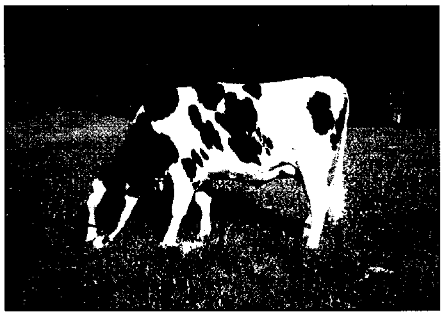
they are mosaics that have the gene in some cells but not in others, including those of the germ line. Each transgenic livestock animal has cost about $500,000 to produce.

Those low success rates prompted the Roslin researchers and others to turn to cloning experiments in which they replicate individuals from somatic cells to increase the numbers of transformants. But in the 24 November issue of the *Proceedings of the National Academy of Sciences*, Robert Bremel, formerly of the University of Wisconsin, Madison, and now managing director of Gala Design, a biotech firm in Sauk City, Wisconsin, his former Wisconsin student Anthony Chan, and their colleagues report that they have achieved a transformation efficiency approaching 100%. They did this by introducing a foreign gene into cow eggs before they were fertilized rather than shortly after, as is currently done.



On the hoof. This heifer, Cressy, produces hepatitis B surface antigen in her milk.

The increased efficiency should be welcome news to researchers who want to introduce genes into livestock, either to improve the strains or to use the animals to produce medically valuable proteins, such as monoclonal antibodies or vaccine proteins. "This is good work," says geneticist Robert Wall of the U.S. Department of Agriculture's Agricultural Research Service in Beltsville, Maryland. He notes that because the gene transfer work is very costly, only about a dozen labs do it now. Improved efficiency might draw others in, however.

In the older techniques, researchers introduce a gene in a carrier, such as the DNA of a retrovirus that can insert itself into the host cell DNA, into an egg that's already been fertilized. But if the DNA doesn't insert until after the egg starts dividing, as is often the case, it ends up only in the descendants of the cell where it integrated, which might be a small minority of the total in the embryo.

To counter this problem, Bremel and his colleagues decided to use unfertilized bovine oocytes isolated in metaphase arrest, when the membrane that normally surrounds the nucleus is absent. The researchers reasoned that this would make it easier to get the foreign gene to the chromosomes so that it could integrate. In addition, putting the gene in the chromosomes of the egg itself would ensure that the gene would end up in all the cells, including the germ cells, of the animal produced when the egg was subsequently fertilized. In cows, "the DNA is incorporated better when inserted earlier," says Bremel.

And that's what the team found. First, they introduced the gene coding for the hepatitis B surface antigen into a retroviral carrier. They chose this gene, Bremel says, partly because the antigen makes an easily detected marker and partly because any transgenic animals could produce the antigen, which is used in hepatitis B vaccines. The researchers then injected the retrovirus into the oocytes, allowed them to mature, and fertilized them.

Of the 836 eggs injected, 174 developed into embryonic blastocysts, and 10 of these were implanted into five foster mothers. This yielded three pregnancies and four healthy calves, two males and two females, now about 2 years old. Tests on skin and blood cells revealed that all four animals carry the hepatitis B gene. In addition, the females, Cressy and Buttons, secrete the antigen in their milk. And mating one of the bulls, Gremlin, with a nontransgenic female produced twin offspring, both transgenic. The researchers say that this technique should work in other species, including primates, where immature egg cells can be manipulated during metaphase. Indeed, if the technique proves as efficient as it now appears, it might even make livestock cloning obsolete. –ANNE SIMON MOFFAT

NANOTECHNOLOGY

AFMs Wield Parts for Nanoconstruction

Nanotechnologists dream of creating useful machines the size of a virus, but for the time being they are in the position of a tinkerer who has a pile of parts but no workbench for assembling them. They have created a handful of molecular blocks, spheres, and rods but don't have a means of manipulating and joining the tiny components. But at the Sixth Foresight Institute Conference on Molecular Nanotechnology held in Santa Clara, California, last week, a team from Washington University in St. Louis and Zyvex, an instrument company based in Richardson, Texas, showed off their technique for wielding individual carbon nanotubes with a trio of robotic arms.

The researchers welded opposite ends of tiny, straw-shaped tubes of carbon atoms to two tiny silicon probes normally used to map surface contours by "feel" in an atomic force microscope (AFM). They then moved the probes to twist, tug, and bend the tubes and even brought in a third arm to give the nanotube a nudge in the middle. All of this was accomplished inside a scanning electron microscope (SEM), allowing them to view and control the nanomanipulation as it happened. "This is very, very beautiful work," says Anupam Madhukar, a materials scientist at the University of Southern California in Los Angeles. Cees Dekker, a nanotube researcher at Delft University of Technology in the Netherlands, says the most exciting demonstration was one showing two probe tips tugging on a nanotube until it broke. "That means they can now determine exactly how strong the nanotubes are," which has long been a goal of the community, he says.

Nanotubes, essentially just rolled-up sheets of graphite with diameters as small as 1 nanometer but lengths up to 100 micrometers, have been proposed for a wealth of jobs in the nanotoolkit (*Science*, 14 August, p. 940). Research teams have already hooked nanotubes to the apex of an AFM tip, a tiny silicon pyramid suspended from a cantilever arm, in an effort to improve the microscope's resolution, but the acrylic adhesive used to bond tube to tip has only moderate strength. For the new work, the Washington-Zyvex team had to figure out how to fasten the tube securely to two AFM tips while imaging it at the same time.

First the team developed a kind of nanoscale jig, incorporating three independently movable AFM tips in different orientations. To attach nanotubes to these tips, the team used its SEM imager as a welding gun. SEMs image an object by scanning an electron beam over its surface and detecting the reflected electrons. Previous teams had shown that an SEM's focused beam can break up stray organic molecules floating in the vacuum chamber. This creates negatively charged hydrocarbon fragments that pile up on positively charged surfaces. So graduate student MinFeng Yu decided to see if those fragments could "weld" the nanotube to their AFM tip.

Yu first dipped an AFM tip into a tiny pile of nanotubes, relying on static electricity to hold one end of a nanotube to the tip. He then focused the SEM beam so that it directed organic fragments in the vacuum toward the junction of the tube and the tip, which was given a positive charge. The result was a tiny carbon-based mound at the base of the nanotube. Then he steered a second AFM tip up next to the other end of the nanotube and repeated the nanowelding procedure. When he then moved the tips relative to one another, the nanotube curved and stretched, showing that the welds were secure—so secure, in fact, that when he pulled the tips apart with enough force, the nanotube broke. "That was a surprise, because we expected that the welds would be weaker than the nanotubes," which are theorized to be stronger than steel,

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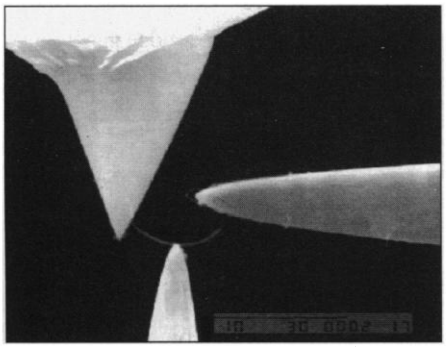


Nanojig. Robotic tips bend, stretch, and prod carbon nanotube.

says physicist and team leader Rodney Ruoff of Washington University.

Ruoff says it's too early to tell how much force it takes to break a single nanotube because the resolution of their SEM is insufficient to judge whether they are looking at a single nanotube or several. The team is hoping to answer that question using a more sensitive SEM or a higher resolution transmission electron microscope. After that, Ruoff says they plan to try welding nanotubes to each other, and then the real construction will begin.

–ROBERT F. SERVICE

ASTRONOMY

Looking South to the Early Universe

A flash of news from the Hubble Space Telescope: The distant universe looks about the same in two opposite directions. When the Hubble was aimed at a small patch of northern sky for 10 days in 1995, astronomers believed that their time exposure had captured a typical sliver of the distant universe. But it never hurts to check. At the beginning of October, they followed up on the original Hubble Deep Field (HDF) with a 10-day exposure of a nondescript patch of sky near the south pole—and found similar swarms of faint galaxies, some of them among the most distant and earliest ever seen.

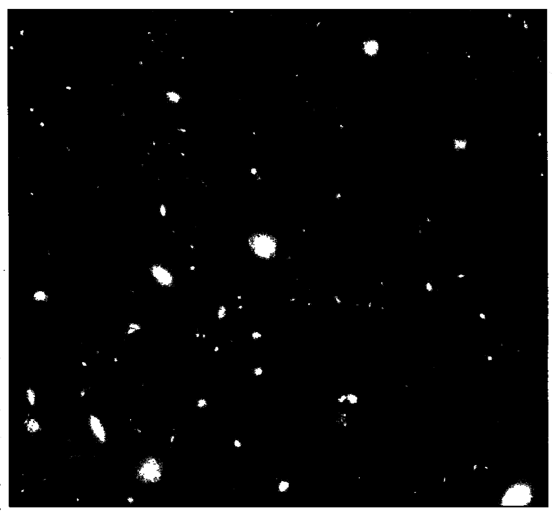
That outcome may sound prosaic, but it's very welcome news to astronomers. "It was crucial to check on our assumption that the HDF is typical of the universe" with a second line of sight, says Alex Filippenko, a galaxy expert at the University of California, Berkeley. And the new view is more than just a reprise of the first: Instruments installed on the orbiting telescope since 1995 have enabled it to harvest far more detail this time around.

"We should call the new results not the Deep Field South but the Southern Fields," says Robert Williams, former director of the Space Telescope Science Institute in Baltimore and now a staff astronomer there, who devoted much of his "director's discretionary time" to the northern and southern deep fields. "This time we obtained three separate images, and comparisons among them will yield significant new results" about how galaxies formed and evolved.

One of the southern images was made with the same camera system used in 1995. Equipped with color filters, it recorded the galaxies' colors, which hold clues to their distances. The reddest galaxies, their light "redshifted" to longer wavelengths by the expansion of the universe, are likely to be the most distant. A second field, slightly offset from the first because it was made with a different instrument, the NICMOS infrared camera, may have captured even more distant galaxies, their light stretched all the way into the infrared. And a third field, recorded with the Space Telescope Imaging Spectrometer (STIS), broke light from the early universe into spectra that may yield new details about galaxy formation.

The HDF and the Southern Fields both record cosmic history, because they offer not a snapshot but a palimpsest of cosmic epochs, seen one behind another out to the most distant galaxy. Already, astronomers studying the HDF have traced how galaxy shapes and numbers change over time. "Look at the [most distant] galaxies: There's not a normal-looking one among them" in comparison with nearby galaxies, seen after 12 billion to 14 billion years of cosmic evolution, says Harry Ferguson, an associate astronomer at the Space Telescope Science Institute.

The STIS image in the new Southern Fields could flesh out this picture by showing how clouds of intergalactic gas fed galaxy formation long ago.



Déjà vu, almost. The clutter of galaxies, up to 12 billion light-years away, in Deep Field South resembles the northern view.

CREDITS: (TOP) ZYVEX LLC; (BOTTOM) R. WILLIAMS/STSCI/THE HUBBLE DEEP FIELD-SOUTH TEAM/NASA

ScienceScope

REPORT ON R&D STRAINS COULD STRESS ACADEMIA

The White House is finishing a report defining its relationship with the research community. But the document, a 2-year effort in response to concerns that those ties are fraying, may disappoint academic administrators seeking relief from a handful of regulations they say drain their schools' time and wallets.

White House sources say the interagency report, expected out in draft form in January, concludes that the relationship is strong but in need of attention. It reaffirms the importance of peer review and of both teaching and research in training students and asks agencies to set uniform policies on scientific misconduct. But it ducks such contentious issues for universities as the tax status of graduate students and recommends further study of how to simplify federal accounting practices and whether to remove limits to recovering the full cost of administering federally funded research.

Milton Goldberg, head of the Council on Government Relations, which last year funneled complaints from university administrators to the panel, says he's glad the report upholds the value of the government's investment in research. But he warns that individual federal agencies need clearer guidelines to avoid "subverting" such principles when they set policies for specific programs.

EUROPEAN UNION AGREES ON R&D BUDGET

The European Union's R&D program finally got a budget last week. After lengthy negotiations, a council of research ministers and the European parliament agreed to spend $18 billion over the next 4 years on the 5th Framework research plan, which supports projects jointly funded by the 15 EU nations.

The sum was less than parliamentarians had pushed for, but it was still the first real increase the program has seen since 1990. But only next year's $3.7 billion outlay is definite, because Spain pushed through a "guillotine" clause. It allows Spanish officials to renegotiate spending if they conclude next year that some regions aren't getting a fair share of the EU's full 2000-2002.

Parliamentarians are grumbling about the uncertainty. But members of the Framework's commission are "rather pleased with the outcome" because the program can begin without delay, says a spokesperson.

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