

**Figure 1 | A two-pronged attack system.** Bacteria can attack target cells using cellular machinery called the type VI secretion system. Ahmad *et al.*<sup>2</sup> find that the type VI system of one bacterium, *Pseudomonas aeruginosa*, secretes a previously unknown toxin, which the authors name Tas1. Tas1 uses energy-carrying ATP molecules to produce the signalling molecule (p)ppApp, rapidly reducing ATP levels. In turn, (p)ppApp blocks production of ATP by inhibiting the first enzyme in the ATP-synthesis pathway, PurF. This two-pronged attack depletes target cells of essential ATP within minutes, causing death.

(ppApp) and adenosine pentaphosphate (pppApp) molecules. The authors therefore named the toxin type VI secretion effector (p)ppApp synthetase I, or Tas1 for short. This is the first example of an alarmone-producing enzyme being transported between bacteria – a remarkable fact, given that these enzymes are found in nearly all bacteria.

Type VI systems often secrete enzymes that destroy essential cellular structures, such as the cell wall, the cell membrane or the genome itself<sup>4</sup>. But Ahmad *et al.* found that the toxicity of Tas1 is linked to its synthesis of (p)ppApp from ATP (Fig. 1). ATP is crucial for almost every cellular process, from DNA replication to the production of proteins and maintenance of the cell's structural integrity. Tas1 synthesizes (p)ppApp from ATP strikingly quickly – one molecule of toxin produces 180,000 (p)ppApp molecules per minute. At such a rate, the toxin depletes the target cell of ATP within minutes, simultaneously disrupting several essential metabolic pathways. Of note, *P. aeruginosa* secretes other toxins alongside Tas1, some of which attack cellular structures that require ATP for their synthesis, including the cell wall and membrane. Tas1 activity might therefore compound the effects of these other toxins.

Ahmad and colleagues went on to highlight the toxic role of (p)ppApp in influencing bacterial physiology. Little has been reported about how (p)ppApp is produced and what it does in bacteria<sup>5</sup>. The authors found that (p)ppApp blocks ATP synthesis in the target cell by binding and inhibiting PurF, a key enzyme in the synthesizing process. Thus, (p)ppApp probably prevents the cell from regenerating ATP and so escaping the death spiral induced by the alarmone's own production. More work is needed to delineate how much this role for (p)ppApp contributes to the overall toxicity of Tas1 in target cells.

Alarmone production is highly regulated to ensure that the molecules are synthesized only when needed, and degraded when stress has passed. Tas1 production of (p)ppApp overrides

these rules – (p)ppApp is synthesized with abandon and, as the authors show, there are unlikely to be any enzymes that can degrade (p)ppApp quickly enough to avoid cell death. Nonetheless, this newfound understanding of (p)ppApp can augment our knowledge of other alarmones. (p)ppGpp, which is structurally similar to (p)ppApp, controls cell growth in part by inhibiting proteins involved in the synthesis of energy-carrying molecules such as ATP and GTP<sup>3,6–8</sup>, including PurF. The fact that both (p)ppApp and (p)ppGpp inhibit this protein, along with the structural similarity between the two alarmones, led Ahmad *et al.* to hypothesize that the molecules could have many overlapping targets.

Tas1 is the only dedicated (p)ppApp-synthesizing enzyme found so far. However, (p)ppApp has been detected in some bacteria, in which its physiological role has yet to be determined<sup>8</sup>. Clearly, it is unlikely to act as

a toxin in these cells. Ahmad and colleagues' discovery that (p)ppApp inhibits PurF is the first step towards mapping the network of targets regulated by this alarmone in healthy cells. Doing so should help us to gain a broader understanding of how alarmone regulatory pathways rewire bacterial physiology.

Type VI secretion systems provide bacteria with weapons against competitors, increasing their ability to thrive in a range of environments – from plants to the human intestinal tract to hospitals<sup>9,10</sup>. The discovery of a toxin that so irreversibly suppresses competitor metabolism opens a new chapter in our understanding of the ammunition used in interbacterial warfare. It will be exciting to see whether other examples of this toxin are found across the bacterial domain, or perhaps even in bacterium–host interactions.

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Solid-state physics

# Surface polarization feels the heat

Gustau Catalan & Beatriz Noheda

A crystal's surface has been found to behave as a distinct material that has temperature-dependent electrical polarization – despite the rest of the crystal being non-polar.

When crystals of certain materials are squeezed, the compression causes a separation of internal charge – a polarization – that generates a voltage. This phenomenon is known as piezoelectricity. Some piezoelectric materials also exhibit spontaneous polarization that changes in magnitude with

increasing temperature. These materials are said to be pyroelectric, and are useful in heat sensors and for solid-state cooling (because pyroelectrics change temperature in an applied electric field)<sup>1</sup>. Pyroelectrics have thus been intensively investigated, with research naturally focusing on electrically

polar materials. Writing in *Advanced Materials*, however, Meirzadeh *et al.*<sup>2</sup> report that the non-polar material strontium titanate (SrTiO<sub>3</sub>) is also pyroelectric, suggesting that the net needs to be cast more widely in the search for pyroelectrics.

Conventional piezo- and pyroelectricity ultimately arise from the fact that the repeating unit (the unit cell) of the crystal lattice is asymmetrical. A perfect, infinite crystal of strontium titanate is symmetrical and therefore should not be pyroelectric. But perfection, alas, does not exist. Many crystals contain defects whose concentration varies across the crystal; the resulting concentration gradient breaks the macroscopic symmetry of the crystal, causing residual piezoelectricity and pyroelectricity<sup>3</sup>.

Moreover, even the most perfect crystals are finite, which means that they inevitably have one kind of ‘defect’: surfaces. And surfaces break symmetry, because what is above the surface is different from what is below. Hence, irrespective of the intrinsic symmetry of the bulk, surfaces can, in theory, be polar and even pyroelectric. This seems to be the case for strontium titanate, a cubic crystal commonly used as a substrate for growing films of other oxides.

Determining whether pyroelectricity comes from the surface, rather than from inside a crystal, is not trivial. Meirzadeh and co-workers did so by heating the surface of strontium titanate with fast laser pulses, and measuring how the resulting pyroelectric current evolves with time (Fig. 1). The rate at which the current decays is related to the rate at which the surface reaches thermal

equilibrium, a process called thermalization: fast decay of the current implies quick thermalization and therefore suggests that the depth of the pyroelectric region is shallow.

From the time-dependence of the signal, the authors estimate that the depth of the polarized layer in strontium titanate is about 1.2 nanometres, equivalent to 3 unit cells. This coincides with an intrinsic region of polar distortion that has been predicted by first-principles calculations to form at the surface of strontium titanate as a result of surface tension<sup>2,4</sup>. Therefore, the pyroelectricity seems to arise from an inherent surface distortion.

The authors took precautions to discard alternative explanations: they checked that the direction of the heat-induced current does not depend on the orientation of the crystal, ruling out a bulk effect; and that the local heating produced by the laser is very small (the temperature increases are at the sub-kelvin scale), which means that the strain gradients induced by thermal expansion are insignificant. Other experiments and data analysis were carried out to exclude the possibility that the induced current is due to molecules (typically water) adsorbed to the surface, charges trapped by lattice defects, excitation of free electrons induced by light, or the thermoelectric Seebeck effect (which generates currents in semiconductors that contain temperature gradients). Importantly, the pyroelectricity disappeared when Meirzadeh *et al.* deposited an atomically thin layer of amorphous silica (SiO<sub>2</sub>) on top of the strontium titanate, consistent with the idea that the phenomenon originates at the surface.

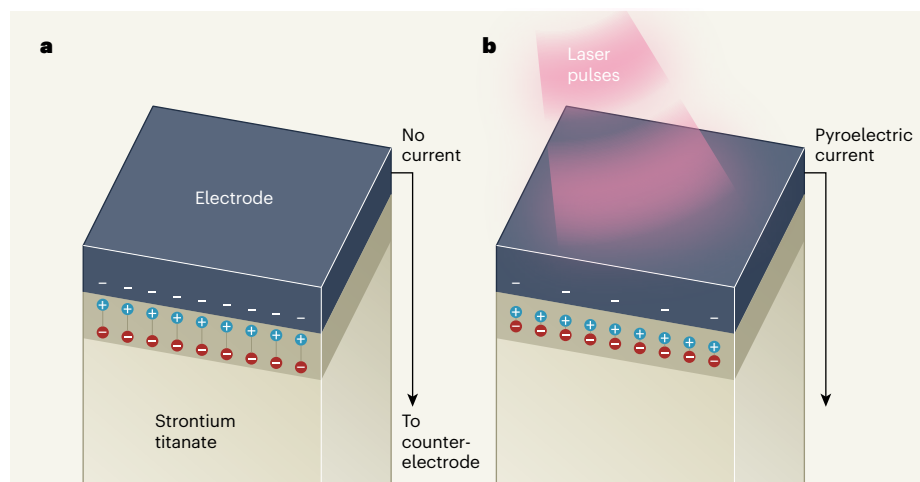
Moreover, the temperature dependence of the surface polarization suggests that a phase transition occurs that is not observed in the bulk. This is interesting, because it implies that the pyroelectricity does not simply arise from thermal expansion of the piezoelectric surface<sup>5</sup>, but from a true phase transition confined to the surface.

Surface layers of crystals known as skin layers, which have different properties from those of the bulk, are found in various materials<sup>6,7</sup>, including strontium titanate<sup>8</sup>. However, such skin layers tend to be much thicker than the atomically thin one described by Meirzadeh and colleagues, and are probably induced by defects introduced during polishing, rather than being intrinsic. Rearrangements of surface atoms in strontium titanate have also previously been reported<sup>9</sup>, but it has not been established whether the resulting surfaces are pyroelectric. Meirzadeh and colleagues’ findings are therefore new.

This discovery matters for many reasons. One is pointed out by the authors: multilayered thin-film devices could be designed to take advantage of the surface polarization at the interface between each layer<sup>10,11</sup>. There are also consequences for bulk crystals. When a crystal of any symmetry is bent, it can become electrically polarized as a result of strain being produced non-uniformly in the material – a phenomenon called flexoelectricity. If the surfaces are already polar, then the surface polarization will also contribute to the total flexoelectricity<sup>12,13</sup>. In fact, the surface termination of a strontium titanate crystal (that is, whether the last atomic layer is TiO<sub>2</sub> or SrO) can theoretically change the sign of the flexoelectric voltage – even for macroscopic crystals<sup>14</sup>.

Surfaces are also interesting in themselves, being 2D entities in a 3D world. If a pyroelectric phase transition does occur in the surface of strontium titanate, it would offer an excellent playground for testing models of the effects of dimensionality on phase transitions in general, because of the universality of the laws that underpin such transitions<sup>15</sup>. It will also be interesting to study the nature of the dipoles that form at surfaces and, specifically, whether their orientation can be switched by an applied voltage – in other words, whether the surface of strontium titanate is not just a 2D pyroelectric but also a 2D ferroelectric.

Electrical polarity might not be the only surprising thing about the surface of strontium titanate. Although this material is an insulator, its surface conducts electricity<sup>16</sup>. The surface might therefore be a polar metal: an exotic type of metal that contains electric dipoles<sup>17,18</sup>. Polar metals have been much sought after, partly out of fundamental curiosity (polar materials are normally insulators



**Figure 1 | Pyroelectricity at the surface of strontium titanate.** Meirzadeh *et al.*<sup>2</sup> report that the surface of crystals of strontium titanate undergoes temperature-dependent changes of electrical polarization – a phenomenon known as pyroelectricity. **a**, In the authors’ experiments, the surface layers (darker tint) have an initial amount of intrinsic polarization, which is balanced (screened) by free charges in an overlying electrode. **b**, Laser light heats up the surface and lowers the polarization (reduces the distance between charges in the dipoles). This causes a current to flow, to balance out the modified polarization. The current disappears once the temperature stabilizes; the time taken for this to happen carries information about the time taken to reach thermal equilibrium, which is proportional to the volume of pyroelectric material. The authors thus find that the volume is very small, consistent with a thin surface layer.

or, at most, semiconductors), but also because they are expected to have unique electronic properties<sup>19</sup>. Meirzadeh and colleagues' findings hint that polar metals might have been under our noses all along, paradoxically on the surfaces of non-polar insulators.

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## Evolution

# The balancing act of growth and expansion

Henry Mattingly & Thierry Emonet

Bacteria move along gradients of chemical attractants. Two studies find that, in nutrient-rich environments, bacteria can grow rapidly by following a non-nutritious attractant – but expanding too fast leaves them vulnerable. **See p.658 & p.664**

Bacteria can sense chemical attractants and use that information to navigate towards resources or away from harm – a process called chemotaxis. But why bacteria chase signals that often do not have much nutritional value has been a long-standing puzzle. Cremer *et al.*<sup>1</sup> show on page 658 that bacterial populations can use non-nutritious attractants as cues for rapidly expanding through nutrient-rich areas, ensuring that plentiful nutrients are available for their future growth. And on page 664, Liu *et al.*<sup>2</sup> build on this work to reveal an unanticipated rule of bacterial evolution: the safest way for a bacterial population to colonize a habitat is not necessarily to expand as fast as possible, because rapid expansion can leave the population vulnerable to invasion by competitors.

In the 1960s, the biochemist Julius Adler demonstrated that a group of cells consuming a chemical attractant can form a rapidly expanding wave that follows a moving concentration gradient that the cells create on their own<sup>3</sup>. That is, by consuming the attractant in their immediate vicinity, the cells create a gradient between their current location and the

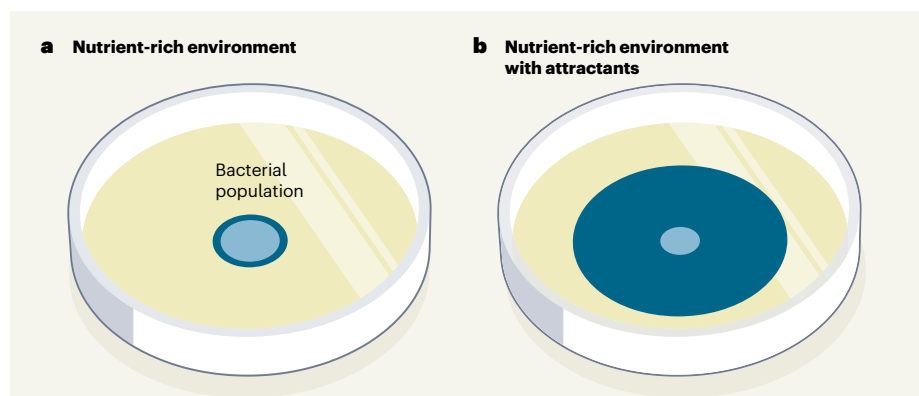
surrounding regions in which the chemical has not yet been consumed. The cells then chase the higher concentration – rather like a horse chasing a carrot on a stick. The wave's

expansion speed is determined by how fast the travelling cells deplete the local attractant<sup>4</sup>.

Cremer *et al.* examined how a cell population's use of chemotaxis to expand (defined as the occupation of more space), as in Adler's experiments, affects its growth (the increase in cell numbers). The authors seeded small colonies of bacteria in a Petri dish, and measured population size over time as the cells grew and filled the available space. As Adler had observed, the colonies formed expanding waves, and some cells fell behind the wavefront, seeding the newly covered ground.

Importantly, when Cremer and colleagues added small amounts of a non-nutritious chemical attractant that was different from the nutrient on which the cells were growing, the population capitalized on chemotaxis to expand before the local nutrient had become depleted. This increased the number of cells that had access to nutrients at a given time and allowed the population to grow much faster than it did without the directional cue of the attractant (Fig. 1). This gain relied on a separation between chemotaxis and growth: the attractant served as a cue, rather than as a nutrient source<sup>5</sup>, to direct the cells towards unoccupied territory. When the attractant is the only nutrient, the population does not grow as fast; either the attractant is abundant, and the cells can't consume it fast enough for rapid expansion, or the attractant is limited, and expansion can be fast but the settlers behind the wavefront are starved and don't grow.

This work demonstrates that – in a nutrient-rich environment – the faster a single population expands, the faster it grows. But what happens when competitors (including spontaneously generated mutants in the population) expand into the same territory? Last year, we and our colleagues<sup>6</sup> showed that bacteria with different chemotactic abilities



**Figure 1 | How bacteria maximize growth in nutrient-rich environments.** **a**, Populations of bacteria can spread out within a nutrient-rich habitat through cell division and random motion. But this approach causes most of the population to stay in a small location and deplete local nutrients – so, many cells starve (light blue) and only the outer edge grows (dark blue). **b**, Cremer *et al.*<sup>1</sup> grew bacteria in the same environment but included low levels of a non-nutritious attractant chemical (not shown). The cells chased the attractant through a process called chemotaxis, expanding rapidly across the dish before the local nutrients were depleted, so that most of the population had the nutrients needed to grow.