Amateur hobbyists are creating home-brew molecular-biology labs, but can they ferment a revolution?

Life hackers

BY HEIDI LEDFORD

Rob Carlson's path to becoming a biohacker began with a chance encounter on the train in 1996. Carlson, a physics PhD student at the time, was travelling to New York to find a journal article that wasn't available at his home institution, Princeton University in New Jersey. He found himself sitting next to an inquisitive elderly gentlemen. Carlson told him about his thesis research on the effects of physical forces on blood cells, and at the end of the journey, the stranger made him an offer. "You should come work for me," said the man, "I'm Dr Sydney Brenner." The name meant little to Carlson, who says he thought: "Yeah, OK. Whatever, 'Dr Sydney Brenner.'"

It wasn't until Carlson got back to Princeton and asked a friend that he realized that "Dr Sydney Brenner" was a famed biologist with a knack for transforming the field. He took the job.

Within a year, Carlson was working with a motley crew of biologists, physicists and engineers at Brenner's Molecular Sciences Institute (MSI) in Berkeley, California, learning molecular biology techniques as he went along. The institute was a hotbed of creativity, and reminded Carlson of the scruffy hacker ethos that had spurred the personal-computing revolution just 25 years earlier. He began to wonder if the same thing could happen for biotechnology. What if a new industry, even a new culture, could be created by giving everyone access to the high-tech tools that he had at his fingertips? Most equipment was already for sale on websites such as eBay.

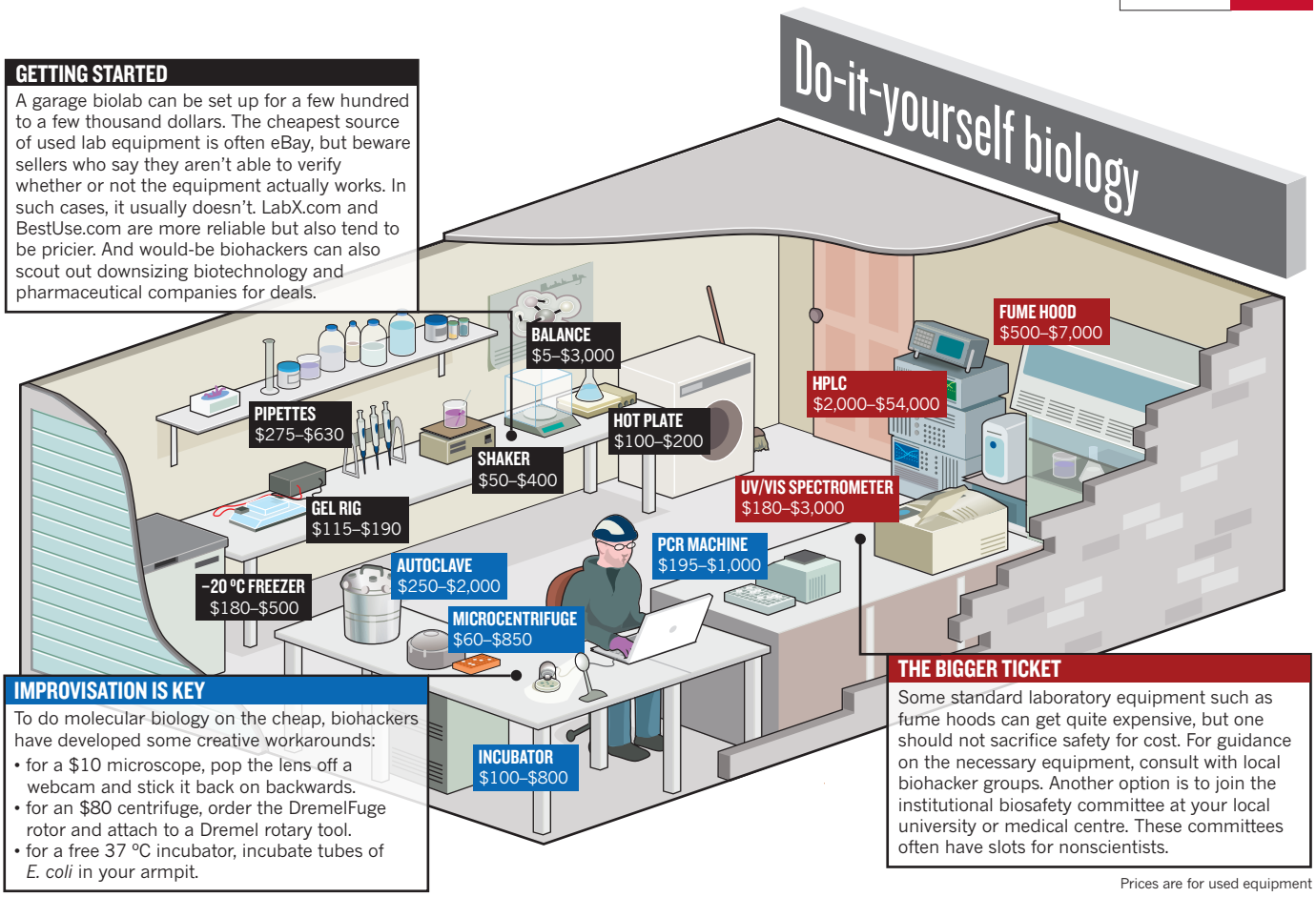
Carlson penned essays and articles that fanned the embers of the idea. "The era of garage biology is upon us," he wrote in a 2005 article in the technology magazine *Wired*. "Want to participate?" The democratization of science, he reasoned, would bring in new talent to build and improve scientific instrumentation, and maybe help to uncover new industrial applications for biotechnology. Eventually, he decided to follow his own advice, setting up a garage lab in 2005. "I made the prediction," he says, "so I figured maybe I should do the experiment."

Carlson is not alone. Would-be 'biohackers' around the world are setting up labs in their garages, closets and kitchens — from professional scientists keeping a side project at home to individuals who have never used a pipette before. They buy used lab equipment online, convert webcams into US$10 microscopes and incubate tubes of genetically engineered *Escherichia coli* in their armpits. (It's cheaper than shelling out $100 or more on a 37 °C incubator.) Some share protocols and ideas in open forums. Others prefer to keep their labs under wraps, concerned that authorities will take one look at the gear in their garages and label them as bioterrorists.

For now, most members of the do-it-yourself, or DIY, biology community are hobbyists, rigging up cheap equipment and tackling projects that — although not exactly pushing the boundaries of molecular biology — are creative proof of the hacker principle. Meredith Patterson, a computer programmer based in San Francisco, California, whom some call the 'doyenne of DIYbio', made glow-in-the-dark yogurt by engineering the bacteria within to produce a fluorescent protein. Others hope to learn more about themselves: a group called DIYgenomics has banded together to analyse their genomes, and even conduct and participate in small clinical trials. For those who aspire to change the world, improving biofuel development is a popular draw. And several groups are focused on making standard instruments — such as PCR machines, which amplify segments of DNA — cheaper and easier to use outside the confines of a laboratory, ultimately promising to make DIYbio more accessible.

"We're making $10 microscopes and the discussion around us is about weaponized anthrax."

Many traditional scientists are circumspect. "I think there's been a lot of overhyped and enthusiastic writing about this," says Christopher Kelty, an anthropologist at the University of California, Los Angeles, who has followed the field. "Things are very much at the beginning stages." Critics of DIY biology are also



Prices are for used equipment

dubious about whether there is an extensive market for garage molecular biology. No one needs a PCR machine at home, and the accoutrements to biological research are expensive, even if their prices fall daily (see graphic). Then again, the same was said about personal computers, says George Church, a geneticist at Harvard Medical School in Boston, Massachusetts. As a schoolboy, he says, he saw his first computer and fell in love. "Everybody looked at me like, 'Why on earth would you even want to have one of those?'"

Carlson started his garage lab as something of a hobby, but he needed to do it without sapping resources from his lab at the University of Washington in Seattle. He bought equipment such as refurbished micropipettes — a staple in any molecular biology lab — and a used centrifuge on eBay. In 2007, fed up with grant applications and eager to spend more time working in his garage lab, he gave up his position at the university altogether.

Carlson decided to follow up on work at the MSI. There, he had been part of a team developing a way to quantify small amounts of proteins in single cells using 'tadpoles', in which a protein 'head' is attached to a DNA 'tail'. The head was designed to bind to a protein of interest, and the DNA tail could be amplified and quantified by PCR, allowing researchers to calculate the number of proteins present (see *Nature Meth.* **2**, 31–37; 2005). The tadpoles have economic potential, providing an alternative to the standard approach of using fluorescently tagged antibodies, which provide at best only rough estimates of protein levels. But the original formulation was too expensive to commercialize, says Carlson. "If I could use this protein in the garage in a simple way to show that it would work, then hopefully it would be a product that would be useful in a low-tech setting, out in the field or in a doctor's office," he says.

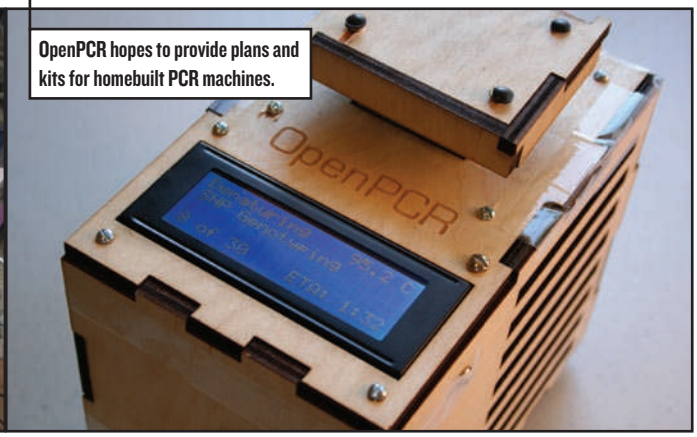
As Carlson worked, the idea of garage biohacking was taking off. In May 2008, Jason Bobe, director of community outreach for the Personal Genome Project at Harvard Medical School, and Mackenzie Cowell, a web developer in Cambridge, Massachusetts, organized the first meeting of DIYbio at the Asgard Irish pub, up the road from the Massachusetts Institute of Technology. About 25 people turned up. Two years later, there are more than 2,000 subscribers on the DIYbio e-mail list.

No one knows how many of those 2,000 are serious practitioners — Bobe jokes that 30% are spammers and the other 70% are law-enforcement officials keeping tabs on the community. But many DIY communities are coalescing: not only in Cambridge, but also in New York, San Francisco, London, Paris and the Netherlands. Some of these aim to develop community lab spaces with equipment that users could share for a monthly fee. And several are already affiliated with local 'hacker spaces', which provide such services to electronics enthusiasts. For example, the New York DIYbio group meets every week at the work-space of an electronics-hacker collective called NYC Resistor, which now has a few pieces of basic molecular biology equipment, including a PCR machine.

DIYbio is an offshoot of the open-science movement, which encourages an open exchange of materials, data and publications and has its origins in the push for open-source software in the 1990s, says Kelty. Many biohackers are also keen to tackle projects that involve engineering cells by piecing together new genetic circuits, an approach often called 'synthetic biology'. DIYbio has picked up both momentum and stigma from this field, which has been alternately hyped and decried as the solution to society's ills or the nursery for a bioterrorist scourge. The thought of hundreds of biohackers creating pathogens in unmonitored garage biology labs set off alarm bells, and in 2009, the Federal Bureau of Investigation (FBI) began sending representatives from its directorate for weapons of mass destruction to DIYbio conferences.

Biohackers are wary. They recall what happened to Steve Kurtz, an artist who was using bacteria shipped to him by a Pittsburgh geneticist. In 2004, federal agents stormed his house in hazmat suits with guns drawn. Kurtz was arrested and saddled with mail-fraud charges


Rob Carlson in his chilly garage biolab in 2005.



OpenPCR hopes to provide plans and kits for homebuilt PCR machines.

S. KELLER (LEFT); J. PERFETTO (RIGHT)

that took him four years to clear. Bobe has interacted with and advised the FBI, but says he finds many of the biosecurity fears of the FBI and the public to be unfounded. "The amateur activity right now is at the seventh- or eighth-grade level," he says. "We're making $10 microscopes and all of the discussion around us is about weaponized anthrax. Sure we're concerned about that just like everybody else, but I don't know what to say except 'Yeah, that sounds scary as hell. Let's be sure nobody does that.'"

The FBI seems to have taken that message on board, and has adopted what some call a 'neighbourhood watch' stance. The approach relies on biohackers monitoring their own community and reporting behaviour they find threatening, says Edward You, a special agent in the FBI's bioterrorism unit.

Carlson's projects are more advanced than those of the average DIYbio hobbyist, and he has found that the garage-hacker ethos eventually suffered. He says he sometimes found it hard to persuade companies to deliver lab supplies to a residential address. Carlson also wanted his garage back to restore a boat.

So, Carlson and his business partner, engineer Rik Wehbring, moved their lab out of the garage and into a small commercial space in 2009. The two fund the space and their experiments through a small consulting firm called Biodesic. Through the firm, they have advised companies on a range of technology issues from biosecurity to designing brainwave-based game controllers.

Other biohackers have also come up with creative ways to fund their projects. Several have used websites such as Kickstarter, which allows inventors to post their projects and funding targets online. Visitors to the site make donations, usually small ones, but the hope is that enough visitors making tiny contributions will add up. Two California garage biohackers, Tito Jankowski and Josh Perfetto, used Kickstarter to fund the development of a small, low-cost PCR machine known as OpenPCR. They reached their fundraising goal of $6,000 in ten days. By the time their Kickstarter listing closed 20 days later, they had doubled that figure. Another group of biohackers used Kickstarter to raise funds for a hackerspace called BioCurious, based in Silicon Valley, California. They raised more than $35,000.

But all of this is tiny compared to the cost of launching an actual business. Joseph Jackson, a self-proclaimed "professional entrepreneur-slash-activist" from Mountain View, California, and Guido Nunez-Mujica, a computational biologist from Venezuela, have teamed up with other hackers to build a portable PCR machine known as LavaAmp, which can be run from a computer's USB port. The team has poured tens of thousands of dollars into the project, says Jackson, but will need closer to $100,000 to achieve its goal of producing PCR machines that could be used by hobbyists, teachers and by researchers in developing countries.

Jim Collins, a synthetic biologist at Boston University, says that the costs of doing molecular-biology research make the comparison between amateur biologists and the hackers who drove the personal-computer revolution inappropriate. There's a vast chasm between these tinkerers and those with access to a traditional lab. Faculty members, Collins says, typically ask for hundreds of thousands of dollars from a university to start a molecular-biology lab. Smart amateurs might be able to bring fresh perspective, he says, but they face an uphill battle. "I'm not saying you need to be appropriately pedigreed. I'm saying you need to be appropriately resourced."

Carlson says that the cost of biological research is decreasing. "The predominant thought about biology used to be that it was expensive and hard," he says. "And it's still hard. It's just not so expensive." In 2003, he projected the falling costs of sequencing and synthesis of DNA and proteins, and the accelerating pace of research into areas such as protein structure determination (R. Carlson *Biosecur. Bioterror.* **1,** 1–12; 2003). His predictions echo Moore's law of computing, and some have dubbed them the 'Carlson curves'.

But the curve trajectory isn't as steep as Carlson might like. He has redesigned the protein heads of his tadpoles, and decided early on that instead of producing the protein himself — an expensive and arduous process — he would pay a company to make it for him. He could either buy cheap protein that was contaminated with other proteins, for about $3,000, or buy clean protein for about $50,000. "There was nothing in between," he said. He took the cheap route, but found that the batches he received weren't clean enough to publish his results or start selling the finished tadpoles. The project stalled.

A few months ago, Carlson realized that more protein-synthesis companies had entered the scene, including several that filled the middle range pricing gap. He ordered a fresh batch of protein that was supposed to arrive more than a month ago, but still hasn't been delivered. "If we had a million dollars in the bank, this problem would have been solved a long time ago," he says. "And if I had an experienced biochemist or molecular biologist at the bench for a year or two it probably would have cost the same and would have been done faster."

> "I'm not saying you need to be appropriately pedigreed, just appropriately resourced."

Still, five years after taking science into his garage, Carlson says he's convinced that biohacking has the potential to trigger a technological revolution. "We're going to see a lot more at the garage level that will produce a variety of products in the marketplace, one way or another," he says.

Once his tadpoles have been optimized, Carlson hopes that publishing his work will attract further investors. Meanwhile, he feels his experiment in garage-based innovation has so far been a success, despite the delays and personal sacrifices. "Part of the exercise was to determine whether or not we could bootstrap this thing," he says. "The answer appears to be 'yes'. As long as you are willing to be patient and to eat nothing but rice for dinner occasionally." ■ SEE EDITORIAL P.634

Heidi Ledford *writes for* Nature *from Cambridge, Massachusetts.*