

Department of Complexity Science and Engineering

Graduate School of Frontier Sciences

The University of Tokyo

2021

Master Thesis

**Molecular underpinnings enabling
the emergence of spontaneous patterned
activity in developing motor circuits**

Submitted February 25, 2022

Adviser: Professor Akinao Nose

Co-Adviser: Dr. Xiangsunze Zeng

駒野目ゆう子

Yuko Komanome

Keyword: *Drosophila*, Neuroscience, Molecular biology

Abstract

Spontaneous neural activity is widely observed in developing circuitry throughout the nervous system. A conserved feature of such activity is the progressive transition from sporadic to spatiotemporally orchestrated patterns over time. Whilst a wealth of research centered on the sensory systems has demonstrated that spontaneous patterned activity contributes to fine-tuning neural circuits via acting synergistically with environmental stimuli, much less is known about the roles of spontaneous activity in developing motor circuits.

A widespread nature during animals' motor development is the appearance of premature movements preceded by sophisticated motor behaviors. For instance, while a human fetus makes a constellation of involuntary movements such as wiggling and kicking in mother's womb, it develops the capability of crawling and walking successively after birth, suggesting that motor activity generated in central circuits transits from primitive to harmonic patterns so as to enable the behavioral maturation. But how spontaneous activity emerges in developing motor circuits and neurobiological mechanisms underpinning the pattern transition remain a conundrum in developmental neuroscience. Here, I address these issues by harnessing a novel model in *Drosophila* embryos that we characterized recently. In this system, a motor circuit composed of M and A27h neurons takes the lead to initiate nascent spontaneous activity inducing premature movements, which eventually kicks off a functional network by generating patterned motor activity driving coordinated locomotion. However, the molecular bases underlying spontaneous activity in the M/A27h circuit and the cellular/circuit mechanisms entailing the emergence of patterned activity thereof are yet to be explored.

In this study, by combining cell-type-specific gene knockdown with behavioral screen and calcium imaging, I identify the molecules essential for kick-starting spontaneous patterned activity in the M/A27h circuit. Moreover, using pharmacological dissections coupled with neural activity recording, I show that the formation of inhibitory chemical synapse paves the way for emerging patterned activity in developing motor network. Finally, I investigate the

roles of spontaneous activity at various embryonic stages by temporary manipulations and unveil a critical period during which spontaneous activity in the M/A27h circuit contributes essentially to motor development.

Collectively, these findings tease apart the molecules, cells, and circuit that lie at the heart of spontaneous patterned activity in developing motor circuits, which add insightful values towards understanding how brain circuits are nurtured during development.