splits up, there's a good chance that the fates of the "extra" copies in the two resulting groups will diverge. In one group, one copy might jump to a new chromosome, while in the other, the copy might move to a different spot in the genome. If the populations merge again, these gene shifts will have made their genomes incompatible. Individuals from the two groups could still mate, but this incompatibility would likely make their offspring less fit.

But several researchers question how Lynch and Conery came up with their duplicate genes and worry about some of the resulting estimates. Manyuan Long, an evolutionary biologist at the University of Chicago, thinks that their analysis doesn't adequately take into account the long-lived gene copies, many of which also exist in these genomes.

Even if the estimates are rough, counters Wagner, "for my work, they are very, very relevant." And he expects that others will take these results as starting points for their own work: "We can plug these estimates into models [to study] the evolution of many interesting things." –ELIZABETH PENNISI

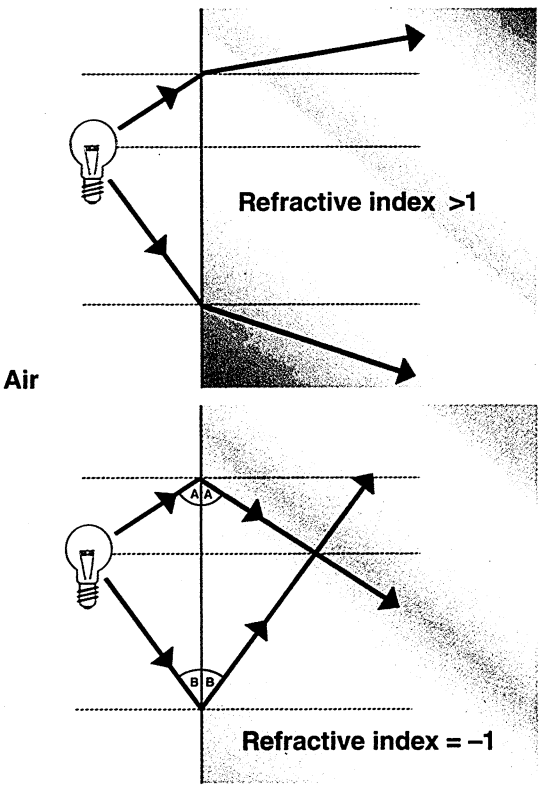
THEORETICAL PHYSICS

Offbeat Lenses Promise Perfect Fidelity

A battleship spied by periscope, a kestrel watched with binoculars, a nebula under the Hubble Space Telescope's gaze: What do these images have in common? None faithfully represents the real thing. A seemingly ineluctable property of any lens is that it cannot focus all wavelengths of light shed by a distant object. What's viewed, therefore, is to some degree a washed out, grainy version of the original. But now a British physicist has found an ingenious solution that lights the way to building a perfect "superlens." That notion has set other experts abuzz. "This is kind of amazing," says Eli Yablonovitch, a physicist at the University of California (UC), Los Angeles. "It's a real theoretical breakthrough."

Most of the time, light travels in an arrow-straight line. But when a beam passes from one material into another, its speed changes, causing it to veer in a slightly different direction. The amount of bending depends on the refractive indexes of the two materials—roughly speaking, measures of light's speed in those materials. By shaping a lens just right, opticians can exploit this bending to make rays converge at a point beyond the lens. But even the best conventional lenses are unable to focus all the light rays; some wavelengths are inevitably lost.

Some deft calculations, however, point to the surprising conclusion that it doesn't have to be that way. Physicist John Pendry of Imperial College, London, used Maxwell's equations—the basic laws governing electromagnetic waves—to examine the behavior of individual wavelengths of light as they pass through a lens. A distant object is blurry because various wavelengths get out of step, like a collection of metronomes, once in sync, that start beating at different tempos. "The function of the lens is to correct that phase difference," says Pendry. It's as if the lens selectively slows each metronome so that the assembly can again sound off in lockstep: When the metronomes synchronize, the image comes into focus. But not all wavelengths can be salvaged. According to the equations, some waves evanesce before reaching the focal point. That means the reconstructed image is missing some of the reflection's original components. Even with the best lens, details are lost.



Sharper image. Negatively refractive materials that bend light in exotic ways *(bottom)* could make perfect lenses, calculations show.

But Pendry discovered a loophole in the equations. His insight was inspired by work described at a meeting of the American Physical Society last March by Sheldon Schultz and colleagues at UC San Diego. Most materials have a positive refractive index; the bigger the index, the slower light moves. The refractive index of air, for example, is 1; that of water, 1.33. Schultz's group found a way to make a material with a negative refractive index—one in which light bends in the opposite direction from the way it bends on entering a glass lens.

Pendry calculated that evanescent waves are not lost when passing through a hypothetical material with a refractive index of –1. "It's a very strange property," he says. "The slab of material grabs hold of the evanescent waves and removes their decay" by shoring up the waves. "It is almost as if it acts as an amplifier," adds Yablonovitch. "It's a feat that is hard to believe." As a result, all the light waves passing through a negative refractive lens reach the focal point intact, preventing any loss of resolution and creating an image that perfectly duplicates the original. Pendry's calculations appear in the 30 October *Physical Review Letters*.

More conventional materials might also make perfect lenses if other electromagnetic properties of theirs were tuned just right, Pendry says. He thinks a very thin film of silver could do the trick. But whatever its composition, a superlens would have drawbacks. For instance, to capture evanescent waves, the lens must be placed only nanometers away from the object being observed and would focus the image roughly the same distance from the lens. That scale isn't useful for naval warfare or bird-watching—let alone astronomy—but Pendry hopes that tiny superlenses will find uses in such pursuits as lithography and medical imaging.

–CHARLES SEIFE

CELL BIOLOGY

New Clues to How Genes Are Controlled

The transformation of a single cell into a complex organism requires an exact system for regulating gene expression. It wouldn't do, say, to have hormone-secreting cells make liver proteins, or even the wrong hormone. Cell biologists don't know exactly how developing cells achieve this precision, but they do know it involves so-called transcription factors—proteins that can turn genes on or off. Now, researchers have intriguing new information about how the transcription factor called Pit-1 works.

Pit-1 is needed to activate the genes for three hormones—growth hormone, prolactin, and thyrotropin—each of which is made by a different type of cell in the pituitary gland. But how Pit-1 turns on the right gene in each cell type without activating the other two has been a mystery. Work described on page 1127 by Kathleen Scully and Michael G.

ILLUSTRATION: CAMERON SLAYDEN

Rosenfeld of the University of California, San Diego, and Aneel Aggarwal of Mount Sinai School of Medicine in New York City and their colleagues points to an answer.

To exert its effects, Pit-1, like other transcription factors, has to bind to a regulatory sequence on its target genes. The Rosenfeld-Aggarwal team has shown that a small sequence variation between the regulatory elements of the prolactin and growth-hormone genes causes Pit-1 to bind very differently to the two. As a result, when Pit-1 binds to the regulatory region of the growth-hormone gene in prolactin-producing cells, it apparently attracts proteins that suppress the gene's activity, whereas on the prolactin gene it attracts activating coregulators. "They're basically arguing that a given regulatory factor can act as a switch, in some cases causing activation and in others repression," says developmental biologist Michael Levine of the University of California, Berkeley (UCB).

It's not unusual for transcription factors to have dual functions, but until now Pit-1 was thought to be an activator only. Beyond that, the finding supports the idea that the sequences that bind transcription factors are more than just docking sites. Instead, as work with another set of transcription factors, the so-called nuclear receptors, has already shown, small changes in these sequences can influence the three-dimensional structure of the bound factor. And that structural change can in turn influence which other proteins bind to the transcription factor on the regulatory site—and ultimately, whether genes are turned on or off. "The information is in the primary DNA sequence, as Watson and Crick told us," Rosenfeld says.

The Rosenfeld team started their experiments by asking what role Pit-1 binding sites might play in selective expression of a target gene. To find out, Scully introduced two genes separately into mice: one with the normal regulatory region for growth hormone and one in which the Pit-1 binding regions were replaced by a comparable element from the prolactin gene.

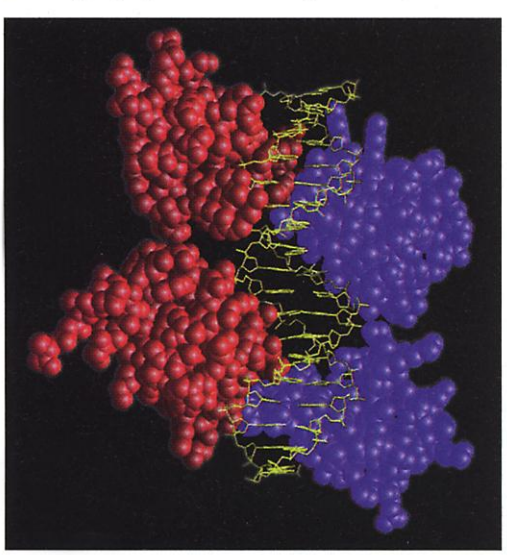
As expected, the gene with the normal regulatory element was expressed only in the growth hormone–producing cells (somatotropes) in the animals' pituitaries. But the gene with the mutant sequences was expressed in both the growth hormone– and prolactin-producing cells (lactotropes). These results indicate that Pit-1, when bound to the normal growth-hormone sequence, somehow keeps the gene "off" in the prolactin-producing cells while allowing it to be "on" in the growth-hormone cells. Indeed, cell biologist Keith Yamamoto, also of UCB, notes that the Rosenfeld team's results imply that gene repression is Pit-1's default activity. That finding, he says, "is a real surprise," and suggests that "the growth hormone and prolactin elements evoke distinct configurations of Pit-1 that somehow produce distinct patterns of activity."

X-ray crystallographic studies performed by Aggarwal and his Mount Sinai colleague Eric Jacobsen in collaboration with the Rosenfeld group support that idea. They showed, for example, that two of the protein's characteristic regions, or "domains," end up on perpendicular faces of the DNA of the prolactin element but are on the same face of the DNA of the growth-hormone sequence. This difference can be traced to the presence of two extra bases in the Pit-1 binding site of the growth-hormone gene. Further work indicates that the shape change induced in Pit-1 by this difference enables it to recruit repressive proteins to the growth-hormone gene.

These results help explain why growth hormone is "off" in lactotropes; what is still unclear is how the gene is turned on in somatotropes. "That's the crucial question," Rosenfeld says. "You have to have an override mechanism" to eliminate the repressive effects of the gene's regulatory sequences.

Despite the unanswered questions, Levine is impressed that the team has gone so far—"from transgenic animals to crystallography"—in explaining the cell specificity of Pit-1's effects. Given that a similar mechanism has already been found by Yamamoto and others for nuclear receptors, which regulate gene expression in response to steroid hormones and retinoids, Levine suspects it may be widespread: "You can envision many proteins where this can happen."

–JEAN MARX



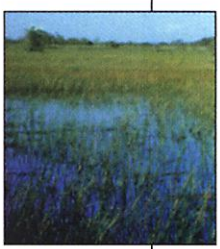
CREDITS: (LEFT TO RIGHT) H. VIADIU; USGS

Off site. When bound to the regulatory element of the growth hormone gene, as shown here, Pit-1 represses the gene expression in lactotropes.

ScienceScope

Everglades Green Light Environmentalists last week celebrated congressional approval of the first phase of a $7.8 billion Everglades restoration plan, but some scientists are withholding their applause until outside experts review the project.

Under the Everglades "restudy," the U.S. Army Corps of Engineers would undo one of its main engineering feats: a system of pumps and levees that since 1948 has diverted water that once flowed south from Lake Okeechobee to Florida Bay. To restore water needed by wildlife, the corps now plans to rip out levees and canals and store water in aquifers and reservoirs.



The bill, headed for President Clinton's signature, allots the first $1.4 billion for the 20-year project. But some scientists say the plan relies too much on engineering solutions and should have been peer-reviewed. Until a National Academy of Sciences advisory committee weighs in, says Columbia University ecologist Stuart Pimm, "it's an open question whether this plan [will] have any ecological benefit."

Next Question? The U.S. Equal Employment Opportunity Commission (EEOC), which has been investigating alleged discrimination against minorities and women at Lawrence Livermore National Laboratory (LLNL) in California (see p. 1072), is catching some flak from lab officials over a survey.

After the EEOC e-mailed the questions to many nonwhite and female Livermore employees on 13 October, lab managers shot back with an e-gram of their own. The survey was "a unilateral action taken by EEOC without our knowledge," LLNL's public affairs office wrote. "We have serious concerns about their methodology and we don't believe the confidentiality of the survey responses can be maintained." It added that staff were "not obligated to respond."

Several Asian-American staff protested, saying the lab e-mail amounted to intimidation. And the EEOC warned survey recipients not to answer electronically, as "email from LLNL may be read by LLNL." But Livermore managers say they were merely answering employees' questions about the survey. And one says the EEOC was sloppy: "They missed half the Asian Americans in the lab." Since the flap, lab director Bruce Tarter has met with some Asian-American employees, assuring them that the lab will be working closely with EEOC investigators.

Contributors: Eliot Marshall, Michael Balter, Jocelyn Kaiser, Andrew Lawler