the very heart of the planet, as now seems likely, then the circle will be closed: Earth's surface not only sinks into the depths but deep rock feeds the surface, offering scientists another window into the planet's deepest depths.

–RICHARD A. KERR

TRANSGENIC ANIMALS

Fertility Therapy May Aid Gene Transfer

The premillennium frenzy about cloned drug-secreting sheep and cows, or pigs that have been given human genes in hopes of using them as organ donors, tends to gloss over the fact that introducing foreign genes into animals other than mice is still very difficult. Because current techniques—which primarily involve injecting DNA directly into fertilized eggs—have only a modest success rate, costs can soar to more than $300,000 for a single cow carrying a foreign gene. Now, genome tinkers may have a new tool for beefing up animal genomes with exotic DNA: sperm.

On page 1180, embryologists Anthony Perry, Teruhiko Wakayama, and Ryuzo Yanagimachi of the University of Hawaii School of Medicine in Honolulu and their colleagues report that they have used sperm to transfer a foreign gene into mice. The technique is a modification of a method originally developed by Yanagimachi for injecting sperm into eggs that is now standard for in vitro fertilization of human eggs. About 20% of the mouse pups born in the group's experiments carried the transgene—which is "definitely on the high side of what's done routinely," says George Seidel, a reproductive physiologist at Colorado State University in Fort Collins. Adds embryo physiologist Gary Anderson of the University of California, Davis, "If this works in other species, people will jump on it like a banshee."

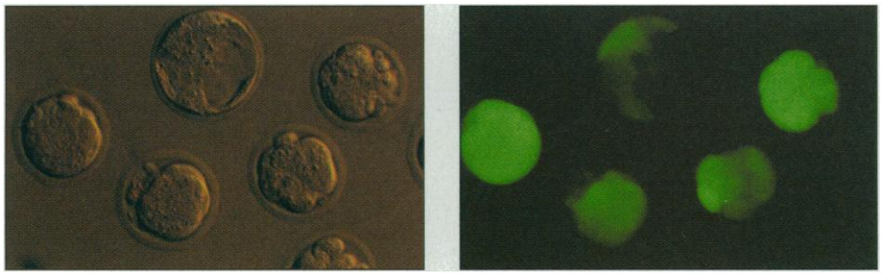
For some this is a giant "if," however. Reproductive biologist James Robl of the University of Massachusetts, Amherst, describes the technique as "very interesting." But he adds, "I'm not sure how widespread its applicability will be." He and others note that before the mouse work, the sperm injection method, known as ICSI for intracytoplasmic sperm injection, had been shown to work well only in humans.

Researchers have been trying to use sperm to create transgenic animals for about 10 years. In early experiments, they simply mixed the DNA to be transferred with sperm and used the mixture for in vitro fertilization. Although the technique initially appeared to work, Anderson says, "even leading people in the field haven't been able to repeat the original result." Today, there seems to be general agreement that such sperm-mediated gene transfer succeeds, but with highly variable efficiency.

About 2 years ago, Perry decided to take a quick shot at seeing whether Yanagimachi's ICSI method would do better. The researchers first removed the propellant tails from sperm and subjected the sperm heads to freezing or detergents to disrupt their cell membrane. They then mixed the sperm heads with a gene encoding green fluorescent protein (GFP). To inject this mixture, the team used a so-called piezoelectric device, which drives the tiny injection pipette very fast and precisely into mouse eggs.

Compared to the manual injection devices used in human fertility clinics, piezoinjection seems to be far less disruptive for the egg. "The mouse egg is the most fragile of [all species]. This study would have been impossible without the piezodevice," says Robert Wall, a geneticist at the U.S. Department of Agriculture's Agricultural Research Service in Beltsville, Maryland.

When the researchers injected the GFP gene along with untreated sperm, only 26% of the embryos carried the transgene. But it was present in up to 87% of the early embryos produced by the detergent-treated or frozen sperm—as indicated by the embryos glowing green under an ultraviolet lamp. Ultimately, however, only about 20% of the newborn pups that developed from the injected eggs carried the GFP gene. Perry suspects that GFP has a deleterious effect on embryonic development, so the transgenic fetuses tend to be selectively aborted. Whatever happens, a majority of the animals that end up with the transgene trans-



Greening up. These mouse embryos glow green under ultraviolet light *(right)* because they acquired the gene for green fluorescent protein along with injected sperm.

CREDITS: PERRY *ET AL.*

ScienceScope

Clinical Clampdown A member of the U.S. biomedical elite—Duke University's Medical Center in Durham, North Carolina—was ordered to freeze most of its clinical research this week. Duke University stopped enrolling new patients in government-sponsored studies after receiving an order to halt from the Office for Protection from Research Risks (OPRR), which is part of the Department of Health and Human Services.

OPRR officials could not be reached for comment, but Duke disclosed in a statement on 11 May that OPRR has been asking the university since December to bring its procedures into line with OPRR rules. Among other things, OPRR has asked Duke to keep more extensive records and create a second review panel to monitor a growing number of clinical trials. Duke offered some changes in March and April. But OPRR, displeased with "the scope and pace of [Duke's] implementation of corrective actions," suspended patient enrollment in government-sponsored trials on 10 May.

Duke's chancellor for health affairs, Ralph Snyderman, says "hundreds" of studies will be disrupted. University officials "absolutely were not" prepared for OPRR's order, he says, adding that it "would be an understatement" to say it took them by surprise. "From our perspective," Snyderman says, "I don't believe any patient was put at risk," but he is satisfying OPRR's requirements and hopes to get clinical research on track in a week.

Pulling Up Their Genes France's genome research may soon get a big boost. The government is considering plans to pump an additional $330 million over the next 3 years into a gene research complex in the Paris suburb of Evry, according to a report this week in *Le Monde*.

The extra spending is reportedly driven by worries that the French genome program is being left behind by major investments in gene research in the United States and the United Kingdom. Officials hope that by following suit, France will get its share of potentially lucrative genome patents.

Officials at Génopôle—which includes the national gene sequencing center and several corporate labs—were not available for comment as *Science* went to press.

mit it to their offspring.

Experts in the field of transgenic animals welcome the new study for adding yet another gimmick to their arsenal of techniques. "It's always nice to have a large collection," Robl says. And the longer the list, he adds, the easier it might become to make transgenics in other species. "This study will create a stir of activity," Seidel says. "I'm sure a lot of people will be trying it."

Whether the expected activity will pay off is, however, a matter of debate. "It will probably not supersede anything that is out there because the efficiency is not that much better than [DNA] microinjection," says Wall. (Current DNA microinjection has a success rate of about 10% in mice.) But Perry says that comparing his new technique to the much more advanced DNA microinjection is unfair. He notes that the efficiency of the latter has increased by three- to fourfold since the first experiments. "If we have a similar increase, almost every animal will be transgenic," Perry concludes.

But the skeptics contend that even if that can be accomplished for mice, using ICSI to transfer genes into other species still might not work. "ICSI is technically quite challenging; it's not as simple as DNA microinjection," says Wall. Perry disagrees, saying that it can't be that hard because "three of the four people who performed the injections had never made a transgenic animal in their lives. It'll take a little time [to perfect the technique]; we're only at the start."

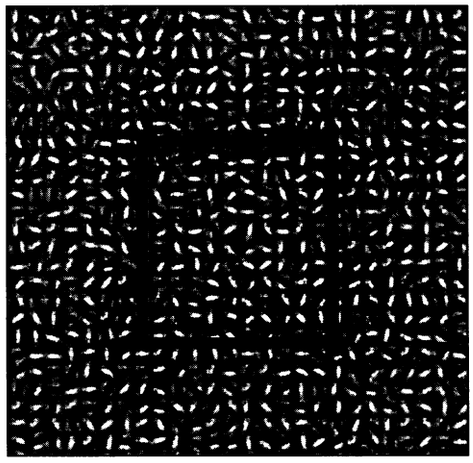
And he should have help in the effort. Despite his reservations, Wall recently purchased one of the $10,000 piezodevices to see for himself whether ICSI lives up to the claims. **–MICHAEL HAGMANN**

NEUROBIOLOGY

Time Cues Help the Brain See Objects

One of the most critical jobs our visual system performs is to group the myriad features of a visual scene into the discrete objects that form the scene. As New York University neuroscientist Anthony Movshon explains, "It is very hard to analyze an image until you have broken it into the objects it contains." Fortunately our brains are virtuosos at this task, called binding, linking even the disjointed parts of an object that is heavily obscured, such as a figure seen through dense woods. Work described in this issue reveals one of the brain's tricks for sorting through scenes so efficiently.

Using psychophysics experiments, in which human volunteers solve visual puzzles, neurobiologists had already shown that cues such as color, continuity, texture, and movement help the brain assemble objects from their parts. On page 1165, Randolph Blake and graduate student Sang-Hun Lee of Vanderbilt University in Nashville, Tennessee, provide the most convincing demonstration yet that the visual system can also exploit timing information, even in the absence of any other cues, grouping features of the scene that change at the same time into coherent objects.



Hidden shapes. No shape emerges from a static image of random circular patches; only when the patch is put in motion does the timing of motion changes reveal the outlined rectangle. For a demonstration, visit www.psy.vanderbilt.edu/faculty/blake/Demos/TS/TS.html

CREDIT: SANG-HUN LEE & RANDOLPH BLAKE

This is "perhaps the most interesting new work in visual psychophysics to come out in the past 10 years," says neuroscientist William Newsome of Stanford University School of Medicine. "It gives us even more appreciation than we had before for the clever approaches that biological visual systems take to make sense of the visual world." In addition, the work has spurred a vigorous debate among neuroscientists about whether it provides support for a controversial hypothesis postulating that neurons in the visual system that are responding to different parts of the same object become bound together by firing in synchrony.

For their experiments, Blake and Lee tested people's ability to see shapes in abstract patterns of small circular patches on a computer screen. As anyone knows who has watched a well-drilled marching band spell out the school's letters by having some members march in a different direction than the rest, a common direction of motion can make shapes jump out of such a pattern. But Blake and Lee wanted to test whether the brain could see a shape based not on common motion, but simply on common timing of visual changes. Several recent studies had suggested that the brain could use timing information for binding, but Blake notes that those tests—based on flickering patterns of dots—contained other cues as well. He and Lee wanted a test in which timing was the only cue to the form hidden in the scene.

To do this they used an array of patches that resembles a completely chaotic marching band, whose members move about the field in a random way. In a rectangular region at the center of the field, however, all of the patches repeatedly changed their direction of movement simultaneously, at irregular intervals. People viewing the test could see the rectangle well enough to tell whether it was oriented vertically or horizontally.

"They have very carefully removed all the spatial information," says Movshon, and "demonstrated that ... you can drive a binding process purely with temporal stimuli." It is reasonable that timing would be a binding cue, says Movshon, because when a real object moves, all its parts generally begin to move at the same time. What's more, in some natural situations, timing alone, rather than a shared direction of motion, might be the main cue. "Imagine a disturbance in a forest, created by a predator moving around in a tree," he says. A synchronous change in the movement of leaves on that branch may be the only clue to the predator's presence.

Lee and Blake's experiment doesn't identify the brain neurons responsible for seeing the rectangle, but Newsome notes that movement-sensitive neurons reacting to the synchronous change in motion are likely to fire synchronously. And that notion sounds familiar, says Stanford neuroscientist David Heeger. It "makes you think immediately," he says, about the hypothesis advanced by neuroscientist Wolf Singer of the Max Planck Institute for Brain Research in Frankfurt, Germany, and others, that synchronous firing binds together neurons perceiving the same object (*Science*, 24 August 1990, p. 856).

Heeger notes, however, that the subjects in Blake and Lee's experiments are responding to synchronous timing in the visual image itself. Singer, on the other hand, holds that neurons responding to different parts of an object will synchronize even if there is no timing signal coming from the object. "I don't think [this new experiment] bears at all on the question of whether the brain uses temporal synchrony to signal binding for other kinds of patterns," says Movshon, and Newsome, Heeger, and others adamantly agree.

But Singer does not. He is elated, he says, to see "direct evidence that synchrony is interpreted by the cortex as a signature of relatedness when it is induced externally. It would be strange," he adds, "if internally generated synchrony ... were interpreted in