Modularity, graded connectivity, and recurrence in a vertebrate sensorimotor neural circuit

Runzhe Yang[1,2], Ashwin Vishwanathan[1], Jingpeng Wu[1], Mark Goldman[3,4], Emre Aksay[5,6], Sebastian Seung[1,2]

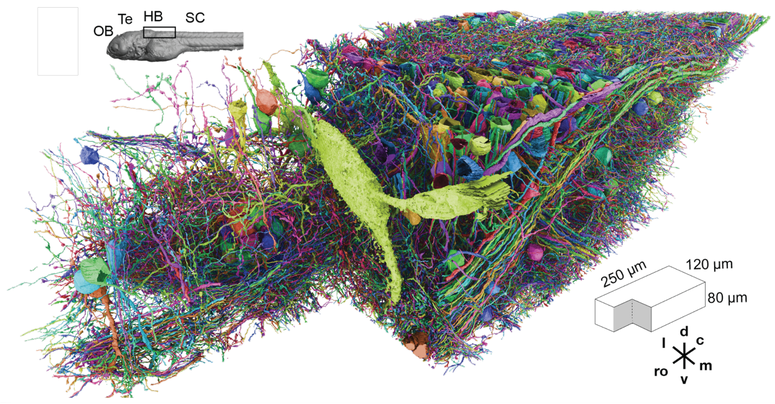
[1]Neuroscience Institute, [2]Computer Science Department, Princeton University, [3]Department of Neurobiology, Physiology, and Behavior, [4]Department of Ophthalmology and Visual Science, UCSD, [5]Institute for Computational Biomedicine, [6]Department of Physiology and Biophysics, Weill Cornell Medical College

Highlights

- We present **the first vertebrate sensorimotor circuit map** with a **synaptic resolution**, encompassing over 3000 neurons reconstructed from **electron microscopy images** of **a larval zebrafish hindbrain**.
- **[Modular structure]** We identify an **oculomotor module (modO)** and an **axial module (modA)** of highly interconnected neurons, which are specialized for **the eyes and body movements**, respectively.
- **[Functional significance of weak connections]** Unlike the *C. elegans* mating circuits (Jarrell et al. 2012), the **modularity** of the zebrafish sensorimotor circuit is **maintained even if all strong connections are discarded**, suggesting that **weak connections are functionally significant** for zebrafish.
- **[Recurrence quantification]** **3-neuron cyclic motifs** are **overrepresented** in the oculomotor module and aligned with a **global cyclic block structure**, which indicates that this vertebrate sensorimotor circuit is highly recurrent.

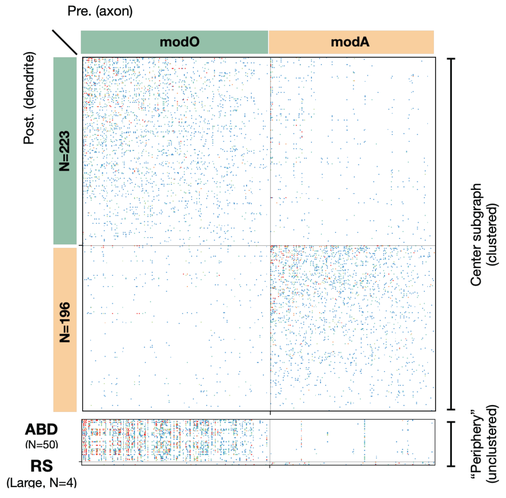
Reconstructed wiring diagram

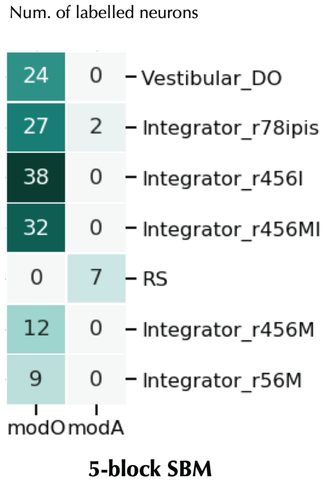
- We apply serial section electron microscopy (ssEM) to reconstruct synaptic wiring diagram of a zebrafish brainstem, which contains 2,883 “nodes” and 44,969 “edges” (75,195 synapses).
- Our analysis is based on a less truncated center subgraph identified by thresholding number of synapses per neuron.

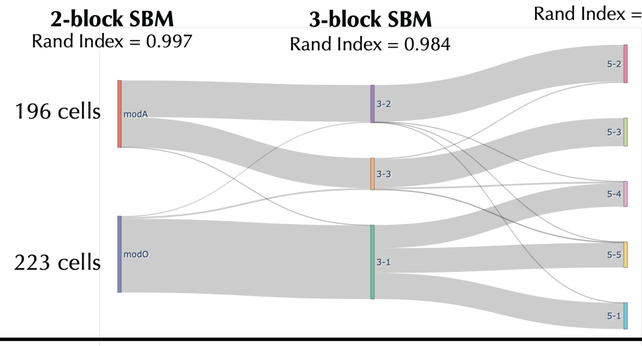


Oculomotor and axial modules

- The degree-corrected stochastic block modeling (DC-SBM) algorithm stably discovers a 2-module structure (*Q=0.37*):
  - **modO** sends more synapses to abducens neurons (ABD), and contains mostly neural integrators.
  - **modA** sends more synapses to large periphery RS neurons, and contains all center RS neurons.

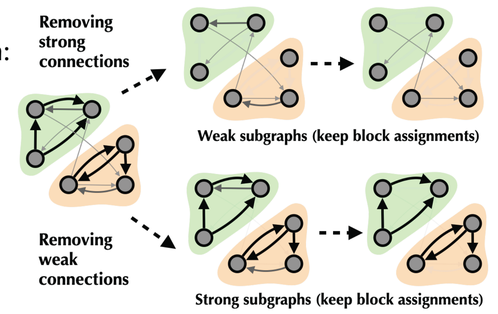


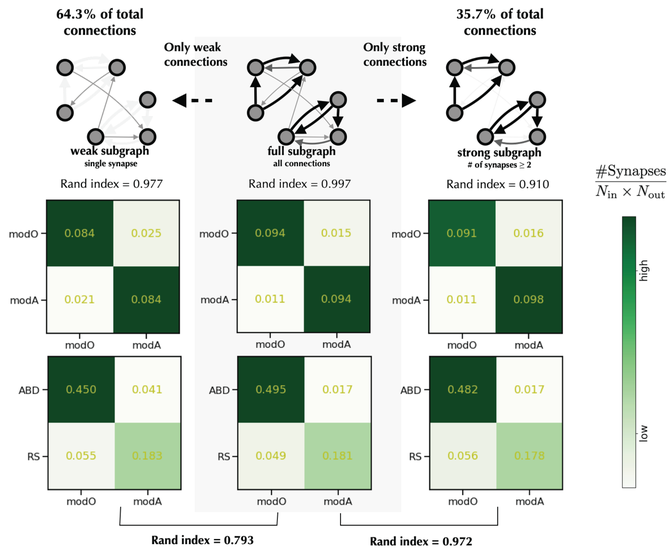


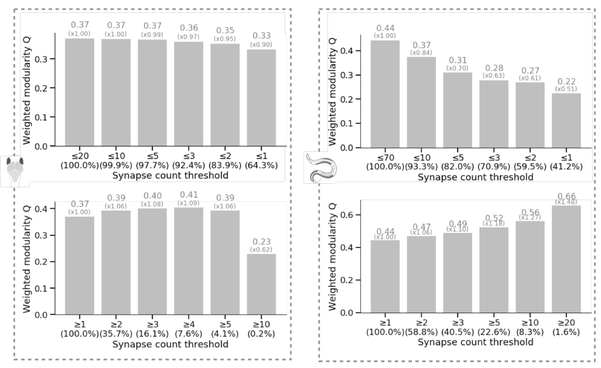


Strong vs weak connections

- There are more than 60% connections are single-synapse (“weak”). Unlike those in *C. elegans*, zebrafish weak connections are non-random:
  - DC-SBM finds similar modules in the weak subgraph.
  - The modularity maintains when removing strong connections.

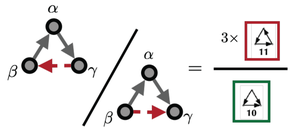






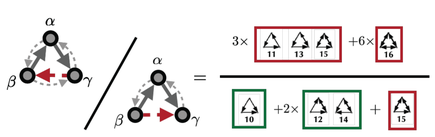
3-cycle motifs in modO

- We quantify the recurrence of modO via two metrics U_3 and C_3 based on the 3-neuron connectivity motifs.
- 3-unicycle motifs is highly overrepresented in zebrafish modO, but not in *C. elegans*. modO is more recurrent than the *C. elegans* interneuron circuit.



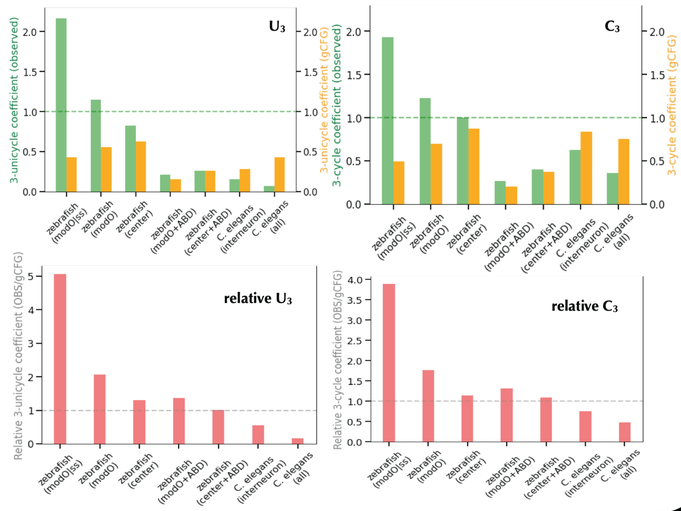
$$U_3 = \frac{\Pr[\gamma \vec{\not\to} \beta | \beta \vec{\not\to} \alpha \wedge \alpha \vec{\not\to} \gamma]}{\Pr[\beta \vec{\not\to} \gamma | \beta \vec{\not\to} \alpha \wedge \alpha \vec{\not\to} \gamma]}$$

3-unicycle coefficient



$$C_3 = \frac{\Pr[\gamma \to \beta | \beta \to \alpha \wedge \alpha \to \gamma]}{\Pr[\beta \vec{\not\to} \gamma | \beta \to \alpha \wedge \alpha \to \gamma]}$$

3-cycle coefficient



3-cycle blocks in modO

- DC-SBM reveals a cyclic 3-block structure in modO
- Blocks are biologically validated by input specificity.
- 87.2% 3-neuron cycles are aligned with these blocks.