sion features have also been reported for the disks around the stars MWC480 (*9*) and SVS 13 (*10*), although these studies only probed distances <0.3 AU from the central star. Interestingly, water appears to be depleted in SVS 13 relative to what is predicted in stagnant disk models (*10*). The variation of observed water abundances in these disks mirrors that which has been inferred for our own solar nebula.

To date, these observations do not distinguish which of the models developed for our solar nebula is correct but rather lend support to recent models for the dynamic evolution of water and other volatiles in protoplanetary disks. However, as the techniques used by Carr *et al*. are applied to other disks, correlations between their chemical compositions and their physical properties can be identified. Models for water evolution predict that the enhancement of water in inner disks should be followed by periods of depletions, so systematic variations with age are expected. Also, larger disks would provide more water ice to drift inward and thus would produce greater enhancements in the inner disk. Searching for such correlations will thus allow us to test models developed for our own solar nebula and determine whether it evolved in a similar way as other disks in our galaxy or if, instead, our planetary system is the result of one or multiple unique circumstances. Right now, these new results, combined with the discovery of high temperature grains in comets (*11*) and in the outer regions of protoplanetary disks (*12*), suggest that the manner by which our solar system formed may have been the rule.

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SYSTEMS BIOLOGY

Customized Signaling Circuits

Altering cellular behaviors can be achieved through a synthetic approach by refashioning signaling circuitry.

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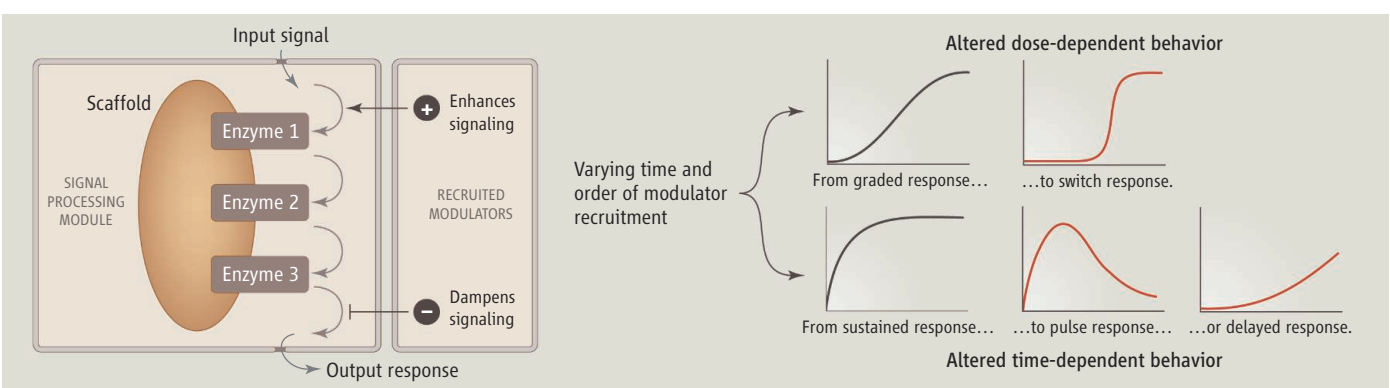
For nearly three decades, cell biologists have labored to identify and dissect the elaborate intracellular signaling pathways that control cellular responses to external stimuli. The emerging field of "synthetic biology" now seeks to move beyond mere understanding of these existing biological systems, and to begin exploiting the acquired knowledge for new purposes such as creating custom-configured signal transduction pathways (*1*–*3*). Much as an engineer assembles new electronic circuits from a toolbox of pre-existing parts, the study by Bashor *et al.* on page 1539 in this issue (*4*) modifies and reconnects components of a well-characterized cellular signaling pathway to reshape fundamental input-output processing behaviors such as temporal dynamics and dose response.

The system chosen for modification is the signaling pathway that responds to mating pheromones in the budding yeast *Saccharomyces cerevisiae*. Because this pathway has long been a model for eukaryotic signal transduction (*5*), the depth of knowledge and the ease of experimental manipulations make it an ideal system for testing new theories of pathway engineering.

In principle, two general strategies can be used to alter signaling circuitry: a bottom-up approach involving de novo design of proteins with new properties (e.g., new interactions, substrate specificities, or kinetic parameters), or a modular approach in which existing proteins are co-opted as parts to be connected in new ways. Bashor *et al.* follow the latter scheme, which exploits the modular property of many natural signaling proteins (*6*). At the core of this effort lies a "scaffold" protein called Ste5, which serves as an assembly platform for a series of sequentially acting enzymes (protein kinases) that propagate signals through the pathway (*7*). The role of scaffold proteins as central signal processing hubs makes them a natural choice as the framework upon which to



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Changing behavior. The response of a cellular signaling pathway to a stimulus can be altered with positive and negative modulators. When such modulators are recruited to the scaffold protein in specific temporal sequences, through the use of feedback loops that control their expression and competitor recruitment sites that act as binding sinks, the time or dose dependence of the signaling response can be adjusted to adopt a variety of useful circuit behaviors.

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?

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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.

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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?