ments with those of another virus that has infected the same cell. Although segment swapping differs from the sexual reproduction technique of eukaryotes, it still produces a hybrid progeny and "so is another form of sex," Chao says.

But there was no joy of segmented sex for Chao's φ6 viruses. Instead, by some careful chaperoning, he forced them to reproduce asexually. He began by infecting a bacterial host with a single virus. As soon as this virus began to reproduce, he randomly selected just one of its progeny and used it to infect a new bacterial cell. The virus never had a chance to reshuffle its segments with those of another particle that had infected the same cell. "We pushed them through 40 of these bottlenecks," says Chao.

At this stage, Chao suspected that Muller's ratchet probably had a firm lock on the virus, impairing its reproductive fitness—a hunch he confirmed by placing one particle of the bottleneck virus and one of the original virus in fresh bacterial cultures for a day to see which reproduced more abundantly. In 20 such reproductive-competition bouts, the original strain of the virus always won. Next, Chao allowed different reproductively enfeebled viral populations to co-infect the same cells and reproduce sexually with each other. In about 30 generations, they had regained much of their reproductive fitness.

But was their renewed fitness actually due to sex, or simply the result of new mutations that made up for the deleterious ones? To answer this question, Chao staged a fresh series of experiments. In one, he crossed reproductively handicapped viruses with themselves to create a large population of "selfed" viruses. He then allowed the viruses to evolve freely over 30 generations. Because this population was not passing through bottlenecks, beneficial mutations would be likely to accumulate. But because the particles had nearly identical genomes, sex wouldn't offer any advantage.

The selfed virus increased its fitness by 21% compared to its original, reproductively deficient ancestor. "That increase was solely due to the virus's high mutation rate," says Chao. But when he added the benefits of sex by allowing the selfed virus to interbreed with other populations, the resulting population gained another 9% in fitness.

"We knew that the virus could recover its fitness from mutations alone," says Chao, "and people used to think that this effect would be so great, it would swamp out any advantage of sex." But that was not the case. "[The study] shows that sex is advantageous," he says. Riley adds that in Chao's experiment "sex does affect Muller's ratchet; it provides an escape"—which is just what most sex researchers have always said.

–Virginia Morell

EVOLUTION

Viruses Scout Evolution's Path

ARNHEM, THE NETHERLANDS—Sex can lead to many things—even the merging of two seemingly incompatible evolutionary theories. So says Lin Chao of the University of Maryland, College Park, who realized that the fast-evolving viruses he uses to test theories about the evolution of sex (see previous story) could help settle another debate. At a meeting of the European Society for Evolutionary Biology here in August, Chao described how the viruses pointed to a possible resolution of a decades-old dispute about the trajectory of evolution.

SAM KITTNER

Pathfinders. Christina Burch and Lin Chao traced the course of evolution in viruses that infect these bacterial cultures.

R. A. Fisher of Cambridge University had argued in the 1930s that evolution is like a staircase, on which organisms evolve through a series of small genetic steps, each one leading to a higher level of fitness. They continue to climb the same staircase, refining existing adaptations, unless a dramatic shift in the environment forces them to begin scaling a different set of stairs. In contrast, Sewall Wright, working at about the same time at the University of Chicago, imagined that genetic changes, as well as environmental ones, could derail the evolutionary process. He pictured evolution as taking place on a landscape of numerous peaks and valleys. In his eyes, harmful mutations can displace an organism from a peak into a valley. In overcoming such mutations, organisms may begin climbing a new peak, setting them on a different evolutionary course.

Chao's virus cultures suggested that both metaphors may be valid. He and his graduate student Christina Burch had originally set out to test Fisher's model of adaptive evolution, which holds that large mutations that dramatically increase fitness are likely to be rare because such mutations tend to have large, deleterious side effects. "Fisher's model is such a pretty idea," says Chao, "because it makes a very strong, straightforward prediction." Yet despite its elegance, Chao notes, "good data to support it don't exist."

Chao and Burch thought they might find supportive data by experimenting with RNA viruses because of their breakneck evolution. They multiply 100-fold every hour or so and pick up many mutations along the way. To see if viral evolution matches Fisher's model, the researchers studied a population whose members had all suffered from a deleterious mutation, which cut the number of progeny they produced. "We wanted to see how—either through large or small steps—it would regain its fitness via natural selection," explains Chao.

The researchers used populations of the severely mutated virus ranging in size from 10 to 10,000 particles. Each population was allowed to grow freely on a bacterial host. At the end of each day, Chao and Burch staged experiments comparing the test viruses with the original, unmutated strain to see how quickly the different populations were regaining their fitness.

In populations below 1000 particles, "fitness increased in multiple steps," Chao says, "which surprised and delighted us." In populations of more than 1000 particles, the virus came roaring back in one large step, presumably because large compensatory mutations were more common in the larger populations. But Chao argues that the combined results support Fisher, "because his model predicted that compensatory mutations of large effect would be rare, and that's exactly what we found. They don't occur except in very large populations."

Burch and Chao's experiment is "the first really serious empirical test of Fisher's model," says Bruce Levin, a population geneticist at Emory University in Atlanta. He adds that it shows "the power of using microbial systems to test general evolutionary hypotheses." But even if Fisher was right about the pace of evolutionary change, Chao adds, the results also support Wright's view that evolutionary shifts can occur

without major environmental change.

The populations regaining their fitness via small compensatory mutations necessarily ended up at new adaptive peaks, says Chao, which represent different ways of attaining the same fitness. "The only way to go back to the same peak you started on" is via a "back mutation" that reinstates the gene in its original form—which should occur only in a single, big step, he explains. In contrast, "a compensatory mutation implies that you're headed toward a new peak." He adds, "At least in this one case, it seems that Fisher's model fits with Wright's view of an evolutionary landscape."

"It's absolutely intriguing," says Hope Hollocher, an evolutionary biologist at Princeton University. "Chao has opened the door toward merging these two viewpoints." She notes, however, that his experiments need some fine-tuning before biologists will be convinced that Fisher and Wright aren't always at odds.

–Virginia Morell

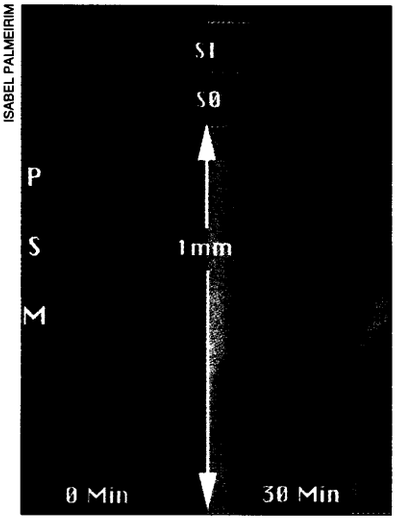
DEVELOPMENTAL BIOLOGY

New Developmental Clock Discovered

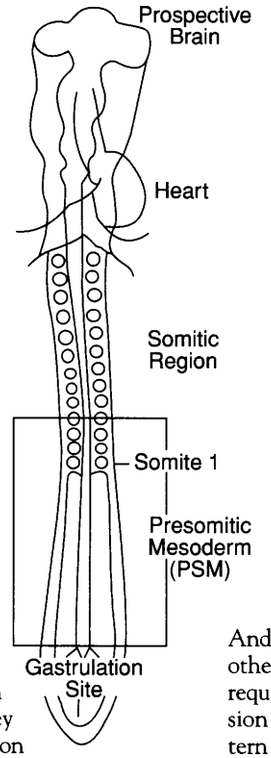
Biological clocks are turning up all over, and in the most unexpected places (see p. 1560). But they all typically keep to a 24-hour schedule, which is logical because it helps keep organisms in tune with the normal day length. But now, a team of French and British scientists has come across a new kind of biological clock, one that not only has a much shorter cycle—only 90 minutes—but also appears to be driven by a different kind of mechanism.

In today's issue of *Cell*, Olivier Pourquié, a developmental biologist at the Developmental Biology Institute of the University of Marseille in France, and his colleagues report evidence indicating that such a clock paces the development of the somites, blocks of tissue that form in regular arrays along the spinal cord of vertebrate embryos and give rise to vertebrae and muscles. The researchers found that in the developing chick embryo, a gene called *chairy* undergoes repeated 90-minute cycles of activity, its expression narrowing each time to a thin band that defines the rear edge of a new somite. These cycles seem to specify the orderly delineation of somites in the growing embryo.

ISABEL PALMEIRIM



Moving target. Two embryos differing in age by about 30 minutes have different patterns of *chairy* expression (dark blue). Embryo images correspond to the boxed area in the diagram *(right)*.



Now the Pourquié team and others are eager to know what makes this clock tick. "It's the first time that very clearly there is a clock associated with a developmental process," says clock biologist Paolo Sassone-Corsi of the University of Strasbourg in France.

The finding also has evolutionary consequences, because *chairy* is the chicken equivalent of a fruit fly gene called *hairy* (*chairy* is short for *chick hairy*), which helps drive formation of the segmented insect body plan. Developmental biologists have long debated whether the segmentlike somites of higher organisms and insect segments arose independently or had a common origin. Until now, they have failed to find common genes involved in forming these structures, but the new *chairy* results provide just such a link. "It's cool stuff," says Eddy De Robertis, a developmental biologist at the University of California, Los Angeles, who has proposed a common origin for insect and somite segmentation (*Science*, 4 July, p. 34).

David Ish-Horowicz's team at the Imperial Cancer Research Fund Laboratory in London originally cloned *hairy* more than a decade ago and showed that it is expressed in a series of stripes that help define the segments of the developing fruit fly embryo. He and Domingos Henrique in his lab then used *hairy*'s sequence to track down *chairy*, a comparable gene in the chicken. But neither they nor Pourquié, a collaborator on another project, could make sense of *chairy*'s seemingly variable expression pattern in the chick embryo.

To try to sort out the problem, Pourquié and his student Isabel Palmeirim divided chick embryos, fixing one half while maintaining the other in culture. When they then compared the gene's expression in the two halves at different times, the link to somite formation emerged. As chick embryos grow, cells are added behind the head to form a long, broad "tail." Once this tail reaches a certain size, somites begin to form one at a time, starting with the one closest to the head and working tailward. Each somite—there are 50 of these visible blocks of tissue in all—takes about 90 minutes to appear.

When the Pourquié team monitored *chairy* expression as the somites formed, they found that the gene was pacing the process. It first becomes active across the rear 70% of the presomatic tissue, starting from the tip of the tail. Over the next 30 to 40 minutes, that band of expression narrows and shifts forward toward the head, where the next somite will develop. Finally, after 90 minutes, the expression band becomes a thin stripe marking the rear edge of the new somite. At the same time this stripe appears, the gene comes back on again over the same broad region where it was initially expressed and begins the cycle anew until all 50 somites develop. "[Expression] spreads along the tissue in a very coordinated fashion," Pourquié says. This repeated, coordinated expression, he suggests, dictates to cells when it is their turn to form a somite. But he has yet to determine what coordinates the gene expression.

It's not controlled by signals from elsewhere in the chick embryo, because *chairy* cycled on and off even after the tissue where it was expressed was teased out of the embryo and grown separately. And it's not a clock like those found in other organisms, because those clocks require protein synthesis. Gene expression still followed this repeating pattern even when protein synthesis was blocked, his group reports.

But these results make the find all the more intriguing, say other researchers. They suggest that this developmental clock keeps time using a new clock type of mechanism, one that Pourquié and his colleagues are working hard to pin down. Sassone-Corsi also predicts that this new developmental clock will inspire other researchers to look for other types of clocks and timing mechanisms, and that, he adds, "is exciting."

–Elizabeth Pennisi