

“WikiGenes,” (not to be confused with the GeneWiki!) a project described in *Nature Genetics* in September 2008. WikiGenes was developed by **Robert Hoffmann, PhD**, at the Massachusetts Institute of Technology. It’s part of his Memoir project, which has, he says, “the ambitious goal to create a free collaborative knowledge base for all of science—where authorship matters.”

Though the creators of the various Wikis have not yet formally quantified participation, Su says that there’s been an uptick in Gene Wiki activity since the *PLoS Biology* paper came out. “It gives me hope that the system is right and that the framework is there, so if we are tapping into a desire in the community to share knowledge and harness community intelligence, then we have the structure to do it now.”

More information is available at: www.wikiprofessional.org (WikiProteins) and http://en.wikipedia.org/wiki/Portal:Gene_Wiki (Gene Wiki).

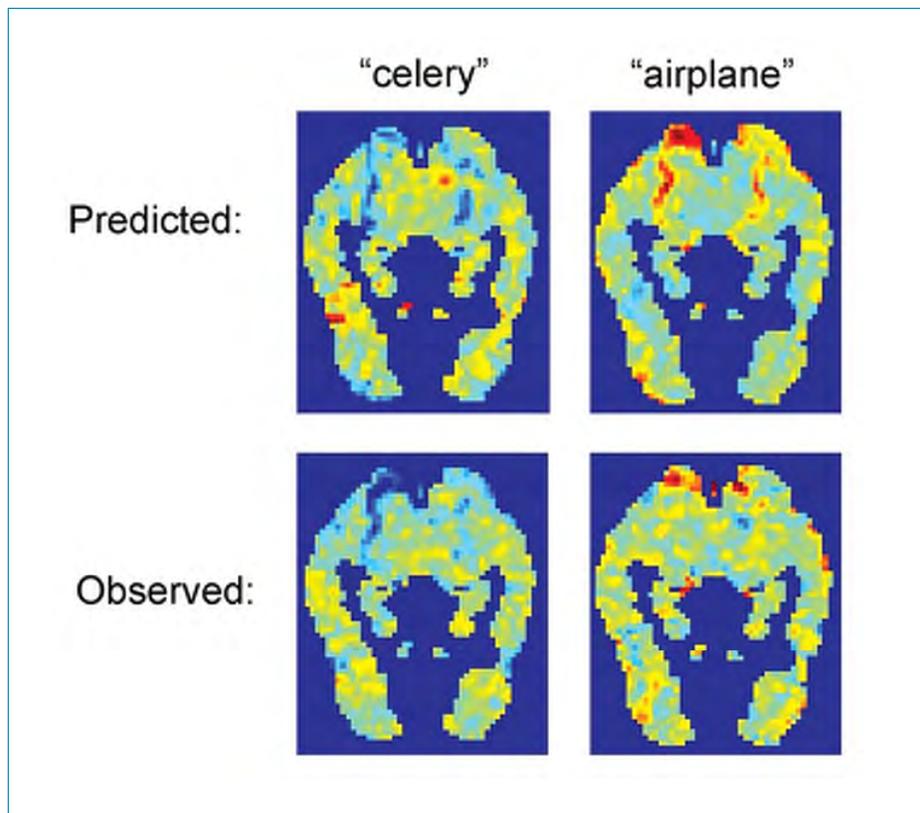
—By *Kristin Sainani, PhD*

Predicting Brain Response To Nouns

Thinking of a noun—a peach, train, or bird, for example—activates specific parts of the brain. Now, scientists have trained a computer to predict such activation patterns. The achievement represents a step toward understanding language processing and could one day contribute to treatments for cognitive decline.

“If we had a better model of how the

brain represents language, we’d be better able to make sense of disorders like dementia,” says **Tom Mitchell, PhD**, a professor of computer science at Carnegie Mellon in Pittsburgh and lead author of the research published in the



Brain activation patterns in response to nouns: The computer algorithm predicted the response to newly encountered words with 77% accuracy. Courtesy of Tom Mitchell. From Mitchell, TM, et al., Predicting Human Brain Activity Associated with the Meanings of Nouns, Science, 320 (5880): 1191 (2008) DOI: 10.1126/science.1152876. Reprinted with permission from AAAS.

May 30 issue of *Science*.

Functional magnetic resonance imaging, or fMRI, registers changes in blood flow within peoples’ brains as they are asked to do a specific task—

computer to produce fMRI images like those generated by humans. The training process uses two sources of data: fMRI images collected from nine people viewing 60 nouns; and a database

The computer model was able to produce a pattern of brain activity in response to words it had never before encountered with greater than 70 percent accuracy.

such as thinking of a specific word. Since 2000, Mitchell and **Marcel Just, PhD**, professor of psychology at Carnegie Mellon and co-director of the Pittsburgh Brain Imaging Research Center have collaborated to train a

(derived from a trillion words of text from the Internet) describing pairings of nouns and the verbs that accompany them most frequently in written text. Noun-verb pairings are the basis of language, as anyone knows who has

raised a toddler, Mitchell notes.

Once trained, the computer model was able to produce a pattern of brain activity in response to words it had never before encountered with greater than 70 percent accuracy. “We now have a model that is capable of extrapolating beyond the data on which it was trained,” Mitchell says. For example, after training, the model could predict that a food noun would provoke activity in the area of the brain mediating eating sensations, the so called gustatory cortex: “peach,” for example, frequently occurs in English paired with the verb “eat.” Similarly, a noun will activate motor areas of the brain to the degree that it co-occurs with the verb, “push,” or cortical regions related to body motion to the degree that it co-occurs with “run.”

Harvard cognitive psychologist **Alfonso Caramazza, PhD**, cautions that the model may be imperfect. He says it fails to capture an area of the brain that is damaged in semantic dementia, one form of brain damage in which people cannot understand the meaning of words. “Our understanding of concepts, and representation of this information in the brain, is not only sensory-motor,” Caramazza says. Evolution likely has sculpted our brains to react appropriately to inanimate things that may be either potentially dangerous or pleasurable. Emotional areas of the brain respond differently to a hammer than to a dog, he points out.

“These are deep questions to which no one has the answers, so one should be cautious,” Caramazza says, adding, “I think (the Pittsburgh team) would agree, these tools are in their infancy and we are only beginning to know how to use them.”

—By **Roberta Friedman, PhD**

A Finer Fat Model

When it comes to heart disease risk, “bad” and “good” cholesterol—also known as low density lipoproteins [LDL] and high density lipoproteins

[HDL]—do not tell the whole story. These particles that carry fat through the blood can be broadly classified based on their density, but they actually vary widely in their composition and clinical risk. A new computational model, described in the May issue of *PLoS Computational Biology*, allows scientists to see this diversity for the first time, providing additional information to aid in diagnoses and treatment planning.

“We look at lipoprotein profiles in greater detail in order to find possibly

Unlike previous models of blood lipid metabolism, Hübner and colleagues modeled the whole spectrum of individual lipoproteins.

relevant abnormalities in the lipid values that would remain undetected by looking only at LDL or HDL,” says lead author **Katrin Hübner, PhD**, a postdoctoral research fellow at the University of Heidelberg who completed much of the work while a PhD student at the Charité University hospital in Berlin. The model has several potential clinical applications.

Unlike previous models of blood lipid metabolism, which considered just four lipoprotein density classes (very low, low, intermediate, and

high), Hübner and colleagues modeled the whole spectrum of individual lipoproteins—by combining any of three proteins (apoB, apoA, and other) and three fat molecules (cholesterol, triglycerides, and phospholipids) in varying amounts. The particles undergo 20 reactions, including particle birth from the liver, particle death from cell uptake, and transfer of fats between particles.

In initial simulations, Hübner and colleagues generated virtual blood lipoprotein profiles that closely matched experimental values from healthy individuals. Then they tweaked the parameters in their model to mimic three known lipid disorders. For example, to simulate familial hypercholesterolemia, which involves a malfunctioning LDL receptor, they decreased the rate of cellular uptake of apoB-containing particles (which are recognized by the receptor) by 75 percent. The simulations accurately reproduced the characteristic lipid profiles of the three diseases.

The model could help pinpoint the underlying molecular defect in patients with abnormal lipid profiles of unknown origin, Hübner says. It could also be used to predict the impact of specific treatments, such as drugs or lifestyle changes, on a patient’s lipid profile.

“This work addresses an important issue in modeling lipoprotein metabolism, which is the heterogeneity of lipoproteins,” says **Brendan O’Malley, PhD**, Project Leader of Systems Biology of Lipid Metabolism at Unilever Corporate Research in the United Kingdom, who also works on lipoprotein modeling (using a different approach).

“This is one of the first works in this area, so there’s still quite a lot of work to be done,” he says. For example, the model needs to be further validated with high quality patient data. But, in the future, it could lead to improved diagnostics and personalized treatments for cardiovascular disease, he adds.

“It’s not ready for the clinic yet,” Hübner agrees. “But we’ve made a promising first step.”

—By **Kristin Sainani, PhD** □