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RESEARCH NEWS

How dendritic spines shape calcium dynamics

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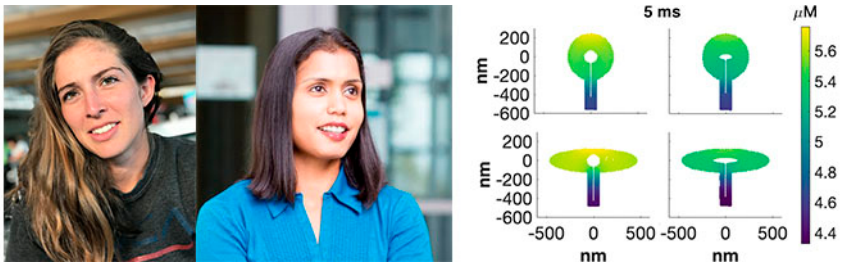
***JGP* study develops mathematical model that describes how calcium signaling could be influenced by spine geometry and ultrastructure.**

Dendritic spines are small, actin-rich structures that protrude from neuronal dendrites and receive inputs from neurotransmitters released by neighboring axons. Calcium ions flood into the spine immediately after neurotransmitter binding, triggering a wide variety of signaling pathways that are crucial for synaptic remodeling and plasticity. A new *JGP* study by Bell et al. describes how the spatiotemporal dynamics of dendritic calcium are affected by both the size and shape of individual spines and by a specialized organelle within spines called the spine apparatus (1).



Miriam Bell (left), Padmini Rangamani (right), and colleagues develop a 3-D multicompartment reaction–diffusion model of calcium dynamics in dendritic spines. The model shows that altering the shape of the spine head or the specialized ER known as the spine apparatus has complex, nonlinear effects on calcium's spatial distribution 5 ms after stimulation.

Calcium dynamics in dendritic spines have been extensively studied (2, 3), and researchers have identified numerous proteins that influence these dynamics and/or respond to them. In recent years, however, high-resolution imaging has shown that individual spines can adopt a variety of sizes and shapes that could have important impacts on their function (4). "We were interested in the physical aspects of this," explains Padmini Rangamani from the University of California, San Diego. "How are calcium dynamics affected by spine geometry?"

Rangamani and her graduate student Miriam Bell are computational biologists rather than neuroscientists, but thanks to a Multidisciplinary University Research Initiative grant from the United States Air Force, they were able to collaborate with Tom Bartol and Terrence Sejnowski to build a 3-D, multicompartment model of how spine calcium dynamics respond to stimulation.

"There's a wealth of information out there, so the most challenging part for me was deciding what proteins to include in the model," says Bell. In the end, the researchers incorporated numerous proteins, including NMDA receptors and voltage-sensitive calcium channels that transport calcium into spines, membrane pumps that remove the metal, and calcium-binding proteins that buffer cytosolic calcium. The model also incorporated the spine apparatus (5), a specialized type of endoplasmic reticulum that can mop up calcium from the cytosol and is present in ∼14% of spines, particularly mature ones.

When Bell and colleagues adjusted the size of the spine head in their mathematical model, they found that smaller spines generate higher peak calcium concentrations, but the total amount of calcium they see over time is reduced. "So there's an interesting trade off that could have important functional implications," explains Bell. "Larger spines tend to be more stable, and even though they have lower calcium peaks, they are exposed to more total calcium, which corresponds to them seeing more information overall."

The effect of spine shape was far more subtle, however. "We thought that adjusting the spine head from a spheroid to an ellipsoid would have a much more dramatic effect," Rangamani admits. Instead, dendritic spine shape showed a complex, nonlinear relationship with calcium dynamics. This is because, while altering spine shape changes its surface area to volume ratio, thereby affecting calcium flux across the cell membrane, it also changes the distance between the postsynaptic density (a major location of calcium influx) and the spine apparatus (a major calcium sink that removes calcium from the cytosol).

Accordingly, changing the size or shape of the spine apparatus altered its capacity to act as a calcium sink and had similar nonlinear effects on calcium dynamics. Bell et al. speculate that spines may dynamically regulate their size and shape and control the presence or absence of the spine apparatus to fine tune their calcium dynamics for optimal synaptic function.

The researchers' model also reveals that calcium dynamics are affected by the spatial distribution of membrane fluxes and calcium buffers. Rangamani stresses that all of these factors should be taken into account when modeling the signals received by individual spines. The next step, the researchers say, is to model how all of these individual signals are integrated by the dendrite as a whole.

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2. Augustine, G.J., et al 2003. *Neuron.* 40:331–346.
3. Bartol, T.M., et al 2015. *Front. Synaptic Neurosci.* 7:17.
4. Berry, K.P., and E. Nedivi. 2017. *Neuron.* 96:43–55.
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