therefore expected it to behave like one of these fragments — not too dissimilar from the comets that form on the outskirts of our own Solar System.

From the beginning, however, something was amiss. 'Oumuamua did not look like a comet and did not display the usual defining features of comets[2] — a tail and a fuzzy envelope called a coma, both made from gas and dust. Instead, it resembled an inactive object, like an asteroid, which moves mainly as a result of gravity. However, it soon became evident that the motion of 'Oumuamua was not exclusively due to gravity: it was being pushed along its path in a similar way to that routinely observed in comets, which are subject to an acceleration caused by the recoil of emitted gas and dust. How was it possible that this object looked inactive, but was showing indirect evidence of activity?

'Oumuamua was observed by most major observatories in the four months following its discovery, but after that, it quickly became too faint for even our most powerful telescopes. Astronomers were left with a large amount of data that needed to be tied together in a consistent model to describe the nature and composition of this unusual object. Such a model would have to reconcile the conflicting properties of 'Oumuamua's trajectory. Many models were proposed, some involving exotic compositions or origins[5]. Bergner and Seligman's paper offers perhaps the first simple and physically realistic explanation of the peculiarities of this object (Fig. 1).

The authors' basic idea echoes that of many previous attempts: it explains 'Oumuamua's acceleration as being a result of the object releasing gas from its surface — in this case, molecular hydrogen. But Bergner and Seligman's innovation is in how they explain the existence of such hydrogen. They assert that 'Oumuamua was born in its home planetary system as a normal, water-rich planetesimal, resembling a comet, and that it was constantly irradiated by galactic cosmic rays during its travel through interstellar space. The energetic particles in these rays caused the water molecules to dissociate and produce molecular hydrogen, which remained trapped in the water–ice matrix that makes up most of the object's body. Then, when 'Oumuamua approached the Sun, this ice changed its crystalline structure and released the trapped gas, propelling the object forwards.

Bergner and Seligman substantiate their claim by showing that there is enough ice under 'Oumuamua's surface — and that it can get hot enough — to release the hydrogen gas necessary to explain the observed acceleration. More importantly, their model does not require an amount of hydrogen that would be visible to astronomers on Earth, nor does it require the same of water, which might also be emitted by such a water-rich body. This explains how 'Oumuamua could have seemed inactive while emitting enough hydrogen to push it around.

The authors' proposal is compatible with our current understanding of how interstellar objects form, and doesn't assume that they contain any exotic material that is not present in comets that originate in the Solar System. At the same time, the idea that these foreign objects closely resemble our own comets leads to an obvious question: why don't we see similar non-gravitational forces acting on the thousands of comets we've observed so far in our Solar System?

Bergner and Seligman's explanation for this is simple: the mechanism they describe is a surface effect, in that heat from the Sun penetrates only a small layer close to the surface of the object. This means that, the larger the object, the less dominant the effect becomes. With a diameter of roughly 100 metres, 'Oumuamua is much smaller than normal comets, which are usually a few kilometres in size, so the surface effect is more pronounced in 'Oumuamua that it is in most observed comets.

If the authors' model is correct, however, we should expect the effects of their mechanism to be observed in comets that are similar in size to 'Oumuamua, but that originate in our own Solar System. We haven't yet spotted such objects, but the hope is that future telescopes will find them, and that instruments such as the James Webb Space Telescope will help us to investigate them in detail. Such discoveries would be welcome, given that 'Oumuamua is no longer observable. And, now that we know what to look for, we are a step closer to the key observations that can conclusively prove whether we finally understand the nature of this fascinating object.

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Synthetic biology

An antiviral molecular language barrier

Benjamin A. Blount

Bacteria with a synthetic genome were engineered to alter the way that the DNA code instructs cells to make proteins. This 'language barrier' serves to isolate the cells genetically, and makes them immune to viral infection. **See p.720**

As scientists gain an increasing ability to build synthetic genomes to specific design criteria, this is enabling the production of cells that have beneficial properties not found in the natural world. Nyerges *et al.*[1] report on page 720 that they have engineered bacteria to be immune to viral infections and to acquire properties that could be useful for microbial biocontainment. The work has implications for the development of safe and efficient applications in biotechnology, and is a compelling demonstration of the possibilities that are opened up by the use of synthetic genomes.

Unlike genome-engineering techniques in which an existing genome in living cells is modified, synthetic genomes can be designed and built from scratch. This means that the scale of changes to a genome, and consequently to a cell's behaviour, is no longer limited by the ability to edit existing DNA.

A functioning synthetic genome has previously been built[2] for the model bacterium *Escherichia coli*. A feature of this genome is a change to how the bacterium translates the information encoded by its DNA into proteins.

DNA determines the order and content of amino acids in a protein, and sequences of three DNA bases, termed codons, encode a given amino acid. This code is almost universally evolutionarily conserved across biology. To produce a protein, DNA-sequence information is copied into a corresponding messenger RNA. A transfer RNA (tRNA) recognizes each codon and then 'translates' it into a specific amino acid to be incorporated into a growing protein chain. There is redundancy

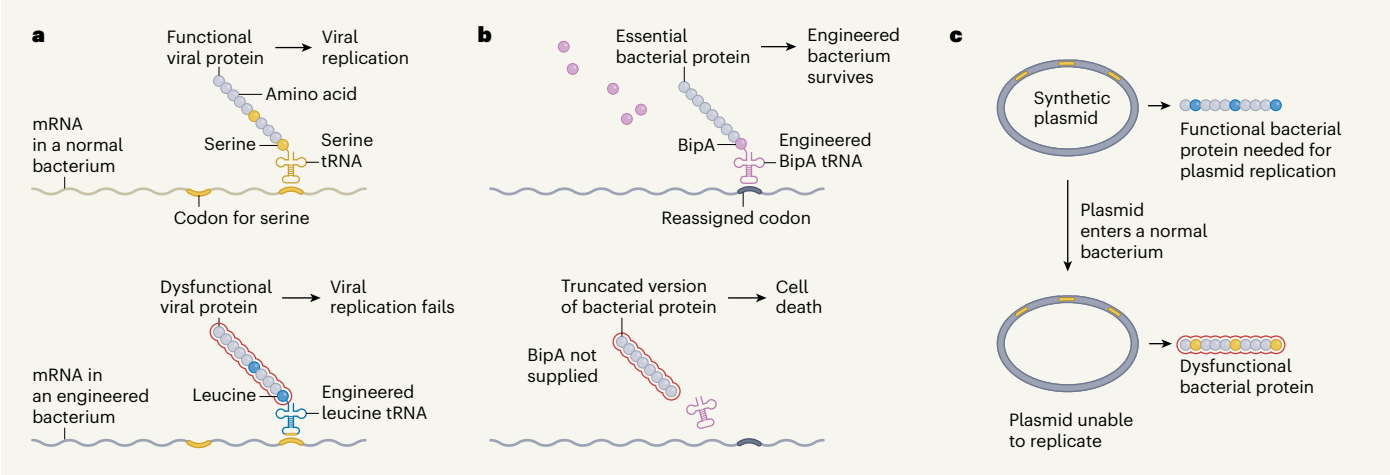

Figure 1 | Engineering bacteria to evade viral infection and to need human intervention for survival. a, Nyerges *et al.*[1] engineered a strain of the bacterium *Escherichia coli* containing a synthetic genome to change some aspects of how the microorganism's genetic code is recognized. Nucleotide sequences in messenger RNA (mRNA), called codons, are recognized by transfer RNA (tRNA) molecules that carry a particular amino acid, such as serine. Thus, the amino acid encoded by the mRNA is added during protein synthesis. When a virus invades a bacterium, it can hijack bacterial machinery to produce the viral proteins needed for replication. The authors used bacteria that lack certain codons for serine, and engineered the bacteria to have tRNAs that recognize the serine codons but carry the amino acid leucine. Viruses can't replicate in these cells because the abnormal leucine content disrupts viral proteins. **b**, The authors reassigned a codon in the engineered bacteria to be recognized by a tRNA that carries the artificial amino acid BipA. The mRNA for an essential bacterial protein contains this reassigned codon, and these bacteria need BipA to survive, offering a potential strategy for biocontainment. **c**, Nyerges *et al.* generated circular DNA molecules called plasmids that rely on the modified system for codon recognition used in the engineered bacteria. These plasmids could not replicate in *E. coli* that have a standard system for codon recognition, reducing the risk of synthetic DNA spreading in wild populations.

in this code, because most amino acids can be encoded by several codons. This makes it possible to swap equivalent codons, changing the DNA sequence while maintaining the amino-acid content.

By swapping codons on a genomic scale, the synthetic *E. coli* genome was designed to exclude all instances of three particular codons. Two of these normally encode the amino acid serine and the other instructs protein assembly to stop. The tRNAs responsible for translating these excluded codons can be removed from the cells or repurposed for a new function. This process of recoding a genome to change the way a cell interprets the DNA code has many implications, not least for how cells interact with viruses.

Viruses typically lack the resources for producing the proteins they need to make copies of themselves and to attack the host cell. Instead, they hijack the host's resources, including its pool of tRNAs. In this case, it would follow that, in synthetic cells in which some tRNAs have been removed from the genome, the viral genetic information wouldn't be translated properly, rendering the virus incompatible with the host. Previous work has indeed shown that cells that have synthetic genomes and have some tRNAs removed can evade infection when challenged with certain viruses[3].

Nyerges and colleagues identified viruses from environmental and wastewater samples that carry their own copies of tRNAs, and showed that these viruses did not rely on host tRNAs and could infect the recoded cells. To protect the engineered cells from this class of virus, Nyerges *et al.* developed tRNAs that changed the link between the DNA code and the protein content. These tRNAs recognize two of the codons removed from the synthetic genome. However, rather than translating them into the hydrophilic amino acid serine during protein assembly, as would normally occur for the universal genetic code, these tRNAs directed the incorporation of the hydrophobic amino acid leucine (Fig. 1a).

This change has consequences if any DNA sequences containing the codons corresponding to those recognized by these tRNAs are introduced into these cells. During protein synthesis, the resulting insertion of leucine, which has different chemical properties from those of serine, would probably alter a protein's structure and properties, inactivating it. These bacteria therefore speak a different 'language' from the rest of nature, including viruses.

Parallel work[4] by the team behind the *E. coli* synthetic genome has shown that this approach is sufficient to prevent infection by selected viruses that have their own tRNAs. Surprisingly, however, Nyerges *et al.* found that the viruses they had isolated could nevertheless infect and kill cells with the modified tRNAs. Further analysis of cells undergoing infection revealed that virally encoded tRNAs were produced at high levels, rapidly outnumbering the host tRNAs and leading to most of the viral proteins being properly assembled and functional.

Faced with this superiority of the viral tRNAs, the team decided to turn that strength back on the invading viruses by co-opting viral tRNAs and generating new versions of them to force a coding switch from serine to leucine. With these virus-derived alternative tRNAs, the engineered bacterial cells could drive the incorporation of the 'incorrect' amino acids into viral proteins. The problematic viruses, along with all other viruses tested, could not overcome this molecular language barrier and couldn't infect the engineered cells.

Crucially, the authors considered that bacteria with an engineered synthetic genome that grants such an unprecedented capacity to evade viral infection could have a competitive advantage over natural bacterial populations. The microorganisms might thus pose a serious challenge if accidentally released outside a controlled environment.

The authors therefore set about enhancing the biosecurity of the engineered strains by further exploiting the codon changes made to the synthetic genome. Building on some of their previous work[5], Nyerges and colleagues made the strains 'addicted' to a synthetic amino acid called L-4,4′-biphenylalanine (BipA). Cells were modified to recognize a repurposed codon as an instruction to incorporate BipA into a protein that the bacterial cells need to survive, thus limiting the microbes' growth to environments in which this non-natural molecule is supplied to them (Fig. 1b).

Finally, the authors demonstrated that the recoding strategies can be used to prevent the spread of synthetic DNA on sequences called mobile genetic elements. Microbes naturally exchange genetic information between cells in various ways, including by the transfer of circular DNA molecules called plasmids — elements

From the archive

Remembering a key advance in our understanding of the cell cycle, and a tale of perilous Antarctic exploration.

50 years ago

Stephen R. Pelc, who died suddenly ... at the age of 65, was internationally famous for his pioneer work on the techniques of autoradiography and for his use of these techniques in cellular biological research. ...[A]t the Hammersmith Hospital, London, ... he began his studies on the action of ionizing radiations on photographic film which led to his development of stripping-film autoradiography ... He is most famous for work begun in the early nineteen-fifties with Dr Alma Howard. By incorporating ^{32}P into dividing cells and removing all but the DNA by acid hydrolysis he was able to time the incorporation of ^{32}P into nuclear DNA. He showed that DNA synthesis did not occur after prophase, as had been believed previously from staining evidence, nor did it occur continuously throughout interphase. He and Howard showed that, for each type of nucleus, there was a particular period of interphase, which he called the "S" (synthesis) stage, during which the DNA content doubled; this DNA was stable and became divided equally into the two daughter nuclei. Before and after the "S" there was a gap in his knowledge of what metabolic processes occurred in the nuclei and, understandably, he named these "G_1" and "G_2".

From *Nature* 23 March 1973

100 years ago

The Worst Journey in the World: Antarctic, 1910–1913. By Apsley Cherry-Garrard — This is the sixth book to give the story, or part of the story, of Capt. Scott's last expedition, and it is in some ways the most remarkable of them all. Mr. Cherry-Garrard took part in three of the worst journeys ever made in the Antarctic or anywhere else, and the iron of his sufferings has entered into his soul and imparted a ferric quality to his recollections ... If poetry be indeed definable as "emotion recollected in tranquillity," Mr. Cherry-Garrard has given us a true epic of exploration.

From *Nature* 24 March 1923

that researchers use to transfer DNA into cells. The authors created a set of plasmids that use the modified codon language of the engineered cells to encode components required for plasmid replication in bacteria. These plasmids can function only in cells with a synthetic genome and engineered tRNAs, a scenario that strikingly reduces the risk of engineered DNA being unintentionally transferred to wild bacterial populations (Fig. 1c).

It currently takes a huge effort to establish a working synthetic genome, with only a handful completed so far. Our capabilities on this front are slowly scaling up, with a full synthetic genome for a eukaryotic cell (one that contains a nucleus) expected to be finalized in the next few years[6], and work towards a human synthetic genome project also under way[7]. As the number, size and ambition of synthetic-genome projects increases, so, too, will our ability to study and manipulate biology. The impressive feats achieved through codon repurposing in this work will be immensely valuable to bacterial biotechnology, in which viral contamination is a persistent and expensive problem.

The biggest impact of this work will probably be in providing a foundation for similar strategies in synthetic genomes for other organisms. Increasingly, key medical products, such as vaccines and protein therapeutics, depend on the use of mammalian or human cell-culture systems that are vulnerable to viral infection, with substantial implications for cost and product safety[8]. Controlled, reliable manufacturing processes that are protected from problems of viral infection will be crucial for maximizing these industries' positive impact on health and well-being, while ensuring that the processes are safe, contained and retain public confidence.

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Engineering

Hazards help autonomous cars to drive safely

Colin Paterson & Chiara Picardi

Collecting training data by focusing on dangerous scenarios offers an efficient way for artificial intelligence to improve the safety of autonomous vehicles. Augmented reality allows the approach to be tested without risking lives. **See p.620**

Every year, collisions involving road vehicles kill or seriously injure tens of thousands of people in the United Kingdom alone (see go.nature.com/3ekkex4). Autonomous vehicles could reduce these numbers, but their safety is yet to be guaranteed (see go.nature.com/3ykw43v). Identifying potentially hazardous situations and testing how an autonomous agent will react are crucial parts of the safety-assurance process. But people are not necessarily adept at recognizing situations that would be hazardous for non-human drivers because they do not register small changes in visual information that might confuse a machine. On page 620, Feng *et al.*[1] introduce a method that uses artificial intelligence (AI) to validate the AI of autonomous vehicles.

The challenge of thinking like a machine is not the only reason it is difficult to test situations that pose a hazard for autonomous vehicles. The first barrier is the sheer volume of data to assess. Human drivers in the United States are estimated to crash once every 850,000 kilometres. Autonomous vehicles currently fare even worse than this: a human operator has to take control of a self-driving vehicle around once every 80,000 kilometres to avoid a crash. However, this still amounts to a lot of safe driving between collisions, which means that searching for test cases is like looking for a needle in a haystack. Simply gathering more data is, therefore, unlikely to improve road safety.

The hazard itself also complicates the task of testing for safety. Trialling autonomous vehicles by placing real people in danger is out of the question, so instead researchers must examine data from a limited set of real-world