FlyBrainLab: Accelerating the Discovery of the Functional Logic of the Fruit Fly Brain in the Connectomic/Synaptomic Era

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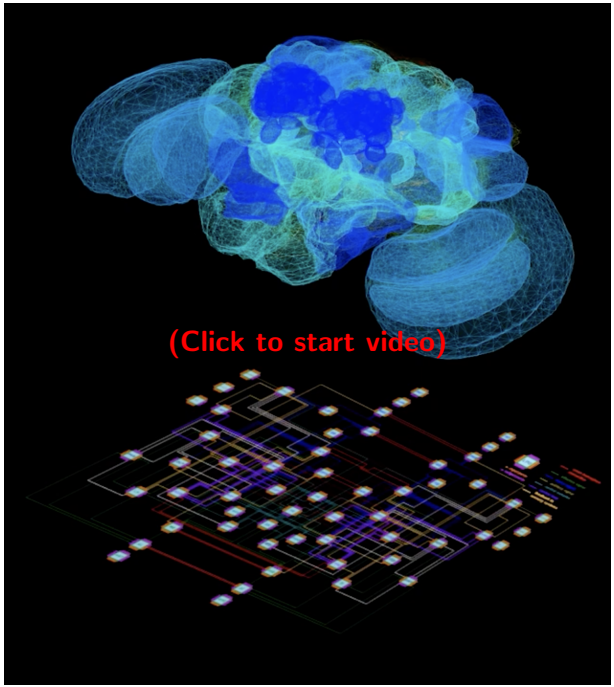
Part I

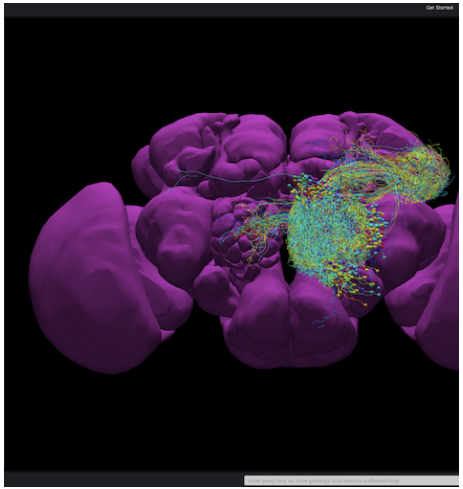
The Fruit Fly Brain Observatory



3D view of the neuropils of the fruit fly brain. Central question: What is the functional logic of the fruit fly brain?

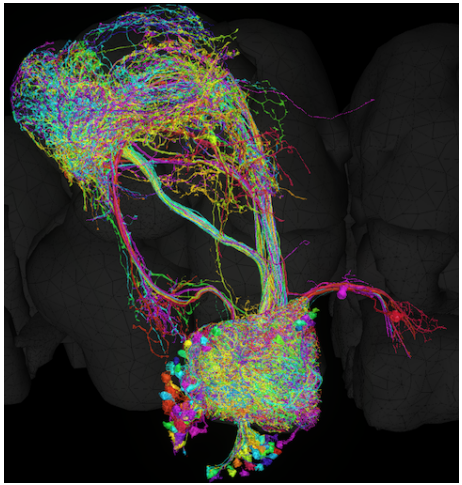
3D circuit diagram depicting a hypothesized systems level architecture of the "local processing units" modeling the neuropils.

FlyCircuit Dataset



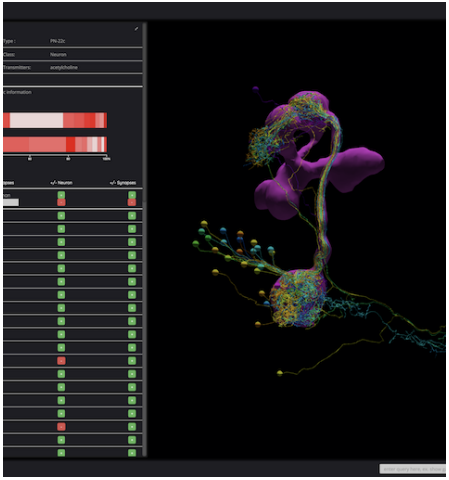
Ann-Shyn Chiang et al., Current Biology 2011, 21(1), pp.1-11.

Hemibrain Dataset



C. Shan Xu et al., A Connectome of the Adult Drosophila Central Brain. bioRxiv 2020.

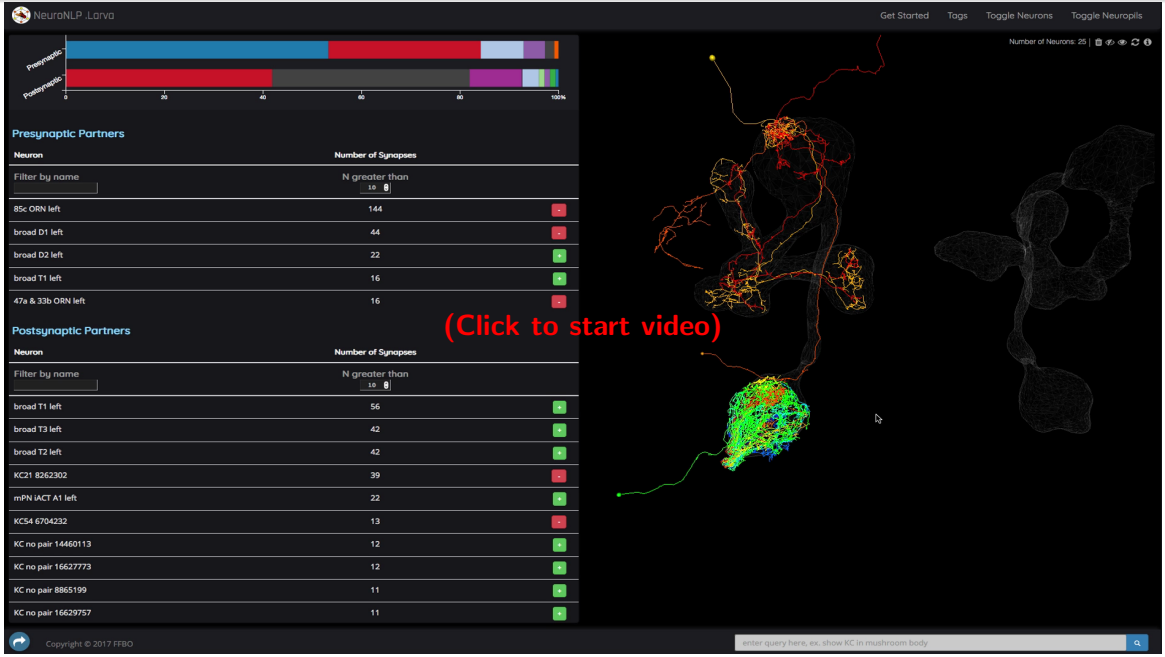
Larva Datasset



Berck et al., ELife 5 (2016):1-21. Eichler et al., Nature 548, 175-182 (2017).

Visualizing the Larva Early Olfactory System

Exploring Antenna > Antennal Lobe > Mushroom Body Neuronal Pathways



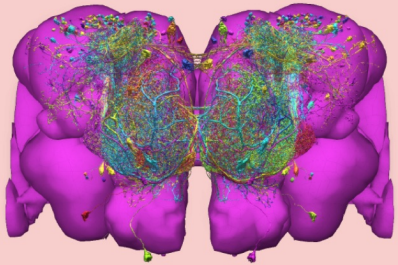
NeuroNLP at https://neuronlp.larva.fruitflybrain.org

NeuroNLP at https://neuronlp.adult.fruitflybrain.org

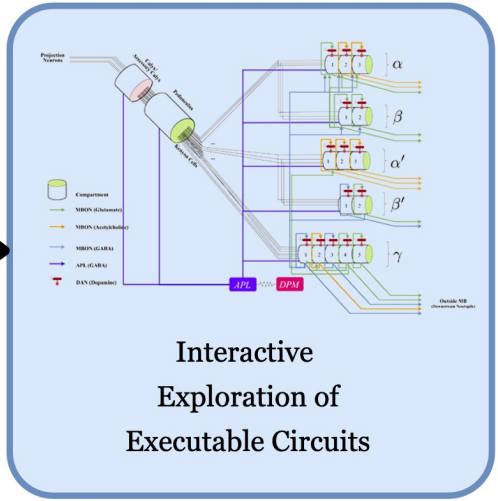
Part II

The FlyBrainLab Interactive Computing Platform

FlyBrainLab: Vision and Requirements



3D Exploration and
Visualization of
Fruit Fly Brain Data

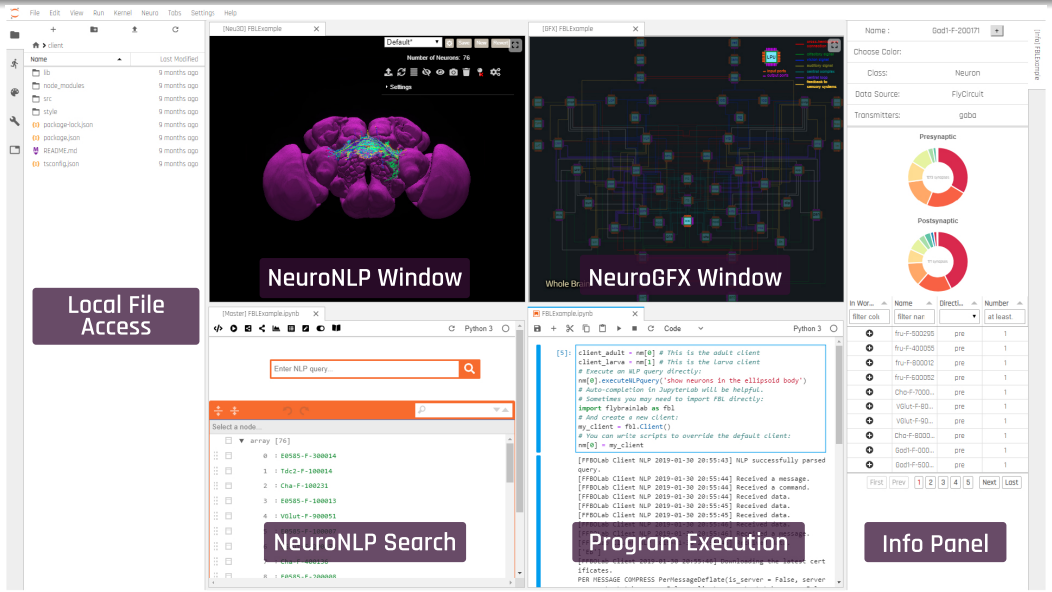


Interactive
Exploration of
Executable Circuits

FlyBrainLab is designed with three main capabilities in mind:

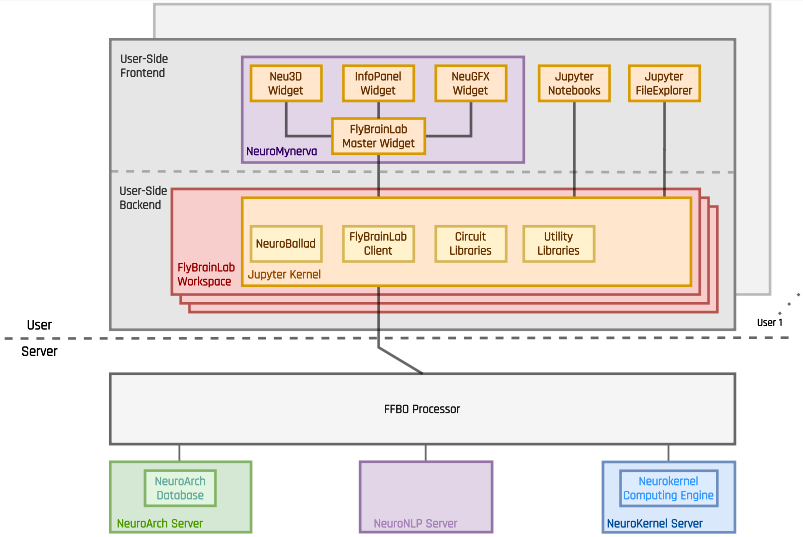
- 3D exploration and visualization of fruit fly brain data,
- creation of executable circuits directly from the explored and visualized fly brain data,
- interactive exploration of the functional logic of the devised executable circuits.

The User Interface of NeuroMynerva



(**top left**) NeuroNLP 3D visualization window. (**top right**) NeuroGFX executable circuits window. (**bottom left**) NeuroNLP Search window for querying data using English. (**bottom right**) Program Execution window with Jupyter Notebook. (**far right**) Information Panel for individual neurons/synapses. (**far left**) Local File Access with Jupyter FileBrowser widget.

The Architecture of FlyBrainLab



- The server-side architecture consists of the NeuroNLP Server, the NeuroArch Server and the Neurokernel Server.
- The user-side provides the local execution environment as well as an easy-to-use GUI for multi-user access to the services provided by the server-side.
- The Utility Libraries and Circuit Libraries can be loaded into the workspace of the user-side backend.

FlyBrainLab Utility and Circuit Libraries

The FlyBrainLab Utility Library of the Fruit Fly Connectome/Synaptome include:

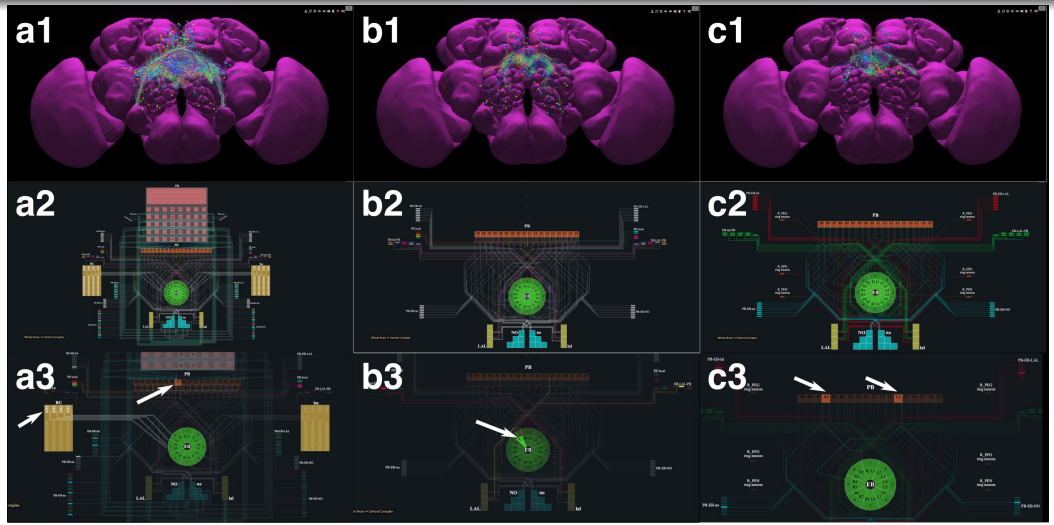
- **NeuroEmbed**: Cell Classification and Cell Type Discovery,
- **NeuroSynapsis**: High Level Queries and Analysis of Connectomic and Synaptomic Data,
- **NeuroGraph**: Connectivity Pattern Discovery and Circuit Visualization Algorithms,
- **NeuroWatch**: 3D Fruit Fly Data Visualization in Jupyter Notebooks,
- **NeuroMetry**: Morphometric Measurements of Neurons.

The FlyBrainLab Circuit Library for Analyzing, Evaluating and Comparing Fruit Fly Brain Circuits

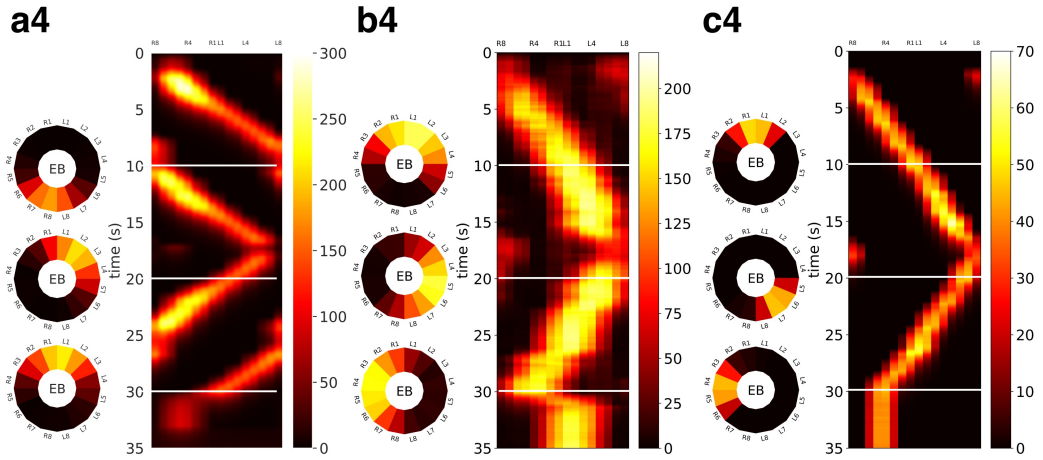
- **CXcircuits**: Library for Central Complex Circuits,
- **EOScircuits**: Library for Larva and Adult Early Olfactory Circuits,
- **MolTrans** Library for Molecular Transduction in Sensory Encoding.

Part III

Analyzing, Evaluating and Comparing *Drosophila* Circuit Models



- (a1, b1, c1) Morphology of the neurons visualized in the NeuroNLP window.
- (a2, b2, c2) Neurons in the NeuroNLP window depicted in the NeuroGFX window as abstract interactive circuit diagrams.
- (a3, b3, c3) When a single vertical bar is presented in the visual field, different sets of neurons/ subregions receive either current injections or external spike inputs for each of the models, respectively.

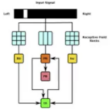


- (a4, b4, c4) Mean firing rate of neurons in each of the EB subregions. Insets show the rates at 10, 20, and 30 seconds, respectively.

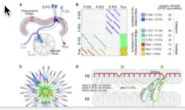
Analyzing, Evaluating and Comparing 3 Circuit Models of the CX (cont'd)

FlyCircuit Dataset

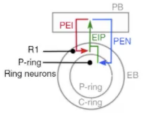
Model from Givon et al., 2017



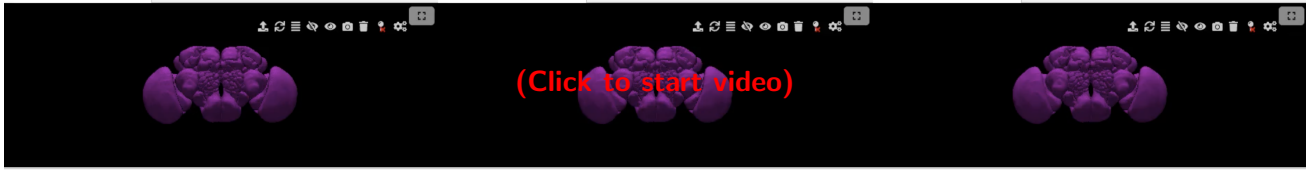
Model from Kakaria & de Bevort, 2017



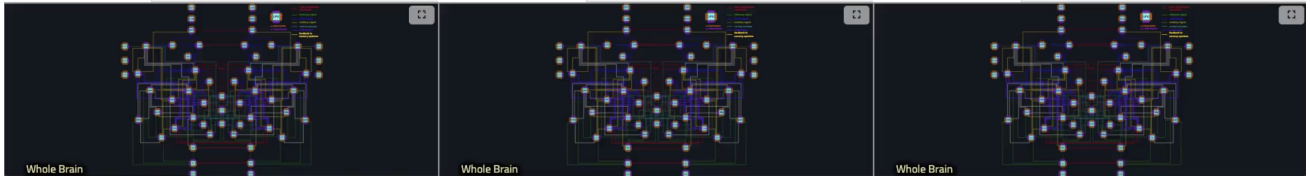
Model from Su et al., 2017

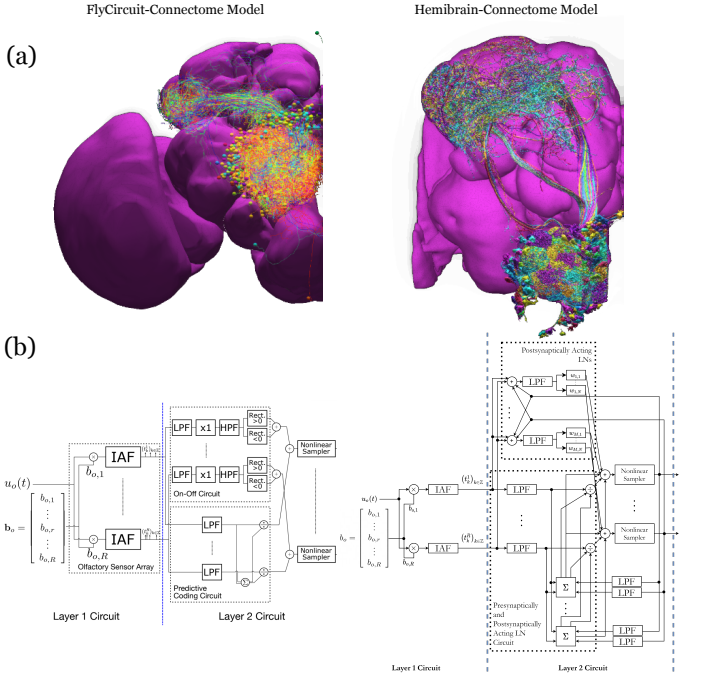


[Neu3D] Untitled5 | [Neu3D] Untitled3 | [Neu3D] Untitled8



[GFX] Untitled5 | [GFX] Untitled3 | [GFX] Untitled8



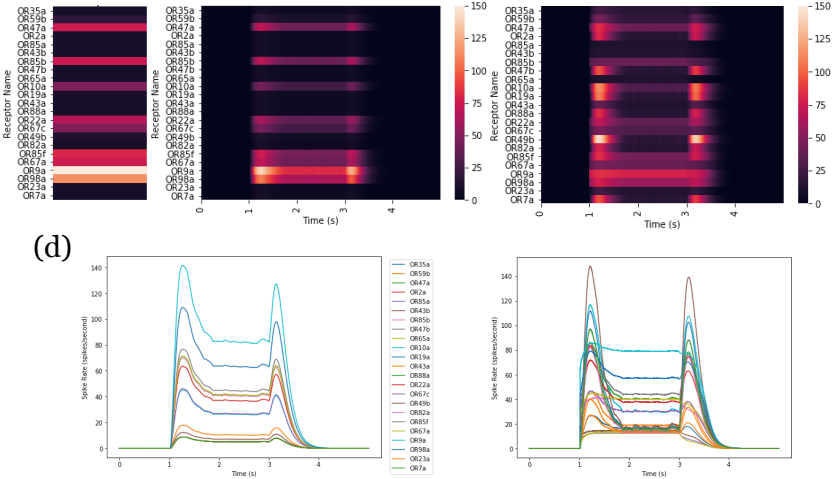


(a) Morphology of olfactory sensory neurons, local neurons and projection neurons in the antennal lobe for the FlyCircuit and Hemibrain datasets.

(b) Circuit diagrams depicting the antenna and antennal lobe circuit motifs derived from the two datasets.

Analyzing, Evaluating & Comparing of 2 Antenna and Antennal Lobe Models (cont'd)

Adult Fly Based on the FlyCircuit (left) Dataset and an Exploratory Model Based on the Hemibrain (right) Dataset

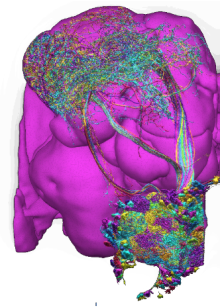


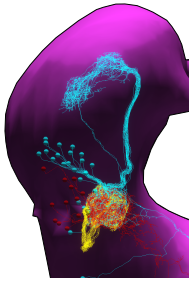
(**top**) Response of the antenna/antennal lobe circuit to a constant ammonium hydroxide step input; (**left**) interaction between the odorant and 23 olfactory receptors captured as the vector of affinity values; (**middle and right**) a heatmap of the uniglomerular PN PSTH values (spikes/second) grouped by glomerulus for the 2 circuit models.

(**d**) The PN response transients of the 2 circuit models for uniform noise input with a minimum of 0ppm and a maximum of 100ppm preprocessed with a 30Hz low-pass filter and delivered between 1s and 3s.

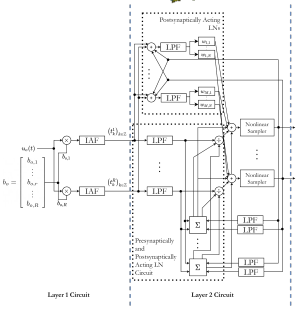
Evaluating and Comparing 2 *Drosophila* Early Olfactory System (EOS) Models

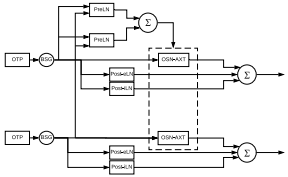
Adult (*left*, Developed Based Hemibrain Dataset) and Larval (*right*, Developed Based on LarvaEM Dataset) Circuits





Morphology of Olfactory Sensory Neurons (OSNs) in the Antenna (ANT), Local Neurons (LNs) in the Antennal Lobe (AL) and Projection Neurons in the AL of the adult (left) and larva (right).

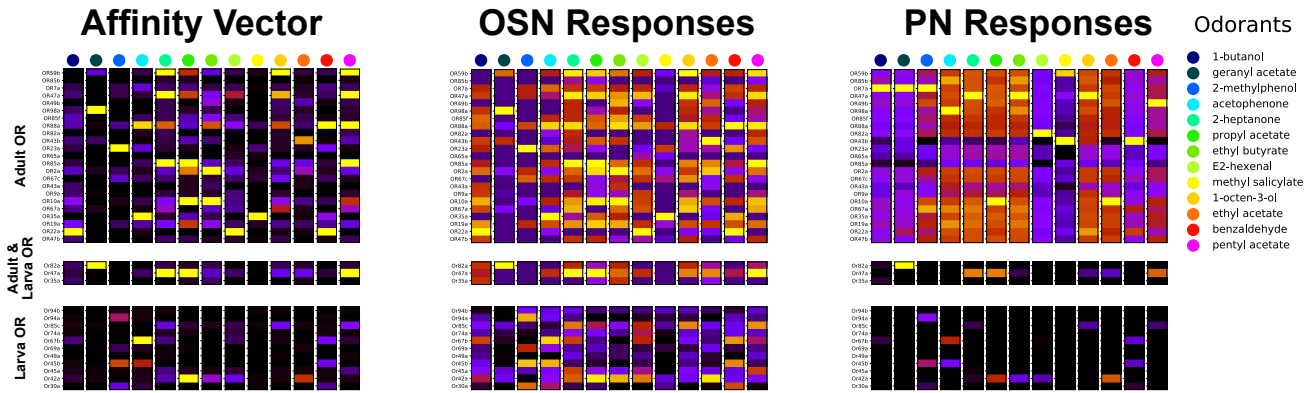




Circuit diagrams depicting the Antenna and Antennal Lobe circuit motifs of the adult (left) and larva (right).

Evaluating and Comparing 2 *Drosophila* Early Olfactory System (EOS) Models (cont'd)

Adult (*left*, Developed Based Hemibrain Dataset) and Larval (*right*, Developed Based on LarvaEM Dataset) Circuits



(**left**) Interaction between 13 odorants and 37 odorant receptors (ORs) characterized by affinity values. The ORs expressed only in the adult fruit flies are grouped in the top panel; the ones that are expressed in both the adult and the larva are grouped in the middle panel; and those expressed only in the larva are shown in the bottom panel.

(**middle and right**) Steady-state outputs of the EOS models to a step concentration waveform of 100 ppm are used to characterize combinatorial codes of odorant identities at the OSN level (**middle**) and the PN level (**right**).

Further Reading

- N. H. Ukani, C.-H. Yeh, A. Tomkins, Y. Zhou, D. Florescu, C. L. Ortiz, Y.-C. Huang, C.-T. Wang, M. K. Turkcan, T. Liu, P. Richmond, C.-C. Lo, D. Coca, A.-S. Chiang, and A. A. Lazar, The Fruit Fly Brain Observatory: From Structure to Function, bioRxiv, Volume 580290, March 2019, https://doi.org/10.1101/580290.
- Aurel A. Lazar, Tingkai Liu, Mehmet K. Turkcan, and Yiyin Zhou, FlyBrainLab: Accelerating the Discovery of the Functional Logic of the Fruit Fly Brain in the Connectomic/Synaptomic Era, bioRxiv, June 2020, https://doi.org/10.1101/2020.06.23.168161.