

pathway and AKT/PKB, which are known to be involved in E-cadherin-mediated cell–cell recognition<sup>10</sup>.

Given that TrkB enables cells to survive when homeless, and thus to metastasize, might blocking this protein be an effective anticancer treatment? Perhaps, but we should be realistic about this expectation. Tumour cells can survive by means of an autostimulatory (autocrine) signalling loop, such as that mediated by TrkB and BDNF, or through a paracrine cross-communication with their environment (Fig. 1). Such cross-talk might use the same molecules: for example, BDNF is produced by the cells that line blood vessels, and production is enhanced by low oxygen conditions<sup>11</sup>; these events could promote the survival of both tumour cells and newly formed blood vessels, in the primary tumour or at a metastatic site. But there are other molecules involved in paracrine signalling, and we should be prepared for the possibility that strategies that target TrkB could be thwarted through these channels.

Homelessness is only one of a multitude of environmental stresses that can befall a cell. One way to overcome such problems is to seek a new and more salubrious location. Thus cells frequently need to migrate in order to survive. For instance, yeast that are poorly nourished extend migratory strands (hyphae) to seek better conditions. Similarly, slime-mould colonies that are deprived of nutrients send out scouts. And cancer cells, faced with a shortage of oxygen, hormones or nutrients, or with overcrowding, might survive by metastasizing — invading local tissue, entering the lymph and blood streams, exiting the circulation at a distant site, and, finally, establishing a secondary colony.

Avoiding death in a harsh or foreign environment seems to be a basic requirement for all types of nomadic behaviour. A mechanism such as that described by Douma *et al.*<sup>3</sup>, which promotes both survival and migration, would give tumour cells (and new blood vessels) a significant advantage. It might even be essential for tumour cells to pass the fitness test for metastasis.

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Materials science

# Silicon carbide in contention

Roland Madar

Silicon carbide is a highly desirable material for high-power electronic devices — more desirable even than silicon. And now the problem of producing large, pure wafers of the carbide could be solved.

After a period of intense scientific and industrial development, the semiconductor silicon carbide (SiC) is at last proving capable of outperforming silicon in electronic devices for high-power, high-frequency and high-temperature applications. Its potential as a replacement for silicon has been known since the 1950s, but its late emergence is principally due to the difficulty of growing large SiC crystals of sufficient quality. That difficulty is set to evaporate, thanks to the crystal-growing process introduced by Nakamura *et al.*<sup>1</sup> on page 1009 of this issue.

A major problem encountered in growing crystals of SiC is that the material doesn't have a liquid form. This means that the traditional methods of crystal growth developed for silicon and other semiconductors, based on controlled solidification from the liquid phase, cannot be used for SiC. However, the invention in 1978 of the 'modified Lely method'<sup>2</sup> (or physical vapour transport, PVT) opened the way to the production of large-area SiC wafers. This is a seeded sublimation technique: supersaturated SiC vapour condenses onto a single crystal seed inside a graphite crucible. Impressive progress has been made, but the quality of the SiC grown in this way is still too poor and remains an obstacle to be overcome if SiC technology is to make a commercial breakthrough. Improving the structural properties and at the same time increasing the size of SiC wafers that can be grown are key areas of research in this field.

As well as the classic defects, such as different kinds of dislocation, that are common

to most materials, SiC wafers produced by PVT tend to have some peculiar defects of their own. Known as 'micropipes', these defects are a consequence of the crystal structure of SiC and profoundly affect the reliability of electronic devices based on this material. The basic unit of the crystal structure is a silicon–carbon bilayer; within each bilayer, carbon atoms are arranged in a two-dimensional hexagonal pattern, with silicon atoms directly on top of them. Three-dimensional lattices are then built by stacking the bilayers along the normal direction, called the *c*-axis, of the hexagonal structure, and a surface polarity effect results, with one face of the crystal formed of silicon atoms and the other of carbon atoms (Fig. 1). In fact, several crystal structures, or polytypes, are possible — all described in terms of stacked hexagonal layers, but with different rotational offsets between the layers. Micropipes are

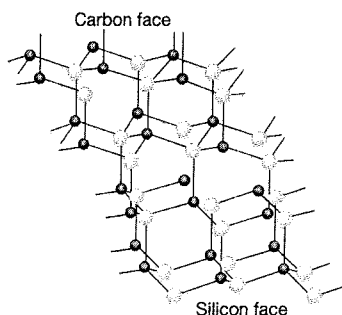


Figure 1 The structure of silicon carbide. The three-dimensional lattice is composed of hexagonally patterned bilayers of carbon (black) and silicon (white) in this 4H polytype. The termination of the crystal structure at a surface results in a face of carbon atoms or of silicon atoms.

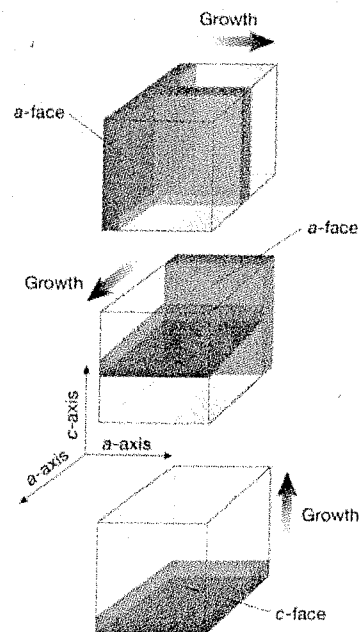


Figure 2 The repeated *a*-face growth process. In the first stage, silicon carbide (SiC) is grown on the *a*-face of a seed crystal. A segment of the newly grown crystal then becomes the *a*-face seed of the next growth stage. A slice of that growth seeds the final stage, but now the new crystal is grown on the *c*-face. The inventors of the process, Nakamura *et al.*<sup>1</sup>, say that repeating the step of *a*-face growth before the more usual *c*-face stage eliminates faults in the resulting crystal.

hexagonal tube-like cavities, with diameters in the sub-micrometre to few-micrometre range, that develop parallel to the *c*-axis of the hexagonal structure (which is the common direction of crystal growth). They are the most harmful defects in SiC.

Intensive work on various aspects of the PVT growth technique — reactor design, growth conditions, seed orientation and surface preparation — has led to a considerable reduction in the number of these defects in SiC ingots and wafers. The best commercially available 3-inch-diameter wafers (of the 4H polytype) have micropipe densities of  $10\text{--}100\text{ cm}^{-2}$  and dislocation densities of  $10^3\text{--}10^4\text{ cm}^{-2}$ . This quality of crystal is good enough for use in some commercial SiC devices, such as Schottky diodes<sup>3</sup>, but not for others. For instance, in high-power bipolar devices, there is a degradation in the material's electrical properties that seems to be related to the development of extended stacking faults, originating from in-plane dislocations in the SiC (ref. 4).

So reducing the density of dislocations in an SiC wafer, and in the epitaxial layer on top of it that forms the active part of the device, is an absolute necessity for the development of high-power SiC technology. Nakamura *et al.*<sup>1</sup> have succeeded: their new process produces SiC crystals with a dramatically lower dislocation density — although, perversely, the first step of the process actually creates a high density of stacking faults.

Most SiC crystals are grown on the *c*-faces

(perpendicular to the *c*-axis) of other crystals. In fact, it has already been shown that growing SiC crystals on surfaces with a different crystal orientation — the *a*-faces — fully suppresses the formation of micropipes. However, crystals made in this way are affected by basal-plane stacking faults. Nevertheless, Nakamura *et al.* started with a SiC single crystal that had been grown on an *a*-face, inheriting a high density of dislocations from its seed crystal. Then, taking a section of the crystal along the *a*-axis of that face, they allowed the crystal to develop on the other *a*-face (Fig. 2), afterwards continuing with classic growth on the *c*-face. Nakamura *et al.* call this the repeated *a*-face (RAF) growth process. It is the repetition of the *a*-face step that ensures that stacking faults are eliminated and dislocations suppressed. The ingots of SiC produced are, say the authors, “virtually dislocation-free”.

These results are spectacular: the RAF process is a major innovation in materials science. Silicon carbide has become, at last, a contender for silicon's crown. ■

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## Social evolution

# Kinship is relative

David C. Queller

Kinship fosters the evolution of cooperation. However, a once-heretical theory and an unconventional social organism show that the cooperation-enhancing effect of kinship is sometimes negated.

As evolutionary biologist W. D. Hamilton showed more than 40 years ago, selfish genes can lead to cooperation and altruism<sup>1</sup>. A gene can spread by helping other individuals that carry copies of the gene. This extension of individual selection, called kin selection, works best with the recognition of close relatives, but Hamilton also thought that if the dispersal of individuals is limited, this might build up enough local genetic similarity to favour a less targeted kind of altruism towards neighbours in general. Because local dispersal is very common, this mechanism might greatly expand the range of cooperation in nature. However, later models<sup>2–4</sup> suggest that this is not necessarily so: when limited dispersal makes neighbours close relatives, it also makes them close competitors, and this can negate the effect of kinship. On page 1024

of this issue<sup>5</sup>, Griffin and colleagues provide the first experimental test of this effect, confirming that both kinship and the scale of competition matter.

The study is part of a growing trend towards using microorganisms to study social evolution<sup>6</sup>. Sociobiologists have been slow to recognize that microorganisms have social interactions worthy of study. However, any reader of John Bonner's work on cellular slime moulds<sup>7</sup> will realize that these single-celled amoebae interact in interesting ways; some give up their lives to form a stalk that furthers the dispersal of others. Analogous behaviour occurs in Myxobacteria<sup>8</sup>. And interesting behaviour is not limited to the exotica of the microbial world; the old laboratory workhorse *Escherichia coli* has strains that aid their own type by wielding poison-antidote systems to destroy other

strains that lack the same system<sup>9</sup>. Perhaps the most common form of microbial cooperation is the secretion of substances outside the cell to do various kinds of work, such as digestion. The work provides a public good, in which the benefits are available not just to the secretor, but to anyone in the neighbourhood. This puts individuals into a social bind. Why work to help others when you can be lazy and freeloader off your neighbours? The obvious answer is kin selection. If your effort helps others with the same genes, it is not wasted.

Once it is recognized that microbes have interesting social behaviour, two clear advantages can be exploited. First, many microbes are well understood biochemically and genetically. Second, it is easy to manipulate entire populations of microbes over space and to select them over time. Griffin *et al.*<sup>5</sup> made full use of these advantages in their study of a freeloading mutant of the bacterium *Pseudomonas aeruginosa*. This ‘cheater’ mutant is deficient in production of a public benefit called siderophores. Siderophores are synthesized and excreted in response to iron deficiency. They then bind iron, making it available for uptake — either by the secretor or by its neighbours. The mutant saves on the cost of producing siderophores but can still obtain iron if it has secretor neighbours.

Griffin *et al.* selected populations, starting with equal numbers of cheaters and secretors, over six cycles of group interaction, each lasting about seven generations (Fig. 1, overleaf). In natural populations with limited dispersal, neighbours tend to be both relatives and competitors, but Griffin *et al.* were able to vary the relatedness and scale of competition independently. High or low relatedness was imposed by allowing bacteria to grow and interact in groups derived from a single bacterium (a cheater or a secretor) or from two bacteria (initially in a ratio of one cheater to one secretor), respectively. The scale of competition was manipulated during the transfers to form each next cycle of groups. Global competition was allowed by mixing the groups and then choosing random individuals to start the next cycle. The more productive groups thus contributed more to the next cycle. Local competition was imposed by taking an equal number of individuals from each group, without mixing between the cycles. Crossing the relatedness and competition treatments yields a simple two-by-two design that permits the study of both factors and their interaction.

As expected, at the end of the experiment the high-relatedness treatments yielded higher frequencies of the cooperative secretors than the low-relatedness treatments, demonstrating the importance of kinship in the evolution of cooperation. But the greater novelty of the study comes from another theory-