The Economist

How to back up a country

Hacking your brain

Space hoppers in orbit

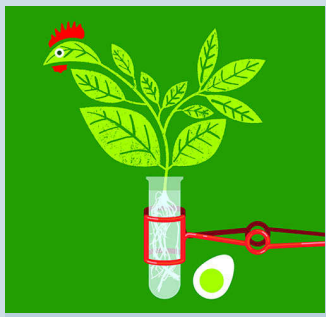
Technology Quarterly

March 7th 2015

Green food from Silicon Valley

Tech firms start cooking up sustainable produce

Contents



On the cover
Silicon Valley-funded startups are moving into the sustainable food business. Their idea is to disrupt the industry by using plant protein to mimic meat and dairy products—and provide a taste which is as good, if not better than, animal-derived produce, page 11

How to back up a country

Internet security: To protect itself from attack, Estonia is finding ways to back up its data

WIPING a country off the map is one thing. Wiping its data is another. Estonians know what the former is like. They are determined to avoid the latter. Just as computer users back up their laptops in case they break or are lost, Estonia is working out how to back up the country, in case it is attacked by Russia.

Estonia has already shown notable prowess in putting government services online. It has pioneered the use of strong digital identities for every resident, enabling them to sign and encrypt documents, access government services, and conduct e-commerce.

But the latest project, termed "digital continuity", is the most ambitious yet. It aims to ensure that even if Estonia's government is sabotaged it will continue to function over the internet, providing services and enabling payments. The lessons will be valuable to any organisation concerned about disaster recovery.

Estonia, which regained independence in 1991 after being occupied by the Soviet Union, was the target of what many regard as the first instance of cyber-warfare. In 2007 its main websites were overwhelmed with traffic from multiple sources in a distributed denial of service attack during a row with Russia over a war memorial. The episode crippled the country's online banking system and came within a whisker of disabling emergency services. Lately Russian airspace intrusions and propaganda attacks are a constant headache.

Estonia's first dry run of digital continuity, carried out in September last year in conjunction with Microsoft, had several elements. One was to maintain e-government services by using back-up computers within Estonia. If that became impossible, the services migrated abroad.

One part of the experiment involved the website of the president, Toomas Hendrik Ilves. A digital-savvy, American-educated advocate for e-government—and a hate figure for the Kremlin—his website is a likely target for Russian attack. During the war in Georgia in 2008, unknown hackers defaced the website of that country's president, Mikheil Saakashvili. Mr Ilves's website was moved fairly smoothly to the "cloud"—networks of third-party computers—in this case Microsoft data centres in Dublin and Amsterdam.

The load and the stress

A more complicated effort involved the State Gazette—the official repository of all Estonian laws. These do not exist in paper form. As well as backing up the data, the experiment tried to see how accessible it would be in an emergency. It applied two tests: one of load (if an unusually large number of people were trying to access the sites); and the other of stress (if outsiders were, for instance, swamping the system with bogus requests for information). ▸▸

The result was broadly a success—the experimenters even succeeded, for a brief planned period, to run services from outside Estonia. But it also highlighted numerous obstacles. "It became clear that no matter how ready you think you are, you are never ready enough," notes a draft report jointly compiled by the Estonian authorities and Microsoft.

One set of issues is legal. Laws on personal data, and public expectations of privacy, are strict in European countries; just as with back-up services for computers, users need to be sure that their data will be properly safeguarded if they are sent abroad. Storing such personal information in "digital embassies"—computers in Estonian diplomatic missions abroad—helps as they are Estonian sovereign territory. But internet law is still unclear.

Technical problems included the way the internet deals with addresses—the Domain Name System (DNS). How would the Estonian authorities ensure that people trying to reach president.ee, for example, would actually get there in an emergency—particularly if a massive cyber-attack were under way? Sorting this out required "extensive manual operations", the report notes dryly.

Digital continuity would become even trickier if the back-up operation were to include more complex services. Estonia's public and private databases exchange information over a peer-to-peer network called the X-Road, a kind of information federation. Users give their digital consent, by using their ID card and PIN, to allow one database to get information from another (for example, if a hospital needs to check a patient's status with a health insurer). So it is not just the data, but also the software that deals with them, that would need to be exported.

The experiment's designers soon spotted several snags. One was that Estonia's system uses lots of different software, in multiple versions, some of them out of date. That works fine when they just need to exchange data, but makes it hard to replicate the system in the cloud.

Another was that the architecture of Estonia's system is poorly documented, and that rules for classification of data as sensitive, personal, secret or public were not suitable for digital continuity: "frequently only a small number of experts understand the workings of the system," the report notes.

The main conclusion of the exercise is both simple to articulate and difficult to achieve: the better data and networks are organised, the better the system is documented, and the more standardised and up-to-date the software, the easier it is to back up and restore. That may be no surprise to any computer user, but it will be a spur to improvement on top of Estonia's already impressive efforts. ■

DIY telecoms

Mobile networks: Fed up with the failings of the big operators, remote Mexican communities are acting for themselves

IN THE cloud forests of the Sierra de Juárez mountains in southern Mexico, a new kind of tree is springing up: the mobile telephone mast. Unlike most phone masts in the world these are installed, owned and operated by small, mostly indigenous communities. Providing a mobile service in these villages was not profitable enough for big telecoms companies to bother with, unless the locals stumped up $50,000. But improvements in software and the falling price of hardware has made it possible to build a local mobile-phone base station for around $7,500, which non-profit operators and small communities can muster.

Sixteen communities in this remote corner of Mexico now count on local mobile services which cost much less than that of Mexico's dominant operator, América Móvil, or its nearest rival, Movistar. Eliel López, a motorcycle-taxi driver, says the business he gets using the community-owned network in Villa Talea de Castro in the state of Oaxaca more than pays his monthly fee of 40 pesos ($2.71), which covers local calls, and per-minute call costs of 0.82 pesos to mobiles on other networks in Mexico. The big networks charge around 3 pesos a minute.

Calls to mobiles on other networks can be dialled using pre-paid credit. But ringing someone in the United States might actually be cheaper. This is thanks to a series of repeater antennae scattered through the mountains and providing a connection to Oaxaca city, the state capital. It allows voice-over-internet calls.

Local networking

The cost of mobile equipment is falling thanks to open-source systems and a new generation of base stations that make use of a process called software-defined radio. As its name suggests, this uses software to manage the network instead of lots of dedicated hardware. Such kit is now available to groups such as Rhizomatica, a non-profit operating from the state capital. Peter Bloom, its founder, has been installing the equipment aided by a bevy of Italian, Spanish and other engineers.

They have been able to do this because Mexico's constitution gives indigenous community radio stations the right to use radio spectrum in places neglected by national concession-holders. Rhizomatica teamed up with a lawyer to persuade regulators that the principle also applies to wireless telephony. "Communication is an essential human right," says Mr Bloom. In the spring of 2014 the national telecom regulator awarded Rhizomatica a two-year experimental, non-profit licence to operate in the region. It also helps that this area of Oaxaca has long governed itself under Mexico's so-called indigenous customary practices, which include communal land and labour-sharing.

Now that Rhizomatica's network is sprouting new nodes, the communities are encountering some of the same difficulties faced by larger operations, such as people from one local network wanting to use their mobiles in another area. The local networks do not use SIM cards to identify users, who must register their phones with the local network's administrator. When someone registered in one community visits another they can automatically use the network there, too. At present they are not charged, but roaming fees could be introduced.

In December Mexico's regulator issued a plan to reserve some of the radio spectrum for indigenous and community use under 15-year non-profit licences. This could encourage more communities to set up their own mobile services. But the non-profit requirement might dissuade outside investors from putting money into such schemes, making it difficult for them to scale up.

In some countries community-based networks form partnerships with incumbent telecoms firms to provide services at a profit. Endaga, an American firm spun out of the University of California, Berkeley, set up such a network in Indonesia in 2013. In Mexico a similar partnership would probably require a change in the rules. As is often the case, technology moves faster than regulators. ■

Smartphone diagnosis

Medical apps: From exposure to HIV to a nasty throat infection or confirmation of a heart attack, the phone will know

BY SOME accounts, one in five Americans use health apps on their smartphones. The apps can also connect to sensors worn on the body to monitor vital signs, such as a runner's heart rate. Others assist with diagnostics, for instance by using the phone's camera to analyse the colour of test strips dipped in samples. Plug-in devices are also appearing to enable phones to take biological measurements directly. Two of the latest can detect exposure to HIV, the virus which causes AIDS, and diagnose other conditions.

Samuel Sia and his colleagues at Columbia University in New York have miniaturised a laboratory-based blood test called an ELISA (for enzyme-linked immunosorbent assay). It detects biological markers, such as antibodies made in response to an infection. A sample of blood from a finger prick is placed in a small disposable plastic cassette that contains reagents necessary for an ELISA. The cassette is inserted into the test-device itself, which is small enough to fit into the hand of the user and contains what is known as a "lab-on-a-chip". This, in turn, is plugged into the phone. An app manages the test and after 15 minutes a negative or positive result is displayed on the phone's screen.

The equipment was recently tried out by health-care workers in Rwanda testing pregnant women, from a single sample of blood, for HIV and syphilis. The results were encouraging and the team are now exploring how to bring their smartphone test to market. Dr Sia says he estimates the device itself would cost about $35 to manufacture. An ELISA machine in a laboratory could cost more than $18,000.

The other idea is from Descue Medical, a Salt Lake City-based startup founded by two brothers, Christopher and Andrew Pagels. They have come up with a product called iTest. The pair, both biomedical-engineering students, hope to have their first test-kit on sale in 2016 after obtaining clearance from America's Food and Drug Administration. It can diagnose "strep throat", a nasty infection by *Streptococcus*

Rounding up oil slicks

Pollution: a quick way to contain oil spills with lightweight booms

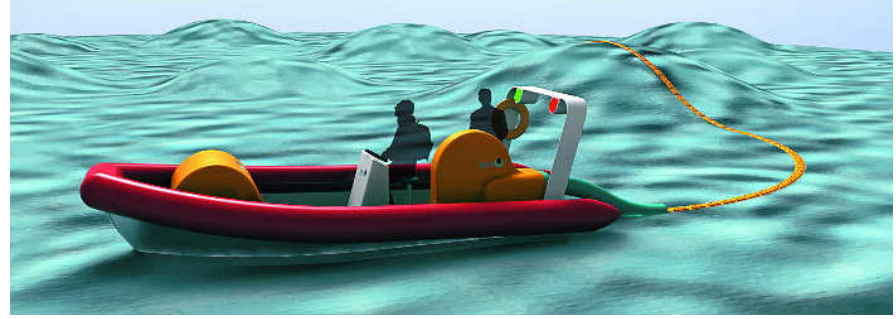
SINCE the disaster in the Gulf of Mexico in 2010 after the Deepwater Horizon drilling rig exploded, there has been a flurry of ideas on how to clear up oil spills. Various machines called "skimmers" have been developed to recover oil from the surface. New chemical methods have been tried to disperse oil and biological ones to digest it. An Italian project even found that coarse wool is particularly good at mopping up oil. But much depends on how quickly an oil slick can be prevented from spreading with floating booms. Now an Israeli startup reckons it has come up with the quickest way to do that.

There are a wide variety of booms which can be used as a physical barrier to contain an oil spill. The booms can be made of plastic, metal and other materials. They typically consist of a solid or inflatable floating section with a "skirt" hanging below and weighed down with a chain. Such booms are bulky and heavy. They also have to be transported by boat or barge to the site of the spill, where a specialist crew is required to launch the boom into the water. All this takes time—sometimes days—which gives oil a chance to spread further and break up into smaller slicks, making the eventual clean-up harder.

The idea which Boaz Ur, the chief executive of HARBO Technologies, and his colleagues came up with is an extremely lightweight plastic boom which can be deployed rapidly from a small craft. It is so compact that an experimental version was delivered in a suitcase to Ohmsett, America's testing facility for oil-spill response equipment in New Jersey. The booms tested there usually arrive in shipping containers.

A lightweight boom can be easily upset by wind and waves, allowing oil to spill over the top or seep out from below. The HARBO system overcomes this in a number of clever ways. As it is deployed the top is filled with air for flotation while the bottom is filled with water for ballast. To prevent the boom tipping over its cross section is T-shaped. The wings on each arm of the T are designed in such a way to provide stability in winds, currents and waves. In the trials at Ohmsett a 30-metre-long prototype boom managed to successfully contain around three tonnes of oil.

The company is now developing a way to deploy the boom rapidly. As the boom weighs just 300 grammes a metre, the operation could be carried out by a small boat with just two operators (as illustrated below). Mr Ur says it would take no more than a day to train the crew. As both the boom and the vessel are small and lightweight, the complete system could be installed close to where oil spills are likely, such as ports, and carried on oil rigs and tankers. Being near to hand, a rapid-response boom team might prevent an oil spill from becoming a nightmare to clean up.



pyogenes, a bacterium. The condition needs treatment with antibiotics. It is most common in children and young teenagers and can cause complications, such as inflamed kidneys and rheumatic fever.

Their kit includes a swab that is rubbed against an infected patch of throat. This is placed into a vial containing a liquid, which washes the sample into solution. The vial is then fitted into the iTest device, which in turn is plugged into a phone. The brothers say the device uses a technique called voltammetry, which measures the current in a sample as a function of the voltage applied to it. Rapid strep tests are not new, but usually involve mixing solutions and looking for a visible reaction.

The strep test, though, is only the beginning of the brothers' ambitions. The idea is to offer a variety of different test kits that can be used by the same iTest device to diagnose a range of conditions, says Andrew Pagels. The brothers say they have already developed tests for HIV and MRSA, a bacterial infection which is particularly difficult to treat, and are working on tests for the flu, sexually transmitted diseases and a combination test for dengue fever and malaria. Another test would allow a smartphone to detect troponin. Elevated levels of this protein in the blood can verify that someone has had a heart attack. The brothers anticipate the main iTest device would sell for about $150 with the test kits available separately.

By offering lab-type diagnostics to almost any population with access to a smartphone, such devices would be particularly useful in remote and resource-poor areas. But they are bound to give hypochondriacs yet another reason to fiddle with their handsets. ■

Ebola's low-down on high tech

Disease control: Advanced equipment has been developed to help protect health-care workers, but the gear may not be helpful in poor countries

DELIRIOUS and occasionally thrashing around, an Ebola patient wracked with acute symptoms may shed as much as ten litres a day of highly infectious blood and other body fluids, faeces and decomposing tissue. It makes caring for patients suffering from this dreadful disease difficult and dangerous—so much so that some health-care workers quit their jobs rather than face another stressful day. As in all Ebola episodes, preventing infection in west Africa during what has been the worst outbreak in history has placed a lot of effort on looking after those dealing with the victims. New high-tech equipment is now available for use by health-care workers, but in some countries it may be inappropriate.

The Ebola virus is spread by direct contact, which can be through the tiniest piece of broken skin or via mucous membranes in, for instance, the eyes, nose or mouth. The source can be contaminated blood or other body materials and objects like needles and syringes. Protective equipment is needed. But when Nichodemus Gebe, head of biomedical engineering at Ghana's Ministry of Health, started looking for specialist gear he was unable to find any easily transportable treatment units able to contain the virus. In July last year he asked Odulair, an American company based in Cheyenne, Wyoming, if they could help. The firm makes mobile medical clinics.

Two months later Odulair put a modular Ebola-isolation unit on the market. The firm says it can be manufactured, air-freighted and set up within a month. The unit maintains a differential air pressure between rooms to help prevent the virus from spreading; although not an airborne disease it can attach to particles which drift in the air. A higher pressure is maintained in areas reserved for medical staff and those awaiting diagnosis. The air in each room is purified up to 36 times an hour with filters that trap almost all particles larger than a third of a micron, or three millionths of a metre, which is smaller than the Ebola virus. Air is also zapped with germ-killing ultraviolet light.

The video doctor

The doors in the unit can open automatically, allowing a "telepresence" robot to patrol. It displays live video of a doctor or nurse, allowing them to speak to a patient. The RP-VITA, as the robot is called, greatly reduces the number of times staff must put on protective suits and step inside, says Anita Chambers, Odulair's boss.

All fluid and solid waste, including things like needles and mattresses, is fed into a cylindrical chamber housed in a shipping container. This grinds it up with a macerator and then cooks it with scalding steam under high pressure until all that is left is a sterile greyish powder. Odulair's isolation unit also incorporates a fogging system that sterilises unoccupied rooms with hydrogen-peroxide vapour. Some hospitals disinfect rooms with remote-controlled machines, such as the Q-10 made by Bioquell, a British manufacturer, or a robot produced by Xenex Disinfection Services in Texas, which can sterilise a room in ten minutes.

Last autumn the UN Office for Project Services in Abidjan, Ivory Coast, suggested some governments in Africa might invest in such kit. But only two Odulair isolation units have been sold. Neither was for Africa or even a country that has an Ebola patient. One unit was delivered to a contractor working for America's Department of Homeland Security and the other will soon be sent to Trinidad and Tobago. For poor countries such equipment is unaffordable, says Ghana's Dr Gebe. An Odulair unit to house ten confirmed and eight suspected patients costs about $900,000—robot not included. A Q-10 comes in at around $53,000 and a Xenex robot at some $100,000.

Cost is not the only reason high-tech solutions are failing to be deployed in ▸▸

Ebola hotspots. Repairing and servicing mechanical and electronic systems is tricky. Sharp metal parts and tools can slice through protective clothing and into skin, increasing infection risks. Local staff, unfamiliar with such technology, are sometimes less keen to maintain it, says Agnès Lamaure, a logistics expert with Médecins Sans Frontières (MSF), a French charity which has led much of the international response to Ebola.

Another difficulty is that Ebola field clinics typically must generate their own electricity. Assessing the value of a system or device therefore involves taking into account not just its cost, but also the precious power it will consume, Ms Lamaure adds. The most practical way to vaporise disinfectants at Ebola centres in Africa is with hand-pumped sprayers typically used for garden pesticides. And rather than import a machine to destroy infected material, which could cost $300,000, Ebola centres burn their waste in pits which are sealed and covered in concrete.

On with the scrubs

Nevertheless, some new technology is helping in west Africa, where the number of cases has fallen, but the disease is hanging on. The bible on stopping transmission in poor countries was for many years a 1998 report by the World Health Organisation and America's Centres for Disease Control and Prevention (CDC) entitled "Infection Control for Viral Haemorrhagic Fevers in the African Health Care Setting". It enshrined a "sort of lowest common denominator" realism based on what was widely available rather than most appropriate, says Armand Sprecher, an MSF epidemiologist. It helped to establish surgical garb as the thing to wear.

But clothing designed for operating theatres is not the best for, say, collecting corpses lying in infectious body fluids. Aprons and surgical gowns leave the wearer's back mostly unprotected so, when squatting to lift a body, material on their boots is likely to wet the cotton surgical scrubs on their buttocks and thighs. "That's an uncomfortable feeling," says Dr Sprecher. He began working on Ebola outbreaks with MSF in 2000 several years before coveralls made with a DuPont synthetic fibre called Tyvek became widely available.

Tyvek is produced from high-density polyethylene fibres. These are not woven, as most fabrics are, but "flashspun" in a process which involves the evaporation of a solvent. Although tear-resistant and waterproof, Tyvek does allow air molecules under high pressure to pass through. This has now led to the wide adoption of a more impermeable laminated DuPont fabric called Tychem.

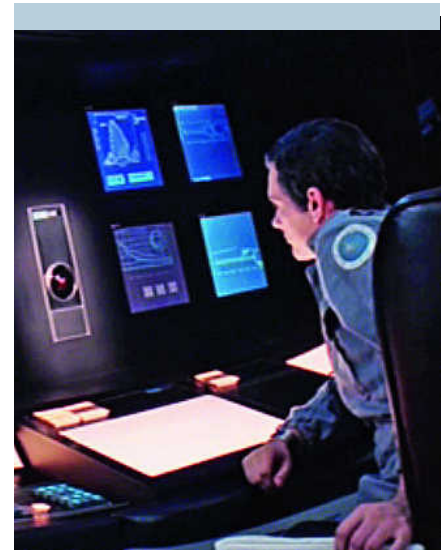
Coveralls made with Tychem, however, have a big drawback. The material restricts gas exchange enough to prevent evaporative cooling, so wearers in hot weather may quickly overheat, becoming confused or even suffering a heat stroke. Sweat and fatigue build so fast that staff in west Africa are limited to two or sometimes three 45-minute sessions in coveralls a day, says Hélène Esnault, a MSF nurse now working in the Democratic Republic of Congo. Dr Sprecher hopes that research by CDC will lead to a more breathable Ebola-resistant fabric.

In the past decade latex gloves have largely been replaced by those made with nitrile, a synthetic rubber that better resists disintegrating in chlorine disinfectants. Goggles are increasingly designed with ventilation slits not placed on the top, lest sweat or rain wash contaminants into the eyes. And surgical masks are now more widely used in Africa's poorest countries because their cost has dropped some 75% in the past 15 years, says Juan Martínez Hernández, an epidemiologist and Ebola expert based in Madrid.

Surgical masks, however, lose effectiveness when soaked with sweat. More expensive "duckbill" designs that protrude from the face work better. MSF is field testing a handful of respirators, which are powered by a battery pack worn on the belt. Filtered air is supplied via a rubber hose into a hood with a plastic visor. More air is delivered than can be inhaled, so pressure under the hood is slightly higher than that outside, which helps to keep particles out.

At about $1,600 apiece, few "positive-air-pressure respirators" are used in west Africa. And wearing them can have consequences, says Dr Martínez Hernández. He was one of the authors of a letter discouraging their use which was published in the *Lancet*. Health-care workers who see colleagues using the respirators are less willing to settle for a traditional passive face-mask even though, used with care, it is good enough, he says. Many African health ministries do not want to see protection standards "get dialled up" to unaffordable levels, adds MSF's Dr Sprecher.

One practical way to prevent infection and lessen the risk to health-care workers is to educate the general population about the disease, says Khadija Sesay, head of the Open Government Initiative in Sierra Leone. With help from IBM, the group uses software to analyse text messages and phone calls to government hotlines. This allows maps to be generated showing the prevalence of people whose actions risk spreading infection. Eating bushmeat, for instance, can transmit Ebola. It is unlikely, then, that the most sophisticated technologies will play much of a role in containing Ebola in Africa, especially if the number of infected remain high. Ebola has come and gone before, but if it abates, one day it will be back. ■



Watch what you say

Speech recognition: Better automated acquisition of speech may be more about seeing than it is about hearing

"IF HE were proven to be malfunctioning, I wouldn't see how we'd have any choice but disconnection." In the film "2001" (pictured above), Frank Poole, an astronaut played by Gary Lockwood, considers what should be done with HAL, the homicidal computer in charge of the ship. HAL learns of his human masters' plan to unplug him by lip-reading their conversation through a window—an idea that researchers and companies are getting closer to realising. Their goal is less about spaceship-driving robots and more about improving voice-controlled helpers such as Apple's Siri and Microsoft's Cortana.

No matter how good voice-recognition software becomes, it will always be hostage to its sonic environment. Ask your digital assistant to dial a number in a quiet office and it might hear the right numbers. Try again near a busy road or at a noisy party and you will probably be disappointed. If only your phone could read your lips.

Ahmad Hassanat, a researcher in artificial intelligence at Mu'tah University, in Jordan, has been trying to teach a computer program to do just that. Previous attempts to get computers to lip-read have focused, understandably enough, on the shape and movement of the lips as they produce phonemes (individual sounds like "b", "ng" or "th"). Such shapes-of-sounds are called visemes. The problem is that there are just a dozen visemes for the

40 to 50 phonemes in English; "pan" and "ban", for example, look remarkably similar to a lip-reader. That makes it rather taxing to reconstruct words from visemes alone. Instead, Dr Hassanat has been trying for the past few years to detect the visual signature of entire words, using the appearance of the tongue and teeth as well as the lips.

His method has had some success. In a paper published late last year, Dr Hassanat described how he had trained his system by filming ten women and 16 men of different ethnicities as they read passages of text. The computer first compared these recordings with a text it knew, then tried to guess what they were saying in a second video. When the computer was allowed to use the same person's training speech, it was fairly accurate—around 75% of words spoken for all subjects and up to 97% for one speaker. But when the person's own training video was excluded from the analysis—just like untrained digital assistants—the program's accuracy plunged to 33% on average and as poor as 15% in some cases (moustaches and beards, it seems, are particularly confusing to the system).

Another idea is not to focus on the mouth. In 2013 Yasuhiro Oikawa, an engineer at Waseda University in Japan, used a high-speed camera capable of shooting 10,000 frames a second of a speaker's throat. This measures tiny, fleeting vibrations in the skin caused by the act of speaking. The precise frequencies present in the vibrations can then, in principle, be used to reconstruct the word being spoken. So far, however, Dr Oikawa's team has managed to map the visual vibrations of just a single Japanese word.

The best results come when a system does more than just passively watch. VocalZoom is an Israeli startup whose idea is to point a low-power laser beam at a speaker's cheek to measure vibrations, and use those to infer the frequencies of speech. The system combines those results with ordinary speech audio from a microphone, subtracting unwanted ambient noise or other talkers and leaving just the cheek-wobble frequencies.

In January the firm took its technology to CES, a giant technology trade show in Las Vegas and a notoriously ear-splitting environment, and impressed the tech press. But the system is not yet ready for the mass market. The prototype is still larger than the smartphones it is intended to be built into, and tempting manufacturers into adding components to ever-slimmer, ever-sleeker handsets will not be easy. The company may have more luck getting its technology into cars, another industry increasingly reliant on voice control; VocalZoom claims to be in early talks with a big carmaker. Perhaps the company will, one day, even get its kit into space-faring vehicles. ■

Out of the groove

Materials science: A simple treatment using a laser can produce surfaces with the ability to clean themselves

A LIGHTNING strike lasting just a few tens of millionths of a second might seem, well, lightning-fast. Elsewhere, though, nature often gets its work done in periods far shorter than that. In recent years, scientists' attention has been caught by lasers that produce pulses lasting just femtoseconds—that is, millionths of a billionth of a second—which can act as flashbulbs that illuminate the fastest processes in biology and physics. Now femtosecond pulses have shown off their abilities in a more quotidian task: making surfaces water-repellent.

Nature has plenty of examples of hydrophobicity, as water-shedding is known, not least the duck's idiomatic back. But a superlative degree of it is of particular interest, because superhydrophobic surfaces are also, in effect, self-cleaning. As they shed water, any dust or dirt on them sticks better to the passing water beads than to the surface. Exposed to the elements, such surfaces stay clean, dry and free of rust or ice (water does not stick around long enough to make either).

There are myriad applications that could make use of such properties: aircraft or power lines that never get icy, and ships or toilets that never get dirty. The idea is already employed by industry, typically by covering surfaces with polymers to achieve hydrophobic effects. But even the best of these do not perform as well as nature's superstars, such as the Morpho butterfly, the leaves of the lotus plant or the garden nasturtium.

Scientists investigating such natural surfaces have found they exhibit patterns and structures on more than one scale—what is known as hierarchical structuring. Morpho wings, for example, are made of tile-like structures about a millionth of a metre long. On each, however, lies a series of grooves measuring just nanometres, or billionths of a metre. In some configurations, hierarchical structuring leads to a reverse effect: an extreme water-loving property called superhydrophilicity.

Chunlei Guo and Anatoliy Vorobyev, physicists at the University of Rochester, in New York, have become experts in using femtosecond lasers to make surfaces with hierarchical structuring. Unlike industrial lasers, femtosecond lasers release their energy in pulses leaving no time for a material to heat up appreciably. As that energy dissipates, single atoms and clusters of varying sizes evaporate off the surface, leaving nanometre-scale bumps and valleys where the laser has removed differing amounts of material.

By scanning a laser beam repeatedly across samples of metal, the researchers are able to cut arrays of grooves about 100 millionths of a metre wide (the width of a human hair). Within each of the grooves, though, lies structure at the nanometre scale. That arrangement, as the pair have shown in a paper in the *Journal of Applied Physics*, results in an astonishing level of superhydrophobicity on platinum, brass and titanium. It is not just that water dropped onto the surfaces does not stick; it actually bounces.

Dr Guo admits, however, that the team have an incomplete understanding of why it works so well. A great many physical mechanisms may be involved, and these need to be unravelled. But making the surfaces is simple, so applications may not be long coming. The pair believe it will work on any metal and, with some tweaking, on materials such as plastics, semiconductors and ceramics. So perhaps a self-cleaning toilet that sparkles after every flush is not far in the future. ■

The little engine that could

Car engines: Downsizing to a car with a smaller engine is being made easier by the latest turbochargers. They can transform a standard four-cylinder engine into a much more powerful motor

FRUGAL four-cylinder engines used to be found only in the cheapest cars. But today they are being fitted to even luxury models. What has made them more acceptable—indeed, desirable—is the development of advanced turbochargers that cram more air than normal into the fixed volume of their cylinders, allowing the engines to burn proportionally more fuel. The result is a compact unit that punches way above its weight in terms of power and torque, a turning force which makes that power available at lower revs. These engines also provide better fuel economy and emit less pollution.

A turbocharger works by tapping the hot exhaust gas from the engine to spin a small turbine which, in turn, drives an equally small air compressor. For higher performance, an intercooler is sometimes placed between the compressor and the engine's inlet manifold. This lowers the temperature of the compressed air and raises its density still further. In general, a turbocharged 1.8-litre four-cylinder petrol engine can deliver the power and torque of a naturally aspirated 3-litre six-cylinder unit. By the same token, a turbocharged V6 can be more than a match for a conventional V8.

Turbochargers are not to be confused with superchargers, made famous by the 4.5-litre Blower Bentleys of the 1920s. While they serve broadly the same purpose—to squeeze more air into an engine—they function differently. A supercharger does not rely on an exhaust-driven turbine but is driven directly by the engine. Superchargers are better in one respect: they do not suffer from "turbo lag" (the time taken for a turbocharger to spool up to speed). The disadvantage is that a supercharger robs the engine of power and, thermodynamically, it is nowhere near as efficient.

Carmakers started to take turbocharging more seriously in 2010, after the American government announced that its CAFE (corporate average fuel economy) target would rise to 35.5 miles per US gallon (6.63 litres/100km) by the 2016 model year. Turbocharged four-cylinder engines typically use 15% less fuel than larger, naturally aspirated, motors of comparable output. Also, with an abundant supply of oxygen to support combustion, the mixture in the cylinders gets burned more thoroughly. The result is a cleaner exhaust all around.

In Europe, where half of all cars and light trucks sold are diesel models, the benefits of turbocharging are well understood. Because diesels ignite their fuel using the heat of compression (rather than spark plugs), they need much higher compression ratios to function. To cope with the greater internal pressure, a diesel's engine block and cylinder head, as well as all its reciprocating and rotating parts, are made much stronger, and thus are heavier.

Unfortunately, heavy rotating masses do not like being spun rapidly. As a result, diesels tend to operate in a lower, more narrow band of engine speeds. And because they spin relatively slowly, they never get enough air needed to fill the cylinders properly during intake strokes, which is why diesel engines have long used turbochargers to overcome their inherent shortness of breath.

The modern turbocharged petrol engine owes much to its diesel equivalent. But there are significant differences that require design changes. For instance, petrol is more volatile than diesel—igniting faster, burning hotter and requiring a lower air/fuel ratio. Petrol engines are also expected to operate over a much wider range of crank speeds, and to respond much more rapidly when called upon by the driver to do so. If turbo lag is longer than a few seconds, the vehicle can be tricky to drive—with nothing happening initially, and then the boost suddenly arriving with a wallop.

The reverse is also true. If the turbocharger does not come off boost quickly enough when the driver lifts his foot from the accelerator pedal—which causes the throttle to shut off the air flow to the engine—pressure waves can surge back to the turbocharger and damage the compressor. To prevent that a "blow-off" valve, which dumps surplus compressed air into the atmosphere, is fitted between the turbocharger and the inlet manifold.

On the exhaust side, a "wastegate" regulates the turbocharger's output by bleeding off some of the hot exhaust gas so that it bypasses the turbine. This makes it possible to match the amount of energy the turbine receives to the amount the compressor needs, so only as much boost is produced as is required. With their more sedentary nature, diesels avoid much of this complexity.

Numerous other tricks have been tried to make turbochargers more responsive. Obviously, the smaller and lighter the rotating parts in a turbocharger are, the faster it can respond to changes in the throttle setting. Unfortunately, small turbochargers quickly run out of puff. Bigger ones produce all the boost required, but are slow to spool up to speed. A number of hybrid designs have emerged that combine the best of both worlds.

Two are better than one

The most popular type today is the "twin-scroll" turbocharger. This works like a pair of turbochargers connected in parallel, one for each of two separate exhaust manifolds. However, while using a pair of turbochargers reduces turbo lag, it doubles the cost and complexity of the installation. The twin-scroll design gets around this by having two exhaust-gas inlets and two nozzles feeding a single turbocharger. One nozzle injects exhaust gas at a steeper angle to the turbine blades, for quick response, while the other injects the exhaust gas at a shallower angle, for peak performance.

Having two exhaust manifolds on a four-cylinder engine adds, of course, to the cost. But by pairing cylinders so their power strokes do not interfere with one another, the two exhaust streams can be injected into separate spirals in the turbocharger, causing it to spin more smoothly. Apart from making the turbine more efficient, this helps to improve the scavenging of burned gases from the cylinders, lowers the exhaust temperature (and thus emissions of nitrogen oxides) and reduces the turbo lag still further. Small turbocharged engines mean that far from fearing the deprivations of downsizing, motorists could be pleasantly surprised. ■

A lightness of being

Microgravity rovers: Space vehicles that can operate in the ultra low-gravity on asteroids and comets are having to employ novel locomotive systems

AFTER hurtling more than 6 billion kilometres through space for over a decade, the European Space Agency's (ESA) probe *Rosetta* began orbiting comet 67P/Churyumov–Gerasimenko last year. In November the mother ship released its lander, *Philae*, which appeared to descend to the surface successfully. But elation at the European mission-control centres soon turned to concern. *Philae* had bounced back up again due to a failure of the explosives-powered harpoons that were supposed to anchor it to the surface. The harpoons were necessary because a small body like a comet generates little gravity. So little, in fact, that if *Philae* bounced faster than 44cm per second it was in danger of exceeding the comet's escape velocity, the speed that an object needs to be travelling to break free of a body's gravity.

As luck would have it, *Philae* fell back to the surface and eventually came to a stop where insufficient sunlight could reach its solar panels. The craft managed to deliver some data until its batteries ran out of power 64 hours later. One day *Philae* might be revived if 67P happens to move into more sunlight. Even so, the difficulties the mission encountered help to explain why space agencies are putting so much effort into designing machines which are capable of not only landing on bodies with microgravity but also travelling around them without flying off in all directions.

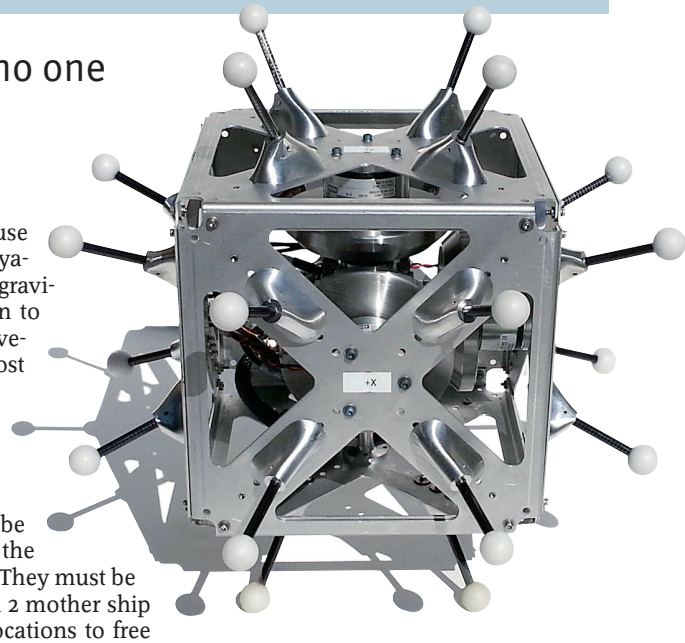
Wheeled rovers have long trundled across the Moon and Mars, but their gravities are merely low—a sixth and a third, respectively, of that on Earth, which has an escape velocity of 11km per second. Wheeled and tracked rovers could probably be made to work in gravity as low as a hundredth of that on Earth, says Issa Nesnas, head of the Robotic Mobility Group at NASA's Jet Propulsion Laboratory in Pasadena, California. But in the far weaker microgravity of small bodies like asteroids and comets, they would fail to get a grip in fine regolith. Wheels might also hover above the ground, spinning hopelessly and using up power. So an entirely different system of locomotion is needed for rovers operating in a microgravity.

Surprising as it may seem, one promising form of transportation in microgravity is a space hopper. These machines are nothing like the bouncy toys made popular in the 1970s-1980s. But they share the same idea, because bouncing from one place to another has its advantages.

The first hop

No one has yet demonstrated if a space hopper will work in space. But in a few years that opportunity will arise. A spacecraft loaded with four robotic hopping rovers blasted off from Japan's Tanegashima Space Centre on December 3rd. The mission, called Hayabusa 2, is being run by the Japan Aerospace Exploration Agency (JAXA). The aim is to collect samples from an asteroid called 1999 JU3 and return them to Earth. The spacecraft will arrive at ▸▸

Until they are tested in a real microgravity no one can be sure these rovers will work



the asteroid in the summer of 2018 and spend about a year surveying it. It will then move in extremely close to fire projectiles into the asteroid's surface. This will throw up material which the spacecraft will suck in with a suction nozzle.

With a diameter of only about 1km, 1999 JU3 has an escape velocity of just 32cm per second. To hop across its surface the rovers will use a moving internal mass. The largest rover on board the Hayabusa 2 spacecraft is a 10kg cube-shaped machine called *MASCOT* (for Mobile Asteroid Surface Scout, and illustrated on the previous page with its mother ship). *MASCOT* employs a weighted internal swing-arm, a bit like a pendulum. An electric motor swings the arm around and then suddenly brakes the movement. This jolt transfers inertia to the body of the rover, pushing it down into the surface, which results in the machine bouncing up. To ensure that the rover drops back down again and does not drift off into space, its hopping speed will be capped at about two-third's of the asteroid's escape velocity.

MASCOT was built by DLR, Germany's aerospace centre. Besides hopping it can use its swing-arm to tumble over if it lands the wrong way up. This is to ensure that its instruments—a camera, magnetometer (to measure magnetic fields), radiometer (to measure temperature and radiation), and an infra-red microscope (to study minerals)—are all pointed in the right direction.

Hopping mechanisms such as these are lighter and less intricate than wheeled and tracked systems. And by hopping the rovers do not require detailed information about the terrain to ensure safe routes. Even if a space hopper lands on a sharp rock it is unlikely to damage itself, because in microgravity objects are a fraction of their weight on Earth. Hopping also requires less energy than turning wheels. The equivalent amount of power required to run an iPad for not much more than 30 seconds will toss *MASCOT* 70 metres or so, reckons Tra-Mi Ho, who leads the project at DLR.

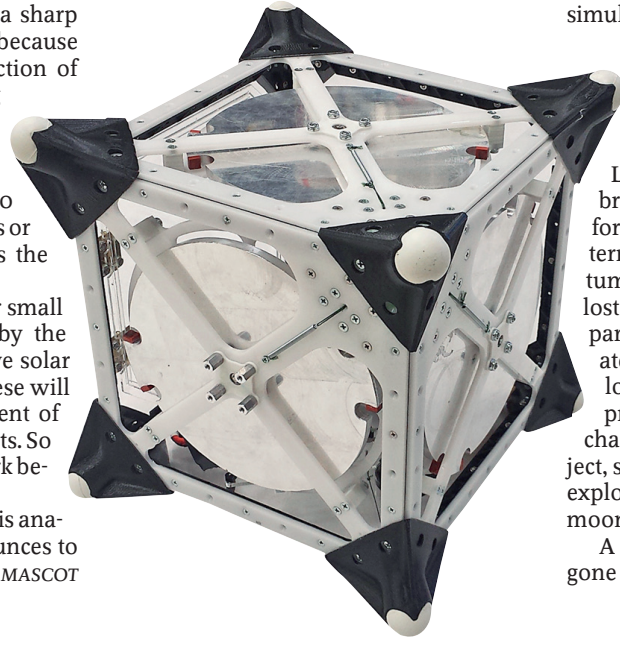
To keep the €28m ($32m) rover small and light enough to be carried by the mother ship *MASCOT* does not have solar panels to recharge its batteries. These will last for just 16 hours, the equivalent of two of the asteroid's days and nights. So the rover has to pack in a lot of work between its hops.

CNES, the French space agency, is analysing data on *Philae*'s ill-fated bounces to better calibrate the hops which *MASCOT* will undertake. CNES will use information from the Hayabusa 2 survey of 1999 JU3's gravity and surface composition to calculate the swing-arm velocities needed for the most efficient hops, says Pierre Bousquet, head of microgravity projects.

In free fall

The biggest challenge will be getting the four rovers onto the asteroid, says DLR's Dr Ho. They must be ejected from the Hayabusa 2 mother ship at precise velocities and locations to free fall to the surface from about 100 metres, she adds. Such separations are tricky, as the first Hayabusa mission showed. In 2005 its mother ship released a space hopper named *MINERVA* 200 metres above an asteroid called Itokawa. That was 130 metres too far. *MINERVA* was not captured by the asteroid's gravity and floated off into space. The three *MINERVA-II* Japanese space hoppers on the current Hayabusa 2 mission are improved variations of the lost original.

If Hayabusa 2's space hoppers work well such rovers would help to broaden extraterrestrial exploration, particularly on asteroids and comets. Scientists are interested in these bodies because they are the purest remnants of the early solar system, unadulterated by many of the chemical and geological transformations that have taken place on planets. Some may contain matter that predates the formation of stars. Many appear rich in complex organic molecules containing carbon, hydrogen, oxygen and nitrogen—elements that were needed for life to begin on Earth.



Asteroids that orbit near Earth can be easier and cheaper to reach than many planets or moons. And because the escape velocities of small bodies are so slow, only a little fuel needs to be carried for a space vehicle to take off from one. Asteroids could therefore serve as stepping stones to get astronauts into deep space, says Marco Pavone, a Stanford University roboticist who is designing a microgravity space hopper for NASA. The rocks could also be mined for elements such as oxygen and hydrogen to replenish supplies of water, breathable air and fuel.

The space hopper which Dr Pavone and his colleagues are working on (pictured below) sports three internal flywheels, one for each axis of motion. Each flywheel is powered with an electric motor, so they can reach different speeds. In order to hop, the inertial energy from each flywheel must be transferred to the robot's frame simultaneously.

Some microgravity space hoppers using a similar system are known as "hedgehogs" because of their protective spikes. Once such prototype built at the Jet Propulsion Laboratory (pictured above) uses brakes to stop the flywheels. The Stanford team are experimenting with an alternative method that delivers momentum more suddenly and with less energy lost as braking heat. It uses a small metal part to snag each flywheel to an immediate halt. Having multiple flywheels allows hops to be more steerable and precise. Benjamin Hockman, a mechanical engineer working on the project, says hedgehogs could also be used to explore moons, such as Phobos, a Martian moon with a tiny microgravity.

A team at the University of Tokyo has gone about things in a different way. They

Digging its claws in

have built a spherical space hopper that generates motion with electromagnets. Four electromagnets are fixed to the sphere's inner wall and a small iron ball is suspended in the centre. Using battery power to activate one or more electromagnets results in the ball being pulled across to the side of the sphere. This imparts momentum to the robot's frame and thus initiates a hop. If more precision in hopping is required then two additional electromagnets could be used. Such a set-up would also allow the rover to roll along, says its designer, Yoshihiko Nakamura.

Rolling is another option for a rover operating in low gravity. One type, known as "structurally compliant" rovers, are designed specifically to roll along. These are constructed from a latticework of rigid rods connected with elastic cables. Mechanical actuators are used to shorten and lengthen the cables, so that the rovers change shape as they repeatedly tip over in the direction they want to go. Although more jerky than graceful, little traction is needed resulting in a "punctuated rolling motion", says Alice Agogino, a NASA-funded researcher working on such a project at the University of California, Berkeley. The rovers' instruments and power supply would be suspended in the centre of the structure.

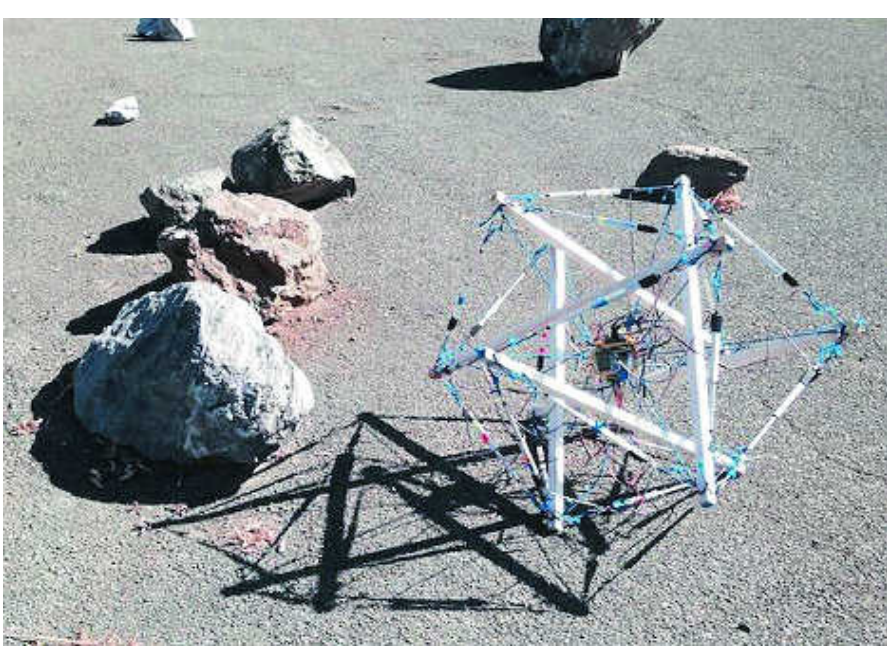
A partner team at NASA's Ames Research Centre is developing structurally compliant rovers they call Super Ball Bots (one of which is pictured right). The researchers hope their robots could be used on Phobos or Titan, one of Saturn's moons. The two moons differ greatly. With a seventh of Earth's gravity, Titan could be traversed with a conventional wheeled rover. A Super Ball Bot, however, makes sense for such a place because it could double as both the locomotion system and a landing mechanism, says Vytas SunSpiral, an Ames roboticist. The structures, lacking rigid joints, are able to absorb large shocks without damage. Conventional rovers dropped on Mars are cushioned with expensive, elaborate and heavy airbag systems. A Super Ball Bot could fall from orbit or roll off a cliff and become its own airbag, says Dr SunSpiral.

Yet mobility in a microgravity will only take a rover so far. Sometimes they must stop and analyse samples. The reason the Hayabusa 2 spacecraft will fire projectiles into the surface of 1999 JU3 to kick up samples is that drilling is not much of an option. No robotic microgravity anchoring system has yet been successfully used, and without one it is the spacecraft or the rover, rather than the drill bit, that would spin. Giving rovers claws might be a solution. Aaron Parness, who works in the Jet Propulsion Laboratory's "extreme environment" robotics lab has developed a machine which uses hundreds of tiny claws to grip the rough surfaces often found on bodies like asteroids. The machine (pictured left) is still under development but it has the potential to climb vertical rock faces and even creep along upside down on overhead formations.

Until they are tested in a real microgravity no one can be sure these rovers will work. There is no practical way to fully replicate a mission in a simulated microgravity on Earth. Some components of the MASCOT system have been tested in a 146-metre drop tower in Bremen, Germany, which uses a catapult to produce 9.3 seconds of near weightlessness. The Draper Laboratory, an independent research centre in Cambridge, Massachusetts, tested the guidance and control systems on a space hopper which it has developed during a reduced-gravity flight on board a NASA aeroplane known as a "vomit comet". But it will be one of Hayabusa 2's space hoppers that may be the first to complete such a mission, although which rover that will be has yet to be decided.

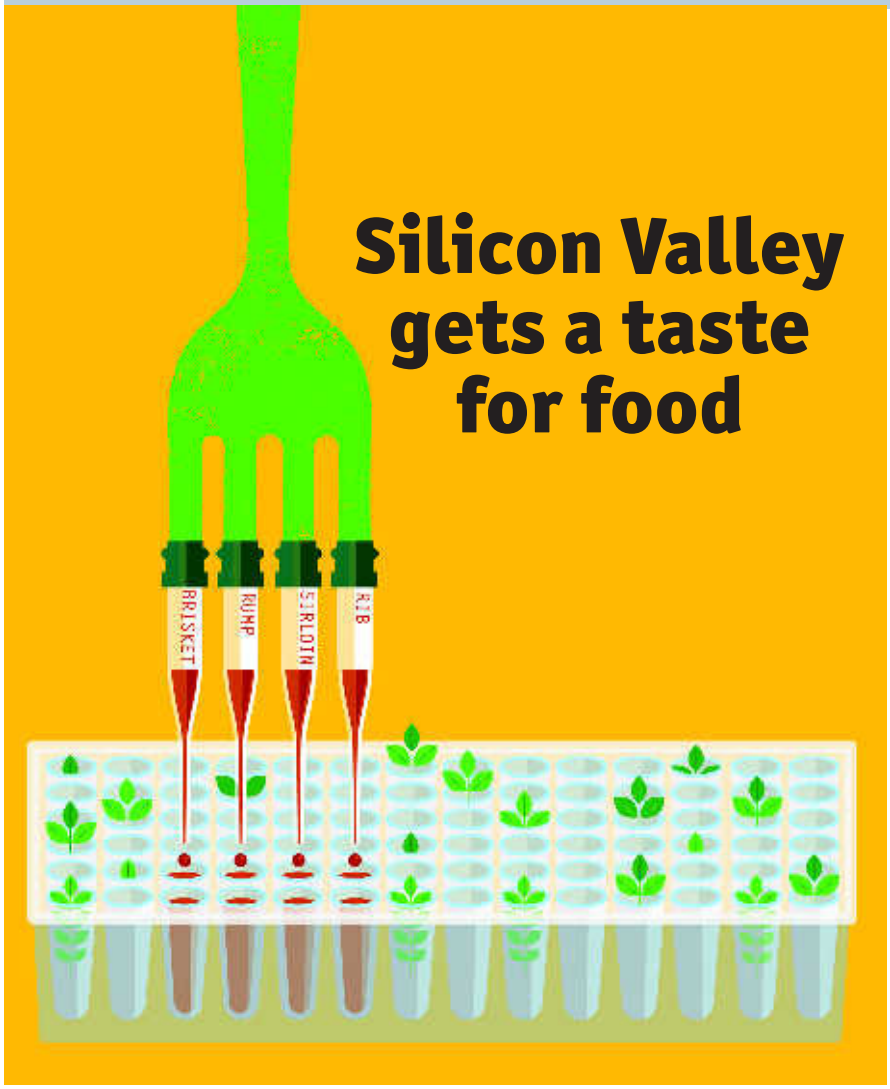
Saving the planet

The importance of a successful deployment is higher than you might imagine. For although they are designed for exploration, microgravity rovers might one day save Earth from a catastrophic collision with an asteroid. Many asteroids are composed of loosely coalesced rocks and would be hard to push or pull into a safe orbit. A paint job, however, might do the trick, reckons CNES's Mr Bousquet. Just as space hoppers rely on every action having an equal and opposite reaction, light and heat reflected off an asteroid's surface exerts a tiny pressure. So increasing the reflectivity of the rocks would alter this gentle pushback and, over time, the asteroid's trajectory. However they move, rovers that can operate in extremely low gravity may one day have a very important job to do. ■



Rocking and rolling along

Silicon Valley gets a taste for food



Green food: Tech startups are moving into the food business to make sustainable versions of meat and dairy products from plants

A PLANT-BASED hamburger patty that bleeds. Meatless chicken strips with the same fleshy and fibrous texture as cooked poultry. Mayonnaise made without eggs that is creamy and smooth. And a vegan beverage that contains all the ingredients for human sustenance, making it unnecessary to bother eating ordinary food every again. Hungry yet?

These are the offerings from a recent crop of Silicon Valley-funded startups which are trying to change the way people eat. The idea of making such products is attracting entrepreneurs and venture-capital firms who think that the traditional food industry is ripe for disruption because it is inefficient, inhumane and in need of an overhaul. The companies have different approaches, but they share the ambition of creating new plant-based food that they say will be healthier, cheaper and just as satisfying as meat, egg, dairy and other animal-based products—but with a much lower environmental impact.

"Animal farming is absurdly destructive and completely unsustainable. Yet the demand for meat and dairy products is going up," says Patrick Brown, founder of one such startup, Impossible Foods, based in Redwood City in the heart of Silicon Valley. It has raised $75m to develop plant-based meat and cheese imitations.

According to the United Nations, livestock uses around 30% of the world's ice-free landmass and produces 14.5% of all greenhouse-gas emissions. Making meat also requires supplying animals with vast amounts of water and food: in the United States producing 1kg of live animal weight typically requires 10kg of feed for beef, 5kg for pork and 2.5kg for poultry. Yet between now and 2050, the world's population is expected to rise from 7.2 billion to over 9 billion people—and the appetite for meat to grow along with it. To keep up with demand, food production will need to increase significantly.

It is a big challenge, but also an economic opportunity. "Anytime you can find a way to use plant protein instead of animal protein there's an enormous efficiency in terms of the energy, water and all sorts of other inputs involved—which translates at the end of the day to saving money," says Ali Partovi, a San Francisco-based entrepreneur and investor in tech startups, such as Dropbox and Airbnb, as well as half-a-dozen sustainable-food companies.

The problem is many people shun vegetables and prefer to eat meat or dairy products. Dr Brown and others think the solution is to mimic the taste of meat and other animal-derived foods with plants and take the animal out of the equation. In theory at least, there would be plenty of food for everyone and fewer resources needed to produce it. "We're reinventing the entire system of transforming plants into meat and milk," he says. Other startups have similar aspirations. Beyond Meat, which makes plant-based chicken strips and beef "crumbles", is already selling its products in stores. As is Hampton Creek, whose eggless mayonnaise has become a bestseller at Whole Foods Market, a big American chain.

Beyond vegetarianism

Of course, the food giants already offer a variety of meat and dairy alternatives that many vegetarians and vegans buy. What is different with this new approach is that the startups are not targeting the small percentage of the population who largely live on a plant-based diet already. They are after people who love meat and dairy products, and that means replicating the meaty, cheesy or creamy flavours and textures that so many people crave. "We want to have a product that a burger lover would say is better than any burger they've ever had," says Dr Brown.

This is also different from "growing" meat in a laboratory using tissue engineering, which involves culturing cells taken from live animals. Modern Meadow, a New York company, is working on this technology, although its more immediate aim is to grow unmarked cultured leather.

Introducing a new food category is risky as it takes a lot of time and money. Big food firms prefer to acquire innovative products rather than develop them internally, explains Barb Stuckey, chief innovation officer at Mattson, a California-based food and beverage consultancy which has developed many new products. "It may take someone from outside the food industry to really disrupt it," reckons Ms Stuckey. And Silicon Valley has enough hubris to do so.

The business has already attracted a fair ▸▸

"Change happens by making something so delicious and so affordable, everyone chooses it"

share of famous venture-capital firms and investors, including Kleiner Perkins, Google Ventures, Andreessen Horowitz, Khosla Ventures, Bill Gates and others. "If we can provide [plant-based] food that's healthier, tastes equal to better, at an equal to lower cost, it'll go everywhere," says Khosla's Samir Kaul. If the companies they are backing succeed, the returns could be massive. The US beef industry alone is worth $88 billion. And even for condiments, such as mayonnaise, the market totals $2 billion. Still, not everyone is bullish on the prospects. These are high-risk endeavours and some of them might fail, cautions Michael Burgmaier of Silverwood Partners, an investment bank involved in dozens of food and beverage deals. The question is, he says: "Is the consumer ready for some of these products?"

Impossible Foods' Dr Brown thinks they are. The inventor of a DNA chip now widely used in gene-expression analysis, his firm has been developing meat and cheese imitations from plants for three years. For meat, the aim is to recreate its key components—muscle, connective and fat tissue—using suitable plant materials. The company's first product, a hamburger patty, already looks and cooks like meat, and will taste as good or better by the time it reaches the shops, Dr Brown promises.

To do this he has assembled a team comparable to one at a biotech or pharma company. It is largely made up of molecular biologists and biochemists, as well as some physicists; only a few members of his staff have a background in food science or have culinary training. In the company's laboratory scientists break down plant materials and extract individual proteins with functional properties that can, for example, make foods firm up or melt down during cooking or baking.

The company has also spent a lot of time working out what gives meat its unique flavour. According to Dr Brown, the secret to a burger's taste is haem, a compound found in all living cells, including plants. It is especially abundant in haemoglobin in blood, and in muscle tissues as myoglobin. It also gives a burger its red colour. During the cooking process haem acts as a catalyst that helps transform the amino acids, vitamins and sugars in muscle tissue into numerous volatile and flavourful molecules, he explains. To create the meaty flavour in its burger patties, the company uses a heme protein equivalent to one found in the roots of legumes.

Development of the burger has come a long way. Dr Brown says one person described the taste of the very first prototype as "rancid polenta". Recent versions have been reviewed much more favourably as "better than a turkey burger". In terms of nutrition, the patty's protein content may be slightly higher than that of a conventional burger and have at least as many micronutrients. Because it is made from plants, it will not contain any traces of antibiotics, hormones or cholesterol. The company hopes to start selling the burger before the end of this year.

Getting the flavour

Beyond Meat, based in Southern California, has also been studying the components of meat to emulate its texture and flavour. "We're smart enough now to understand the architecture and the composition of a piece of muscle," says Ethan Brown (no relation to Dr Brown), the company's CEO. The firm's flagship product, Beyond Chicken Strips, has been on sale since 2012, and has a surprisingly authentic feel when eaten. When several Whole Foods Markets accidentally sold mislabelled chicken salads with the company's plant-based strips there were no complaints. Only when an employee discovered the mix-up after two days were the salads officially recalled. The product's texture is based on years of research at the University of Missouri, and it can now be created in a process that takes less than two minutes. An extruder rapidly heats, cools and pressurises a mixture of proteins and other ingredients into a structure that mimics the fibrous tissue of muscle.

The company's most recent product, the Beast Burger, was released last month. It has more protein, more iron and is overall more nutritious than actual meat burgers. "The entire quest for meat in human evolution is really about a nutrient-dense source of food," explains Mr Brown. "I wanted to build on that theme."

But marketing plant-based burgers to carnivores is not easy. "My view is that meat has a masculine bent to it. You can't sell it the same way you sell lettuce," says Mr Brown. Hence the company is building the brand with images of vitality, fitness and health. In promotions it is using athletes. David Wright, captain of the New York Mets baseball team, has already signed up. In return, he is getting a small stake in the company.

Still under development is what may be Beyond Meat's most ambitious product to date—a raw ground beef equivalent which it hopes will be offered in supermarkets' meat sections right next to actual beef. Due for release later this year, it can be cooked and moulded into a meatloaf or meatballs—or, as Mr Brown hopes, even supplied to a fast-food chain to make burgers.

San Francisco-based Hampton Creek has replaced eggs with plant proteins in the products it has released so far. Its Just Mayo and Just Cookie Dough are now distributed in 30,000 stores, including Kroger and Walmart. Other items in the works include a ranch salad dressing, a scrambled-egg alternative and pasta. The goal is to create products that make it easy for people to choose sustainable plant-based foods over conventional items. "Change happens by making something so delicious and so affordable, everyone chooses it," says the firm's boss, Josh Tetrick.

To accomplish this, Hampton Creek has assembled a team that includes experts in biochemistry, bioinformatics and food science along with a number of chefs. Scientists extract and isolate proteins from plant materials and conduct basic biochemical studies to understand their characteristics and possible applications for a variety of foods. The promising ones are tested in recipes in the company's bakery and culinary sections to see how they perform.

So far, Hampton Creek has analysed more than 7,000 plant samples and identified 16 proteins that might prove useful in food applications. Several are already being used in its commercial food products,

"It's much easier to make a cookie dough without egg than it is to create a scrambled egg without egg"

including a type of Canadian yellow pea in its mayonnaise. The team are looking for proteins with functional properties such as foaming, gelling and moisture retention. Mayonnaise, for example, requires a substance that binds the right amount of oil with water to create a stable emulsion. For its version in stores the company tested more than 1,500 different formulations.

Dan Zigmond, the former lead data scientist for Google Maps and now Hampton Creek's vice-president of data, is in charge of simplifying the process of finding useful proteins. There are an estimated 400,000 plant species in the world, each of which may have tens of thousands of proteins. To search this vast number more efficiently, his team are feeding data the company has already gathered into machine-learning models, which are designed to predict which types of proteins could be useful in specific food applications without having to go through all the biochemical tests.

Last October Unilever, a consumer-goods giant, sued Hampton Creek for false advertising, saying its product should not be called "mayo" because it does not contain eggs. (Based on food standards from America's Food and Drug Administration that date back to 1938, mayonnaise includes eggs.) Unilever also complained that the plant-based product had taken market share away from its well-known brand Hellmann's, which is made with eggs. Some people saw the lawsuit as a frivolous food fight in which a big company tries to bully a fledgling one. Andrew Zimmern, a celebrity chef who had preferred Just Mayo over Hellmann's in a blind taste-test, even started an online petition to urge Unilever to drop the lawsuit. It gathered over 100,000 signatures.

"This was great for Hampton Creek because it got their name out there and people on their side," says Matthew Wong, a research analyst at CB Insights, an analytics firm. Initially Unilever demanded that Hampton Creek rename its product, take existing inventory off the shelves and pay damages. But in December, the company suddenly dropped its lawsuit. It was on the same day that Hampton Creek announced its latest funding round of $90m, bringing its total raised to $120m.

Hampton Creek has been successful with the products it already sells. However, it is not trying to build a burger patty from scratch with plants, as Impossible Foods is trying to do, and it has not yet released its scrambled-egg replacement. "It's much easier to make a cookie dough without egg than it is to create a scrambled egg without egg," says Mattson's Ms Stuckey. In a cookie dough or mayonnaise there are plenty of other ingredients to work with. But in creating an egg or meat analogue there is a higher bar in the consumer's mind, she adds, because the product is not combined with other ingredients it can hide behind.

Perhaps the most radical approach to disrupting the food industry comes from Soylent, whose beverage is designed to be a complete substitute for food and not just one of the many diet drinks or nutritional supplements. Sold as a powder to be mixed with water, it contains all the ingredients needed for sustenance, says Rob Rhinehart, Soylent's founder. It also eliminates the need to plan meals, cook and clean up afterward. "I see it as a life-simplification tool," he says.

The name originates from the sci-fi novel "Make Room! Make Room!" in which people in an overcrowded, apocalyptic world live on foods made of soy and lentils. (A twist in the movie version "Soylent Green" is that its secret ingredient is human flesh.) The company moved from the San Francisco area to Los Angeles in late 2013 in search of cheaper office space.

Some users of the first version of the beverage complained of flatulence because of the high fibre content. That problem has now largely been solved by changing the carbohydrate blend and adding some digestive enzymes. Mr Rhinehart likens the improvements to the continuous updates to software that tech companies make. Soylent 1.3, the most recent version, has a smoother texture than the original, a more neutral taste and its omega-3s now come from algae as opposed to fish oil.

Out with the dishes

Mr Rhinehart himself uses Soylent for about 80% of his dietary needs. As a result he has not made a trip to the grocery store in years. He owns neither a fridge nor dishes. And he has turned his kitchen into a library. "I've also been able to separate the feeling of biological hunger from the craving of food from an experiential aspect," explains Mr Rhinehart, who still enjoys "recreational food" on occasion.

As of mid-February his firm had a four-to-five-month backlog for new orders. Customers subscribe online to receive monthly shipments with a "meal" costing roughly $3. According to Mr Rhinehart, his company is already profitable and will use a recent $20m cash infusion to expand production and sales.

Mr Rhinehart is, to put it mildly, a little extreme. Not everyone may want to separate eating into utility versus pleasure. Impossible Foods' Dr Brown does not believe such a compromise is necessary. "I don't see any reason why you can't have it all—the best tasting food, healthiest, best for the planet and most affordable."

But even if the scientific hurdles of making plants taste like meat and other animal-based products are overcome, the bigger obstacle these companies face may be cultural. People have been eating meat and having meals together for thousands of years. Meat in particular is not only prized for its taste but also perceived as a force of vitality, strength and health.

A recent study by the Humane Research Council, an animal advocacy group, says most vegetarians and vegans, about 2% of America's population, go back to eating meat eventually. In the future that may not be an option. "We can't sustain the number of people that we're going to need to feed over the next couple of decades with the current way that we're eating, " says Ms Stuckey. Whether out of necessity or choice, Silicon Valley's vision of a big shift to plant-based foods may be inevitable. ■

Hacking your brain

Neurostimulation: With a DIY bundle of electronics or a ready-made device it is possible to stimulate the brain. But does it work and is it safe?

"IT'S like coffee times ten," raves one enthusiast. "I use it a couple of times a week and problems solve themselves. At the end of the day, I haven't wasted hours on frivolous websites. At the end of the week, my apartment is clean." This marvel of productivity is not a new energy drink or an experimental wonder drug but a simple electrical device that he built at home for less than $10. Whenever this physicist feels like an extra burst of motivation, he places electrodes on his skull and sends a jolt of electricity into his brain.

The currents, which are typically applied for ten to 20 minutes, are hundreds of times smaller than the seizure-inducing shocks used in electroconvulsive therapy. Plans to make such transcranial direction current stimulation (tDCS) machines are freely available online and their components can be bought at hobbyist stores. Kits cater to those lacking soldering skills, and now companies are emerging offering nicely designed and packaged brain zappers for mainstream consumers.

Not everyone using tDCS is seeking to become more efficient in their daily life. Some hope to enhance their concentration for study or video gaming; others want to boost their memory, speed up learning or induce meditative calm. Yet more are trying to self-medicate for conditions such as depression, chronic pain and motor, sensory or neurological disorders. The benefits might sound implausible, but there is some science to support them. The idea goes back a long way. Scribonius Largus, a first-century Roman physician, prescribed the shock of an electric ray for headaches, and in the 19th century electrical pioneers such as Luigi Galvani and Alessandro Volta toyed with crude bioelectric experiments. It was not until the 1960s, however, that the first rigorous studies of electrical brain stimulation took place.

Directing the flow

The theory behind tDCS is that a weak direct current alters the electric potential of nerve membranes within the brain. Depending on the direction of the current, it is said to make it easier or more difficult for neurons in a brain circuit to fire. Position the electrodes correctly and choose the right current, so the idea goes, and you can boost or suppress all kinds of things. Some researchers have reported that tDCS can reduce pain, ease depression, treat autism and Parkinson's disease, control cravings for alcohol and drugs, repair stroke damage, and accelerate recovery from brain injuries, to say nothing of improving memory, reasoning and fluency. Remarkably, some effects seem to persist for days or even months. And the closer that scientists look at tDCS, the more they seem to find. Scientific papers about the technology appear at an ever-faster rate.

Hardly surprising, then, that DIY brain hackers want in on the action. Christopher Zobrist, a 36-year-old entrepreneur based in Vietnam, is one of them. With little vision he has been registered as blind since birth due to an hereditary condition of his optic nerve that has no established medical treatment. Mr Zobrist read a study of a different kind of transcranial stimulation (using alternating current) that had helped some glaucoma patients in Germany recover part of their vision. Despite neither the condition nor the treatment matching his own situation, Mr Zobrist decided to try tDCS in combination with a visual training app on his tablet computer. He quickly noticed improvements in his distance vision and perception of contrast. "After six months, I can see oncoming traffic two to three times farther away than before, which is very helpful when crossing busy streets," he says.

Online communities dedicated to tDCS are full of similar stories. More still claim to have gained cognitive enhancements that give them an edge at work or play. Users follow the latest scientific papers avidly and attempt to replicate the results at home, discussing the merits of different currents, waveforms and "montages" (arrangements of the electrodes on the skull).

Dissenting voices are rare. Here and there are tales of people who experienced headaches, nausea, confusion or sleeplessness after tDCS, while temporary visual effects and mild skin burns are fairly common. There have been no reports of seizures, serious injuries or deaths. But that does not mean it is without risk, says Peter Reiner, co-founder of the National Core for Neuroethics at the University of British Columbia. He says DIY users may place electrodes incorrectly, thus stimulating the wrong part of their brain, or reverse the polarity of current, potentially impairing the very things they are trying to improve. No one really knows how tDCS interacts with chemical stimulants or recreational drugs like marijuana, or with pre-existing conditions like epilepsy. Even something as fundamental as being left-handed can alter the functional organisation of the brain. ▸▸

Happiness and health may always be more than just a 9-volt battery away

And if the benefits of tDCS can persist for weeks, perhaps its side-effects can linger, too. Many neuroscientists are particularly worried that the use of tDCS by children and young adults could affect their long-term neural development.

Some of these concerns can be addressed by manufacturing tDCS devices to make it difficult, or impossible, to exceed recommended currents or to apply the electrodes incorrectly. One such product already exists. The Foc.us v2, made by Transcranial, a London company, is advertised as a $199 pocket-sized controller that pairs with a $99 headset intended to help with concentration and reaction speed while videogaming. Donning the headset automatically positions the electrodes on the left and right temples, and both the duration and maximum current are capped. A second headset provides a different montage aimed at improving performance and motivation while exercising.

In reality, however, there is no guarantee that even slick products are any safer than a pocket-money brain stimulator assembled at home from a 9-volt battery, electrodes, a few wires and other components. Unlike the tDCS machines used for medical trials and clinical research, consumer versions may not have been assessed by any official body for safety or effectiveness. If the maker insists they are for use only by healthy adults to enhance cognition or leisure activities and make no diagnostic or therapeutic claims, such "wellness" devices have slipped under the regulatory radar of both the Medical Devices Directive in Europe and the Food and Drug Administration (FDA) in America.

That worries some experts. A recent paper from the Institute for Science and Ethics at the University of Oxford points out that consumer tDCS products are mechanically and functionally equivalent to medical neurostimulation devices that require licensing. Why regulate the version that is likely to be operated responsibly by health professionals, and not the one freely available to unskilled and inexperienced users? The Nuffield Council on Bioethics agrees, recommending in 2013 that the European Commission should consider regulating all such gadgets under its medical devices regime, regardless of the purposes for which they are marketed.

The Institute for Science and Ethics proposes a graded regulation system that errs on the side of consumer choice for tDCS devices, requiring comprehensive, objective information about risks and benefits to allow users to make informed decisions. But it wants supplying brain zappers to children to be made illegal. Last year the FDA allowed transcutaneous electrical nerve stimulator (TENS) machines for headache relief as it rated them as low-to moderate-risk devices. TENS devices use a different waveform to tDCS and target cranial nerves rather than the brain itself, but they rely on a similar controller and head-mounted electrodes. Before allowing new TENS products to be sold, the FDA now wants to see evidence that the components are not likely to cause injury, that the controller can reliably provide the correct output, that there are no thermal or mechanical hazards, and that clinical data demonstrate the device is safe and effective as a headache treatment. Recent draft FDA guidelines for wellness devices suggest tDCS machines may eventually be regulated in a similar way.

Going underground

The University of British Columbia's Dr Reiner doubts that any manufacturer today can provide such information for tDCS. Even if they could, the cost of gathering it would make consumer devices more expensive. "When you can make a tDCS device yourself for less than $20, we would advise strongly against heavy regulation because it will only drive the technology underground," he says.

Proving the effectiveness of brain stimulation will be difficult. Although it may well do something, exactly what is open to question. As the hype around tDCS grows, some neuroscientists are starting to question whether the technology really is the panacea it appears to be.

In 2013 Teresa Iuculano and Roi Cohen Kadosh of the Department of Experimental Psychology at the University of Oxford split volunteers up into three groups and asked them to learn a made-up mathematical notation system. The first two groups received tDCS to different parts of the brain previously associated with numerical understanding and learning, while a non-functional "sham" device was used on the third group as a control. After a week, all three groups were tested on how well they had learned the new notation system, and whether they could use it in practice. The first group showed an improvement in learning compared with the control group, but a decrease in their ability to apply their knowledge, while the second group experienced the opposite result. This suggests that the brain is actually rather well balanced: boost performance in one cognitive realm through stimulation, and aptitude in another will naturally diminish.

There is also the possibility that a variation in individual responses to tDCS will overshadow any general effects. In a study published last year, Dr Cohen Kadosh set up two groups: one of people who were anxious when presented with mathematical problems, and another who had confidence in their ability to breeze through numerical quizzes. When treated with tDCS to their prefrontal cortices, the nervous individuals improved their reaction time on simple arithmetical problems and showed reduced levels of stress. Given the same treatment, the confident group had longer reaction times and no less stress. "If you can get exactly the opposite results with a different population, that shows DIY brain hackers and companies marketing stimulation to improve gaming or other abilities are not on the right track," says Dr Cohen Kadosh. "We need to understand how the brain works in different people."

Felipe Fregni, director of the Laboratory of Neuromodulation at Harvard Medical School, says tDCS has been shown to accelerate the learning of new skills. But he agrees that individual variation is important, noting that younger people sometimes do not improve as much as older subjects, and that people at later stages of learning may even experience detrimental effects. "The more science you know, the more confused you can become of what really is the effect of tDCS," says Dr Fregni.

One advantage of the deluge of scientific papers is that they can be subjected to meta-analysis, whereby studies can be statistically combined to tease out new discoveries. Last year, Jared Horvath, a neuroscientist at the University of Melbourne in Australia, published a meta-analysis of 30 measurements taken during tDCS studies, including neural responses, oxygen levels and electrical activity in the brain. Surprisingly, he found that tDCS had a reliable effect on only one: the electrical response of muscles to stimulus, and even that has steadily declined in studies over the last 14 years. Mr Horvath believes this indicates that the response has historically been measured poorly and that it too will eventually disappear as techniques mature.

Equally troublesome is a meta-analysis of the cognitive and behavioural effects on healthy adults that Mr Horvath subsequently carried out. As before, he included only the most reliable studies: those with a sham control group and replicated by other researchers. It left 200 studies claiming to have discovered beneficial effects on over 100 activities such as problem solving, learning, mental arithmetic, working memory and motor tasks. After his meta-analysis, however, tDCS was found to have had no significant effect on any of them.

If tDCS alters neither the physiology of the brain nor how it performs, thinks Mr Horvath, then evidence suggests it is not doing anything at all. Marom Bikson, a professor of biomedical engineering at City University of New York, disagrees. "I can literally make you fall on your butt using the 'wrong' type of tDCS," he says. Dr Bikson thinks the biggest challenge for tDCS is optimising techniques, such as the dose.

Mr Horvath notes that many papers measure 20 or more outcomes, with brain stimulation showing a weak effect on one or two. "But in the title and abstract, that's all they talk about," he says. "No one mentions the tons of effects that tDCS didn't have an impact on but that technically it should have if it is doing what the researcher thinks it is."

Another problem might be the small sample size, sometimes as few as ten or 15 people. Mr Horvath says future studies should use at least 150 subjects. There is, of course, the possibility that Mr Horvath's analyses are flawed. His paper included only one-off sessions, while many scientists believe the effects of tDCS accumulate with repetition. However, too few multiple-session studies exist for a valid meta-analysis. Dr Cohen Kadosh points out that individual variations could make the technology look as though it is doing nothing when in fact it has real but opposing effects in different people. Mr Horvath insists that his analysis allows for this possibility.

Critics might also wonder why Mr Horvath omitted tests where tDCS seems to have been most effective, in alleviating, for instance, clinical conditions such as depression. He admits that would be useful but says, "If something doesn't demonstrate any type of effect in healthy people, it becomes incredibly difficult, if not impossible, to argue why it would work within a clinical population."

Not all neuroscientists are defending the status quo. "I'm not surprised that he found no effect from conventionally applied tDCS," says Jamie Tyler, a professor at Arizona State University and one of the founders of Thync, a Silicon Valley startup that recently unveiled a smartphone-controlled tDCS device. Thync tried to replicate some basic tDCS findings on cognition but could not do so. Dr Tyler now believes that tDCS may not directly stimulate the brain at all but instead modulates cranial nerves in the skull, like the headache-busting TENS technology. He designed the Thync device, a pocket-sized unit with disposable pre-shaped electrodes, to target these nerves with the aim of generating either relaxed or energetic mental states.

A shot of caffeine

Dr Tyler recently published a study of 82 people with a control. Its results suggest that Thync's device can reduce psychophysiological stress by altering skin conductivity (a measure used in pseudoscientific lie detectors), stress enzymes and heart rate variability. He likens Thync's "modified tDCS" programs to ingesting either a third of a cup of coffee or a glass of wine, and says no effect has been found on cognitive processes like working memory. While Thync's stimulator is not yet available to the public, the firm was willing to give your correspondent a pre-launch trial.

The Thync device attaches with one sticky electrode on the right temple and one behind the right ear. The unit is controlled via a smartphone app, with the user able to adjust the intensity but not the duration of the session. At first, the unit generated a barely perceptible crawling feeling on the skin near the electrodes, building gradually to a pronounced tingling sensation. Over the 20-minute session, the strength of the signal varied up and down according to a preset routine. It felt itchy at times and, at its most powerful, caused muscles in the forehead to spasm alarmingly. Although the experience was not altogether unpleasant, any extra energy or focus proved, alas, elusive. Dr Tyler acknowledged that perhaps one in four people do not perceive any immediate benefit from the device.

Even for those who find themselves susceptible to its charms, the challenges for a product like Thync are formidable. The cognitive enhancements of a strong cup of tea or a glass of vintage Burgundy are well established. And partaking of them can be socially acceptable, deliciously enjoyable and rapidly achieved. None of these can be said of a disconcerting gizmo that needs half an hour to work and causes eyebrows to raise, both literally and socially.

Regardless of their questionable utility and effectiveness, tDCS gadgets are too novel, cheap and alluring to simply dismiss. Consumer-wellness devices like Thync may appeal to those who cannot use caffeine or alcohol for medical or religious reasons, and there will always be healthy overachievers seeking to supercharge their cognition for study or work. More importantly, tDCS presents the tantalising promise of relief from some medical conditions for which traditional therapies are either ineffective or unaffordable. As the University of Melbourne's Mr Horvath says, "If there are ten percent of people who are feeling a huge effect, even if that's placebo, who are we to say no to them?"

If people want to experiment with tDCS, there seems to be no reason to prevent them, provided it is done in the safest way possible. Devices could be regulated lightly with a view to safety rather than effectiveness, and neuroscientists encouraged to design future studies with more rigour. Happiness and health may always be more than just a 9-volt battery away, but brain hacking looks like it is here to stay. ■

Medicine by numbers

Susan Ellenberg is a biostatistician trying to avoid mistakes in an era of Big Data and high-tech personalised medicine

"IF WE didn't take any risks, we wouldn't approve any drugs," says Susan Ellenberg, a professor of biostatistics at the University of Pennsylvania. "Some people will always want a new drug sooner and say they're willing to take a chance. Others will ask, why didn't you study it longer and find out about this horrible side-effect?"

During her long career, Dr Ellenberg has used data to quantify and communicate those risks. Along the way she has helped to shape a discipline that owes as much to ethics and philosophy as it does to pure mathematics. Now medicine is entering a new digital age, one of Big Data and high-tech personalised treatments that are tailored to an individual's genetic make-up. But more data does not necessarily mean better data, so amid the increasing complexity it will be as important as ever to measure correctly which treatments work and which do not.

It is a job Dr Ellenberg is well suited to. She has already played a big part in improving the data-monitoring committees that now oversee virtually all clinical trials; she has helped establish standard practices for tracking dangerous treatments; and she has encouraged patient lobbies to find a voice in clinical testing.

But Dr Ellenberg nearly missed becoming a statistician at all. As a high-school maths teacher in the 1970s, she took a summer job analysing clinical trial data. Luckily, she became so engrossed that she quit her job and returned to graduate school for a doctorate in statistics. The basics of randomising subjects into different groups and leaving the patient (and ideally health-care workers as well) unaware of the treatment each was receiving were well known. However, there were still plenty of mistakes being made.

"In the old days, people used to throw out some of their data," says Dr Ellenberg. "If a patient didn't comply with their treatment, the researchers would say, how can they possibly contribute to the question of how that treatment works? So they just dropped them." In one case Dr Ellenberg worked on in the 1970s, doctors wanted to test whether chemotherapy could help people recovering from colon cancer surgery. The study required patients to start chemotherapy within six weeks of their operation for the best chance of catching any remaining cancer cells. Those who missed the deadline were automatically excluded from the analysis.

Dr Ellenberg realised that most reasons for starting treatment late, such as a slower recovery from surgery because of old age or a particularly large tumour, would probably mean a poorer prognosis regardless of any subsequent treatment. Excluding those people would leave the chemotherapy group with healthier members on average, making a drug look beneficial even if it did nothing. Dr Ellenberg insisted that the investigators track everyone who had been randomised into the study, even if they were treated late or not at all.

In 1988, Dr Ellenberg became the first chief of biostatistics for AIDS at the US National Institute of Allergy and Infectious Diseases. She arrived at a desperate time. HIV appeared to be a death sentence, patients were demanding treatments, however unproven, and doctors were struggling to catch up. With most infectious diseases, patients could be treated and followed up within weeks to see whether the pathogen had disappeared. With HIV/AIDS, they might have to monitor trial members for years to see who lived and who died.

Measuring surrogates

Dr Ellenberg championed a concept called surrogate endpoints that she had pioneered in cancer trials. These are biochemical measures that can indicate quickly whether a patient in a trial is likely to improve, remain stable or deteriorate in the long-term. For example, blood pressure can be a surrogate endpoint for cardiovascular mortality. The challenge with AIDS was working out which of dozens of biological markers had the best predictive value. Dr Ellenberg helped narrow these down to ones that were strongly associated with long-term survival, such as CD4 white-blood-cell counts. "I wish I could tell you that led to wonderful results and now we know how to do it," she says, "But we're still limping along."

The problem is that a surrogate for one treatment may not work with another, either because the second treatment functions differently or has side-effects. But it was still a step forward, allowing investigators to screen potential drugs more quickly. Nothing could be fast enough for some activists, however, who wanted early access to anything that might slow the progression of AIDS. "The clinical

Without the right analytical methods, more data just gives a more precise estimate of the wrong thing

leadership was unwilling to talk with activists at that point," says Dr Ellenberg, "But I saw that the Act Up group in New York had a very carefully thought-out set of principles for doing AIDS trials."

Dr Ellenberg welcomed Act Up to her statistical working group on AIDS, and changes began to trickle through. Until then, some studies had not allowed trial patients to take drugs other than the one being tested, even though many AIDS sufferers needed a cocktail of medications to fight opportunistic infections. Dr Ellenberg showed that a study could deliver useful results while allowing its members to continue with life-saving medicines. Patient groups are now routinely involved in planning clinical trials.

The role of placebos in clinical testing was a thornier problem. The most reliable results can always be obtained by comparing two identical groups, one of which receives a treatment and the other an inert placebo. Ethically, however, doctors are loth to withhold an effective treatment where one exists, so many trials simply compared a new drug to an existing one. In 1993 Dr Ellenberg moved to the US Food and Drug Administration (FDA). In a series of scientific papers, she and a colleague demonstrated that such trials can often fail to demonstrate the effectiveness of new treatments. In 2002, the World Medical Association changed its recommendations to permit placebo-controlled trials explicitly where patients would not suffer serious or irreversible harm.

The same year, Dr Ellenberg wrote a book about the importance (and the dangers) of analysing data as it accumulates during a clinical trial. Her ideas of how data-monitoring committees should function quickly became standard practice. It had long been realised, for example, that a trial might reveal one treatment to be much better than another. The only ethical thing to do in that case would be to stop the trial and give everyone the superior drug. In the past, statisticians keen to find such magic bullets would crunch their data every few weeks or months. "But if you look at your data often enough, sooner or later you'll observe by chance that one arm of the test looks better," says Dr Ellenberg. "There is now a mistrust of the whole concept of early termination."

She also cautions against the temptation to set statistics aside when faced with something that appears to be urgent: "There are groups saying they would be opposed to doing randomised trials for drugs or vaccines for Ebola because it's so serious. But we're not doing anybody any favours if we don't find out whether these drugs or vaccines actually work."

Much of Dr Ellenberg's work at the FDA focused on the safety of medicines, particularly vaccines, once they were on the market. No clinical trial can ever catch the rarest side-effects but tracking those down from sporadic reports, anecdotes and coincidences is incredibly difficult. She notes that most infants are vaccinated and sometimes children get very sick. But is it the vaccine or just coincidence? "I was trying to make something out of the worst, dirtiest kind of data that you could possibly imagine," adds Dr Ellenberg.

The arrival of electronic medical records and the advent of Big Data promises massive statistical analyses that can uncover everything from uncommon side-effects to how peoples' genes might affect their future well-being. The technology is likely to be particularly useful in detecting bad treatments, thinks Dr Ellenberg. While most reported problems may continue to be coincidences, at least biostatisticians will be able to compare reliable lists of who took a drug and who experienced unpleasant reactions. The problem, says Dr Ellenberg, is detecting the signal from the noise. "The more people you have the richer your database will be but also the more ways there are to be misled by the data." Without the right analytical methods, she believes, more data just gives a more precise estimate of the wrong thing.

From the genes

Dr Ellenberg points out that services like 23andMe, which provide ancestral and medical interpretations of individuals' genetic information, have not yet delivered the revolution in health that many had expected. In the early days of genomics, excited mathematicians thought they had discovered thousands of correlations, most of which were chance findings. Dr Ellenberg also worries that presenting people with links between particular genes and health outcomes might lead them to worry needlessly or seek out potentially harmful treatments for conditions they do not yet suffer from.

In his state-of-the-union address, Barack Obama lauded personalised medicines. But these are tricky to approve. When a disease affects millions, large clinical trials can reliably spot even small differences between drugs. But for personalised treatments, or ones targeting rare "orphan diseases" that affect only a few people, those differences become much harder to spot. Nevertheless, Dr Ellenberg believes statistics can help by integrating evidence from other trials.

Dr Ellenberg continues to work on surrogate endpoints and clinical trials, including a new study testing an innovative approach to attacking HIV. She also recently travelled to Botswana to help statisticians and clinicians there develop their own biostatistics programmes. Like most medical academics, Dr Ellenberg would like to see an end to the practice of some pharmaceutical companies quietly burying trial data that is inconvenient to them. Thousands of clinical trials have never been registered with oversight agencies and results from around half of all clinical trials (often those with unfavourable results) remain unpublished. Making that data available to statisticians would almost certainly lead to new discoveries and clinically useful findings.

However there could also be negative consequences. "Sharing raw data could promote inappropriate re-analyses," warns Dr Ellenberg. She says there are many who would be ready to believe any analysis claiming to prove that vaccines caused harm.

That the dry world of statistics is becoming a battleground of ideas and commercial interests, affecting the future of medical care and the lives of people around the world, may shock some. For Dr Ellenberg, who has spent her professional life emphasising the life-saving importance of accuracy, it is no surprise at all. "We've got all this data," she says. "The answer isn't to ignore it. The answer is to figure out how to limit the number of mistakes we make." ■