Serotonin-dependent Pulse-Width-Modulation control of food uptake

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***Short Abstract* — In this study, we examined how food uptake is regulated in *C. elegans*. Combination of microfluidics and automated image analysis enabled longitudinal measurement of individual worms at high temporal resolution in precisely defined environment. We identified the bi-phasic nature of feeding regulation of the worms, where feeding behavior alternates between fast regular pumping and slow irregular pumping. The rate of food uptake is modulated in response to food availability by adjusting the duration of the two modes via the control mechanism as known as Pulse-Width Modulation, where the neurotransmitter serotonin plays essential role.**

***Keywords* — Pharyngeal Pumping, Regulation of food uptake, Serotonin, Pulse-Width Modulation**

I. Background information

THE regulation of food uptake is a critical mechanism with major physiological impact [1-4]. To understand the mechanism of how food uptake is regulated, there has been interest in using feeding of *C. elegans* as a model system [5, 6]. The nematode feeds on bacteria, and it is facilitated by the action of the pharynx, a neuromuscular pump that draws bacteria suspended in liquid into the mouth from the surrounding environment, and transports them to the intestine after concentrating and grinding [7, 8]. Pharyngeal pumping is therefore a primary indicator of food intake and consequent growth.

Previous results suggest that pharyngeal pumping depends on feeding history and quality of food through a mechanism that involves the neurotransmitter serotonin (5-HT, 5-hydroxytryptamine) [9-11]. Serotonin increases feeding rate of *C. elegans* [12] and has been suggested as a putative food signal that controls feeding of the animal [13].

II. Summary of results

Conventional feeding assays are performed on dense bacterial lawns which do not allow fine control of food concentration. Thus, to probe how food uptake is regulated in response to food availability, we employed a custom microfluidic device [14] that enabled us to precisely control the concentration of available food and to monitor the dynamics of pharyngeal pumping at high resolution. At various food concentrations, we probed the time courses of pumping of individual worms, which revealed switching dynamics between two pumping modes. In one mode, worms pump regularly at maximum rate and, in the other mode, they pump sporadically. We show that the durations of the two modes are modulated in response to food concentrations, and the average feeding rate is determined by the fraction of time spent in the fast mode.

Using strains that lacks serotonin biosynthesis or serotonin receptors, the essential role of the neurotransmitter serotonin in the regulation of feeding in the nematode was demonstrated.

III. Conclusion

With our data, we show that feeding of *C. elegans* is controlled by a serotonin-dependent Pulse-Width-Modulation mechanism, with a duty cycle that depends on the availability of food.

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