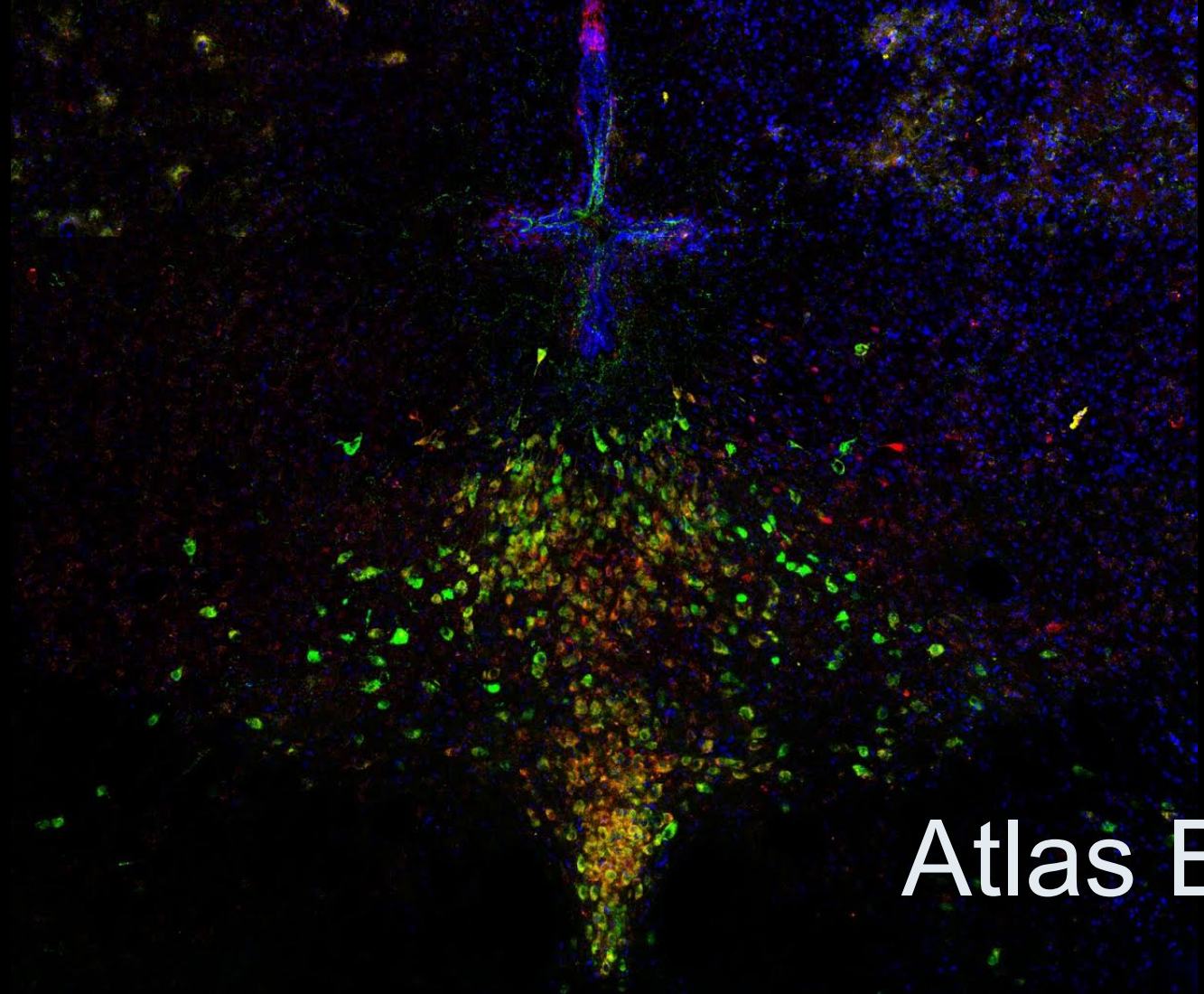


Atlas Building

Charless Fowlkes
Computer Science Department
University of California, Irvine

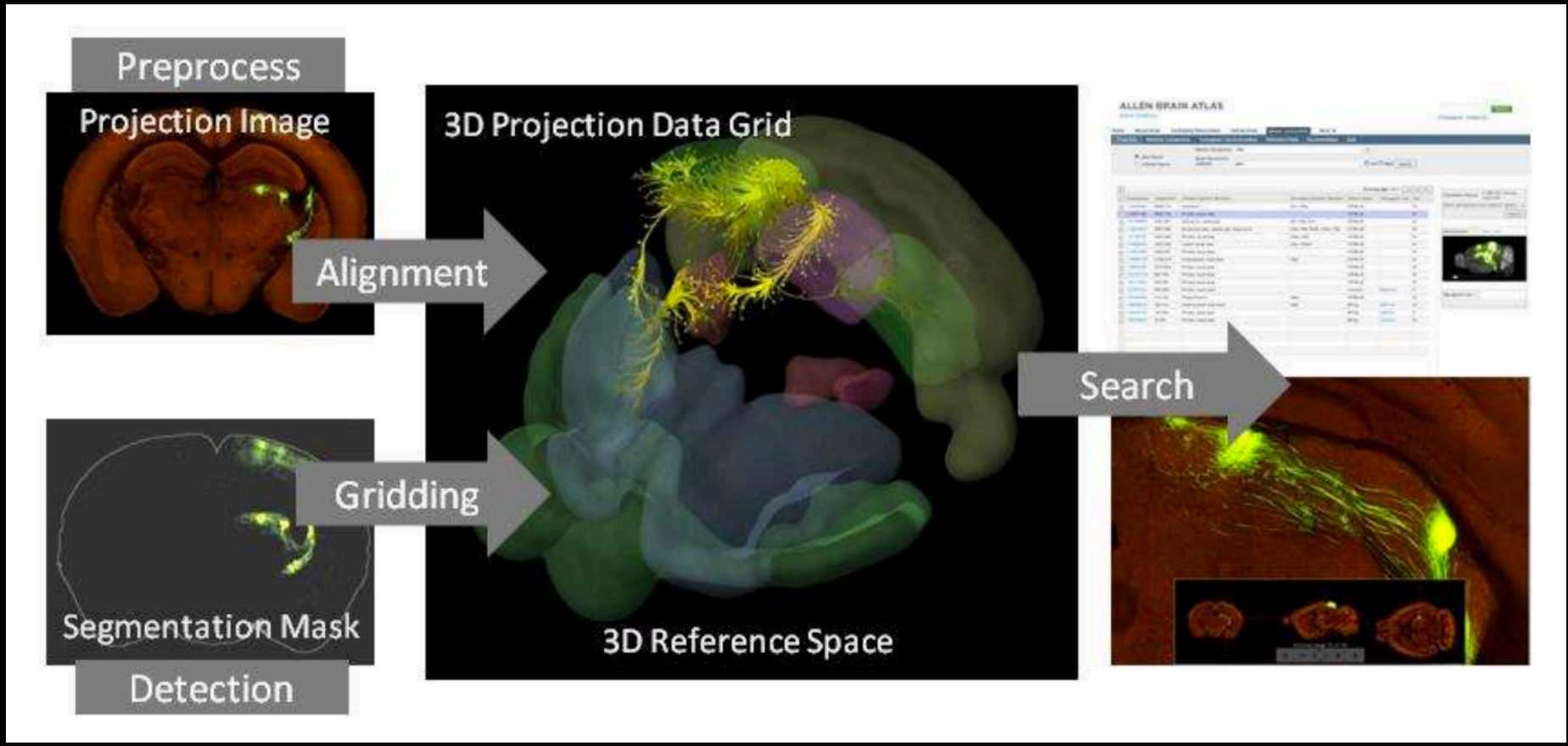
Optical mapping and atlases

- Improved methods for labeling, clearing and optical imaging place cellular-resolution whole brain acquisition within reach even for small labs without titanic resources.

- Computational outlook: need data structures and algorithms for capturing, curating and querying spatial data

- General types of queries:
  - What cell types are present in a particular area?
  - What other regions do these neurons project to?
  - Are these two cell populations directly connected?

Allen Mouse Brain Atlas



- Mechanically sectioned, computational registration based on large scale anatomical features
- Gene expression (*in situ*) and projection data (rAAV + Cre)
- Very large scale!

Registration and Correspondence

Align data collected across different experiments into a standardized spatio-temporal coordinate system

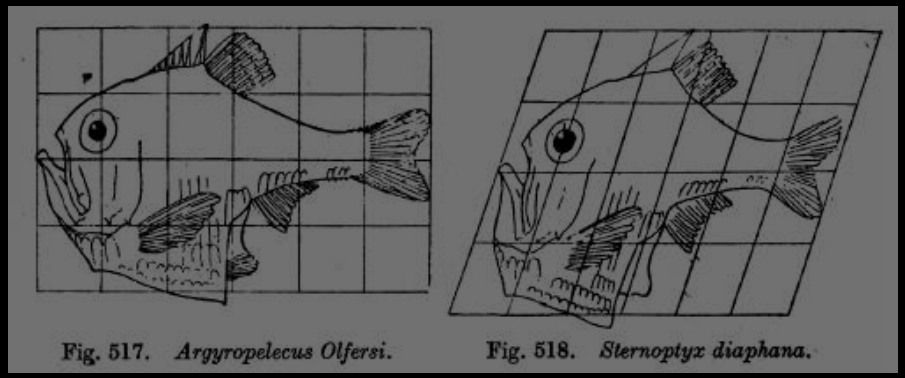


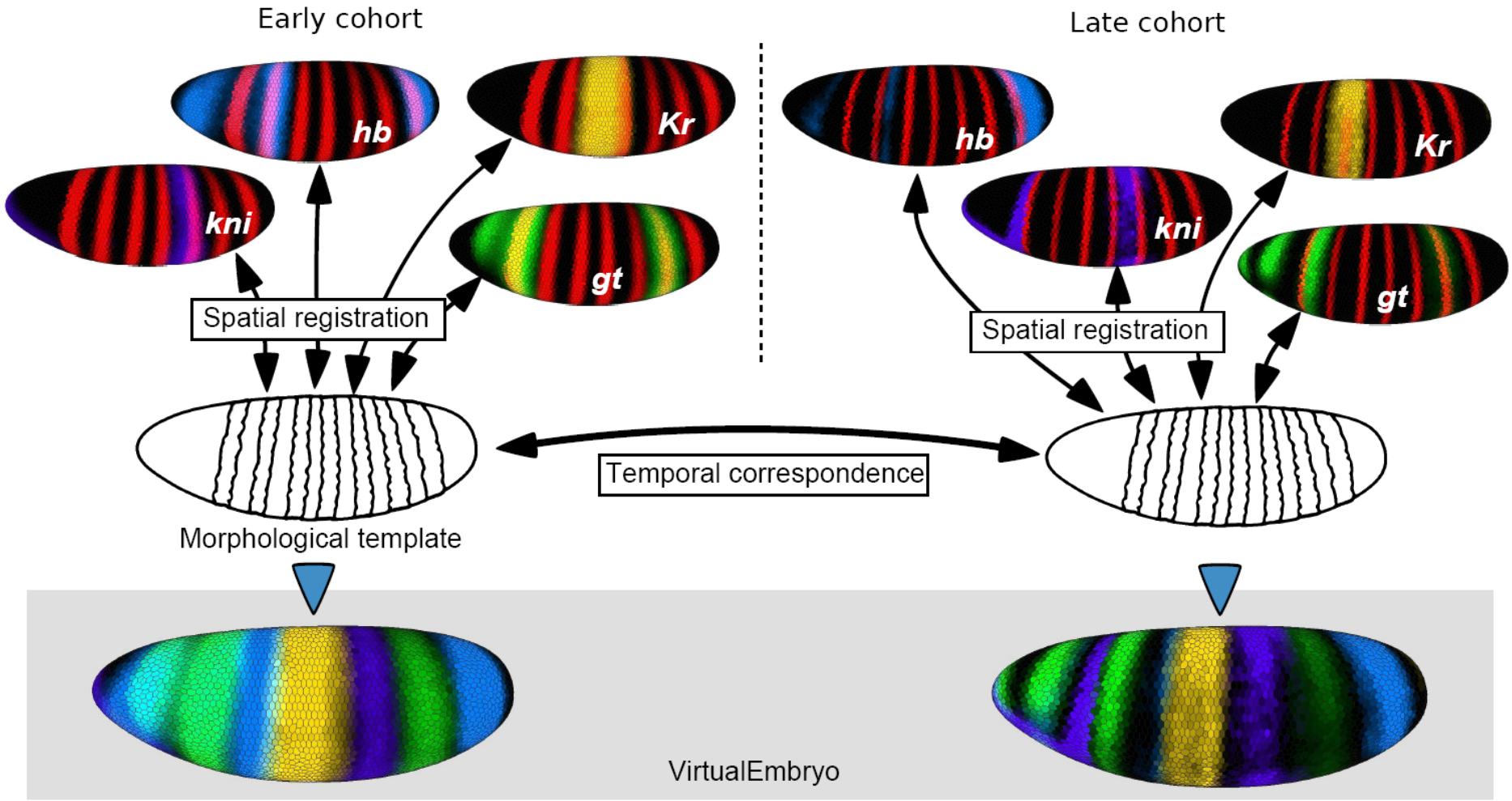
Fig. 517. *Argyropelecus Olfersi.* Fig. 518. *Sternoptyx diaphana.*

Correspondences between samples is the key:

- Composite / average measurements across experiments
- Factor out unimportant modes of spatial variability when making comparisons among individuals
- Measure and characterize remaining variability

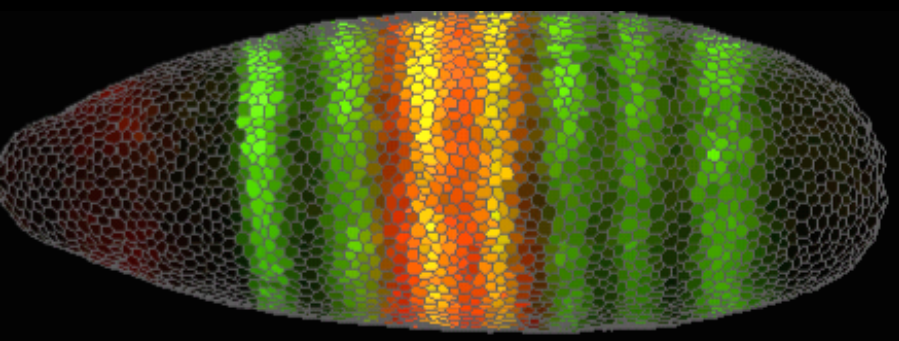
Drosophila gene expression atlas

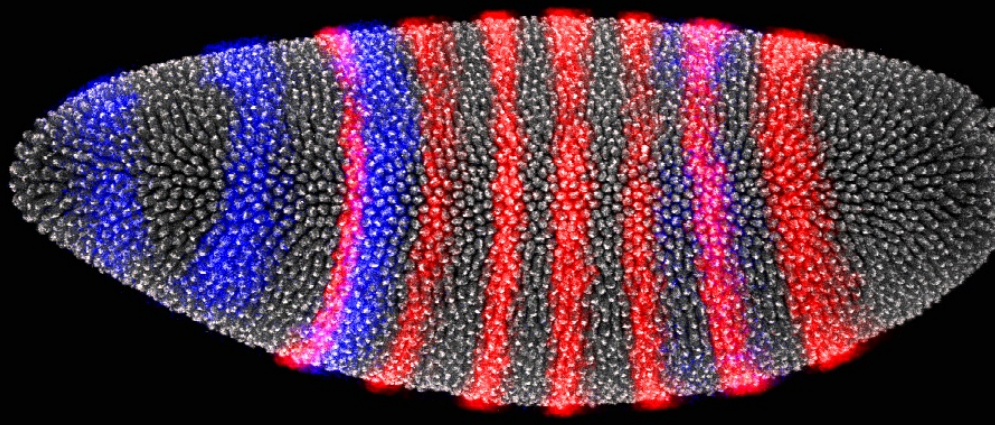
D. melanogaster

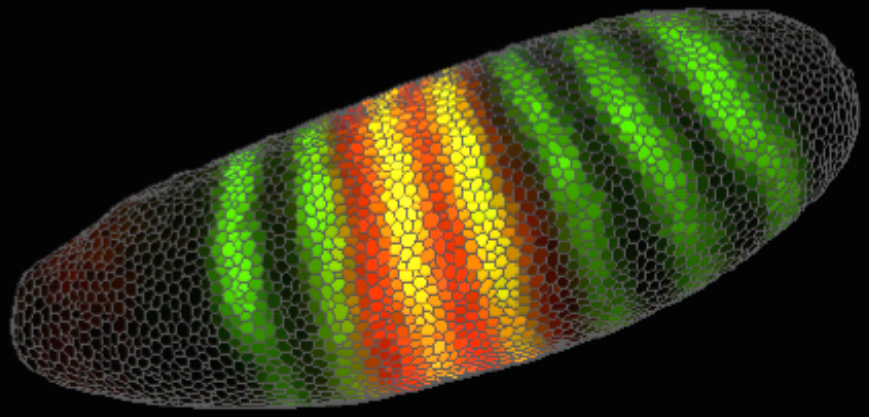


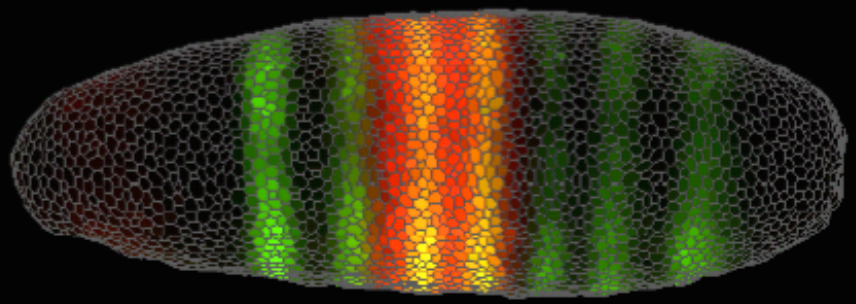
[Fowlkes, et. al., *Cell*, 2008]

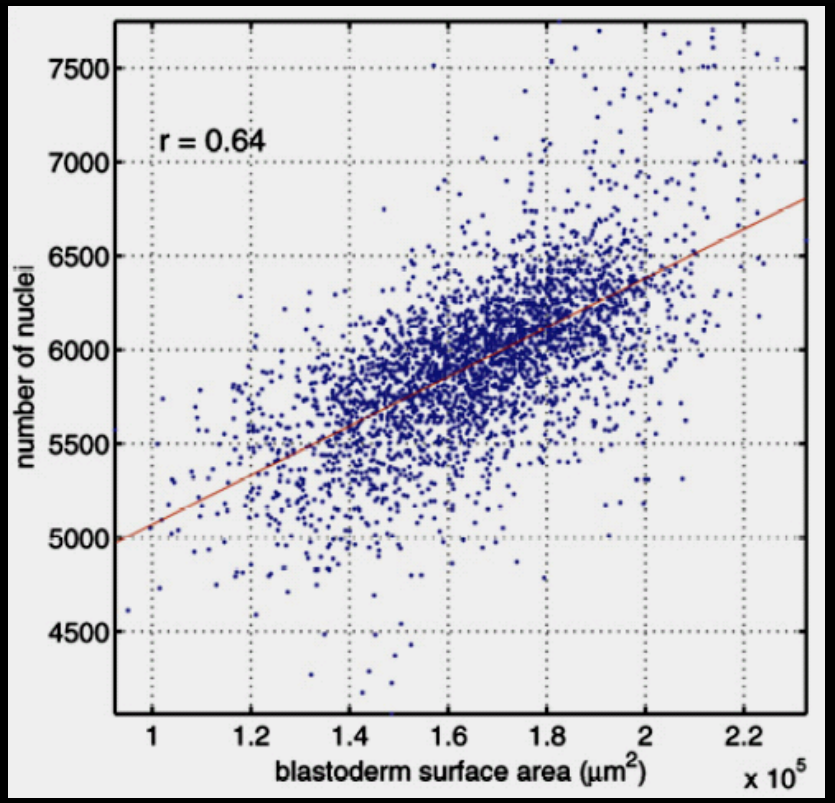
Embryo shape and number of cells varies







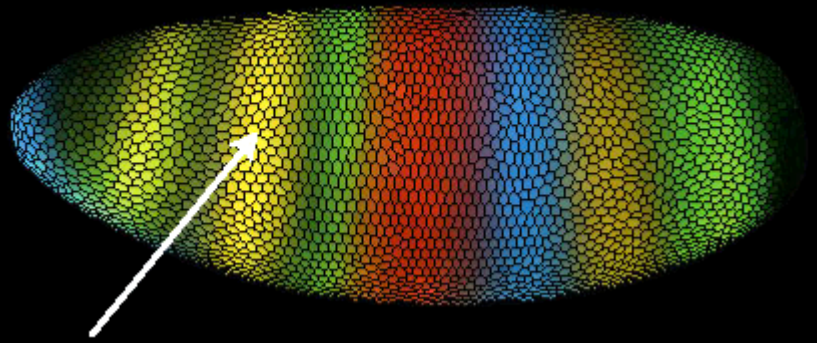




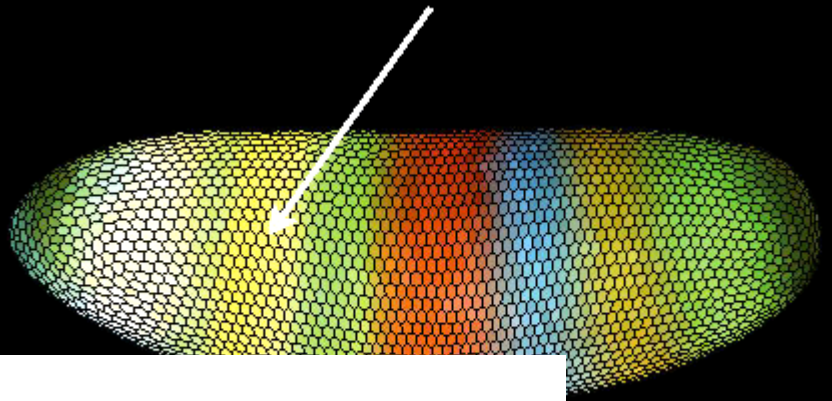
D. melanogaster

D. pseudoobscura

Gene 1 @ t1, t2, t3, t4, t5, t6
Gene 2 @ t1, t2, t3, t4, t5, t6
.
.
.
Gene 8 @ t1, t2, t3, t4, t5, t6

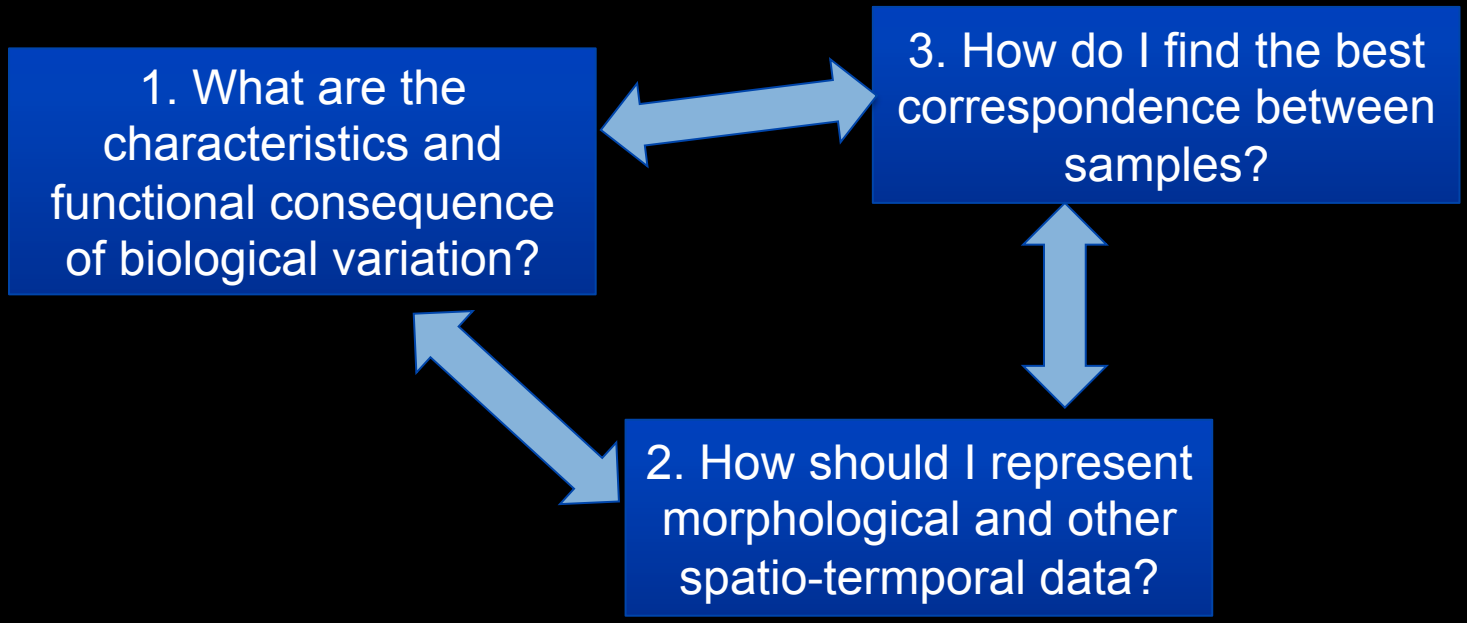


ID1
Gene 1 @ t1, t2, t3, t4, t5, t6
Gene 2 @ t1, t2, t3, t4, t5, t6
.
.
.



[Fowlkes, et. al., PLoS Genetics, 2011]

How do you represent correspondence and assemble a comprehensive, cellular-resolution description of the brain when the *tissue is heterogeneous* and there is no *simple one-to-one* mapping between functionally equivalent circuits?



1. Understanding Variability

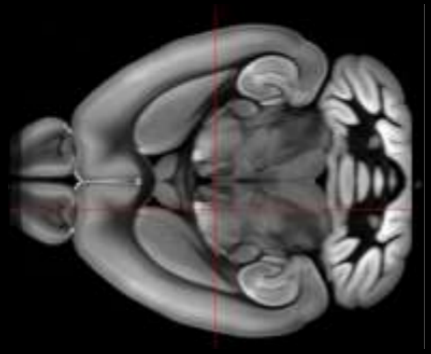
- What are the modes of variation in spatial organization (cell morphology, genetics, circuits, activity, development) across individuals?

- How does function depend (or not) on these differences?

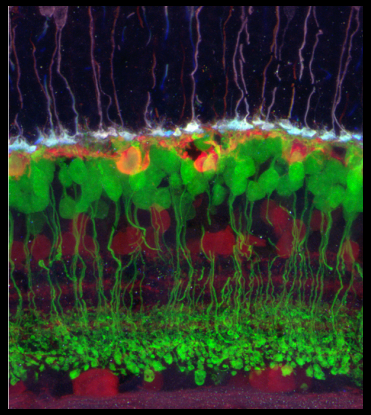
- In what way would we expect comprehensive maps of the brain to represent individual variation? Does a mean or “typical” connectome make any sense?

2. Spatial Representations

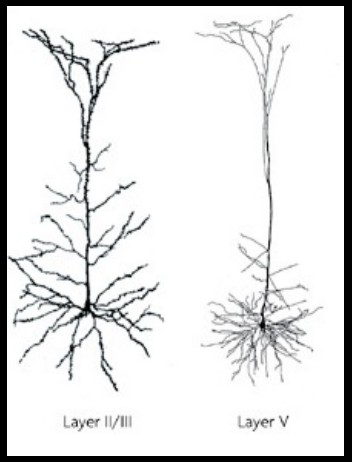
anatomical shape



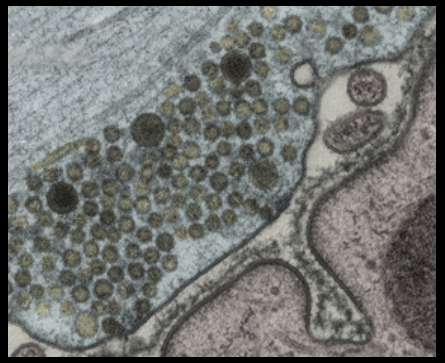
circuit wiring



cell morphology



distribution of subcellular components



shape-like ????? texture-like

- Variability/stochasticity in spatial organization has different characteristics at different spatio-temporal scales
- How do we represent these different types of information in a common computational framework? What are the criteria for deciding if we are using the "right" representations?

3. Robust computational tools

- How do we get quantitative mapping data to interact computationally with new experimental data collected by individual labs?

- Are atlases only built by specialized, large-scale efforts or could they be assembled from more heterogeneous data collected by the "long tail" of small labs focused on specific research questions?

- Need robust pipelines for extracting quantitative morphological descriptions from images and aligning them to atlases. Opportunities for user-trainable and human-in-the-loop approaches to automating data analysis and curation