

dynamic phase diagram of possible behaviours of the filaments. Just how universal this diagram will be — whether it describes the behaviour of everything from flocks of birds to catalytic colloids — can be tested only by comparison to experiments on the many realizations of active matter. ■

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MICROBIOLOGY

Altruistic defence

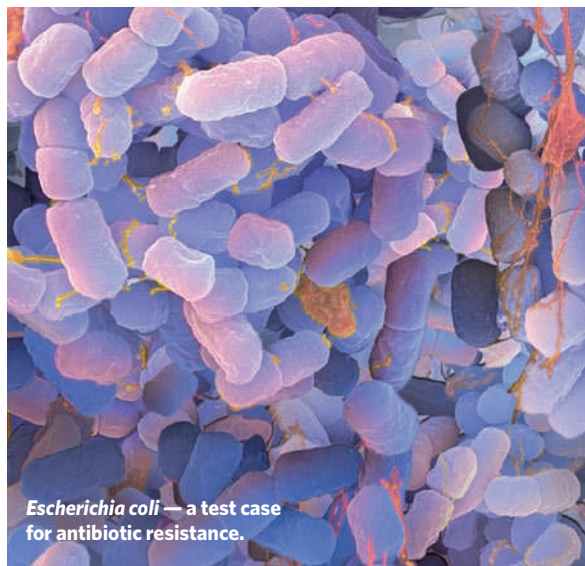
Hyun Youk and Alexander van Oudenaarden

A charitable deed by a few cells in a bacterial culture can help the rest of that population survive in the presence of antibiotics. This finding can aid further research into a major problem in public health.

Bacterial resistance to an antibiotic arises when mutations in the DNA of a few cells in a bacterial population enable them to fend off the harmful effects of the antibiotic. This gives such cells a selective growth advantage through, for example, being able to pump out the antibiotic faster than it can kill them. The mutant bacteria pass on the advantage to their daughter cells and to subsequent generations. Through such amplification, they can outgrow their non-resistant neighbours and eventually come to dominate the population, making an antibiotic generally ineffective. This, then, is the cause of the global challenge of widespread resistance to antibiotics¹.

On page 82 of this issue, Lee *et al.*² offer a new angle from which to view this picture, one that reveals collective action on the part of bacteria exposed to an antibiotic threat. The work highlights the importance of quantitatively understanding microbial population dynamics in developing the correct strategies for prescribing antibiotics for patients.

Imagine that a cell that developed resistance can help its non-resistant neighbours by, say, secreting some substance that assists those neighbours in fighting off an antibiotic. This type of behaviour might make it easier for the whole bacterial population to avoid extinction. From the point of view of the bacterial species as a whole, it would avoid the need to wait for the rare resistant mutant to come to dominate the population. It would also ensure that population-level genetic diversity is maintained.



Lee *et al.*² describe just such a charitable deed carried out by individual bacteria in a population of *Escherichia coli* subjected to an antibiotic. The authors show that mutations that develop in a few cells enable them to assist neighbouring cells that have not undergone resistance-conferring mutations. The actions of these few cells lead to a population-wide resistance. But they do so in a roundabout way that illustrates how antibiotic resistance can emerge from seemingly harmless and unrelated processes.

Lee *et al.* used the antibiotic norfloxacin, which targets a protein that is essential for DNA replication, and so for bacterial cell division and population growth. They studied how mutant cells within initially genetically

identical *E. coli* cells arise over time under the selective pressure imposed by the presence of norfloxacin in the growth media. When kept on media containing a moderate, not fully lethal, level of norfloxacin, the bacterial cells initially suffered from stunted growth. But within a couple of days, the overall population growth rate increased because the pool of cells had together become more resistant to the constant level of antibiotic.

The authors then increased the amount of norfloxacin, which slowed the overall population growth again. But within a couple of days the population developed resistance once more, and the growth rate recovered. This tug-of-war, presenting an ever-increasing challenge to the cells, was continued for ten days, at the end of which the population could withstand some five times higher levels of norfloxacin than it could initially. But that did not mean that every bacterial cell in the population had become resistant through mutations.

The novelty of Lee and colleagues' study² lies in their temporal characterization of the mechanisms responsible for resistance to norfloxacin in individual cells as they developed. The authors found that almost all of the resistant mutants were less effective at staving off the growth defect imposed by norfloxacin than

was the whole population from which they were isolated. In other words, when almost all of the isolated mutants were subjected to norfloxacin, their growth rate was lower than that of the overall population containing mixtures of both resistant and non-resistant cells. But a small minority, just one or two, of the isolated resistant mutants grew faster than the whole population when they alone were exposed to norfloxacin.

Lee *et al.* show that this is due to these few, highly resistant mutants producing a small molecule called indole, which readily diffuses into neighbouring cells and triggers molecular defence against norfloxacin. Notably, the mutations in these highly resistant mutants do not directly cause this altruistic behaviour. Indole is a molecule that is usually produced by the bacteria when antibiotic

is not present, but is shut down when it is. The authors demonstrate that the highly resistant mutants developed mutations that could help them survive in the presence of norfloxacin in the first few days as well as allow indole production to continue. This enabled them to assist their much less resistant neighbours in counteracting the antibiotic. Because the highly resistant mutants invest energy to produce indole, which is not required for their own resistance, their help for their kin can be considered a form of altruism. Lee *et al.* repeated their experiments with another antibiotic, gentamicin, and found that the bacterial response was the same (that is, it was not drug specific).

Research such as this — tracking how and

which mutations develop in the presence of an antibiotic by isolating individual cells from a bacterial population — is essential for optimizing a dynamic strategy for prescribing antibiotics. Such information can help in assessing the need for changes in the dosage and duration of treatments, for example. The approach also highlights the fact that interaction between different communities of resistant mutants that form in a bacterial population can enable them to mount a more formidable defence against antibiotics. Single-cell behaviour that is markedly different from that at the population level has been a subject of intense investigation in systems biology. Lee *et al.* provide another valuable example of such studies.

Furthermore, the collective behaviour of single-celled organisms — as seen in the phenomena of quorum sensing³ and metabolism

in a biofilm⁴, and now in antibiotic resistance — shows that a pool of microbes can act in concert. Apart from its implications for research in tackling antibiotic resistance, the new work² adds to previous studies in challenging the conventional definition of what constitutes a multicellular organism. ■

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ASTROPHYSICS

Unexpected warm water

Bengt Gustafsson

The detection of water vapour in a carbon star has challenged the understanding of ageing stars. The discovery that such water can be warm shows that our knowledge of these objects is still rudimentary.

In the short time since its launch on 14 May 2009, the European Space Agency's Herschel Space Observatory has delivered several astronomical discoveries in the infrared and submillimetre regions of the electromagnetic spectrum. On page 64 of this issue, Decin *et al.*¹ report yet another of Herschel's exciting findings: the detection of warm water vapour in the circumstellar envelope of the carbon star IRC +10216.

Carbon stars were first recognized in the 1860s by William Huggins and Angelo Secchi. On the basis of his purely visual inspection of spectroscopic observations, Secchi defined this new group of objects as class IV in his classification system of stellar spectra. These extremely red stars, he noted², were remarkably different from the orange stars of class III: "we cannot identify precisely the sources of the lines and the bands. We can say however that there is a marked analogy with the reversed spectrum of carbon." Further observations by Hermann Carl Vogel and Nils Dunér later strengthened his conclusion.

The distinctive spectral features that characterize carbon stars — notably the dominant spectral bands of carbon compounds, such as the C₂ Swan bands in the green part of the spectrum, and the lack of bands from oxides such as TiO and H₂O, which are characteristic of other types of cool star — is due to their atmospheres being richer in carbon than in oxygen, as was suggested by Charles Donald Shane³ and demonstrated by Henry Norris Russell⁴. If there is

more carbon than oxygen, oxygen is mostly bound to carbon in the form of carbon monoxide (CO) because the molecule has a high binding energy (11 electronvolts). As a result, little oxygen is left free to form other oxides in such stellar atmospheres, whereas carbon atoms are available to form other carbon compounds. By contrast, in normal stars such as the Sun, the atmosphere contains more oxygen than carbon and the opposite occurs: carbon-containing molecules other than CO become rare.

During the 1950s, investigators showed that a peculiar class of ageing red giant stars known as asymptotic giant branch (AGB) stars — to which carbon stars belong — have important roles in nucleosynthesis processes. For example, the heavy 's-elements' found in the Milky Way (so called because they are created by relatively slow, hence the 's', neutron capture by heavy atomic nuclei), as well as nitrogen and carbon⁵, are believed to be produced in AGB stars and later expelled into the interstellar medium. But the details of these processes have remained unclear: we still lack a complete understanding of key mechanisms, not least of those that drive the intensive winds from such stars.

There is therefore good reason to study carbon stars — not least, as we shall see, the Milky Way's pulsating star IRC +10216. This visually faint, extended object is, as seen by an observer on Earth, the brightest source outside the Solar System in the 5-micrometre waveband⁶. Radio observations have demonstrated that the optically thick, dusty shell that surrounds the star

is a rich source of complex molecules. More than 70 molecular species, which are characteristic of a carbon-rich chemistry, had already been detected there before the Herschel era⁷. In fact, about 50% of all molecules observed in astronomy have been detected in this object⁸.

Data from the IRAS infrared satellite have shown^{9,10} that about 4% of all Galactic carbon stars have signs of silicate grains in their expanding circumstellar envelopes. This suggested — contrary to what one would expect under thermal-equilibrium conditions and for well-mixed gas mixtures — that the gas envelopes of these carbon stars contain both oxygen-rich and carbon-rich material, thereby posing a challenge to the conventional understanding of the chemistry and evolution of ageing stars. One possible explanation for this astonishing observation is that the stars' evolutionary transition from an oxygen-rich to a carbon-rich phase occurred quite recently, so that the remains of previous epochs can still be traced in the stars' outer envelopes. The subsequent detection¹¹, with the SWAS submillimetre satellite, of circumstellar water vapour in IRC +10216 — a characteristic of oxygen-rich stars — has caused further astonishment.

This observation¹¹ was based on the identification of a single water-vapour spectral line of low excitation, which corresponds to a transition between two energy levels that are populated even at low temperatures. The fact that the line is a low-excitation one may suggest that the water vapour originates from the outer, cold regions of the stellar gas envelope. Another possibility is that the vapour arises from the vaporization of icy bodies, such as comets or minor planets, in orbit around the star^{11,12}.

In their study, Decin *et al.*¹ identify not just one but numerous water-vapour lines in the spectra of IRC +10216 (see Fig. 1 on page 65). However, many of these are high-excitation lines, which — if the water molecules are thermally excited — means that the temperature of the gas in which the lines are formed is of the order of 1,000 kelvin. These results point to the existence of warm water vapour in the inner regions of the stellar envelope, and seem to rule out models — including the vaporization-of-icy-bodies hypothesis — that posit that water vapour originates only from the stellar envelope's cooler intermediate and outer regions.

The strength of the newly discovered lines also goes against another hypothesis: that the existence of water vapour in the envelope's inner regions is due to shock waves that are induced by the star's pulsation and generate the non-thermal-equilibrium chemistry needed to form water in a carbon-rich gas. The authors¹ suggest, instead, that the non-thermal-equilibrium chemistry is the result of the penetration of ultraviolet photons into the inner regions of the envelope, possibly from the star but more likely from interstellar space. But for these hypotheses to work, a highly clumpy circumstellar envelope is required, so that enough of the ultraviolet radiation penetrates into its