

## EVOLUTIONARY BIOLOGY

## Twinned Genes Live Life in the Fast Lane

The financial rewards of genome sequencing may go to the companies, but the intellectual fruits of this multimillion-dollar enterprise are going to the likes of evolutionary biologist Mike Lynch and computer scientist John Conery. On page 1151, this duo at the University of Oregon, Eugene, describes new insights into how genes arise and fuel evolution. By trolling through sequence data for nine very distinct organisms, they have uncovered evidence that genes are copied far more frequently—and the duplicates are lost from the genome far faster—than researchers had thought. What's more, the work suggests that some duplicate genes play a key role in the evolution of new traits and in speciation.

Although some researchers question the Oregon team's conclusions, the report is nevertheless "a very nice example of how the creative analyses of genomic databases can provide valuable but previously inaccessible information about evolution," says Loren Rieseberg, an evolutionary biologist at Indiana University, Bloomington.

More than 30 years ago, geneticist Susumo Ohno of the City of Hope Hospital in Los Angeles proposed that genomes grow and diversify by gene duplication, an idea that most evolutionary biologists have since come to accept. It seems that when—by some quirk of DNA replication—a gene, piece of a chromosome, or whole genome is copied twice, the "extra" genes can take on a new function and expand the organism's genetic repertoire. This extra copy might become active at a different time in development or in a different tissue, or it may undergo base changes that alter the properties of the protein encoded by that gene. Yet until recently, researchers had no good way to determine whether Ohno was right. "They have had only a few duplicates" with which to try to estimate the life-spans of twinned genes, explains Andreas Wagner, an evolutionary biologist at the University of New Mexico, Albuquerque, and the Santa Fe Institute.

But thanks to the recent flurry of genome sequencing—the genomes of the fruit fly, yeast, and nematode are virtually complete, and others are close behind—Lynch and Conery were able to get a more comprehensive view of the potential of duplicate genes for furthering evolution. To do so, Lynch

and Conery used a computer program to find duplicate genes in the three completed genome sequences and among all the protein-coding sequences available for the mouse, chicken, human, rice, and the plant *Arabidopsis thaliana*.

The researchers relied on sequence differences in the matched copies to estimate the age of each copy, as differences accumulate through time. Specifically, they counted the number of silent nucleotide base changes—those that didn't alter the protein code—to date the duplication event. Then they compared the number of silent changes to the number of base changes that caused protein alterations. This ratio told them whether the copy was changing faster or slower than expected.

Lynch and Conery found that most of the duplicated genes are relatively young and that extra genes disappear quickly, at least on an



**No matter the species.** Genes in organisms as diverse as the mouse, fruit fly, chicken, and rice (clockwise from upper left) undergo frequent duplications.

evolutionary time scale. In the human and mouse, for example, about half of new copies disappear within 7.3 million years.

Perhaps most surprising, the two found an "astronomical rate of gene duplication," says Sally Otto, an evolutionary biologist at the University of British Columbia in Vancouver, Canada. In fact, duplications occur as often as single-base changes within genes, which have long been considered the primary means by which genomes evolve. The rates are similar among such disparate organisms as fruit fly and yeast, notes Lynch; a genome with 15,000 genes could acquire between 60 and 600 duplicate genes over a million years as fodder for speciation. "Gene duplications are so frequent that we really need to take them into account as an important source of genetic variation," says Wagner.

Nor do genes need to morph much before they begin to divide one species into two, Lynch suggests. For example, if a population carrying a recently twinned gene

## ScienceScope

**Silver Lining** Advocates of more controls on human subjects research will be getting help from Paul Gelsinger, father of 18-year-old Jesse Gelsinger, who died last year in a gene therapy trial at the University of Pennsylvania in Philadelphia (*Science*, 12 May, p. 951). Gelsinger received a "significant" financial settlement from Penn last week, his attorney says, after agreeing to end a malpractice suit. As part of the deal, Gelsinger dropped two defendants—former medical school dean William Kelley and Penn bioethicist Arthur Caplan, who gave informal advice on the trial's design. Caplan says, "It would be horrible to have anyone sued for expressing an opinion to a colleague."

Gelsinger intends to use the funds to form "a private foundation to support a few organizations that we consider ethical," including the National Organization for Rare Disorders in New Fairfield, Connecticut, and Citizens for Responsible Care & Research in New York City. Gelsinger adds: "We need legislation to protect research subjects by imposing stiff fines and jail time for violators."

**Planning Ahead** When you are shelling out \$2.4 million per day, it pays to plan ahead. That is the conclusion of Britain's mammoth biomedical charity, the Wellcome Trust, which this week released its first-ever 5-year plan. The roadmap will guide the \$22 billion charity's increasing spending, which has tripled over the last 3 years to about \$900 million per year, says trust director Mike Dexter.

According to the 14-page document, the trust will spend nearly \$4.5 billion by September 2005 on a wide variety of projects around the globe, including research grants, lab construction, education, and its share of constructing the new Diamond synchrotron near Oxford. The trust will also create a \$390 million fund to support unexpected "emerging research opportunities." Wellcome, however, will not feel bound by the document if priorities change, Dexter says: "The plan is not written in stone. Every year we will be evaluating things."

**Drilling Denunciation** Scientists have taken a stand against drilling in Alaska's oil- and wildlife-rich Arctic National Wildlife Refuge. More than 240 scientists and resource managers released a letter to President Clinton on 1 November asking him to permanently protect the refuge. The long-running issue came up again in this year's presidential election, with candidate George W. Bush saying he would consider drilling and Al Gore vowing to bar it. The impacts of drilling, the letter signers say, have not "been adequately considered."

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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

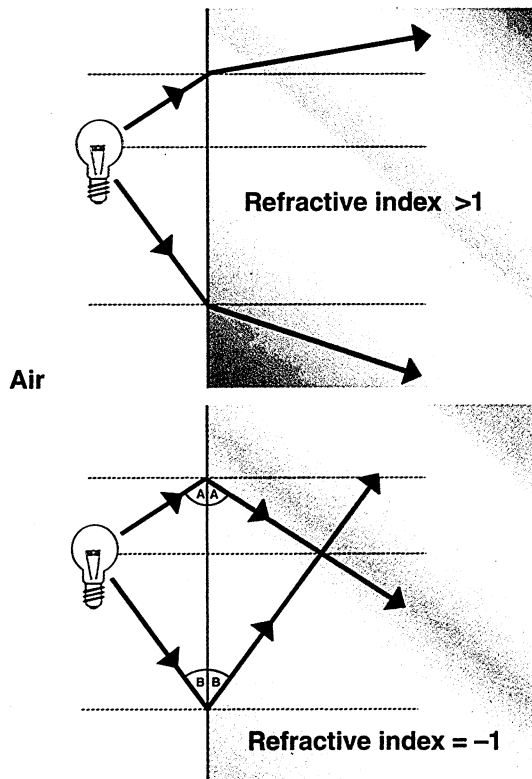
## THEORETICAL PHYSICS

### 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



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

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.

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.

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