also the growth inhibition brought about when cells come into contact with another.

Since, as cancer gene expert Tony Hunter of the Salk Institute puts it, "any negative regulator of the cell cycle is a potential target for inactivation"—and therefore cancer development—the discovery of these inhibitors raises the possibility that they might themselves be tumor suppressors. Mutations in these genes might, for example, contribute to the development of the 50% of human cancers in which mutations in *p53* itself do not occur, although this has yet to be demonstrated.

Researchers clearly still have a lot to do to pin down the role of the cell cycle components in causing cancer. One of the biggest gaps in their knowledge concerns the identity of the targets of the cell cycle kinases, information they want to help understand exactly what turns on DNA synthesis and moves cells through the cycle. So far one such target has been identified, and it's an important one from the point of view of understanding cancer: the protein product of the retinoblastoma (*Rb*) gene, which is another tumor suppressor.

A few years ago, researchers in several labs found that *Rb* suppresses cell growth by binding to a transcription factor and preventing it from doing its normal job of turning on gene expression. That block is relieved when the cell cycle kinases are activated and add phosphates to *Rb*, causing it to release the transcription factor (*Science*, 14 June 1991, p. 1492). More recently, several groups have evidence that the D and E cyclins and their associated kinases are particularly important in overriding *Rb*'s inhibitory effects, and moving cells from G1 into DNA synthesis and cell division. But, predicts Harlow, whose own research includes *Rb*, "*Rb* is not going to be the only one [cell cycle target]."

Indeed, there are now numerous links between the cell cycle and growth factors on one hand and tumor suppressors on the other. Add the idea that intrinsic defects in the operation of the cell cycle can also lead to cancer, and it's clear that cell cycle research will be going around at a high rate of speed for a long time to come.

–Jean Marx

Additional Reading

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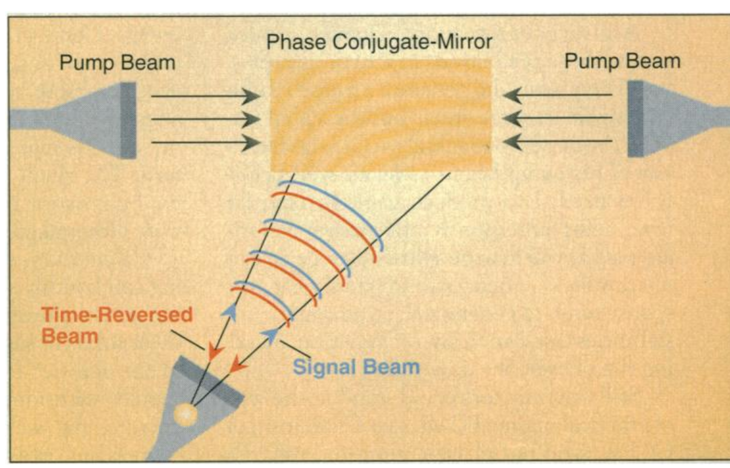
TECHNOLOGY

Researchers Try to Build Time Machines for Microwaves

"Ginger Rogers did everything Fred Astaire did," say feminists. "She just did it backward and in high heels." Physicists trying to "time-reverse" beams of microwaves have a vivid appreciation of how difficult it can be to do things backward. These researchers are trying to design reflectors that undo distortion in a microwave signal by sending it back to its source exactly as it was originally transmitted. A simple mirror won't suffice; all it can do is change a signal's direction. Instead, the reflecting medium has to shape the outgoing beam so that it precisely reverses every motion of the incoming beam. If the original beam came from the left, for example, the outgoing beam has to angle to the left; if the original beam fanned out, the outgoing beam has to converge; if the original beam got distorted, the outgoing beam has to be distorted in reverse—so that it will lose the distortion on the return trip.

Just as Ginger Rogers might have turned an ankle or toppled a lamp during a grueling routine, physicists trying to master this feat have gotten used to setbacks. But in the last couple of years, several of them of them have taken a crucial step: They've developed exotic materials that can serve as wave-reversing mediums for microwaves —plasmas, stacks of tiny polysilicon pendulums, and liquid suspensions of graphite fibers. None of these materials so far produces a time-reversed signal strong enough for practical applications. But Harold Fetterman of the University of California, Los Angeles, for one, thinks he and his colleagues are on the track of what he calls "a definitive experiment in opening up the technology."



Return to sender. In four-wave mixing, incoming microwaves interfere with a pump beam *(right)* in a special medium, perturbing it. The perturbations scatter a second pump beam, time-reversing the signal.

SOURCES: *SCIENTIFIC AMERICAN*, DOMIER ILLUSTRATION: C. FABER SMITH

Motivation for this work comes from earlier successes with visible light. Phase-conjugate mirrors (PCMs), as they are called, have found dozens of important applications in the visible spectrum, from undoing distortion in laser beams to reconstructing images that get scrambled when transmitted through long stretches of optical fiber. For phase conjugation of microwaves, the potential applications are, if anything, more numerous. Equipped with a PCM, a satellite could beam data unerringly to a ground station; a radar system could turn a weak reflection from a distant object into a powerful, directed probe.

These goals have been tough to achieve for microwaves because phase conjugation requires each incoming signal to, in effect, reshape the "mirror." The PCM has to record the contours and phases of the incoming wavefronts by temporarily changing its own characteristics, such as its index of refraction. The outgoing beam will then pick up this "phase information," acquiring exactly the same contours and phases—but in reverse temporal order—as it passes through the altered regions of the PCM.

In a common scheme for time-reversing an optical signal, called four-wave mixing, other beams help to record the phase information, then write it into the outgoing beam. The incoming beam (wave *1*) interferes with a "pump" beam (wave *2*), creating a pattern of light and dark regions within the PCM that encodes information about the incoming beam. This interference pattern reshapes the optical properties of the PCM. When a second pump beam (wave *3*) travels through the medium in the opposite direction from the first, some of it gets imprinted with a record of the incoming beam's characteristics and leaves the medium as the phase-conjugated wave (*4*). Because the pump beams can be far more intense than the incoming beam, four-wave mixing yields a valuable bonus: The PCM can exhibit "gain," amplifying the original signal to generate a far stronger time-reversed beam.

Although this scheme, developed for visible light, is attractive for microwave radiation as well, it has proved difficult to put into practice. The central problem is that the phase-conjugating medium must be "nonlinear"—its refractive properties have to change in response to incoming radiation. And while that condition is easy to meet for visible light, which can elicit nonlinear behavior from crystals, semiconductors, and high-pressure gases, it's not so easy for microwaves. At those lower frequencies, with their lower energy levels, matter is frustratingly unresponsive. "The problem with most matter is that it becomes very well behaved [at] low frequencies," says Calvin Domier, a physicist at the University of California, Davis.

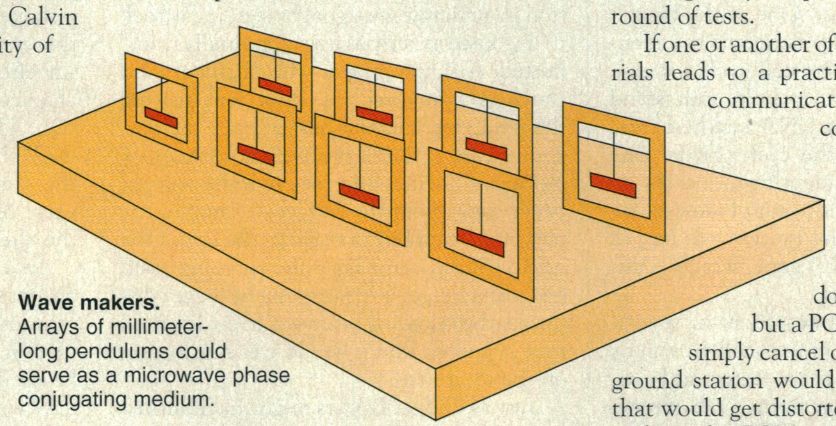
Domier and some other physicists thought they saw the answer in plasmas, whose mobile electric charges make them highly responsive to the electromagnetic field of microwaves and other radiation. "Plasmas are nonlinear at virtually every single frequency," says Domier, and unlike solids, their densities can be adjusted to improve their nonlinear properties. Moreover, a plasma's nonlinear response should be as quick as a microsecond, says Martin V. Goldman, a plasma theorist at the University of Colorado in Boulder.

A little over a year ago, Domier decided to test those predictions in a hydrogen plasma. The plasma did generate a phase-conjugate signal in short order. But the signal was weak, because Domier had to hold the intensity of his pump beams to levels well below those needed to produce gain. In fact, far from being unresponsive like other materials, plasmas seem to be a little too sensitive to microwaves: Their strong nonlinear response tends to generate electromagnetic instabilities that can throw off radiation, masking the phase-conjugate signal.

Still other factors could stand in the way of practical plasma PCMs, says Chan Joshi of UCLA, who has phase-conjugated infrared light in plasmas. "A plasma tends to be inhomogeneous... and to flow"—effects that can degrade the reflected beam. Domier himself emerged skeptical from his experience of digging weak phase-conjugate signals out of background noise, but he isn't closing the door on plasmas. He thinks that with better microwave equipment than his funding now permits, he could "wait out" some of the instability and achieve better phase conjugation after the plasma settles down.

If plasmas haven't lived up to expectations so far, UCLA's Fetterman remains upbeat about prospects for a very different class of materials: minute, electrically conductive rods. Fetterman says his original motivation was simple curiosity. "I used to be in the quantum electronics group at Lincoln Lab, MIT," he says. "People there would do all sorts of really neat things with nonlinear materials. I just wanted to see if I could bring some of these effects to microwaves." At the top of his list was phase conjugation.

Doing the twist. Fetterman naturally looked for ordinary solids capable of doing the job—and quickly reached the discouraging conclusion "that it's impossible to do" for microwaves. But after discussions with colleagues at the Rockwell Science Center in Thousand Oaks, California, including Dan Rogovin, Bob McGraw, and W. Ho, he cooked up the idea of structures that would act like an array of tiny weather vanes—actually moving in response to microwave energy. Conductive ellipsoids or rods a millimeter or so long, suspended in a matrix that doesn't absorb microwaves, would tend to align with the strong microwave electric field in, say, the maxima of an interference pattern. The result would be an optical "grating," consisting of regions in which the rods were either aligned or randomly oriented.



Wave makers. Arrays of millimeter-long pendulums could serve as a microwave phase conjugating medium.

SOURCE: FETTERMAN ILLUSTRATION: C. FABER SMITH

Calculations show that this kind of grating can handily scatter a pump beam, creating a time-reversed signal. And because these solids or suspensions shouldn't be prey to instabilities like those in plasmas, they should withstand powerful pump beams, opening the way, Fetterman estimates, to gains as high as a million. On the other hand, the rods would respond to the interference pattern much more slowly than a plasma, taking about a second to spin—still sufficient, perhaps, for communicating with satellites, which move slowly across the sky.

In Fetterman's first effort to test this promise, he and his students Robert Shih and Bradley Bobbs beamed a signal into a medium made up of graphite rods suspended in heptane and mineral oil. That was enough for a proof-of-principle: The group was able to produce phase conjugation in one dimension by time-reversing a signal in a waveguide. But the pump beams heated the oil excessively, prompting Fetterman and another University of California, Los Angeles (UCLA), collaborator—former Russian scientist Boris Tsap—to try a new medium: three-dimensional arrays of pendulums that hang from minuscule frames.

Fetterman has high hopes for his new PCM, which UCLA's Kristofer Pister produces by micromachining blocks of polysilicon, then coating the pendulums with a film of metal. Although making these devices is painstaking work, Fetterman insists that this solution isn't as extravagant as it sounds. "You don't need a lot of pendulums per wavelength [about three centimeters] to get fantastic gain—five or 10 is enough," Fetterman predicts. He and his collaborators are now building arrays of pendulums for their first round of tests.

If one or another of these candidate materials leads to a practical PCM, the job of communicating with satellites could get a whole lot easier. The sloshing, turbulent plasma of Earth's ionosphere now limits data rates and sometimes shuts down communication, but a PCM on a satellite could simply cancel out the distortion. The ground station would emit a "guide beam" that would get distorted on its way up; after striking the PCM and being encoded with information, the time-reversed wave-fronts would scoot back along the same path to the ground, shedding distortion along the way. Similarly, a PCM placed near the usual radar dish along an airport approach path could catch weak radar echoes, boost them, and send them straight back to the planes, thereby "brightening" the targets seen by the radar system by orders of magnitude.

Microwave phase conjugation could also be a key to visionary schemes for collecting solar energy in space, then funneling it to Earth in the form of microwave beams. To target the intense microwaves precisely, the ground station would send up a probe beam; the solar collector would respond with a vastly more powerful phase-conjugated beam. Without phase conjugation's pinpoint accuracy, says physicist Norman Rostoker of the University of California, Irvine, who has studied these energy schemes, "you maybe miss, and there goes New York."

But all those visions will have to wait on painstaking laboratory work. "It all boils down to materials," says David Pepper of Hughes Research Laboratories, who works on optical phase conjugation. "Once you observe the effect, the question is, 'What's the most efficient way to produce the time-reversed wave?'" Agrees Fetterman, "There are extraordinary things you can do with [a PCM for microwaves]... if the blasted thing works."

–James Glanz

James Glanz is a science writer in Chicago.