sponge (like a kitchen sponge) in a reactor to culture, for the first time, a deep-sea archaeon from the eukaryote-like clade known as Asgard archaea[9].

For hints as to where to start, researchers can check the BacDive database, which lists characteristics and culture conditions for more than 80,000 cultured strains from 34 bacterial and 3 archaeal phyla. Genomic information, when available, can also provide clues, says Christian Jogler, a microbiologist at Friedrich Schiller University Jena in Germany.

But even pedestrian concerns can make a difference, Jogler warns. Rather than relying on ultrapure water-purification systems, such as Milli-Q, that many labs use, Jogler's group makes its own pure water by distilling it, twice. Milli-Q water can contain chemicals that block the growth of some cultures, he says. Plus, Jogler adds, the agar commonly used as a gelling agent might inhibit growth, so he sometimes tries alternatives such as gellan gum.

Even the way that the agar is prepared can be important, Kamagata's group has found. When agar is heat-sterilized together with phosphates, it produces hydrogen peroxide that prevents some microbes from growing. Autoclaving the components separately eliminates the problem, and has allowed the team to grow previously uncultivated microbes[10].

Patience is key. It took Kamagata and his colleagues more than 12 years to grow their archaeon, tentatively christened '*Prometheoarchaeum syntrophicum*'. But once microbiologists obtain the first culture of a new organism, that microbe usually grows faster.

Epstein calls the process domestication. He suggests that during the first, sluggish growth cycle, some microbes alter their epigenome – the molecular markers on DNA that control gene expression – to adapt to lab conditions. Then, they grow faster.

Earth and sky

Now, Epstein is developing technology to isolate and cultivate new microbes entirely *in situ*.

He calls the devices Gullivers, in honour of the adventurer in Jonathan Swift's 1726 book *Gulliver's Travels*. Gullivers are little boxes filled with sterile gel, with a semipermeable-membrane surface, like that of the ichip, to allow nutrients and signals to diffuse in. A single pore, one micrometre across, allows an individual microbe to enter from the environment. That microbe should plug the entryway, but its descendants could populate the gel inside the box, forming a colony.

Eventually, Epstein says, it might be possible to get results from a Gulliver without opening or even retrieving it. Nanosensors could collect and send back data on oxygen or carbon dioxide levels, or the production of signalling compounds or antibiotics, he imagines. After dropping the device into, say, the depths of the Arctic Ocean, researchers could simply go on holiday and wait for results to pour in, he jokes.

In the coming months, Epstein plans to test Gullivers at Mount Erebus, an active Antarctic volcano. But his ultimate goal is beyond Earth, deploying the devices on potentially life-hosting bodies such as Mars or Jupiter's moon, Europa.

Time will tell whether microbes exist in such places. In the meantime, there's plenty of microbial diversity on Earth to keep researchers busy. With the right techniques, says Raoult, it should be possible to domesticate and study any microorganism – eventually.

"Unculturable", he sniffs, "is an insult to the future."

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1. Lagier, J.-C. *et al. Nature Rev. Microbiol.* **16**, 540–550 (2018).
2. Ngom, I. I. *et al. New Microbes New Infect.* **33**, 100624 (2020).
3. Yimagou, E. K. *et al. New Microbes New Infect.* **32**, 100606 (2019).
4. Berdy, B., Spoering, A. L., Ling, L. L. & Epstein, S. S. *Nature Protoc.* **12**, 2232–2242 (2017).
5. Rheims, H., Rainey, F. A. & Stackebrandt, E. J. *Indust. Microbiol.* **17**, 159–169 (1996).
6. He, X. *et al. Proc. Natl Acad. Sci. USA* **112**, 244–249 (2015).
7. Cross, K. L. *et al. Nature Biotechnol.* **37**, 1314–1321 (2019).
8. Gich, F., Janys, M. A., König, M. & Overmann, J. *Environ. Microbiol.* **14**, 2984–2997 (2012).
9. Imachi, H. *et al. Nature* **577**, 519–525 (2020).
10. Tanaka, T. *et al. Appl. Environ. Microbiol.* **80**, 7659–7666 (2014).

CHLOE COLLYER/BLOOMBERG/GETTY

Alexa-powered tools allow researchers to quickly access laboratory-specific information.

VOICE-ACTIVATED ASSISTANTS COME TO THE LAB

The research-optimized tools enable hands-free note-taking, reminders, instrument control and more. **By Jeffrey M. Perkel**

Funsho Fakuade has spent a lot of time in the dark. As a PhD student studying ion channels and cardiac arrhythmias at Georg August University in Göttingen, Germany, his work typically involves measuring the electrical output and fluorescence intensity of cells under a microscope. But because such measurements must be made in darkness, he needed to document his experiments in the dim glow of a computer monitor. Often, he wrote nothing at all.

"I had to prioritize the information I wrote," Fakuade says. "It's one thing to be looking at the screen to look at [cellular] changes, and another thing to be trying to strain your eyes to write something down."

Then, in early 2019, team members from Berlin-based company LabTwin visited the university, looking for researchers to test-drive its voice-based note-taking system. Fakuade volunteered.

"Sometimes you do these experiments for weeks," he says. "That's when you find it difficult to remember all the stuff that you've been doing. LabTwin helped me with that."

Voice-activated electronic assistants such as Apple's Siri and Amazon's Alexa are wildly popular in the consumer market. Now a handful of tools is bringing this technology to research laboratories as well.

LabTwin's offering — which is free for academics — operates on iOS and Android devices. "We want to bring scientists closer to their data," says Guru Singh, head of growth at the company. Researchers keep a headset on and their mobile device nearby. To activate the software, they say the 'wake word' — avocado, blueberry or dragonfly — and the software begins recording and transcribing what they say. The system can also dictate protocols, log completed steps, set timers and reminders, and more. "The way I describe it is, imagine Siri with a PhD," says Magdalena Paluch, LabTwin co-founder and chief executive.

Ernesto Díaz-Flores, who studies childhood leukaemias at the University of California, San Francisco, says LabTwin's software makes it easy to move from bench to bench without a lab notebook. "I can use it whenever I need it."

Several Alexa-powered tools have also hit the lab bench. One such tool, myNEB, from New England Biolabs in Ipswich, Massachusetts, offers quick access to the company's enzyme product information through an Alexa device. The firm that built myNEB, HelixAI, based in Rome, Georgia, also has its own Alexa-enabled platform, which labs can use to build 'private skills' to access laboratory-specific information, such as protocols and inventory, according to James Rhodes, who co-founded the company along with his wife, microbiologist DeLacy Rhodes. The system is currently in beta testing for use with corporate clients; an academic version is anticipated later this year.

"Not having to take off gloves or eye protection to go back over and look at something is certainly convenient."

Thermo Fisher Scientific in Waltham, Massachusetts, has incorporated Alexa software into two models of its Applied Biosystems QuantStudio Pro Real-Time PCR System (6 and 7), which are high-throughput instruments for quantifying nucleic acids.

Such voice-controlled tools allow researchers to work hands-free — particularly useful when working in a fume cupboard or handling sensitive samples. "Not having to take off gloves or eye protection to go back over and look at something is certainly a convenient time saver," says Jason Furrer, a microbiologist at the University of Missouri School of Medicine in Columbia, who uses myNEB to double-check his enzymatic protocols at the bench. The ability to set timers and play podcasts is useful, too, he adds.

According to Santhosh Nair, who leads Thermo Fisher's qPCR instrument business, QuantStudio Pro currently supports ten voice commands, with more in development. Among the most popular, he says, is 'change block', which reduces a complex procedure to a single command. "This was a huge delight for our current users," he says.

Developers admit that researchers have been slow to embrace voice activation, despite the popularity of their consumer-market counterparts. But they're coming around.

"Voice activation in the lab will come, it's just a matter of when," says Penny Devoe, product marketing manager for DNA-cloning products at NEB. "Hopefully, we will be right there when people are ready to make that leap."

Jeffrey M. Perkel is technology editor for *Nature*.