Seminar

GTR Nagoya University

Two Sexes, Two Minds: Whole-Brain Dynamics Beyond the Connectome

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Brains are dynamic organs in which neural circuits are continually reprogrammed to change behavior. During sexual maturation, each sex must add its own sex-specific mating behaviors while retaining existing nonsexual behaviors, such as avoiding dangerous chemicals. How nervous systems are reprogrammed to accommodate both remains largely unknown.

To address this, we compared whole-brain activity between both sexes of *C. elegans*, neuron-by-neuron, to identify dimorphisms in sensory-processing circuits (Seyedolmohadesin et al., *bioRxiv* 2025). Using NeuroPAL (Yemini et al., *Cell* 2021), we simultaneously measured neuron identities and activity across a broad set of stimuli: food, pheromone, osmotic stress, toxic stress, and olfactory and gustatory stimuli at low and high concentrations.

These stimuli evoked responses across nearly every head neuron, revealing surprising dimorphisms. Nearly every neuron responds both monomorphically and dimorphically, suggesting that sex and stimulus interact to activate either shared or sex-specific circuits. Strikingly, neurons with the strongest functional dimorphisms show negligible differences in synaptic connectivity (and vice versa) underscoring the need for dynamic activity maps to complement the static connectome. This extends earlier work showing similar disconnects between functional and synaptic connectivity in *C. elegans* hermaphrodites (Yemini et al., *Cell* 2021; Uzel et al., *Current Biology* 2022; Randi et al., *Nature* 2023).

These findings raise three questions: What drives sensory dimorphisms? Why do functional and synaptic connectivity diverge? Can whole-brain activity predict neural circuits? We address each in turn: showing that the cell-autonomous sexual identity of sensory neurons in the head shapes circuit function to balance the addition of mating behaviors while retaining nonsexual survival behaviors; that monoaminergic signaling, underrepresented in the connectome, contributes to sensory-behavioral circuit function; and introducing algorithms that infer and predict neural circuits from whole-brain dynamics – taking us beyond the connectome.

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