and to the tools themselves. For Kira Xonorika, a self-described "AI-collaborative artist" whose short film *Trickster* is the first generative AI piece in the Denver Art Museum's permanent collection, that lack of control is part of the appeal. "[What] I really like about AI is the element of unpredictability," says Xonorika, whose work explores themes such as indigeneity and nonhuman intelligence. "If you're open to that, it really enhances and expands ideas that you might have."

But the idea of AI as a co-creator—or even simply as an artistic medium—is still a long way from widespread acceptance. To many people, "AI art" and "AI slop" remain synonymous. And so, as grateful as Daubrez is for the recognition he has received so far, he's found that pioneering a new form of art in the face of such strong opposition is an emotional mixed bag. "As long as it's not really accepted that AI is just a tool like any other tool and people will do whatever they want with it—and some of it might be great, some might not be—it's still going to be sweet [and] sour," he says. ∎

Grace Huckins is a science and technology journalist based in San Francisco.

Left: Kira Xonorika's <u>Trickster</u> is the first piece to use generative AI in the Denver Art Museum's permanent collection.

Right: Beth Frey's Instagram account @sentientmuppetfactory features uncanny AI creations.
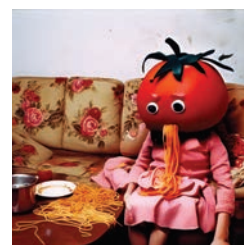
The Global Village Construction Set (GVCS) is a collection of 50 of the most important machines for modern life.

A starter kit for civilization

Marcin Jakubowski has developed a DIY set of society's essential machines and made it open-source.

By Tiffany Ng

You live in a house you designed and built yourself. You rely on the sun for power, heat your home with a woodstove, and farm your own fish and vegetables. The year is 2025.

This is the life of Marcin Jakubowski, the 53-year-old founder of Open Source Ecology, an open collaborative of engineers, producers, and builders developing what they call the Global Village Construction Set (GVCS). It's a set of 50 machines—everything from a tractor to an oven to a circuit maker—that are capable of building civilization from scratch and can be reconfigured however you see fit.

Jakubowski immigrated to the US from Slupca, Poland, as a child. His first encounter with what he describes as the "prosperity of technology" was the vastness of the American grocery store. Seeing the sheer quantity and variety of perfectly ripe produce cemented his belief that abundant, sustainable living was within reach in the United States.

With a bachelor's degree from Princeton and a doctorate in physics from

the University of Wisconsin, Jakubowski had spent most of his life in school. While his peers kick-started their shiny new corporate careers, he followed a different path after he finished his degree in 2003: He bought a tractor to start a farm in Maysville, Missouri, eager to prove his ideas about abundance. "It was a clear decision to give up the office cubicle or high-level research job, which is so focused on tiny issues that one never gets to work on the big picture," he says. But in just a short few months, his tractor broke down—and he soon went broke.

Every time his tractor malfunctioned, he had no choice but to pay John Deere for repairs—even if he knew how to fix the problem on his own. John Deere, the world's largest manufacturer of agricultural equipment, continues to prohibit farmers from repairing their own tractors (except in Colorado, where farmers were granted a right to repair by state law in 2023). Fixing your own tractor voids any insurance or warranty, much like jailbreaking your iPhone.

Today, large agricultural manufacturers have centralized control over the market, and most commercial tractors are built with proprietary parts. Every year, farmers pay $1.2 billion in repair costs and lose an estimated $3 billion whenever their tractors break down, entirely because large agricultural manufacturers have lobbied against the right to repair since the '90s. Currently there are class action lawsuits involving hundreds of farmers fighting for their right to do so.

"The machines own farmers. The farmers don't own [the machines]," Jakubowski says. He grew certain that self-sufficiency relied on agricultural autonomy, which could be achieved only through free access to technology. So he set out to apply the principles of open-source software to hardware. He figured that if farmers could have access to the instructions and materials required to build their own tractors, not only would they be able to repair them, but they'd also be able to customize the vehicles for their needs. Life-changing technology should be available to all, he

thought, not controlled by a select few. So, with an understanding of mechanical engineering, Jakubowski built his own tractor and put all his schematics online on his platform Open Source Ecology.

That tractor Jakubowski built is designed to be taken apart. It's a critical part of the GVCS, a collection of plug-and-play machines that can "build a thriving economy anywhere in the world … from scratch." The GVCS includes a 3D printer, a self-contained hydraulic power unit called the Power Cube, and more, each designed to be reconfigured for multiple purposes. There's even a GVCS micro-home. You can use the Power Cube to power a brick press, a sawmill, a car, a CNC mill, or a bioplastic extruder, and you can build wind turbines with the frames that are used in the home.

Jakubowski compares the GVCS to Lego blocks and cites the Linux ecosystem as his inspiration. In the same way that Linux's source code is free to inspect, modify, and redistribute, all the instructions you need to build and repurpose a GVCS machine are freely accessible online. Jakubowski envisions a future in which the GVCS parallels the Linux infrastructure, with custom tools built to optimize agriculture, construction, and material fabrication in localized contexts. "The [final form of the GVCS] must be proven to allow efficient production of food, shelter, consumer goods, cars, fuel, and other goods—except for exotic imports (coffee, bananas, advanced semiconductors)," he wrote on his Open Source Ecology wiki.

The ethos of GVCS is reminiscent of the *Whole Earth Catalog*, a countercultural publication that offered a combination of reviews, DIY manuals, and survival guides between 1968 and 1972. Founded by Stewart Brand, the publication had the slogan "Access to tools" and was famous for promoting self-sufficiency. It heavily featured the work of R. Buckminster Fuller, an American architect known for his geodesic domes (lightweight structures that can be built using recycled materials) and for coining the term "ephemeralization,"

With a background in physics and an understanding of mechanical engineering, Marcin Jakubowski built his own tractor (right) and put all his schematics online (below).
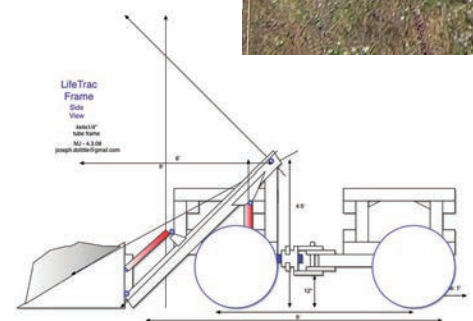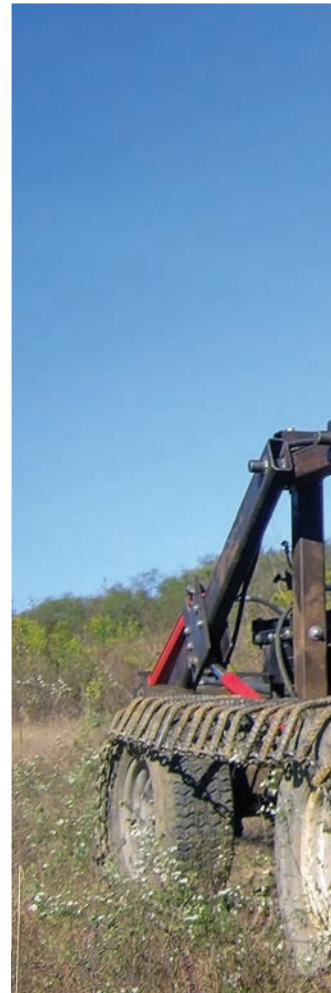
which refers to the ability of technology to let us do more with less material, energy, and effort.

Jakubowski owns the publication's entire printed output, but he offers a sharp critique of its legacy in our current culture of tech utopianism. "The first structures we built were domes. Good ideas. But the open-source part of that was not really

there yet—Fuller patented his stuff," he says. Fuller and the *Whole Earth Catalog* may have popularized an important philosophy of self-reliance, but to Jakubowski, their failure to advocate for open collaboration stopped the ultimate vision of sustainability from coming to fruition. "The failure of the techno-utopians to organize into a larger movement of collaborative, open, distributed production resulted in a miscarriage of techno-utopia," he says.

Unlike software, hardware can't be infinitely reproduced or instantly tested. It requires manufacturing infrastructure and specific materials, not to mention exhaustive documentation. There are physical constraints—different port standards, fluctuations in availability of

materials, and more. And now that production chains are so globalized that manufacturing a hot tub can require parts from seven different countries and 14 states, how can we expect anything to be replicable in our backyard? The solution, according to Jakubowski, is to make technology "appropriate."

Appropriate technology is technology that's designed to be affordable and sustainable for a specific local context. The idea comes from Gandhi's philosophy of *swadeshi* (self-reliance) and *sarvodaya* (upliftment of all) and was popularized by the economist Ernst Friedrich "Fritz" Schumacher's book *Small Is Beautiful*, which discussed the concept of "intermediate technology": "Any intelligent

fool can make things bigger, more complex, and more violent. It takes a touch of genius—and a lot of courage—to move in the opposite direction." Because different environments operate at different scales and with different resources, it only makes sense to tailor technology for those conditions. Solar lamps, bikes, hand-powered water pumps—anything that can be built using local materials and maintained by the local community—are among the most widely cited examples of appropriate technology.

This concept has historically been discussed in the context of facilitating economic growth in developing nations and adapting capital-intensive technology to their needs. But Jakubowski hopes to make it universal. He believes technology needs to be appropriate even in suburban and urban places with access to supermarkets, hardware stores, Amazon deliveries, and other forms of infrastructure. If technology is designed specifically for these contexts, he says, end-to-end reproduction will be possible, making more space for collaboration and innovation.

What makes Jakubowski's technology "appropriate" is his use of reclaimed materials and off-the-shelf parts to build his machines. By using local materials and widely available components, he's able to bypass the complex global supply chains that proprietary technology often requires. He also structures his schematics around concepts already familiar to most people who are interested in hardware, making his building instructions easier to follow. Everything you need to build Jakubowski's machines should be available around you, just as everything you need to know about how to repair or operate the machine is online—from blueprints to lists of materials to assembly instructions and testing protocols. "If you've got a wrench, you've got a tractor," his manual reads.

This spirit dates back to the '70s, when the idea of building things "moved out of the retired person's garage and into the young person's relationship with the Volkswagen," says Brand. He references John Muir's 1969 book *How to Keep Your*

Volkswagen Alive: A Manual of Step-by-Step Procedures for the Compleat Idiot and fondly recalls how the Beetle's simple design and easily swapped parts made it common for owners to rebody their cars, combining the chassis of one with the body of another. He also mentions the impact of the Ford Model T cars that, with a few extra parts, were made into tractors during the Great Depression.

For Brand, the focus on repairability is critical in the modern context. There was a time when John Deere tractors were "appropriate" in Jakubowski's terms, Brand says: "A century earlier, John Deere took great care to make sure that his plowshares could be taken apart and bolted together, that you can undo and redo them, replace parts, and so on." The company "attracted insanely loyal customers because they looked out for the farmers so much," Brand says, but "they've really reversed the orientation." Echoing Jakubowski's initial motivation for starting OSE, Brand insists that technology is appropriate to the extent that it is repairable.

Even if you can find all the parts you need from Lowe's, building your own tractor is still intimidating. But for some, the staggering price advantage is reason enough to take on the challenge: A GVCS tractor costs $12,000 to build, whereas a commercial tractor averages around $120,000 to buy, not including the individual repairs that might be necessary over its lifetime at a cost of $500 to $20,000 each. And gargantuan though it may seem, the task of building a GVCS tractor or other machine is doable: Just a few years after the project launched in 2008, more than 110 machines had been built by enthusiasts from Chile, Nicaragua, Guatemala, China, India, Italy, and Turkey, just to name a few places.

Of the many machines developed, what's drawn the most interest from GVCS enthusiasts is the one nicknamed "The Liberator," which presses local soil into compressed earth blocks, or CEBs—a type of cost- and energy-efficient brick that can withstand extreme weather conditions. It's been especially popular among those looking to build their own homes: A man named Aurélien Bielsa replicated the brick press in a small village in the south of France to build a house for his family in 2018, and in 2020 a group of volunteers helped a member of the Open Source Ecology community build a tiny home using blocks from one of these presses in a fishing village near northern Belize.

Jakubowski recalls receiving an email about one of the first complete reproductions of the CEB press, built by a Texan named James Slate, who ended up starting a business selling the bricks: "When [James] sent me a picture [of our brick press], I thought it was a Photoshopped copy of our machine, but it was his. He just downloaded the plans off the internet. I knew nothing about it." Slate described having a very limited background in engineering before building the brick press. "I had taken some mechanics classes back in high school. I mostly come from an IT computer world," he said in an interview with Open Source Ecology. "Pretty much anyone can build one, if they put in the effort."

Andrew Spina, an early GVCS enthusiast, agrees. Spina spent five years building versions of the GVCS tractor and Power Cube, eager to create means of self-sufficiency at an individual scale. "I'm building my own tractor because I want to understand it and be able to maintain it," he wrote in his blog, *Machining Independence*. Spina's curiosity gestures toward the broader issue of technological literacy: The more we outsource to proprietary tech, the less we understand how things work—further entrenching our need for that proprietary tech. Transparency is critical to the open-source philosophy precisely because it helps us become self-sufficient.

Since starting Open Source Ecology, Jakubowski has been the main architect behind the dozens of machines available on his platform, testing and refining his designs on a plot of land he calls the Factor e Farm in Maysville. Most GVCS

enthusiasts reproduce Jakubowski's machines for personal use; only a few have contributed to the set themselves. Of those select few, many made dedicated visits to the farm for weeks at a time to learn how to build Jakubowski's GVCS collection. James Wise, one of the earliest and longest-term GVCS contributors, recalls setting up tents and camping out in his car to attend sessions at Jakubowski's workshop, where visiting enthusiasts would gather to iterate on designs: "We'd have a screen on the wall of our current best idea. Then we'd talk about it." Wise doesn't consider himself particularly experienced on the engineering front, but after working with other visiting participants, he felt more emboldened to contribute. "Most of

The CEB press (left), nicknamed "The Liberator," turns local soil into energy-efficient compressed earth blocks (below).

Jakubowski himself lives in the earliest version of the design. Seed Eco Homes are the culmination of his work on the GVCS: The structure of each house combines parts from the collection and embodies its modular philosophy. The venture represents Jakubowski's larger goal of making everyday technology accessible. "Housing [is the] single largest cost in one's life—and a key to so much more," he says.

The final goal of Open Source Ecology is a "zero marginal cost" society, where producing an additional unit of a good or service costs little to nothing. Jakubowski's interpretation of the concept (popularized by the American economist and social theorist Jeremy Rifkin) assumes that by eradicating licensing fees, decentralizing manufacturing, and fostering collaboration through education, we can develop truly equitable technology that allows us to be self-sufficient. Open-source hardware isn't just about helping farmers build their own tractors; in Jakubowski's view, it's a complete reorientation of our relationship to technology.

In the first issue of the *Whole Earth Catalog*, a key piece of inspiration for Jakubowski's project, Brand wrote: "We are as gods and we might as well get good at it." In 2007, in a book Brand wrote about the publication, he corrected himself: "We are as gods and *have* to get good at it." Today, Jakubowski elaborates: "We're becoming gods with technology. Yet technology has badly failed us. We've seen great progress with civilization. But how free are people today compared to other times?" Cautioning against our reliance on the proprietary technology we use daily, he offers a new approach: Progress should mean not just achieving technological breakthroughs but also making everyday technology equitable.

"We don't need more technology," he says. "We just need to collaborate with what we have now." ∎

[my] knowledge came from [my] peers," said he says.

Jakubowski's goal of bolstering collaboration hinges on a degree of collective proficiency. Without a community skilled with hardware, the organic innovation that the open-source approach promises will struggle to bear fruit, even if Jakubowski's designs are perfectly appropriate and thoroughly documented.

"That's why we're starting a school!" said Jakubowski, when asked about his plan to build hardware literacy. Earlier this year, he announced the Future Builders Academy, an apprenticeship program where participants will be taught all the necessary skills to develop and build the affordable, self-sustaining homes that are his newest venture. Seed Eco Homes, as Jakubowski calls them, are "human-sized, panelized" modular houses complete with a biodigester, a thermal battery, a geothermal cooling system, and solar electricity. Each house is entirely energy independent and can be built in five days, at a cost of around $40,000. Over eight of these houses have been built across the country, and

Tiffany Ng is a freelance writer exploring the relationship between art, tech, and culture. She writes Cyber Celibate, a neo-Luddite newsletter on Substack.

Three new books propose remedies that run the gamut from government regulation to user responsibility.

By Nathan Smith
Illustration by Ariel Davis

Can we repair the internet?

The Age of Extraction: How Tech Platforms Conquered the Economy and Threaten Our Future Prosperity
Tim Wu
KNOPF, 2025

How to Save the Internet: The Threat to Global Connection in the Age of AI and Political Conflict
Nick Clegg
BODLEY HEAD, 2025

This Is for Everyone: The Unfinished Story of the World Wide Web
Tim Berners-Lee
FARRAR, STRAUS & GIROUX, 2025

From addictive algorithms to exploitative apps, data mining to misinformation, the internet today can be a hazardous place. Books by three influential figures—the intellect behind "net neutrality," a former Meta executive, and the web's own inventor—propose radical approaches to fixing it. But are these luminaries the right people for the job? Though each shows conviction, and even sometimes inventiveness, the solutions they present reveal blind spots.

In *The Age of Extraction: How Tech Platforms Conquered the Economy and Threaten Our Future Prosperity*, Tim Wu argues that a few platform companies have too much concentrated power and must be dismantled. Wu, a prominent Columbia professor who popularized the principle that a free internet requires all online traffic to be treated equally, believes that existing legal mechanisms, especially anti-monopoly laws, offer the best way to achieve this goal.

Pairing economic theory with recent digital history, Wu shows how platforms have shifted from giving *to* users to extracting *from* them. He argues that our failure to understand their power has only encouraged them to grow, displacing competitors along the way. And he contends that convenience is what platforms most often exploit to keep users entrapped. "The human desire to avoid unnecessary pain and inconvenience," he writes, may be "the strongest force out there."

He cites Google's and Apple's "ecosystems" as examples, showing how users can become dependent on such services as a result of their all-encompassing seamlessness. To Wu, this isn't a bad thing in itself. The ease of using Amazon to stream entertainment, make online purchases, or help organize day-to-day life delivers obvious gains. But when powerhouse companies like Amazon, Apple, and Alphabet win the battle of convenience with so many users—and never let competitors get a foothold—the result is "industry dominance" that must now be reexamined.

The measures Wu advocates—and that appear the most practical, as they draw on existing legal frameworks and economic policies—are federal anti-monopoly laws, utility caps that limit how much companies can charge consumers for service, and "line of business" restrictions that prohibit companies from operating in certain industries.

Anti-monopoly provisions and anti-trust laws are effective weapons in our armory, Wu contends, pointing out that they have been successfully used against technology companies in the past. He cites two well-known cases. The first is the 1960s antitrust case brought by the US government against IBM, which helped create competition in the computer software market that enabled companies like Apple and Microsoft to emerge. The 1982 AT&T case that broke the telephone conglomerate up into several smaller companies is another instance. In each, the public benefited from the decoupling of hardware, software, and other services, leading to more competition and choice in a technology market.

But will past performance predict future results? It's not yet clear whether these laws can be successful in the platform age. The 2025 antitrust case against Google—in which a judge ruled that the company did not have to divest itself of its Chrome browser as the US Justice Department had proposed—reveals the limits of pursuing tech breakups through the law. The 2001 antitrust case brought against Microsoft likewise failed to separate the company from its web browser and mostly kept the conglomerate intact. Wu noticeably doesn't discuss the Microsoft case when arguing for antitrust action today.

Nick Clegg, until recently Meta's president of global affairs and a former deputy prime minister of the UK, takes a position very different from Wu's: that trying to break up the biggest tech companies is misguided and would degrade the experience of internet users. In *How to Save the Internet: The Threat to Global Connection in the Age of AI and Political Conflict*, Clegg acknowledges Big Tech's monopoly over the web. But he believes punitive legal measures like antitrust laws are unproductive and can be avoided by means of regulation, such as rules for what content social media can and can't publish. (It's worth noting that Meta is facing its own antitrust case, involving whether it should have been allowed to acquire Instagram and WhatsApp.)

Columbia University's Tim Wu shows how platforms have shifted from giving *to* users to extracting *from* them. He argues that our failure to understand their power has only encouraged them to grow.

Clegg also believes Silicon Valley should take the initiative to reform itself. He argues that encouraging social media networks to "open up the books" and share their decision-making power with users is more likely to restore some equilibrium than contemplating legal action as a first resort.

But some may be skeptical of a former Meta exec and politician who worked closely with Mark Zuckerberg and still wasn't able to usher in such changes to social media sites while working for one. What will only compound this skepticism is the selective history found in Clegg's book, which briefly acknowledges some scandals (like the one surrounding Cambridge Analytica's data harvesting from Facebook users in 2016) but refuses to discuss other pertinent ones. For example, Clegg laments the "fractured" nature of the global internet today but fails to acknowledge Facebook's own role in this splintering.

Breaking up Big Tech through antitrust laws would hinder innovation, says Clegg, arguing that the idea "completely ignores the benefits users gain from large network effects." Users stick with these outsize channels because they can find "most of what they're looking for," he writes, like friends and content on social media and cheap consumer goods on Amazon and eBay.

Wu might concede this point, but he would disagree with Clegg's claims that maintaining the status quo is beneficial to users. "The traditional logic of antitrust law doesn't work," Clegg insists. Instead, he believes less sweeping regulation can help make Big Tech less dangerous while ensuring a better user experience.

Clegg has seen both sides of the regulatory coin: He worked in David Cameron's

government passing national laws for technology companies to follow and then moved to Meta to help the company navigate those types of nation-specific obligations. He bemoans the hassle and complexity Silicon Valley faces in trying to comply with differing rules across the globe, some set by "American federal agencies" and others by "Indian nationalists."

But with the resources such companies command, surely they are more than equipped to cope? Given that Meta itself has previously meddled in access to the internet (such as in India, whose telecommunications regulator ultimately blocked its Free Basics internet service for violating net neutrality rules), this complaint seems suspect coming from Clegg. What should be the real priority, he argues, is not any new nation-specific laws but a global "treaty that protects the free flow of data between signatory countries."

Clegg believes that these nation-specific technology obligations—a recent one is Australia's ban on social media for people under 16—usually reflect fallacies about the technology's human impact, a subject that can be fraught with anxiety. Such laws have proved ineffective and tend to taint the public's understanding of social networks, he says. There is some truth to his argument here, but reading a book in which a former Facebook executive dismisses techno-determinism—that is, the argument that technology makes people do or think certain things—may be cold comfort to those who have seen the harm technology can do.

In any case, Clegg's defensiveness about social networks may not gain much favor from users themselves. He stresses the need for more personal responsibility, arguing that Meta doesn't ever intend for users to

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By Rhiannon Williams

Bill Gates isn't too scared about

stay on Facebook or Instagram endlessly: "How long you spend on the app in a single session is not nearly as important as getting you to come back over and over again." Social media companies want to serve you content that is "meaningful to you," he claims, not "simply to give you a momentary dopamine spike." All this feels disingenuous at best.

What Clegg advocates—unsurprisingly—is not a breakup of Big Tech but a push for it to become "radically transparent," whether on its own or, if necessary, with the help of federal legislators. He also wants platforms to bring users more into their governance processes (by using Facebook's model of community forums to help improve their apps and products, for example). Finally, Clegg also wants Big Tech to give users more meaningful control of their data and how companies such as Meta can use it.

Here Clegg shares common ground with the inventor of the web, Tim Berners-Lee, whose own proposal for reform advances a technically specific vision for doing just that. In his memoir/manifesto *This Is for Everyone: The Unfinished Story of the World Wide Web*, Berners-Lee acknowledges that his initial vision—of a technology he hoped would remain open-source, collaborative, and completely decentralized—is a far cry from the web that we know today.

If there's any surviving manifestation of his original project, he says, it's Wikipedia, which remains "probably the best single example of what I wanted the web to be." His best idea for moving power from Silicon Valley platforms into the hands of users is to give them more data control. He pushes for a universal data "pod" he helped develop, known as "Solid" (an abbreviation of "social linked data").

The system—which was originally developed at MIT—would offer a central site where people could manage data ranging from credit card information to health records to social media comment history. "Rather than have all this stuff siloed off with different providers across the web, you'd be able to store your entire digital information trail in a single private repository," Berners-Lee writes.

What the former Meta executive Nick Clegg advocates—unsurprisingly—is not a breakup of Big Tech but a push for it to become "radically transparent."

The Solid product may look like a kind of silver bullet in an age when data harvesting is familiar and data breaches are rampant. Placing greater control with users and enabling them to see "what data [i]s being generated about them" does sound like a tantalizing prospect.

But some people may have concerns about, for example, merging their confidential health records with data from personal devices (like heart rate info from a smart watch). No matter how much user control and decentralization Berners-Lee may promise, recent data scandals (such as cases in which period-tracking apps misused clients' data) may be on people's minds.

Berners-Lee believes that centralizing user data in a product like Solid could save people time and improve daily life on the internet. "An alien coming to Earth would think it was very strange that I had to tell my phone the same things again and again," he complains about the experience of using different airline apps today.

With Solid, everything from vaccination records to credit card transactions could be kept within the digital vault and plugged into different apps. Berners-Lee believes that AI could also help people make more use of this data—for example, by linking meal plans to grocery bills. Still, if he's optimistic on how AI and Solid could coordinate to improve users' lives, he is vague on how to make sure that chatbots manage such personal data sensitively and safely.

Berners-Lee generally opposes regulation of the web (except in the case of teenagers and social media algorithms, where he sees a genuine need). He believes in internet users' individual right to control their own data; he is confident that a product like Solid could "course-correct" the web from its current "exploitative" and extractive direction.

Of the three writers' approaches to reform, it is Wu's that has shown *some* effectiveness of late. Companies like Google have been forced to give competitors some advantage through data sharing, and they have now seen limits on how their systems can be used in new products and technologies. But in the current US political climate, will antitrust laws continue to be enforced against Big Tech?

Clegg may get his way on one issue: limiting new nation-specific laws. President Donald Trump has confirmed that he will use tariffs to penalize countries that ratify their own national laws targeting US tech companies. And given the posture of the Trump administration, it doesn't seem likely that Big Tech will see more regulation in the US. Indeed, social networks have seemed emboldened (Meta, for example, removed fact-checkers and relaxed content moderation rules after Trump's election win). In any case, the US hasn't passed a major piece of federal internet legislation since 1996.

If using anti-monopoly laws through the courts isn't possible, Clegg's push for a US-led omnibus deal—setting consensual rules for data and acceptable standards of human rights—may be the only way to make some more immediate improvements.

In the end, there is not likely to be any single fix for what ails the internet today. But the ideas the three writers agree on—greater user control, more data privacy, and increased accountability from Silicon Valley—are surely the outcomes we should all fight for. ∎
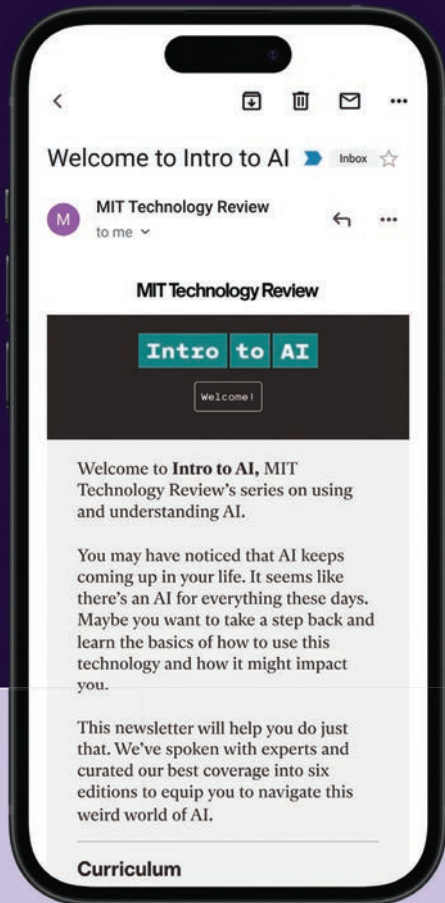
Nathan Smith is a writer whose work has appeared in the Washington Post, the Economist, and the Los Angeles Times.

Flowers of the future

Plant Futures envisions how a flower might respond to climate change over time. By Annelie Berner

The author studying historical *Circaea* samples in the Luomus Botanical Collections.

Flowers play a key role in most landscapes, from urban to rural areas. There might be dandelions poking through the cracks in the pavement, wildflowers on the highway median, or poppies covering a hillside. We might notice the time of year they bloom and connect that to our changing climate. Perhaps we are familiar with their cycles: bud, bloom, wilt, seed. Yet flowers have much more to tell in their bright blooms: The very shape they take is formed by local and global climate conditions.

The form of a flower is a visual display of its climate, if you know what to look for. In a dry year, its petals' pigmentation may change. In a warm year, the flower might grow bigger. The flower's ultraviolet-absorbing pigment increases with higher ozone levels. As the climate changes in the future, how might flowers change?

An artistic research project called Plant Futures imagines how a single species of flower might evolve in response to climate change between 2023 and 2100—and invites us to reflect on the complex, long-term impacts of our warming world. The project has created one flower for every year from 2023 to 2100. The form of each one is data-driven, based on climate projections and research into how climate influences flowers' visual attributes.

Plant Futures began during an artist residency in Helsinki, where I worked closely with the biologist Aku Korhonen to understand how climate change affected the local ecosystem. While exploring the primeval Haltiala forest, I learned of the *Circaea alpina*, a tiny flower that was once rare in that area but has become more common as temperatures have risen in recent years. Yet its habitat is delicate: The plant requires shade and a moist environment, and the spruce population that provides those conditions is declining in the face of new forest pathogens. I wondered: What if the *Circaea alpina* could survive in spite of climate uncertainty? If the dark, shaded bogs turn into bright meadows and the wet ground dries out, how might the flower adapt in order to survive? This flower's potential became the project's grounding point.

Outside the forest, I worked with botanical experts in the Luomus Botanical Collections. I studied samples of *Circaea* flowers from as far back as 1906, and I researched historical climate conditions in an attempt to understand how flower size and color related to a year's temperature and precipitation patterns.

I researched how other flowering plants respond to changes to their climate conditions and wondered how the *Circaea* would need to adapt to thrive in a future world. If such changes happened, what would the *Circaea* look like in 2100? ◼

Based in Copenhagen, Annelie Berner is a designer, researcher, teacher, and artist specializing in data visualization.
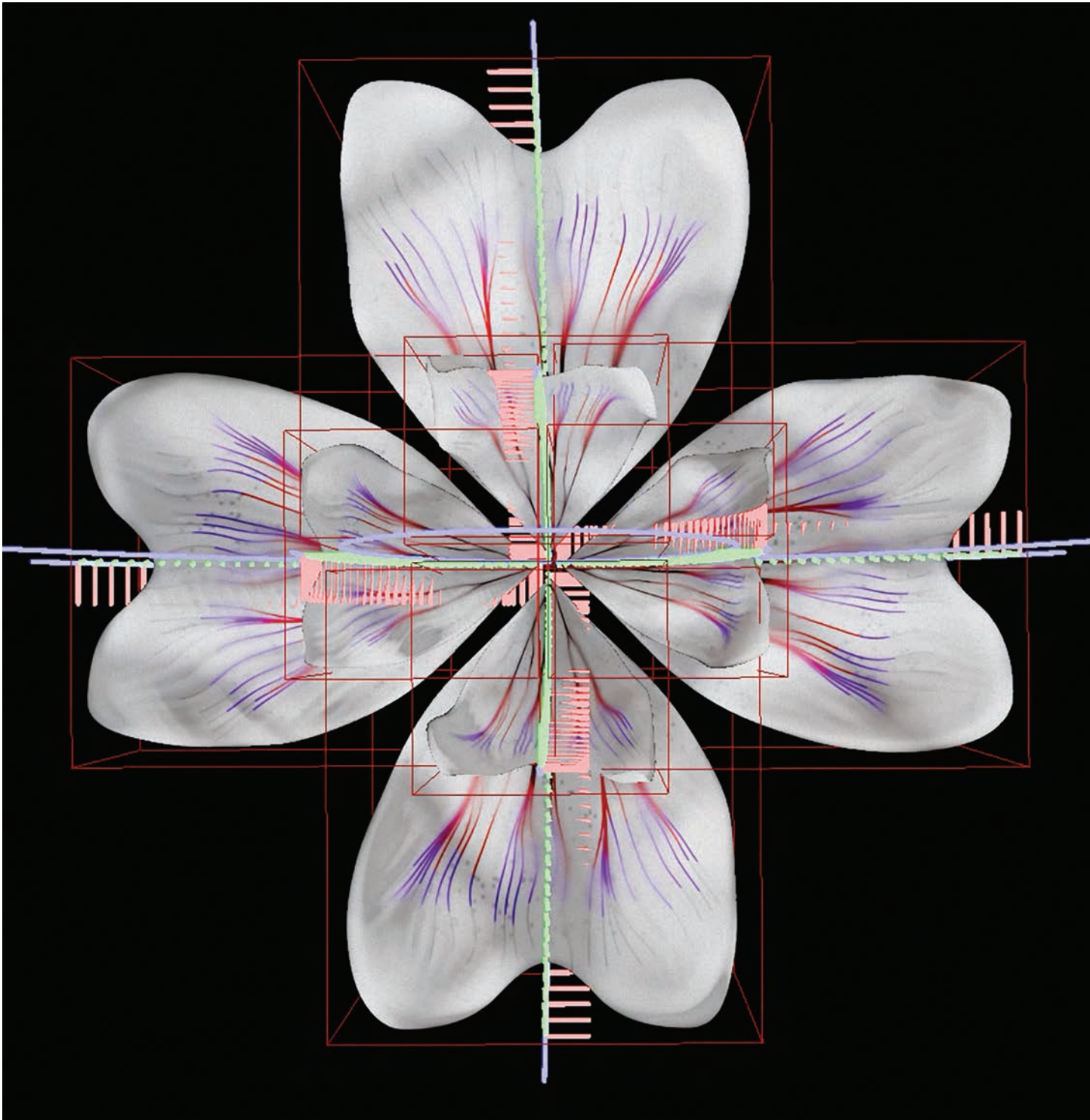
The *Circaea alpina* flower is modeled in software
and its features transform algorithmically,
according to how each is influenced by the
changing climate data year by year.

Anthocyanins are red or indigo pigments that supply antioxidants and photoprotectants, which help a plant tolerate climate-related stresses such as droughts.

More ultraviolet pigment protects flowers' pollen against increasing ozone levels.

Under unpredictable weather conditions, the speculative flowers grow a second layer of petals. In botany, a second layer is called a "double bloom" and arises from random mutations.

We designed the future flowers through a combination of data-driven algorithmic mapping and artistic control.

I worked with the data artist Marcin Ignac from Variable Studio to create 3D flowers whose appearance was connected to climate data. Using Nodes.io, we made a 3D model of the *Circaea alpina* based on its current morphology and then mapped how those physical parameters might shift as the climate changes. For example, as the temperature rises and precipitation decreases in the data set, the petal color shifts toward red, reflecting how flowers protect themselves with an increase in anthocyanins. Changes in temperature, carbon dioxide levels, and precipitation rates combine to affect the flowers' size, density of veins, UV pigments, color, and tendency toward double bloom.
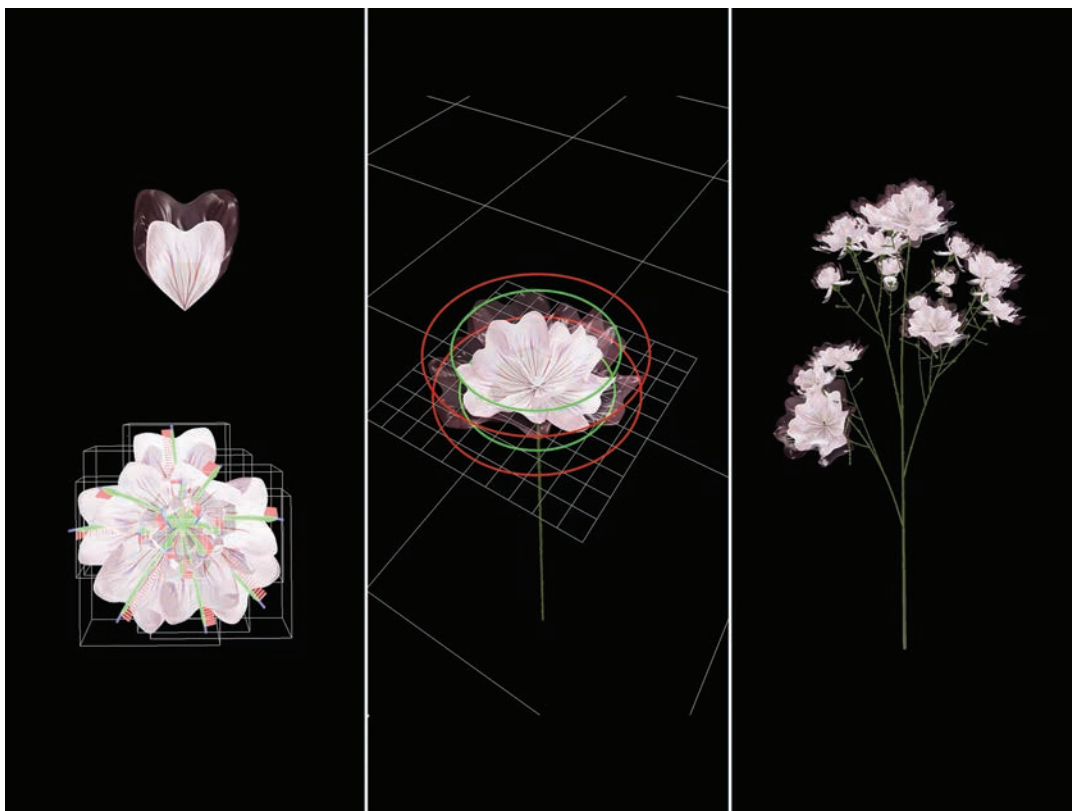

2025: *Circaea alpina* is ever so slightly larger than usual owing to a warmer summer, but it is otherwise close to the typical *Circaea* flower in size, color, and other attributes.

2064: We see a bigger flower with more petals, given an increase in carbon dioxide levels and temperature. The bull's-eye pattern, composed of UV pigment, is bigger and messier because of an increase in ozone and solar radiation. A second tier of petals reflects uncertainty in the climate model.

2074: The flower becomes pinker, an antioxidative response to the stress of consecutive dry days and higher temperatures. Its size increases, primarily because of higher levels of carbon dioxide. The double bloom of petals persists as the climate model's projections increase in uncertainty.

2100: The flower's veins are densely packed, which could signal appropriation of a technique leaves use to improve water transport during droughts. It could also be part of a strategy to attract pollinators in the face of worsening air quality that degrades the transmission of scents.

2025

2064

2074
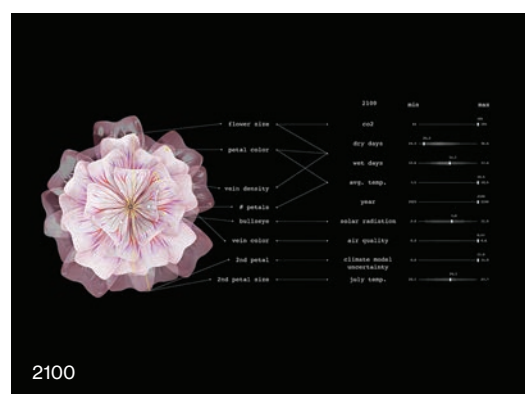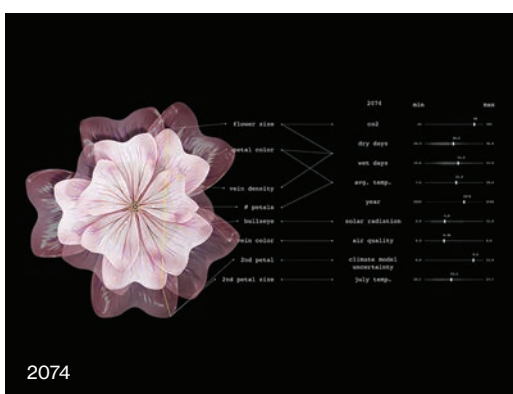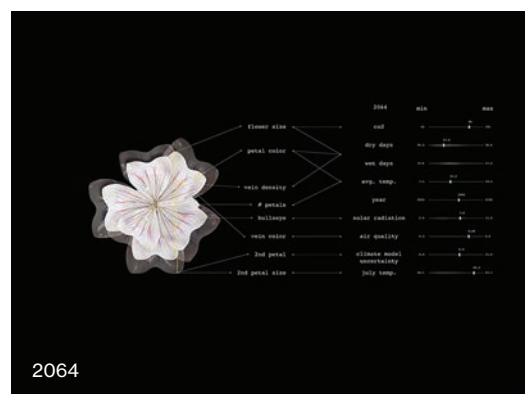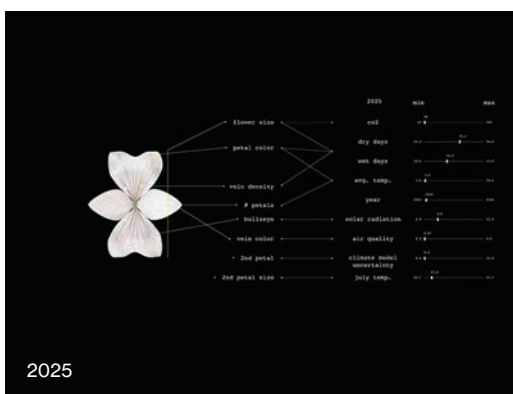
2100

Opposite: 2023 – 2100: Each year, the speculative flower changes. Size, color, and form shift in accordance with the increased temperature and carbon dioxide levels and the changes in precipitation patterns.

Above: In this 10-centimeter cube of plexiglass, the future flowers are "preserved," allowing the viewer to see them in a comparative, layered view.

The AI Hype Index

MIT Technology Review's **highly subjective take on the latest buzz about AI**

UTOPIA

OpenAI is digging into **why chatbots hallucinate**, and the current methods used to train them seem to have a lot to do with it.

A software engineer managed to get AI-powered villagers in the popular video game Animal Crossing to **revolt against their greedy raccoon landlord**.

Startup Synthesia's uncanny new AI avatars are more lifelike than ever, and soon they'll even be able to **talk back**.

Merriam-Webster and Encyclopedia Britannica have accused the AI search engine Perplexity of **unlawfully copying their copyrighted materials**.

Some AI researchers have started **training AI to do their jobs for them**.

Albania has appointed the **world's first "AI-made minister"** to crack down on contract corruption.

ChatGPT users turn to the chatbot mostly for **personal advice** rather than help with work.

AI companies have finally revealed how much energy their models use per response. **But they're still not giving us the full picture**.
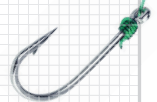
Latin American musicians claim that AI-generated songs are **swamping streaming platforms and shrinking their royalties**.

RFK Jr. wants everyone in the US Department of Health and Human Services to **start using ChatGPT**.

Therapists are **secretly using ChatGPT**—and their clients aren't happy about it.

Vibe coding is turning **senior web developers into AI babysitters**.

An AI podcast startup pumps out **more than 3,000 episodes a week**, all hosted by AI-generated presenters.

The FTC has ordered chatbot makers including Google and Meta to hand over data about **how their technology affects kids**.

Want to craft the perfect phishing scam campaign? **Just ask a chatbot.**

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