

FROM SENSORY INPUT TO MOTOR OUTPUT AND BACK: CLOSING THE LOOP IN DROSOPHILA LARVA CHEMOTAXIS

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Chemotaxis is a paradigm to study decision making. Orienting in a chemical environment requires a non-trivial repertoire of computational abilities to transform external sensory information into motor responses. We recently discovered [1] that odor-search behavior in the fruit fly larva represents an active sampling process more elaborated than the biased random walks of *Escherichia Coli*, and analogous to sniffing in rats and humans. By quantitatively measuring behavior and inferring olfactory experience during unconstrained motion, we showed how larvae control when, where and how much to turn. However, motor output and sensory input are coupled in a feedback loop that can be challenging to investigate experimentally. We now combine real-time tracking, electrophysiology, optogenetics, quantitative analysis and modeling. In numbers, we can both monitor and stimulate a 4 millimeter creature at a spatial and temporal resolution of 8 micrometers and 30 milliseconds respectively. We created blind transgenic animals retaining olfactory function in just one sensory neuron expressing channel-rhodopsin, a light-gated ion-channel. Rather than using odor molecules, this allows us to deliver very precise and fast stimulation patterns with light. We found that wild type and light smellers demonstrate the same basic orientation strategy in real odor gradients. Surprisingly, so do light smellers when chemotaxing in synthetic light gradients. Therefore, we are in position to systematically investigate the computational bases of spatiotemporal integration during orientation behavior by re-engineering olfactory responses with light, either preset or contingent upon the animal decisions. Trained and tested in our closed-loop virtual reality arena, we built a model that accurately predicts behavioral decisions from sensory data. Overall, our work clarifies at multiple levels how a simple brain uses active sampling and makes decisions to control behavior.

[1] Alex Gomez-Marin, Greg J. Stephens and Matthieu Louis, "Active sampling and decision making in *Drosophila* chemotaxis", *Nature Communications* 2:441 doi: 10.1038/ncomms1455 (2011).