Probing Neural Dynamics with Behavioural Genetics 2019

**A trial-by-trial associative-learning paradigm reveals differential effects of neuromodulators on the dynamics and efficacies of learning by C. elegans.**

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Associative learning allows animals to adapt to multiple environmental stimuli that occur close together in space and time. Temporal order and contiguity of stimuli presentation is a key feature of associative learning. How molecular and cellular interactions gate and control the formation, maintenance and degradation of the learnt memories in precise spatiotemporal terms remains under active investigation. The nematode *C. elegans* can be trained to associate multiple cues and exhibit learnt locomotor responses. Comprehensive genetic and cellular manipulation tools and a deep understanding of its neural circuits allow a single-cell level resolution of analysis to be applied to *C. elegans* learning and memory. Short wavelength light is an aversive stimulus that triggers an escape response by *C. elegans* and also causes worms to stop feeding. We have developed a novel trial-by-trial conditioning paradigm for *C. elegans* that utilizes the pairing of a noxious light stimulus and a neutral odour stimulus. After training, worms not only learnt to reverse to the once-neutral smell but also learnt to stop feeding - a new learnt response that has not been previously described. Interestingly, one pair of training stimuli (light/odour) can result in learning over distinct timescales across multiple behavioural circuits (reversals/feeding). As neuromodulators are crucial factors in learning and memory processes, we conducted a preliminary candidate screen of neuromodulator mutants. Mutants defective in dopamine, glutamate, and octopamine exhibited defects in learning rates and efficiencies. Intriguingly, mutants defective in serotonin learnt faster and more consistently than wild-type worms. By varying the temporal order of stimuli presentation under different genetic backgrounds and probing neural dynamics (calcium imaging), we will attempt to determine the molecular, cellular and circuit mechanisms that underlie this learning behaviour.