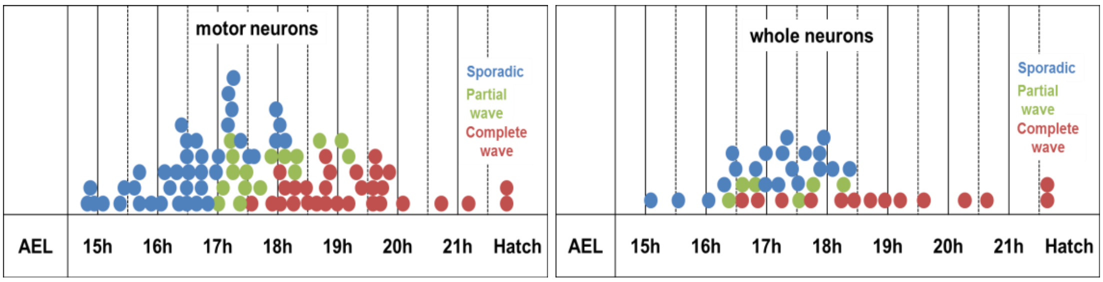
論 文 の 内 容 の 要 旨

論文題目
Development of Coordinated Neural Activities in the Motor Circuits of *Drosophila* Larvae: the Role of Sensory Feedback and Gap Junctions
（ショウジョウバエ幼虫の運動回路における協調的活動の発生：感覚フィードバックとＧＡＰ結合の役割について）

氏　名　川崎　達平

Most animals possess the ability to move. Aristotle defined and classified animals as beings that have nutritive power, self-motion and sense-perception. Many stereotyped motor outputs are composed of a combination of various simple patterned activities of muscles. Such simple patterned activities are controlled by the CPGs. Over decades studies about CPGs reveal many things about this circuit, but the detail mechanism underlying this circuit is not well known yet. In this study, I used the peristaltic locomotion of *Drosophila* embryos as a model to study the mechanism of how coordinated neural activities emerge during the development of the nervous system. The *Drosophila* larva is an ideal model to study the mechanism of motor systems from the following reasons. First, its behavior is stereotypic and easy to quantify. Second, highly sophisticated genetic tools can be used to visualize and manipulate specific component neurons in the system. Third, its short life cycle (~10 days) allows efficient genetic crosses and developmental analyses. Peristaltic locomotion in *Drosophila* embryos is achieved by propagation of muscle contractions from anterior to posterior or posterior to anterior of the body. The muscle movements are in turn generated by sequential activation of motor neurons (MNs) in the corresponding neuromeres (segmental units of the central nervous system). Previous studies examined the development of the motor circuits in *Drosophila* larvae indirectly by observing the development of muscle activity. However, since these studies observed a global movement of muscles using muscle contraction as a measure, development of more local activities (such as activities in a single muscle or a small group of muscles) remained unknown. More importantly, activity of neurons that generates the muscle movement had not been studied. In this study, I first used calcium imaging of muscles to examine the activity of individual muscles during development and found local activity of muscles that were unnoticed in the previous studies. I then performed calcium imaging of central neurons and revealed for the first time the emergence of neuronal activity that generates larval locomotion during embryonic development. As the result, I found that Coordinated Activities in interneurons (INs) Emerging Earlier than Those in Motor Neurons (**Figure1**). This result suggests that some interneurons other than cholinergic neurons play leading roles in the organization of the circuits Finally, I show essential roles of gap junctions in the embryonic central circuits that autonomously (without the aid of sensory feedback) generate motor waves. The requirement of gap junctions is transient since gap junctions are no longer required in the 3rd instar larvae. My results suggest the possible model that there are two independent and complementary circuits in the embryos that generate motor waves, one involving GJs and the other mediated by sensory feedback and they are gradually integrated with the maturation (**Figure2**).



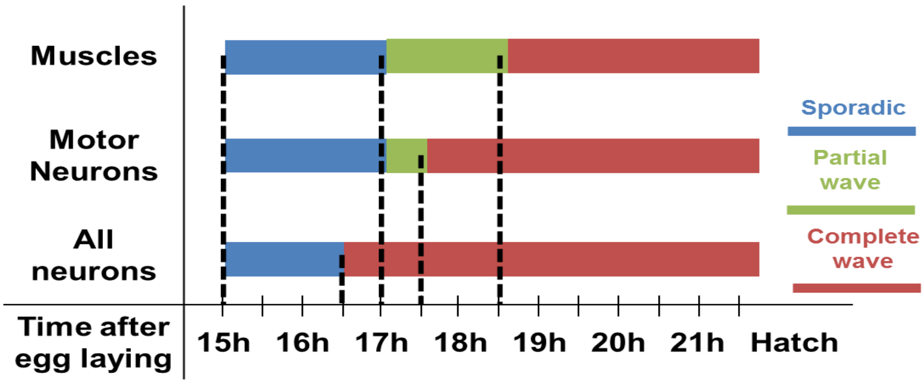


Figure1

Patterned Activities Appear at Different Timings between MNs and INs. MNs and all neurons in the CNS. INs show coordinated activity ~1h prior to MNs.

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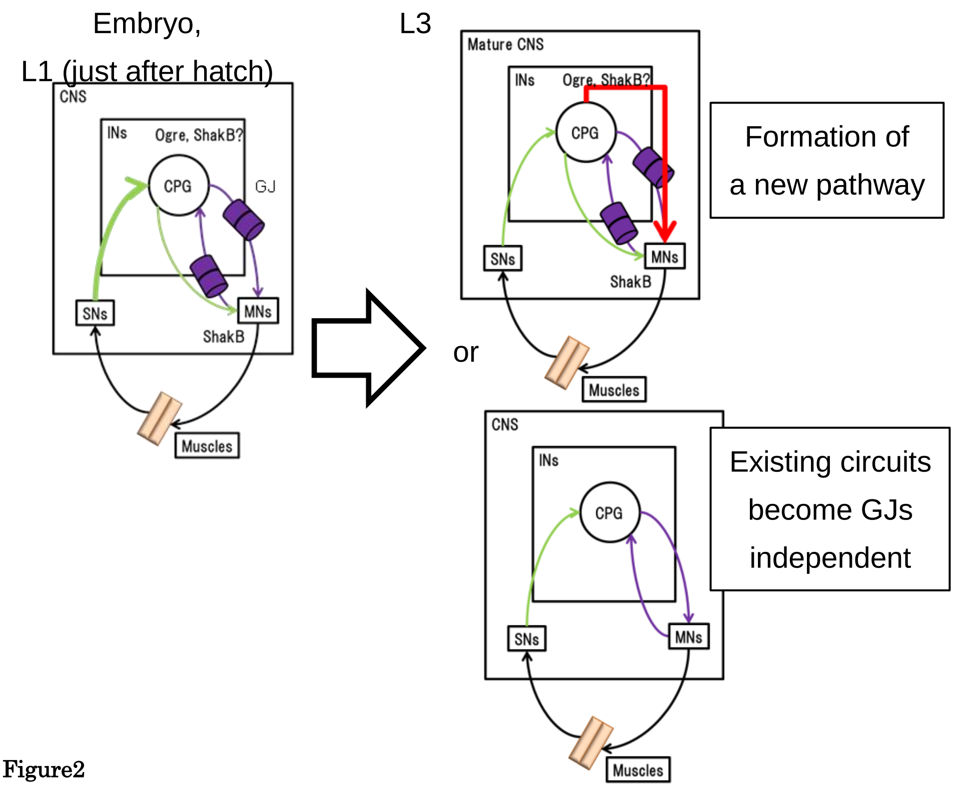

Figure2

In immature CNS (embryo, 1st instars just after hatch, left), two pathways, one dependent on gap junctions and the other mediated by SFs, generate the motor wave. Either one of the two pathways is sufficient for wave generation but eliminating both pathways abolishes the wave. In mature CNS (3rd instars, right), motor waves can occur even when both GJs and SFs are absent. This may be because of the formation of a new pathway (top) or because the existing circuits become GJ-independent (bottom).