Preface

Techniques to stimulate neural networks can help us understand the roles of specific neural populations in physiological processes, like learning and feeding. Existing techniques such as electrodes and chemicals have poor specificity and cannot provide specific stimulation to densely packed neural tissues. To overcome some of these limitations, I developed a technology for noninvasive control of neural activities using magnetic forces and magnetic nanoparticles (MNPs). By performing the experiments with different neurotoxins and experimental conditions; I found that the mechanism of magnetic neural stimulation involves membrane-bound MNPs transducing magnetic forces into mechanical stretching of the cell membrane to open mechano-sensitive N-type calcium channels for calcium influx.

Neural networks actively regulate their ratio of excitatory to inhibitory ion channel/receptor to maintain network homeostasis. I thus performed chronic magnetic stimulation on fragile X syndrome (FXS) model neural networks. I found that chronic magnetic stimulation reduced the density of N-type calcium ion channels whose expression is increased in FXS. This technique demonstrates the potential of using biomagnetic/biomechanical forces to modulate expressions of mechanosensitive ion channels where they are overexpressed in diseases such as hypersensitivity to pain and epilepsy.

Nonetheless, there are still a few areas where magnetic neural technique can be improved. Firstly, it is the use of MNPs with more uniform properties to have greater control on magnetic stimulation. Secondly, the technique needs to be useful for in vivo studies. Therefore, I started researching on magnetotactic bacteria (MTB) which produce biological MNPs with superior properties such as homogenous magnetic properties with the goal of harvesting MNPs from them.

MTB, however, grow extremely slowly, and the number of MNPs produced/bacterium is low. One way to overcome this problem is to evolve MTB over-producers of MNPs. I combined random chemical mutagenesis and selection using a magnetic ratcheting platform to generate and isolate MTB over-producers that produce twice as many MNPs/bacterium after five rounds of mutation/selection. I next designed a magnetic microfluidic device and demonstrated as a proof of concept that it can be coupled to a bioreactor for high-throughput microfluidic selection of MTB over-producers.

Magnetic neural stimulation technique is especially useful to study and modulate neural activities in deep tissue organs and the peripheral nervous system which have attracted more attention in recent years. We anticipate that with improvements of magnetic neural stimulation technique in areas like temporal resolution and ease of experimental setup, its use will become more prevalent.

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