of Medicine, says both methods work well. "Both the DeepMind and Baker lab advances are phenomenal and will change how we can use protein structure predictions to advance biology," she says. A DeepMind spokesperson wrote in an email, "It's great to see examples such as this where the protein folding community is building on AlphaFold to work towards our shared goal of increasing our understanding of structural biology."

But AlphaFold2 solved the structures of only single proteins, whereas RoseTTAFold has also predicted complexes, such as the structure of the immune molecule interleukin-12 latched onto its receptor. Many biological functions depend on protein-protein interactions, says Torsten Schwede, a computational structural biologist at the University of Basel. "The ability to handle protein-protein complexes directly from sequence information makes it extremely attractive for many questions in biomedical research."

Baker concedes that, in general, AlphaFold2's structures are more accurate. But Savvides says the Baker lab's approach better captures "the essence and particularities of protein structure," such as identifying strings of atoms sticking out of the sides of the protein—features key to interactions between proteins. Agard adds that Baker's and Baek's approach is faster and requires less computing power than DeepMind's, which relied on Google's massive servers. However, the DeepMind spokesperson wrote that its latest algorithm is more than 16 times as fast as the one it used at CASP in 2020. As a result, she wrote, "It's not clear to us that the system being described is an advance in speed."

Beginning on 1 June, Baker and Baek began to challenge their method by asking researchers to send in their most baffling protein sequences. Fifty-six head scratchers arrived in the first month, all of which have now predicted structures. Agard's group sent in an amino acid sequence with no known similar proteins. Within hours, his group got a protein model back "that probably saved us a year of work," Agard says. Now, he and his team know where to mutate the protein to test ideas about how it functions.

Because Baek's and Baker's group has released its computer code on the web, others can improve on it; the code has been downloaded 250 times since 1 July. "Many researchers will build their own structure prediction methods upon Baker's work," says Jinbo Xu, a computational structural biologist at the Toyota Technological Institute at Chicago. Moult agrees: "When there's a breakthrough like this, 2 years later, everyone is doing it as well if not better than before." ■

NEUROSCIENCE

# Brain signals 'speak' for person with paralysis

## Algorithm creates words, sentences from neural activity

*By* **Kelly Servick**

A man unable to speak after a stroke has produced sentences through a system that reads electrical signals from speech production areas of his brain, researchers report this week. The approach has previously been used in nondisabled volunteers to reconstruct spoken or imagined sentences. But this first demonstration in a person who is paralyzed "tackles really the main issue that was left to be tackled—bringing this to the patients that really need it," says Christian Herff, a computer scientist at Maastricht University who was not involved in the new work.

The participant had a stroke more than a decade ago that left him with anarthria—an inability to control the muscles involved in speech. Because his limbs are also paralyzed, he communicates by selecting letters on a screen using small movements of his head, producing roughly five words per minute. To enable faster, more natural communication, neurosurgeon Edward Chang of the University of California, San Francisco, tested an approach that uses a computational model known as a deep-learning algorithm to interpret patterns of brain activity in the sensorimotor cortex, a brain region involved in producing speech (*Science*, 4 January 2019, p. 14). The approach has so far been tested in volunteers who have electrodes surgically implanted for nonresearch reasons such as to monitor epileptic seizures.

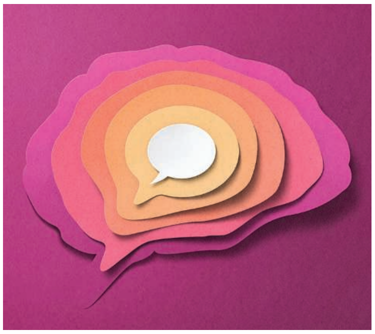

ILLUSTRATION: EIKO OJALA

In the new study, Chang's team temporarily removed a portion of the participant's skull and laid a thin sheet of electrodes smaller than a credit card directly over his sensorimotor cortex. To "train" a computer algorithm to associate brain activity patterns with the onset of speech and with particular words, the team needed reliable information about what the man intended to say and when.

So the researchers repeatedly presented one of 50 words on a screen and asked the man to attempt to say it on cue. Once the algorithm was trained with data from the individual word task, the man tried to read sentences built from the same set of 50 words, such as "Bring my glasses, please." To improve the algorithm's guesses, the researchers added a processing component called a natural language model, which uses common word sequences to predict the likely next word in a sentence. With that approach, the system only got about 25% of the words in a sentence wrong, they report this week in *The New England Journal of Medicine*. That's "pretty impressive," says Stephanie Riès-Cornou, a neuroscientist at San Diego State University. (The error rate for chance performance would be 92%.)

Because the brain reorganizes over time, it wasn't clear that speech production areas would give interpretable signals after more than 10 years of anarthria, notes Anne-Lise Giraud, a neuroscientist at the University of Geneva. The signals' preservation "is surprising," she says. And Herff says the team made a "gigantic" step by generating sentences as the man was attempting to speak rather than from previously recorded brain data, as most studies have done.

With the new approach, the man could produce sentences at a rate of up to 18 words per minute, Chang says. That's roughly comparable to the speed achieved with another brain-computer interface, described in *Nature* in May. That system decoded individual letters from activity in a brain area responsible for planning hand movements while a person who was paralyzed imagined handwriting. These speeds are still far from the 120 to 180 words per minute typical of conversational English, Riès-Cornou notes, but they far exceed what the participant can achieve with his head-controlled device.

The system isn't ready for use in everyday life, Chang notes. Future improvements will include expanding its repertoire of words and making it wireless, so the user isn't tethered to a computer roughly the size of a minifridge. ■





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