somes delivered an infectious agent that provided a seed, enabling endogenous Sup35p to convert to the self-propagating prion form. This form was subsequently transmitted from the original yeast cells to daughter cells through cell division, and was then propagated over a number of generations of growth. Two variants of the Sup35pNM fragment known to be defective in seeding conversion of normal Sup35p to the prion form (*9*) were unable to seed this conversion when delivered by liposomes to yeast cells.

These experiments prompt the question, What is the nature of the Sup35p seed that catalyzes Sup35p conversion? Sparrer and co-workers show that only a small percentage of the Sup35pNM-loaded liposomes contain, or at least are able to deliver, seeding activity. This hints that it is not simply aggregated Sup35p that acts as the seed. Fibrils of Sup35p formed by conversion of the normal protein to the prion form exist for the most part as amyloid-like fibrils (*7*), although there has been no direct demonstration that these fibrils are the seeds that initiate the normal-to-prion conversion. Tellingly, agitation (and the presumed consequent fragmentation of Sup35p fibrils) greatly increases their seeding activity in vitro (*7, 9*). In vivo, the picture is even less clear. Sedimentation analysis of Sup35p has confirmed that it is found primarily as part of an aggregate (that can be pelleted by centrifugation) in [*PSI*$^+$] cells. But there is no evidence that these aggregates consist of fibrillar polymers of Sup35p even though they can seed prion conversion in vitro.

Fibrils of Sup35p formed in vitro and the high molecular weight Sup35p aggregates found in vivo may simply be "dead-end" products of the polymerization process. The prion-forming seeds may be lower molecular weight, possibly monomeric, forms of Sup35p that have acquired a new and inheritable conformation. We know from studies of chemically induced [*PSI*$^+$] loss in yeast that there are at least 60 seeds per haploid cell (*11*). Until the identity of these seeds has been established, we can only speculate about the mechanism of protein-mediated inheritance in yeast and the transmission of prions in mammals.

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PERSPECTIVES: APPLIED PHYSICS

How to Be Truly Photonic

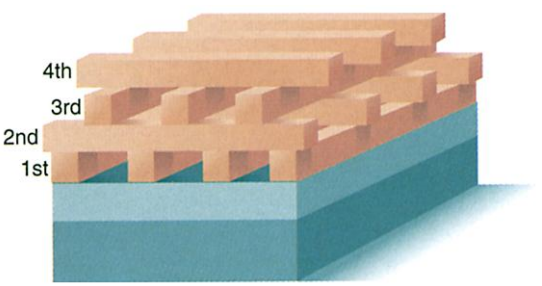
E. Yablonovitch

Photonic crystals are three-dimensional (3D) dielectric structures with a forbidden gap for electromagnetic waves, analogous (*1*) to the electronic band gap in semiconductors that lies at the heart of silicon technology. A photonic band gap allows light to be trapped in the tiniest volumes and optoelectronic devices, which interface optical and electronic components, to reach their ultimate limit of miniaturization.

The dream of photonic integrated circuits—microchips for light—remains yet to be fulfilled, and many believe that tiny photonic crystal devices will hold the key. The Internet is demanding more and more communications capacity that will require vast numbers of such optical components. As reported on page 604, Noda *et al.* (*2*) now bring these devices one step closer to reality by creating a photonic crystal with unprecedented performance.

The first photonic crystals were reported about 10 years ago (*3*, *4*), but they were hardly photonic at all. They were large structures and had gaps at microwave frequencies and centimeter wavelengths. Since then, the race has been on to shrink the structures down to optical wavelengths. This has not been an easy task, not least because photonic crystals are intricate 3D objects that must be created with nanometer precision.

Among the variety of optical materials, only those with a refractive index greater than roughly 2.0 are capable of supporting a photonic band gap. For fully functional optoelectronics, the classic III-V semiconductors, such as GaAs, will ultimately be preferred, because they combine both optical and electronic function. Although there has been considerable progress with other substances, such as TiO_2 and silicon, the III-V semiconductors remain the preeminent materials of choice.



Stacking assembly of photonic crystals. Just eight layers make a respectable photonic crystal. With the strategy of Noda *et al.* (*2*), this requires only three stacking and alignment steps.

The ideal structure for photonic band gaps must recreate, at the optical wavelength scale, the beautiful valence bond structure of diamond crystals at the atomic scale. Diamondlike connectivity or geometry in photonic crystals has provided the widest photonic band gaps observed to date even for relatively low refractive index contrast. Other crystal structures are easier to make. For example, face-centered cubic (fcc) crystals will self-assemble from microspheres in many types of colloidal solutions. But these fcc crystals have a relatively feeble gap that requires a refractive index greater than 2.8. These materials are likely to have other optical applications but are unlikely to provide full optoelectronic function, wherein electricity directly creates light.

Strategies for meeting the exacting set of requirements for a 3D, diamondlike nanostructure, with a III-V material base, for photonic crystals have long been sought. There have been some mildly successful efforts in the past (*5*, *6*). A figure of merit has emerged to measure their success, with the rejection of optical intensity within the forbidden band gap becoming the accepted gauge. For a photonic band gap to be interesting, a rejection factor of 10 is deemed rather inadequate. Optical rejection should be much higher, at least 100 and up to 10,000 or more according to need.

The excellent report by Noda *et al.* (*2*) represents a watershed in photonic crystal research. The authors demonstrate unprecedented optical rejection >10,000 in a GaAs photonic band gap structure. All of the key requirements for photonic crystal–based optoelectronics are demonstrated in this work.

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CREDIT: FROM (*3*).

Their strategy, pursued for several years, has been marked by clear vision with few compromises. The particular diamondlike structure that Noda *et al.* fabricate is sometimes called the stack-of-logs structure, or the layer-by-layer structure introduced by the Iowa State group (*7*). (Actually, all 3D photonic crystal structures can be built up layer by layer.) The stack-of-logs structure (see the figure) represents the cubic <100> face of a diamond crystal. Its main advantage is that each face has a rectilinear appearance, easily programmed into electron-beam–writing lithography equipment. When the layers are precisely stacked above one another, the 3D structure emerges as diamondlike, with a strong photonic band gap.

The stacking of successive layers can be accomplished by wafer fusion, where temperature and pressure allow two semiconductor crystal layers to merge. Here, Noda *et al.* have realized an excellent strategy. To make a full crystal requires many layers, each step necessitating exacting alignment, allowing errors to creep in. The authors noticed, however, that after stacking the first two layers, they could then work with both to stack four at a time, thus reducing the number of fabrication steps. Eight layers already make a respectable photonic crystal but require only three stacking and alignment steps (*2*).

This fabrication strategy has been fully vindicated by the excellent results presented in this issue. The internal waveguides demonstrated in the 3D crystal structure of Noda *et al.* may be the precursor of photonic integrated circuits. Soon we can expect to see tiny electromagnetic cavities, fully isolated from their surroundings in all three dimensions, that will exhibit unusual quantum effects.

Nevertheless, there are competing approaches. It has been noted that full 3D confinement, although meritorious, is not always essential. Excellent results have emerged recently in thin film semiconductor slabs perforated by a hexagonal array of holes, which form two-dimensional (2D) photonic crystals (*8*). These structures are much easier to make than 3D structures, while providing adequate index guiding in the third dimension. Recently, nanocavity lasers were demonstrated in such 2D photonic crystals (*9*). It appears that the race for technological supremacy will continue.

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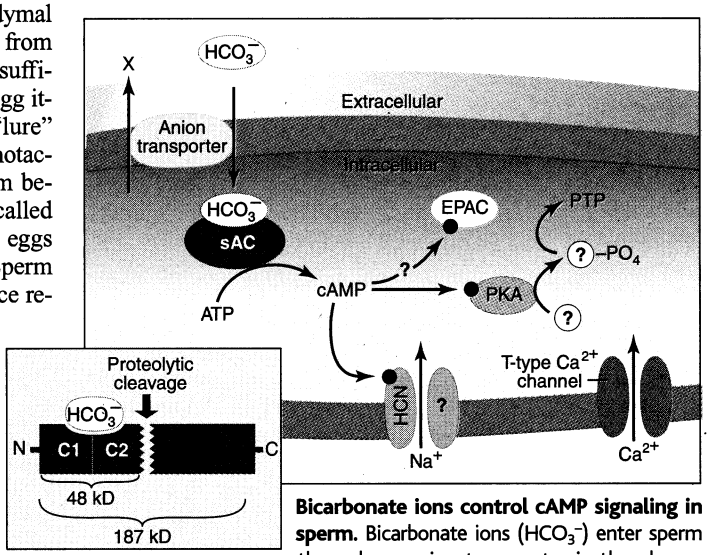
PERSPECTIVES: CELL BIOLOGY

A Universal Bicarbonate Sensor

U. Benjamin Kaupp and Ingo Weyand

Sperm cells are equipped with a limited repertoire of behaviors that exclusively subserve their purpose—to fertilize eggs (*1*). When produced in the testis, sperm are immotile; they acquire the ability to swim as they transit through the epididymal tract of mammals or after ejaculation from invertebrates. But motility alone is not sufficient to direct a sperm to an egg. The egg itself (or associated structures) must "lure" the sperm by releasing diffusible chemotactic factors (*2*). After mammalian sperm become motile, they mature (a process called capacitation) and are able to fertilize eggs within the female reproductive tract. Sperm and egg initially interact through surface receptors, then the proteolytic contents of the sperm's acrosomal vesicle are released. This proteolytic cocktail helps the sperm to penetrate the outer coat of the egg and to reach the egg's plasma membrane.

The three principal events in sperm mobilization—motility (and chemotaxis), capacitation, and the acrosome reaction—each depend on the intracellular cyclic nucleotides: adenosine 3′,5′-monophosphate (cAMP), or guanosine 3′,5′-monophosphate (cGMP), or both (*1*). It has been established that bicarbonate ions activate sperm capacitation and that this activation can be blocked by membrane-permeant cAMP analogs. This suggests that sperm capacitation is activated by a rise in intracellular cAMP induced by bicarbonate ions (*3*). Now, on page 625 of this issue, Chen *et al.* (*4*) provide compelling support for this possibility. They show that bicarbonate ions directly stimulate the soluble form of adenylyl cyclase (AC), the enzyme that synthesizes cAMP from adenosine triphosphate. Activation of this enzyme results in an increase in cAMP and induction of the signaling pathway that brings about the capacitation response.



Bicarbonate ions control cAMP signaling in sperm. Bicarbonate ions (HCO_3^-) enter sperm through an anion transporter in the plasma membrane and activate the soluble adenylyl cyclase (sAC), resulting in increased synthesis of the signaling molecule, cAMP. The precursor of sAC has a molecular weight of 187 kD. As sperm transit through the epididymal tract, sAC is proteolytically cleaved into several fragments including a 48-kD form that contains the two catalytic domains, C1 and C2 (inset). Potential targets of cAMP in sperm are protein kinase A (PKA), the hyperpolarization-activated, cyclic nucleotide-gated (HCN) channel and guanine-nucleotide-exchange factors (EPAC). HCN channel-mediated depolarization of sperm might lead to Ca^{2+} influx through T-type Ca^{2+} channels. cAMP also stimulates protein tyrosine phosphorylation (PTP).

The soluble form of AC (sAC) in sperm is thought to be different from the transmembrane form (tmAC) found in other cells. The activity of tmAC is controlled by heterotrimeric GTP-binding protein (G protein)–coupled receptors through stimulatory or inhibitory G proteins; in contrast, sAC does not require G proteins for activation. Moreover, forskolin, a powerful stimulator of tmAC, has no effect on sAC, whereas bicarbonate ions increase the production of cAMP in sperm (*5*–*7*). Recently, Chen and colleagues (*8*) showed that sperm sAC is structurally distinct from G protein–regulated tmACs and that, together with AC from cyanobacteria, it falls into a separate family. Notably, its two catalytic domains (C1 and C2) more closely resemble those of cyanobacterial AC than those of mammalian tmACs.

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