

Lee says that further experiments could help his research on infertility, for example, in overcoming deficiencies in the eggs of patients trying to become pregnant. But he says he plans to wait for new regulations that define what procedures to follow.

Such regulations were the topic of two recent public forums. On 18 January, a citizens' group assembled a panel here to discuss what was billed as "a legal response to human cloning." The panel included a lawyer with expertise in litigating medical issues, a Catholic human rights activist, a private-sector biotech safety advocate, and Seo. The panel urged legislators to strike a balance in its regulation of this powerful technology.

The conference was one in a series organized to encourage public dialogue on important civic issues. And the comments reflected a range of views on the subject of cloning. One citizen complained about paying taxes to support work by unethical scientists, while another asked, hopefully, whether this technology might make it easier for lesbian couples to have babies.

On 20 January, national legislator Lee Sang Hee convened a cyber-conference to discuss his plans to amend existing laws governing bioengineering. Lee hopes to address ethical concerns without hindering the country's scientific competitiveness, says an aide.

Lee has proposed a national ethics review that would report to the science minister. Although such a body is essential, says Park Byung Sang of the private Biosafety Ethics Association, it needs to report directly to the prime minister to remain independent of special interests. Whether that is done, academic observers predict that the Kyunghee experiments will spur more universities to establish their own ethical review boards. Such boards now exist at only two universities, Yonsei and Seoul National.

—MICHAEL BAKER

Michael Baker writes from Seoul.

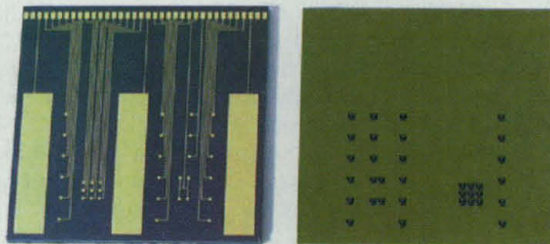
DRUG DELIVERY

Silicon Chips Find Role As in Vivo Pharmacist

Once upon a time, microchips were confined to the hearts of computers. Now they inhabit everything from children's toys to toasters. Before long, according to a team of researchers at the Massachusetts Institute of Technology (MIT) in Cambridge, they will turn up inside your body. In this week's issue of *Nature*, the team reports creating the first drug-delivery microchip, the progenitor of devices that may be capable of releasing variable doses of multiple drugs over an extended time once swallowed or implanted

under the skin. The new chips have yet to be tested in animals or humans, but already some experts believe they have the potential to radically change the way many patients take medication.

"It's conceptually an extraordinarily exciting breakthrough," says Henry Brem, a neurosurgeon and oncologist at The Johns Hopkins University School of Medicine in Baltimore, Maryland. The centimeter-square silicon chips bear a series of tiny wells, sealed with membranes that dissolve and release the contents when triggered by an elec-



Dime store. Implanted chips (shown front and back) could release controllable drug doses.



trical signal. If loaded with potent medications, the chips could administer doses of one or more different drugs for months at a time. "The ability to modulate multiple drugs in a local environment would be an incredible step forward," says Brem. The researchers also hope to engineer the chips so that they can change the drug-release schedule or medication type in response to commands beamed through the skin. Such an ability would aid treatment of conditions such as Parkinson's disease and cancer, where doctors need to adjust medications and dosages.

Controlling how drugs are released in the body is already a big business. Timed-release capsules, nicotine skin patches, and their ilk racked up \$14 billion in sales in 1997. But these either provide a single pulse of a drug as the protective capsule dissolves, for example, or continuously release the drug for a set length of time as a degradable matrix dissolves. "What doesn't exist is a pulsatile delivery system that you can control," says MIT chemist Robert Langer, who led the new effort.

To create one, Langer enlisted the help of MIT doctoral student John Santini and Michael Cima, an MIT colleague and microelectronics fabrication expert. The trio started with a standard silicon wafer, normally used to make computer chips, and

used conventional chip-processing techniques to carve a series of 34 tiny reservoirs in the chip, each capable of holding just 25 nanoliters of liquid, less than the volume of a grain of salt. Additional deposition, patterning, and etching steps created a circuit of gold wires on the top surface of the chip and tiny gold membranes capping each well. The bottom of each well was still open, allowing the researchers to flip the chip over and fill each compartment with fluorescent and radioactive compounds—easy to detect in initial

tests. Finally, they sealed the back with a sheet of either glass or epoxy.

To test the chip, Langer, Cima, and Santini dunked it in a buffer solution mimicking the body's pH and chloride concentration. They then flipped a switch to send a current through one of the gold electrodes covering a single well. Robbed by the current of some of their electrons, positively charged gold ions in the electrode readily reacted with chloride ions in solution to create a metal salt. The gold membrane covering the well dissolved in just seconds, spilling its contents into the solution. Now that the team has demonstrated the principle, they have more ambitious plans. "You can put thousands of [wells] on a chip the size of a dime," says Langer. And because each reservoir-topping electrode can be wired separately, researchers can control exactly when each reservoir releases its contents.

But the new pharmacy chips still have a long way to go before reaching the market, says Langer. Researchers must first test them in animals and humans to ensure that all of the components are biocompatible. To operate autonomously inside the body, the chips will need additional circuitry and battery power. Also, the chips will not be suitable for all drug therapies: Insulin, for example, must be taken in doses of up to 1000 milligrams several times a day, more than the chips can handle. Instead, the pharmacy chips will more likely find use delivering precise amounts of extremely potent compounds, such as hormones and ultrastrong painkillers.

Other uses outside the body could come sooner. Chips designed to stagger the release of different compounds could help automate tasks ranging from laboratory tests to pharmaceutical drug discovery. The team says a chip could even be charged with different fragrances and put in a TV set to release, say, the aroma of pepperoni as accompaniment to a pizza advertisement.

—ROBERT F. SERVICE