Alice Liu

Research Progress Report

Phase response curves for optogenetic manipulation during forward locomotion support a threshold model for rhythm generation

Despite the roundworm *C. elegans'* compact and well-mapped nervous system, the basic mechanisms underlying locomotory rhythm generation and coordination remain largely unknown. To gain insight into motor coordination during forward movement, I delivered brief optogenetic perturbations to muscles and neurons of freely moving worms in viscous liquids while quantifying their behavioral responses in the form of curvature over body coordinate and time. I then calculated phase response curves indicating the magnitude of phase delay or advance as a function of the phase within the locomotory cycle at which a manipulation occurred. It was found that briefly relaxing the head body wall muscles shifts the phase of the locomotory wave in a highly phase-dependent manner, ranging from cycle delays of $\pi/2$ to small phase advances. The phase response curve had a highly asymmetric sawtooth-like shape, with a falling phase approximately 5 times steeper than the rising phase. A graduate colleague in my laboratory also showed computationally that the asymmetry and periodicity of the phase response curve can be explained by a model in which the active moment generated by body wall muscles switches between fixed values in the dorsal and ventral directions upon the curvature reaching thresholds in either direction. This model predicts an asymmetry between the slopes of the rising and falling absolute curvature, which I further verified experimentally. Transiently inhibiting motor neurons exclusively delayed the locomotor cycle, as does transient activation of neurons that inhibit locomotion. These results suggest that rhythm generation in *C. elegans* is highly dependent on proprioceptive feedback and occurs via a threshold-based mechanism.