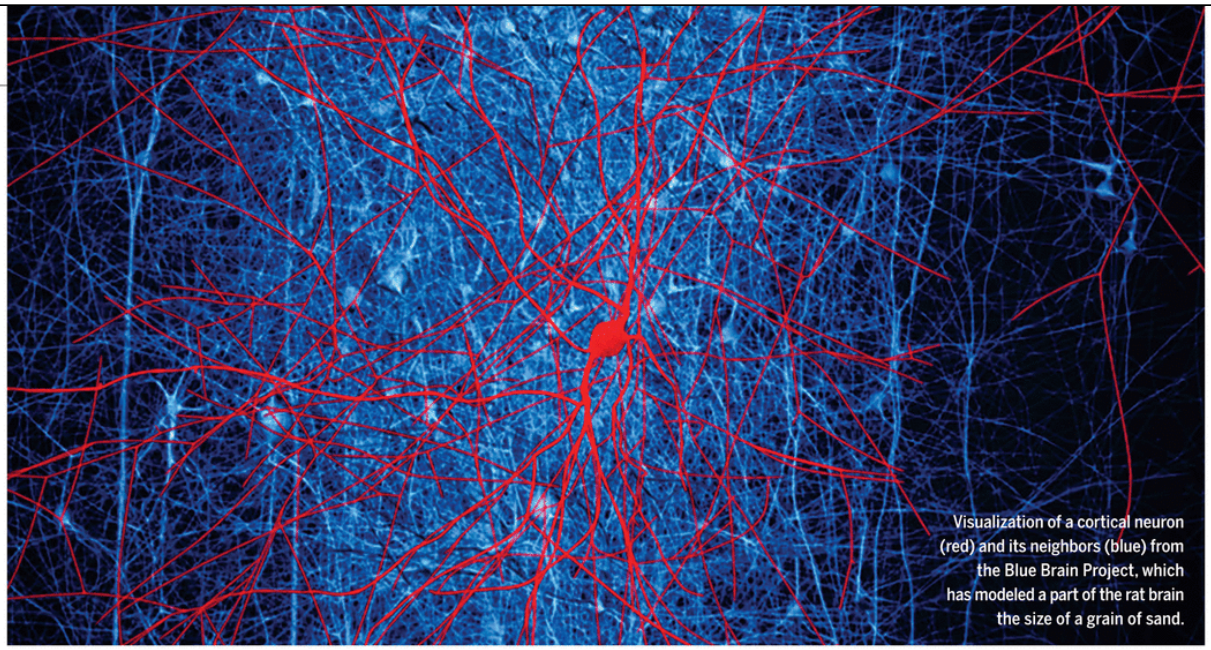

Visualization of a cortical neuron (red) and its neighbors (blue) from the Blue Brain Project, which has modeled a part of the rat brain the size of a grain of sand.

IMAGE: BBP/EPFL 2015

NEUROSCIENCE

Virtual rat brain fails to impress its critics

The Blue Brain Project publishes its simulation of 30,000 neurons

By **Kai Kupferschmidt**

Critics of Henry Markram—and there are many—complain that he promises far more than he can deliver. A charismatic and mediagenic neuroscientist working at the Swiss Federal Institute of Technology (EPFL) in Lausanne, Markram persuaded the European Commission to fund the Human Brain Project (HBP), a €1 billion plan to simulate the entire human brain in a computer—an effort doomed to fail, many scientists say. As proof, they have cited the Blue Brain Project, another Markram endeavor that was lavishly funded by the Swiss government. It set out in 2005 with the more modest target of modeling the rat brain but produced few tangible results.

But now, the Blue Brain Project finally has something to show for the investment. In a *Cell* paper published last week, researchers unveiled the most detailed digital reconstruction of brain tissue ever built: A simulation of 30,000 neurons, connected by almost 40 million synapses, in a piece of rat brain about the size of a grain of sand. The sprawling 37-page paper, co-authored by 82 scientists in eight countries, shows that building an in silico model of the human brain is feasible as well, Markram says—and that he's not selling pipe dreams. "When I started at EPFL, this is what I promised to deliver," he says, "and I have delivered it."

Some scientists are impressed, including Christof Koch, the head of the Allen Institute for Brain Science in Seattle, Washington. "Following Richard Feynman's dictum 'What I cannot create, I do not understand,' this amounts to a hard-nosed, engineering demonstration of how much progress the field has made over the last few decades in synthesizing the behavior of neuronal networks," he says.

But the paper has done little to convince skeptics. "This is an enormous amount of neuroanatomy work and there is no doubt that that is important," says Alexandre Pouget, a computational neuroscientist at the University of Geneva in Switzerland and a longtime critic of the HBP. "But the model teaches us nothing. It computes nothing, it represents nothing." Nor does it prove that the attempt to model the human brain—which is 2 million times the size of the speck covered in the new paper—can achieve anything worthwhile, he adds. But Pouget suspects it's good PR nonetheless. "If we're talking politics and perception, I think this is good news for the [HBP]."

Peter Latham, a neuroscientist at University College London, agrees. "I think the [HBP] is a waste of money, but after reading this paper I am slightly more in favor of it," he says. "This paper may actually save the [HBP]."

The HBP was foundering last year after hundreds of scientists signed an open letter charging that it was badly managed and too narrowly focused scientifically. The signatories threatened to boycott the project unless the program was broadened and its governance improved. An independent review ordered by the European Commission and a mediation panel largely agreed with the critics, which led to a series of structural reforms at the HBP and a diminished role for Markram (*Science,* 27 March, p. 1406). "As you can imagine, publishing this paper was very tough in a climate of extreme prejudice based on second-hand information," Markram says. "Now, at least everyone can judge the science directly for themselves."

The Blue Brain team set out to model a piece of rat sensory cortex that processes information from a hindlimb. In a first step, the scientists had to recreate the anatomy of this area. The team took measurements of thousands of neurons in rat brains, from their form and size to the electrical signals they produced. Based on those data and the scientific literature, the scientists came up with 55 distinctive types of neurons. Guided by measurements of cell type density, the researchers distributed thousands of neurons in the simulated brain tissue.

The model predicted that the virtual neurons would connect and exchange information at 200 million synapses, which was much more than expected in such a

tiny piece of tissue. The scientists used an algorithm to limit the number to a more realistic 37 million. In a second step, each neuron was matched with a certain pattern of electrical activity, based on years of recording neurons, and each synapse assigned to either activate a neighboring neuron or inhibit it. Simulations of electrical activity run on the model match measurements in living cells and animals, the team writes in *Cell*.

The model leaves out many features of brain tissue, such as blood vessels and glial cells, which account for 90% of the cells in the brain but are generally not involved in relaying signals. That's because it's only a first draft, Markram emphasizes: "We will include more data in the future."

Chris Eliasmith, a theoretical neuroscientist at the University of Waterloo in Canada, argues that the model may already have too much information. The researchers were successful in replicating certain of the brain's behaviors, he says. "But you can get all those results with a way less complicated model." In 2012, Eliasmith published a model that includes 2.5 million neurons with about a billion connections, although at a much lower resolution than the Blue Brain version (*Science*, 30 November 2012, p. 1202). "If we build highly detailed neural models, we should ask questions that show how and why those details matter," he wrote in an email. "That was not done here. Complexity for complexity's sake is a mug's game."

The Blue Brain team has made their model available online; anyone can examine it on their PC, but to run a simulation you need the power of a supercomputer, Markram says. He says the model has already proven useful for generating hypotheses. For instance, the researchers found that reducing the amount of calcium ions in the model led to a change in the activity patterns, from synchronized bursts of firing to an asynchronous pattern. "There is a transition there. That is an interesting finding," Markram says—and neuroscientists will be able to uncover other phenomena using the model, he argues.

In the end, the question is whether such new insights are worth the massive investment, Latham says. "Do you want to spend a billion euros on this? That's the question." Markram has no doubt that the answer is yes. A hundred years ago, Spanish biologist Santiago Ramón y Cajal made invaluable contributions to neuroscience by peering through a microscope and drawing the cells he saw in brain tissue, he says. "What do you think Ramón y Cajal would be doing today? He would do what we are doing." ■

HUMAN EVOLUTION

First modern humans in China

Contemporary-looking teeth found in cave suggest that *Homo sapiens* left Africa much earlier than expected

By **Ann Gibbons**

For decades, anthropologists have tried to trace the patchy trail left by the earliest modern humans out of Africa. But they have been stymied by gaps in the fossil record or unreliable dates, especially in East Asia. Now, Chinese anthropologists report 47 teeth of *Homo sapiens* from a cave in southern China, dated to 80,000 to 120,000 years ago. If the dating is accurate, the discovery pushes back the appearance of our species in Asia by at least 30,000 years, wiping out a long-standing picture in which modern humans swept out of Africa in a single wave 50,000 to 70,000 years ago.

These fossil teeth may have belonged to the first *Homo sapiens* in China.

PHOTO: S. XING

"This changes everything. It's the best evidence we have for modern humans in East Asia this early," says archaeologist Michael Petraglia of the University of Oxford in the United Kingdom, who was not part of the work but has long advocated an early migration out of Africa. Others question the dates. "This case is better than the previous similar claims, but it is not fully convincing," says paleoanthropologist Yousuke Kaifu of the National Museum of Nature and Science in Tokyo.

Most researchers agree that modern humans arose in Africa and first ventured out of that continent into the Middle East about 120,000 to 90,000 years ago, as shown by skulls from Israel. But *H. sapiens* remains don't appear in Europe, East Asia, and Australia until 40,000 to 50,000 years ago. Older fossils in Asia proposed as *H. sapiens* are controversial. Genetic studies, too, suggest that humanity's great global expansion began just 50,000 to 70,000 years ago.

But Petraglia and others have unearthed sophisticated stone tools from the Arabian Peninsula and India, persuading him that modern humans left Africa as long ago as 125,000 years, settled in a then-wet Arabia, then pushed into India and eastward (*Science*, 29 August 2014, p. 994). Skeptics counter that other archaic humans could have made the tools, and that fossils are needed as proof.

Hence the excitement about the teeth reported this week in *Nature*, from Fuyan Cave in Daoxian in southern China, about 600 kilometers northwest of Hong Kong. A team led by Wu Liu and Xiu-Jie Wu of the Chinese Academy of Sciences' Institute of Vertebrate Paleontology and Paleoanthropology in Beijing found small teeth with slender roots that barely differed from modern Chinese teeth. Indeed, the wear pattern and shape of the teeth are so modern that some wonder how they could be so old.

The dates come from a small stalagmite, part of a flowstone that capped the layer holding the teeth. The team used the radioactive decay of uranium to thorium to date this stalagmite to 80,000 years ago—a minimum age for the teeth. Fossils of extinct elephants, hyenas, and pandas in the hominin layer are 120,000 years old at most, so the team concluded that the teeth are 80,000 to 120,000 years old, says co-author Maria Martinón-Torres of University College London.

But the dated stalagmite came from a different trench than the teeth, and may be of a different age, says paleoanthropologist Russell Ciochon of the University of Iowa in Iowa City: "The actual dates reported for Fuyan Cave are probably good but I doubt that the teeth are that old."

The authors insist that the stratigraphy in the cave is clear. Liu even argues that the find supports the radical—and minority—view that our species was born in China, not Africa. The discovery is likely to spur "a lot of debate," Martinón-Torres says, "and force a new look at other alleged [*H. sapiens*] sites in China." ■