Medical Xpress

Electrical balance in the brain

June 12 2019

Despite more than a million fold difference in the light intensity, our brains enable us to see the same scene in broad daylight and a dim night by the process of normalization. Credit: Hrishikesh Nambisan

Balance is the key. It's not exactly neuroscience; except that it is.

Since balance is key for almost everything we do—walking, cycling, and a million other things in life—it really is no surprise that electrical balance holds the key to understanding how our brains function.

In neural networks, excitation/inhibition (E/I) balance occurs when the average levels of excitatory signals match those of inhibitory signals received from all connections. Even individual neurons are known to maintain E/I balance, and a loss of this balance is linked to serious problems such as epilepsy, schizophrenia, and autism.

Although E/I balance is known to operate from the whole brain level to individual neurons, this has always been measured by recording electrical activity straight from animal brains, either when the brain is flooded with information about the world, or is chattering by itself. It has only recently been shown that single neurons in small circuits—composed of just 2 or 3 kinds of neurons—insulated from the rest of the brain are also E/I balanced.

The study which shows this, comes from Upinder Bhalla's group at the National Centre for Biological Sciences (NCBS), Bangalore, and has been published in the journal *eLife*.

But what good does it do to the brain to maintain such precise balance between neurons? The work demonstrates that E/I balance, and another phenomenon known as E/I delay, together form the biophysical roots of 'normalization'; 'normalization' being the process by which our brains make sense of the world despite huge variations in the information they receive.

"Our first objective was to investigate if E/I balance was also maintained within a sub-circuit," say Aanchal Bhatia and Sahil Moza, who are two of the researchers behind this work.

Bhatia and Moza stimulated neurons in mouse brain slices with different patterns of light using a technique called optogenetics. To precisely control the stimulation they applied, the team designed a contraption of their own with a disembowelled DLP (digital light processing) projector;

their final setup can now stimulate neurons (from tens to a few hundred) in random patterns. The team focused on a specific circuit in the hippocampal region of the brain called the CA3-CA1 circuit, known for its role in memory formation.

Thousands of measurements later, the researchers had their answer—sub-circuits also maintain a very precise E/I balance, even with totally random patterns of input!

"This was quite a surprise. These random patterns of input don't correspond to any real-world stimulus, and yet, the excitation and inhibition were precisely balanced.", exclaims Bhatia.

"Think of a neuron as a car. Excitation acts like the accelerator pedal, driving neurons to fire off a signal. Inhibition, however, acts like the brake pedal and pushes neurons away from firing," says Moza.

If a neuron is a car running at a constant speed, one understands that its driver must keep the accelerator and brakes in balance to maintain that speed. However, neurons usually do not have just a single driver—most neurons receive hundreds to thousands of inputs from other neurons—which, using the car analogy, translates to an equally large number of drivers. In E/I balance, all of these driver-neurons' inputs are weighted such that the neuron-car maintains its constant speed. However, the numbers of neuron-drivers for a neuron-car can and do keep changing. How then, does the neuron-car respond sensibly to inputs from such a large number and range of neuron-drivers?

"This is a clever trick that our brains use," says Moza. "As the numbers of neuron-drivers increase, each driver keeps shortening the delay between applying the accelerator and brakes, without ever changing the sum total of acceleration and brakes provided," he adds. What Moza describes with this analogy, is the phenomenon of E/I delay, which has also been demonstrated in their study. E/I delay is a distinctive relationship between the strength of excitation and the timing of inhibition—as excitatory inputs become stronger, the delays between excitation and inhibition become shorter.

"The icing on the cake, however, is our discovery that E/I balance and E/I delay create the biophysical mechanism for a new form of normalization called 'subthreshold divisive normalization'," says Bhatia.

To understand what 'normalization' is, imagine that you are gazing out of your bedroom at the familiar outlines of nearby buildings at midday, then imagine the same scene at midnight. Whether in the full blast of the midday sun or drenched in the mellow hues of sodium vapour street lamps at midnight, you would still recognise the scene outside your window as the same.

How are you doing this?

By 'normalization'. The brain literally 'normalizes' its reactions by dividing the response of each neuron with a common factor that is usually the summed activity of a pool of neurons. This is how one picture, despite sending hugely different signals under different conditions can still be recognised by our brains as being the same.

"Neurons calculate first, shoot later," says Moza, to emphasize that neurons 'normalize' all their responses to inputs before they fire off a signal.

"People have been trying to understand how neurons add up and process the inputs they receive. In other words, does 1+1 equal 2 for a neuron, or is it doing something else?" asks Bhatia.

Turns out that neurons are doing something much more complex than just adding-up their inputs. They perform a more complex operation—subthreshold divisive normalization—in which, the output does not increase in proportion to the input. In fact, the output increase rate actually decreases in proportion to the input.

Bhatia neatly sums this up by explaining that for the neurons in this study, "1+1 is close to 2, 1+1+1 is a bit less than 3, 1+1+1+1+1 is further less than 5, and this trend continues such that 1+1+1+1+1+1+1+1+1 is way lesser than 9, and so on".

Upinder Bhalla, the third author on the paper, says that this work has broad implications for how the brain computes. "Imagine that you're a cell in a crowd, with a thousand voices coming your way. Having a close balance means that you can ignore most of the thousand inputs, and selectively pay attention to those few signals that are particularly important, by tweaking the balance." He adds, "The study was also an excellent example of E/I (Experiment/IT) balance, where Aanchal did these delicate experiments, and Sahil provided the Information Theory and analysis."

More information: Aanchal Bhatia et al, Precise excitation-inhibition balance controls gain and timing in the hippocampus, *eLife* (2019). DOI: 10.7554/eLife.43415

Provided by National Centre for Biological Sciences