# Cell Communication

## Buck, Zhang seek understanding of signals in neurological disorders

*Researchers at Case Western Reserve University are continuing a 12-year investigation on how plexin, a protein found in human cell membranes, processes signals through the membrane to facilitate cell communication.*

Plexins receive guidance cues from other proteins and transmit signals through the lipid membrane, regulating cell migration and targeting processes. However, if a signal is not transmitted correctly through plexin, studies have shown that this could result in serious neurological disorders. Biophysical scientists in the lab of Matthias Buck, Ph.D., are studying the signal transduction mechanism of a certain type of plexin that can become destabilized as part of an activation process.

Using Ohio Supercomputer Center services, Buck's lab has performed molecular dynamics simulations using both CHARMM and NAMD programs to understand the structure and dynamics of the transmembrane helixes of plexin and the intracellular and transmembrane domains of plexin in lipid membrane systems.

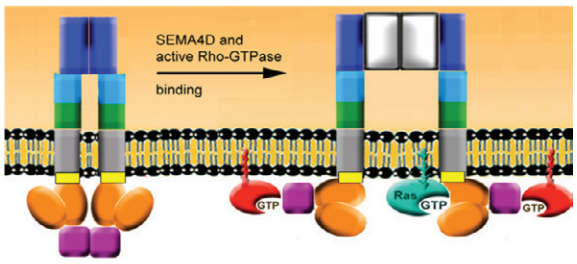
"In the first project, [resource units] were applied to characterize the dynamics of the transmembrane protein receptor in lipid membranes, which is critical for understanding the signal transduction process of plexin through the membrane," said Liqun Zhang, a previous postdoctoral scholar at Case Western; currently, she is an assistant professor in the Chemical Engineering department of Tennessee Technological University.

The initial structure of plexin was predicted with a CHARMM simulation and then virtually inserted into the cell lipid bilayer where further CHARMM simulations refined the possible structure of the protein. Based on the CHARMM simulations, consistent structures were predicted compared to the experimental structures.

"Based on this achievement we then used CHARMM-GUI software to insert the initial structure into the lipid bilayer, then applied explicit lipid and solvent CHARMM simulations to refine the structure," Zhang said.

Overall, three different plexin helix dimer structures were predicted. The results of this simulation were published in PLOS One.

Now, researchers are testing the function of the plexin structures within the cell membrane, with the long-term goal to understand the signal transduction process through the lipid membrane and in the cytoplasmic domain. They intend to continue the computational project in Dr. Buck's lab to give guidance to and synergize with experimental work performed in the lab. •




(Above right) Transmembrane and intracellular domains of plexin-B1 (in blue approaching the lipid bilayer in green). (Right) Schematic model for signal transduction via activation of plexin-B1 by a conformational change of the plexin-B1 dimer upon RhoGTPase binding to the RBD.

**Project Lead:** Matthias Buck, Ph.D., Case Western Reserve University
**Research Title:** Molecular dynamics simulations of plexin-b1 transmembrane plus intracellular domains
**Funding Source:** National Institutes of Health
**Website:** physiology.case.edu/research/labs/buck-lab