doom many research projects, noting that no other facility offers the same combination of highly sensitive and stable receivers to detect faint signals, extremely efficient data collection, and wide frequency coverage in the millimeter range. "I myself won't be able to finish five or six projects," she says.

Others worry that the closure could drive young researchers out of the field. These critics doubt that ALMA will begin even interim operations by 2005, given that NSF has requested $6 million to extend a 3-year, $26 million design and development effort for another year and won't make a bid for construction funds until 2002 at the earliest.

To be sure, the directors of at least two university facilities—the California Institute of Technology's Owens Valley Radio Observatory and the Five College Radio Observatory in Massachusetts—say they would welcome proposals from Kitt Peak researchers. The university community "may well be able to pick up much of the slack," says Anneila Sargent, president-elect of the American Astronomical Society, director of Owens Valley, and a member of the board of Associated Universities Inc., which operates NRAO for NSF. "Compromises and adaptations will be possible." But some astronomers are skeptical that university-run dishes and arrays will be able to accommodate researchers displaced from Kitt Peak. "Yes, the university facilities make time available to outside scientists, but they're not really oriented to the general user like a national observatory," says astronomer Jean Turner of the University of California, Los Angeles.

Whatever the outcome, all parties agree that the decision to close the 12-meter telescope is a sad one. "You'd like to focus on the future without letting go of the present and the past," says Vanden Bout. "Unfortunately, that couldn't happen here."

–MARK MURO

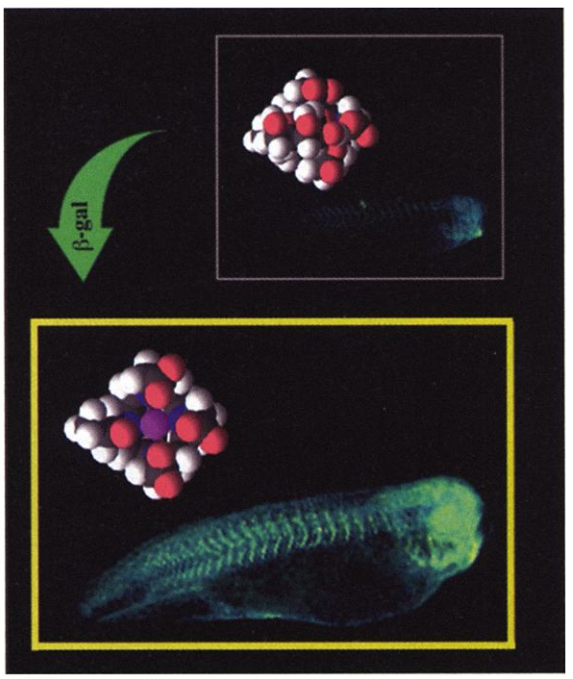
Mark Muro writes from Tucson, Arizona.

MAGNETIC RESONANCE IMAGING

Detecting Enzyme Activity in Live Animals

Thomas Meade and his colleagues at the California Institute of Technology in Pasadena have adapted a technique perhaps best known for peering inside athletes' injured knees to watch genes being turned on in living tadpoles. The researchers report in the March issue of *Nature Biotechnology* that they've used magnetic resonance imaging (MRI) to track the expression pattern of an enzyme called β-galactosidase in living *Xenopus laevis* tadpoles. They were able to see the enzyme being produced deep within the animal's head, where conventional imaging techniques can't reach without slicing through the animal.

"They can see a measurable result in a living animal," says Claude Meares, a chemist at the University of California (UC), Davis. "That's really quite exciting." What's more, the resolution—the highest so far in these types of studies—was good enough to discriminate structures as small as individual cells. Richard Harland, a developmental biologist at UC Berkeley, describes that achievement as "impressive."



Uncaged. When β-galactosidase (β-gal) opens the chemical cage surrounding gadolinium (purple), cells producing the enzyme light up in the MR image of this tadpole.

Meade's team is one of several groups using MRI to probe cellular processes deep inside living organisms (*Science*, 17 December 1999, p. 2261). The payoff could be considerable. By allowing researchers to follow the activity of specific genes in living embryos, for example, the technique should generate new insights into embryonic development. And ultimately, experts hope, it will provide more sensitive methods for diagnosing diseases such as cancer and also help physicians measure how well therapies for cancer and other diseases are working.

Typically, MRI detects perturbations induced in hydrogen atoms—particularly those in water—by an intense magnetic field. To measure the activity of β-galactosidase, Meade and his colleagues needed to find a way to amplify the signal only in those cells where the enzyme is active. They turned to gadolinium, a metal that enhances the contrast in MR images because its unpaired electrons interact with the protons in water, boosting the signal. The researchers enclosed the gadolinium in a chemical cage that normally keeps it from interacting with water, but they provided the cage with a gate, in the form of a sugar molecule, that springs open when clipped off by β-galactosidase. This exposes the gadolinium to water, thus upping the MRI signal wherever the enzyme is active.

To test the technique, Angelique Louie, a postdoc in Meade's lab, injected both of the first two cells of *Xenopus* embryos with the caged gadolinium. Then she injected DNA or messenger RNA that encodes β-galactosidase into just one of the two cells and allowed the embryos to grow into tadpoles.

The researchers generated MR images of the living animals. Then they compared these images with the patterns obtained when they killed the animals and stained them with a reagent that reveals β-galactosidase activity. Bright regions in the MR images correlated strongly with the locations of enzyme production revealed by the staining. "You can see things to a cellular level in deep tissues," says Louie.

The method holds promise for a wide variety of applications. In principle, Meade notes, the chemical properties of the gate that shields the gadolinium can be modified so that it opens in response to any of many different enzymes. In addition to creating agents that could be used to study embryonic development, researchers could, for example, devise compounds that are activated specifically in cancer cells. This might provide a technique for early detection of new tumors or those regrowing after treatment, notes Daniel Sullivan, a radiologist at the National Cancer Institute in Bethesda, Maryland. Similarly, it might someday be possible to monitor the effectiveness of gene therapy by designing the gadolinium cage so that it's opened by a therapeutic gene's product.

Researchers have a long way to go before such applications become reality, however. In order to be medically useful, the caged gadolinium would have to penetrate into the tissues of the body after it is injected into the bloodstream. The next step, Meade says, is to look at how well the compound distributes through small animals such as mice. If it doesn't, he says, he hopes to devise ways to deliver the compound efficiently, say by attaching proteins that can snake their way into cells. "The door's been cracked," Meade say. "Now it's just left to our imagination to see what we can develop."

–EVELYN STRAUS

CREDIT: A. LOUIE AND T. MEADE, *CHEMICAL & ENGINEERING NEWS*