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The New Diamond Age?

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append additional regulatory input. Indeed, previous work indicated that modified scaffolds can alter the flow of signaling between alternate pathways (*8*, *9*). Bashor *et al.* build on these past efforts in a comprehensive and systematic way, generating multiple new layers of control over signaling dynamics.

The authors use heterodimerizing protein interaction motifs called leucine zippers to recruit to the scaffold protein additional positive or negative modulators of pathway signaling. Alone, recruitment of these modulators simply enhances or dampens signaling. To generate more sophisticated behaviors, however, the timing of their recruitment was varied in two ways: by expressing modulators from promoters that themselves are regulated by the signaling pathway, thus generating feedback loops, and by forcing the modulators to compete for access to the scaffold with nonfunctional "decoy" molecules, thus generating delayed action. Different permutations of these variables yielded different effects on either temporal or dose-response behaviors. For example, if expression of the negative modulator is induced by the pathway, but must first saturate a constant number of high-affinity decoy binding sites before it can bind to the scaffold, the pathway is converted from one that shows sustained activation to one that shows a "pulse" of activation followed by a sharp decline (see the figure). A reciprocal arrangement, in which a preexisting negative modulator must be displaced by a decoy protein whose expression is induced by the signaling pathway itself, causes the response to be delayed, rather than immediate. Yet another configuration alters the dose dependence of the pathway, converting it from a graded, rheostat-like response to a sharply sensitive, switchlike response. A related recent study using the same system showed that by expressing pathway components from a promoter that is itself regulated by the same signaling pathway, a positive-feedback loop can be established that maintains signaling even after the stimulus is removed, thus converting the pathway from reversible to irreversible (*10*).

The results of such tinkering illustrate several points. They test whether our concepts about signaling mechanisms are correct. Indeed, the observed results clearly emphasize how colocalization of signaling proteins can play a critical role in shaping pathway behavior. In addition, the observed variations in signaling behavior mimic those in nature (e.g., transient versus sustained, or graded versus switchlike) and, hence, suggest how they could have arisen by evolutionary swapping of promoters or protein-binding sites. The results also show that signaling dynamics can be successfully reengineered by using rational approaches.

One goal of synthetic biology is to establish a set of standard biological parts that can be connected in multiple combinations to accomplish various objectives (*3*). Although some tools developed by Bashor *et al.* may seem pathway specific, it is conceivable that the entire signaling cascade, along with the modifications that confer specific circuit behaviors, might serve as a transferable module that can be connected to different inputs and outputs. Indeed, because a primary output of this pathway is the regulation of gene expression, essentially any gene can be placed under pathway control by simply providing it with the proper promoter. Furthermore, the activating stimulus can be altered either by additional changes to the scaffold (*8*, *9*) or by replacing the upstream receptor of the stimulus (*11*). Therefore, future engineers might potentially generate an extraordinary variety of signaling circuits by mixing and matching one choice from each category: an input, an output, and a signal-processing module. The broad lesson of the modular approach is that complex behaviors do not necessarily require highly evolved proteins, but can be developed from the gradual layering of regulators and connections. These early studies are just the tip of the iceberg in what is likely to become a rapidly accelerating field.

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MATERIALS SCIENCE

The New Diamond Age?

Paul W. May

After the hype, what realistic applications might synthetic diamond films have in the near future?

Diamonds were prized for their scarcity for centuries, and they remain a symbol of wealth and prestige to this day. Apart from their appeal as gemstones, diamonds have remarkable physical properties. Diamond is the hardest known material, has the highest thermal conductivity at room temperature, is transparent over a wide range of wavelengths, is the stiffest and least compressible material, and is inert to most chemical reagents. It is thus not surprising that diamond has been referred to as the ultimate engineering material. Here I highlight some of the exciting new areas where the use of artificial diamond in the form of thin films or coatings may find realistic wide-scale applications in the next few years.

Artificial diamond was first fabricated in the laboratory in the 1950s by the high-pressure, high-temperature growth technique. This method has been used to produce small synthetic diamond crystals, which are used for industrial processes such as cutting and machining mechanical components and for polishing and grinding of optics.

In the late 1980s, a new method of making diamond was developed (*1*). In the chemical vapor deposition (CVD) method, a gas-phase chemical reaction above a solid surface results in deposition onto that surface. For diamond, the process gas is usually a mixture of 99% H_2 and 1% CH_4, activated by a hot (2000°C) metal filament or a microwave plasma. A substrate temperature above 700°C ensures formation of diamond rather than amorphous carbon. Apart from diamond itself, the most common substrate material is silicon; researchers now regularly grow polycrystalline diamond films to thicknesses from micrometers to millimeters on standard Si wafers. Adding a boron-containing gas to the process mixture allows the diamond film to become boron-doped, giving it controllable p-type semiconducting properties.

In the early 1990s, the rapid progress in this field led to speculation that diamond would become the next-generation ideal semiconductor and spark a new "diamond age" for electronics and mechanical components. This technological promise has not yet been realized. Was it all just hype? And what are the realistic applications for CVD diamond in the short to middle term?

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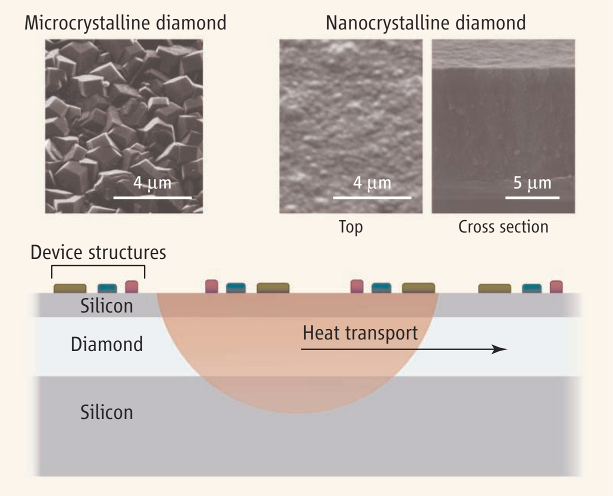

The next generation of integrated circuits? In Si-diamond-Si sandwich structures, the heat generated by the devices (red semicircle) diffuses into the diamond layer, which rapidly transports the heat to a heat sink at the chip edge, preventing overheating. The diamond layer may be microcrystalline diamond (**top left**), which must be polished before use, or nanocrystalline diamond [shown in top view (**top middle**) and cross section (**top right**), with film thickness 10 μm], which conducts heat less well but does not require polishing.

Some of the major problems associated with diamond CVD have now been solved, but many hurdles remain. First, it is difficult to make large-area, single-crystal diamond substrates. Most CVD diamond films are polycrystalline, and the presence of graphitic material at the grain boundaries between the diamond crystallites degrades the material properties. Second, diamond films grow at a rate of only a few micrometers per hour; unless methods are found to speed up growth by a factor of 10 or more, diamond films will remain prohibitively expensive.

Third, the high deposition temperature severely limits the substrates on which diamond can be deposited. Ultra-nanocrystalline diamond with grain diameters below 10 nm can be grown at 400°C (*2*), but most CVD diamond requires temperatures above 700°C. Thus, low-melting-point materials such as glass, plastics, and aluminum are difficult, if not impossible, to coat with diamond by standard CVD methods. Ferrous materials are also problematic, because carbon is highly soluble in iron at these temperatures.

Fourth, doping diamond to make a viable n-type semiconducting material has proved elusive. Phosphorus has been used as a dopant, but the electronic characteristics are not good enough for most devices (*3*). Without an n-type material, diamond electronics will be limited to simple p-type devices such as sensors and detectors. Even if a suitable n-type dopant were discovered, it is doubtful that the resulting material would have high enough carrier mobilities to rival high-performance room-temperature electronics made with silicon. However, for high-power, high-temperature electronics, the properties of diamond reign supreme. High-value specialized applications such as sensors in car or jet engines where temperatures can be above 300°C, or fast high-power switches for train doors or heavy machinery, are areas where diamond may have a substantial impact on the market.

Despite the problems mentioned above, thin, polycrystalline diamond films currently find small-scale specialized applications. They are, for example, used as hard and wear-resistant coatings, cold cathode sources, heat spreaders, microwave and infrared windows, micro- and nanoelectromechanical systems, electrolytic water purifiers, ultraviolet sensors, electrodes for electrochemical processes, and loudspeaker tweeters (*4*).

A promising new application stems from the recent discovery that the usually inert surface of diamond can be functionalized by chemically replacing the hydrogen atoms that terminate the carbon bonds with other, more reactive ligands. Attaching a hydrocarbon chain terminating in an amine group allows selected proteins or DNA fragments to be tethered to the diamond surface (*5*). When immersed in a liquid solution containing biomolecules, the tethered protein/DNA will selectively grab hold of its natural "partner" (for example, a coenzyme or complementary DNA strand). This uptake can be monitored electrochemically or via a fluorescent marker. This approach could be used to make cheap, reusable biosensors for use in genetic screening, disease diagnosis, or day-to-day monitoring of diabetes and other conditions.

The extremely high thermal conductivity of diamond may result in one of the first large-scale applications for CVD diamond films. With the increasing miniaturization of silicon-integrated circuits comes the major problem of heat dissipation. To overcome this, chip manufacturers and diamond companies such as sp^3 Diamond Technologies Inc. (*6*) are beginning to consider replacing the standard Si wafer substrate with a composite wafer comprising a Si-diamond-Si sandwich. To make this wafer, a CVD diamond layer 10 to 20 μm thick is grown onto a standard Si wafer. Next, a thin (<5 μm) layer of Si is deposited. The device components are deposited onto the top Si layer and patterned using standard photolithography and etching processes (see the figure).

Although this sounds relatively straightforward, some serious technological problems remain. These include devising methods to deposit diamond films uniformly onto 300-mm-diameter Si wafers, and then polishing the surface to nanometer smoothness, while avoiding bowing of the wafer that might arise from thermal-expansion mismatch between the diamond and Si. If these challenges are overcome, it is likely that within 5 years, most PC microprocessors may be fabricated on such a diamond-sandwich wafer.

The expense and difficulties of making such complex composite wafers would not be necessary if large single-crystal diamond wafers were commercially available at affordable prices. Progress in growing single-crystal diamond has been slow, but breakthroughs in understanding the growth chemistry in the past 5 years are beginning to yield results. The UK-based company Element Six now makes and supplies single-crystal diamond substrates, although the largest are only about 5 μm by 5 μm (*7*). Ho *et al.* have grown single-crystal CVD diamond gemstones 6.7 mm in diameter and 12 mm high (*8*). The crystals were intended primarily for use in diamond anvil cells, but the same technology can be used to make commercial gems. Companies such as Apollo Diamond (*9*) are beginning to exploit these advances for growing commercial gemstones.

In hindsight, the enthusiastic predictions of the 1990s for diamond were perhaps too ambitious, but the story is not over yet. As well as being essential for a growing number of small but lucrative niche applications, CVD diamond may yet play a crucial role in more mainstream emerging technologies.

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ERRATUM

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Perspectives: “The new diamond age?” by P. W. May (14 March, p. 1490). The largest single-crystal diamond substrates supplied by Element Six are are 5 mm by 5 mm, not 5 μm by 5 μm.