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Are Chiropractors Backing The Anti-Vaccine Movement?

Bruce Y. Lee Senior Contributor

Healthcare

I am a writer, journalist, professor, systems modeler, computational and digital health expert, avocado-eater, and entrepreneur, not always in that order.

This article is more than 4 years old.

Dr Andrew Wakefield (center) was the first clinician to suggest a link between autism in children... [+]

Today Andrew Wakefield was a keynote speaker at the International Chiropractors Association's Annual Conference on Chiropractic and Pediatrics in Maui, Hawaii. Yes, the same Andrew Wakefield, who in 2010 was stripped of his medical license in the United Kingdom for

Exhibit 7

ethical violations and failure to disclose potential financial conflicts of interest. The same Wakefield who published a subsequently discredited and retracted study in the *Lancet* linking vaccines to autism that the *British Medical Journal (BMJ)* described as an "elaborate fraud". The same Wakefield who produced and directed an anti-vaccine "documentary" film, *Vaxxed: From Cover-Up to Catastrophe*, that pushed conspiracy theories about the Centers for Disease Control and Prevention (CDC) and vaccines. The same Wakefield who has not been able to provide scientific evidence to support his claims. Is this really the best way for a professional association and a conference to gain scientific legitimacy?

The Annual Conference on Chiropractics and Pediatrics now has something in common with the "Conspira-Sea Cruise," a week-long cruise hosted by the tour company Divine Travels to have conversations about--you guessed it--"conspiracies." Both have invited Wakefield as a guest speaker. David Gorski writing for *Popular Mechanics* mentioned some of the others on the cruise's preliminary list of speakers such as:

- **Robert O. Young:** who has claimed that the cause of all cancers is excess acidity and has been selling books and programs promoting alkaline diets. (Who would have thought that the Cancer Moonshot is just to make better Tums tablets?)
- **Robert Strecker:** who has claimed that HIV/AIDS is a man-made (or actually human-made) disease that was spread by the government (because the government just does not have enough to problems to address).
- **Len Horowitz:** who describes himself as the "King of Natural Healing" and has been trying to sell an herbal cream that he claims will make skin cancer fall off your body in less than 3

weeks.

The preliminary speaker list probably reflected the final list of speakers, unless the cruise was itself a conspiracy. As April Glaser reported for *Wired*, the cruise speakers included people who have broken the law such as Sean David Morton, who was indicted and fined by the U.S. Securities and Exchange Commission for making false (as opposed to truthful) claims to investors about psychic abilities to predict the stock market. (Apparently, his psychic abilities did not help him predict that the SEC would catch him.)

What Horowitz, Young and a number of others on the cruise have in common is that they are all trying to sell treatments that compete with existing treatments approved and supported by legitimate government agencies such as the Food and Drug Administration (FDA) and the scientific community. So, could conspiracy theorists have something to gain financially by discrediting the government and the scientific community? Could there be personal agendas behind certain conspiracy theories? In other words, could there be conspiracies behind conspiracy theories?

Let's go back to the "anti-vaccine movement." But before we do so, let's clearly distinguish "anti-vaxxers" from those who have earnest concerns or questions about vaccines, but are not staunchly opposed to the idea of vaccination. Vaccines are not 100% safe. Nothing is. Not even stuffed animals. (This is not to say that the risks of vaccines and stuffed animals are the same.) Indeed, vaccines can cause both minor and major side effects. But scientific studies have shown that the risks of major side effects are very low and have not shown any connection between vaccines and autism. The benefits of vaccines seem to far outweigh potential risks. Nonetheless, wondering about vaccine safety is perfectly reasonable. Science, medicine and public health need to keep monitoring the safety of existing products and pushing for even safer products. Products can always get better. Science can always advance. A reasonable amount of skepticism can be healthy.

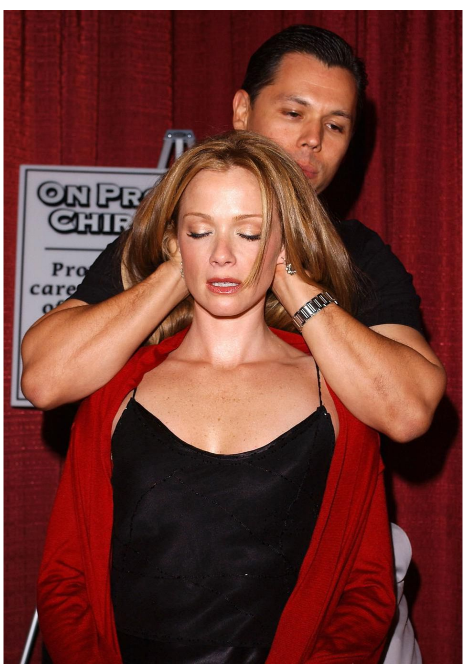
By contrast, the "anti-vaccine movement" seems to include some organized attempts to present information not necessarily supported by science and convince you to stop vaccinating yourself or your children. As she wrote in *Time* (actually in time for *Time*), Meghan Moran, Ph.D., an associate professor of health, behavior and society at the Johns Hopkins Bloomberg School of Public Health, led a study that analyzed 480 anti-vaccination websites and found many false claims and attempts to discredit the government and medical practitioners. In fact, some websites seem to be masquerading as legitimate vaccine authorities by using titles such as "national" and "information." Do these websites really represent honestly concerned citizens or actually organizations with hidden agendas?

How many chiropractors are behind these efforts? Well, some chiropractors may see potential financial gain if vaccination rates go down. Try doing a web search for "chiropractors" and "vaccination," "infectious disease," "influenza," "measles" and other vaccine-related topics and you'll some interesting claims about how chiropractic techniques can help prevent and treat infectious diseases. For example, in a website from the Chiropractic Leadership Alliance, Dr. Christopher Kent wrote:

> Even more impressive are some of the spectacular results reported by early chiropractors in patients with infectious diseases. One example where chiropractic care provided a beacon of light was the 1917-18 influenza epidemic, which brought death and fear to many Americans... The results were

> spectacular. Rhodes reported that in Davenport, Iowa, medical doctors treated 93,590 patients with 6,116 deaths—a loss of one patient out of every 15. Chiropractors at the Palmer School of Chiropractic adjusted 1,635 cases, with only one death. Outside Davenport, chiropractors in Iowa cared for 4,735 cases with only six deaths—one out of 866.

This statement has about as much science as a Barbie doll. Yes, of course, more people died from the flu under a doctor's care than a chiropractor's care, because most people really sick with the flu probably went to doctor rather than chiropractor. You could probably find similar patient mortality statistics for plumbers or cheese-makers. (If you go to a cheese-maker to get medical treatment, you have more problems than you realize.) Kent went on to make similar claims about smallpox, measles, scarlet fever and gonorrhea. He concluded, "In a world where we are faced with antibiotic-resistant bacteria, and viral diseases where effective treatments are lacking, the role of chiropractic care in allowing for optimum immune system function deserves thorough exploration."



A *USA Today* piece reported that "about 19%" of chiropractors are being vocal about opposing vaccines. The story quoted chiropractor Josh Handt as saying, "[The job of] chiropractic is to allow the body to function optimally without taking anything out or putting anything in," which is a very broad, vague, sweeping claim that essentially says nothing and applies to most health

Chiropractic adjustment such as the one actress Lauren Holly (right) is receiving here can help with... [+]

professionals including doctors, physical therapists and nurse practitioners. No, doctors don't think, "Hmm, what can I remove or put into the patient?"

Certainly, chiropractic techniques have proven to be helpful for certain musculoskeletal conditions. But trying to extend techniques and methods well beyond what they are intended to do is analogous to having a hammer and just trying to find ways to make the hammer seem more useful and thus more sell-able. "Oh, look, the hammer can be used as a spatula. Oh, I can use a hammer to brush my teeth. And who needs toilet paper when you have a hammer?"

Again, not all chiropractors necessarily have that agenda. There are chiropractors who use evidence-based approaches and recognize the strengths and limitations of their techniques. However, you have to wonder about the International Chiropractors Association's motivation behind featuring Wakefield as a speaker, especially without providing a balancing scientific talk. When people are staunchly opposed to vaccines, the medical profession or government agencies, how much of it is true belief and how much is a hidden financial agenda? How's that for a conspiracy theory about conspiracy theorists?

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Bruce Y. Lee

I am a writer, journalist, professor, systems modeler, computational and digital health expert, avocado-eater, and entrepreneur, not always in that order. Currently, I am... **Read More**

APRIL GLASER SCIENCE 02.09.2016 08:00 AM

A Skeptic Infiltrates a Cruise for Conspiracy Theorists

Conspira-Sea is a seven-day cruise where fringe thinkers can discuss everything from crop circles to mind control on the open sea.

Exhibit 8

The Ruby Princess cruise ship docked at Port Everglades in Fort Lauderdale on November 3, 2014. ALAMY

SAY YOU'RE NOT one to believe the mainstream media. Maybe you think climate change is an elaborate hoax or the medical community is trying to hide the myriad dangers of vaccinations. Perhaps you are utterly convinced the government is overrun by reptilian beings.

Where on Earth can you go to get away from it all, and mingle with those who share your views? Well, Conspira-Sea, of course. It's a seven-day cruise where fringe thinkers can discuss everything from crop circles to mind control on the open sea. Last month's cruise featured a caravan of stars from a surprisingly vast galaxy of skeptics and conspiracy theorists, including Andrew Wakefield, known for his questionable research and advocacy against vaccines. Also aboard was Sean David Morton, who faced federal charges of lying to investors about using psychic powers to predict the stock market.

But they had an outsider among them, and not one from another planet. Harvard-educated attorney Colin McRoberts is writing a book about people who believe in conspiracy theories, and used a crowdfunding campaign to book passage on the cruise. He blogged about his adventure and told us all about it---including the bit where the IRS arrested Morton when the ship returned to port.

__What were some of the conspiracies discussed on board?

__

We had about a dozen presenters of all different stripes. Some technical or scientific experts, but only one scientific speaker, Wakefield, had a legitimate education. The rest were into new-age or were conspiracy theorists in the traditional sense. Or aliens. They all had their various specialities.

__And what were the attendees like? __

The people on the cruise tended to be there with a primary focus on one or two big issues. They were there to learn about vaccines. Or they were there to find out more about astrology. But they were interested in everything else. I didn't talk to anybody who wasn't willing to kind of go outside their comfort zone.

Most people had advanced degrees, for the most part master's. I talked to at least one woman who had a PhD, in counseling. There were also some people there who were blue collar. I talked to one person who was a metal worker, another who was a nurse. And I talked to a teacher and a couple who own a new-age bookstore. There was a pretty decent diversity in terms of backgrounds.

What was the relationship between the attendees and observers like you on board?

It was a very tense environment on the boat. There were a couple of instances in which the journalists on board had been treated poorly by a couple of the presenters. One of the journalists was ambushed in the Internet cafe by a couple who had accused her of being an agent of the CIA. She managed to persuade them that she was not an undercover agent.

Did anyone succeed in indoctrinating people?

The anti-GMO track was probably the most effective in terms of changing people's behavior. The primary speaker worked very hard, not at convincing people that GMOs are evil, but in giving specific tools for convincing others that GMOs are evil. Which was, the ethics of it aside, a savvy way to activate some communicators and try and shift actual behavior in the real world.

__Wakefield was the most prominent personality on board. What was his presentation like? __

I think Wakefield is unhappy with the fact that his career has now taken him to a conspiracy conference in which he's sharing billing with the third dimensional delegates of the galactic roundtable. He sees himself as someone who can champion his issues as an issue of public health, and instead he winds up in sort of a side show.

In his presentation, he launched into a very direct, very passionate, and I think a very heartfelt defense of his own words, explaining essentially that he was unjustly demonized. I got the impression that he was wanting a sort of redemption story. I think this is his second arc. He's trying to redeem himself and start over, not as a medical expert, but as an issue activist.

What do you think motivates these fringe theory evangelists?

I thought that both of the pseudo-legal speakers were con-men. People left with specific, terrible, dangerous advice that could really ruin their lives. There's definitely a streak of con-artistry in a man that gets up and tells you this is how you get rid of your debts, and doesn't say, oh and by the way, I'm under indictment for doing this. Sean David Morton didn't know that he was going to be arrested right after he got off the boat. But he knew the IRS had raided him, I found out later, and was fighting the raid in trial for using some of the legal tricks he talked about in his presentation.

At the same time I think those presenters believed what they were saying. It turns out that both pseudo-legal speakers were both doing it themselves. And that really surprised me because I didn't think that anybody would really spend that kind of time and effort learning how to pull these tricks off and not realize at some point that it will never work.

__What do the attendees get out of the cruise? __

I think a lot of people who get stuck in an ideology that's based on some irrational idea, like how Bigfoot exists or that vaccines cause autism or that GMOs are poisonous or the legal stuff, they kind of define the idea in opposition to the mainstream. So I think what a lot of them are looking for is a community and a culture that supports them and doesn't judge them for having this unusual belief. They come together not just on a cruise ship, but in a community.

Is there anything we can learn from the attendees?

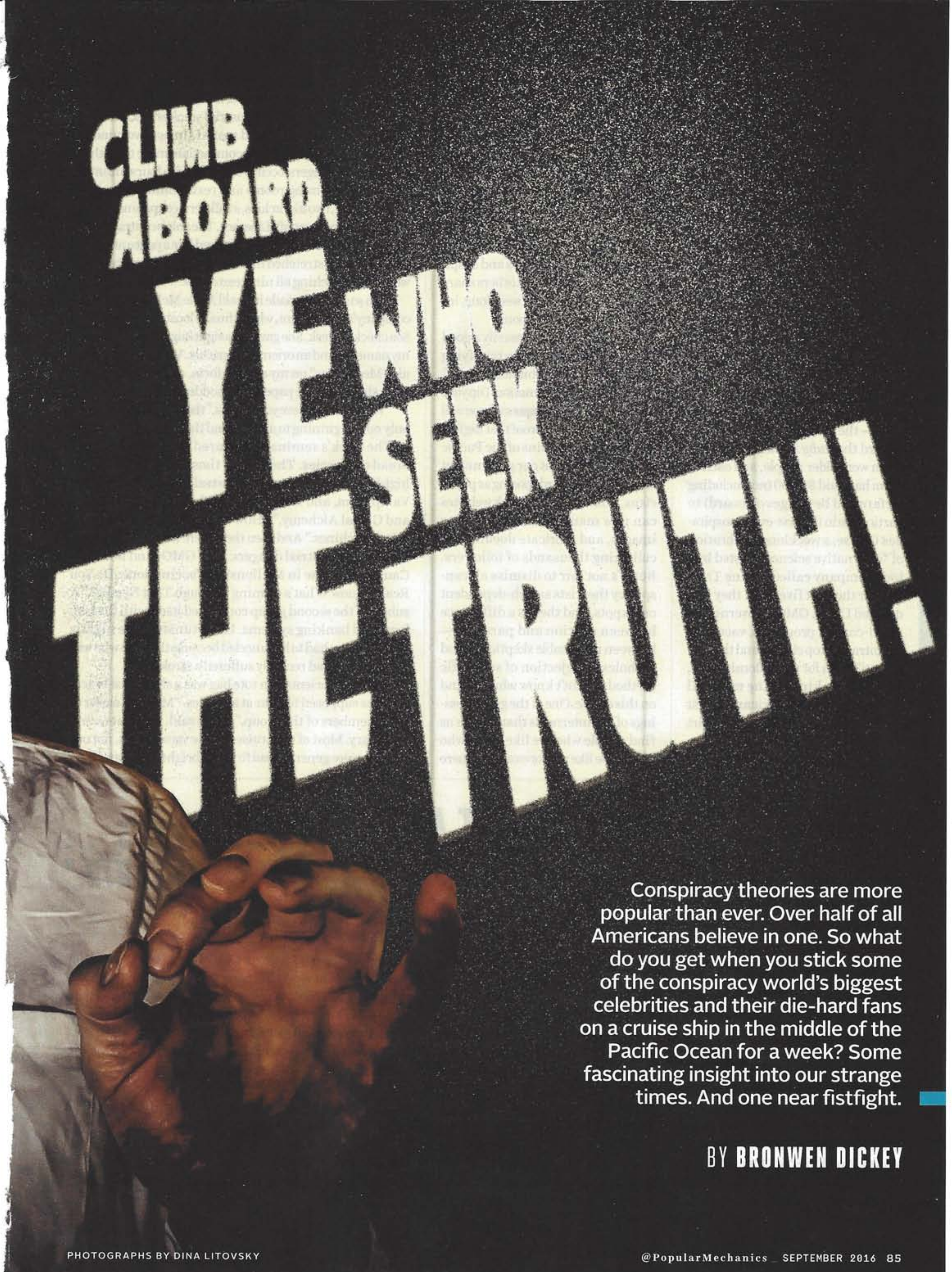
We tend to receive information filtered through our friends, and colleagues, and

science.

That happens to everybody, not just conspiracy theorists. We all do it. And that's why I think it's so important for us to kind of get outside of our little communities, step across the aisle, and have that conversation with someone who is different.

Andrew Wakefield, leader of the anti-vaccine movement and one of the marquee lecturers on the Conspira-Sea Cruise.

Exhibit 9



CLIMB ABOARD, YE WHO SEEK THE TRUTH!

Conspiracy theories are more popular than ever. Over half of all Americans believe in one. So what do you get when you stick some of the conspiracy world's biggest celebrities and their die-hard fans on a cruise ship in the middle of the Pacific Ocean for a week? Some fascinating insight into our strange times. And one near fistfight.

BY **BRONWEN DICKEY**

PHOTOGRAPHS BY DINA LITOVSKY

IT

It was a bit after seven, and I should have been downstairs on Plaza Deck, dressed in formal attire and enjoying dinner with the conspiracy theorists. There were about a hundred of them, and they were nearing the end of their week—the last week in January—aboard the *Ruby Princess*. Many of them were older people, and each of them had paid $3,000 (not including airfare and beverages on board) to participate in the first-ever Conspira-Sea Cruise, a weeklong celebration of "alternative science" hosted by a tour company called Divine Travels. For the past five days, they had debated UFOs, GMOs, government mind-control programs, vaccines, chemtrails, crop circles, and the Illuminati's plan for world domination, all while soaking up the mystical energies of three Mexican tourist towns known mainly for wet T-shirt contests and Señor Frog's.

But I was not on Plaza Deck. I was locked in my stateroom on Baja Deck, picking at a room-service cheeseburger. Earlier that afternoon, a pair of Conspira-Sea presenters had chased me—*chased* me—from a conference room. This wasn't our first confrontation, and now I feared they were tracking me around the ship, waiting to spring out from blind corners and empty doorways.

Understand that I don't consider myself the paranoid type. Although when I had come across the Conspira-Sea Cruise on a science blog a few months earlier, I'd known I wanted to go, but not because I fear dark forces are out to get me. I used to love *The X-Files,* and the prospect of discussing Roswell and JFK over piña coladas sounded like fun. So did getting to know some devoted conspiracy wonks. Wondering whether the world is actually as it seems is a uniquely American sport, and there's plenty of evidence that's worth wondering about—this is the country of Watergate and the Tuskegee experiments and the NSA tapping your phone.

But the *Ruby Princess* was no place for casual wonderers. The *Ruby Princess* was for people who scraped together three grand to be reassured that their fears and suspicions and theories aren't the lonely fever dreams of basement-dwelling outcasts, that those fears and suspicions are valid, and that others share them. It would be like a weeklong, in-person internet chat room.

Not that that's necessarily a good thing. Chat rooms can be terrifying (virtual) places, rabbit holes of self-reinforcing misinformation. Dip your toe into Reddit or Disqus and you will be bombarded with proof that Bigfoot lives in the mountains of the Pacific Northwest and that our government is run by giant lizards posing as politicians. Charlatans with slick websites can now manipulate data, doctor images, and fabricate documents, collecting thousands of followers. But it's not fair to dismiss all conspiracy theorists as web-dependent crackpots, and there's a difference between caution and paranoia—between reasonable skepticism and a wholesale rejection of scientific method. I didn't know what I'd find on this cruise. One of the great blessings of the internet is that it helps us find people who are like us, or who seem to be like us. For example, there are casual Phillies fans, and then there are the kind of Phillies fans who spend endless hours on Phillies fan websites e-conversing with the equally obsessed. Likewise there are people who kind of wonder, fleetingly, whether Lee Harvey Oswald acted alone before their thoughts return to work and family and whether to take the freeway or the local roads. And then there are people who fly far from home, at great expense, to spend a week on the Conspira-Sea Cruise.

Somewhere in the middle was me, deadbolted in my room. Paranoid.

ON A BRIGHTER, happier afternoon five days earlier, I boarded the *Ruby Princess* in San Pedro, California. Flanked by the port's grimy regiment of industrial smokestacks, the ship gleamed majestic white and soared almost two hundred feet into the air. She could accommodate more than three thousand passengers, occupying them with four swimming pools, twelve dining rooms and restaurants, an outdoor movie screen, two nightclubs, a full-service spa, and enough rococo baubles to satisfy Liberace. The ship's central atrium and its giant spiral staircase glittered like a pageant crown. Every corridor stretched into eternity, with identical stairwells crosshatching all nineteen decks.

"I'm so glad you made it!" said Adele McIntosh, the tour company's travel agent, when I finally located the Conspira-Sea check-in desk. She gave me a tight hug, then handed me my name tag and an orientation packet. When I wrote "Popular Mechanics" on my sign-in form, a woman to Adele's right shuffled some papers and nodded approvingly.

"Wonderful to have you with us," the woman said. "We're only now beginning to understand the quantum realm."

The week's seminars appeared to be split into two broad categories. There were those with a magical or highly new age component: "Astral Possession, Psychic Vampirism, and Exorcism," "Gaia-Sophia, Timelines and Global Alchemy," "How to Control the World with Mind Machines." And then there were those that detailed concrete, terrestrial dangers: "Are GMOs and Roundup Causing Disease in Millions?" "Vaccinations: Do You Really Know What's Coming Through That Needle?" A subset of the second group concerned itself with the U.S. legal and banking systems. Unfortunately, the nightly UFO watches had to be canceled because the man who was to lead them had recently suffered a stroke.

Inside my orientation tote bag was a shiny blue bracelet I was supposed to wear at all times. "Makes it easier to find members of the group," Adele said. But that wasn't necessary. Most of the cruisers—the vacationers, not our group—were generally outfitted in bright colors and loud prints. As the days passed, a lot of them began wearing novelty captain's hats from the gift shop. The conspiracy group, on the other hand, was mostly serious-looking senior citizens in "Infowars" T-shirts. Some of them wore casts, others walked with canes. Two relied on motorized scooters. None looked like he or she could afford to spend money frivolously. One eighty-year-old man's toes poked through the tops of his worn leather loafers.

"DEATH IS NOT REAL," HE SAID. "THAT'S THE BIGGEST BUNCH OF CRAP ON EARTH."

I headed to the windowless conference room that had been temporarily renamed the Liberty Lab.

"Welcome everyone," said Dr. Susan Shumsky, the founder of Divine Travels and (claim to fame) one-time

A predinner prayer in the ship's Michelangelo Dining Room; one of the maze-like hallways on the *Ruby Princess*.


EXIT

personal staff member of Beatles' guru Maharishi Mahesh Yogi. (Her doctorate in divinity is from the Teaching of Intuitional Metaphysics in San Diego.) "I'd like to begin with a prayer." Nearly everything the woman wore was either bright pink or sparkled. "Breathe in divine light!" she said. We closed our eyes and inhaled. Across the hall, in Gatsby's Casino, slot machines clanged to a piped-in soundtrack of Taylor Swift and Rihanna.

Then sixteen presenters introduced themselves and gave brief synopses of their seminars. Laura Eisenhower—great-granddaughter of Dwight!—said she had been invited in 2006 to join a secret American colony on Mars and that aliens, including some prominent U.S. politicians, are already living on earth in disguise. Dannion Brinkley, a *New York Times* best-selling author, announced that he had risen from the dead three times, the first after a lightning strike that sent him on a twenty-eight-minute sojourn through the afterlife. "Death is not real," he said. "That's the biggest bunch of crap on earth." Winston Shrout spoke of "commercial redemption," a philosophy that promises each American citizen access to giant piles of secret money.

"Generally I do speak from a little bit of a higher level," Shrout drawled in a thick Kentucky accent. "Because to understand commercial redemption, you have to go into the fifth, and even sixth, dimensions."

The attendees scribbled in their notebooks and eagerly circled items on the schedule. There were pitches for wishing machines, astrological charts, and dowsing rods, followed by screeds against Big Pharma and Monsanto. Sean David Morton, whom AM radio host Art Bell called America's Prophet, vowed to help us get out of debt while sticking it to the American court system. (He did not mention that in 2010 he was sued by the Securities and Exchange Commission for telling a group of investors that he could psychically predict the stock market or that he tried to escape fraud charges by declaring himself the ambassador of a nonexistent country called the Republic of New Lemuria.)

The biggest name on the program was Andrew Wakefield, the discredited former British gastroenterologist who wrote a highly controversial (and since retracted) 1998 paper that claimed to find an association between the measles-mumps-rubella (MMR) vaccine and autism in twelve children. After the U.K.'s General Medical Council stripped Wakefield of his license, he moved to the U.S., where he has assumed rock-star status among the growing American anti-vaccine movement.

Wakefield was superficially charming, if a bit weary. "The story of my life is basically how to take a perfectly good career and flush it down the toilet," he said.

LATER THAT NIGHT, in the Michelangelo Dining Room, Dannion Brinkley was sitting under an airbrushed painting of Poseidon. He is six-foot-four, and the flowing scarf under his sport coat gave him the appearance of an aging linebacker who had just returned from an ashram. Several fans were gathered around him. He motioned me over warmly and I sat down.

"What is your motive for being here," he asked, "and what is your *intention?*"

Puzzled, I looked to the young man on my left, who said he was an orthodontist from Calgary named Leo. He leaned over and whispered in my ear, "Dannion can immediately tell if people are on the right frequency, like tuning a radio. He's trying to figure out what frequency you're on."

"I'm a reporter for Popular Mechanics," I told Dannion, "and I'm here to learn about the conspiracy community."

He beamed and started telling me about his lightning strike. "Whether or not you believe me doesn't matter," Dannion said. "Because ultimately I'm going to win the argument. You are not going to die, and some of us can get up from the dead."

Before he could elaborate, a pair of presenters, Leonard "Len" Horowitz and his girlfriend, Sherri Kane, breezed into the room and sat down at our table. Online, they call themselves "The Horokane." Len bore a strong resemblance to the Count from *Sesame Street,* if you had frozen the Count in 1974 and dressed him in Hawaiian shirts. A former dentist from New Jersey with a degree in public health from Harvard, he is most well-known for writing a 1996 book that theorized the AIDS and Ebola viruses are genocidal weapons engineered by the U.S. government to depopulate the planet through vaccination programs. On the cruise, however, he would be lecturing on the key to lifelong health and world peace: the "miracle frequency" of 528 hertz.

According to Len, everything in the universe emits vibrations, and all the positive, life-affirming forces (including the green/yellow

THE ROCK STARS OF CONSPIRACY THEORY

Other than Andrew Wakefield (pictured on page 84), a few of the biggest draws on the Conspira-Sea Cruise.

LEONARD HOROWITZ

Theorizes AIDS is a genocidal weapon created by the government. Sells crystal pyramids for pain relief. Has a degree in public health from Harvard.

LAURA EISENHOWER

UFO fanatics think her great-grandfather Dwight held meetings with aliens in the White House. She claims many current politicians *are* aliens.

DANNION BRINKLEY

Doesn't believe in death. His book about getting struck by lightning and meeting angels in the afterlife was a *New York Times* best seller.

SEAN DAVID MORTON

Called "America's Prophet." Psychically predicts the stock market. Recently arrested on charges to defraud the IRS. Has amazing taste in neckties.

light in rainbows) "resonate" at a frequency of 528 hertz. Therefore, all music should be tuned in 528 hertz, rather than the 440 hertz of standard tuning, which he asserted was an evil plot imposed by the Rockefeller Foundation to militarize the world's populace. Len believes that standard tuning aggravates the pineal gland, making all of us emotionally distressed, sicker, and more destructive. He called this "musical cult control."

"You," he said to me, and then paused. "Are...a...digital, bio-holo-*graph*-ic, precipitation, crystallization...mi-*rac*-ulous manifestation! Of divine frequency vibrations, forming harmonically in hydrospace."

"Okay," I said.

"That's the frequency that monks used to chant in while making brandy," Dannion added.

Len's face lit up. "When was that?"

"In the 1340s," Dannion said.

"And how do you know that?" Len asked.

Dannion dabbed at the corners of his mouth with his napkin and said, "Because when you die, you know these things. I saw it when I crossed over."

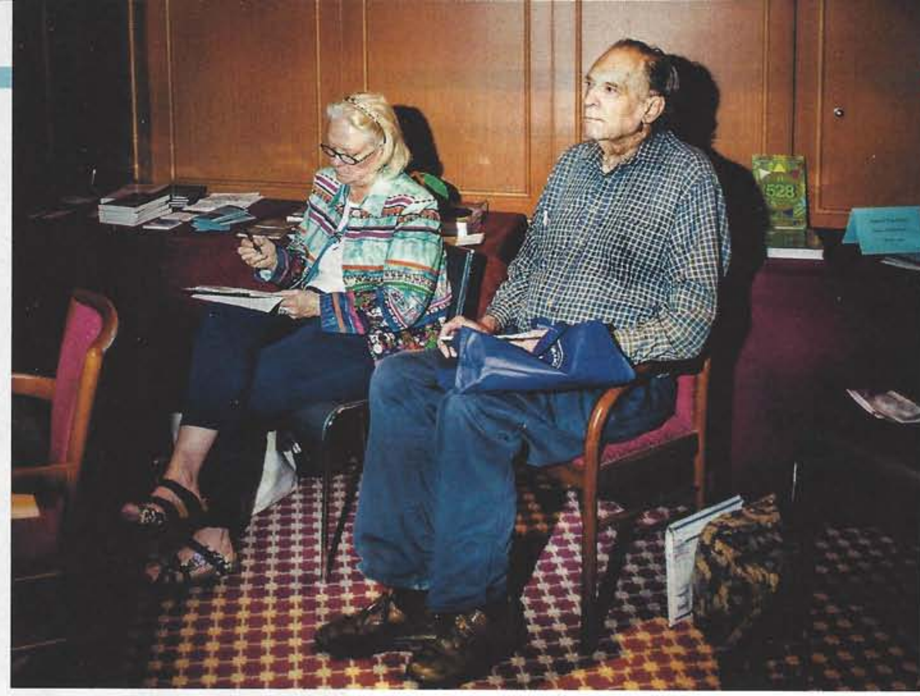
Sherri introduced herself as an investigative reporter who "defected from Fox News." A pretty blond much younger than Len, she seemed to be the great love of his life. "If it weren't for her," Len said, "I might not have known that my ex-wife was working with the CIA to undermine me." (Reached by email, Len's ex-wife denied these allegations.)

"How do you know *I'm* not working for the CIA?" I joked.

Sherri waved the question off, laughing. "Because trust me, it would be obvious. If you were a plant, I would *know*."

When the ship lurched away from the dock and the ice cubes in our water glasses chimed under the drone of the propellers, Dannion requested that we all join hands to pray. Len lowered his voice and leaned across the table.

"The real question," he said, "is whether, after you've learned the truth about all this stuff, your editors at Popular Mechanics will even let you write it."



Cruisegoers paid around $3,000 for the weeklong trip. Not including umbrella drinks.

THE NEXT MORNING, shortly before Wakefield's lecture "Whistleblowing in the Public Interest," a tall, lean man wearing a shiny blue bracelet stood near the elevators. His name was Larry Cook. A soft-spoken fifty-one-year-old anti-vaccination activist from Los Angeles, he said he had joined the trip specifically to meet Wakefield, whom he regarded as something of a personal hero.

"The media has tried to destroy Andy," Larry said as he walked toward the back of a dining room where about fifteen other people were clustered. "But it's all lies and character assassination. We don't *need* drugs and vaccines. If we adopt a healthier lifestyle, we can regain our health without using them. Think about it: If vaccines actually worked, then why do these diseases still exist at all?"

The seminar began. For an hour, Wakefield paced in front of a projection screen, which ballooned his shadow to giant proportions. Slides of children born without arms and others screaming in pain flashed behind him.

"Your bodies are owned by Big Pharma," he said. "It's turning into a science-fiction movie." The audience gasped and shook their heads in disbelief. "This will be the end of the United States of America." During the Q&A portion,

THE TRUTH IS IN HERE

Popular Mechanics has a long history of covering conspiracy theories. Some of our more notable work:

JUNE 1907

"The Truth About Burning Ashes" According to a popular rumor, you could mix a compound with ashes to make a fuel with more energy than anthracite coal. Uh, no.

JUNE 1961

"Facts and Myths About When to Change Oil" Stop trusting your dipstick.

MAY 2001

"When UFOs Land" Most scientists tell you there's no evidence of UFOs. Turns out that's not true.

JANUARY 2005

"Who's Spying on You?" An exploration of the fragile state of personal privacy with the rise of GPS, sensors, and data aggregation.

MARCH 2005

"9/11: Debunking the Myths" We consulted more than 70 professionals in aviation, engineering, and the military to disprove 16 common 9/11 conspiracy theories. We still get crazy emails.

Wakefield added, "This is a deliberate eugenics program, a deliberate population-control program."

I looked around the room. People were sitting and listening attentively. For the first two days, I was heartened by how open and friendly most of the group was, even if they sometimes said surprising things. They told me about their lives and how they were drawn to the conspiracy community.

"Ever since I was little, I've just known that something was off," a fit, stylish forty-seven-year-old office manager named Cary told me. "That we aren't being told everything. My family doesn't believe me, but they are totally brainwashed."

I asked her why she thought the government was poisoning its own citizens with vaccines and GMOs.

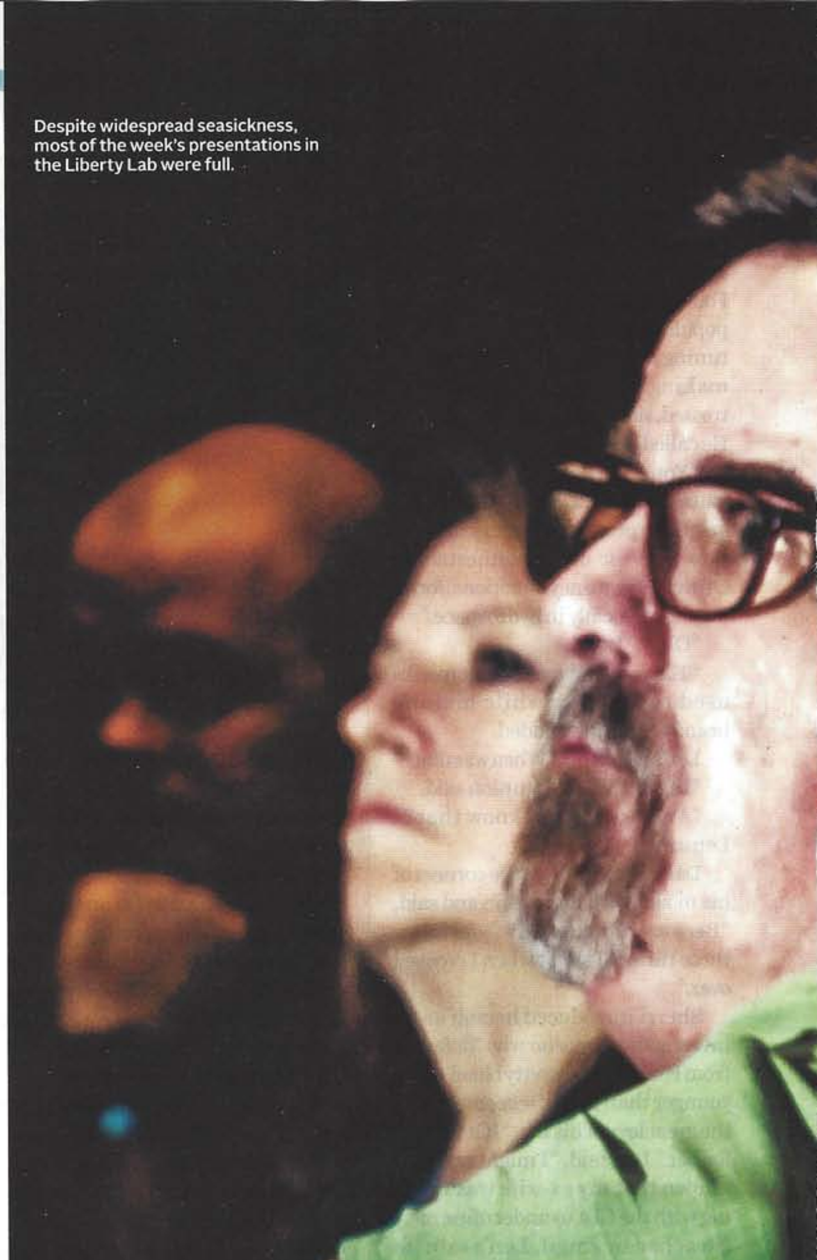
"Because they want to f--king kill us!" she said.

Not everyone was as cynical. Missy and Ron Hill were a married couple from Florida. Missy had a tousled thatch of short blond hair and wore a black leather jacket. Ron wore sandals and floppy fishing hats. The two had met in church roughly fifteen years ago. When Ron, a truck driver for a cryogenics company, was assigned longer runs, Missy went to truck-driving school so that they could see the country together. It was out on the open road that the couple began listening to the late-night AM radio show *Coast to Coast AM,* hosted by Art Bell, who is best known for broadcasting interviews with UFO researchers from a remote station in the middle of the Nevada desert.

"There was so much stuff I had never realized was going on," Ron said. "After that, we were kind of hooked, I guess." The couple's interest in "star gates" and global energy fields inspired them to travel to places like Ireland, France, and Spain. Unlike some of the other cruisers, they explored the world rather than hiding from it.

As the week went on, word spread among the participants that I was writing for a magazine that often covered the world of science. First, Susan Shumsky informed me and Dina Litovsky, the photographer on the story, that Wakefield had requested we not attend the preliminary screening of his documentary, *Injecting Lies,* which alleges that the Centers for Disease Control and Prevention has ironclad evidence that vaccines are linked to autism but has chosen to hide this alarming connection from the public. (Months later, the film—its title changed to *Vaxxed: From Cover-Up to Catastrophe*—would cause a heated national debate when it was accepted, then rejected, by the Tribeca Film Festival. In reviews, *Variety* called it a "scientifically dubious hodgepodge of free-floating paranoia" while *The Guardian* said it was "probably headed straight to the junkheap with all the other conspiracy films." Only when contacted by Popular Mechanics' research department five months later did Wakefield—through his publicist—offer to send me a link to the film.) Then we were asked by Jeffrey Smith, an anti-GMO activist whose previous career involved "yogic flying," to leave two other panels. After that, attendees began ducking out of photos and complaining about Dina's flash.

On Tuesday morning, we sat down in the front row of a presentation we had not yet been barred from: Len Horowitz's lecture on 528 hertz. While Len fussed with the projector, Sherri set out boxes of nutritional supplements and crystal pyramids for sale. Their flagship product, OxySilver, retailed for $49.40. It contained one listed ingredient: purified water, though its nutritional table also included 5 micrograms of colloidal silver.



Despite widespread seasickness, most of the week's presentations in the Liberty Lab were full.

"I took some OxySilver, and I'm already feeling better!" a woman in a scooter who'd suffered a recent bout of cancer announced to the room.

Dressed in a black velour jacket and white shirt with a butterfly collar, Len walked over to me. "I just want you to know that if you degrade and disparage me and libel me in your article," he said, "I will devote everything I have to exposing Popular Mechanics and the people behind it."

"I'm not here to degrade anyone, Len," I said. I was somewhat in shock, because our conversation at dinner the first night had been so

pleasant. "And certainly not to libel them. What is going on?"

"I am living a *nightmare!*" he sputtered, his voice rising like water starting to boil. "Every day of my life is like a roller coaster in *The Twilight Zone*. But I do this because I will not stand by and *watch this genocide!*"

His eyes began to fill with tears. "I think that people should be able to choose how they are going to die, and not be *wiped out by the government!*"

THE INITIAL THRILL of a tropical vacation soon curdled into tension and distrust.

Maybe it was the claustrophobia of all those small, windowless rooms. Or the seasickness that seemed to claim more Conspira-Sea participants by the day. I saw fewer of them relaxing by the pool or playing Texas Hold'em. At breakfast one morning, a woman whose father had survived the Holocaust told me that she broke down in tears when another cruiser claimed it never happened.

(One bright spot: During a day trip to the Las Labra-

Attendee Larry Cook (left) defends the Popular Mechanics team from presenters Len Horowitz and Sherri Kane.

das petroglyphs—carvings etched into large boulders on a beach near Mazatlán—Larry Cook calmly mentioned that the reason few people were now talking to me was that I was "pro-vaccine." We had a civil conversation about the issue—me conceding I was swayed by scientific consensus and the mountain of rigorously controlled peer-reviewed studies that have proved vaccines to be safe and effective, Larry remaining skeptical. Neither of us changed our minds, but we didn't get into a heated shouting match or assault each other's motives. In the two-dimensional world of the internet, it is easy for people on the opposite sides of a controversy to become ciphers to be vanquished rather than human beings with legitimate questions and concerns. It's much harder to dismiss someone right in front of you, a person whose story you know.)

That night the ocean whipped itself into twelve-foot swells. Even more people grew seasick. Still, there were enough to pack the Liberty Lab for the Horokane's screening of their documentary about the Paris terrorist attack on the Bataclan concert hall in November 2015, which they maintained was part of one large false-flag operation. It turned out to be a plotless pastiche of Hollywood movie trailers (*Wag the Dog, Our Brand Is Crisis*), interview segments with survivors of the Bataclan theater attack downloaded from YouTube, and clips of Sherri and Len talking in front of a green screen that had been digitally rendered to look like a news desk. Drawings of Satan and banners denouncing the militant media scrolled behind Sherri's head, as did several advertisements for Len's supplement company, Healthy World Organization.

The film's central thesis went like this: Hollywood superagent Ari Emanuel (who represents Eagles of Death Metal, the band that was playing at the Bataclan when it was attacked) was in cahoots with the Lagardère Group, a French media conglomerate that had purchased the Bataclan in September 2015. Because Qatar Holding has a stake in Lagardère, and because the government of Qatar has been criticized for tacitly allowing terrorist groups to do their banking in the United Arab Emirates, and because—and this is where they totally lost me—Ari Emanuel is the brother of Rahm Emanuel, the mayor of Chicago, the Horokane believed that Lagardère must have orchestrated the attack with the help of Ari Emanuel.

When the film ended, Sherri grabbed the microphone. Her face had turned into a grim, ugly mask, the corners of her mouth pulled downward as if by strings.

"I don't want anybody to leave the room right now," she said. "I have a question." She pointed at Dina, our photographer, who was circling the room taking pictures.

"Come up here," Sherri said. "I want you to tell everybody who you work for."

"I'm with Popular Mechanics," Dina said. "Everybody knows that."

As though she were talking to a small child, Sherri continued, "And can you tell everybody what Popular Mechanics has to do with a *conspiracy cruise?*"

Someone in the audience interrupted, "You know she's the photographer, not the reporter?"

"Let me ask the questions, okay!" Sherri snapped, turning back to Dina. "And can you tell everyone why Popular Mechanics would be interested in people like us?"

Dina just smiled. "What, you don't think you are interesting?"

"You're taking photos so that you can label us conspiracy theorists!"

Dannion Brinkley groaned. "Let's keep it in 528, y'all," he said.

A woman named Abbie, who taught free yoga classes every morning, also stepped in. "That's enough, guys," she said.

"And who are *you?*" Sherri said.

"She's a plant!" someone yelled from the audience.

Eyes rolled. Heads shook. People filtered out.

Someone muttered, "She's the yoga teacher."

WHEN WE ARRIVED at the Liberty Lab the next afternoon, Len accosted Dina in the doorway. His eyes were the size of dinner plates.

"I want you to see something!" he shouted as he tried to force a packet of papers into her hands, then mine. They were articles from Popular Mechanics debunking bad science. Apparently Len and Sherri had been up all night Googling the magazine and printing out documents in the ship's computer center. There was also a Wikipedia entry that linked the magazine's parent company, Hearst, to the Lagardère Group.

I tried to laugh it off and go around him, but Len wouldn't let me pass.

"Look at this!" he shouted, his face contorting with rage. "Look at this! *This is why you're here!* You're here in *bad faith!*"

Larry Cook, who had also been milling around in the hallway, stepped in front of Len to keep him from lunging at me.

"Get your hands off me!" Len shouted at him. "Get your f--king hands off me!"

Armed with a camera, Sherri darted out from behind Len and chased me around the hallway, demanding that I explain myself. As I tried to block my face from the camera, I got trapped against the wall between Len and Larry, who seemed seconds away from a full-on brawl.

"If you don't stop this, I'm calling security," Larry said. Len then challenged Larry to a fistfight in the ship's gym.

That's when I ducked out of the corridor, fled Fiesta Deck, and deadbolted myself in my cabin for the rest of the night. We had sailed far from the Mexican coast, over reason's horizon. We were now bobbing around on the waters of pure insanity.

THE HALLWAY SHOWDOWN turned the rest of the trip into a blur. Wakefield chummily invited me and Dina to his third presentation, which we declined, only to learn from others who attended that he had planned to ambush us by reading aloud from Popular Mechanics. Dannion Brinkley "read my energies" by giving me a long hug. "You were flowing beautifully just then," he said. "But you're putting love out there to someone who isn't giving it back. You're giving this person too much power. You need someone who can appreciate you... like me!" Winston Shrout, in his farewell lecture, reasserted his position as the third-dimensional delegate to the Galactic Roundtable, noting that many of his clients were "fairies and elves." I learned from Laura Eisenhower that Hillary Clinton may have a supernatural agenda for world domination. "She's not even human," Eisenhower said. "You don't want to know what she is."

I also witnessed something called the Baked Alaska Parade. It was the final night of the cruise. I was eating dinner with Dina in the Da Vinci Dining Room, taking long pulls on overpriced beer. The lights dimmed. The waitstaff, holding LED-lit trays of meringue cakes over their heads, formed a conga line and began snaking around the tables to the song "Hot Hot Hot." Someone with a microphone shouted, "Ladies and gentleman, get those napkins up!" And they did. Everybody in the dining room except Dina and I twirled their napkins in the air while singing along. *Olé, o-lé, olé, o-lé.* It was kind of silly, but I think the point was to make people feel they were a part of something bigger.

The conspiracy community does the same thing. Its emotional power is much stronger than facts. It offers a worldview in which chaos, randomness, happenstance—the messy, frightening qualities of life that science depends upon and our minds find so hard to accept—simply do not exist. For some, a sinister reason for life's disappointments is more satisfying than no reason at all.

When we finally disembarked, after Dina and I had driven away, a team of special agents with the Internal Revenue Service arrived at the port and arrested Sean David Morton and his wife, Melissa, on fifty-six counts of fraud, including filing a false tax return that sought a refund of $2,809,921. If convicted, the two face more than six hundred years in prison. (Both have pleaded not guilty.) A couple months later, Winston Shrout was indicted for allegedly printing more than $1 *trillion* in fake financial documents. (He has also pleaded not guilty.) Len and Sherri returned to their home in Hawaii and wrote a long, angry blog post charging me with war crimes and claiming I was part of a top-secret cell of "Pharma Trolls." They also charged Larry, who tried to protect me, as being a double agent for Big Pharma.

WE WERE BOBBING ON THE WATERS OF PURE INSANITY.

Even then, I had a hard time feeling angry at Len.

"I had a brilliant mother who scrubbed the streets at Nazi gunpoint in Vienna," he revealed during one of his last panels, which I attended only after Adele's assurance that she would call security if the Horokane caused any more scenes. "By miracle my mother made it onto one of the last ships out of Europe. By a miracle I am sitting here today. My mother used to say, 'Lenny, you have no idea. Corporate fascism and neo-Nazism could arise at any time and anywhere, in any country.' And I said, 'Mom, I understand your pathology. You're neurotic. Had I been through what you went through, I certainly would feel the same way. You see Nazis everywhere. But I'm sorry, I can't go along with that agenda. I would recommend some good therapy.'"

Then Len's mother received the 1976 swine flu vaccine. After that, she developed Guillain-Barré syndrome, a disease that attacks the peripheral nervous system. She also developed uterine cancer. When she died, Len became convinced that the vaccine—which *was* linked to a small uptick in Guillain-Barré, according to the CDC—was responsible for her illness and subsequent death.

Len Horowitz saw something troubling in the world. When bad things happen without cause, some people turn to religion for comfort. Some look for a scientific reason. Some conclude that bad things happen and there's nothing we can do. Not Len. Len wanted a direct explanation. There had to be one. You just had to know where to look. PM

A sign that was held up to presenters to keep them on schedule.

ICD-10

MICROMD EMR VERSION 10.0

UPDATE GUIDE

Exhibit 10

HENRY SCHEIN®

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Clinical Quality Measures

43 Clinical Quality Measures have been updated for Stage 2 to include ICD-10 codes as well as ICD-9 codes. These updates are done behind the scenes in the reference database.

Form Encounters and the Administrative Form Builder

Users can create forms using the Form Encounter or the Administrative Form Builder to create forms containing ICD-10 codes. The codes will work with checkboxes, options buttons, pick lists and when inserting medical information or assessments with ICD view/print.

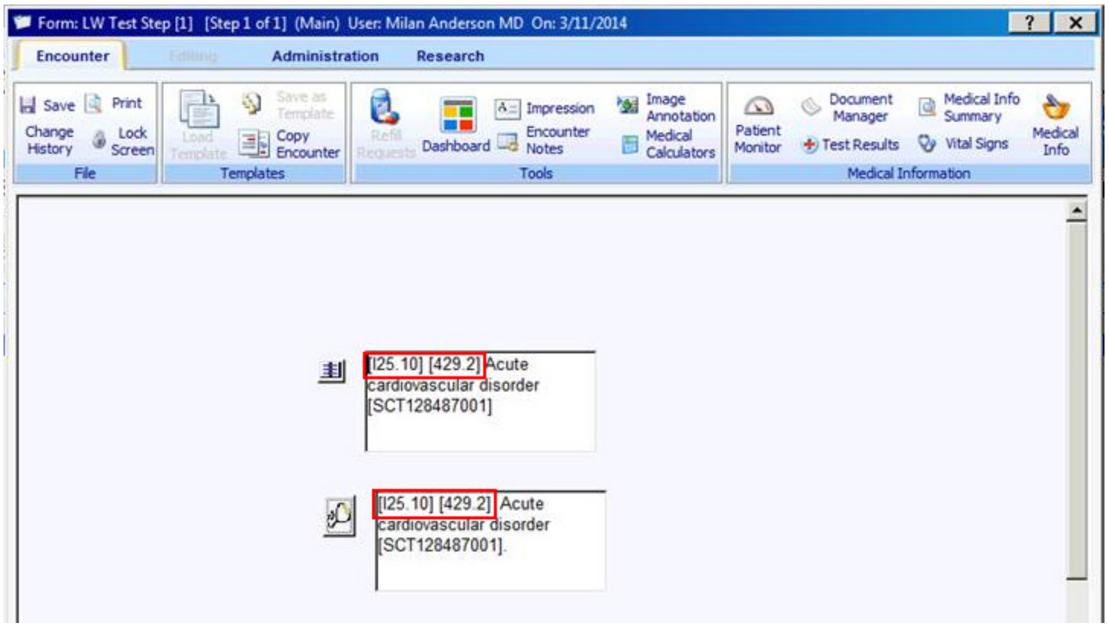

Figure 1.34 ICD-9 and ICD-10 codes in the Form Builder

Drug-to-ICD Warnings

MicroMD has incorporated First DataBank's Medical Lexicon Module, which integrates all existing ICD-10 codes into the EMR, and drug-to-ICD warnings are current with the new code set.

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nature electronics

ARTICLES

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Check for updates

An electrically conductive silver–polyacrylamide–alginate hydrogel composite for soft electronics

Yunsik Ohm[1,2,5], Chengfeng Pan[1,2,5], Michael J. Ford[1,2], Xiaonan Huang[1,2], Jiahe Liao[1,3] and Carmel Majidi[1,2,3,4] ✉

Hydrogels offer tissue-like compliance, stretchability, fracture toughness, ionic conductivity and compatibility with biological tissues. However, their electrical conductivity (<100 S cm^{-1}) is inadequate for digital circuits and applications in bioelectronics. Furthermore, efforts to increase conductivity by using hydrogel composites with conductive fillers have led to compromises in compliance and deformability. Here, we report a hydrogel composite that has a high electrical conductivity (>350 S cm^{-1}) and is capable of delivering direct current while maintaining soft compliance (Young's modulus < 1 kPa) and deformability. Micrometre-sized silver flakes are suspended in a polyacrylamide–alginate hydrogel matrix and, after going through a partial dehydration process, the flakes form percolating networks that are electrically conductive and robust to mechanical deformations. To illustrate the capabilities of our silver–hydrogel composite, we use the material in a stingray-inspired swimmer and a neuromuscular electrical stimulation electrode.

Soft electronics that exhibit high electrical conductivity and match the compliance of biological tissue are important in the development of wearable computing[1,2], soft sensors[3,4] and actuators[5], energy storage/generation devices[6,7] and stretchable displays[8,9]. A variety of material architectures have been used to create soft and stretchable electronics, including deterministic (such as wavy or serpentine) structures[10,11], soft microfluidic channels[12,13] and conductive composites or polymers[14–16]. However, these conductive materials have intrinsic limitations, such as relatively high Young's modulus (≫1 MPa in some cases) or limited deformability, and are not ideally suited for applications related to bioelectronic systems (such as those that require interfacing with biological tissues). Recently, researchers have demonstrated conductive elastomers with enhanced stretchability and compliance by incorporating microdroplets of liquid metal alloys such as eutectic gallium indium (EGaIn)[17,18]. In particular, a highly stretchable and conductive polymer composite has been developed using silver and EGaIn particles embedded in an ethylene vinyl acetate copolymer[18]. Although EGaIn-based polymer composites exhibit an encouraging combination of high conductivity, stretchability and compliance, they require a large volume fraction of metallic filler and their Young's modulus (~0.1–1 MPa) is greater than the modulus of soft gels and biological materials (roughly 1–10 kPa), such as adipose (body fat) tissue[19].

Hydrogels are a promising candidate for soft electronics since they have similar mechanical properties to a range of biological materials and soft tissues[20,21], including epidermal skin[22], brain[23], spinal cord[24] and cardiac tissue[25]. Recent research has highlighted various aspects of hydrogels, including high fracture toughness, tissue-like Young's modulus (<10^2 kPa), high water content (>75%), ionic conductivity, bioactivity and biocompatibility[21,26]. These properties enable unique applications in bioelectronics[27] and soft robotics[28], including soft-matter sensors[9,29] and actuators[30]. However, hydrogels have an intrinsic ionic conductivity (10^{-5} to 10^{-1} S cm^{-1}; refs. [31–33]) that is six to nine orders of magnitude lower than the conductivity of metals, and is inadequate for digital and power electronics[34].

To improve their electrical properties, hydrogel matrices have been filled with conductive materials such as metallic fillers (for example, nanowires or micro/nanoparticles)[35–38], carbon-based conductive materials (carbon nanotubes or graphene)[39,40] and intrinsically conducting polymers (for example, poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) or polyaniline)[3,34,41,42]. These composites demonstrate the potential for engineering hydrogels that are both electrically conductive (~10^{-5}–10^1 S cm^{-1}) and have tissue-like mechanical compliance. However, there is a trade-off between improved electrical conductivity and lowered compliance and deformability in these conductive hydrogel composites. For example, a pure PEDOT:PSS hydrogel[34] has been developed with electrical conductivity of 40 S cm^{-1} but high Young's modulus (~2 MPa) and low maximum strain limit (<35% strain), while a soft graphene hydrogel[40] has been synthesized with favourable mechanical properties (Young's modulus of 50 kPa) but low electrical conductivity (~10^{-4} S cm^{-1}).

In this Article, we report an electrically conductive hydrogel composite that has high electrical conductivity (374 S cm^{-1}), a low Young's modulus (<10 kPa) matching that of soft biomaterials, such as adipose tissue[19], and high stretchability (250% strain). We use a polyacrylamide (PAAm)–alginate hydrogel that is embedded with a low concentration of silver (Ag) flakes. Electrical conductivity is created via a partial dehydration process[34] in which a moderate portion of water is removed to induce percolation and create electrically conductive pathways (Fig. 1a,b). Because the composite has a low concentration of metallic filler, it exhibits only modest hysteresis between loading and unloading cycles. The Ag–hydrogel composite's high conductivity, low Young's modulus, high electrical stability and high stretchability make it a suitable material for applications in soft robotics, bioelectronics and wearable electronics (Fig. 1c, Supplementary Fig. 1 and Supplementary Table 1). We demonstrate the potential applications of this soft conductor by using it in a light-emitting diode circuit that shows high mechanical compliance (Fig. 1d and Supplementary Fig. 2), a stingray-inspired

Exhibit 11

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Non-equilibrium signal integration in hydrogels

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Materials that perform complex chemical signal processing are ubiquitous in living systems. Their synthetic analogs would transform developments in biomedicine, catalysis, and many other areas. By drawing inspiration from biological signaling dynamics, we show how simple hydrogels have a previously untapped capacity for non-equilibrium chemical signal processing and integration. Using a common polyacrylic acid hydrogel, with divalent cations and acid as representative stimuli, we demonstrate the emergence of non-monotonic osmosis-driven spikes and waves of expansion/contraction, as well as traveling color waves. These distinct responses emerge from different combinations of rates and sequences of arriving stimuli. A non-equilibrium continuum theory we developed quantitatively captures the non-monotonic osmosis-driven deformation waves and determines the onset of their emergence in terms of the input parameters. These results suggest that simple hydrogels, already built into numerous systems, have a much larger sensing space than currently employed.

EXHIBIT 12

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Hydrogels play a central role in a wide range of applications[1–11], from drug delivery[12] to microsensors[13] to smart optical[14] and homeostatic[15] materials. Much of the recent interest has focused on enabling hydrogels to deform rapidly in-phase with specific inputs from the environment, such as pH[13,14], temperature[16,17] or chemical concentration[18,19]. In living systems, however, chemical signal transduction—from self-organizing amoebas navigating in fields of chemoattractant waves[20], to heartbeats adapting to ionic bursts and spikes[21], to membranes[22] and genetic material reconfiguring with changing metabolic states[23]—often involves coupling multiple chemical stimuli arriving at separate times and rates. This non-equilibrium integration is driven by materials that convert each incoming stimulus into a long-lived active chemical or mechanical response, often outlasting the duration of the stimulus and thereby enabling it to be coupled to a later one. We considered that even simple hydrogels intrinsically possess these same mechanistic elements. In this way, hydrogels may potentially act as complex chemical signal integrators and in turn exhibit a wide range of previously unexplored transient phenomena and sensing behaviors.

In current strategies, there is a tight, in-phase feedback between the hydrogel deformations, diffusion, and reversible chemical reactions, such as protonation/deprotonation[7,13,14], oxidation/reduction[24], or complexation/dissociation[10,18]. This means that as soon as the stimulus—e.g. protons, divalent ions or reagents—has been removed from the environment, the gel returns to its original state. Then, the gel's response to a subsequent stimulus is a new, separate, independent event. However, we hypothesized that introducing species that complex to the gel with variable, rather than uniformly fast, association/dissociation rates would enable common hydrogels to act as couplers of different stimuli separated across time and space. In particular, a slow dissociation rate should alter the traditional picture: By remaining complexed to the gel, a chemical stimulus would create a kinetically stable state with a characteristic lifetime. In such a case, the gel's deformation would be transiently maintained upon removal of the stimulus from the environment. A second chemical species introduced later could then compete for binding sites, and trigger decomplexation of the first chemical species. As a result, the complexation, diffusion, and gel deformation rates associated with the first stimulus become interlinked with those of the second. In this paper, we show how coupling the dynamics of otherwise separate stimuli in time and space creates specific responses arising from the transient superposition of chemical species entering and exiting the gel.

We explore this concept with a widely used hydrogel, polyacrylic acid (PAA). Our system consists of a thin layer of hydrogel containing an array of embedded microplates, which enable real-time visualization of the gel's deformations at the microscale. The hybrid hydrogel-microplate configuration[25] has previously enabled a class of adaptive materials that catch and release biomolecules[26], switch chemical reactions on and off[27], or control wettability[28], homeostasis[15] and flow[29]. Under neutral or basic conditions, the carboxyl groups (COOH) of the PAA gel exist in a deprotonated form (COO^-), the gel is swelled, and the embedded microplates stand upright. Consistent with the traditional use of PAA gel as a direct pH sensor, exposure to acid protonates the COO^- groups, inducing nearly immediate contraction of the gel and the associated tilting of the microplates (Fig. 1a, yellow). Adding a base rapidly deprotonates the gel and restores the original state. To test our hypothesis, we apply as a first stimulus divalent copper ions (Cu^{2+}), which interacts with COO^- and contracts the gel. Cu^{2+} and COO^- form a kinetically stable chelate complex, which has been reported to maintain localized gel deformation and blue color over months in the absence of external Cu^{2+} (Fig. 1b, blue).[30] Our results demonstrate how this blue color, characteristic for COO^--Cu^{2+}-COO^- complexation, provides a complementary readout mechanism for the complex kinetic interplay between two stimuli. When acid (H^+) is delivered as a second stimulus to a system previously exposed to Cu^{2+}, H^+ competes for COO^- groups (Fig. 1b, gray box) and displaces Cu^{2+}, releasing it into the fluid phase of the gel and then into the initially copper-free supernatant. Cu^{2+} decomplexation will be dependent on the timescale of acid delivery τ_H. Varying τ_H with respect to the timescales of Cu^{2+} diffusion and hydrogel deformation leads to the emergence of a variety of competing non-equilibrium dynamics (Fig. 1, expanded gray box).

Through experiments, scaling laws and a non-equilibrium continuum theory that captures the time-dependent coupling of the two stimuli, we demonstrate how two different, previously unseen responses emerge. (i) Acid-induced Cu^{2+} decomplexation inside the gel triggers transient water influx, driven by the osmosis caused by the Cu^{2+} ions released into the fluid phase of the gel (dependent on the timescale of acid delivery τ_H). At the same time, acid itself contracts the gel (with the mechanical relaxation time $\tau_\perp$). Counterintuitively, even though both Cu^{2+} and H^+ contract the gel upon complexation, the competition between Cu^{2+}-induced osmosis and acid-induced contraction produces traveling osmotic swelling waves when $\tau_H < \tau_\perp$ (Fig. 1c). (ii) If copper is complexed locally in the hydrogel, acid releases Cu^{2+} in region A to diffuse and recomplex to new COO^- groups in previously unoccupied neighboring regions B (Fig. 1d). At the same time, acid also competes with Cu^{2+} and displaces it from these new sites. As a result, traveling color waves appear ahead of a slow-moving acid front when it progresses more slowly than Cu^{2+} diffusion.

Results

Delivering the Cu^{2+} stimulus to the hydrogel microplate system. Our hydrogel system comprises an array of surface-attached, slightly pretilted epoxy microplates embedded in a PAA hydrogel (Fig. 2a). The plates are 18 µm tall. The hydrogel has a height of $H \approx 10$ µm measured from the confocal microscopy z-stack imaging (Supplementary Fig. 1). After deprotonating the PAA hydrogel by rinsing with a base, the hydrogel is swollen and the microplates are oriented nearly upright, 9° with the surface normal (see Methods for details). Upon addition of an aqueous copper(II)sulfate solution (0.8 M $CuSO_4$), the hydrogel turns blue, indicating the formation of COO^--Cu^{2+}-COO^- complexes in the hydrogel (Fig. 2b, c). Concurrently, the hydrogel contracts, and the embedded microplates tilt toward the substrate. This is evidenced by a progressive conversion from a rectangular to a square projection of the microplates in plain-view optical microscopy images. We note that the presence of the microplates and the blue color of the gel provide simple visual reporters on, respectively, (i) the deformation state of the gel, which is quantified by the microplate tilt angle, and (ii) Cu^{2+} complexation, which is quantified by the red channel (r-) value in optical microscopy images (see Methods and Supplementary Fig. 1). Both the microplate tilting and the blue color are maintained after Cu^{2+} is removed from the external solution, even after repeated rinsing with water, indicating a kinetically stable state that stores the Cu^{2+} stimulus upon complexation. The vertical diffusion of Cu^{2+} into the gel layer happens at a timescale $\tau_{Cu2+} \approx H^2/D_{Cu2+} \approx 10$ s, with a diffusion constant of $D_{Cu2+} \approx 10^{-11}$ m^2 s^{-1}. Thus, we expect the local contraction and coloring responses upon Cu^{2+} delivery to occur over a time τ_{Cu2+}.

The Cu^{2+} delivery can be localized and made directional by using a thin copper electrode wire (diameter approx. 100 µm) mounted directly on top of the substrate, covered with a thin

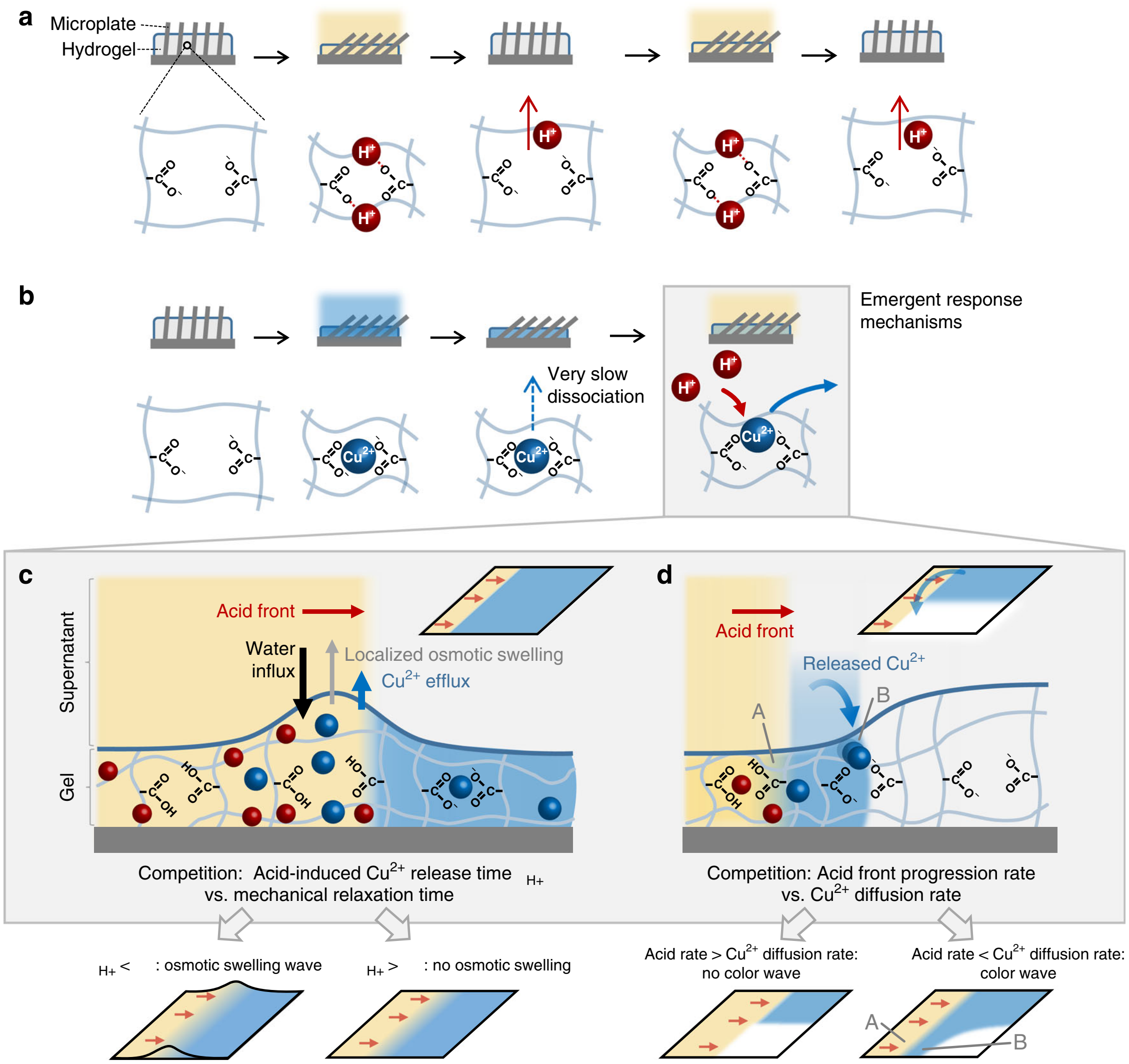

Fig. 1 Non equilibrium coupling of stimuli across time. a Traditionally, a responsive polyacrylic acid (PAA) hydrogel contracts and swells directly in-phase with the presence or absence of an acid stimulus (yellow). Here, hydrogel contraction tilts an array of embedded microplates (gray). **b** In contrast to this rapid reversibility, divalent cations (Cu^{2} , blue) contract the PAA gel by forming a kinetically stable complex with two carboxylate (COO) groups, remaining in the gel after removal of Cu^{2} from the environment. A subsequent acid stimulus then competes for COO groups and triggers dissociation of the Cu^{2} on a timescale determined by its delivery rate ($_H$). The ensuing dynamics of diffusion, complexation, and mechanical deformations in the presence of the entering and exiting stimuli can lead to scenarios depicted in c-d: **c** Competition between transient water in ux, induced by released Cu^{2} , and the mechanical relaxation time of the gel ($_\perp$) creates traveling osmotic swelling waves reporting the speed of an oncoming acid front when $_H$ < $_\perp$; **d** Competition between the diffusion and transient recomplexation of released Cu^{2} (top, curved blue arrow) and its re-release by oncoming acid creates rate-sensitive traveling color waves when the acid progression rate is smaller than the Cu^{2} diffusion rate (bottom right, narrow blue band).

layer of a sodium perchlorate electrolyte solution ($NaClO_4$, 0.05 M, see Scheme in Fig. 2d, Methods and Supplementary Fig. 2). When a voltage of approx. 1 V (current 0.1 mA) is applied, the microplates near the positive electrode begin to tilt as the corresponding region of the hydrogel contracts and turns blue. The region expands outward in time with a gradient of tilt angles and color intensity, consistent with Cu^{2} ions diffusing from the electrode through the electrolyte and binding to the hydrogel (Fig. 2e and Supplementary Movie 1). The slight initial pretilting of the microplates in one orientation results in a uniform tilting direction upon Cu^{2} -complexation. As we noticed a variability in the degree of gel contraction depending on the direction of electrochemical Cu^{2} delivery, all experiments were performed such that the pretilted plates were oriented towards the Cu^{2} source, as schematically represented in Fig. 2d. Both the tilted state and blue color are maintained after Cu^{2} is removed from the external solution by rinsing the substrate with water. Only a slow release of Cu^{2} occurs at the edge of the Cu^{2} -contracted region (Fig. 2f).

Osmotic pulses and waves selective to rapid Cu^{2} release. The kinetically stable complexation creates a unique condition where Cu^{2} is present inside the gel and absent from the external environment. Hence, rapid dissociation of Cu^{2} upon protonation of the carboxylates must yield a transient osmotic pressure within the gel (Fig. 3a): If the release rate of Cu^{2} is fast enough to induce water influx, this triggers an osmotic imbalance across the gel supernatant solution interface. Satisfying this condition requires the relaxation time of the hydrogel deformation $_\perp$ to be smaller than the diffusion timescale of Cu^{2} ($_{Cu2}$), *i e* $_\perp$ < $_{Cu2}$ ($\equiv \epsilon L$ $U^{(0)}$, where $\epsilon \sim$ h H is the ratio of the change in gel lm thickness h over its equilibrium thickness H, L is the horizontal length scale, and $U^{(0)}$ is the inlet speed of the acid).

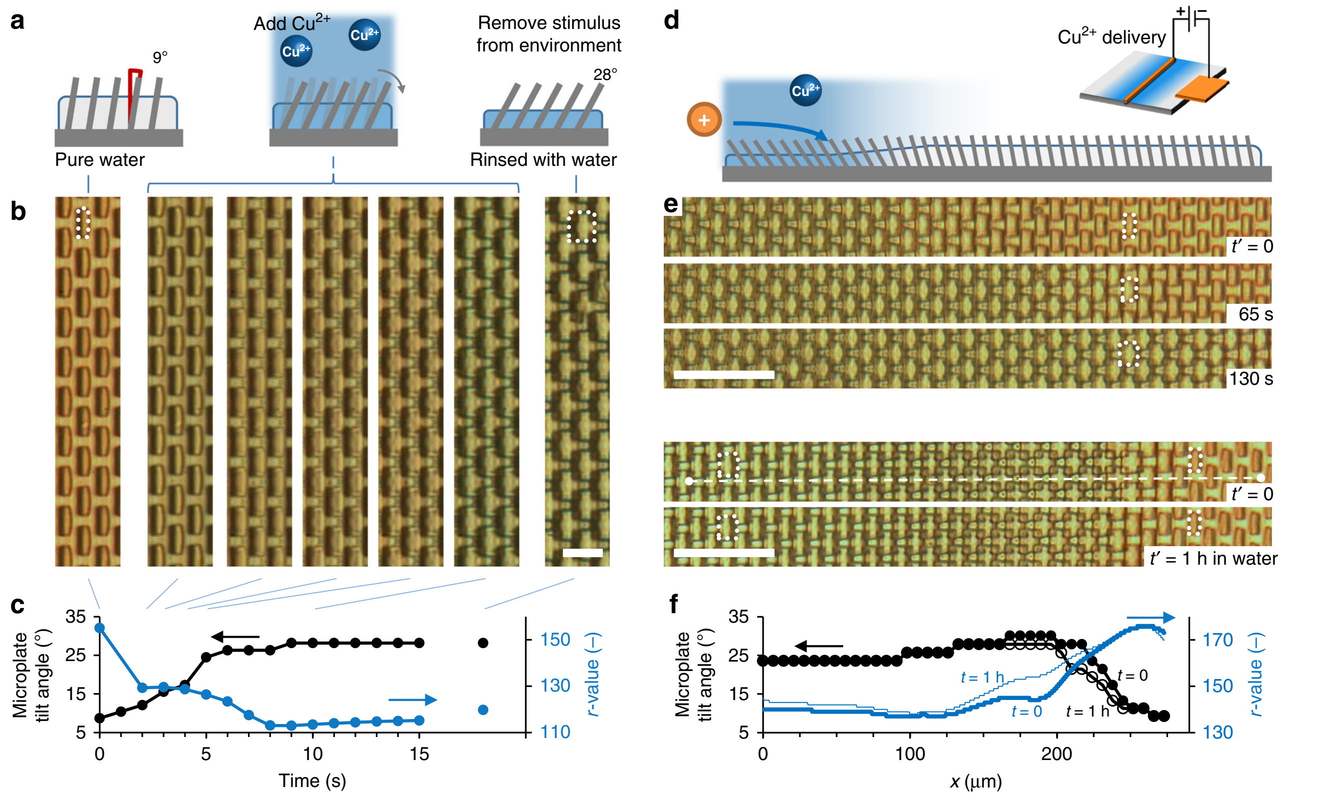

Fig. 2 Delivery and storage of a Cu2 stimulus. a Scheme of the Cu2 complexation, hydrogel contraction, and microplate tilting upon exposure to Cu2 , and the maintenance of this response upon the formation of kinetically stable complexes after the stimulus is removed from the external environment. **b** Optical microscopy images showing that the addition of copper(II) sulfate (see Methods) leads to progressive microplate tilting, concurrent with a progressive colorless-to-blue transition of the hydrogel, indicative of COO -Cu2 -COO complexation. The white dotted outlines indicate the change of the cross-sectional view of a single plate from rectangular (in the upright state) to nearly square (in the tilted state). Scale bar: 15 m. **c** Data corresponding to microscopy images of the microplate tilt angle (black, reported as the angle between microplate and normal to the substrate, see Methods), and Cu2 complexation (blue, reported as value, i.e. red-channel value of the optical micrographs). The tilt angles and blue color are maintained after rinsing the substrate with water (right image in b). **d** Scheme showing Cu2 ions electrochemically delivered from a positively charged copper electrode wire. **e** Upon applying a voltage of approx. 1 V across a copper wire (diameter approx. 100 m), Cu2 ions are released from the electrode (from the left side of the images), diffuse from left to right, and undergo complexation by the COO groups in the hydrogel, inducing blue color and microplate tilting. Scale bar: 50 m. **f** After electrochemical delivery, localized storage of Cu2 remains intact, with only a slow release of Cu2 at the boundary of the contracted region. The value and the microplate tilt angle vs. position *x*, shown in the graph, were acquired along the horizontal white dashed line shown in e. Scale bar: 50 m.

Then, a suf ciently low acid-induced Cu2 release timescale $_H$, such that $_H$ < $_\perp$, is expected to produce an unusual transient gel swelling that would be selective only to fast onset-rates of the acid stimulus.

As an initial test of this scaling prediction, a concentrated acid solution (1 M HCl) was added to a hydrogel-microplate substrate containing complexed Cu2 . Directly after this delivery of a ‘fast arriving acid stimulus, a rapid dissociation of Cu2 was observed, as indicated by the loss of blue color within $_H$ 2 s (Fig. 3b, d and Supplementary Movie 2). Concurrent with this color transition, the initially tilted microplates briefly stood upright at the onset of the acid stimulus, con rming that the system reports the fast acid flow with a transient swelling of the hydrogel when $_H$ < $_\perp$, and then tilted back toward the substrate over $_{Cu2}$ 10 s. Corroborating that this unique transient swelling is indeed driven by an osmotic imbalance induced by Cu2 dissociation, we show that the inclusion of $CuSO_4$ (0.8 M) in the HCl solution—to reduce its hypotonic character—suppresses the swelling pulse (Supplementary Fig. 3).

To assess the selectivity of the swelling response for fast Cu2 release, the same amount of acid was added slowly via a series of progressively concentrated HCl solutions, from 0.01 to 1 M. As shown in Fig. 3c, e, Cu2 dissociates from the hydrogel during the addition step of 0.05 M HCl, over $_H$ 20 s. Since in this case the generation of free Cu2 inside the gel is slower than its diffusion out of the gel (i.e. $_H$ > $_{Cu2}$ 10 s), the accumulation of free Cu2 in the gel is insuf cient to drive the osmotic swelling. As a result, the gel is observed to remain in its contracted state with the microstructures titled to the substrate, and simply changes color as protonation induces the release of Cu2 . We note that when calcium (Ca2) is used as an alternative complexing agent to contract the PAA hydrogel, Ca2 release upon rapid addition of acid induces a transient swelling response as well (Supplementary Fig. 4), suggesting a general applicability of our approach.

The transient osmotic pressure due to rapid Cu2 dissociation can also take the form of traveling swelling waves that are sensitive to the progression rate and direction of an acid front spreading across the substrate. As schematically shown in Fig. 4a, an acid stimulus with a controllable progression rate can be initiated by delivering a drop of acid under one edge of a glass cover (Methods and Supplementary Fig. 5). Cu2 decomplexation at the acid front is indicated by a blue-to-colorless transition that progresses from left to right (Fig. 4b, c), and occurs over a length scale of *L* 100 μm, consistent with free diffusion within the stimulus front (*D* 10 ^{9} m^2 s ^{1}) over $_{Cu2}$ 10 s and $_\perp$ 10 s (see Supplementary Information). To meet the

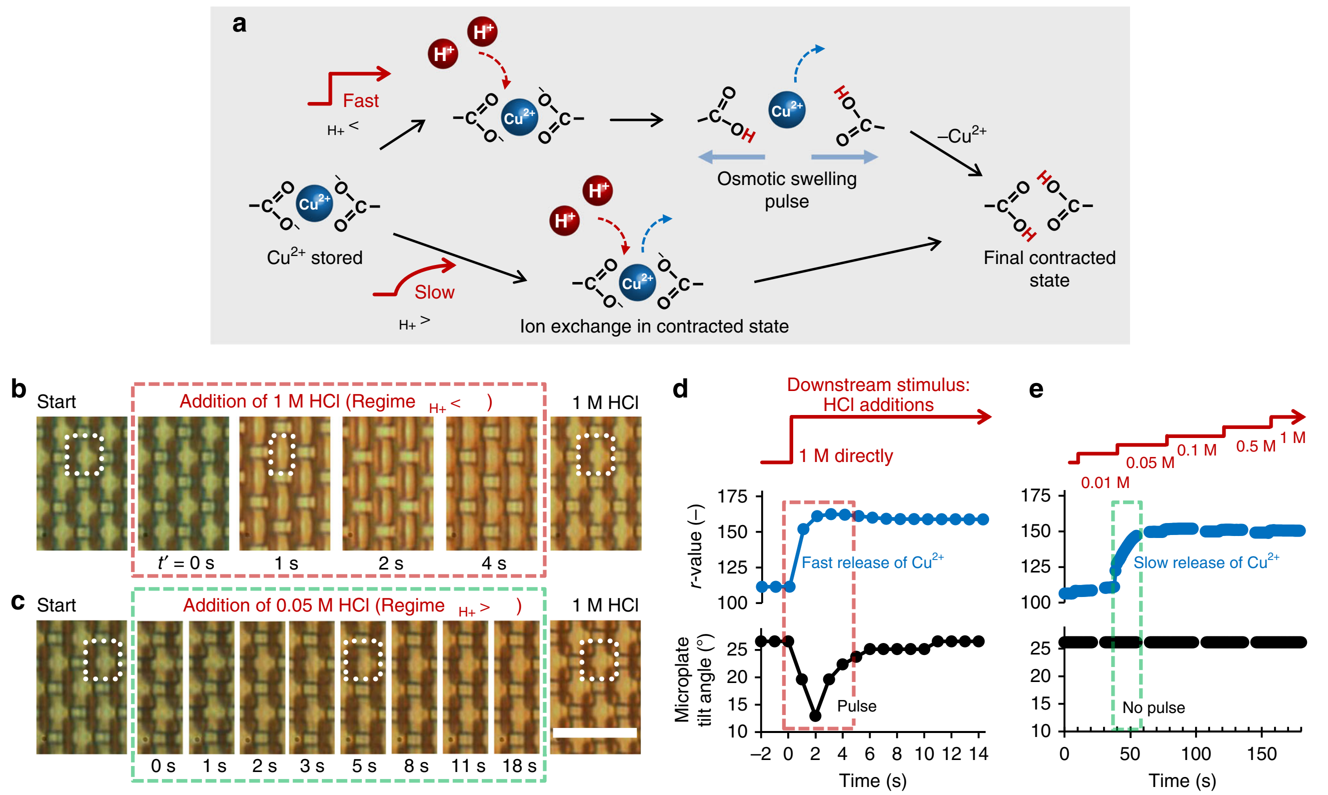

Fig. 3 Cu^{2} ions generate a transient osmotic swelling pulse upon rapid release by an acid stimulus. a Schematic presentation of the mechanism, showing how acid delivered after Cu^{2} has been removed from the external environment of the hydrogel protonates carboxylate groups and thereby releases the complexed Cu^{2}. Fast release would generate an osmotic swelling pulse (top) before acid contracts the hydrogel again, while slow addition of acid should lead to a slow Cu^{2} release without transient swelling (bottom). **b** Experimental demonstration of the fast Cu^{2} release (regime $_{\mathrm{H}}$ < $_{\perp}$), triggered by direct addition of concentrated 1 M HCl, which results in rapid disappearance of the blue color and transient reorientation of the microplates to an upright position. The dotted outlines indicate the change of the cross-sectional view of a single plate from nearly square (in the tilted state) to rectangular (in the upright state), and back to nearly square. **c** Stepwise addition of acid leads to a slow release of Cu^{2}, such that the gel remains contracted without transient swelling (regime $_{\mathrm{H}}$ > $_{\perp}$). Scale bar: 25 m. **d**, **e** Time-dependent microplate tilt angle and value (acid stimulus added at t = 0) for fast (**d**) and stepwise, slow (**e**) addition.

condition of $_{\mathrm{H}}$ < $_{\perp}$ 10 s—the requirement for observing a transient swelling response as discussed above, where $_{\mathrm{H}}$ L/v_{C}—the acid progression speed must be $v_{\mathrm{C}} > 10\,\mu\mathrm{m\,s}^{1}$. Consistent with this prediction, a wave of weakly up-and-down moving microplates is experimentally observed to travel at the front of an acid stimulus moving with a minimum rate of $v_{\mathrm{C}} = 8.6\,\mu\mathrm{m\,s}^{1}$ (Fig. 4c and Supplementary Movie 3). A slower progression yields no swelling pulse at the stimulus front (Supplementary Fig. 6), as exempli ed by the results in Fig. 4b acquired at $v_{\mathrm{C}} = 0.76\,\mu\mathrm{m\,s}^{1}$. In contrast, fast progression ($v_{\mathrm{C}} \geq 95\,\mu\mathrm{m\,s}^{1}$) yields a high-amplitude traveling pulse (Fig. 4d). The pressure that is required to establish a swelling wave spreading over L 100 μm within $_{\mathrm{H}}$ 10 s determines the poroelastic diffusion constant of water inside the hydrogel, given by D_{water} $k_{\mathrm{f}}\,p/\mu_{\mathrm{f}}$ 10 $^{10}\,\mathrm{m}^2\,\mathrm{s}^{1}$, where k_{f} 10 ^{19} 10 $^{18}\,\mathrm{m}^2$ is the hydraulic permeability of the hydrogel and $\mu_{\mathrm{f}} = 10^{3}$ Pa s is the dynamic viscosity of water. The required pressure p equals 1 10 MPa; a pressure that can be generated upon osmosis as the concentration of Cu^{2} ions is estimated to be 2.9 M (Supplementary Fig. 7 and Supplementary Information), implying a maximum osmotic pressure of ~7 MPa (p_{osm} [Cu^{2}]·$k_{\mathrm{B}}T$). We note that the orientation of the microplates with respect to the acid stimulus progression does not have a major effect on the swelling response of the hydrogel.

To further assess the timescales and forces involved in the unique transient swelling responses and traveling waves that arise upon coupling of successive Cu^{2} and acid stimuli, we developed a continuum theory that gives the time-dependent height pro le of a thin hydrogel sheet, based on time- and position-dependent descriptions of (i) Cu^{2} and acid present in the supernatant fluid, in the hydrogel interior fluid, and complexed to PAA; (ii) the osmotic and contractile forces exerted on the gel due to free and complexed Cu^{2} and acid in the gel, and (iii) the mechanical deformation of the gel (see Supplementary Discussion). Simulations based on parameter values, which match experimentally assessed time- and pressure-scales, quantitatively reproduce the experimental vertical deformation waves of the hydrogel, as derived from the experimentally observed microplate tilting waves (Fig. 4e, Supplementary Figs. 8 and 9, and Supplementary Movies 4–6). The transient osmotic vertical flow for thin lm domains is given by Supplementary Eq. 14 and holds at the leading order O(δ^0, ϵ^0), where δ is the aspect ratio of the thin lm; both ϵ and δ are very small. The mobility coef cient in Supplementary Eq. 14 scales with δ ^{2} and is not a free parameter. This osmotic flow term quantitatively reproduces the osmosis-induced traveling waves (Fig. 4, Supplementary Movies 4–6). Thereby, our theory shows that, rst, species released within the hydrogel induce transient osmosis; second, this enables unique signaling routines that selectively report input stimuli occurring at fast rates; and, third, swelling pulses are displayed at timescales that cannot be established by solely breaking crosslinks in the hydrogel.

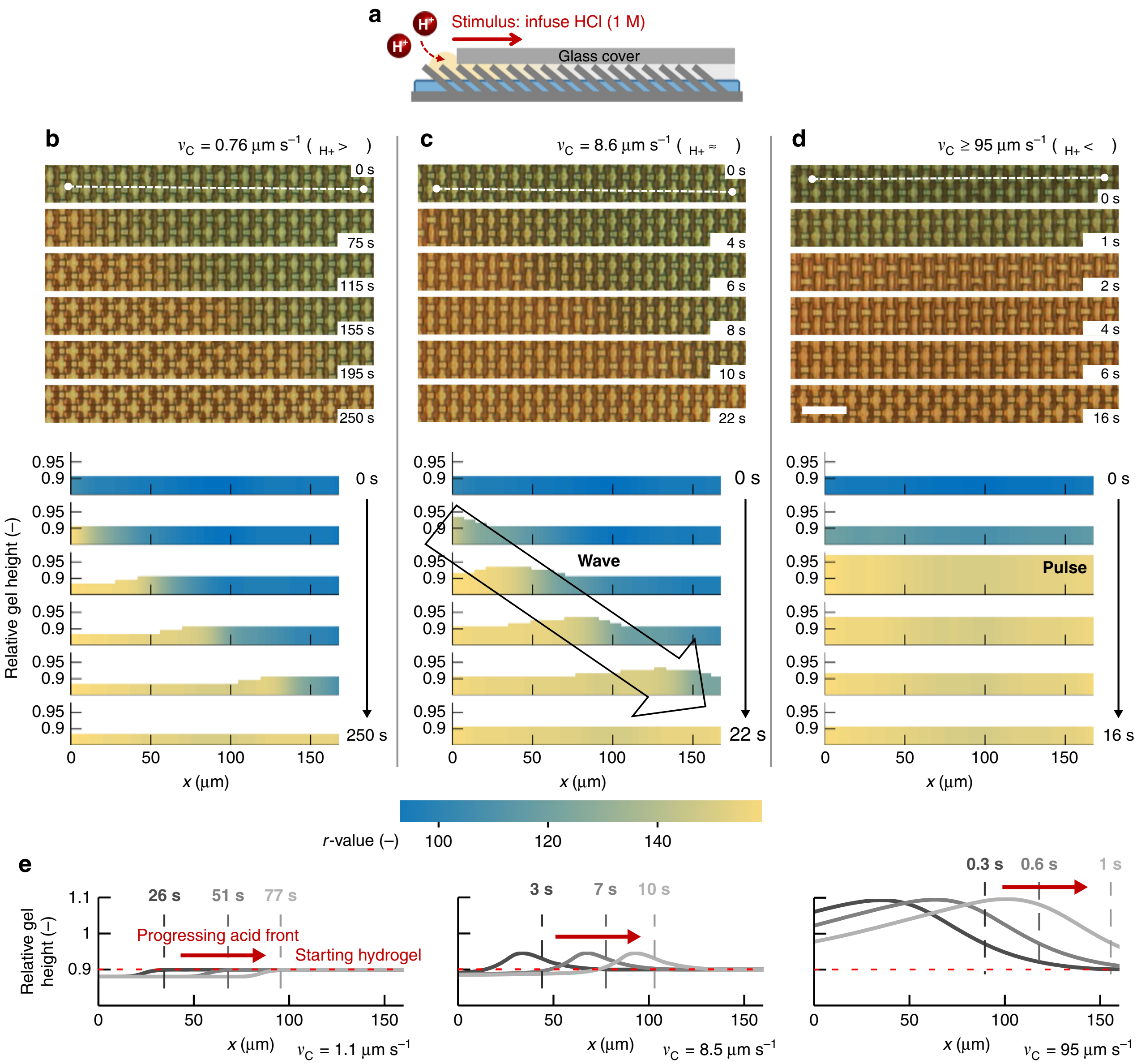

Fig. 4 Traveling swelling waves that are sensitive to the acid progression rate. a Schematic of the experimental design: HCl (1 M) is added from the left side of a Cu^{2} -contracted substrate covered with a thin water film and a glass cover (see Methods). **b**–**d** (Top) Micrographs showing the progression of the acid stimulus at various rates, indicated by a blue-to-colorless transition. (Bottom) The height of the diagrams represents the evolution of the relative hydrogel height in time and space derived from the microplate tilt angle as described in Methods (Supplementary Fig. 1), along the white dashed line for the six micrographs from top to bottom; and the color of the diagrams represents the Cu^{2} release as characterized by the blue-to-colorless transition: **b** No swelling pulse is observed for the acid stimulus that travels from left to right over 190 m in 250 s ($v_C = 0.76$ m s ^{1}); **c**, **d** Faster progression of the acid within 22 s (**c** $v_C = 8.6$ m s ^{1}) and within 2 s (**d** $v_C \geq 95$ m s ^{1}) generates swelling/contraction waves that travel at the acid front. Scale bar: 25 m. **e** The results of our continuum theory show that traveling swelling/contraction waves are only obtained at $v_C \geq 8.5$ m s ^{1} for this set of experimental parameters, in excellent agreement with the experimental data. The red dashed lines indicate the starting height of the Cu^{2} -storing hydrogel; the vertical lines indicate the position of the progressing HCl front at three different times; the curves show the corresponding relative hydrogel height along the horizontal position *x*. The grayscale corresponds to three different times given in the legend of each plot.

Traveling color waves reporting slow acid fronts. Copper ions released by acid from the hydrogel into an otherwise Cu^{2} -free medium not only enable short-term osmotic pressure in the gel, but also give rise to localized patterns of recomplexation as the released Cu^{2} ions diffuse with the moving acid front. While swelling waves require a rapidly moving acid front to trigger a rapid release of Cu^{2} inside the gel, recomplexation of Cu^{2} should in contrast require the acid front to be moving slowly enough for the diffusing Cu^{2} ions to be able to compete with the oncoming protons for new binding sites. Assuming a graded acid concentration at the front, Cu^{2} comigrating with the front will potentially have a time window to recomplex to the gel in the presence of a low acid concentration, before saturating acid overtakes the recomplexed Cu^{2} and releases it again. Consistent with this possibility, flowing a solution containing 1 M HCl and 0.8 M $CuSO_4$ with a slow progression rate along a substrate with a deprotonated PAA hydrogel yields a transient band of Cu^{2} complexation at the solution front ($v_C = 3$ µm s ^{1}, Supplementary Fig. 10). For a system that is exposed rst to Cu^{2} and subsequently to progressing acid, initial release of Cu^{2} by acid at

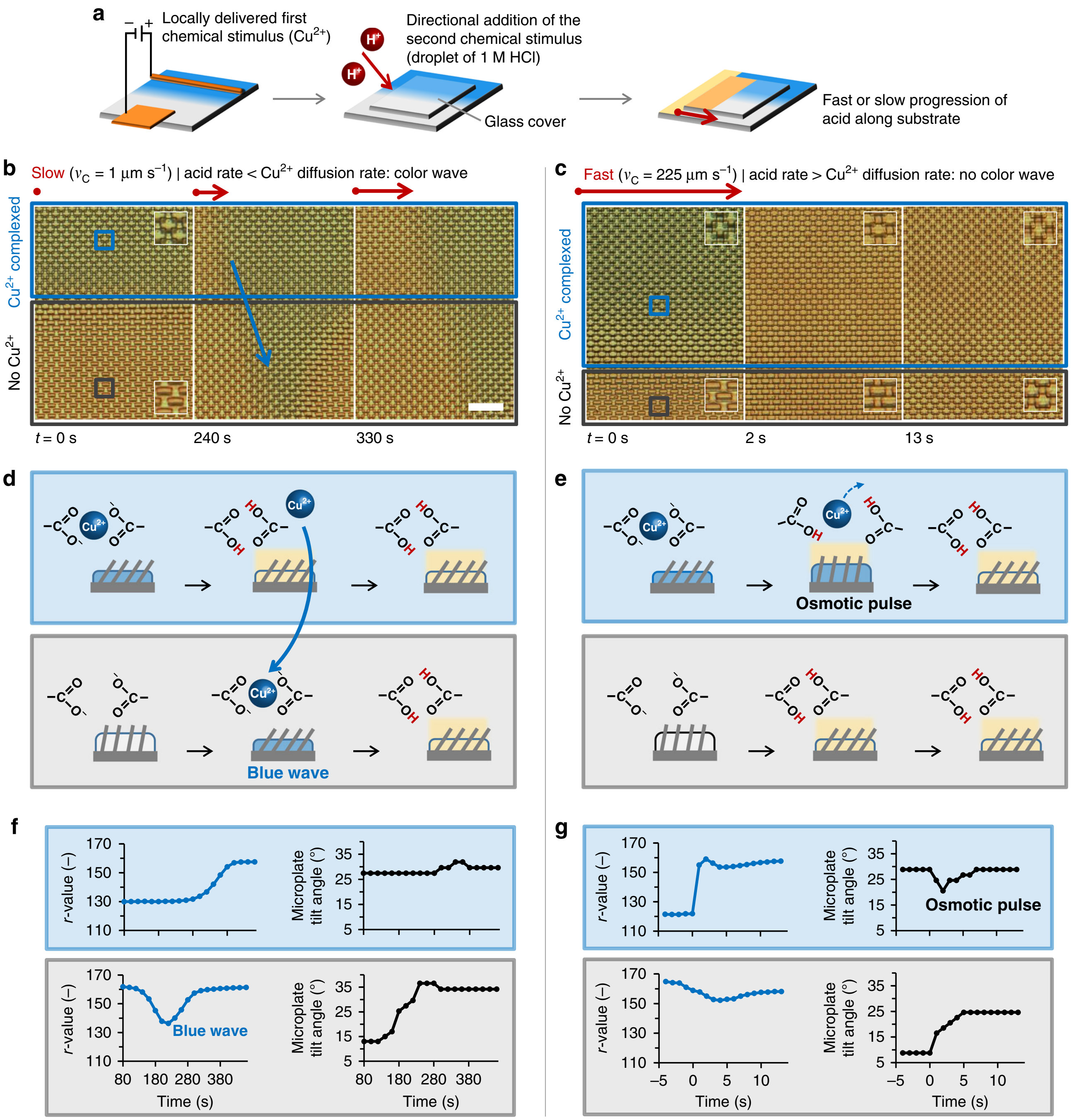

Fig. 5 Traveling color waves selectively reporting slowly progressing acid stimuli. a Schematic presentation showing the mechanism for the appearance of the travelling color waves: Cu2 is initially delivered electrochemically to one side of the substrate (blue region in diagram). A glass cover is then applied and the acid is added from the left and allowed to progress along the substrate. **b** Experimental demonstration of the slow acid progression: Cu2 is complexed in the region of the substrate where it was applied; slow progression of the acid (acid rate < Cu2 diffusion) allows Cu2 , released at the acid front in the Cu2 -complexing region (blue box), to migrate to the adjacent Cu2 -free region (blue arrow), generating a transient blue wave just ahead of the stimulus front (gray box). Scale bar: 50 m. **c** Fast progression of the acid from left to right (acid rate > Cu2 diffusion) induces a swelling/contraction wave in the Cu2 -complexing region (blue box) and a direct contraction of the hydrogel with no color wave in the region with no Cu2 (gray box). **d**, **e** Schematic representation of the subsequent stages for both regions in (**b**) and (**c**), respectively. **f**, **g** Time-dependent value and microplate tilt angle, acquired at the blue and gray squares in (**b**) and (**c**), respectively.

a region A, followed by diffusion of Cu2 through the supernatant solution and recomplexation to the gel at a region B, can result in a transient band of Cu2 complexation. This must only happen when acid migration from A to B is slower than the diffusion of Cu2 and its subsequent recomplexation at B: $L_x/v_C > L_x^2/D^{(a)}_{Cu2}$, where $L_x \sim L$ 100 μm is the distance between A and B, and $D^{(a)}$ is the diffusivity in the supernatant solution.

To test this idea, we electrochemically delivered Cu2 across one half of a gel/microplate system, so that Cu2 is stored on one side while the other remains copper-free (blue and white sides in Fig. 5a, respectively). Acid is then flowed such that the front progresses over both halves in parallel (Fig. 5a, yellow). This con guration potentially allows some of the released Cu2 at the front to diffuse to and recomplex on the copper-free side, subject to the acid-dependent competition and time window. Our experimental results at different progression speeds indeed indicate the ability of this mechanism to produce a distinctive slow-rate-sensitive response: a slow acid progression speed ($v_C = 1\ \mu m\ s^{-1}$) generates a wave of blue color that travels with the acid front through the initially copper-free side (Fig. 5b, d, f and Supplementary Movie 7), featuring the regime where the acid progression is slower than the Cu^{2+} diffusion. This response was further observed with an intermediate rate of $v_C = 3\ \mu m\ s^{-1}$ (Supplementary Fig. 11), and also with a hydrogel without embedded microplates (Supplementary Fig. 12). The inequality $L_x/v_C > L_x^2/D^{(a)} + \tau_{Cu2+}$ only holds when $v_C < 5\ \mu m\ s^{-1}$, assuming $D^{(a)} = 10^{-9}\ m^2\ s^{-1}$ and $\tau_{Cu2+} = 10$ s. Indeed, at fast progression rates ($v_C = 225\ \mu m\ s^{-1}$, Fig. 5c, e, g), no blue color was observed on the copper-free side (acid progression rate > Cu^{2+} diffusion rate). Instead, a wave of osmotic pressure was generated on the copper-storing side, with the associated transient upright movement of the microplates, as discussed above.

Discussion

Our results provide a potentially transformative approach to chemical signal processing and, more generally, suggest that simple hydrogels have a much larger sensing space than is currently made use of. By integrating the complexation-transport-deformation dynamics induced in the gel by two chemical stimuli that occur separately in time and space, we show that a common hydrogel—traditionally used for direct stimulus tracking through nearly in-phase response to an applied stimulus—can produce previously unseen complexity. This is demonstrated by time-sensitive, nonmonotonic osmotic effects accompanied by spikes and waves of gel expansion and contraction, as well as traveling color waves of patterned migration and recomplexation. Our non-equilibrium continuum theory captures how the diverse responses depend on the coupling of diffusion, flow, complexation, and hydrogel deformation as successive chemical stimuli enter and exit the gel. The theory allows the parameter windows to be predicted for a range of phenomena based on the relative timescales involved in signal coupling. Combined with an extensive experimental and scaling analysis, the model provides insight into the competing processes underlying the response mechanisms and emergent behaviors. As exemplary cases, our theory reveals how traveling osmotic swelling waves can emerge in response to the rapid onset of a stimulus that would normally—on its own—contract the gel, if the timescale of acid propagation is smaller than the mechanical relaxation time of the hydrogel. The theory further implies that, when two H^+ signals approach from opposite directions, the accompanying swelling fronts would annihilate each other upon collision. This is because no available bidendate complexation sites would be left ahead of each front to be decomplexed and create osmotic imbalance. Further scaling laws elucidate how a slowly moving acid gradient can induce sequences of migration and recomplexation highly sensitive to the interdependent dynamics of the released and oncoming stimuli.

In conclusion, the framework presented here shows how a hydrogel can be used without specialized modifications to perform complex chemical sensing tasks not previously achieved with electronics-free systems. The exemplary responses we demonstrate likely represent only a small sample of the dynamic phenomena that may emerge. Based on simple, reversible chemistry and trivial hydrogel composition and geometry, our scaling analyses and the theoretical model elucidate distinct outputs able to discriminate among many possible combinations and permutations of rates, times, sequences, and configurations of multiple arriving stimuli. These concepts are potentially applicable to a wide range of hydrogels, stimuli and non-equilibrium molecular systems beyond the ions, acid, and PAA gel used in this study.[31–39] The non-equilibrium concepts and theory can be further applied to readout mechanisms beyond the microplates used in this study, such as via microparticles dispersed within the gel or via focussing and defocussing of light beams by the gel. Additionally, the concept of rate-selective recomplexation waves—exemplified by the blue color waves in our system—can be expanded by selecting alternative pairs of complexing agents (such as Ca^{2+} and H^+), potentially in combination with fluorescent or other indicators. In particular, the non-equilibrium mechanisms revealed in this study may enable micron-scale synthetic soft actuators, analogous to the way Ca^{2+}-based biochemical reaction-transport pathways power the motion of some single-celled organisms, such as *D. discoideum*[40] and the *Vorticella* ciliates[41]. Beyond reporting the gel's dynamics, microstructures embedded in the gel can themselves introduce feedback to the complexation-transport-deformation coupling[42], potentially opening another realm of non-equilibrium sensing. Further developing these capacities may bring about new possibilities for integrating complex chemical sensing and transduction, using simple soft materials, into areas such as soft robotics, catalytic materials, and agricultural and biomedical diagnostics.

Methods

Chemicals and materials. Polydimethylsiloxane (PDMS, Dow-Sylgard 184) was purchased from Dow Corning Corporation (Midland, MI, USA). Epoxy resin OG178 was purchased from Epoxy Technology (Billerica, MA, USA). Glycidyl methacrylate, acrylic acid, sodium acrylate, 2,2′-azobis(2-methylpropionamidine) dihydrochloride, *N-N*′-methylenebisacrylamide, 1-butanol, ethylene glycol, copper (II)sulfate, sodium perchlorate, ethylenediaminetetraacetic acid, potassium hydroxide and hydrochloric acid were purchased from Sigma Aldrich. Irgacure 819 was purchased from BASF Corporation, Lumiprobe BDP FL NHS ester from Lumiprobe Corporation (Hallandale Beach, FL, USA), calcium chloride from J.T. Baker and copper(II)chloride from Fluorochem. All compounds and materials were used as received.

Fabrication of hydrogel-embedded microplate substrates. To prepare the epoxy microplate substrates, first a PDMS negative mold was obtained by curing a 10:1 wt./wt. mixture of base resin and hardener onto a silicon master with the microplates positioned in a staggered array, with a height of 18 μm, a width of 10 μm, a thickness of 2 μm and a spacing of 5 μm in both *x* and *y* directions. The silicon master was fabricated via the Bosch process and functionalized with (tridecafluoro-1,1,2,2-tetrahydrooctyl)trichlorosilane in a desiccator under vacuum at room temperature for at least 24 h, in order to facilitate demolding of the PDMS. The PDMS prepolymer mixture was mixed for 1 min, degassed under vacuum at room temperature, poured over the silicon master in a petri dish, put under vacuum at room temperature to remove bubbles, and then cured at 70 °C. After 2 h, the PDMS molds were cooled and peeled off from the silicon mold. To prepare an epoxy microplate substrate, 35 μL of a 9:1 (wt./wt.) prepolymer mixture of the OG178 epoxy resin and glycidyl methacrylate was added to the PDMS mold and covered with a glass slide (16 × 16 mm^2, pretreated in O_2-plasma for 2 min). UV curing was performed under a UV lamp (100 W, Blak-Ray with a 365 nm band-pass filter, approx. 10 mW cm^{-2} at 365 nm) for 30 min. The microplate substrate was then obtained by carefully removing the glass slide from the PDMS mold.

In order to embed the microplate structures in the hydrogel, 3 μL of a hydrogel precursor solution was added to the substrate. The hydrogel precursor solution was prepared by combining 400 μL of acrylic acid with 20 mg *N-N*′-methylenebisacrylamide crosslinker in 1 mL of a 1:1 v/v mixture of ethylene glycol and 1-butanol. To introduce the Irgacure 819 photoinitiator, 10 μL of a 25 mg mL^{-1} solution in 1-butanol was added to 90 μL of the aforementioned solution to obtain the hydrogel precursor solution. After applying the hydrogel precursor solution to the microplate substrate, it was immediately covered with a thin glass cover slide (cleaned with isopropanol) and the hydrogel was subsequently cured for 5 min under UV, similarly to the epoxy curing. After curing, the hydrogel-microplate substrate was immersed in deionized water to allow the glass cover slide to detach and to exchange the ethylene glycol/1-butanol mixture in the hydrogel for water.

To assess the embedding of the microplates in the hydrogel, the hydrogel was dyed by combining a solution of Lumiprobe BDP FL NHS ester (2.5 mg mL^{-1}) in a 1:1 v/v 1-butanol/ethylene glycol mixture with an equal volume of a double concentrated hydrogel precursor solution (see above). Next, the obtained solution was applied to the microstructures and cured as described above. The dyed hydrogel-microplate substrates were then analyzed by confocal microscopy (λ_{ex} = 488 nm).

To prepare a hydrogel substrate with no microplates embedded, first an epoxy substrate was prepared by photo curing a Norland 68 epoxy resin sandwiched between a flat PDMS support layer and a glass cover (prepared as described above, total exposure time under UV 10 min). Subsequently, 40 µL of a hydrogel precursor (113 mg mL^{-1} sodium acrylate, 11 mg mL^{-1} *N*-*N*′-methylenebisacrylamide and 7.5 mg mL^{-1} 2,2′-azobis(2-methylpropionamidine) dihydrochloride photoinitiator in water) was applied, and covered with a glass slide of 18 × 18 mm^2. Subsequently, the hydrogel was cured under UV (366 nm, 4 min) and the substrate was immersed in water to detach the glass cover. Then, the substrate was vertically immersed for 2 min in an aqueous $CuCl_2$ (0.8 M) solution, such that one half of the hydrogel was complexed to Cu^{2+} as evidenced by the appearance of blue color. The results in Supplementary Fig. 12 were acquired in analogy to the methodology applied for Fig. 5; the images were acquired on a Leica DM 2500 microscope equipped with a Leica DFC 7000T camera.

Assessing complexation of Cu^{2+} and tilting of microplates. All optical microscopy images were acquired with an Olympus IX71 dark field inverted microscope equipped with a QImaging Retiga 2000R camera unless stated otherwise. All colored images were acquired with similar white balance settings and light intensity. Confocal microscopy was performed using a ZEISS LSM 700 microscope. SEM images were acquired on a JEOL JSM 639OLV scanning electron microscope, and the sample was sputter-coated with Au/Pd for imaging.

To quantify the tilting of the microplates, the microplate tilt angle was determined from the microplates′ projection in optical microscopy images. The projection of the microplates was measured in the images and, based on the ratio of this projection to the distance between n rows of microplates in the same image, which equals $(n - 1) \times 7$ µm, converted to the real dimensions p in µm. Based on the height of the microplates $h = 18$ µm and the thickness $t = 2$ µm, the microplate tilt angle α was determined as $\alpha = 90 - \mathrm{acos}((p - t)/h)$ (see Supplementary Fig. 1c). It is assumed that the plates do not curve upon actuation but maintain their straight form and only hinge at the connection to the substrate (see Supplementary Fig. 1b). The relative gel height was derived via $\cos(\alpha)/\cos(\alpha_{\text{gel completely swelled}})$.

The color profiles were acquired using ImageJ 1.50b software. To avoid the profiles being disturbed by the contours of the microplates, the images were blurred (Gaussian blur; Sigma radius 50) prior to acquiring the r value (red channel RGB value).

Absorption spectra were acquired on a Beckman Coulter DU 720 UV/Vis spectrometer, in a polymethyl methacrylate (PMMA) cuvette (optical path length 1 cm) at room temperature, and the background was acquired on a PMMA cuvette with water.

Complexation of Cu^{2+} in the hydrogel. Prior to the contraction of the hydrogel via Cu^{2+} complexation, the hydrogel-microplate substrate was sequentially rinsed with hydrochloric acid (HCl 1 M, 4× the same solution of 2 mL), water (5×), potassium hydroxide (KOH in a concentration of 0.1 M, 4× the same solution of 2 mL, repeated with a fresh solution of 2 mL), and water (5×). Thereafter, excess water was removed from the substrate with a tissue. For Fig. 2b, a thin layer of 50 µL water was applied to the substrate, and subsequently 10 µL $CuSO_4$ 0.8 M was added. To assess the storage of Cu^{2+} upon complexation to the hydrogel, the substrate was rinsed with water (4×).

Electrochemical delivery of Cu^{2+}. Cu^{2+} ions were delivered to the hydrogel-microplate substrate by mounting a copper wire (diameter approx. 100 µm) as a positive electrode and a copper mesh (hole and wire diameter approx. 100 µm) as a negative electrode on top of the substrate with scotch tape, with a distance between the (+) and (–) electrodes of approx. 3 mm, as schematically represented in Fig. 2d. The scotch tape was applied such that it did not allow a short-circuit between the electrodes. One hundred microliters sodium perchlorate ($NaClO_4$) in water (0.05 M) was added as an electrolyte solution, forming a thin electrolyte layer that ensured contact with both the (+) and (–) electrodes. The electrodes were connected via crocodile clips to a Keithley 2450 Sourcemeter power supply, and the current was set at 0.1 mA, resulting in a voltage of approx. 1 V.

Swelling and contraction pulses. To prepare the hydrogel for Cu^{2+} complexation, the hydrogel was rinsed with hydrochloric acid (HCl 1 M, 4× the same solution of 2 mL), water (5×), potassium hydroxide (KOH 0.1 M, 4× the same solution of 2 mL, repeated with a fresh solution of 2 mL), and water (5×). Subsequently, excess water was removed from the substrate with a tissue, 50 µL of a 0.8 M $CuSO_4$ solution was added, excess Cu^{2+} was removed by rinsing the substrate with water and excess water was removed with a tissue. To obtain the swelling/contraction pulse (Fig. 3b), 1 mL 1 M HCl was added. The stepwise addition of HCl solutions with increasing concentrations (Fig. 3c) was performed by adding volumes of 1 mL, with removal of excess HCl solution from the substrate prior to each subsequent addition.

Controlled progression of acid stimulus. Cu^{2+} was first complexed to the hydrogel as described above (swelling and contraction pulses). The substrate was then dried with a tissue, 4 µL water was applied, and the substrate was covered with a 10 × 16 mm^2 glass cover of 1 mm thickness. To initiate the HCl stimulus, a droplet of 30 µL 1 M HCl was added at the edge of the glass cover as schematically shown in Fig. 4a. The color transition progression speed v_C in µm s^{-1} was determined via the time it took the blue-to-colorless front to progress from left to right over the field of view (190 µm). Small-magnification optical microscopy images in Supplementary Fig. 5 reveal a fast progression of the HCl front over the first few millimeters, whereas further away from the edge of the glass cover the progression of the HCl front slows down, enabling variation of v_C for different experiments shown in Fig. 4 and Supplementary Fig. 6. Alternatively, a larger amount of water under the glass cover can be used to slow down the progression.

Spatial patterning of pulses and traveling waves. To obtain a localized Cu^{2+} complexation (Fig. 5), Cu^{2+} was electrochemically delivered via the same procedure as described above (electrochemical delivery of Cu^{2+}). Here, the experiments started with a substrate that was rinsed with hydrochloric acid (HCl 1 M, 4× the same solution of 2 mL), water (5×), potassium hydroxide (KOH 0.05 M, 4× the same solution of 2 mL, repeated with a fresh solution of 2 mL), and water (5×). Subsequently, the electrodes were removed, and the substrate was rinsed with water, dried with a tissue, and covered with 4 µL water and a glass cover (10 × 16 mm^2, 1 mm thick). Similarly to the procedure described above (Controlled progression of acid stimulus), a droplet of 30 µL 1 M HCl was added at the edge of the glass cover to initiate the Cu^{2+} release, as schematically shown in Fig. 5a.

Determining the concentration of Cu^{2+} complexed to gel. The concentration of Cu^{2+} complexed to the COO^- groups in the hydrogel was determined upon extraction of Cu^{2+} from the hydrogel with an ethylenediethylaminetetraacetate (EDTA) solution, as shown in Supplementary Fig. 7. By comparing the optical density of the extract solutions to a calibration line (based on absorption spectra of aqueous EDTA solutions (0.27 M, 1 M KOH) with different $CuSO_4$ concentrations), the total amount of Cu^{2+} ions was determined. For the hydrogel-microplate substrate, we obtained a total Cu^{2+}-amount of 0.0038 mmol. Based on the ratio between the area of the blue region in Supplementary Fig. 7b and the printed squares of the paper background (0.634 × 0.634 cm^2), the hydrogel area in the sample is estimated to be 1.30 cm^2. Based on the estimated thickness of the contracted hydrogel of 10 µm (Supplementary Fig. 1), the volume of the hydrogel is 0.00130 cm^3. Therefore, the Cu^{2+} concentration inside the contracted hydrogel is estimated to be 0.0038 mmol/0.00130 cm^3 = 2.9 M (Supplementary Fig. 7). The concentration of carboxylic acid groups in the hydrogel is estimated from the precursor solution, which was prepared from a solution of 0.4 mL acrylic acid + 0.5 mL ethylene glycol + 0.5 mL 1-butanol, and was subsequently mixed in a 9:1 ratio with the initiator solution, resulting in an acrylic acid concentration of 3.74 M. After the application of the hydrogel precursor, we assume that the solution wets the plates, with a height of 18 µm, as well as the glass cover applied on top of it. Densification of this precursor solution with a thickness of 18 µm to a hydrogel with a final thickness of 10 µm (see Supplementary Fig. 1) results in a final carboxylic acid concentration of 6.7 M. This indicates that after exposing to a concentrated $CuSO_4$ solution, the Cu^{2+} to COO^- complexation in the hydrogel approaches a 1:2 ratio ($Cu^{2+}/COO^-_{max} = 43\%$).

Data availability

The data that support the findings of this study are available within the article (and its Supplementary Information files) and from the corresponding authors on reasonable request.

Code availability

The computer code that was developed to perform the simulations with our model is freely available at Github: https://github.com/nadirkaplan/hydrogels_naturecomm.

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Author contributions

P.A.K., A.G. and J.A. conceived the research. P.A.K. and R.M.R. performed the experiments; C.N.K. developed the theoretical model; all authors analyzed the results; P.A.K., C.N.K., A.G. and J.A. wrote the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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