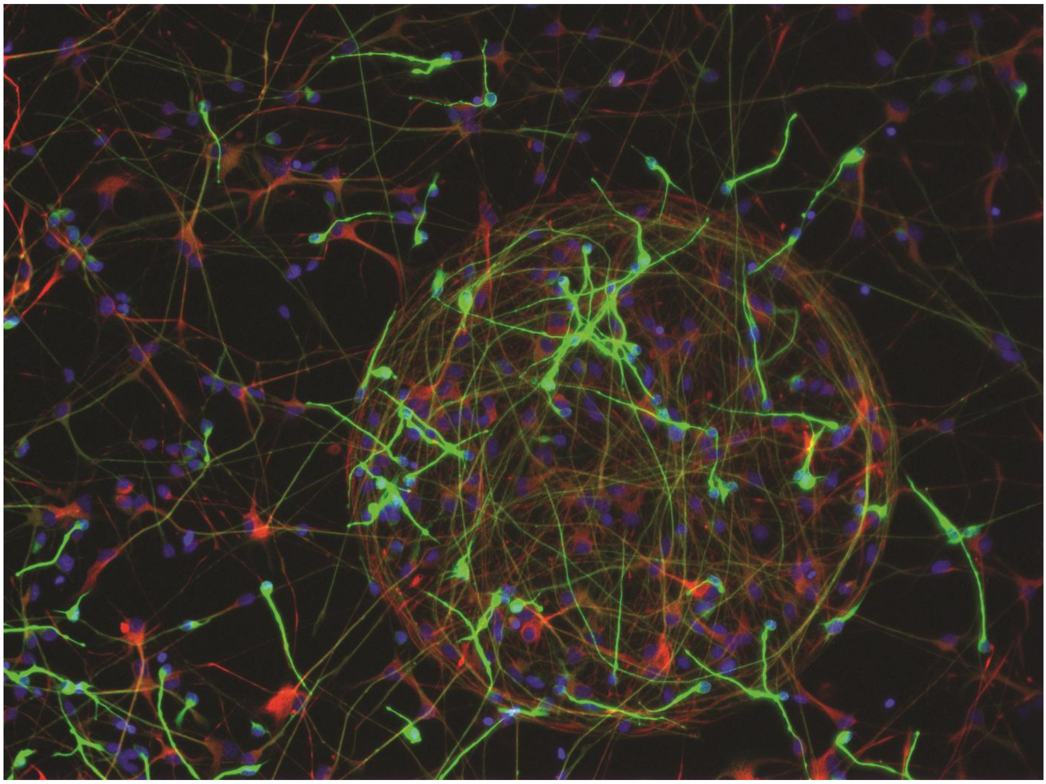
UCSF scientist transforms skins cells into brain cells

New stem-cell technology shows promise in treatment of neurodegenerative diseases.

BY NEEL PATEL



Cellular rewiring. Ding and his colleagues have been able to generate human induced pluripotent stem cells from mature somatics cells by direct reprogramming, which can be used in a wide range of disease studies. Image courtesy of GE Healthcare, http://www.flickr.com/photos/gehealthcare/4253575089/lightbox/.

A recent breakthrough at the Gladstone Institute of Cardiovascular Disease at the University of California, San Francisco has the potential to radically change the way doctors treat neurodegenerative diseases. Sheng Ding and his lab were able to successfully convert human skin cells into functional brain cells. Published in *Cell Stem Cell*, the results of the study could potentially wipe out illnesses like Alzheimer's, Parkinson's, and Huntington's disease.

"Dr. Ding's latest research offers new hope for the process of developing medications for these diseases," said Lennart Mucke, director of neurological research at Gladstone. "There is also the possibility of cell-replacement therapy to reduce the trauma of millions of people affected by these devastating and irreversible conditions."

Embryonic stem cells are pluripotent, meaning they are capable of maturing into any type of cell in the body. Many in the scientific community believe that these cells are critical to the future of regenerative medicine, in which damaged organs and tissues can be easily repaired or replaced.

Ding's research was an extension of the work undertaken by another Gladstone scientist, Shinya Yamakana, who in 2006 discovered a method of turning adult skin cells into embryonic cells. Yamakana was able to derive stem cells without having to destroy embryos. Embryonic stem cell processing remains heavily controversial.

The immediate consequences of this breakthrough are expected to yield more insight into how neurodegenerative diseases work.

"Modeling many human neurodegenerative disorders is difficult in animal models," said Rajesh Ambasudhan, lead author of the study. "Moreover, unlike skin or blood, brain cells cannot be readily taken out from a live patient. This new technology might help to overcome such a hurdle to study many such disorders in a patient-specific way."

"Through this method, there is less likelihood of tumor formation or immune rejection after transplantation," Ambasudhan explained. "However, there are more hurdles to overcome before this process is safer and viable for clinical practice." ■

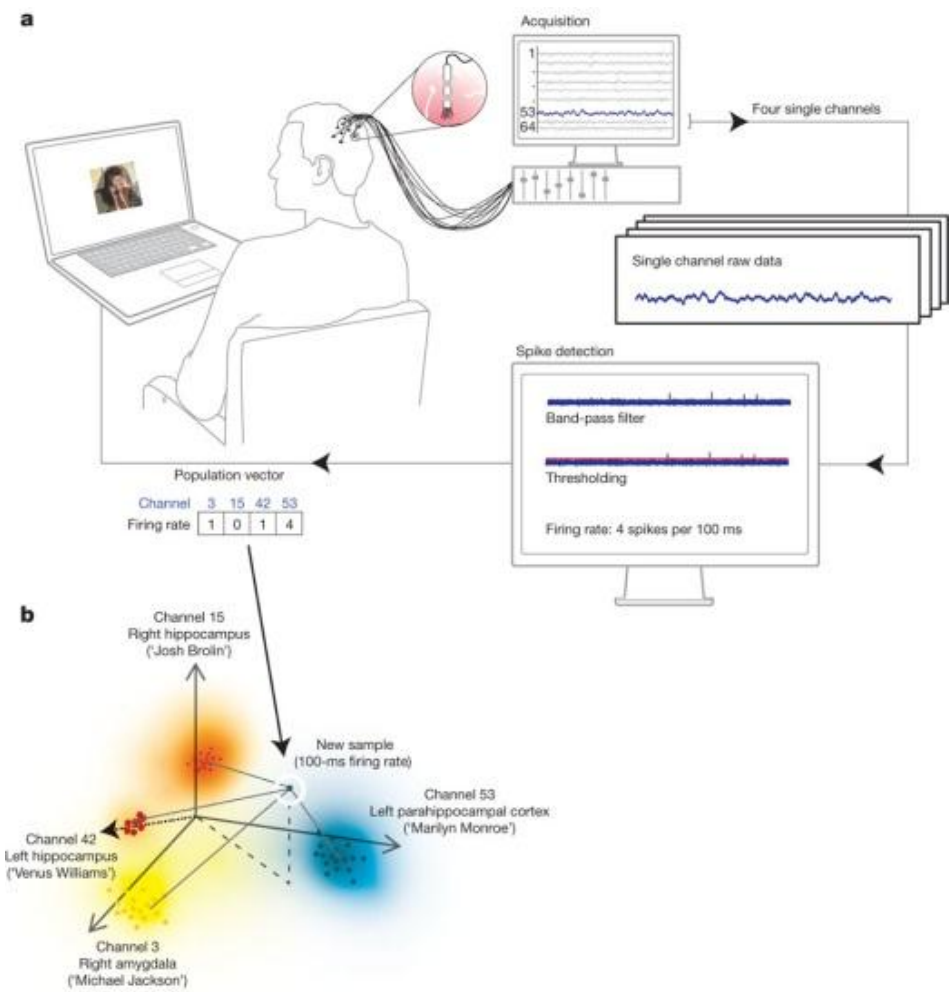
Neel Patel is a senior studying biomedical engineering at the Virginia Polytechnic Institute and State University in Blacksburg, VA, USA.

Brainpower: who's really in control?

Scientists reveal potential therapeutic for quadriplegics, and that mind control is not as far-fetched as we seem to believe.

BY JORDAN HALL

Imagine changing the TV channel just by thinking about it—a mental remote control. What was once a science-fiction fantasy is slowly becoming reality: a team of researchers has demonstrated simple mind control of a screen image. Scientists at the California Institute of Technology and University of California, Los Angeles taught patients to consciously change images on a computer



Experimental setup. **a**, Continuous voltage traces are recorded by 64 microelectrodes from the subject's medial temporal lobe. A four-dimensional vector, corresponding to the number of action potentials of four responsive units in the previous 100 ms, is sent to a decoding algorithm determining the composition of the hybrid seen by the subject with a total delay of less than 100 ms. **b**, The closest distance (weighted by the standard deviation) of this vector to the four clusters representing the four images is computed. If the 'winning' cluster represents the target or the distractor image, the visibility ratio of these two is adjusted accordingly. M Cerf *et al.* *Nature* **467**, 1104-1108 (2010) doi:10.1038/nature09510

screen through the use of individual brain cells. Their study, published last year in *Nature*, revealed an apparent ability to control the energy of an individual neuron.

Patients who volunteered for this study suffered from treatment-resistant epilepsy. While awaiting neurosurgery at the UCLA Ronald Reagan Medical Center, patients had an array of electrodes implanted into their brains to target the specific regions responsible for their severe seizures. The electrodes also enabled UCLA neurosurgeon Itzhak Fried to monitor neuronal firing.

MIND OVER MATTER

Our neurons communicate with each other through chemical and electrical signals. These chemicals, known as neurotransmitters, bind to specific receptors at the tip of a neuron and cause it to "fire," sending an electrical impulse down its long body, which then signals the release of neurotransmitters from its end to restart this process for the adjacent neuron.

Based on observations from prior experiments, Fried and his team determined that an individual neuron can fire when a subject either imagines or recognizes a particular object or person. This observation suggests that the brain can actually filter which sensory information to consider and which to ignore.

In this latest experiment, researchers showed twelve patients a series of familiar images—such as ones of Michael Jackson or Marilyn Monroe—and monitored the patients' electrical brain activity. An image that elicited strong, reliable activity from an individual neuron would then be superimposed over a different image that brought about a similar response from a different neuron. Patients were then instructed to select and think about only one of the images in this competing hybrid. For example, from a collage of Michael Jackson and Marilyn Monroe images, patients who chose to focus on Marilyn Monroe would cause the "Marilyn Monroe neuron" to increase its firing activity, and as a result, fade out the image of Michael Jackson and only be left with the iconic model and actress.

In more than two-thirds of the trials, subjects were successful in enhancing their target image and completely fading out the opposing image. With practice, patients quickly learned how to manipulate this ability by changing which image they wanted to enhance, and achieving this result more rapidly by increasing the firing rate of the related neuron. Live feedback from the computer screen was vital. Without the screen, subjects' success rate fell to less than one-third.

"[Our] environment offers some reality, but [our brains] can shape it and override it with its internal deliberations," said the study's lead author, Moran Cerf.

He believes these mind control results offer great potential for new technologies and capabilities. Cerf imagines that victims of quadriplegia and "locked-in" syndrome, who have no control of their bodies but still have healthy minds, might one day harness individual neurons to signal for concepts such as "water" and "food." But for the foreseeable future, our daily routines will still require the use of the TV remote control. ■

Jordan Hall is a student studying neuroscience at Duke University in Durham, NC, USA.