An 'attractive' man-machine interface

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Researchers at Children's Hospital Boston have developed a new "nanobiotechnology" that enables magnetic control of events at the cellular level. They describe the technology, which could lead to finely-tuned but noninvasive treatments for disease, in the January issue of *Nature Nanotechnology* (published online January 3).

Don Ingber, MD, PhD, and Robert Mannix, PhD, of Children's program in Vascular Biology, in collaboration with Mara Prentiss, PhD, a physicist at Harvard University, devised a way to get tiny beads – 30 nanometers (billionths of a meter) in diameter – to bind to receptor molecules on the cell surface. When exposed to a magnetic field, the beads themselves become magnets, and pull together through magnetic attraction. This pull drags the cell's receptors into large clusters, mimicking what happens when drugs or other molecules bind to them. This clustering, in turn, activates the receptors, triggering a cascade of biochemical signals that influence different cell functions.

The technology could lead to non-invasive ways of controlling drug release or physiologic processes such as heart rhythms and muscle contractions, says Ingber, the study's senior investigator. More importantly, it represents the first time magnetism has been used to harness specific cellular signaling systems normally used by hormones or other natural molecules.

"This technology allows us to control the behavior of living cells through magnetic forces rather than chemicals or hormones," says Ingber. "It may provide a new way to interface with machines or computers in the

future, opening up entirely new ways of controlling drug delivery, or making detectors that have living cells as component parts. We've harnessed a biological control system, but we can control it at will, using magnetic forces."

In a demonstration involving mast cells (a kind of cell in the immune system), Ingber and Mannix showed that the beads, when bound to cell receptors and exposed to a magnetic field, were able to stimulate an influx of calcium into the cells. (Calcium influx is a fundamental signal used by nerve cells to initiate nerve conduction, by heart and muscle cells to stimulate contractions and by other cells for secretion.) Magnetic fields alone, without the beads, had no effect.

The beads' 30-nm size (with an inner 5-nm particle) provides the optimal crystal geometry to make them "superparamagnetic" – able to be magnetized and demagnetized over and over, notes Mannix, who shares first authorship of the paper with Sanjay Kumar, MD, PhD of Children's. (Kumar is now a faculty member in Bioengineering at the University of California at Berkeley.) To give a sense of scale, one nanometer is to a meter (about a yard) as one blueberry is to the diameter of the Earth.

The beads were made to attach to the mast-cell receptors by pre-coating them with antigens; these antigens then bound to antibodies that coated the receptors, similar to the way antibodies bind to antigens in the immune system. "Our goal was to have one antigen coating each bead, so that each bead would bind to just one receptor," Mannix says.

As an accompanying News & Views article notes, "scaling down the interactions to single receptors demonstrates unprecedented control at the individual protein level."

Electrical stimuli have been used to influence the activity of nerve cells,

but isn't effective in cells that aren't electrically excitable by nature, the researchers note. The advantage of a "nanomagnetic" control system is that it can be used in a broad range of cell types and provides a near-instantaneous on-off switch, unlike hormones and chemicals that can take minutes to hours to act and then may linger in the body. In addition, magnets can be portable and have low power requirements, allowing their use in the military and other mobile situations.

Ingber envisions a kind of pacemaker that would involve an injection of nanoparticles into the heart that could then be controlled magnetically. "You could make those cells responsive to magnetic forces that work through the skin, rather than having to do surgical implants or place wires," he speculates.

"You could also have a pacemaker for muscles in different parts of your body, or a pacemaker for producing hormones or insulin," Ingber adds. "If you're a diabetic, you could have cells that produce insulin put under your skin, and then inject nanoparticles that go to those cells. Then, when you have a meal and need more insulin, you could just use a magnet to cause the cells to produce more. So you wouldn't have to keep buying the drug and injecting it."

The nanomagnetic system could also interface with external instruments and computer controls that take in information from the body or the surrounding environment and activate the magnet as needed, Ingber adds.

A diabetic, for example, could have a transdermal glucose sensor that controls the magnet, which then controls the insulin production by itself. In the neonatal intensive care unit, sick newborns could have their heart and breathing rates monitored and their cells rigged to respond through magnetic stimulation, without a tangle of wires and probes. Or, on the battlefield, the magnet could trigger production of an antidote when a

toxin or infectious agent is sensed in the environment.

But these examples are just theoretical. “The applications are hard to define because we’re opening up a whole new area of control that never existed before,” Ingber says.

Source: Children's Hospital Boston