

THIS WEEK

EDITORIALS

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Power of one

New tools that allow biologists to explore the characteristics of individual cells are bringing collaborators from other disciplines into the field of single-cell analysis.

The street-light effect is often used as a criticism in science, because it introduces an observation bias. The concept is based on the old joke about the night-time drunk who looks for his house keys under the light, even though he lost them somewhere else, because that's the only place he can examine.

But if nothing is lost and a street light shines scientific light on a new place, then it would be perverse not to peer underneath. Because that's one of the attractive features of science: discovery and the joy of the unknown. So it is difficult to criticize those scientists who rush to exploit new tools that allow the analysis of single cells. As we describe in a special series of articles this week, advances in the past few years at this technical and computational frontier offer an unprecedented view of what goes on at the cellular level, with implications for everything from genomics and ageing to the treatment of disease (see page 19).

Some of this science is descriptive and discovery-led. It's nearly 180 years since the cell was first proposed as the most basic individual unit of all life on Earth. Yet most of what we know about how cells work at the molecular and biochemical level comes from studying them not as individuals but as groups. This is problematic: researchers know that tissues, and even apparently homogeneous collections of identical cells, can carry significant differences. These ups and downs are missed when cells are mashed together and assessed. It's a classic downside of the tyranny of the average. But that was where the light was, so that's where scientists looked. And now the unexplored territory inside the cell is ripe for adventure.

As the street light of science starts to focus on individual cells and individual characteristics, so it also becomes a spotlight. For the study of the single cell is not just the territory of discovery — it also enables problem-based research. Take cancer. We know that tumours comprise a multitude of vastly different cells, not all of them explicitly cancerous (think of blood and lymph vessels and immune cells). To unravel the ways in which they interact and either fight or maintain tumours has been a major challenge. One way of addressing that is to get more data on all the players, and to extract information from cancer cells about how they developed and what weaknesses they may harbour. And that takes single-cell analysis.

The illumination of this biology of individual cells also shines a light on some interesting cultural differences. To explore this new frontier demands new skills, and so mathematicians and computer scientists are teaming up with cell biologists, developmental biologists and the various systems specialists: immunologists, neuroscientists and others. As they do so, they are bringing with them the more collaborative and open approach seen in their native disciplines. As a result,

and unusually for a dynamic and fast-moving field in the life sciences, single-cell biology has seen

data, tools and results being shared more readily before publication.

This is hugely positive, and is perhaps a benefit of the otherwise-maligned street-light approach to science. The better the search tools, and the more that scientists work together to improve them, the greater the chance of everyone striking lucky. When the goals and rewards of science are less clear, then perhaps the benefits of cooperation outweigh the risks.

It will be instructive to see whether this interdisciplinary ethos continues, and whether it spreads to other subfields as the impact

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of big data forces biologists to rethink their approaches and broaden the expertise in their groups and laboratories. One indication might be the open submission and sharing — or not — of the computer code used to crunch the data presented in journal papers. As this publication pointed out in 2014, the delivery of such code from scientists lags

behind that of other forms of data (*Nature* **514**, 536; 2014). The lack of standardization makes it difficult to mandate open sharing of code, but scientists shouldn't use this as an excuse to keep it to themselves.

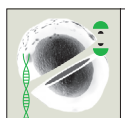
One sign of how far the field of single-cell analysis has come is that it has its own ambitious — some say too ambitious — mega-project. The Human Cell Atlas aims to identify the number of cell types and cell states that comprise a person. That ambition, of course, raises a similar question about the street-light effect. People are as individual as cells, so what if a map of cells in one human says little about the cells' representation in other humans? At some point we're going to have to spread the light around. The effect could be blinding. Or it could be dazzling. ■

Flash machine

In the 50 years since their discovery, pulsars have proved their scientific value.

As scientists know only too well, nature often delivers a scruffier, more inconvenient version of reality than the one they wished for. But there are rare occasions when the Universe presents a real treat. One arrived 50 years ago, with the discovery of pulsars. In the decades since, these extremely precise 'ticking' stars have allowed astronomers to test gravity and explore deep space. They may yet form the Global Positioning System of the future.

Jocelyn Bell Burnell, the first person to detect a pulsar, said it emerged as a “bit of scruff” in the scribbled output from a



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hand-built radio array at the Mullard Radio Astronomy Observatory in Cambridge, UK. After two years of helping to build the array, the PhD student had started operating the equipment in July 1967, analysing 29 metres of chart recordings a day. The weeks that followed revealed spikes in the signal from a particular patch of sky; on closer inspection, these turned out to be repeated at precisely 1.3-second intervals. Three similar discoveries soon followed.

Bell Burnell realized the revolution that she and her supervisor Anthony Hewish had started only when a seminar to announce the results, ahead of their 1968 *Nature* publication (A. Hewish *et al.* *Nature* **217**, 709–713; 1968), drew “every astronomer in Cambridge”. By the end of the year, the craze had gone worldwide, with astronomers finding dozens more such ‘pulsars’ and Austrian astrophysicist Thomas Gold offering an explanation: they were neutron stars, predicted in the 1930s but never before seen. If surrounded by powerful magnetic fields, he said, these extremely dense cores of exploded stars would create a column of radiation that would sweep past Earth like a lighthouse beam.

Pulsars are incredible objects: dead stars the size of a city, with more mass than the Sun and magnetic fields as much as 20 trillion times that of Earth, which spin at speeds of up to 70,000 kilometres a second. But astronomers immediately saw beyond pulsars’ status as objects of curiosity to their potential as cosmic probes.

The flashes of light they emit are as regular as a ticking clock. And the timing, polarization and shape of incoming signals give clues to the environment they were born in, as well as the journey they’ve been on. Since the 1960s, precision studies of pulsar light have allowed astronomers to study everything from the Sun’s corona, or outer atmosphere, to the density of matter in the interstellar medium.

Pulsars also provided a way to study gravity in extreme situations, when, in 1974, astronomers found one orbiting a fellow neutron star

in a binary system. This celestial dance also yielded the first evidence of gravitational waves, when the rate at which the stars slowed in their orbit was found to match predictions from Einstein’s general theory of relativity about how such rapid, heavy objects should lose energy as they emit ripples in space-time. In 1992, precise measurements of bleeping radio waves from pulsar PSR1257+12 even revealed the first exoplanet.

Today, astronomers have seen more than 2,000 pulsars, and the flow of ideas for how to use them has not slowed. Members of the Pulsar

“Pulsars are incredible objects: dead stars the size of a city, with more mass than the Sun.”

Timing Array collaboration hope to be able to use pulsars to detect gravitational waves directly, from the way in which the stretching and contracting of space-time subtly shifts the arrival time of pulses from sources across the sky. Studies of pulsars using NASA’s Neutron Star Interior Composition Explorer (NICER) should reveal how nuclear forces behave in extreme environments (see *Nature* **546**, 18; 2017), and the same mission will test whether pulsars can be used to triangulate position in a navigation system that needs no contact with Earth.

Back in 1967, when Bell Burnell first saw the signal, and she and Hewish had ruled out Earth-based interference, they briefly considered that they might be seeing a message from an alien civilization. Even the thought stoked enormous press interest (and a new-found fame for Bell Burnell, which prompted bizarre questions from the press, such as how many boyfriends she’d had, and her height in relation to Princess Margaret, Queen Elizabeth II’s glamorous sister). Discovering extraterrestrial life would indeed have been momentous. But short of that, pulsars were just about the most exciting thing they could have found. And useful too. In other words, the Universe’s perfect gift. ■

Up and away

A geopolitical crisis in the Middle East underlines the need for helium recycling in science.

The blockade of Qatar by its neighbours is a reminder of how the fragile geopolitics of the world’s helium supply leaves researchers vulnerable. But it doesn’t have to be this way.

Qatar is the second-largest supplier of liquefied helium, which scientists rely on to cool superconducting magnets inside nuclear magnetic resonance spectrometers, magnetic resonance imaging scanners, particle accelerators, and much else besides. Researchers now face price hikes, and, more importantly, could struggle to get their hands on the stuff at all. During shortages, science is far down the delivery list, because bigger customers get priority (see page 16). And without helium, scientists can be forced to reschedule or abandon experiments, and to place costly and complicated equipment in shutdown.

Other helium shortages have caused havoc for labs over the past two decades. Yet there is a simple way for researchers to both insulate themselves from supply shortages and save on their helium bills — a large chunk of running expenses in many labs.

The solution is to prevent millions of research dollars of liquid helium from literally and unnecessarily evaporating into thin air. Helium boils at just 4 kelvin, and during normal lab operations much inevitably evaporates, and is lost forever into the atmosphere (and onwards into space). But by capturing this vented gas, up to 95% of it can be reliquefied, stored and reused.

The recycling technology does not come cheaply — up-front capital investment starts at around US\$100,000 for a facility to supply even a small lab, and often costs several million dollars for larger facilities. So

recycling facilities tend to be found only in industry, large universities and national labs.

Yet even the most rudimentary calculations show how costs can be quickly recouped. The American Physical Society has helped to launch an interactive website that allows researchers to calculate whether recycling would make economic sense for them or their institutions. They should give it a spin. And then they should badger officials and administrators to get it done. As a rule of thumb, research centres using more than 30,000 litres of helium a year should be investing in small-scale reliquefiers. To not do so is folly, especially as political and public scrutiny of investment in science tightens.

Faced with supply cuts due to the Qatar blockade that will inevitably result in shortages around the world, researchers with recycling facilities feel deservedly smug that, with less of their lab helium going to waste and stocks out at the back, they are much better placed than non-recycling colleagues to see through the storm.

Research funders must step up. Stuart Brown, a physicist at the University of California, Los Angeles, testified at a congressional subcommittee hearing in Washington DC on 21 June that rising prices and unstable supplies are having a detrimental effect on research — leading, for example, to scientists hiring fewer staff in order to pay their helium bills, or abandoning altogether research areas that require liquid helium. And universities are sometimes even reluctant to hire faculty members whose work requires liquid helium, because of its high costs.

Brown called for legislation to provide support for researchers to invest in recycling. His case is difficult to fault. Recycling would save money in the long term, prevent the withering of helium-dependent research, and provide a much needed buffer against temporary shortages.

Otherwise, researchers and their funders may as well fill coloured balloons with their vented gas. Then at least we can all contemplate the spectacle of their research cash floating away. ■