The Fruit Fly Brain Observatory

Aurel A. Lazar, Columbia University

The Columbia University Team:
- Wesley Bruning
- Allison L. Fenichel
- Aurel A. Lazar (PI)
- Nikul H. Ukani
- Chung-Heng Yeh
- Yiyin Zhou

The National Tsing Hua University Team:
- Ann-Shyn Chiang (PI)
- Yu-Chi Huang
- Chung-Chuan Lo (PI)
- Cheng-Te Wang

The University of Sheffield Team:
- Daniel Coca (PI)
- Dorian Florescu
- Carlos Luna Ortiz
- Paul Richmond
- Adam Tomkins
Why the Fruit Fly

The brain of the fruit fly serves as a viable model for investigating human neurological and psychiatric disorders

• Over 70% of genes involved in human mental disorders have related sequences in the fruit fly
• Small but sufficiently complex brain and nervous system
• Powerful toolkit of genetic manipulation techniques
• No ethical limitations on in vivo experimentation
• Rapid developmental cycle
Where We Are At

• Current Status
  ✓ Knowledge and information of the detailed neuroanatomy, neuron connectivity and gene expression of the adult fly brain is publicly available thanks to earlier pioneering efforts.
  ✓ Vast amounts of experimental data have yet to be distilled into new models or used to validate and refine existing models of brain function.

• Major Obstacles
  ❖ The lack of open communication/collaboration across the modeling community.
  ❖ The lack of shared models, modeling tools and data repositories.

• What’s Needed
  o an open source, modular software platform for accelerated model development, simulation, sharing and review, which ultimately is capable of simulating efficiently a complete model of the healthy and diseased fruit fly brain.
Fruit Fly Brain Observatory (FFBO)

World’s first science platform specifically developed for
• studying fruit fly brain function,
• investigating fruit fly brain disease models that are highly relevant to the mechanisms of human neurological and psychiatric disorders, and
• accelerating the pace of discovery and the translation of fundamental neuroscience research into drug, cell and gene therapies.

A unique open science platform that
• integrates, within a single database, genetic, anatomical, neurophysiological data with computational models. It provides location, morphology, connectivity and biophysical properties of every neuron
• is equipped with powerful executable tools for circuit generation, numerical simulation and user-friendly query and visualization
• automatically generates models of the fly brain that can be simulated efficiently using multiple Graphics Processing Units to help elucidate the mechanisms of human neurological disorders.

FFBO is built upon a novel architecture
• whereupon researchers can build, share, compare, refine and validate models of neuropil compartments, constituent circuits and connectivity maps,
• supports the research efforts of labs around the world.
NeuroNLP: A Natural Language Portal for Aggregated Fruit Fly Brain Data

NeuroNLP is a unique natural language user interface for querying the fly brain database that

- enables in-depth exploration and investigation of brain structure, using intuitive plain English queries,
- provides powerful interactive visualization of neural circuits functionality,
- integrates neural circuits data from multiple sources,
- provides a modern web-based portal for navigating fruit fly brain circuit data,
- can be accessed from any browser supporting WebGL on laptops and smartphones.
Add cholinergic neurons in Elli
NeuroGFX:
A Graphic Functional Explorer for the Fruit Fly Brain

NeuroGFX is a programming interface that automatically translates biological and modeling data into executable code that can be run on a local or cloud-based GPU servers. It

• provides an intuitive graphical interface to leverage the power of the FFBO computational infrastructure,
• visualizes execution results in the context of biological structure.

NeuroGFX provides an environment where

• computational researchers can present configurable, executable neural circuits, and
• experimental scientists can easily explore circuit structure and function ultimately leading to biological validation.
NeuroAPPs: Apps for Healthy and Diseased Models of the Fruit Fly Brain

NeuroAPPs host integrated healthy and diseased models applications of the fruit fly brain. Early examples:

- **Parkinson’s Disease: Olfaction**
  - an emulation of pathological states of the olfactory system due to excess release of the GABA neurotransmitter, a phenomenon observed in Parkinson’s disease.

- **Parkinson’s Disease: Vision**
  - an interactive demonstration of the poorly-understood effect of the retinal degeneration seen in Parkinson's disease.

- **Epilepsy Model**
  - a model which can be used to reproduce experimental observations and to verify working hypotheses.

- **Retinal Degeneration**
  - a retina app to study the potential of rescuing retinal degeneration by optogenetic means.