

# Untangling the Connectome

**MED'S KASTHURI ON HOW OUR WIRING MAKES US HUMAN** / BY BARBARA MORAN



Bobby Kasthuri needs a map. Not your everyday, get-me-to-Kenmore-Square kind of map. What Kasthuri needs is a map of all the connections in the human brain—kind of a wiring diagram for neurons. Kasthuri, a School of Medicine assistant professor of anatomy and neurobiology, thinks that this map—the so-called connectome—could help explain how our brains develop from childhood and give deep insights into memory and consciousness.

But there's a problem: the data. The map of one mouse brain would consume about two exabytes—that's two billion gigabytes—of storage. (For comparison, the iPhone 6 comes with a mere 128GB.) With some creative help from a handful of high school students, Kasthuri has analyzed a sliver of mouse brain and created stunning images of neurons. The exquisitely detailed images hint at the power of big data, the complexity of the connectome, and some of the secrets that may lie waiting for us in the brain.

Bostonia talked to Kasthuri of mice and men, small worms and bold ideas, and what we can learn from Big Oil.

**Bostonia: What is a connectome?**

*Kasthuri:* It's this idea that, for a brain, you know how every neuron connects to every other neuron.

**Why do we need to know that?**

If you look at a neuron of a human and a neuron of a mouse, they look essentially the same. We share 98 percent of our genome. So the strong hypothesis is that we have the same LEGO blocks, but we build a huge palace with our LEGO blocks, and mice build more of a hut. And if that's true, it would imply that connections are deeply correlative and causative to things like our memories, our personalities, and our fears. The connectome would be the map of that.

**So far, scientists have mapped the connectome of one organism—a worm called *C. elegans*?**

Yes, it's a roundworm about a millimeter long, with exactly 302 neurons. And

they have very simple behavior. I think they squirt forward, they squirt backward. Squirt forward, squirt backward. It took scientists about a decade to do a wiring diagram of *C. elegans*, completely by hand.

**How many neurons do people have?**  
People claim 100 trillion.

**That seems extremely difficult. Where do you start?**

We start with a big volume of an adult mouse brain, let's say a millimeter cubed.

**So you take this tiny part of the mouse brain, and what do you do with it?**

You have to cut it in slices, take a picture of each slice, and then put the images back together on the computer. But here's the problem: a millimeter cubed, at the resolution we would like, is about two million gigabytes of data. The whole human genome is about three to five gigabytes.

When they sequenced the genome in the 1990s, people were like, "three to five gigabytes? That's impossible." But they did it. Now I'm talking about 200,000 times more, but the world is being pushed toward this, independent of what we do.

**Exactly. Everybody needs somewhere to put their data. Maybe the Google guys will figure it out.**

I think Google might figure it out. I've heard that the people who work with the biggest data sets in the world are oil companies, because they make these tremendous models of where the oil is. And for them, finding the oil is worth the investment of supercomputers and huge data sets.



Bobby Kasthuri

Once you've sliced up this little bit of mouse brain, can you do anything with it?

It's a great question. I still haven't gotten to the hard part: analyzing the data. I like to use this Kennedy quote: "We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard." We went to the moon! Right? Is analyzing this data that much harder than sending human beings to the moon and coming back?

So now I have two million gigabytes of information. And now we get to the hard part, the really, truly hard part. We have to figure out a way to analyze two million gigabytes of data with some combination of computers and humans.

Here's my current version of that: I teach neuroscience at one local high school, Masconomet Regional High School. I teach the students what a neuron looks like, I teach them how to trace something, and they work on my data. They're free, which is an advantage for me, and it's educational. And so far, they love it.

How much mouse brain have you been able to analyze?

Barely a fraction of the mouse brain. It's so small, it's embarrassing. We're going to get faster, I hope, if I have any chance of making a career out of this. But this is the new reality. And the question is, do we want to face reality or not?

And?

I have to. I can't turn back now.

What if it turns out that the connectome doesn't matter? Maybe everything that makes us human just lies in the genes and how they are turned on and off.

Yes, it could be. My view is not that we have the right answer, but my view is we've got to try. Let's just do it, man! I guarantee we'll find a surprise that's going to change how we think about brains.

**WEB EXTRA** Watch videos about how Bobby Kasthuri makes detailed images of the brain, and how mapping the way neurons connect could help us understand what makes us who we are, at [bu.edu/bostonia](http://bu.edu/bostonia).

## EMBRYONIC FROGS, AS WELL AS OTHER ANIMALS, CAN LEAVE AN EGG IF DANGER PRESENTS ITSELF / BY CYNTHIA K. BUCCINI

# Escape Hatch

As far as housing goes, an egg is a pretty good place for a frog embryo. It offers physical protection and it keeps its inhabitant from drying out.

But like many homes with great curb appeal, eggs aren't always the ideal dwelling. For some frog eggs, being packed in a gelatinous mass called a clutch can limit the supply of oxygen. Eggs can be swept away by floods or killed by fungal pathogens, and they make a nice lunch for predators like snakes and wasps. Faced with such peril, it might seem that the eggs have little hope of hatching alive, but red-eyed treefrog embryos have a few survival tricks up their sleeve.

Biologist Karen Warkentin has found that these embryos are capable of assessing a variety of threats in surprising ways, and if danger presents itself, they can choose to hatch days earlier than they typically would. The process is called environmentally cued hatching, and in the last decade researchers have found evidence that it works for all kinds of animals—from flatworms to fishes, from frogs and salamanders to turtles and birds. "Hatching is a controlled, regulated response," says Warkentin, a College of Arts & Sciences associate professor of biology. "At some point, the embryos will decide to do it. It's amazing the information they attend to."

Environmentally cued hatching, says Warkentin, is part of a bigger story, and it has led to a collective shift in thinking about development. Until the 1990s, biologists believed that animals that begin life in an

Undisturbed, these five-day-old red-eyed treefrog embryos would remain in the egg for another day or two. But they've been capable of hatching for at least a day and a half.

