FlyWire: online community for whole-brain connectomics

2025-5-29

- **Introduction to Brain Connectomics and Applications in Model Organisms——王姣**
- **Foundational Principles and Operational Guidelines of the FlyWire——李畅**
- **Current Advances in Drosophila Research Using FlyWire——邢丽敏**

连接组学概述

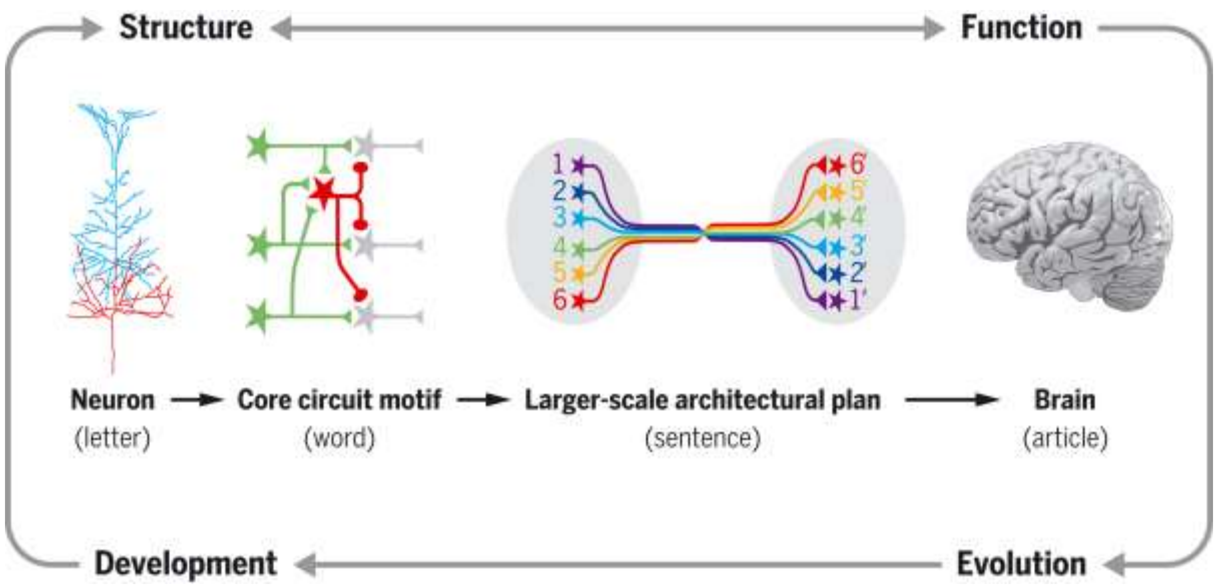
1. Connectome & Connectomics
2. 连接组学中的常用技术
3. 连接组学中的突破性进展

WJ

What is the Connectomics

Connectomics: a branch of biotechnology concerned with applying the techniques of computer-assisted image acquisition and analysis to the structural mapping of sets of neural circuits or to the complete nervous system of selected organisms using high-speed methods, with organizing the results in databases, and with applications of the data.

——Jeff W. Lichtman



- 对大脑进行大范围的观察，明确特定功能与特定区域之间的联系。
- 描述单个神经细胞的特性以及它们如何使用电和化学信号进行通信。

Liqun Luo. *Science*. 2021.

How to get a Neural Connection Diagram

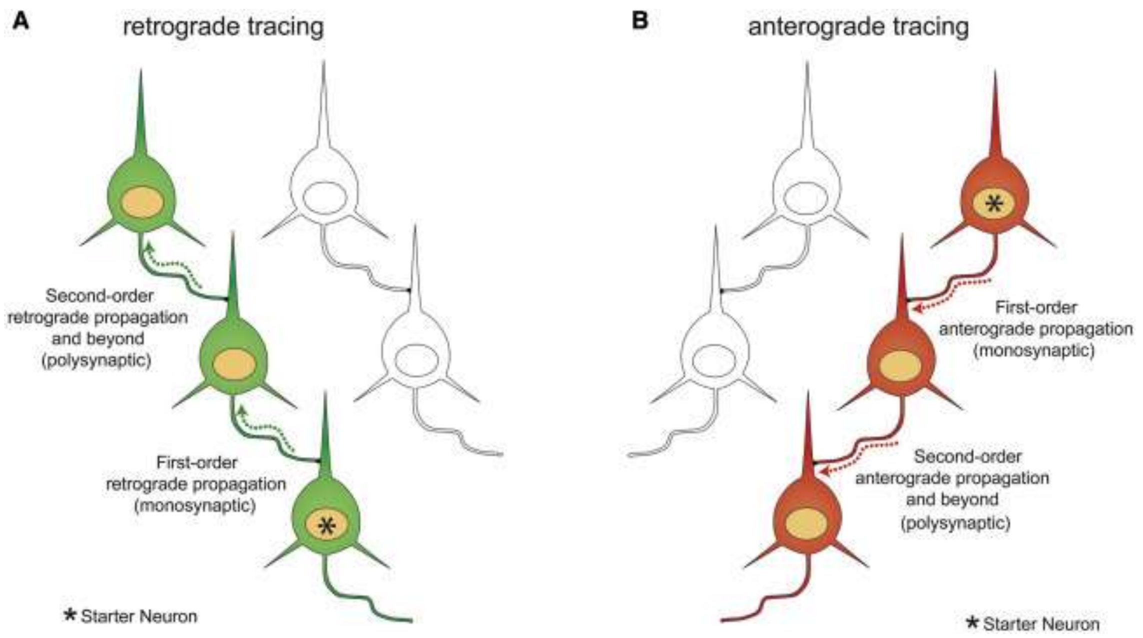
连接组映射依赖于获取和分析大视场（large-field-of-view）高分辨率（high-resolution）大脑图像的方法。
神经环路示踪技术:

传统神经示踪工具:

常用的示踪剂有：HRP（horse radish peroxidase，辣根过氧化物酶），快蓝（fast blue），荧光金（fluorogold），核黄（nuclear yellow），神经生物素（neurobiotin），生物素化葡聚糖胺（biotinylated dextran amine,BDA）等

①无法特异性标记细胞类型；②几乎没有跨突触能力；难以用于多个脑区、多种类型神经元通过突触连接形成的复杂神经网络研究。

跨突触示踪（病毒转导）：



Rozanne M. Sandri-Goldin, et al. *Neuron*. 2020

How to get a Neural Connection Diagram

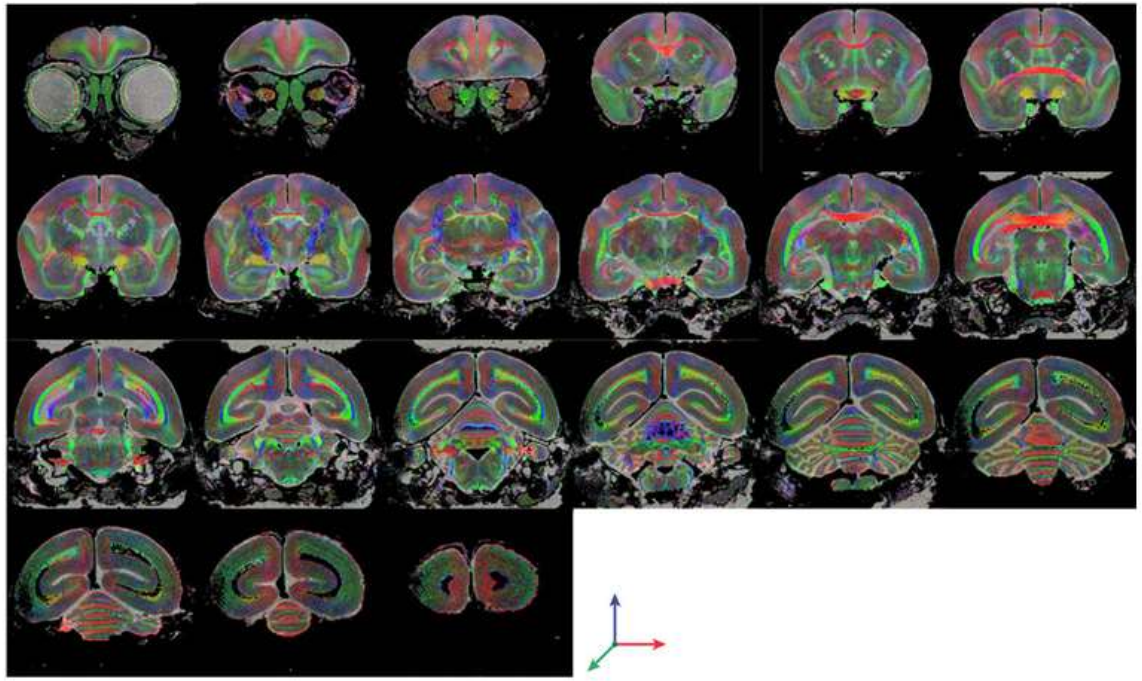
神经影像技术:

	Light/fluorescence microscopy	Magnetic resonance imaging	Electron microscopy
Imaging performed using	Light (fluorescence)	Magnetic resonance	Electron
Resolution	High	Low	Extremely high
Skill level required for imaging	Low	High	High
Expense	Moderate	High	High
Whole-brain imaging	Difficult	Easy	Very difficult
Live imaging	Easy	Easy	Difficult

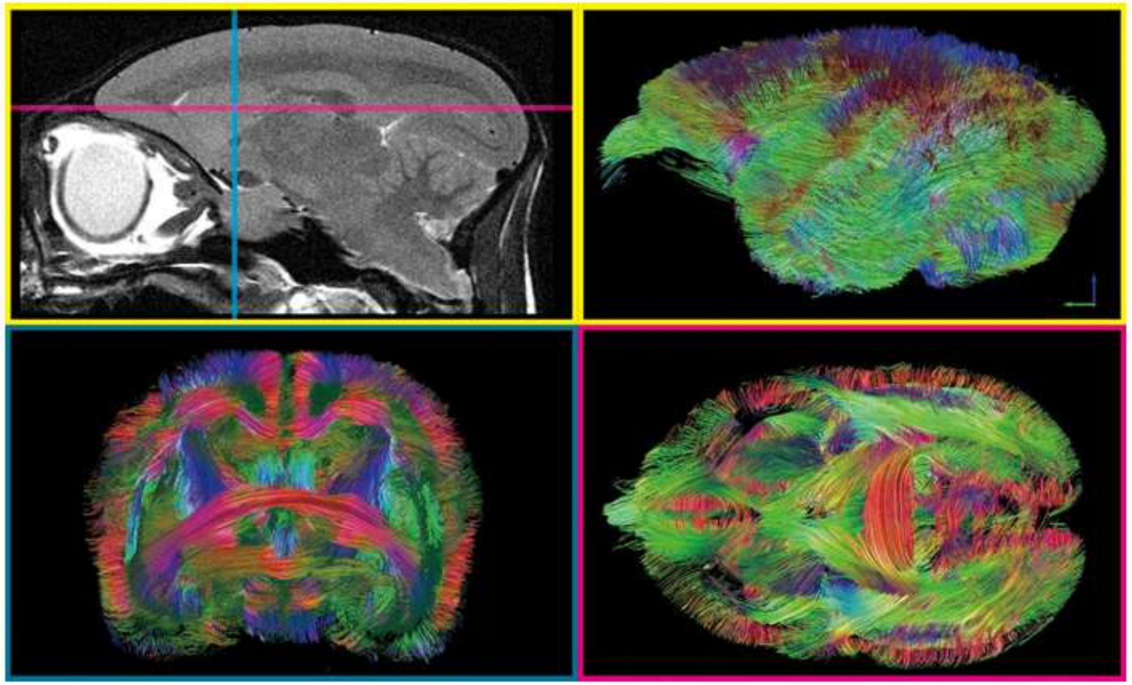
The three major technologies used for connectomics analysis

Shinsuke Shibata, et al. *Microscopy*. 2015.

Macroscale connectomics with MRI



Images from MRI connectomics analysis



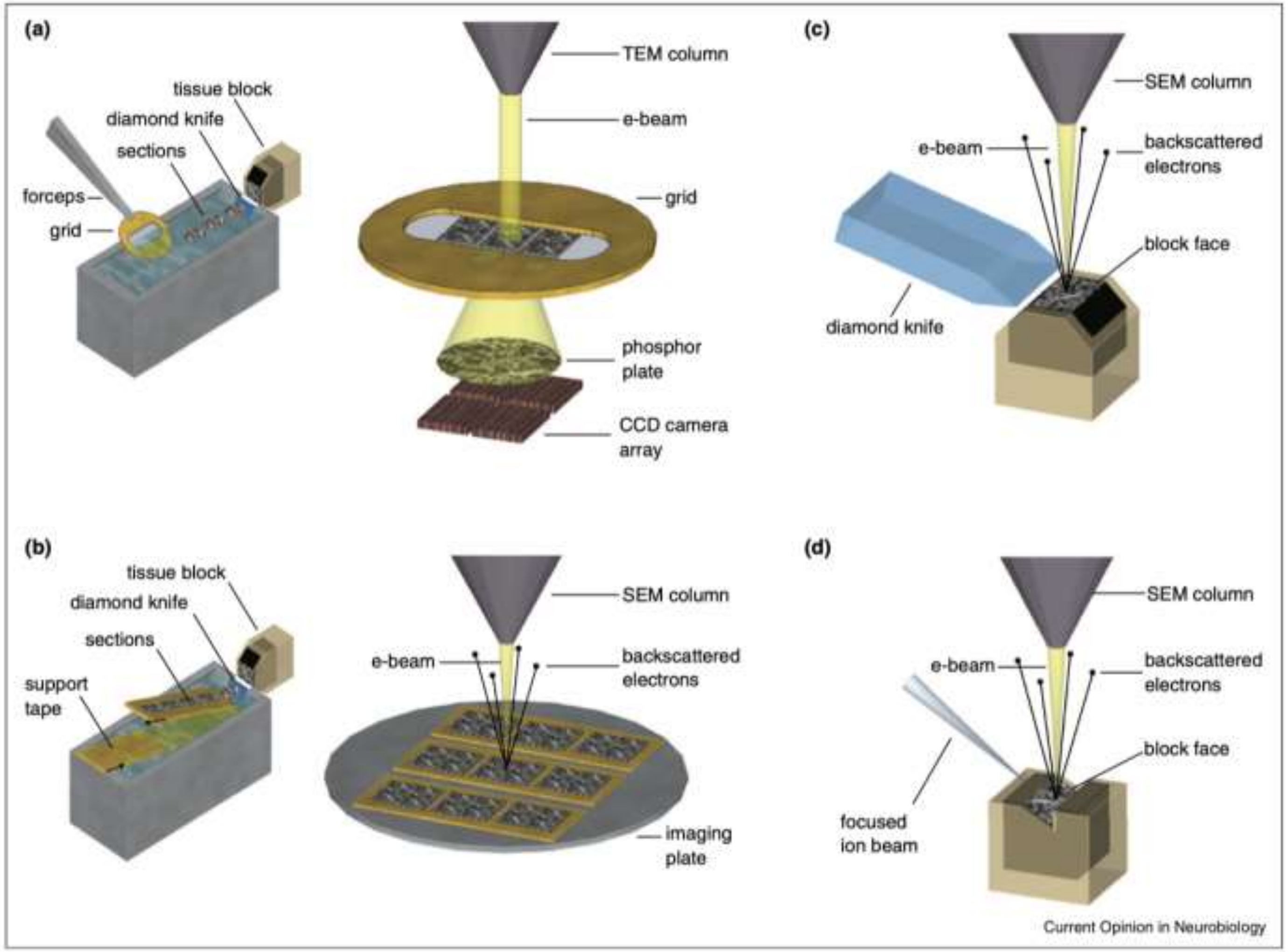
The macroscale fiber connections of the whole brain identified using tractography.

Colors indicate the fiber direction: green, antero-posterior; red, medio-lateral and blue, cranio-caudal.

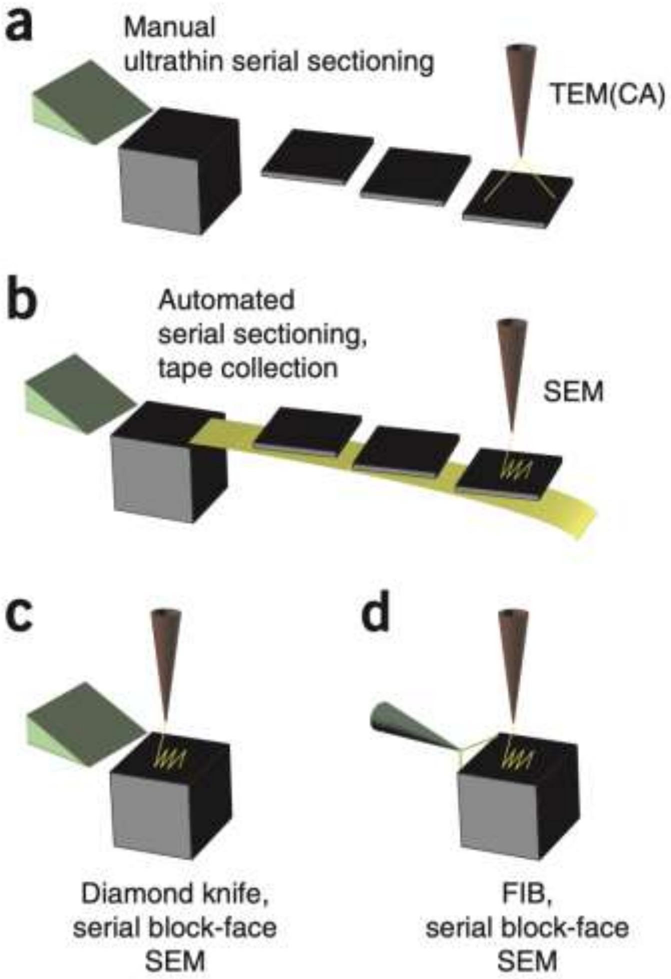
整个大脑的宏观纤维连接

Shinsuke Shibata, et al. *Microscopy*. 2015.

Microscale connectomics with EM



(a)ssTEM. (b)ATUM-SEM. (c)SBEM. (d)FIB-SEM.



(a)TEM或TEMCA.(b)ATUM-SEM.(c)SBEM.(d)FIB-SEM

Kevin L Briggman, et al. Current Opinion in Neurobiology. 2012

Mesoscale connectomics with LM

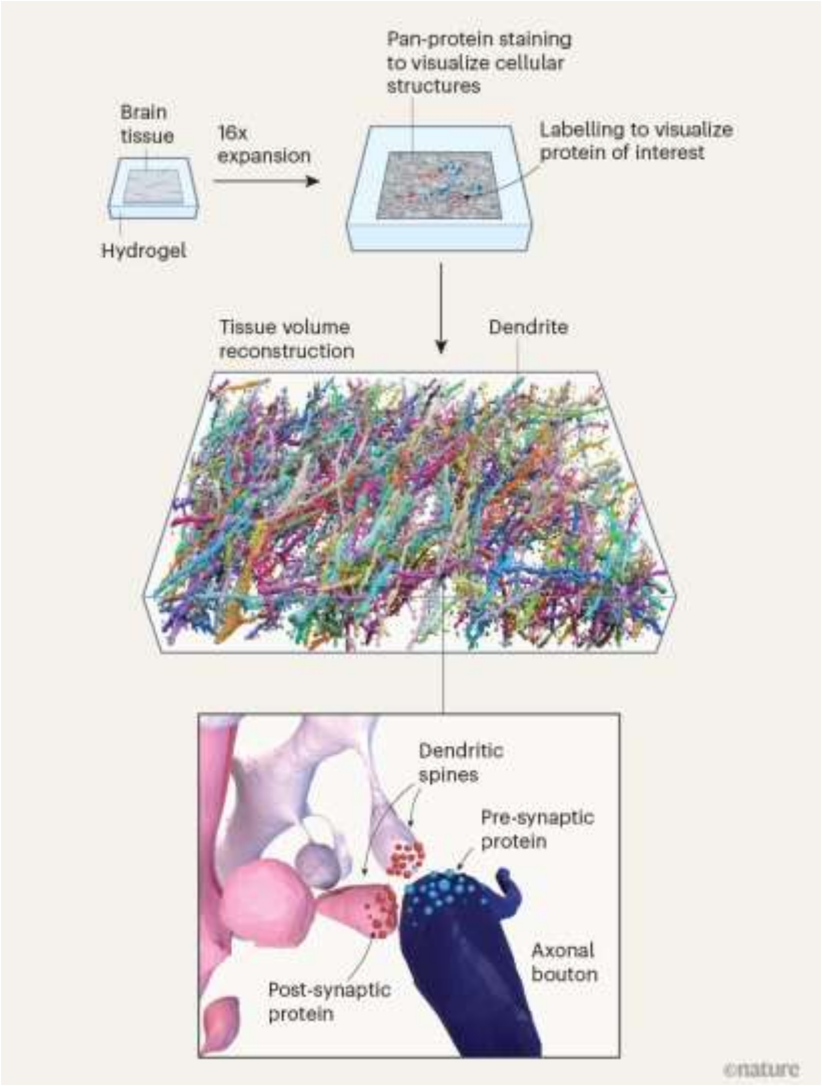
nature

Light-microscopy-based connectomic reconstruction of mammalian brain tissue

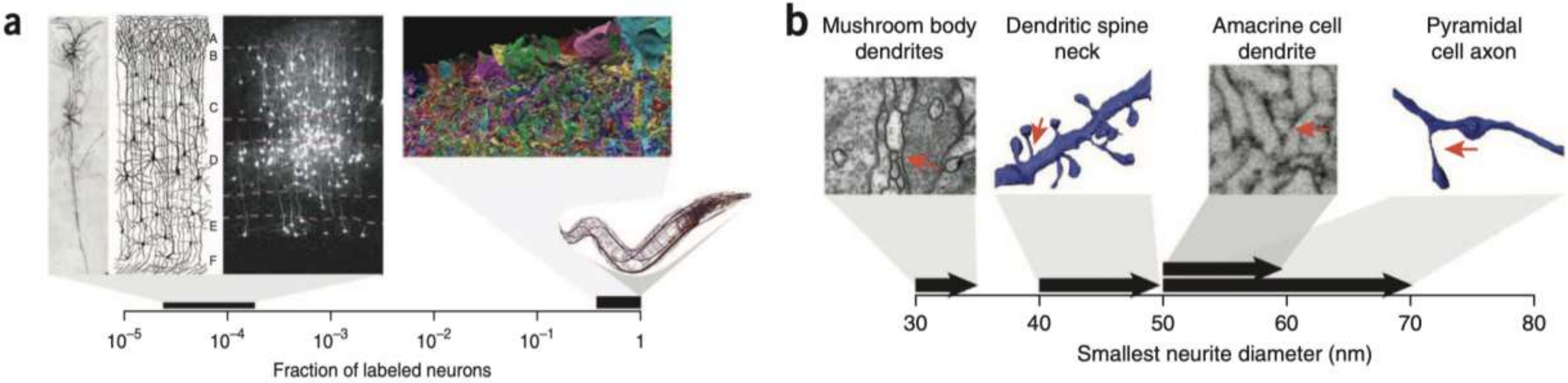
Mojtaba R. Tavakoli, Julia Lyudchik, Michał Januszewski, Vitali Vistunou, Nathalie Agudelo Dueñas, Jakob Vorlaufer, Christoph Sommer, Caroline Kreuzinger, Bárbara Oliveira, Alban Cenameri, Gaia Novarino, Viren Jain & Johann G. Danzl

Nature (2025) | Cite this article

LICONN——利用传统光学显微镜实现类似电子显微镜分辨率的连接组重建，并且还能获得有价值的分子信息。



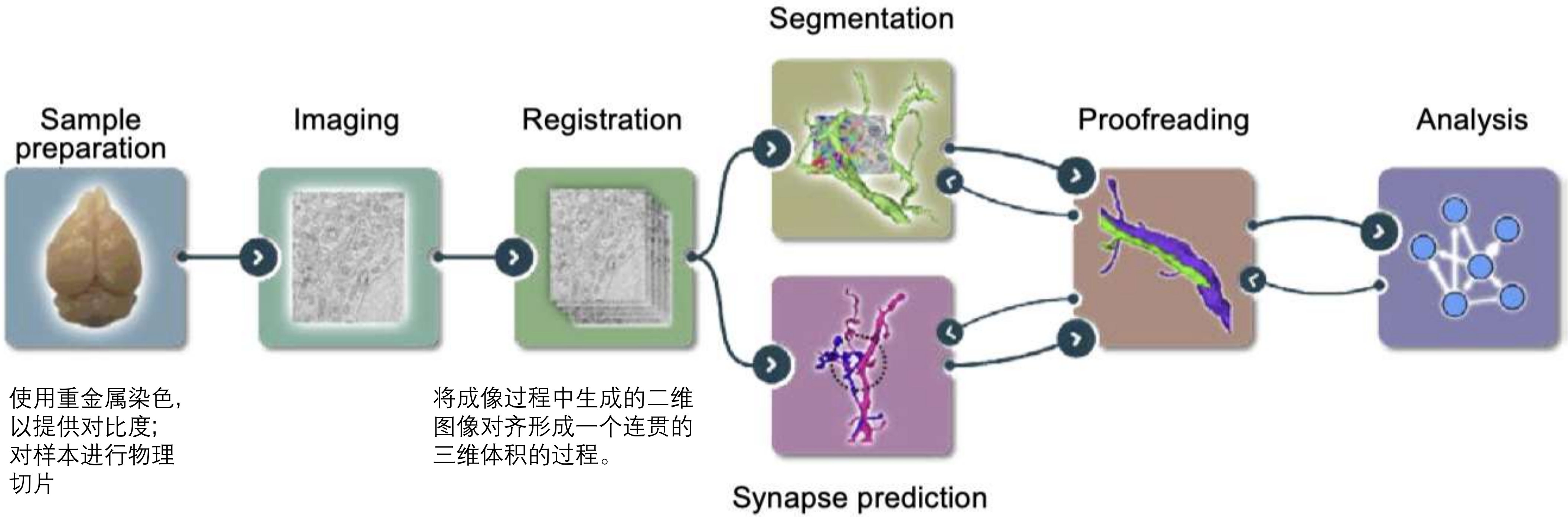
Microscale connectomics with EM, comparing to the mesoscale



EM 的分辨率比 LM 高，是实现转录组研究的主要方法

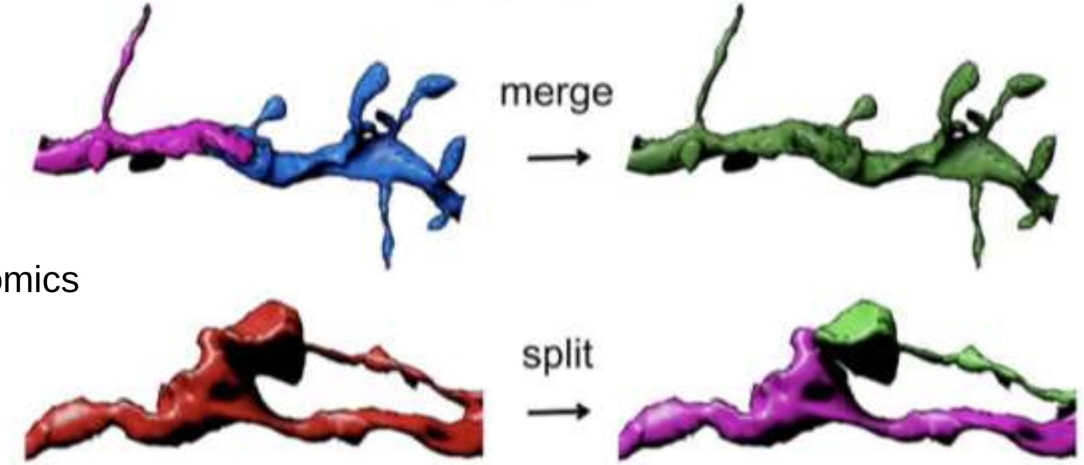
Moritz Helmstaedter. Nature methods.2013

Schematic pipeline for whole-brain connectomics



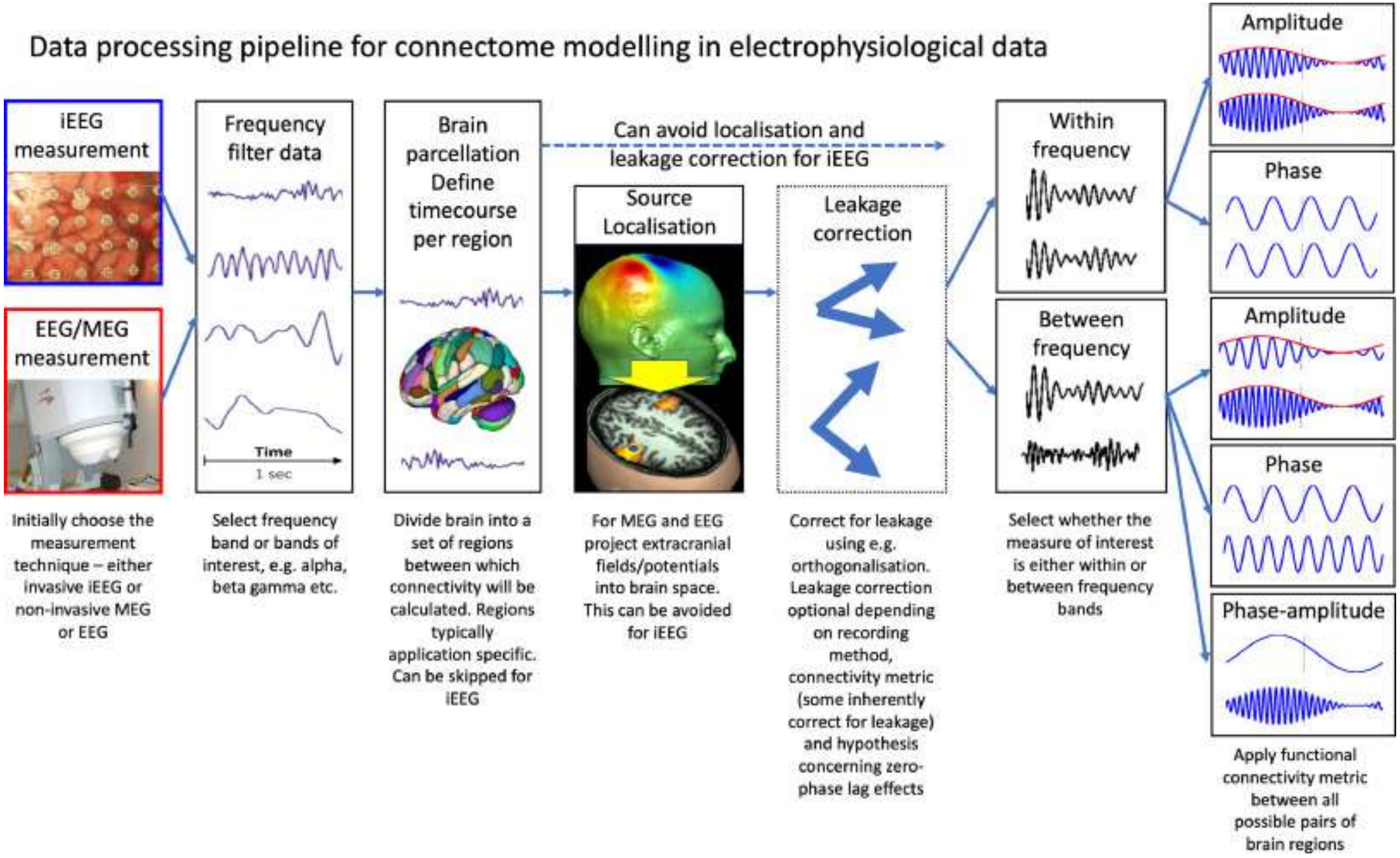
使用重金属染色，
以提供对比度;
对样本进行物理
切片

将成像过程中生成的二维
图像对齐形成一个连贯的
三维体积的过程。



https://wellcome.org/reports/scaling-connectomics

Connectomics of electrophysiology



Sepideh Sadaghiani. et al .*NeuroImage*. 2022.

AI for Connectomics

限制连接组重建的主要计算问题是图像分割，其目标是识别图像中属于各个对象的特定像素集。

“segment anything model”（SAM）

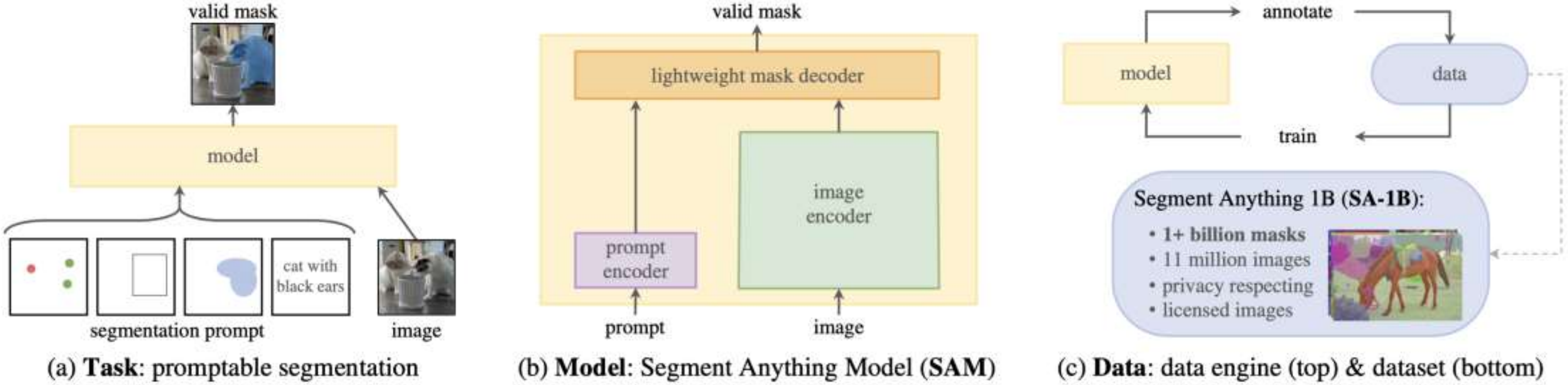


Figure 1: We aim to build a foundation model for segmentation by introducing three interconnected components: a promptable segmentation *task*, a segmentation *model* (SAM) that powers data annotation and enables zero-shot transfer to a range of tasks via prompt engineering, and a *data* engine for collecting SA-1B, our dataset of over 1 billion masks.

Kirillov, A. et al. *ICCV*. 2023.

The Landmark studies in connectomics
1. Whole-animal connectomes of Caenorhabditis elegans

The Structure of the Nervous System of the Nematode *Caenorhabditis elegans*

(The Mind of a Worm)

J.G. White, E. Southgate, J.N. Thomson, and S. Brenner

Sydney Brenner
Facts

Photo from the Nobel Foundation archive.

Sydney Brenner
The Nobel Prize in Physiology or Medicine 2002

Born: 13 January 1927, Germiston, South Africa

Died: 5 April 2019, Singapore

Affiliation at the time of the award: The Molecular Sciences Institute, Berkeley, CA, USA

Prize motivation: "for their discoveries concerning genetic regulation of organ development and programmed cell death"

Prize share: 1/3

1986年，Brenner等人首次构建了线虫的大脑连接组。

线虫脑内包含大约300个神经元（共302个），他们的工作使人类第一次在神经元水平上看到了脑连接的全貌。

在这项工作中，共计302个神经元，被划分为118个类别，建立了5,000个化学突触、2,000个神经肌肉接头和600个电隙连接。

The Landmark studies in connectomics
1. Whole-animal connectomes of Caenorhabditis elegans

Circuit diagrams of nervous system:

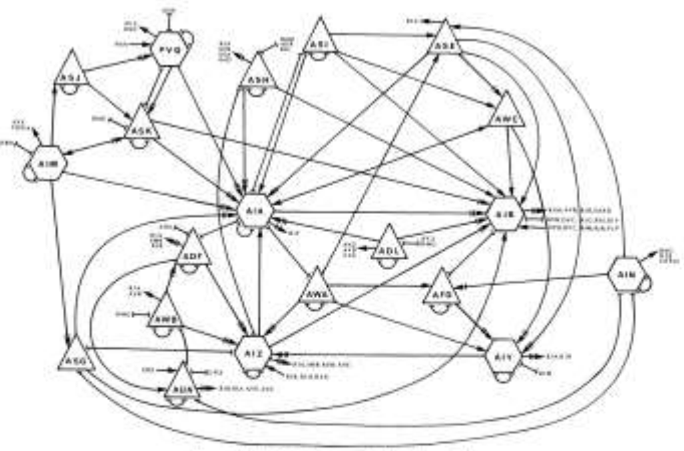


FIGURE 21. (a) Circuitry associated with amphids.

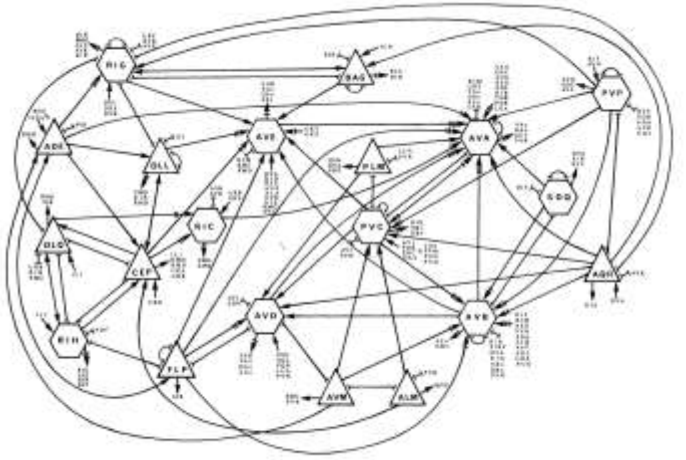


FIGURE 21. (b) Circuitry associated with other sensory receptors in the head.

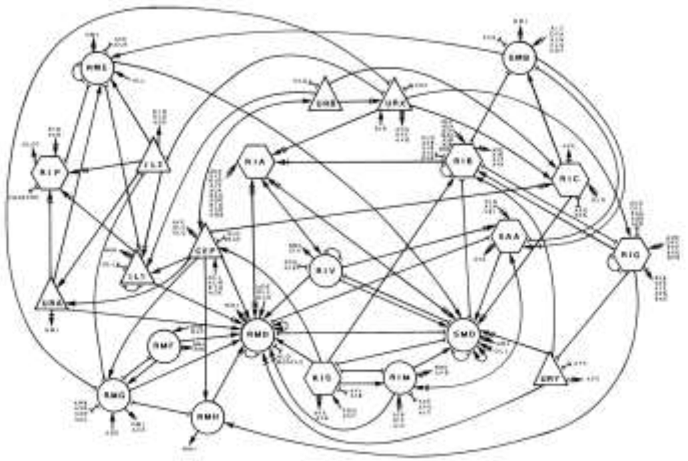


FIGURE 21. (c) Circuitry associated with the motoneurons in the nerve ring.

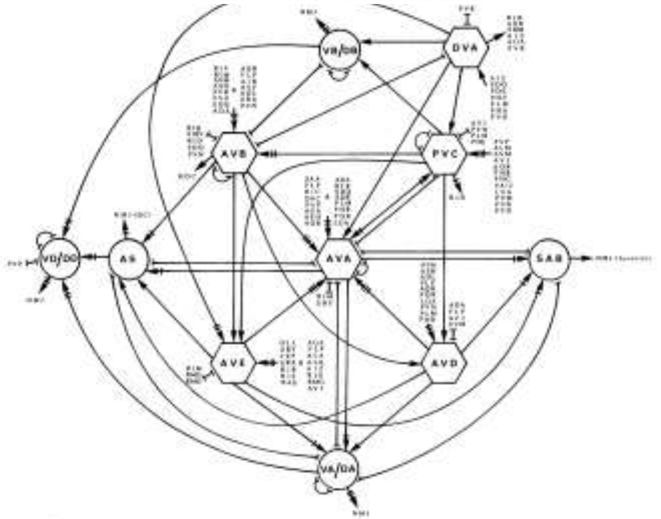


FIGURE 21. (d) Circuitry associated with the motoneurons of the ventral cord.

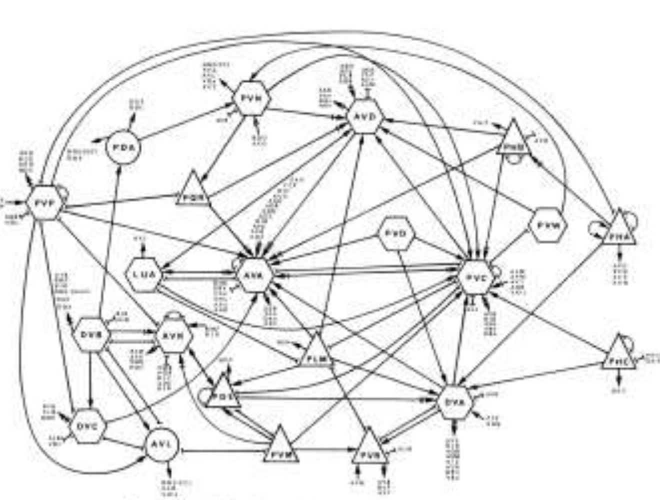


FIGURE 21. (e) Circuitry associated with neurons in the tail ganglia.

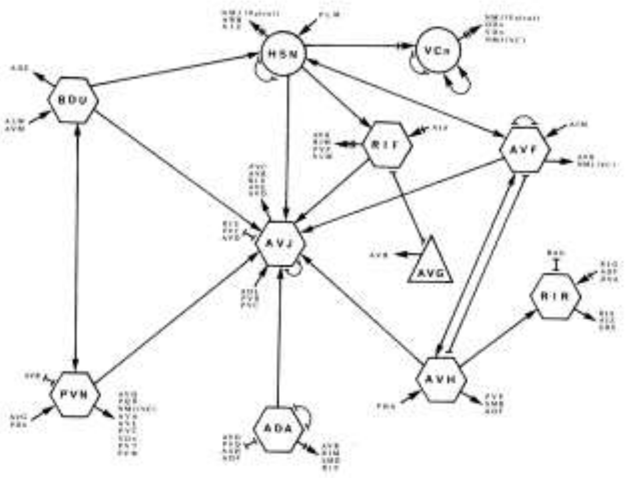
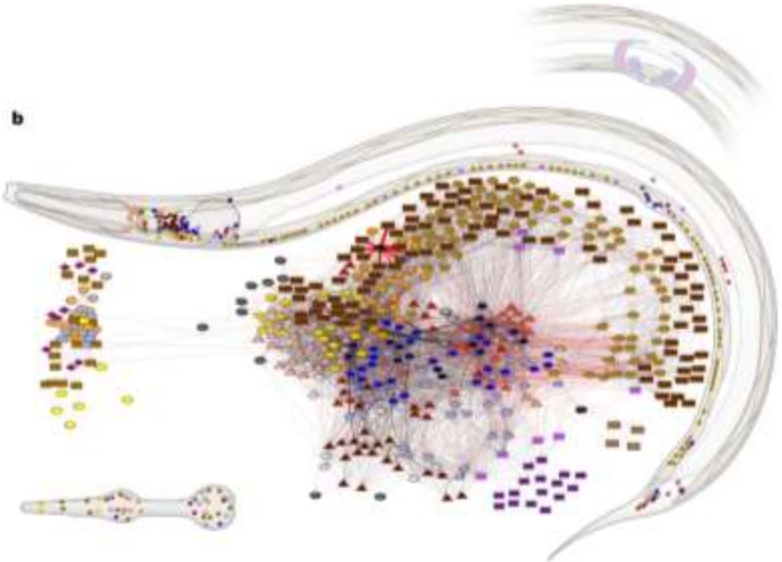
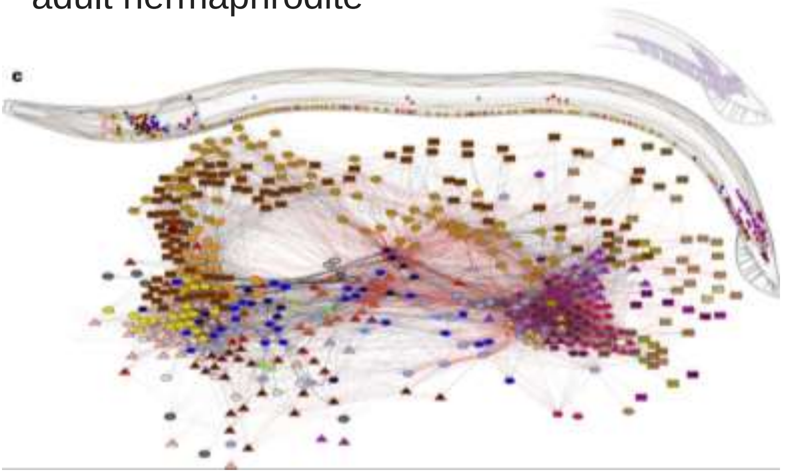


FIGURE 21. (f) Egg-laying circuitry.

The Landmark studies in connectomics
1. Whole-animal connectomes of Caenorhabditis elegans



adult hermaphrodite



adult male

nature > articles > article

Article | Published: 03 July 2019

Whole-animal connectomes of both *Caenorhabditis elegans* sexes

Steven J. Cook, Travis A. Jarrell, Christopher A. Brittin, Yi Wang, Adam E. Bloniarz, Maksim A. Yakovlev, Ken C. Q. Nguyen, Leo T.-H. Tang, Emily A. Bayer, Janet S. Duerr, Hannes E. Bülow, Oliver Hobert, David H. Hall & Scott W. Emmons

Nature **571**, 63–71 (2019) | Cite this article

- 利用EM绘制了线虫的两性（雌雄同体和雄性）的完整神经系统
- 对神经系统进行分层排列
- 性别差异

The Landmark studies in connectomics
2. The FlyWire connectome: neuronal wiring diagram of a complete fly brain(2024)

nature > articles > article

Article | Published: 20 April 2015

A multilevel multimodal circuit enhances action selection in *Drosophila*

Tomoko Ohyama, Casey M. Schneider-Mizell, Richard D. Fetter, Javier Valdes Aleman, Romain Franconville, Marta Rivera-Alba, Brett D. Mensh, Kristin M. Branson, Julie H. Simpson, James W. Truman, Albert Cardona & Marta Zlatic

Nature **520**, 633–639 (2015) | Cite this article

28k Accesses | **279** Citations | **114** Altmetric | Metrics

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Research Advance

Neuroscience

Conserved neural circuit structure across *Drosophila* larval development revealed by comparative connectomics

Stephan Gerhard, Ingrid Andrade, Richard D Fetter, Albert Cardona, Casey M Schneider-Mizell

Howard Hughes Medical Institute, United States; University of Cambridge, United Kingdom

Oct 23, 2017 • https://doi.org/10.7554/eLife.29089

对果蝇幼虫中枢神经系统完整的电子显微镜体积成像和组装。

使用基于网络的协作工具逐步重建了第一龄幼虫大脑中2,500个神经元的形态和连接性。

The Landmark studies in connectomics
2. The FlyWire connectome: neuronal wiring diagram of a complete fly brain(2024)

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Research Article

Computational and Systems Biology, Neuroscience

A connectome and analysis of the adult *Drosophila* central brain

Louis K Scheffer, C Shan Xu, Michal Januszewski, Zhiyuan Lu, Shin-ya Takemura, Kenneth J Hayworth, Gary B Huang, Kazunori Shinomiya, Jeremy Maitlin-Shepard ... Stephen M Plaza see all »

Janelia Research Campus, Howard Hughes Medical Institute, United States; Google Research, United States; Life Sciences Centre, Dalhousie University, Canada; Google Research, Google LLC, Switzerland; Institute for Quantitative Biosciences, University of Tokyo, Japan; MRC Laboratory of Molecular Biology, United States; Institute of Zoology, Biocenter Cologne, University of Cologne, Germany; Department of Zoology, University of Cambridge, United Kingdom

Sep 3, 2020 • https://doi.org/10.7554/eLife.57443

nature > articles > article

Article | Open access | Published: 02 October 2024

Neuronal wiring diagram of an adult brain

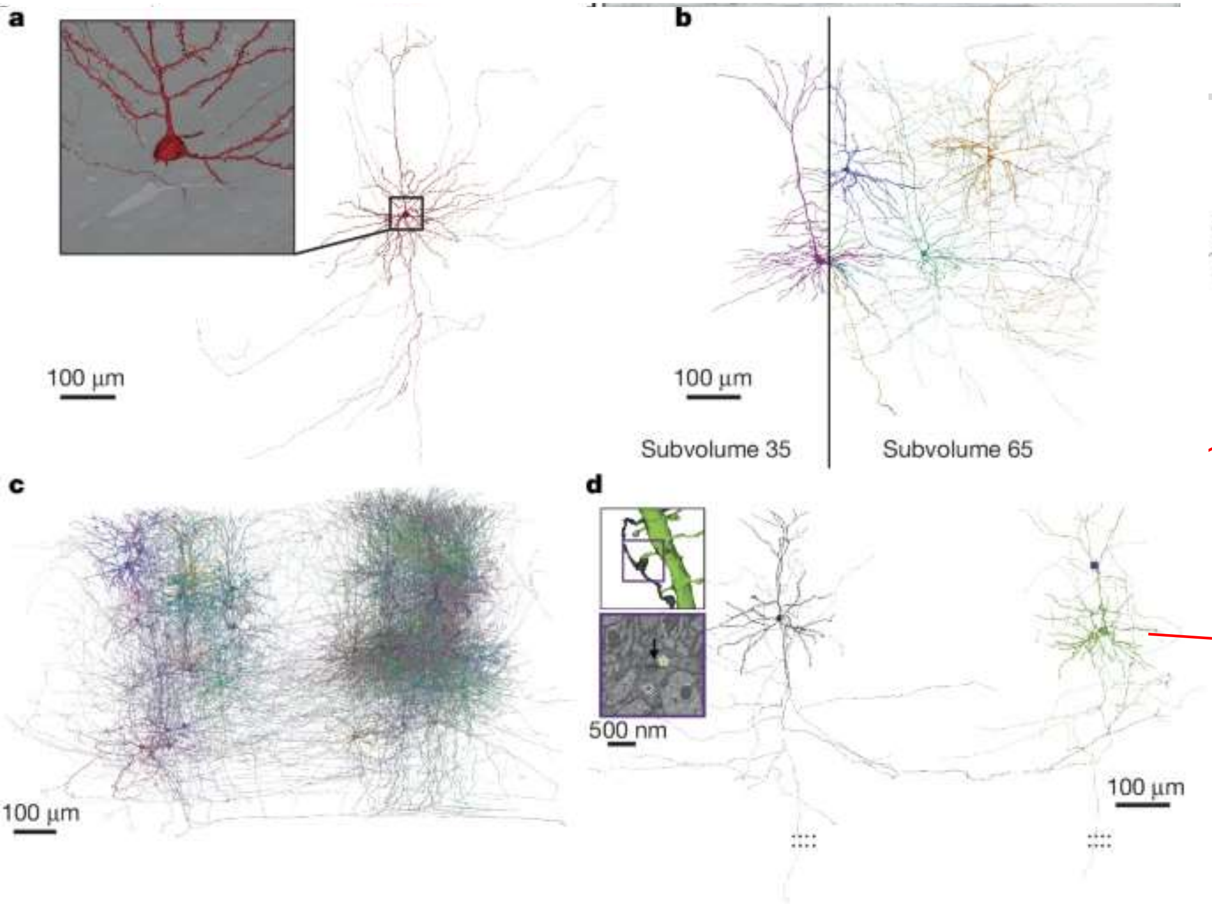
Sven Dorkenwald, Arie Matsliah, Amy R. Sterling, Philipp Schlegel, Szi-chieh Yu, Claire E. McKellar, Albert Lin, Marta Costa, Katharina Eichler, Yijie Yin, Will Silversmith, Casey Schneider-Mizell, Chris S. Jordan, Derrick Brittain, Akhilesh Halageri, Kai Kuehner, Oluwaseun Ogedengbe, Ryan Morey, Jay Gager, Krzysztof Kruk, Eric Perlman, Runzhe Yang, David Deutsch, Doug Bland, The FlyWire Consortium + Show authors

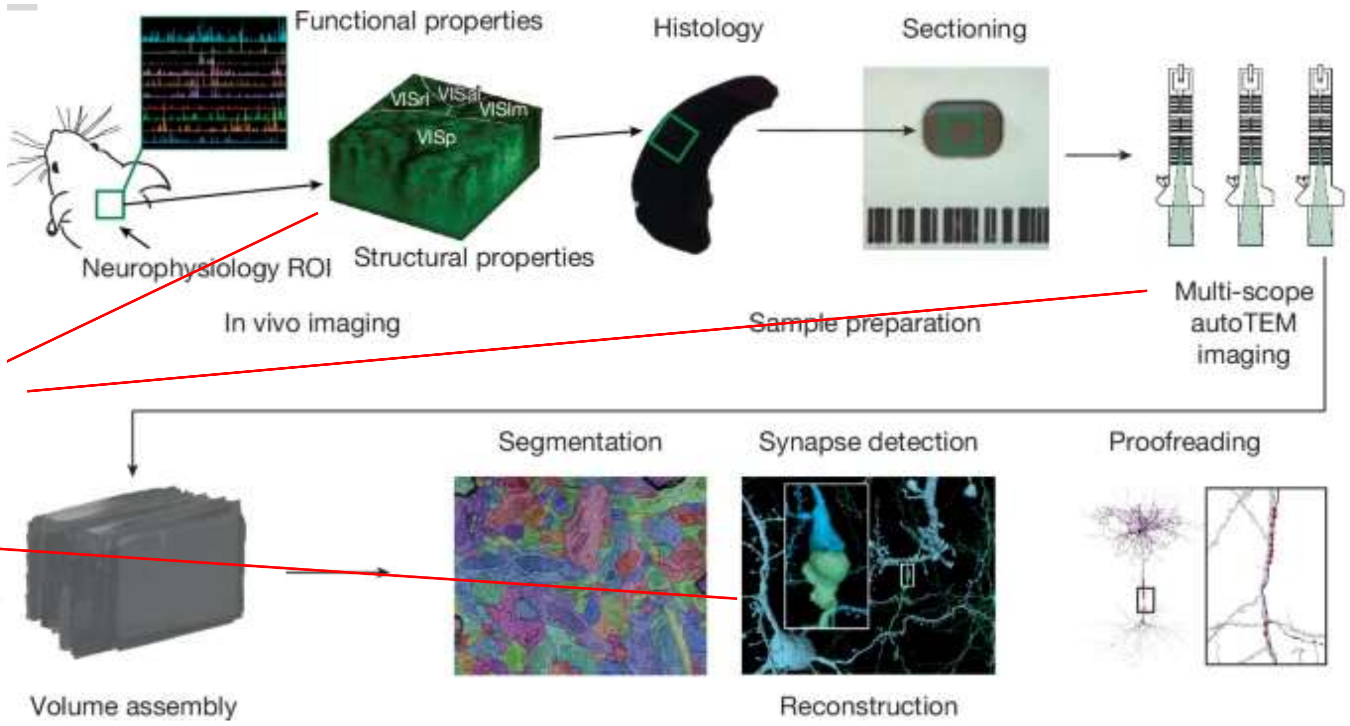
Nature **634**, 124–138 (2024) | Cite this article

果蝇半脑连接组图

首个雌性果蝇大脑的完整神经元连接组

The Landmark studies in connectomics
3. MICrONS（Machine Intelligence from Cortical Networks）（2025）

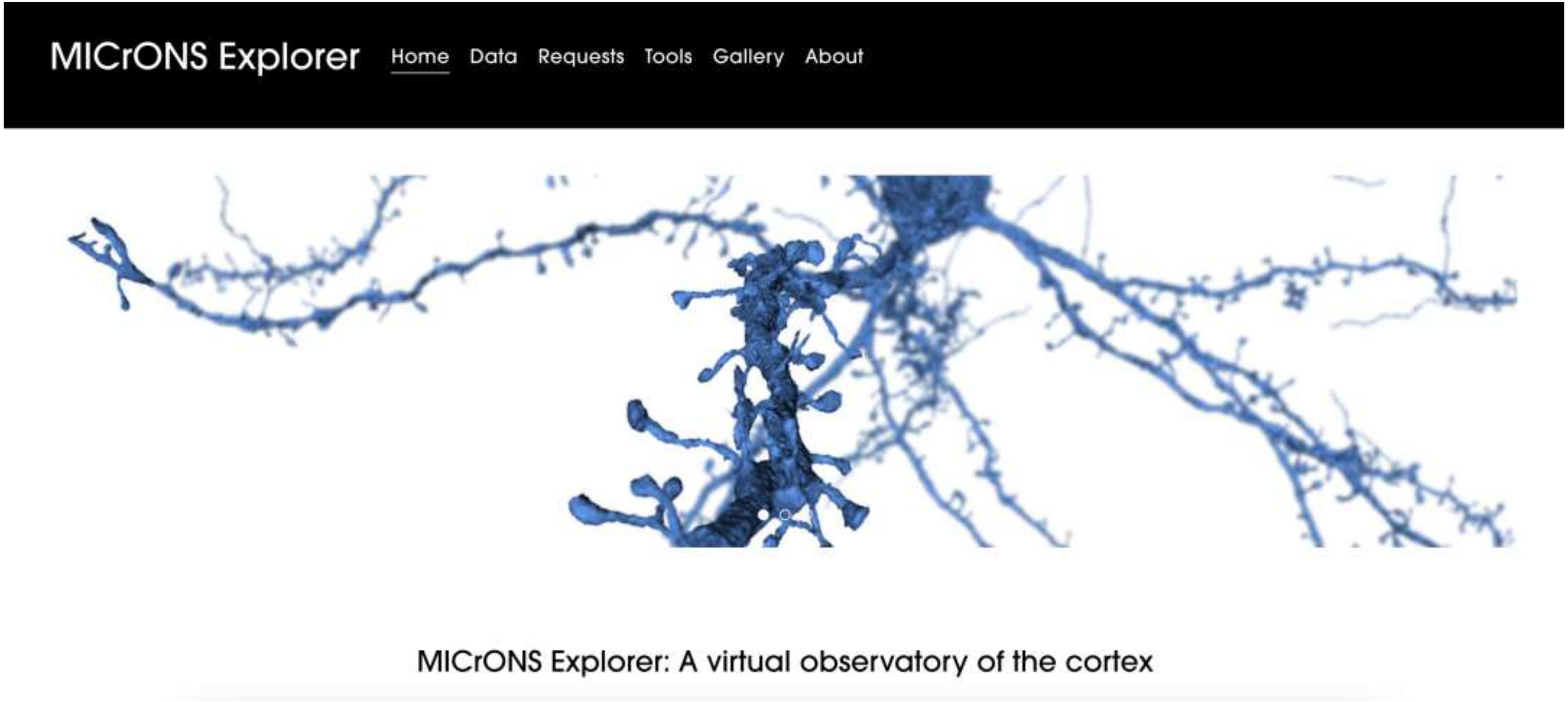




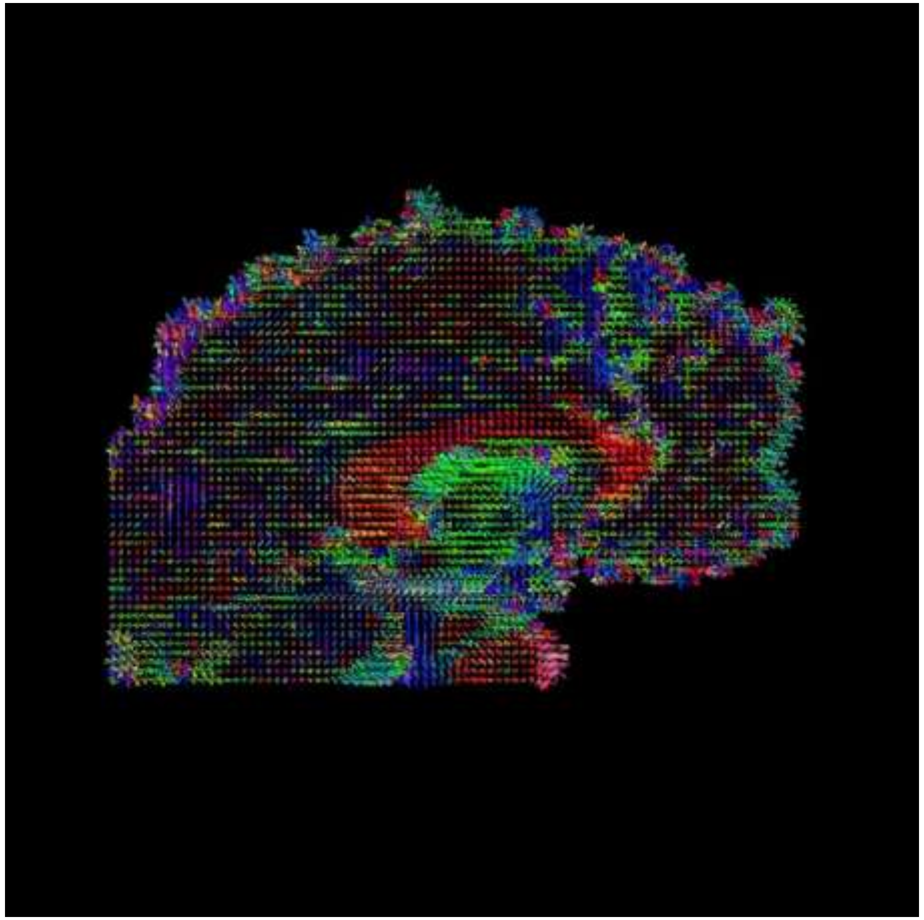
卷积神经网络

ChunkedGraph 校对系统

The Landmark studies in connectomics
3. MICrONS（Machine Intelligence from Cortical Networks）（2025）

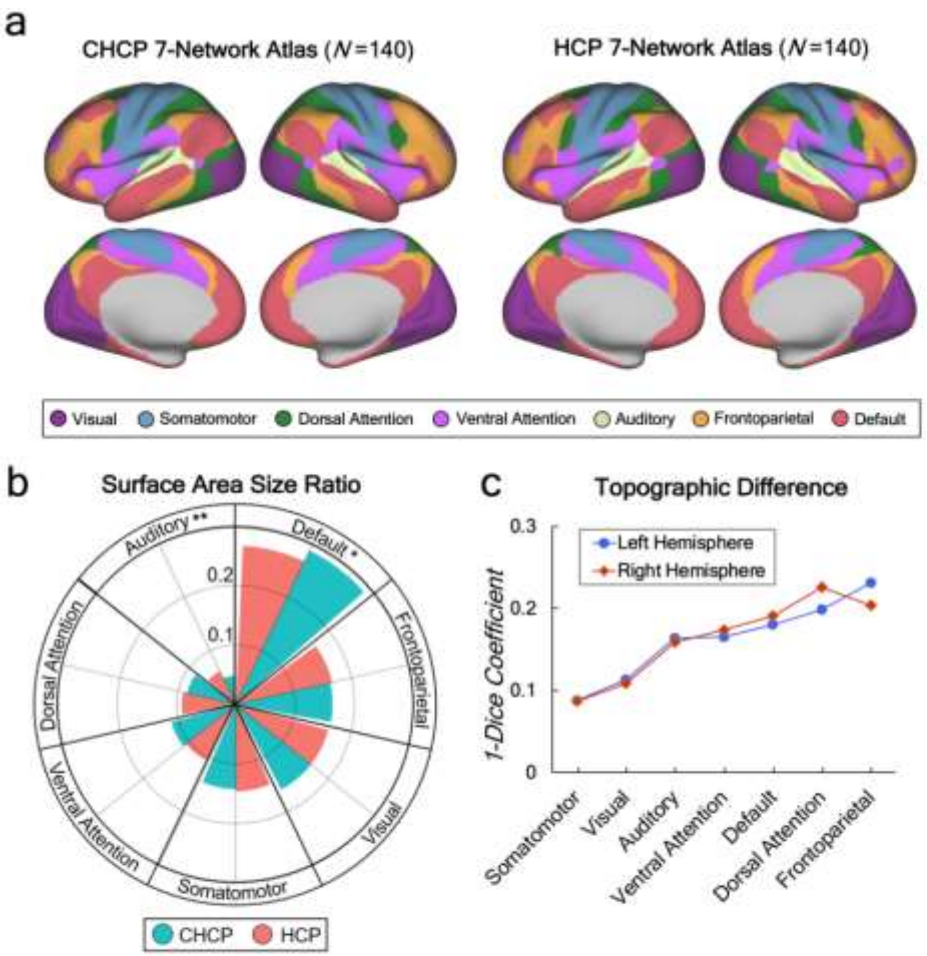


The Landmark studies in connectomics
4. The Human Connectome Project （2010）



The Human Connectome Project (HCP) is a project to construct a map of the complete structural and functional neural connections in vivo within and across individuals. The HCP represents the first large-scale attempt to collect and share data of a scope and detail sufficient to begin the process of addressing deeply fundamental questions about human connectional anatomy and variation.

The Landmark studies in connectomics
4. The Chinese Human Connectome Project（2017）



Differences in the seven-network atlases between the CHCP and HCP.

CHCP 与 HCP 在功能网络上表现出的差异，可能受到人类认知、情感和动机中与文化相关的影响。

Jia-Hong Gao, et al. Nature Neuroscience. 2022

Foundational Principles and Operational Guidelines of the FlyWire

- Data Sources and Foundational Principles of Flywire
- FlyWire Platform Overview and Operational Guidelines

LC
25.5.29

1

Data Sources and Foundational Principles of Flywire

Murthy Lab

image: Mary Sym

Mala Murthy	
Born	1975 (age 49–50)
Nationality	American
Alma mater	Massachusetts Institute of Technology Stanford University
Scientific career	
Institutions	California Institute of Technology Princeton University
Doctoral advisor	Thomas Schwarz Richard Scheller
Website	https://mala-murthy.squarespace.com

Mala Murthy (b. 1975) is an American neuroscientist and Professor of Neuroscience at Princeton University and leads the Murthy lab in the Princeton Neuroscience Institute – their work focuses on the neural mechanisms that underlie social communication, using the fruit fly Drosophila as a model system. In July 2022, she was named Director of the Princeton Neuroscience Institute.

Seung Lab

Homepage

RESEARCH AREAS

- Machine Learning
- Computational Biology

Sebastian Seung

Professor of Computer Science and Princeton Neurosciences Institute

CONTACT

153 Princeton Neuroscience Institute

sseung@cs.princeton.edu

(609) 258-7713

Ph.D., Harvard University, 1990

● Murthy Lab

image: Mary Sym

Mala Murthy	
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- Arthur, BJ, Sunayama-Morita, T, Coen, P, Murthy, M* and Stern, DL*. *Multi-channel acoustic recording and automated analysis of Drosophila courtship songs*. **BMC Biology**. 2013. January vol. 11(1): 11. *co-corresponding authors BMC Biology website
- Calhoun, AJ, Pillow, JW, and Murthy, M. *Unsupervised identification of the internal states that shape natural behavior*. **Nature Neuroscience 2019**. Nov 25. #
  - News&Views: Opening the black box of social behavior
  - Princeton Discovery Magazine: Neuroscientists develop models to identify internal states of the brain
  - Nature: Inside the Mind of an Animal
- Pereira, TD, Tabris, N, Matsliah, A, Turner, DM, Li, J, Ravindranath, S, Papadoyannis, ES, Normand, E, Deutsch, DS, Wang, ZY, McKenzie-Smith, GC, Mitelut, CC, Castro, MD, D'Uva, J, Kislin, M, Sanes, DH, Kocher, SD, Wang, SSH, Falkner, AL, Shaevitz, JW, Murthy, M. *SLEAP: A deep learning system for multi-animal pose tracking*. **Nature Methods 2022**. Vol 19 April 486–495. doi.org/10.1038/s41592-022-01426-1.
  - News&Views: Tracking together: estimating social poses
- Cowley, BR, Calhoun, AJ, Rangarajan, N, Turner, M, Pillow, JW, Murthy, M. *Mapping model units to visual neurons reveals population code for social behaviour*. **Nature 2024** 629, 1100–1108. https://doi.org/10.1038/s41586-024-07451-8

Seung Lab

Our Research

Interpretation of connectomes

We are devising concepts and methods for interpreting neuronal wiring diagrams. The fly connectome includes as a corollary the first wiring diagram of a visual system. By studying this wiring diagram, we have discovered a new circuit for form vision in the fly brain. We have also discovered that many inhibitory interneuron types function as a highly diverse set of normalization mechanisms in fly vision. Both of these discoveries draw on the striking analogy between the fly visual system and convolutional nets.

Reconstructing neural circuits

In ongoing collaborations, we are applying and refining connectomic technologies to reconstruct more fly connectomes (Mala Murthy), as well as a patch of mouse retina (Thomas Euler). We are reconstructing mouse neural circuits for memory (David Tank), decision making (Adrian Wanner and Jeff Lichtman), and reinforcement learning (Ilana Witten). These collaborations make use of the high throughput EM facility at the Princeton Neuroscience Institute. In many of the projects, neural circuit reconstruction is preceded by calcium imaging of neural activity *in vivo*.

Scaling up to mammalian brains

Today's connectomic technologies are sufficient for reconstructing an entire fly brain, and are also being applied to millimeter-scale chunks of mammalian brains . A mouse brain is 1000× larger, and a human brain 1000× larger still. *There is plenty of room at the top*. We are participating in a "transformative project" of the NIH BRAIN Initiative that aims to scale up connectomics to a whole mouse brain. The Princeton Neuroscience Institute is the only site in the world with both of the EM image acquisition technologies that are being scaled up to the mouse connectome, beam-deflection transmission electron microscopy and multi-beam scanning electron microscopy .

Scaling down to molecules

The fly connectome was reconstructed from EM images with 4×4×40 nm³ voxels, which is sufficient for detecting chemical synapses and tracing the "wires" of the brain. This resolution might seem very fine, but is actually coarse compared to the 0.1 nm theoretical limit of EM. *There is plenty of room at the bottom*. Serial section EM tomography can improve resolution; the challenge is to deliver this improvement over much larger volumes than before. One can imagine, for example, imaging an entire fly brain at 4×4×4 nm³ or 2×2×2 nm³ resolution. This would reveal brain cell biology in fantastic detail, within the full context of neurons and their connections.

Homepage

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- Computational Biology

Sebastian Seung

Professor of Computer Science and Princeton Neurosciences Institute

CONTACT

153 Princeton Neuroscience Institute
sseung@cs.princeton.edu
(609) 258-7713
Ph.D., Harvard University, 1990

Technical Support Required to Establish Flywire

Data Sources

- Cell segments were auto-generated from electron-microscopy images with AI
- Cell reconstructions were assembled from segments (proofread) by the FlyWire community (see FlyWire)
- Synaptic connections were automatically detected using the Buhmann et al. method and refined with synapse segmentations from Heinrich et al.
- Free-form labels (cell identification tags) were provided by the FlyWire community - see the labeling leaderboard and detailed credits in each cell info page
- Hierarchical annotations (side, flow, super class, cell class, cell type, Hemibrain type, nerve and hemi-lineage) were provided by Schlegel et al. (Jefferis lab)
- Neurotransmitter types were predicted by Eckstein, Bates et al.
- Morphological similarity scores (NBLAST based) were computed for the central brain cells by Philipp Schlegel
- Links from FlyWire neurons and cell types to Virtual Fly Brain and FlyBase were curated by Clare Pilgrim
- Repository of known functions for cell types is curated by Yijie Yin and synced periodically; see source spreadsheet for credits (corrections/contributions welcome)
- Refer to the table below or contact flywire@princeton.edu for additional info / questions on data credits

When using the FlyWire resource, please co-cite the Dorkenwald et al. and Schlegel et al. manuscripts. To give credit for specific aspects of data creation (=columns) please select the appropriate citations based on this table.

citation	doi	Data										
		reconstruction	annotations						hemibrain matching	connectivity tags	synapses & connectivity	neurotransmitter information
			community	hierarchical	nerves	hemilineages	gene	cell_type				
Dorkenwald et al., 2024	https://doi.org/10.1038/s41586-024-07558-y	x	x	x	x	x		x	x		x	x
Schlegel et al., 2024	https://doi.org/10.1038/s41586-024-07686-5	x		x	x	x		x	x			
Zheng et al., 2018	https://doi.org/10.1016/j.cell.2018.06.019	x	x	x	x	x		x	x		x	x
Buhmann et al., 2021	https://doi.org/10.1038/s41592-021-01183-7										x	
Heinrich et al., 2018	https://doi.org/10.1007/978-3-030-00934-2_36										x	
Eckstein, Bates et al., 2024	https://doi.org/10.1016/j.cell.2024.03.016											x
Matsliah, Yu et al., 2024	https://doi.org/10.1038/s41586-024-07981-1							x				
Lin et al., 2024	https://doi.org/10.1038/s41586-024-07968-y									x		
Deutsch et al., 202X	TBD						x	x				

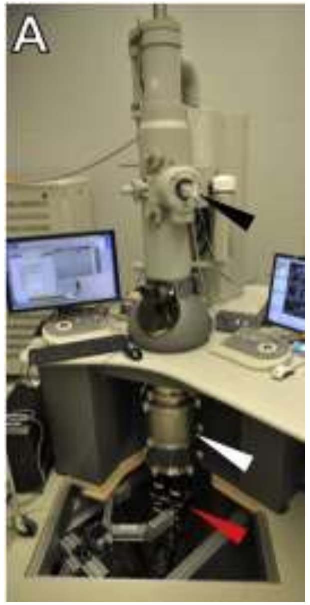
A complete adult Drosophila brain was imaged with EM and has been made publicly available

› Cell. IF: 45.5 Q1 2018 Jul 26;174(3):730-743.e22. doi: 10.1016/j.cell.2018.06.019. Epub 2018 Jul 19.

A Complete Electron Microscopy Volume of the Brain of Adult Drosophila melanogaster

Zhihao Zheng [1], J Scott Lauritzen [1], Eric Perlman [1], Camenzind G Robinson [1], Matthew Nichols [1], Daniel Milkie [2], Omar Torrens [2], John Price [3], Corey B Fisher [1], Nadiya Sharifi [1], Steven A Calle-Schuler [1], Lucia Kmecova [1], Iqbal J Ali [1], Bill Karsh [1], Eric T Trautman [1], John A Bogovic [1], Philipp Hanslovsky [1], Gregory S X E Jefferis [4], Michael Kazhdan [5], Khaled Khairy [1], Stephan Saalfeld [1], Richard D Fetter [1], Davi D Bock [6]

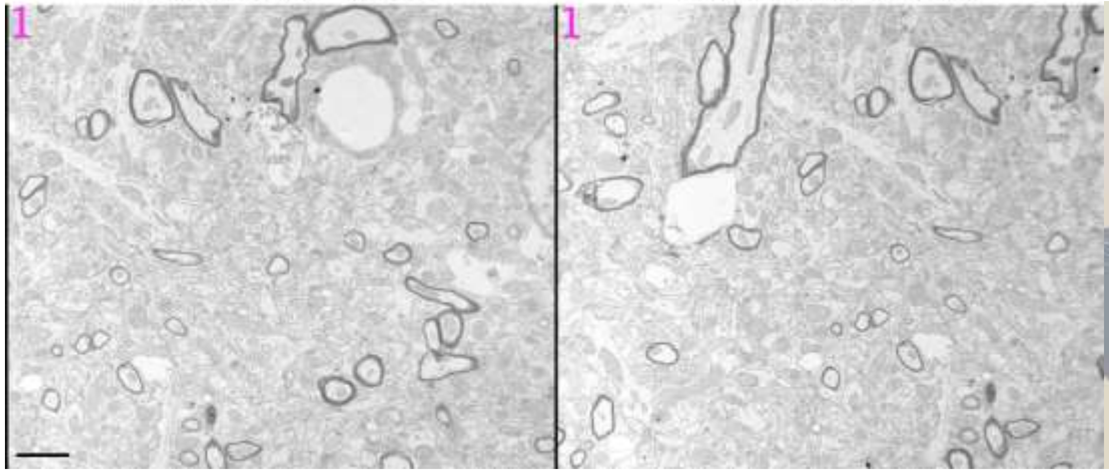
PMID: 30033368 PMCID: PMC6063995 DOI: 10.1016/j.cell.2018.06.019



Fast Stage

elongated vacuum chamber

2 × 2 camera array



Zheng, Zhihao et al. *Cell* vol. 174,3 (2018): 730-743.e22.

Automatic detection of synaptic partners in a whole-brain Drosophila electron microscopy data set

Nat Methods. IF: 36.1 Q1 2021 Jul;18(7):771-774. doi: 10.1038/s41592-021-01183-7.
Epub 2021 Jun 24.

Automatic detection of synaptic partners in a whole-brain Drosophila electron microscopy data set

Julia Buhmann [1, 2], Arlo Sheridan [1], Caroline Malin-Mayor [1], Philipp Schlegel [3], Stephan Gerhard [4, 5], Tom Kazimiers [1], Renate Krause [1, 2], Tri M Nguyen [4], Larissa Heinrich [1], Wei-Chung Allen Lee [6], Rachel Wilson [4], Stephan Saalfeld [1], Gregory S X E Jefferis [3], Davi D Bock [7], Srinivas C Turaga [1], Matthew Cook [2], Jan Funke [8]

PMID: 34168373 PMCID: PMC7611460 DOI: 10.1038/s41592-021-01183-7

Funke Lab

Our lab at HHMI Janelia develops machine learning methods for the life sciences, with a focus on microscopy image analysis.

We are particularly interested in:

1. Identification of Structures of Interest in Large Datasets

   In the field of connectomics, we develop methods to segment neurons, detect synapses, and to classify synapses in very large electron microscopy datasets.

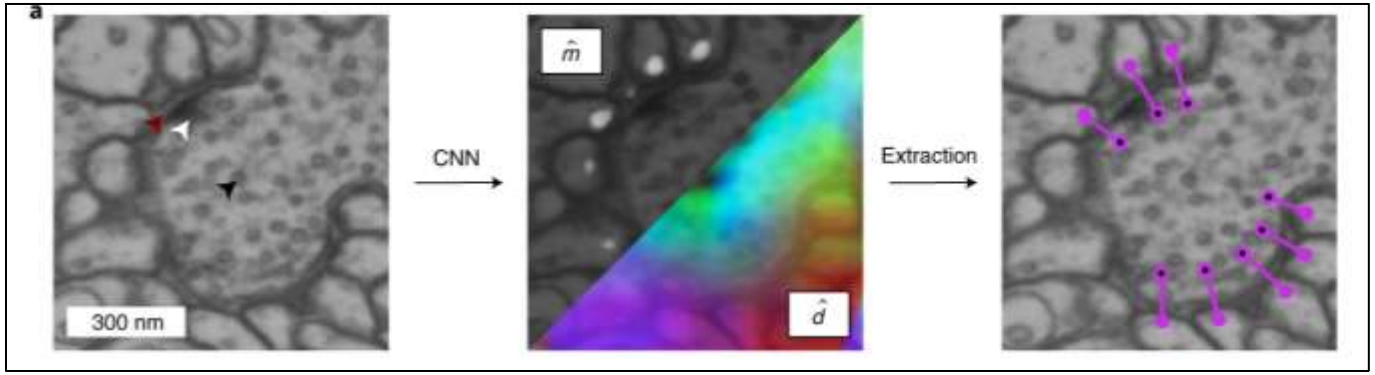
   We also work on the segmentation and tracking of cells in live-cell imaging datasets.

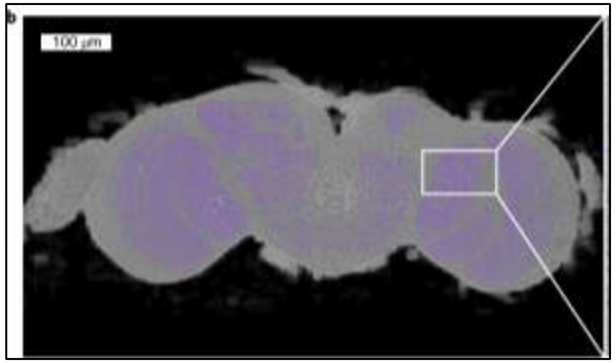
2. Explainable Machine Learning Methods

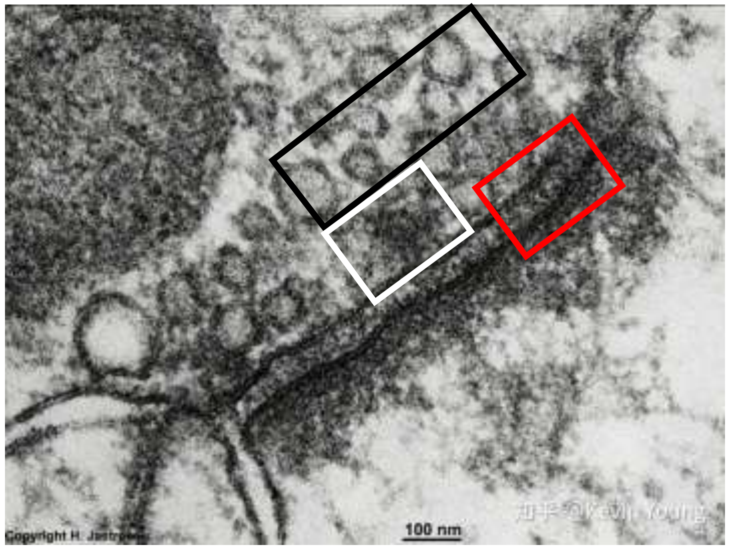
   We develop methods that use machine learning to identify and visualize subtle patterns in biological datasets. Those methods can reveal previously unknown phenotypical differences, e.g., in image data.

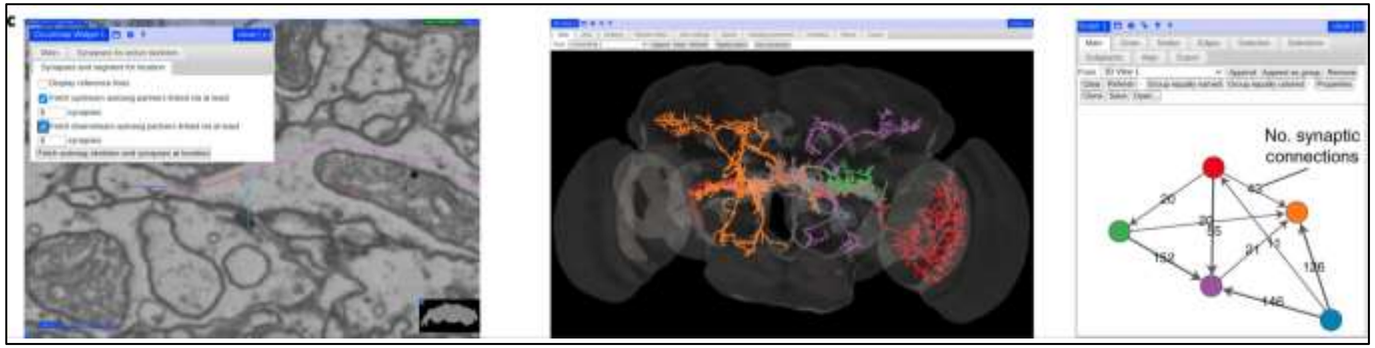
3. Mechanistic Machine Learning

   To increase the utility and interpretability of machine learning methods, we design models that directly incorporate biophysical constraints and domain knowledge. So far, our models have been used to count fluorophores beyond the diffraction limit and to infer synaptic plasticity rules from behavioral measurements.









Buhmann, Julia et al. *Nature methods* vol. 18,7 (2021): 771-774

Artificial neural networks can predict transmitter types for presynapses from electron micrographs (acetylcholine, glutamate, GABA, serotonin, dopamine, octopamine)

> Cell. IF: 45.5 Q1 2024 May 9;187(10):2574-2594.e23. doi: 10.1016/j.cell.2024.03.016.

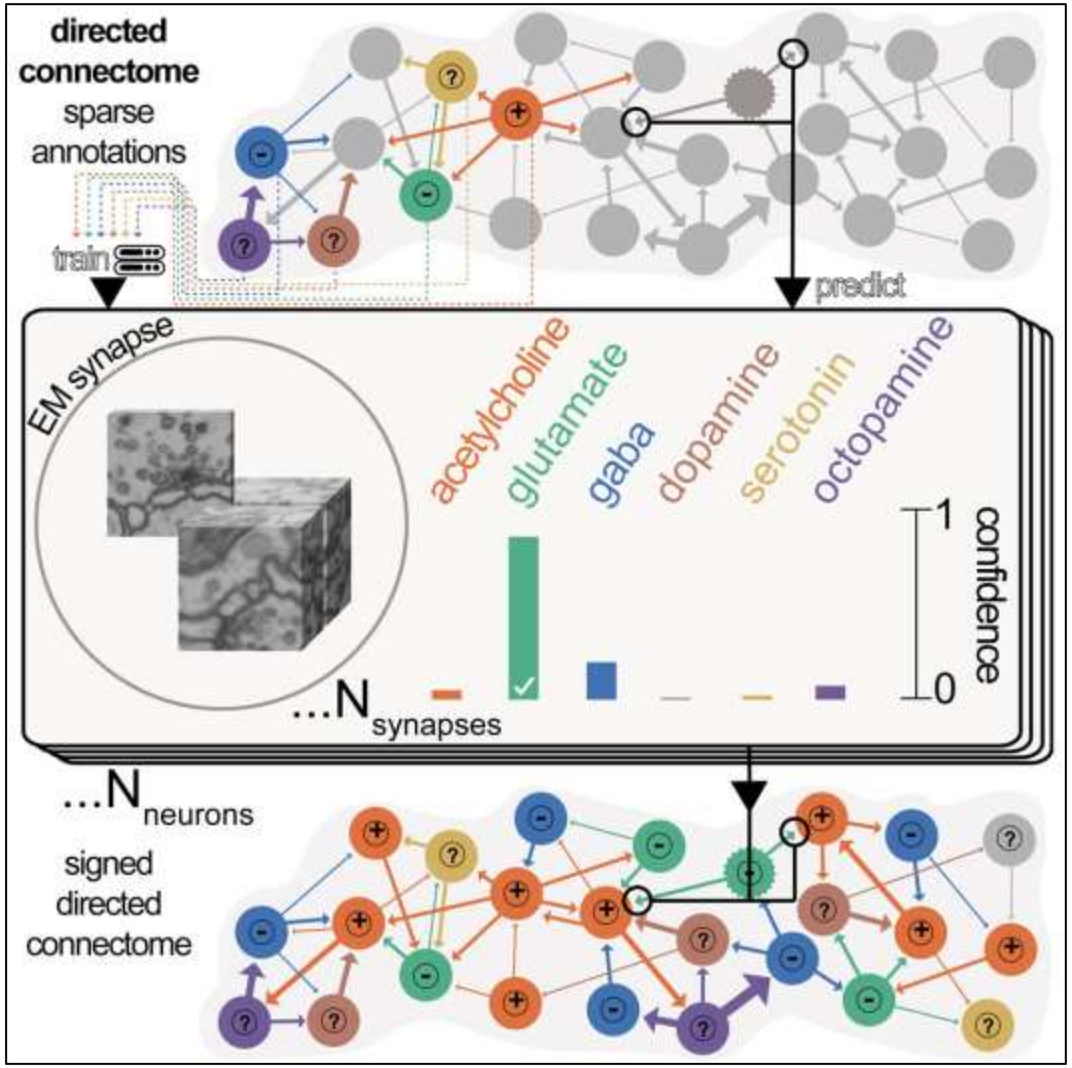
Neurotransmitter classification from electron microscopy images at synaptic sites in Drosophila melanogaster

Nils Eckstein [1], Alexander Shakeel Bates [2], Andrew Champion [3], Michelle Du [4], Yijie Yin [3], Philipp Schlegel [5], Alicia Kun-Yang Lu [4], Thomson Rymer [4], Samantha Finley-May [4], Tyler Paterson [4], Ruchi Parekh [4], Sven Dorkenwald [6], Arie Matsliah [6], Szi-Chieh Yu [6], Claire McKellar [6], Amy Sterling [6], Katharina Eichler [3], Marta Costa [3], Sebastian Seung [6], Mala Murthy [6], Volker Hartenstein [7], Gregory S X E Jefferis [8], Jan Funke [9]

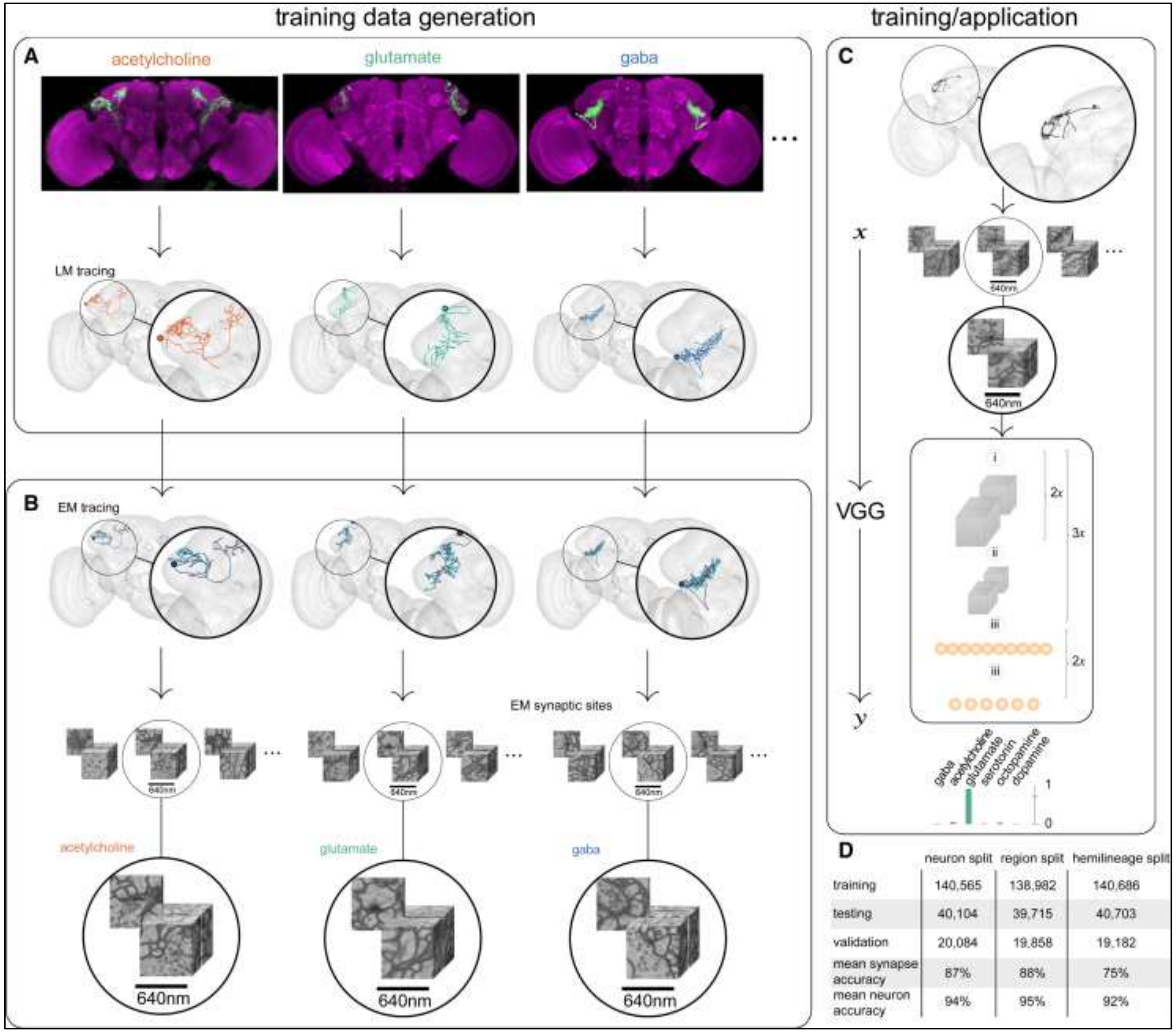
PMID: 38729112 PMCID: PMC11106717 DOI: 10.1016/j.cell.2024.03.016

Highlights

- Machine learning identifies synaptic transmitters from electron micrographs
- Six transmitters predicted across the whole fly brain connectome
- Explainable AI reveals ultrastructural differences between transmitter identities
- Fly brain hemilineages predominantly express one fast-acting transmitter



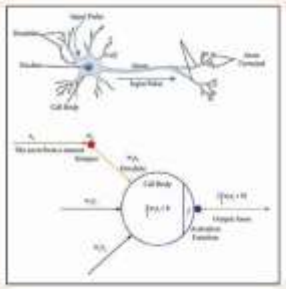
Eckstein, Nils et al. Cell vol. 187,10 (2024): 2574-2594.e23.



D

	neuron split	region split	hemilineage split
training	140,565	138,982	140,686
testing	40,104	39,715	40,703
validation	20,084	19,858	19,182
mean synapse accuracy	87%	88%	75%
mean neuron accuracy	94%	95%	92%

Dale's law, also known as **Dale's principle**, states that a neuron releases the same neurotransmitter or group of neurotransmitters at all its synaptic connections. However, this principle has been shown to be incorrect for many neurons, as research indicates that some neurons can release multiple types of neurotransmitters. Current neuroscience suggests that Dale's law has been partially or totally disproven, reflecting a more complex understanding of neurotransmitter release. Oxford Reference +2



Lacin's law: In the ventral nerve cord Lacin et al. comprehensively showed that only one of acetylcholine, glutamate, or GABA is expressed per hemilineage. By analogy with Dale's law, we call this observation Lacin's law.

C

acetylcholine	→ glutamate	dimmer cleft, darker t-bar
acetylcholine	→ gaba	dimmer cleft
acetylcholine	→ serotonin	thinner cleft, more dense core vesicles (DCVs)
acetylcholine	→ dopamine	filled vesicles, fewer PSDs, fewer synaptic partners
acetylcholine	→ octopamine	thinner cleft, larger vesicles, less circular vesicles
glutamate	→ gaba	smaller vesicles
glutamate	→ serotonin	thinner cleft, more DCVs
glutamate	→ dopamine	thinner cleft, larger vesicles, fewer PSDs

Eckstein, Nils et al. Cell vol. 187,10 (2024): 2574-2594.e23.

> Nat Methods. IF: 36.1 Q1 2022 Jan;19(1):119-128. doi: 10.1038/s41592-021-01330-0. Epub 2021 Dec 23.

FlyWire: online community for whole-brain connectomics

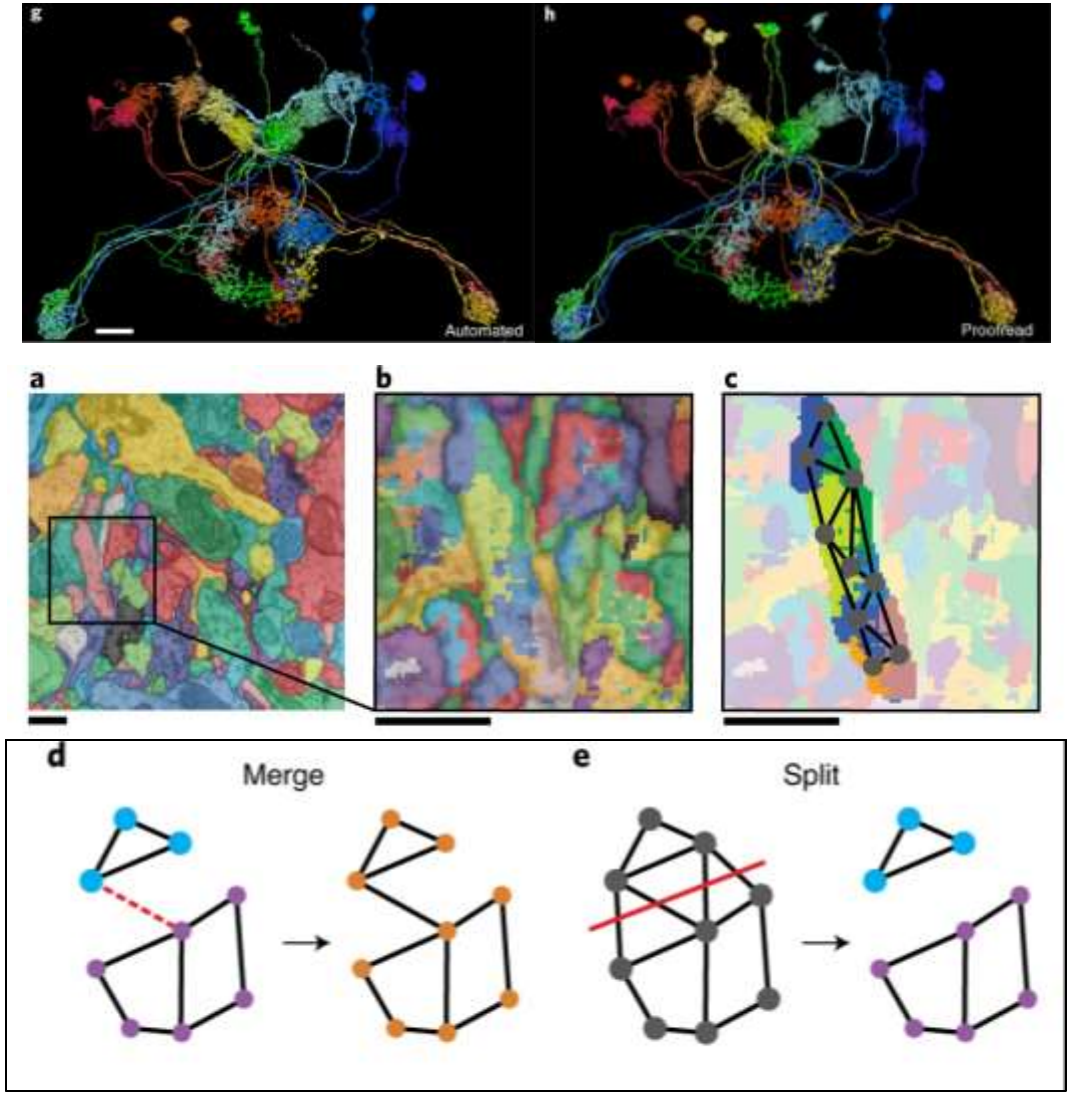
Sven Dorkenwald [#,1,2], Claire E McKellar [#,1], Thomas Macrina [#,1,2], Nico Kemnitz [#,1], Kisuk Lee [#,1,3], Ran Lu [#,1], Jingpeng Wu [#,1], Sergiy Popovych [1,2], Eric Mitchell [1], Barak Nehoran [1,2], Zhen Jia [1,2], J Alexander Bae [1,4], Shang Mu [1], Dodam Ih [1], Manuel Castro [1], Oluwaseun Ogedengbe [1], Akhilesh Halageri [1], Kai Kuehner [1], Amy R Sterling [1], Zoe Ashwood [1,2], Jonathan Zung [1,2], Derrick Brittain [5], Forrest Collman [5], Casey Schneider-Mizell [5], Chris Jordan [1], William Silversmith [1], Christa Baker [1], David Deutsch [1], Lucas Encarnacion-Rivera [1], Sandeep Kumar [1], Austin Burke [1], Doug Bland [1], Jay Gager [1], James Hebditch [1], Selden Koolman [1], Merlin Moore [1], Sarah Morejohn [1], Ben Silverman [1], Kyle Willie [1], Ryan Willie [1], Szi-Chieh Yu [1], Mala Murthy [6], H Sebastian Seung [7,8]

PMID: 34949809 PMCID: PMC8903166 DOI: 10.1038/s41592-021-01330-0

Proofreading time calculation for a full fly brain

We based our estimate of the proofreading time for an entire fly brain on the measured mean proofreading time of 19.1 min multiplied by an estimated 116,000 neurons in the fly brain[58]. We assumed 2,000 h of work per year per person.

FlyWire: online community for whole-brain connectomics



Dorkenwald, Sven et al. Nature methods vol. 19,1 (2022): 119-128.

A whole-brain connectome of the fruit fly, including ~130k annotated neurons and tens of millions of typed synapses!

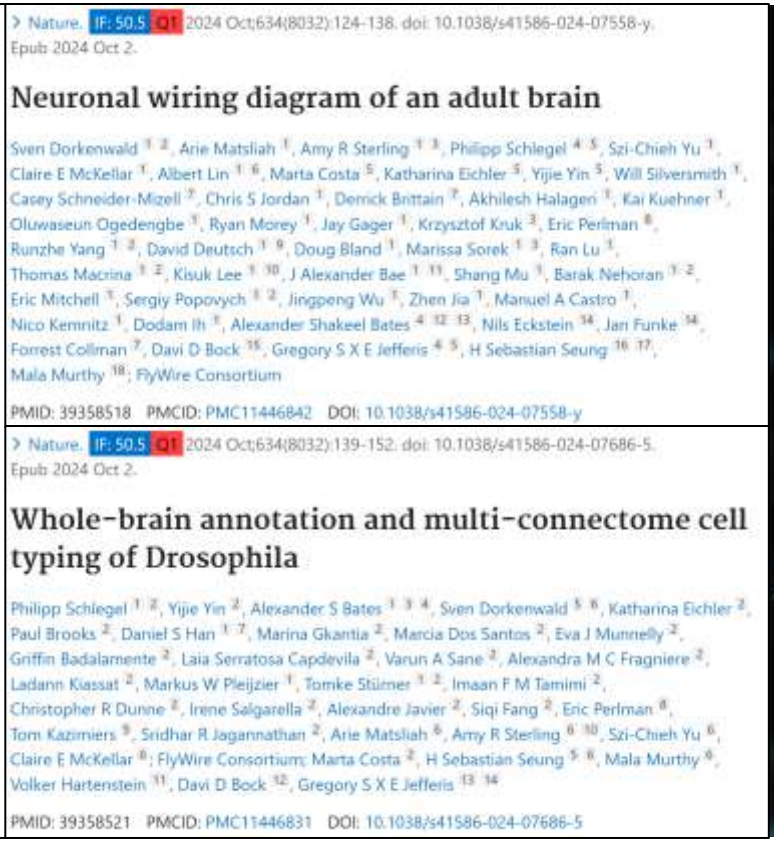
FlyWire @FlyWireNews · Jul 1, 2023

4 years. 250 people. 2.7 million edits to proofread 127,000 neurons. The fly connectome is here!

Preprint: Neuronal wiring diagram of an adult brain
biorxiv.org/content/10.110...

Explore it in Codex: codex.flywire.ai

0:06 / 2:19



Nature. IF: 50.5 Q1 2024 Oct;634(8032):124-138. doi: 10.1038/s41586-024-07558-y.
Epub 2024 Oct 2.

Neuronal wiring diagram of an adult brain

Sven Dorkenwald [1,2], Arie Matsliah [1], Amy R Sterling [1,3], Philipp Schlegel [4,5], Szi-Chieh Yu [1], Claire E McKellar [1], Albert Lin [1,6], Marta Costa [5], Katharina Eichler [5], Yijie Yin [5], Will Silversmith [1], Casey Schneider-Mizell [7], Chris S Jordan [1], Derrick Brittain [7], Akhilesh Halageri [1], Kai Kuehner [1], Oluwaseun Ogedengbe [1], Ryan Morey [1], Jay Gager [1], Krzysztof Kruk [3], Eric Perlman [8], Runzhe Yang [1,2], David Deutsch [1,9], Doug Bland [1], Marissa Sorek [1,3], Ran Lu [1], Thomas Macrina [1,2], Kisuk Lee [1,10], J Alexander Bae [1,11], Shang Mu [1], Barak Nehoran [1,2], Eric Mitchell [1], Sergiy Popovych [1,2], Jingpeng Wu [1], Zhen Jia [1], Manuel A Castro [1], Nico Kemnitz [1], Dodam Ih [1], Alexander Shakeel Bates [4,12,13], Nils Eckstein [14], Jan Funke [14], Forrest Collman [7], Davi D Bock [15], Gregory S X E Jefferis [4,5], H Sebastian Seung [16,17], Mala Murthy [18]; FlyWire Consortium

PMID: 39358518 PMCID: PMC11446842 DOI: 10.1038/s41586-024-07558-y

Nature. IF: 50.5 Q1 2024 Oct;634(8032):139-152. doi: 10.1038/s41586-024-07686-5.
Epub 2024 Oct 2.

Whole-brain annotation and multi-connectome cell typing of Drosophila

Philipp Schlegel [1,2], Yijie Yin [2], Alexander S Bates [1,3,4], Sven Dorkenwald [5,6], Katharina Eichler [2], Paul Brooks [2], Daniel S Han [1,7], Marina Gkantia [2], Marcia Dos Santos [2], Eva J Munnelly [2], Griffin Badalamente [2], Laia Serratosa Capdevila [2], Varun A Sane [2], Alexandra M C Fragniere [2], Ladann Kiassat [2], Markus W Pleijzier [1], Tomke Stürner [1,2], Imaan F M Tamimi [2], Christopher R Dunne [2], Irene Salgarella [2], Alexandre Javier [2], Siqi Fang [2], Eric Perlman [8], Tom Kazimiers [9], Sridhar R Jagannathan [2], Arie Matsliah [6], Amy R Sterling [6,10], Szi-Chieh Yu [6], Claire E McKellar [6]; FlyWire Consortium; Marta Costa [2], H Sebastian Seung [5,6], Mala Murthy [6], Volker Hartenstein [11], Davi D Bock [12], Gregory S X E Jefferis [13,14]

PMID: 39358521 PMCID: PMC11446831 DOI: 10.1038/s41586-024-07686-5

Dorkenwald, Sven et al. Nature vol. 634,8032 (2024): 124-138.
Schlegel, Philipp et al. Nature vol. 634,8032 (2024): 139-152.

Take home message

- FlyWire is created at Princeton University

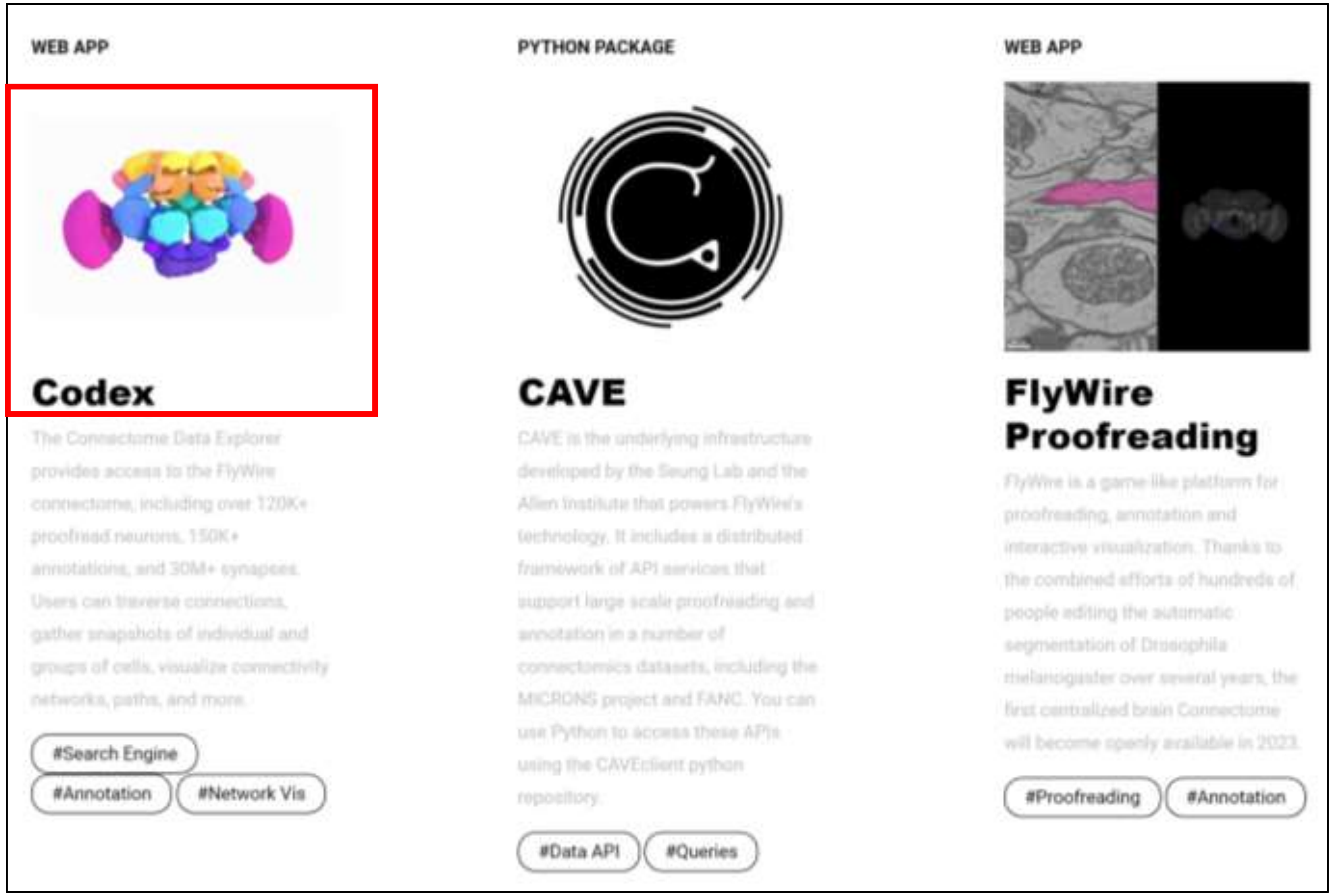
image: Mary Sym

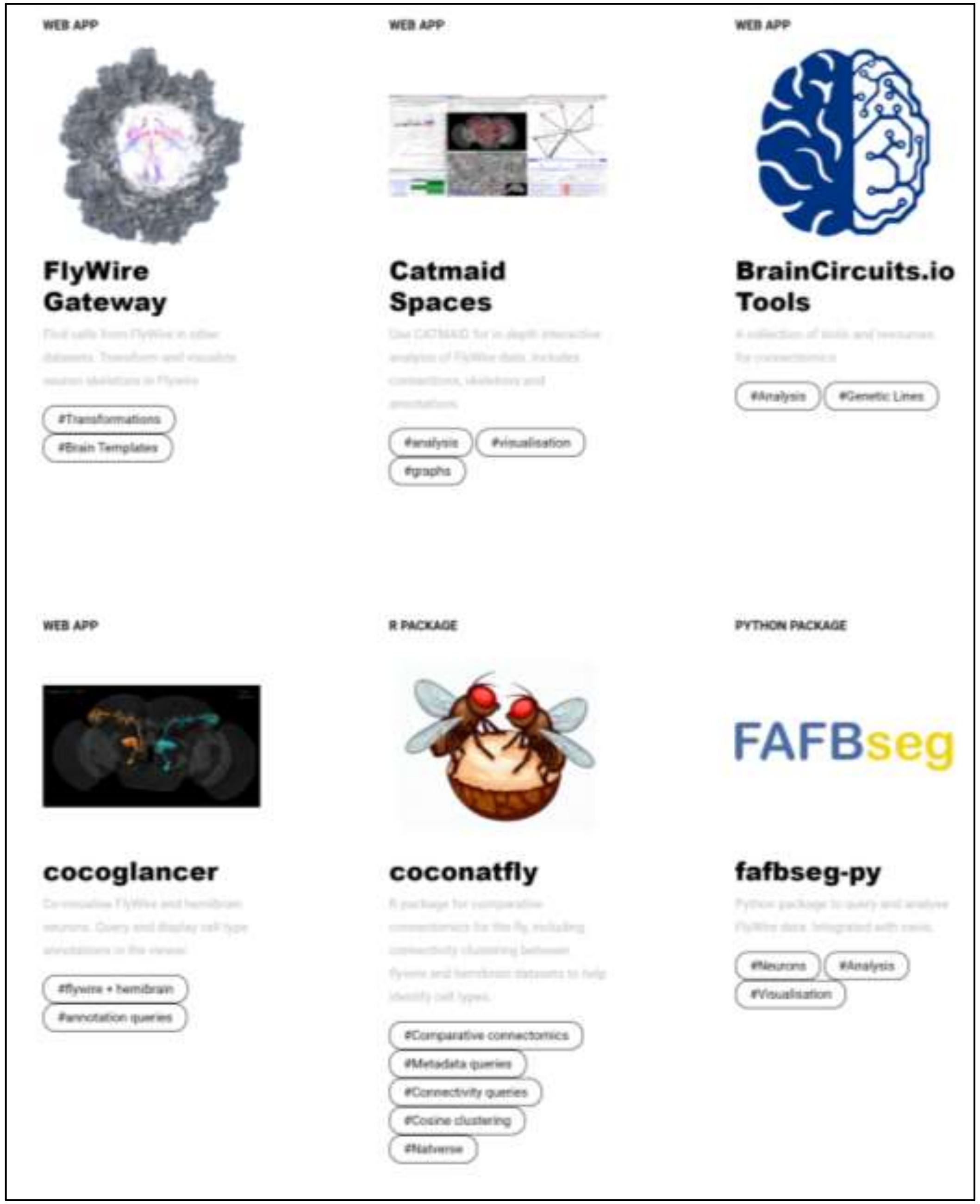
Data Sources

- Cell segments were auto-generated from electron-microscopy images with AI
- Cell reconstructions were assembled from segments (proofread) by the FlyWire community (see FlyWire)
- Synaptic connections were automatically detected using the Buhmann et al. method and refined with synapse segmentations from Heinrich et al.
- Free-form labels (cell identification tags) were provided by the FlyWire community - see the labeling leaderboard and detailed credits in each cell info page
- Hierarchical annotations (side, flow, super class, cell class, cell type, Hemibrain type, nerve and hemi-lineage) were provided by Schlegel et al. (Jefferis lab)
- Neurotransmitter types were predicted by Eckstein, Bates et al.
- Morphological similarity scores (NBLAST based) were computed for the central brain cells by Philipp Schlegel
- Links from FlyWire neurons and cell types to Virtual Fly Brain and FlyBase were curated by Clare Pilgrim
- Repository of known functions for cell types is curated by Yijie Yin and synced periodically; see source spreadsheet for credits (corrections/contributions welcome)
- Refer to the table below or contact flywire@princeton.edu for additional info / questions on data credits

2

FlyWire Platform Overview and Operational Guidelines





https://flywire.ai

Codex Search Stats Cell Info 3D Explore Connectivity fafb v783

Codex

Connectome Data Explorer : tutorials
Developed at Princeton Neuroscience Institute

FlyWire Brain Dataset (FAFB v783)

Connectome of a female adult fly brain (see FlyWire Brain homepage for details). Exploring version v783 that includes:

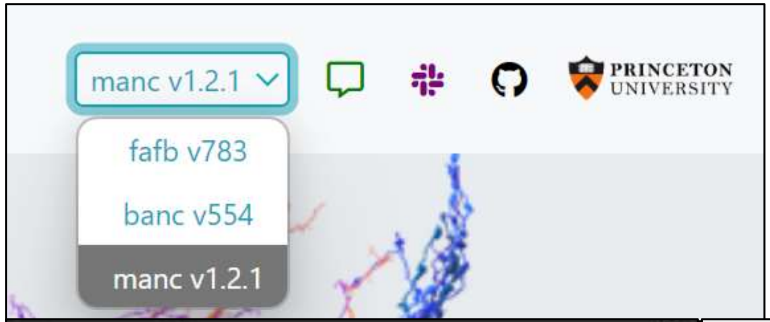
139,255 proofread cells	**138,059 (99%)** typed or labeled cells
2,700,513 connections [?]	**34,153,566** synapses [?]

See About FlyWire and FAQs pages for more details.
Switch datasets from the drop-down menu in the top-right corner.

search cells and annotations

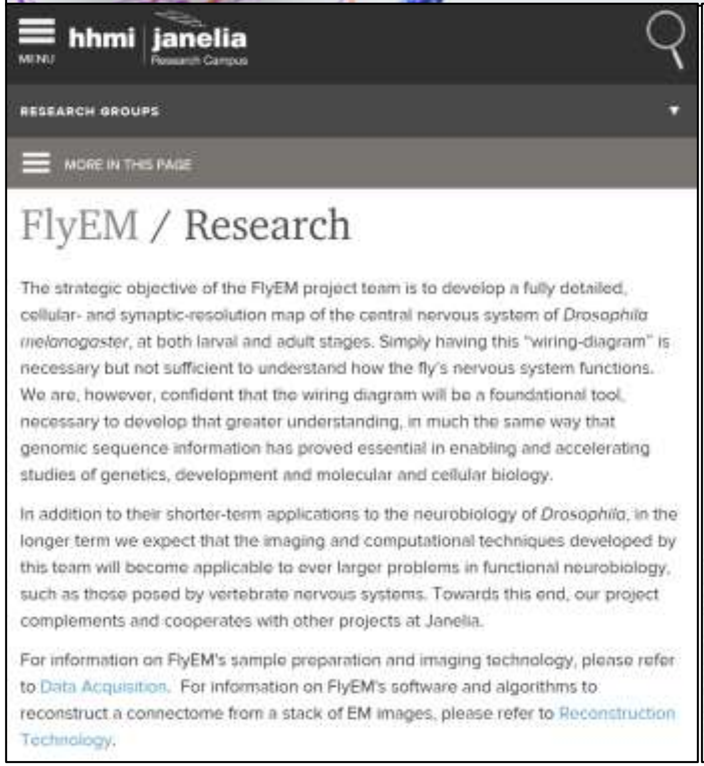
Datasets in Codex (May 2025)

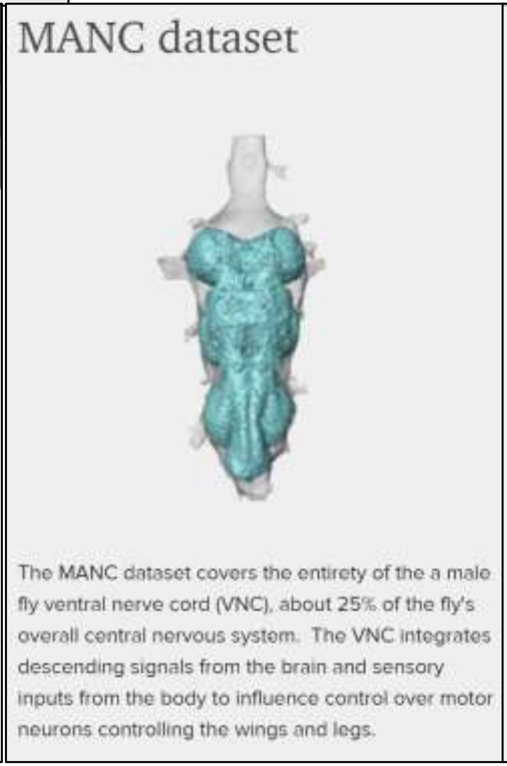
- FlyWire FAFB - female brain
- BANC - female brain and nerve cord (requires access token)
- MANC - male nerve cord
- Optic Lobe - male optic lobe (coming soon)
- Mouse datasets (coming later)

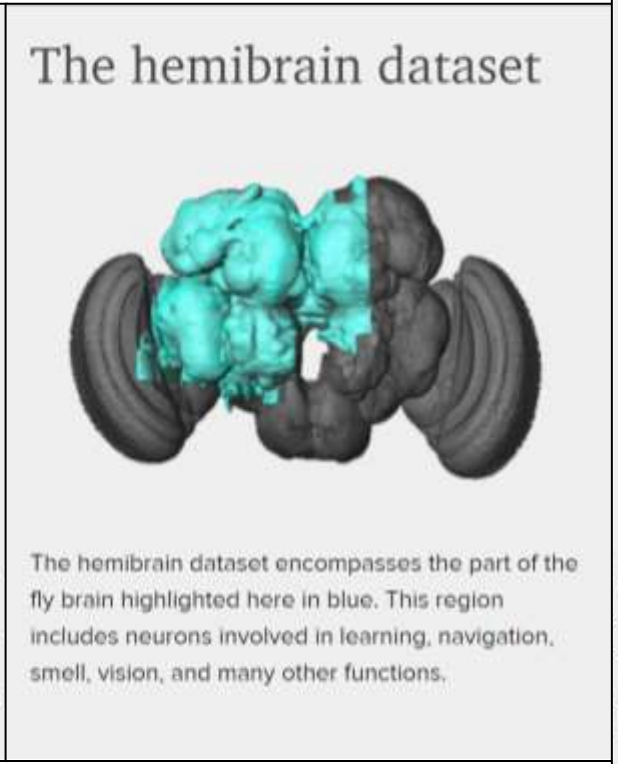


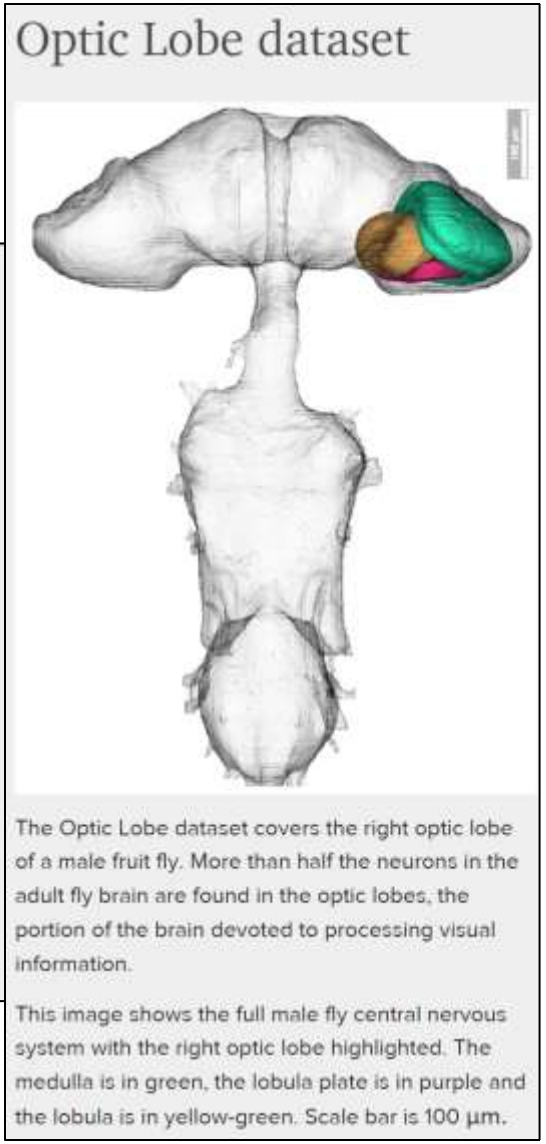
- **MANC**

  Male Adult Nerve Cord

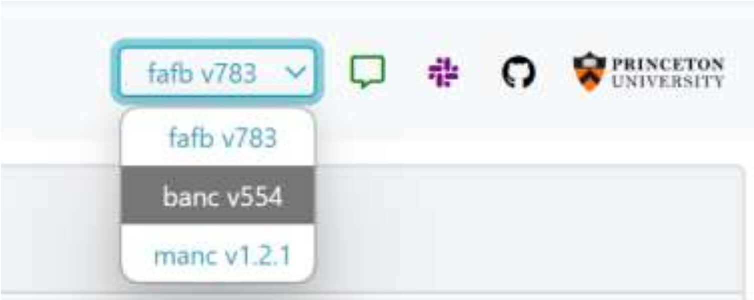






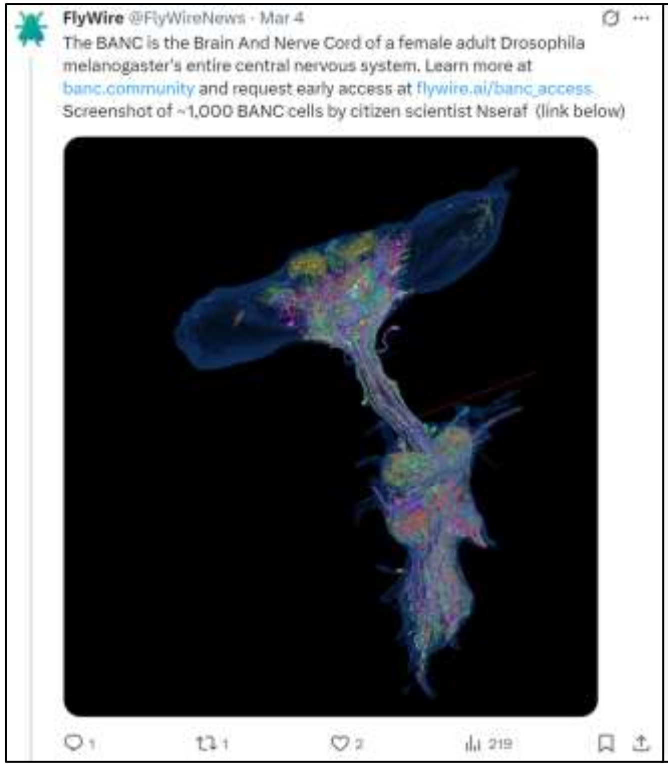


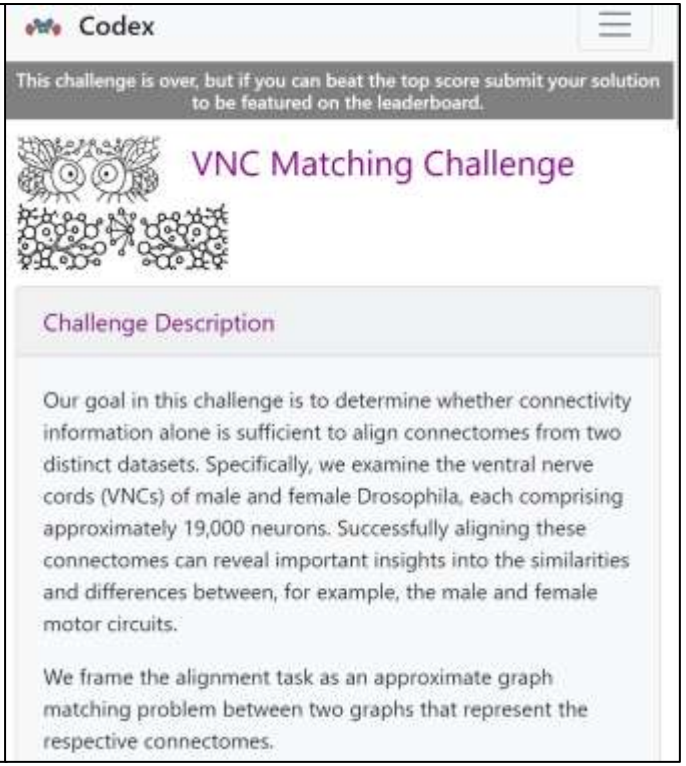
Shin-ya Takemura et al. eLife13:RP97769



- **BANC**

The Brain And Nerve Cord of a female adult *Drosophila melanogaster*





The connectome of an insect brain

Science. IF: 44.7 Q1 2023 Mar 10;379(6636):eadd9330. doi: 10.1126/science.add9330.
Epub 2023 Mar 10.

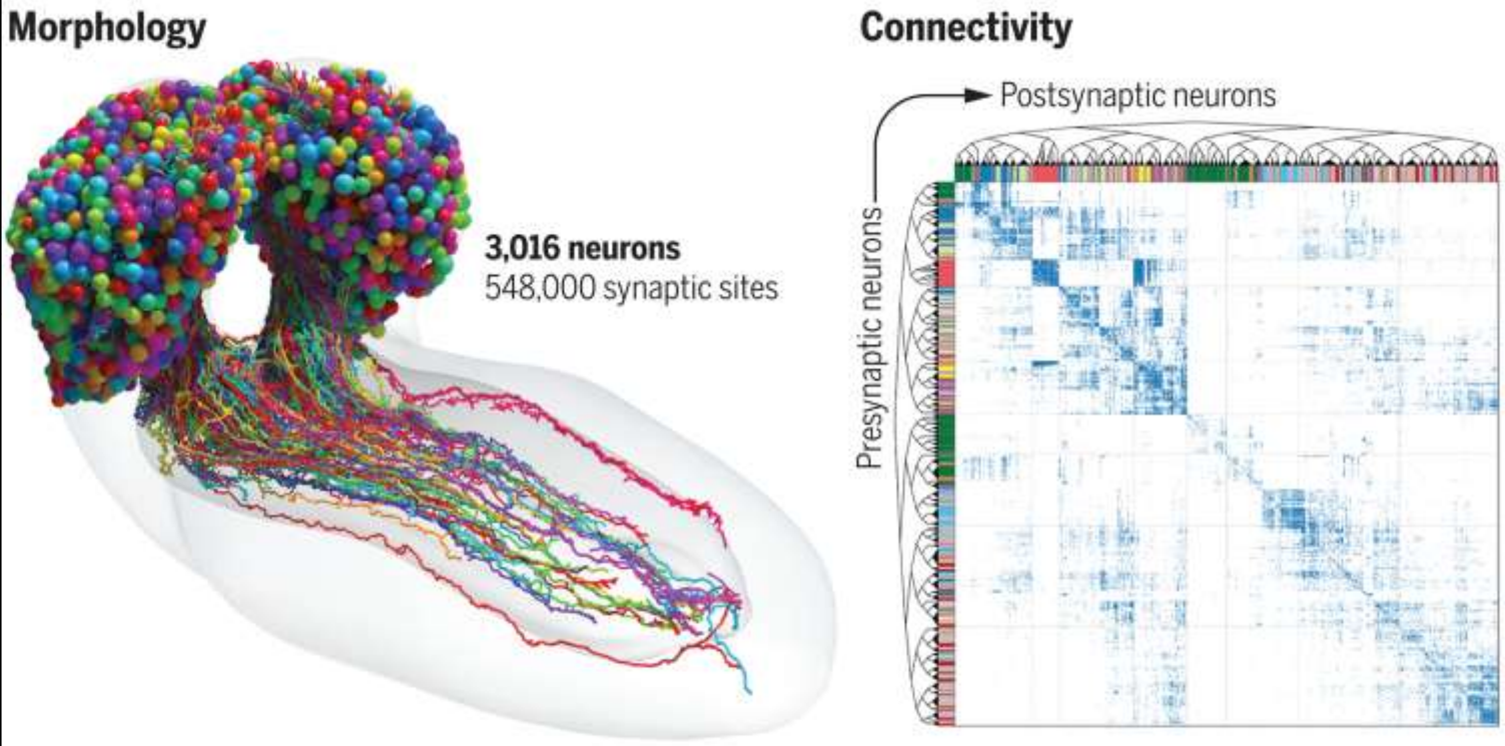
The connectome of an insect brain

Michael Winding [1,2,3], Benjamin D Pedigo [4], Christopher L Barnes [2,5], Heather G Patsolic [6,7], Youngser Park [8], Tom Kazimiers [3,9], Akira Fushiki [3,10], Ingrid V Andrade [11], Avinash Khandelwal [3], Javier Valdes-Aleman [1,3], Feng Li [3], Nadine Randel [1,2], Elizabeth Barsotti [2,5], Ana Correia [2,5], Richard D Fetter [3,12], Volker Hartenstein [11], Carey E Priebe [6,8], Joshua T Vogelstein [4,8], Albert Cardona [2,3,5], Marta Zlatic [1,2,3]

PMID: 36893230 PMCID: PMC7614541 DOI: 10.1126/science.add9330

Neurobiology

Marta Zlatic
Circuit mechanisms of learning and action-selection
mzlatic@mrc-lmb.cam.ac.uk



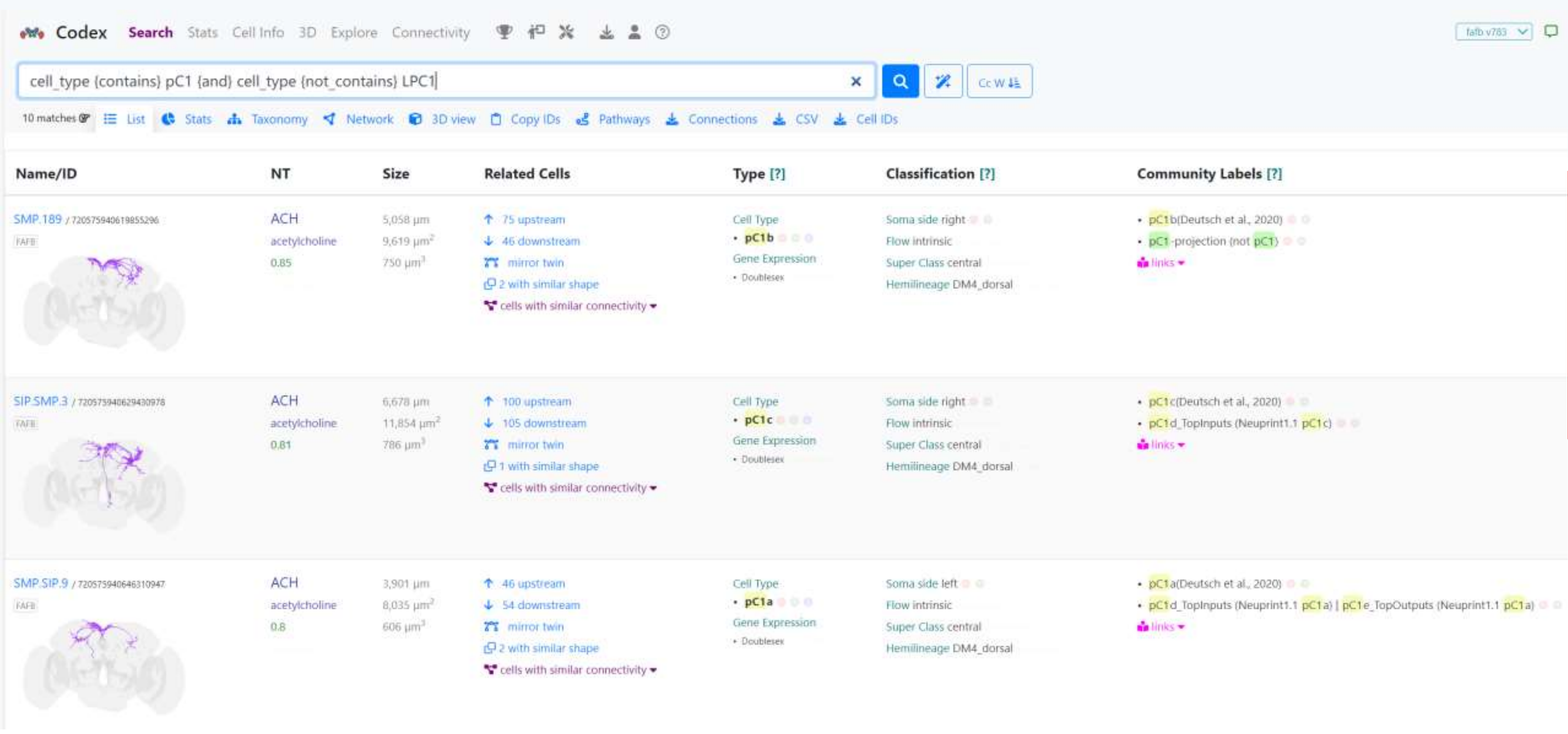
Winding, Michael et al. Science (2023)

3 Codex 常用功能

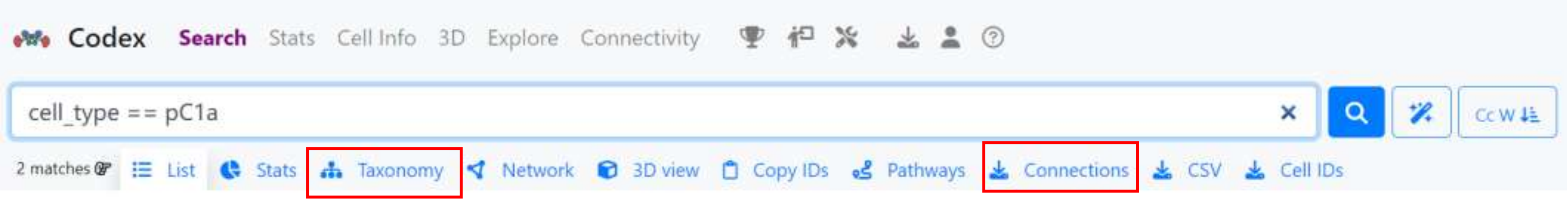
红色标注的功能是最常使用的。

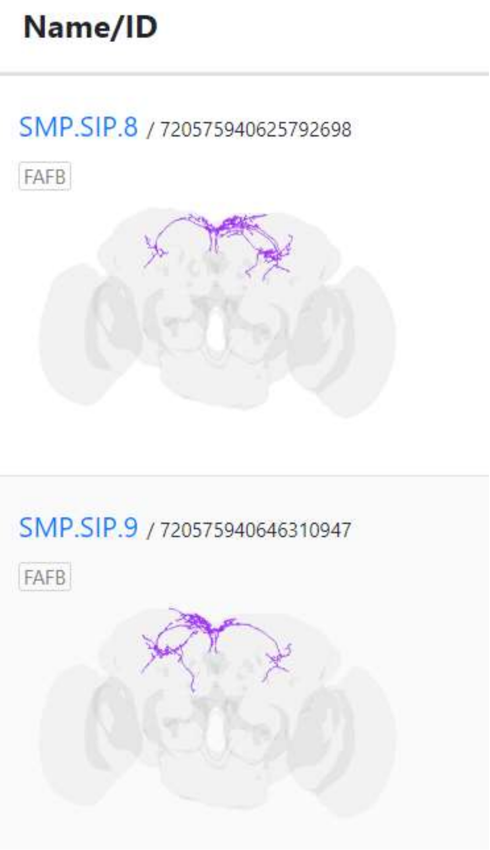
By GC

Search: Find neurons using free-form or structured queries



Search: Find neurons using free-form or structured queries





Taxonomy

Annotation Taxonomy

Context : flow : super_class : class : sub_class : resolved_type : side : number of cells

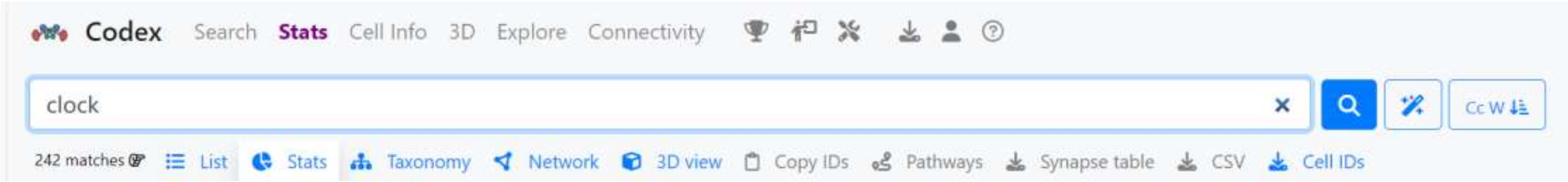
query : intrinsic : central : [class] : [sub_class] : pC1a : right : 1 cells; left : 1 cells

Connections

From	To	Neuropil	Synapses	Neuro Transmitter
720575940625792698	720575940646310947	SMP_R	11	ACH
720575940625792698	720575940646310947	SIP_L	7	ACH
720575940625792698	720575940646310947	SIP_R	5	ACH
720575940625792698	720575940646310947	MB_VL_R	1	ACH
720575940625792698	720575940646310947	SMP_L	10	ACH
720575940646310947	720575940625792698	SIP_L	4	ACH
720575940646310947	720575940625792698	SMP_L	3	ACH
720575940646310947	720575940625792698	SMP_R	6	ACH
720575940646310947	720575940625792698	SIP_R	10	ACH

Schlegel, Philipp et al. Nature vol. 634,8032 (2024): 139-152.

Stats: See statistics and charts for various attributes of all or subset of neurons in the dataset



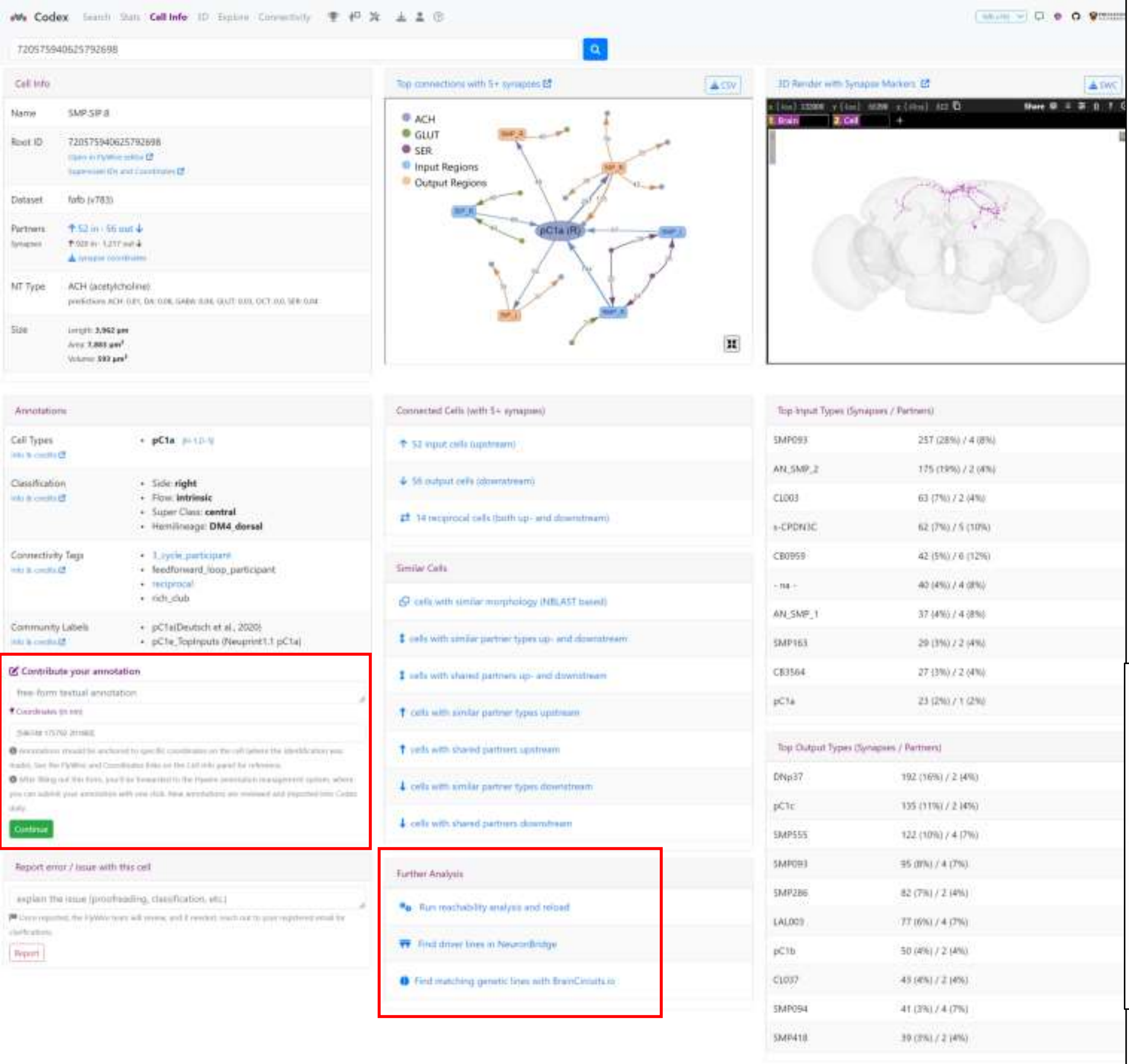
Cells	242
- Cell Types	21
- Typed cells	242
- Internal connections / syns	711 / 7,166
- Ext. upstream partners / syns	866 / 29,300
- Ext. downstream partners / syns	1,182 / 32,940
- Combined length	359,664 μm
- Combined area	774,900 μm²
- Combined volume	64,771 μm³

Top Types	
s-CPDN3A	38
s-CPDN3D	37
s-CPDN3C	32
s-CPDN3E	25
s-CPDN3B	25
APDN3	12
l-LNv	8
DN1pA	8
DN1pD	8
s-LNv	8

Top Input Types (Synapses / Partners)	
s-CPDN3D	1,734 (5%) / 26 (3%)
aMe3	1,577 (4%) / 2 (0%)
DN1pA	1,507 (4%) / 8 (1%)
aMe8	1,195 (3%) / 4 (0%)
SMP517	1,059 (3%) / 9 (1%)
CB0710	737 (2%) / 4 (0%)
aMe1	725 (2%) / 4 (0%)
SMP202	725 (2%) / 2 (0%)
cM04	694 (2%) / 6 (1%)
SLP270	644 (2%) / 2 (0%)

Top Output Types (Synapses / Partners)	
DN1pD	1,210 (3%) / 8 (1%)
CL086_a	1,185 (3%) / 10 (1%)
s-CPDN3D	964 (2%) / 34 (3%)
SMP234	830 (2%) / 2 (0%)
DN1pC	805 (2%) / 4 (0%)
SMP285	801 (2%) / 2 (0%)
DNd01	705 (2%) / 4 (0%)
LNd_CRY+_ITP+	672 (2%) / 2 (0%)
- na -	616 (2%) / 26 (2%)
SMP335	597 (1%) / 2 (0%)

Neurotransmitter Types
GLUT
ACH
SER
0
100
Num Cells
Top Input Regions
SMP_R
SMP_L
SLP_R
MB_CA_R
SLP_L
PLP_R
MB_CA_L
LH_L
PLP_L
SCL_L
0
50
100
Num Cells
Top Output Regions
SMP_R
SMP_L
SLP_R
SLP_L
PLP_R
MB_CA_R
SCL_R
MB_CA_L
SCL_L
PLP_L
0
50
100
150
Num Cells
Side
50.4%
49.6%
left
right
Flow
intrinsic
Super Class
90.1%
central
optic
visual_projection
Sub Class
circadian_clock
241
242
Num Cells
Connectivity Tag
feedforward_l...
3_cycle_partic...
reciprocal
rich_club
0
100
200
Num Cells
Class
bilateral
7
8
Num Cells
Hemilineage
SLPpl1
putative_primary
SMPpd2
SLPav1_lateral
SMPpv2_dorsal
0
100
Num Cells
Cell Type
s-CPDN3A
s-CPDN3D
s-CPDN3C
s-CPDN3E
s-CPDN3B
DN3A
CB1791
CB2901
CB2989
APDN3
0
20
40
Num Cells

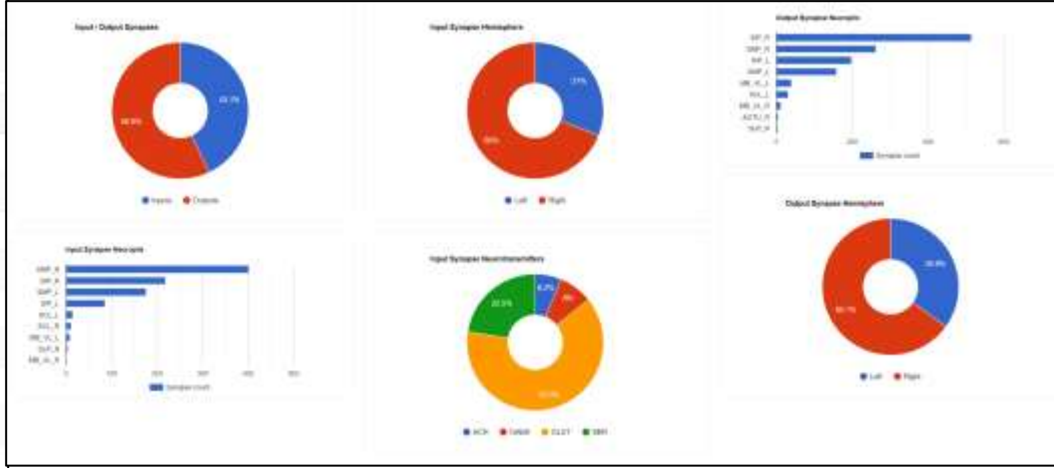


Cell Details:

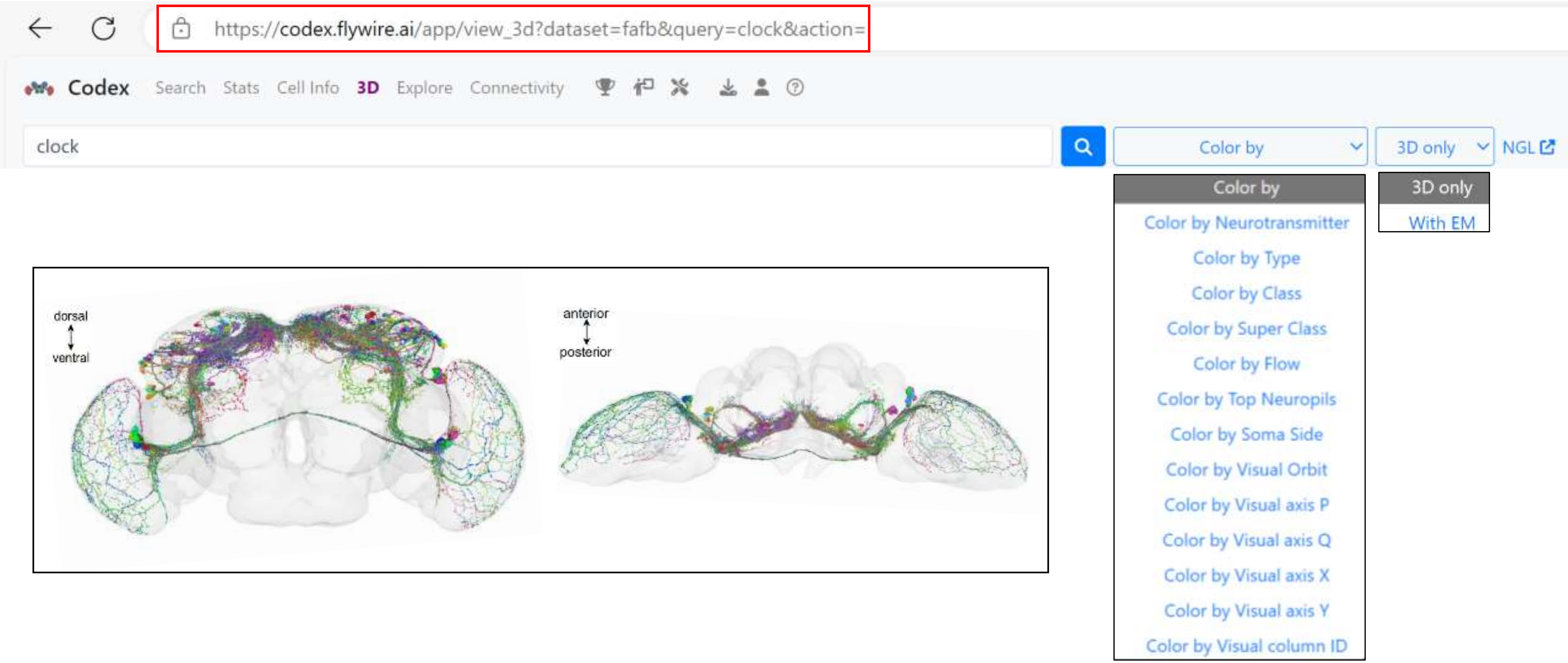
Information about individual cells, their connectivity, similar/twin cells, 3D rendering and annotations

References and external links

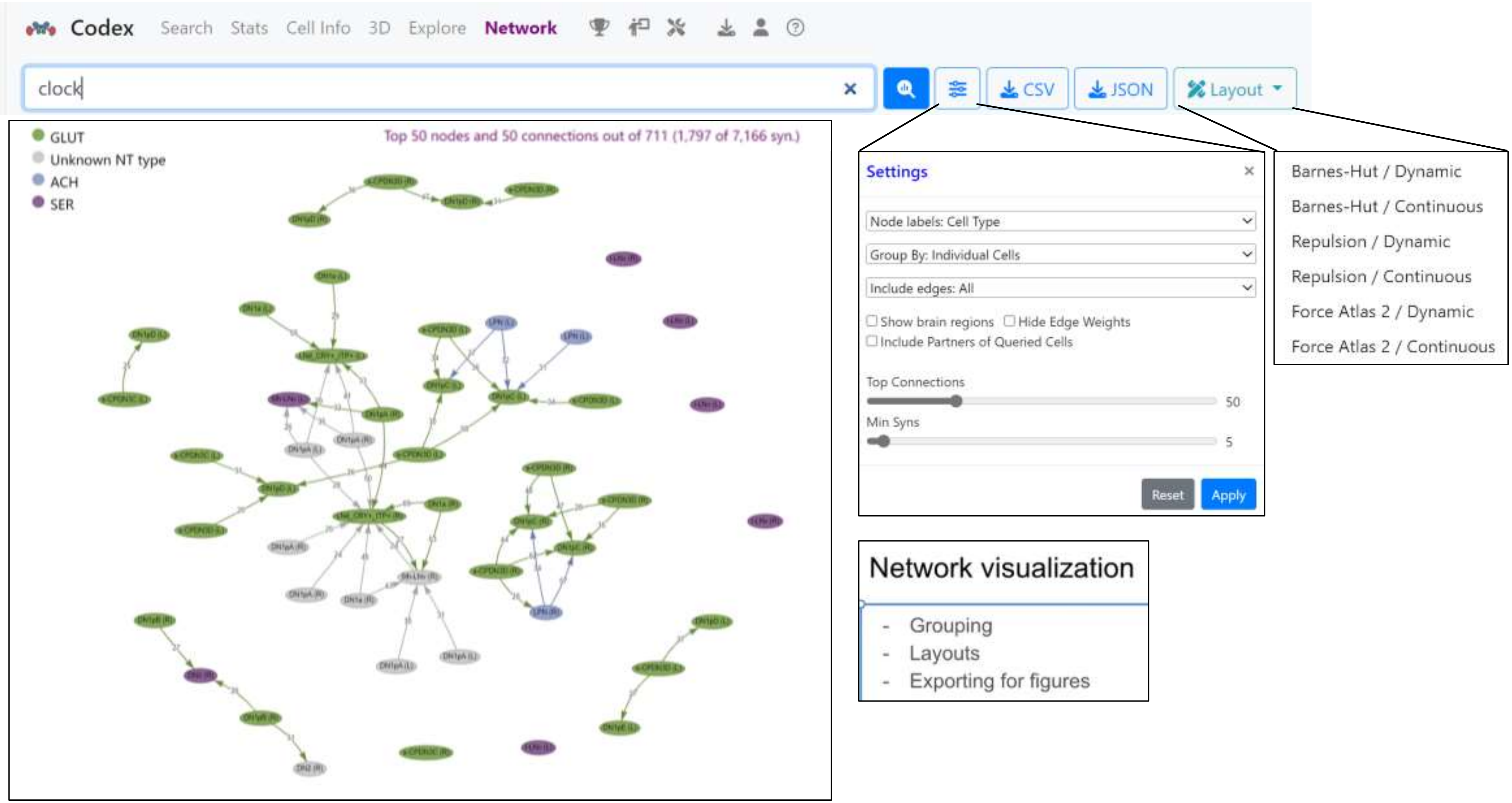
- Neuron bridge (matching driver lines)
- Braincircuits.io (genetic lines)
- Virtual Fly Brain and FlyBase (neuron and cell type information)
- Automated summary and literature citations (not very useful yet)
- Coming soon: known function of certain cell types



3D Viewer: Visualize queried neurons and synapses in annotated Neuroglancer scenes



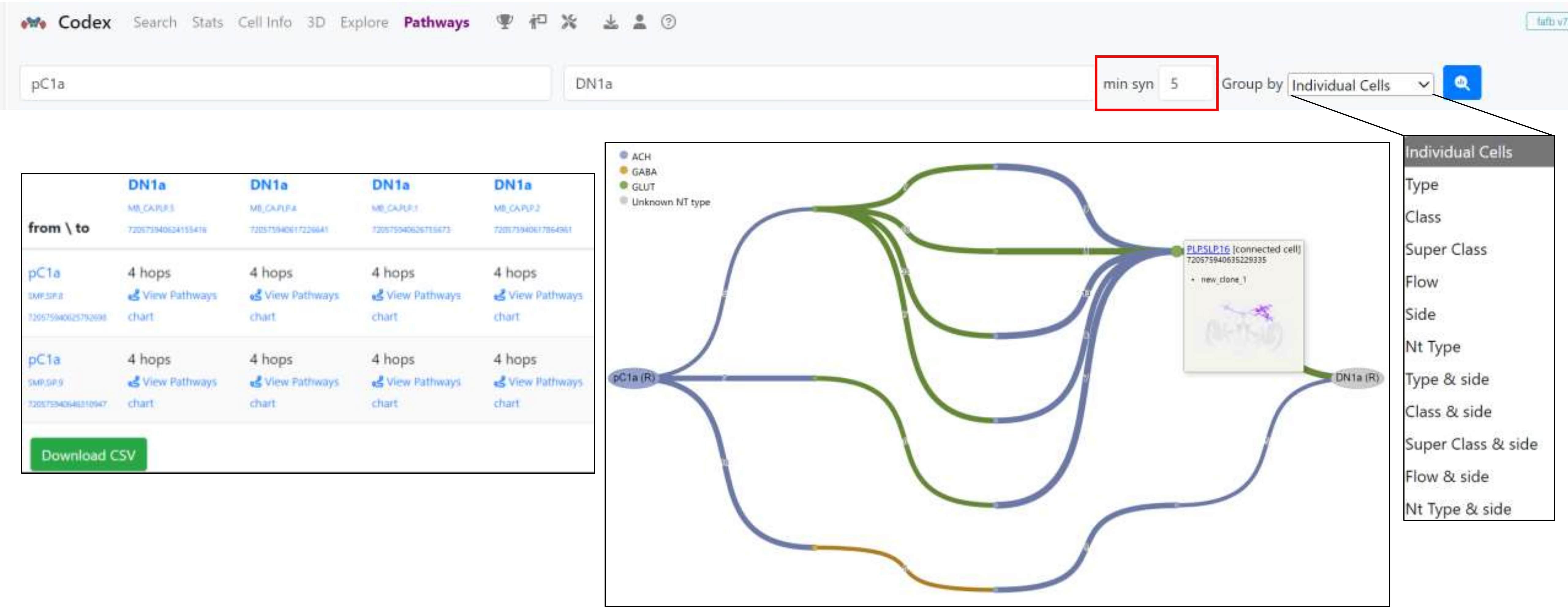
Network Graphs: Visualize connectivity of neurons and their synaptic links



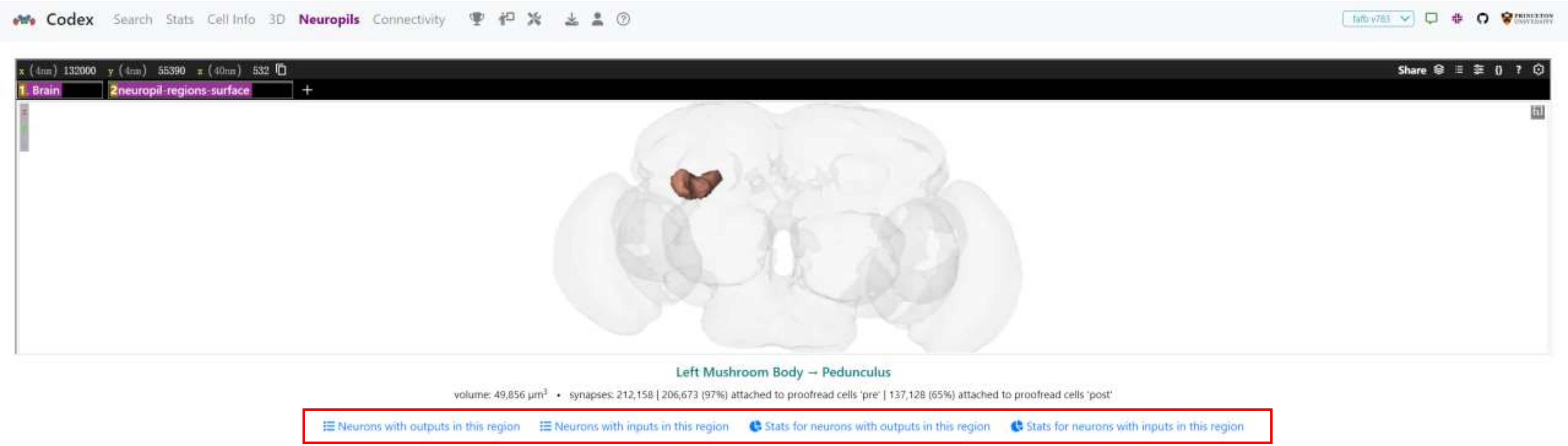
Network visualization

- Grouping
- Layouts
- Exporting for figures

Pathways: Analyse shortest-paths between pairs of neurons



Neuropils: Visualize and query connections in specific brain regions



Take home message

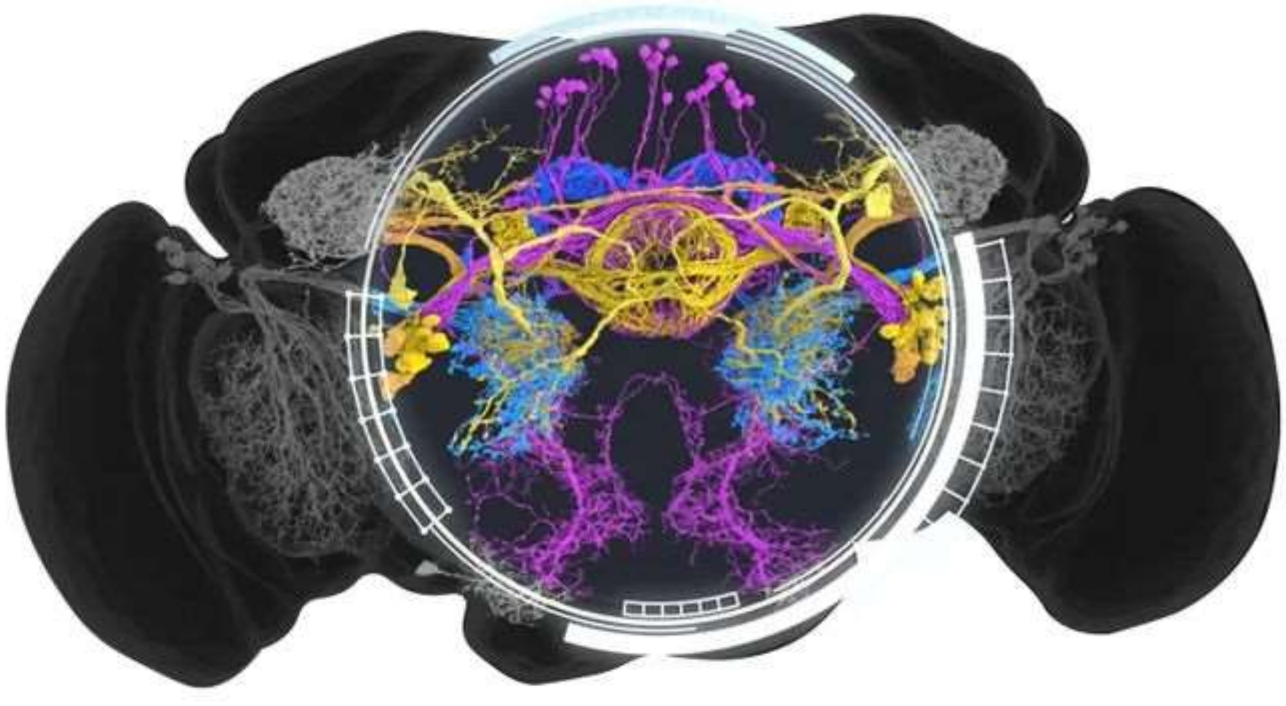
Datasets in Codex (May 2025)

- FlyWire FAFB - female brain
- BANC - female brain and nerve cord (requires access token)
- MANC - male nerve cord
- Optic Lobe - male optic lobe (coming soon)
- Mouse datasets (coming later)

PART 3:

Current Advances in *Drosophila* Research Using FlyWire

XLM

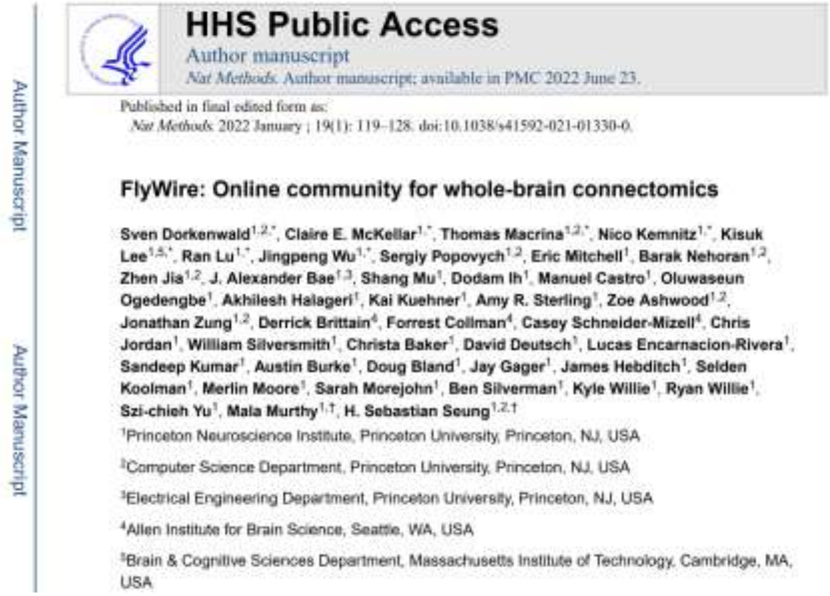


From the Flywire to scientific researches:

What research areas are covered by FlyWire's applications?

What can we inspire from these researches using FlyWire?

Development and application of flywire



HHS Public Access
Author manuscript
Nat Methods. Author manuscript; available in PMC 2022 June 23.

Published in final edited form as:
Nat Methods. 2022 January ; 19(1): 119–128. doi:10.1038/s41592-021-01330-0.

FlyWire: Online community for whole-brain connectomics

Sven Dorkenwald[1,2,*], Claire E. McKellar[1,*], Thomas Macrina[1,2,*], Nico Kemnitz[1,*], Kisuk Lee[1,5,*], Ran Lu[1,*], Jingpeng Wu[1,*], Sergiy Popovych[1,2], Eric Mitchell[1], Barak Nehoran[1,2], Zhen Jia[1,2], J. Alexander Bae[1,3], Shang Mu[1], Dodam Ih[1], Manuel Castro[1], Oluwaseun Ogedengbe[1], Akhilesh Halageri[1], Kai Kuehner[1], Amy R. Sterling[1], Zoe Ashwood[1,2], Jonathan Zung[1,2], Derrick Brittain[4], Forrest Collman[4], Casey Schneider-Mizell[4], Chris Jordan[1], William Silversmith[1], Christa Baker[1], David Deutsch[1], Lucas Encarnacion-Rivera[1], Sandeep Kumar[1], Austin Burke[1], Doug Bland[1], Jay Gager[1], James Hebditch[1], Selden Koolman[1], Merlin Moore[1], Sarah Morejohn[1], Ben Silverman[1], Kyle Willie[1], Ryan Willie[1], Szi-chieh Yu[1], Mala Murthy[1,†], H. Sebastian Seung[1,2,†]

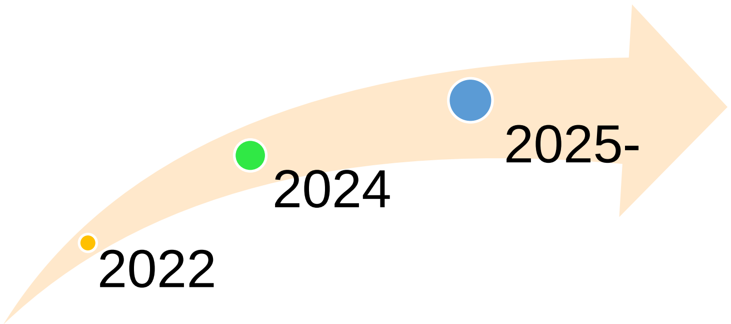
[1]Princeton Neuroscience Institute, Princeton University, Princeton, NJ, USA

[2]Computer Science Department, Princeton University, Princeton, NJ, USA

[3]Electrical Engineering Department, Princeton University, Princeton, NJ, USA

[4]Allen Institute for Brain Science, Seattle, WA, USA

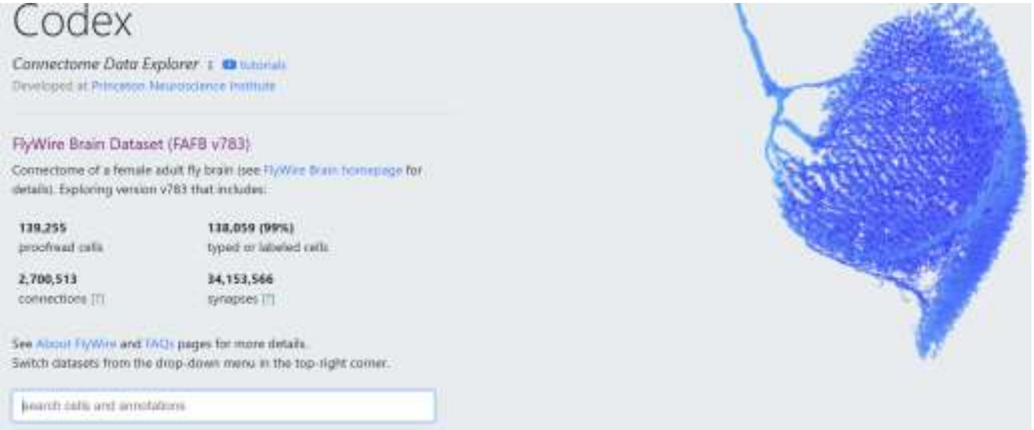
[5]Brain & Cognitive Sciences Department, Massachusetts Institute of Technology, Cambridge, MA, USA



Establishment of FlyWire
The auditory pathway relating to courtship

Whole-brain connectome
The connectome of sensory system
Circadian rhythm

Clock neurons



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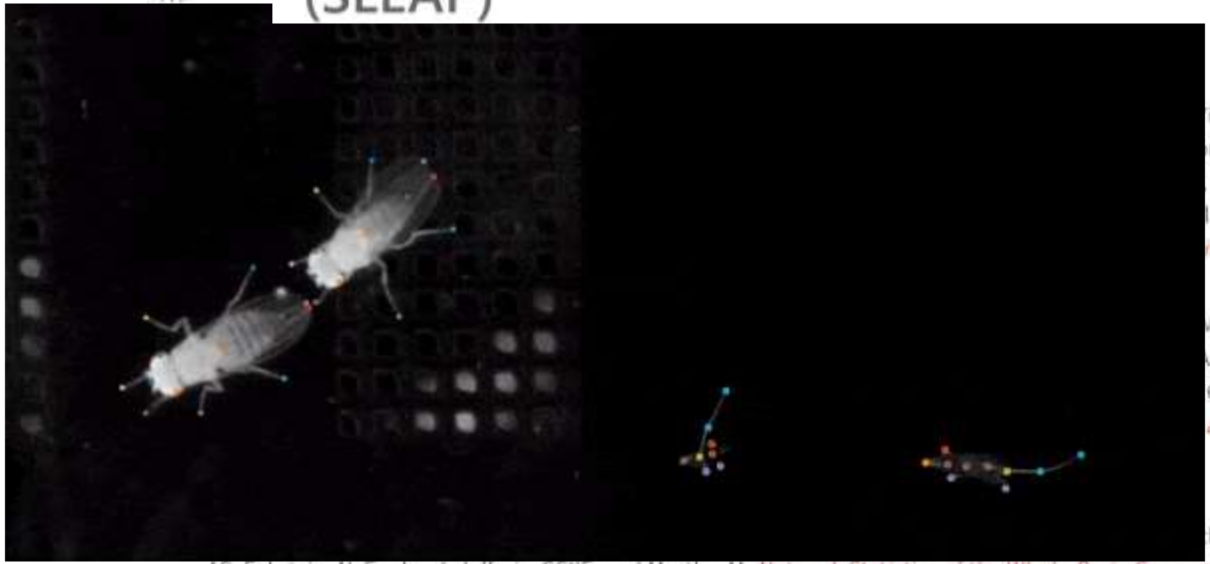
2024

- Brezovec, L... *co-correspondi... Vol. 121, No. 47.

Social LEAP Estimates Animal Poses (SLEAP)



...in, Y, ...rey, R, Gager, ... Nehoran, B, ...llman, F, ...iring diagram

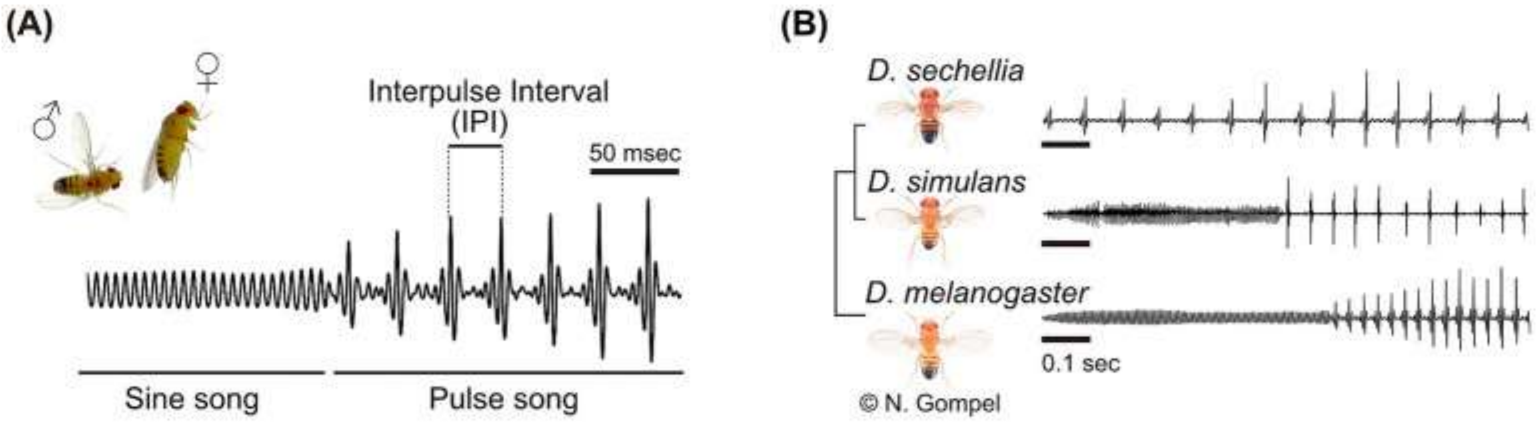
...Munnelly, EJ, ..., Fang, S, ... Consortium, ...and multi-

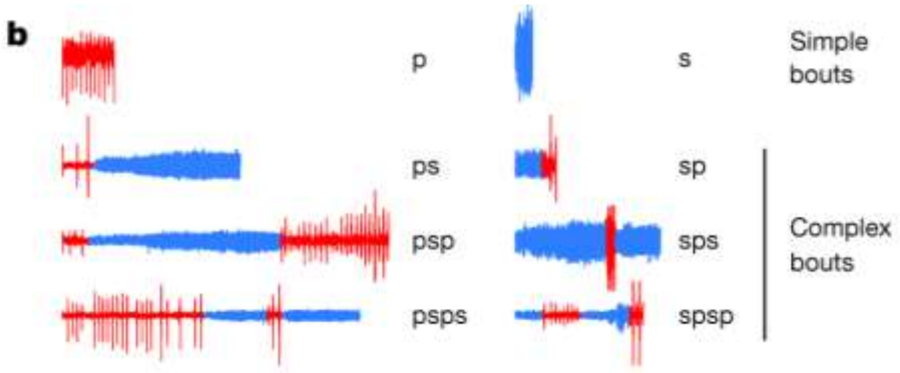
...hler, K, Bates, AS, Eckstein, N, Funke, J, Jefferis, GSXE, and Murthy, M. *Network Statistics of the Whole-Brain Connectome of Drosophila.* **Nature 2024**. 634, 153–165. doi.org/10.1038/s41586-024-07968-y #

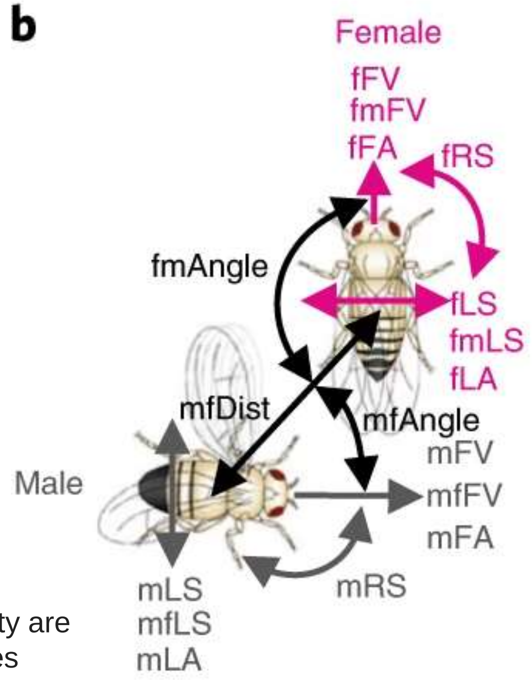
- Matsliah A, Yu SC, Kruk K, Bland D, Burke A, Gager J, Hebditch J, Silverman B, Willie K, Willie R, Sorek M, Sterling AR, Kind E, Garner D, Sancer G, Wernet M, Kim SS, Murthy M, Seung HS, and the FlyWire Consortium. Neuronal "parts list" and wiring diagram for a visual system. **Nature 2024**. 634, 166–180. doi.org/10.1038/s41586-024-07981-1 #
- Shiu, PK, Sterne, GR, Spiller, N, Franconville, R, Sandoval, A, Zhou, J, Simha, N, Kang, CH, Yu, S, Kim, J, Dorkenwald, S, Matsliah, A, Sterling, AR, Yu, S-C, McKellar, CE, Schlegel, P, Costa, M, Eichler, K, Jefferis, GSXE, Murthy, M, Bates, AS, Eckstein, N, Funke, J , Bidaye, SS, Hampel, S, Seeds, AM, and Scott, K. *A leaky integrate-and-fire computational model based on the connectome of the entire adult Drosophila brain reveals insights into sensorimotor processing.* **Nature 2024**. 634, 210–219. doi.org/10.1038/s41586-024-07763-9 #

Mala Murthy (b. 1975) is an American neuroscientist and Professor of Neuroscience at Princeton University and leads the Murthy lab in the Princeton Neuroscience Institute – their work focuses on **the neural mechanisms that underlie social communication,** using the fruit fly *Drosophila* as a model system.

Courtship song is an important factor for the successful mating





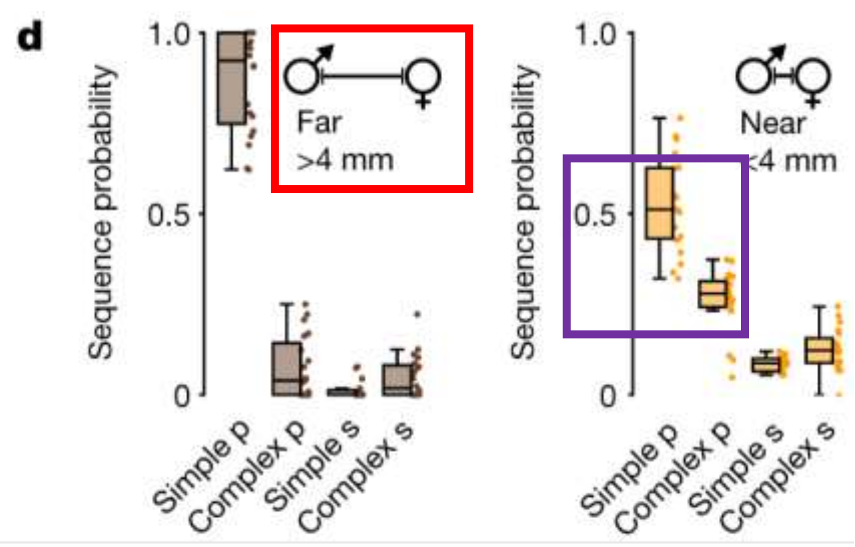


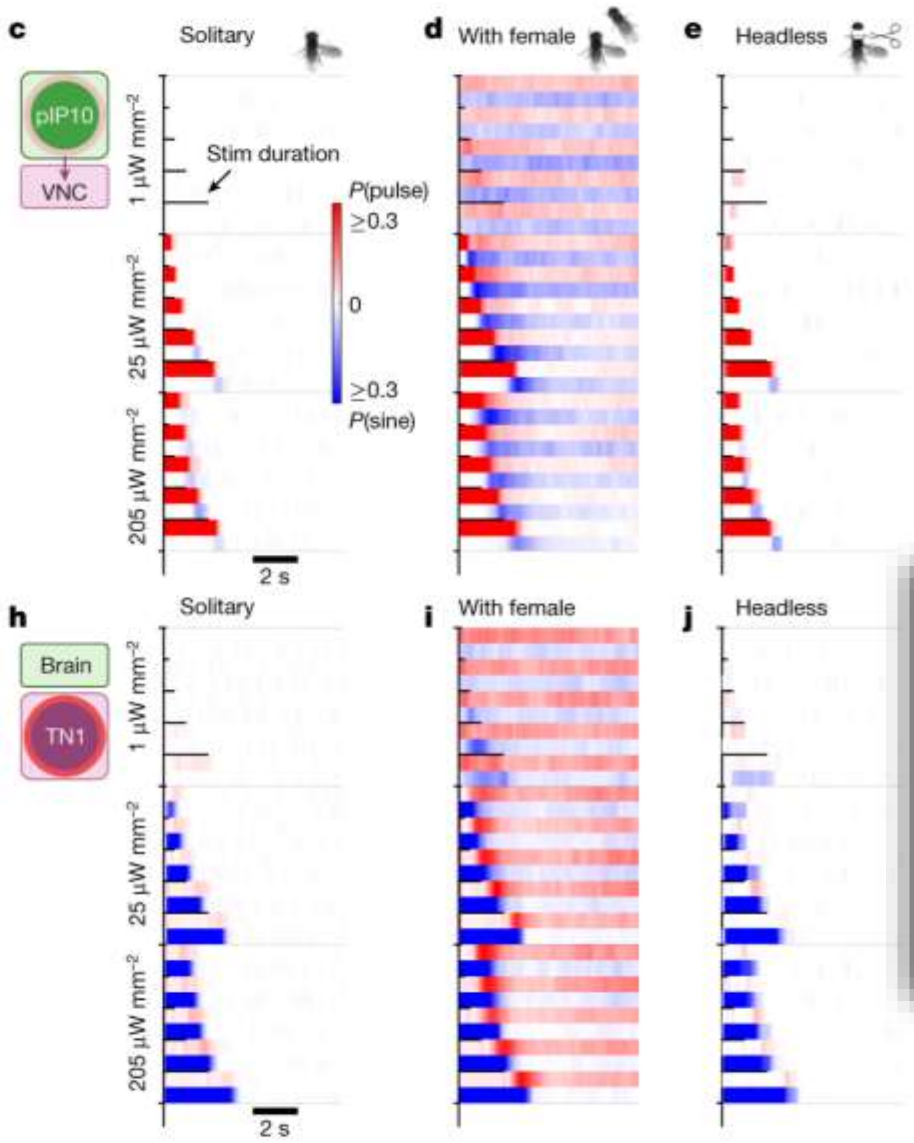
Receptive females reduce locomotor speed in response to multiple features within conspecific song.

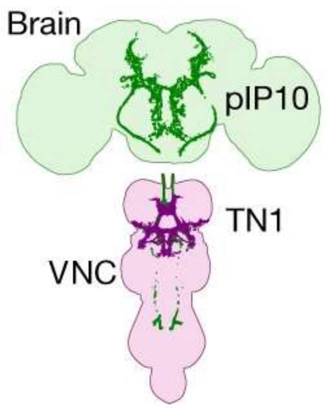
Male song patterning, timing and intensity are known to be modulated by feedback cues stemming from the female

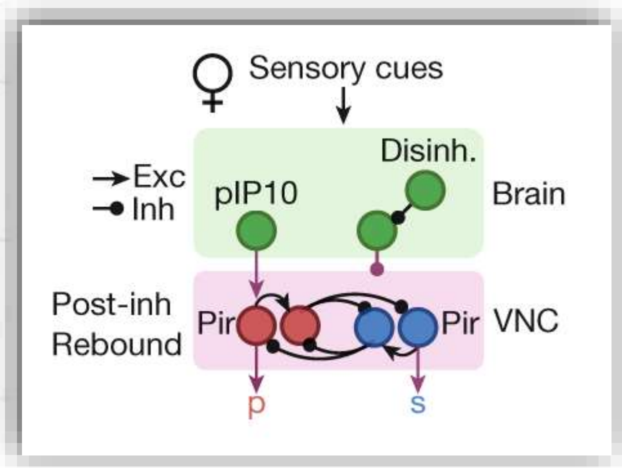
Kamikouchi A, Li X. *Front Neural Circuits.* 2024
Roemschied, F.A. *et al. Nature*. 2023
Calhoun, A.J., *et al*. *Nat Neurosci* .2019

Reciprocal interactions between pulse-producing and sine-producing neurons in the presence of a female







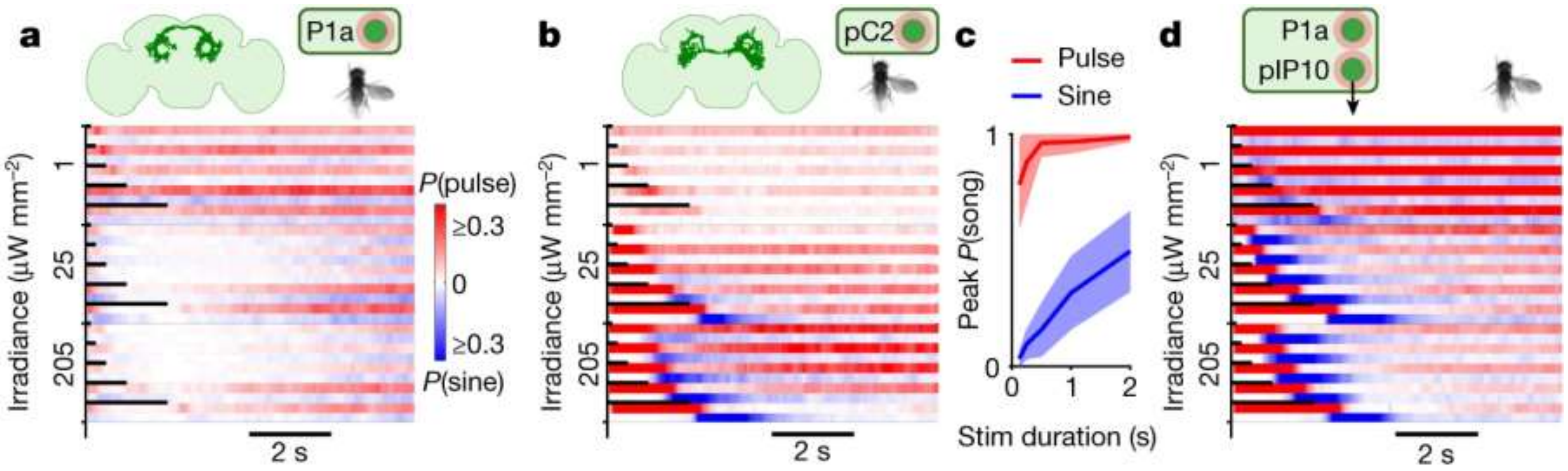


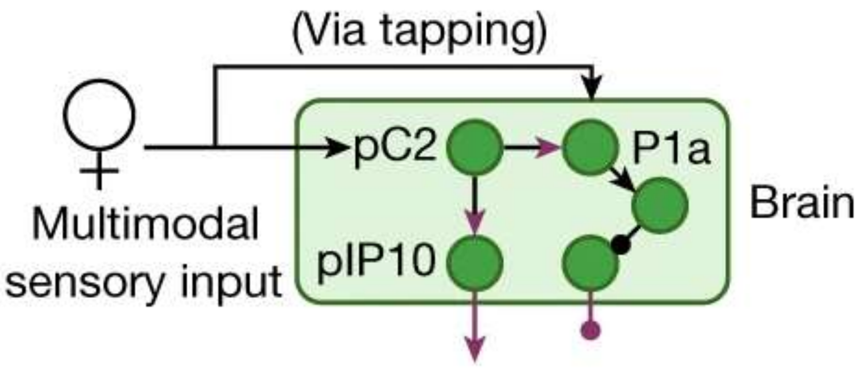
Context alters sequencing of male song

Pulse-neurons are activated initially

Roemschied, F.A. *et al. Nature*. 2023

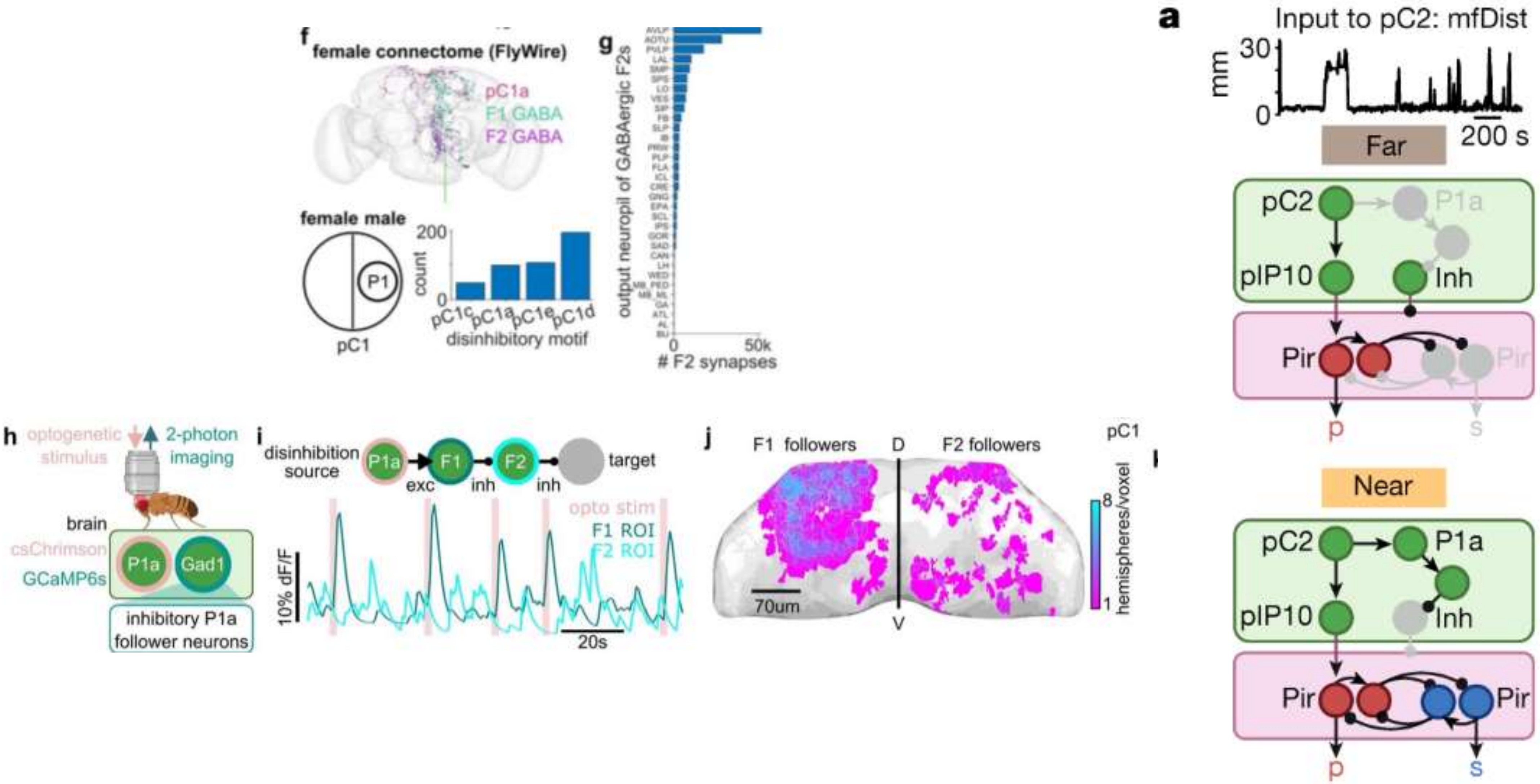
Female sensory cues promote complex song bout generation





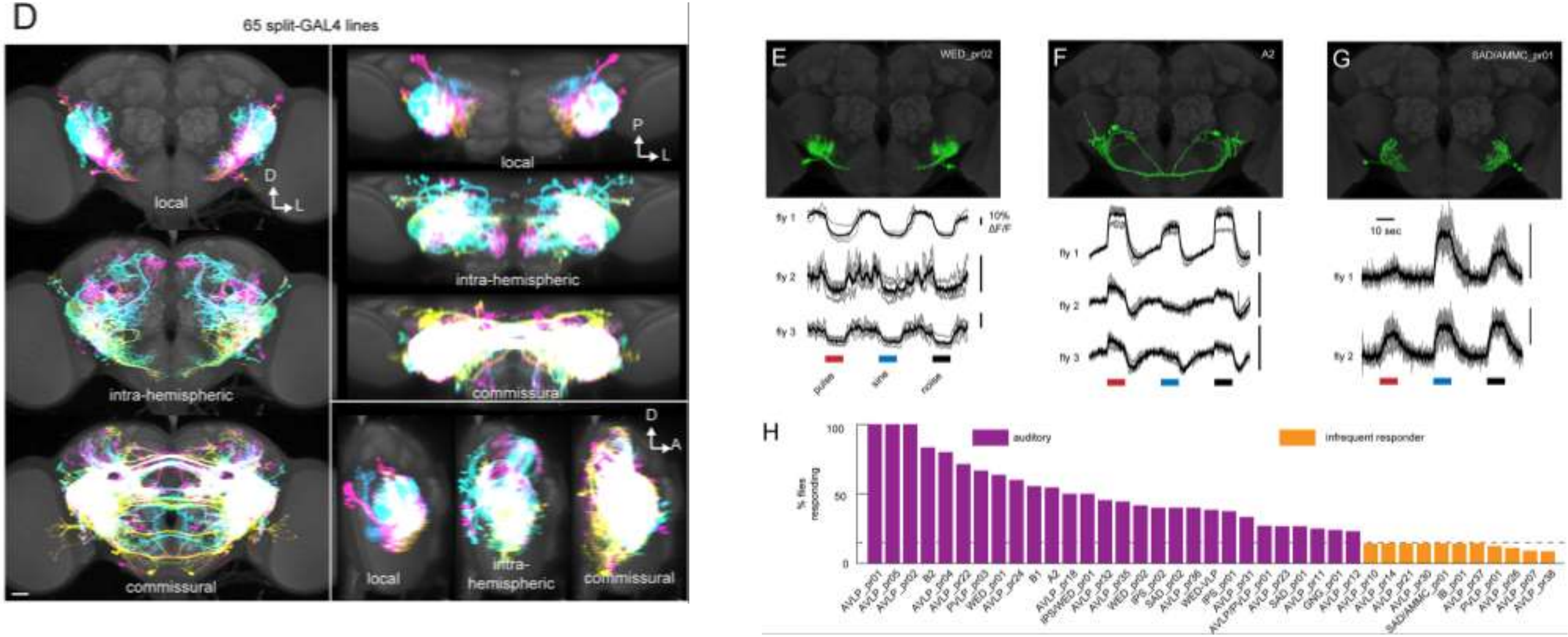
Roemschied, F.A. *et al.* *Nature*. 2023

Neural circuit model of context-dependent song patterning



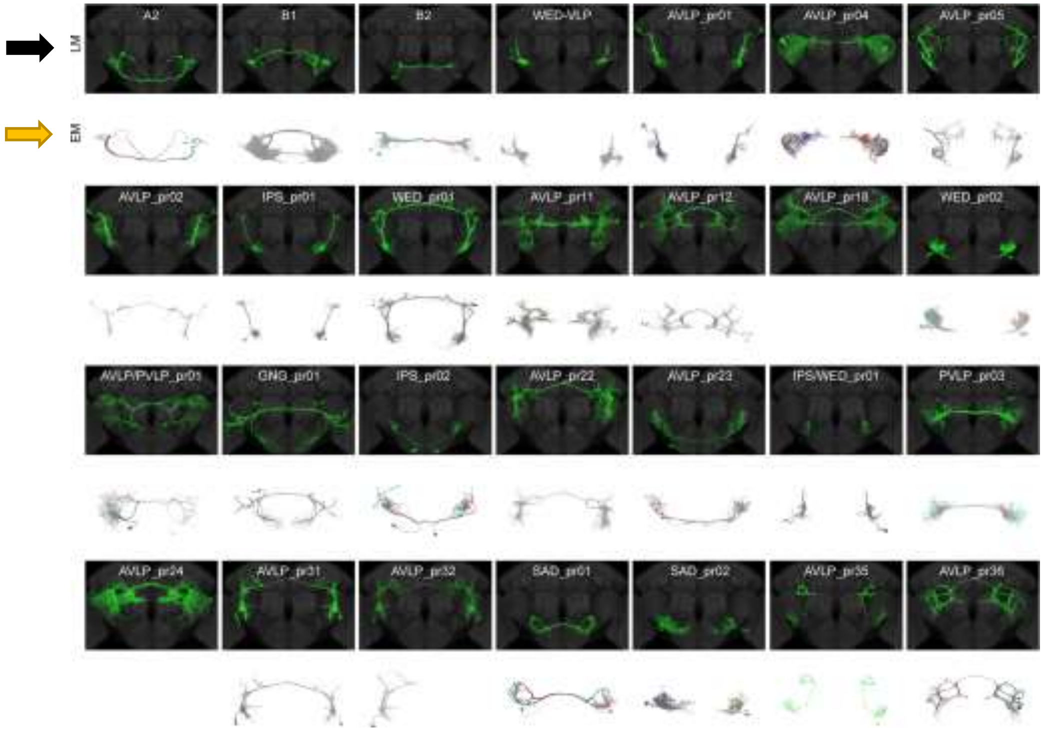
Roemschied, F.A. *et al. Nature*. 2023

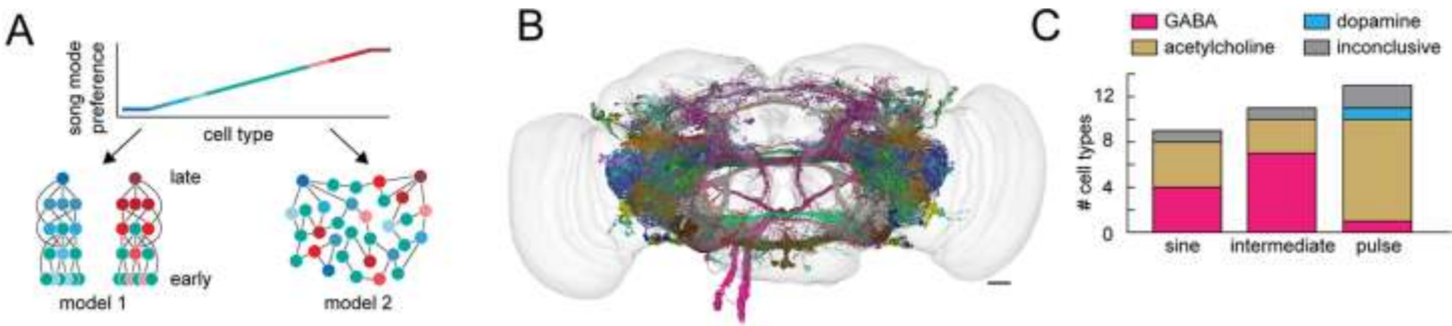
Anatomic and functional screen for auditory neurons

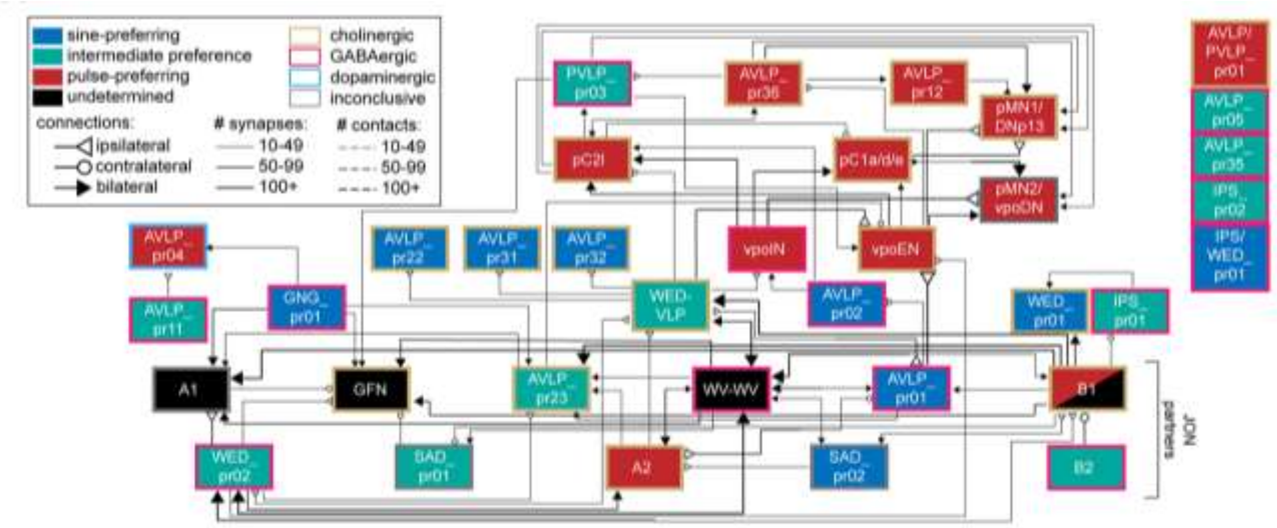


Baker CA. et al. Curr Biol. 2022

Identifying the connectome of *Drosophila* auditory neurons







To identify the preferred responses of different neurons to sine song and pulse song

The first circuit-level map of the auditory pathway

Baker CA. et al. Curr Biol. 2022

nature COMMUNICATIONS

Nat Commun. 2024 Dec 5;15:10392. doi: 10.1038/s41467-024-54694-0

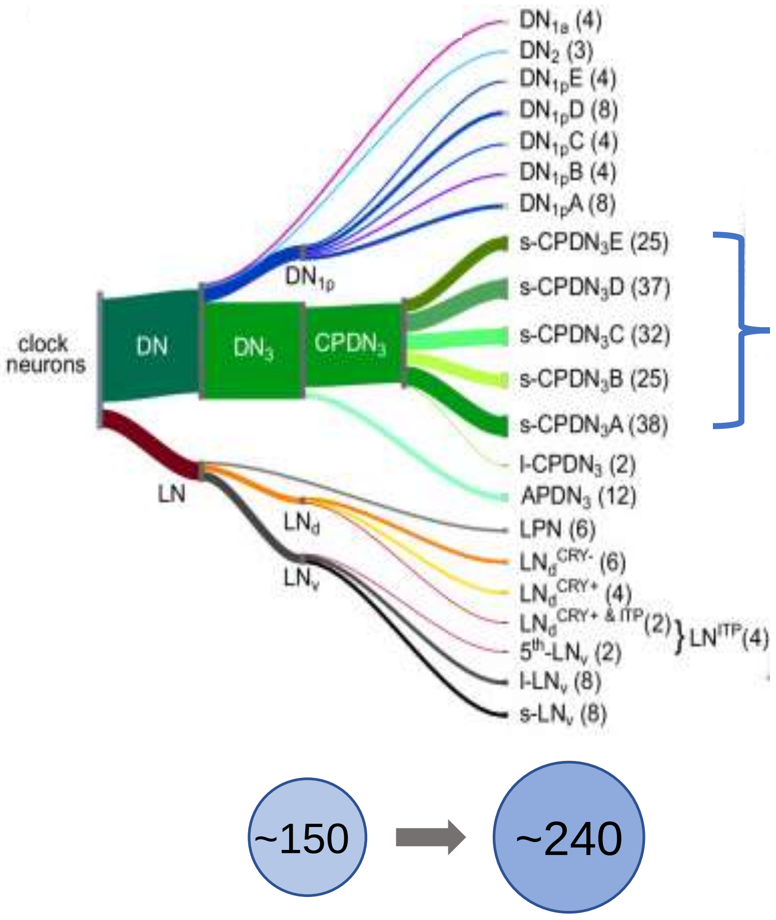
Synaptic connectome of the *Drosophila* circadian clock

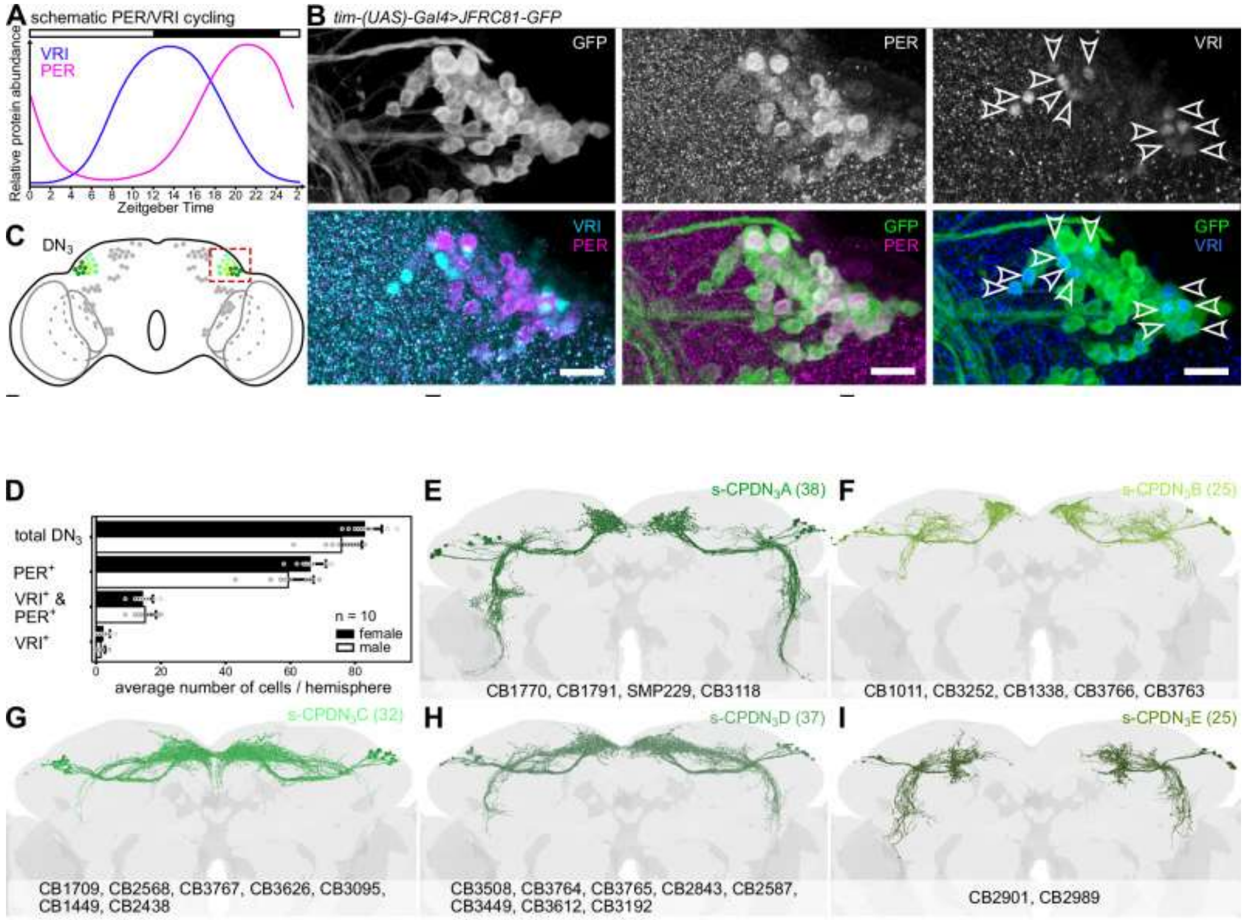
Nils Reinhard [1,#], Ayumi Fukuda [2,#], Giulia Manoli [1], Emilia Derksen [1], Aika Saito [2], Gabriel Möller [1], Manabu Sekiguchi [2], Dirk Rieger [1], Charlotte Helfrich-Förster [1,✉], Taishi Yoshii [2], Meet Zandawala [1,3,✉]

Author information · Article notes · Copyright and License information

PMCID: PMC11621569 PMID: 39638801

Additional dorsal clock neurons are identified, by using FlyWire

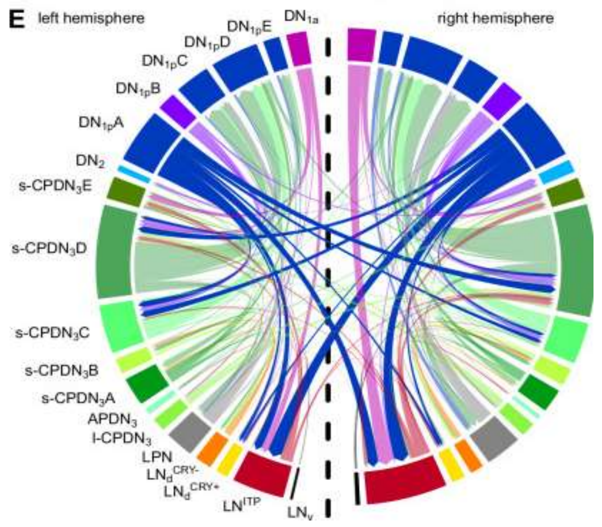


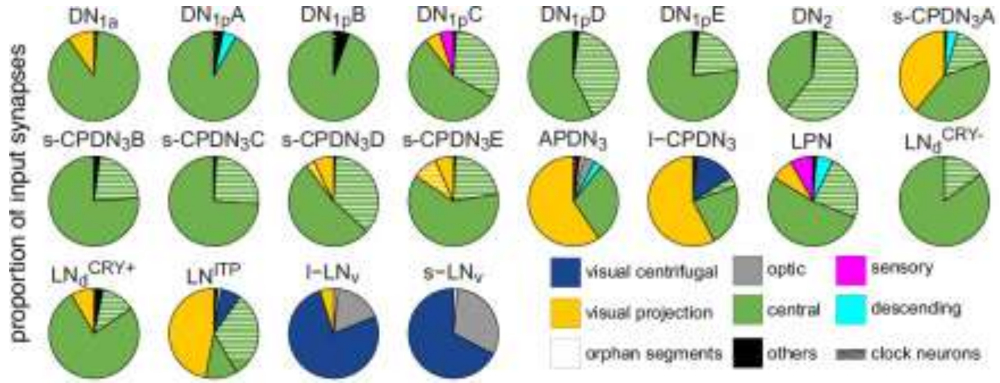


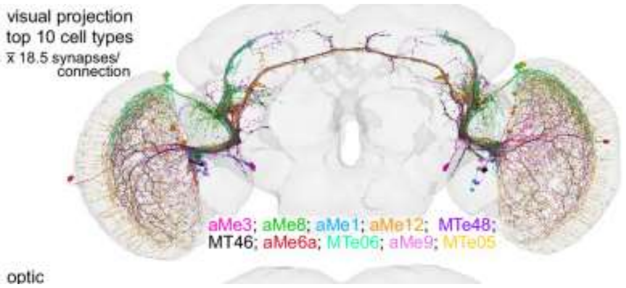
根据形态学、先前确定的连通性及其胞体位置的组合鉴定了 242 个时钟神经元

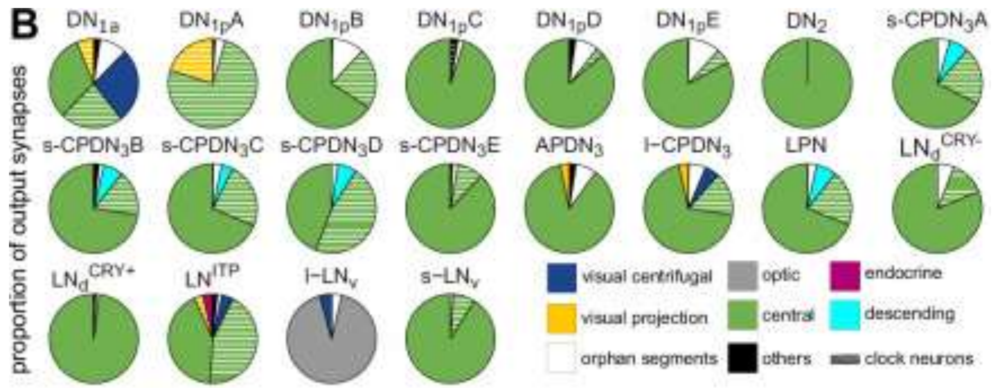
Reinhard N. *et al. Nat Commun*. 2024

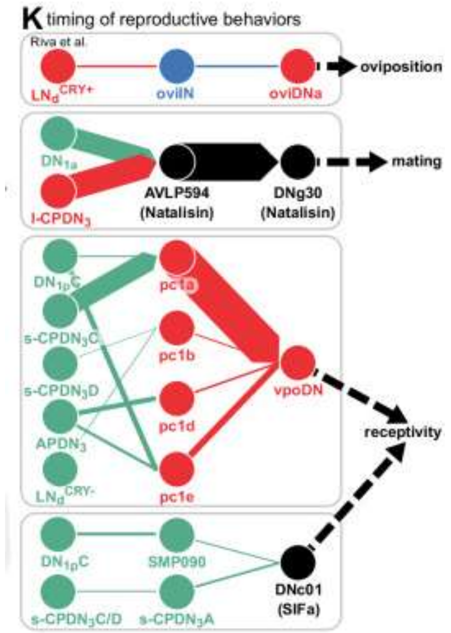
The upstream and downstream neural networks centered on rhythmic neurons are described in more detail



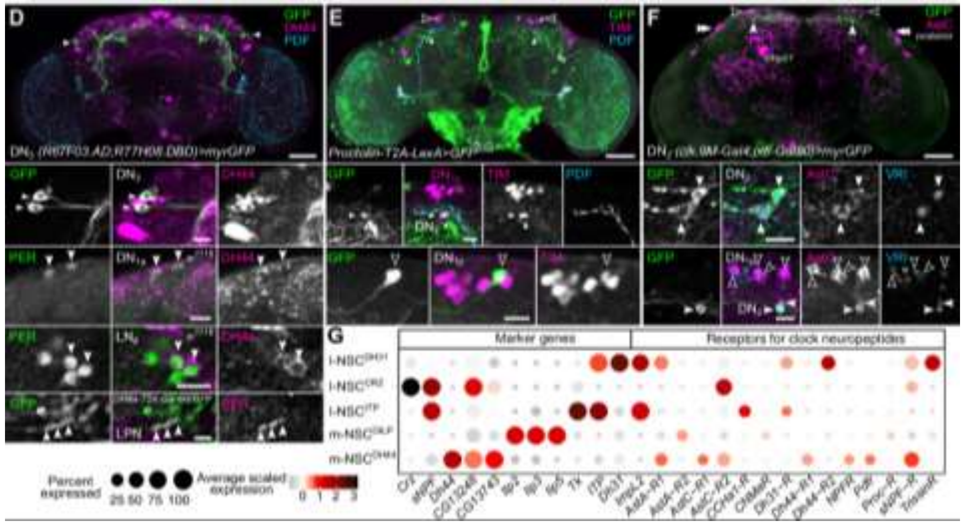


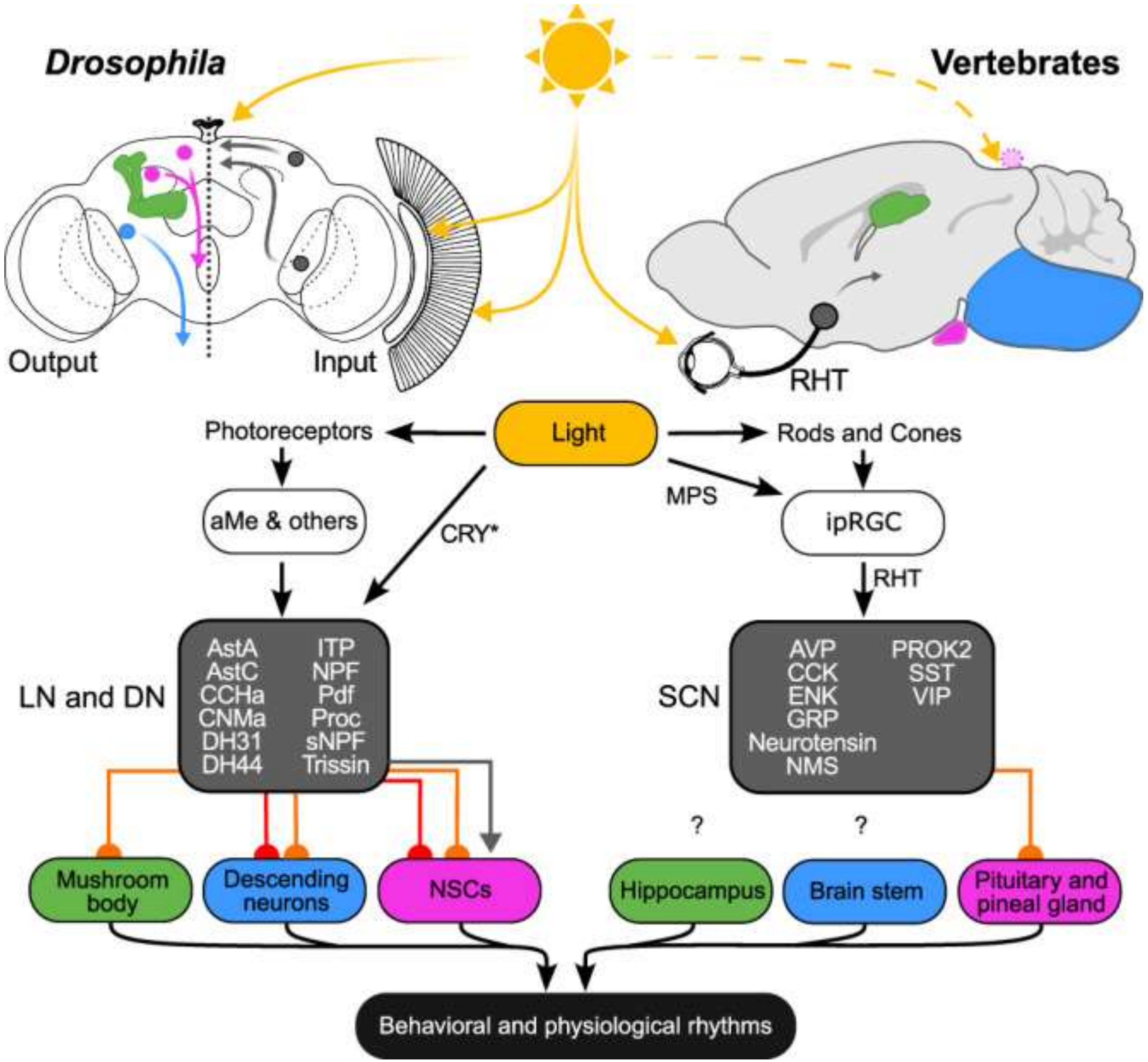






Reinhard N. *et al. Nat Commun*. 2024


D
E
F
G
Marker genes
Receptors for clock neuropeptides


Drosophila
Vertebrates
Output
Input
RHT
Photoreceptors
Light
Rods and Cones
MPS
aMe & others
CRY*
ipRGC
RHT
LN and DN
AstA
AstC
CCHa
CNMa
DH31
DH44
ITP
NPF
Pdf
Proc
sNPF
Trissin
SCN
AVP
CCK
ENK
GRP
Neurotensin
NMS
PROK2
SST
VIP
?
?
Mushroom body
Descending neurons
NSCs
Hippocampus
Brain stem
Pituitary and pineal gland
Behavioral and physiological rhythms

郭方

教授、博士生导师

地址：医学院教学楼A406

电话：0571-88206510

E-mail：gfang@zju.edu.cn

实验室网站 ：https://person.zju.edu.cn/guofang#0

研究方向 ：生物节律调控行为的分子和神经机制

Current Biology

Article

Regulation of pre-dawn arousal in *Drosophila* by a pair of trissinergic descending neurons of the visual and circadian networks

Highlights

- DNp27 neurons integrate circadian and visual signals
- Calcium oscillations in DNp27 peak at night and decline at day
- Activating trissinergic DNp27 reduces activity, and silencing advances the morning peak
- DNp27 inhibits light-responsive activity, promoting sleep stability before dawn

Authors

Ruihan Jiang, Yue Tian, Xin Yuan, Fang Guo

Correspondence

gfang@zju.edu.cn

In brief

Jiang et al. investigate two trissinergic DNp27 neurons in the *Drosophila* brain, which exhibit extensive innervation and integrate circadian and visual inputs. These neurons modulate the onset of the morning anticipation peak through Trissin-TrissinR signaling, inhibiting activity in downstream brain regions to regulate arousal thresholds.

PLOS BIOLOGY

RESEARCH ARTICLE

Temperature cues are integrated in a flexible circadian neuropeptidergic feedback circuit to remodel sleep-wake patterns in flies

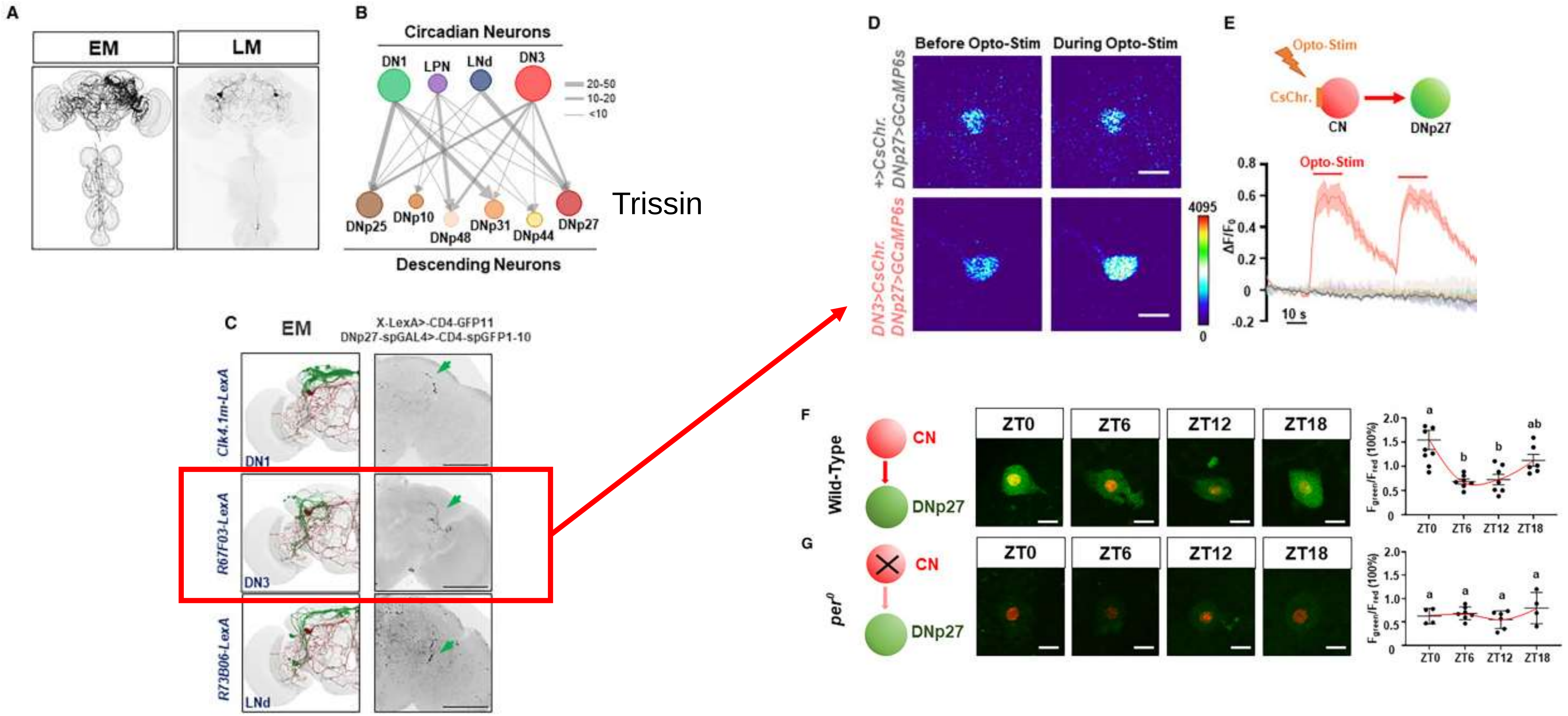
Xin Yuan[1,2,3], Hailiang Li[2,3,4], Fang Guo[1,2,3,4*]

1 Department of Neurology of Children's Hospital and School of Brain Science and Brain Medicine, Zhejiang University School of Medicine, Hangzhou, China, 2 MOE Frontier Science Center for Brain Research and Brain-Machine Integration, State Key Laboratory of Brain-machine Intelligence, Zhejiang University, Hangzhou, China, 3 NHC and CAMS Key Laboratory of Medical Neurobiology, Zhejiang University, Hangzhou, China, 4 Department of Neurobiology, Department of Neurology of Sir Run Run Shaw Hospital and School of Brain Science and Brain Medicine, Zhejiang University School of Medicine, Hangzhou, China

* gfang@zju.edu.cn

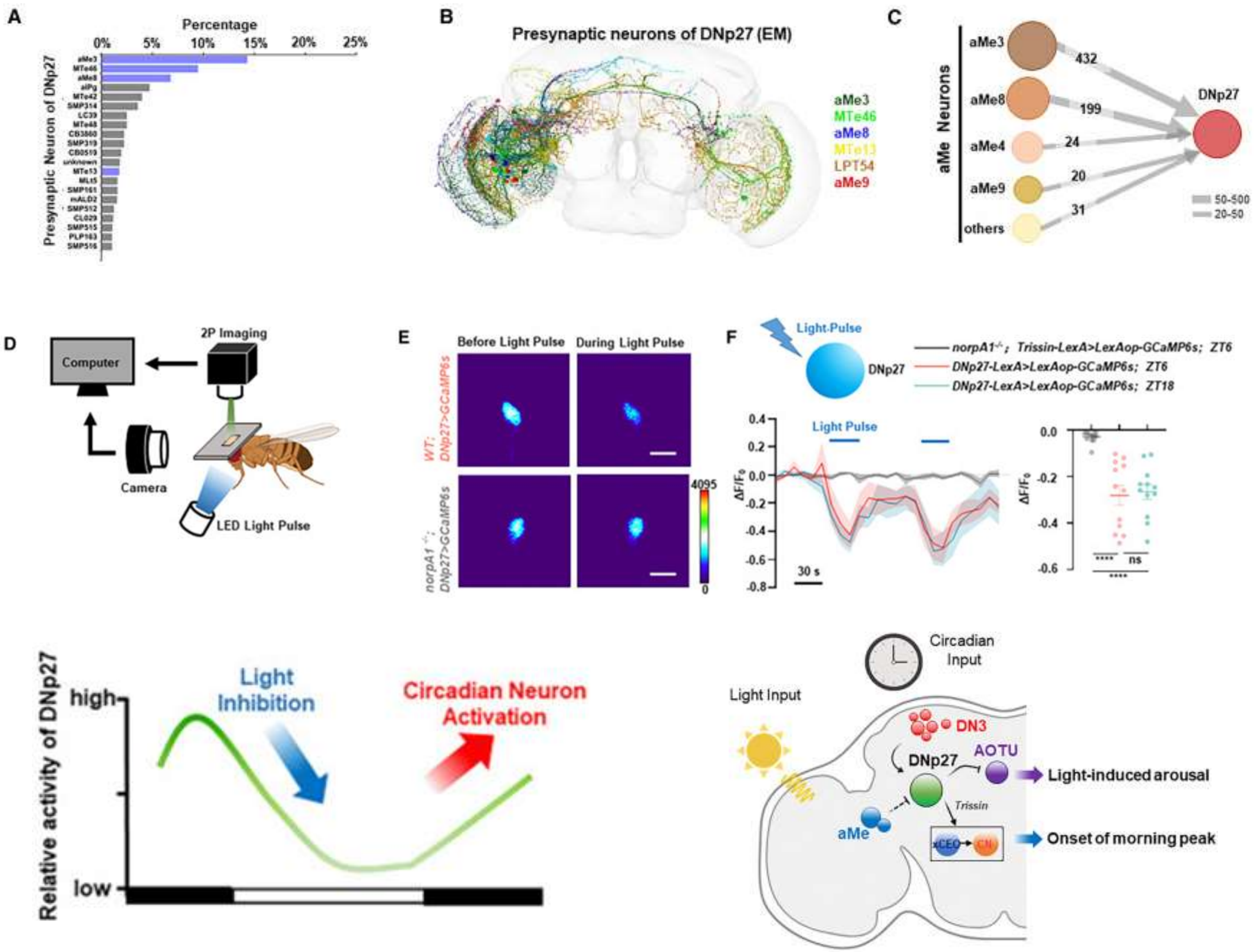
Check for updates

Searching in Flywire: DNp27 receives excitatory input from circadian neurons DN3



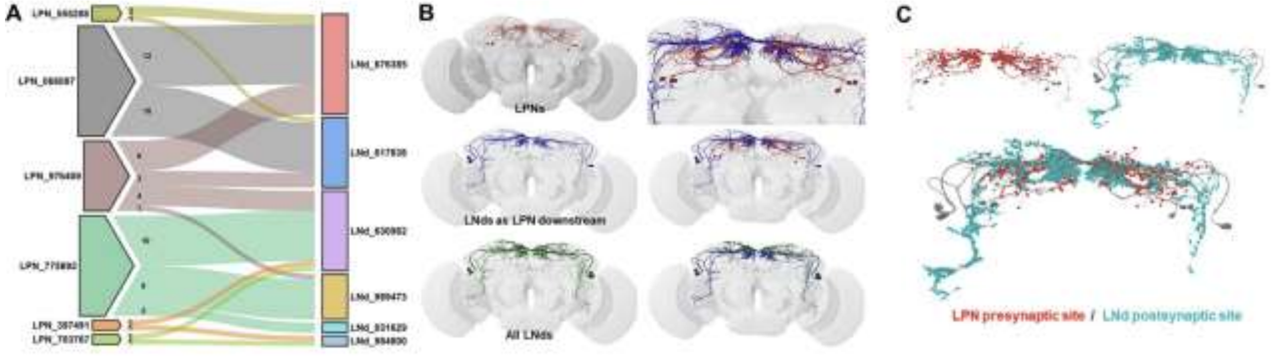
Jiang R. *et al. Curr Biol.* 2025

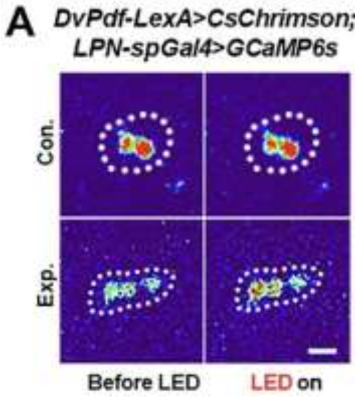
Nighttime circadian excitatory input and daytime photo-inhibitory input induce the daily fluctuating calcium pattern of DNp27

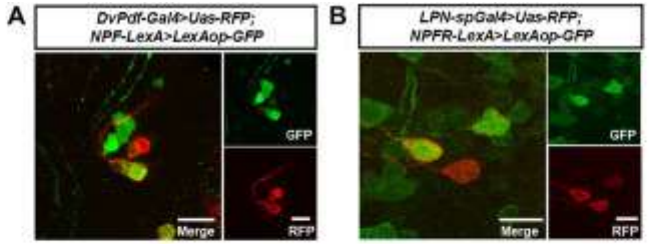


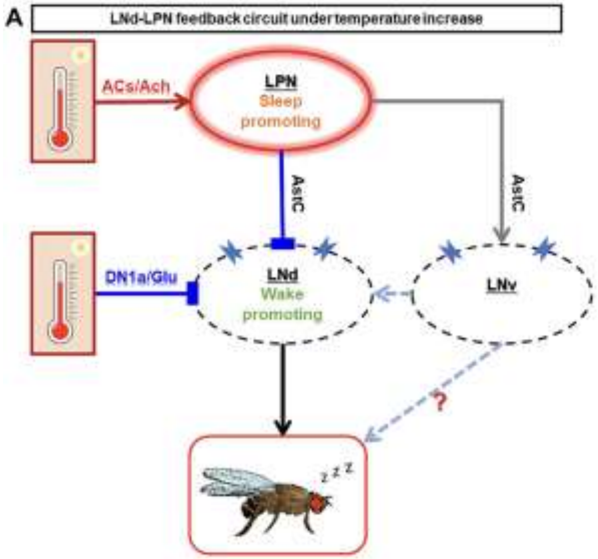
Jiang R. *et al. Curr Biol.* 2025

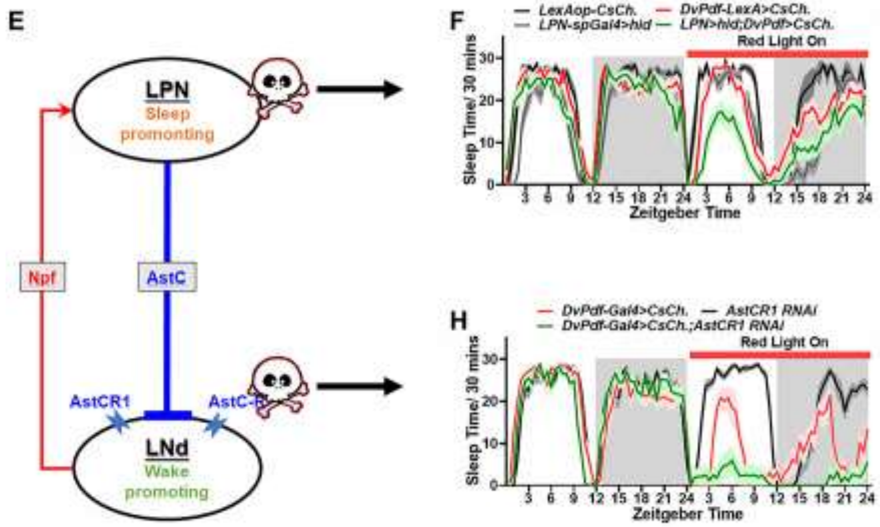
Temperature cues are integrated in a flexible circadian neuropeptidergic feedback circuit to remodel sleep-wake patterns in flies







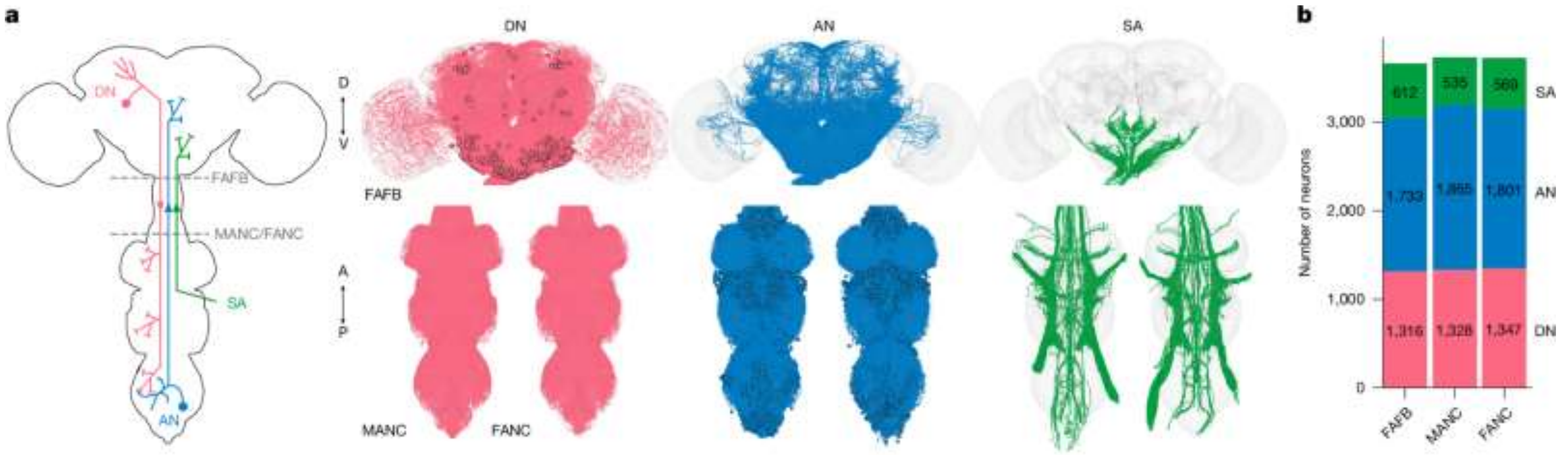


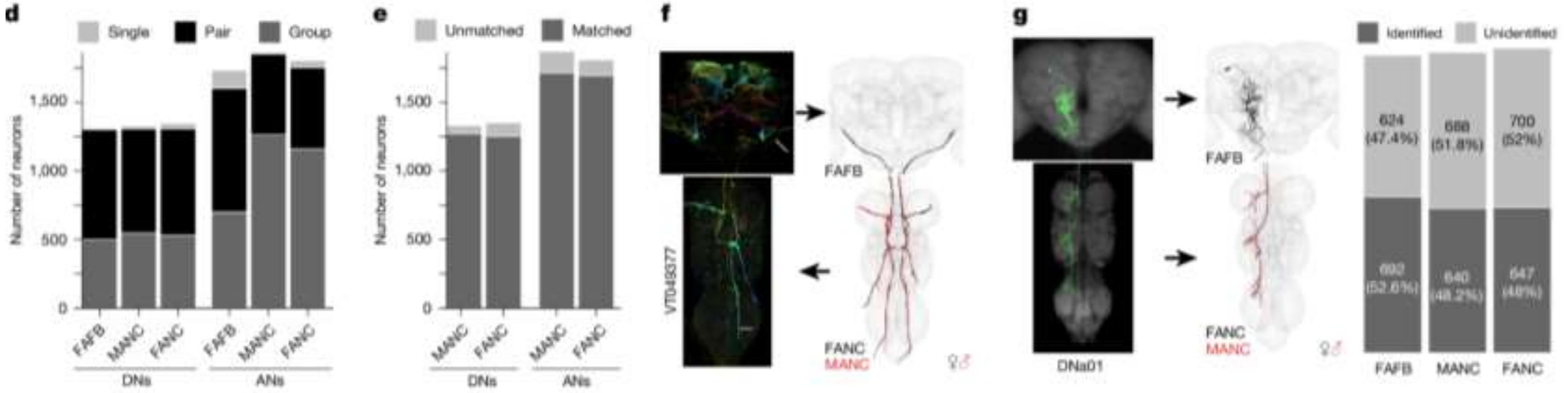


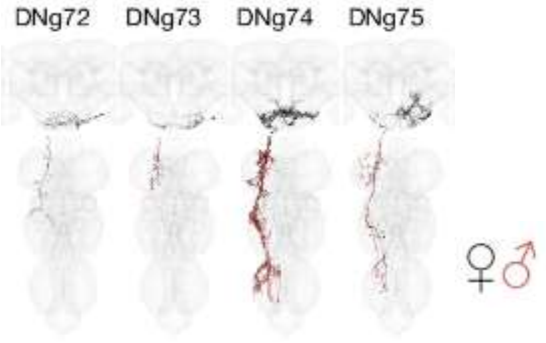
Yuan X, *et al. PLoS Biol.* 2024

Matching neurons across three datasets

female adult fly brain (FAFB-FlyWire), female adult nerve cord (FANC), MANC



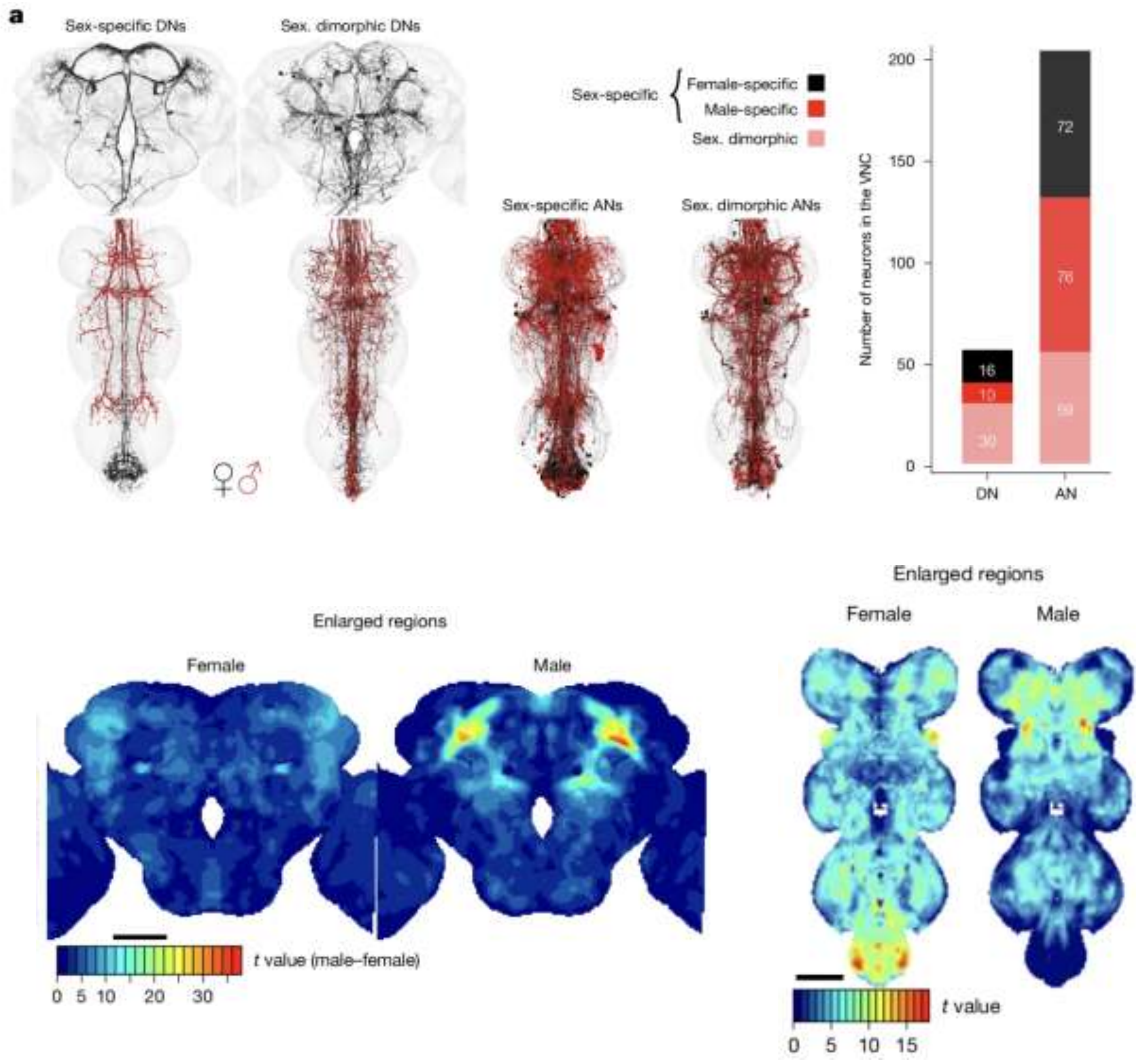




https://tinyurl.com/NeckConnective
https://github.com/flyconnectome/2023neckconnective

Stürner, T. et al.*Nature*. 2025.

Sex-specific or sexually dimorphic neurons



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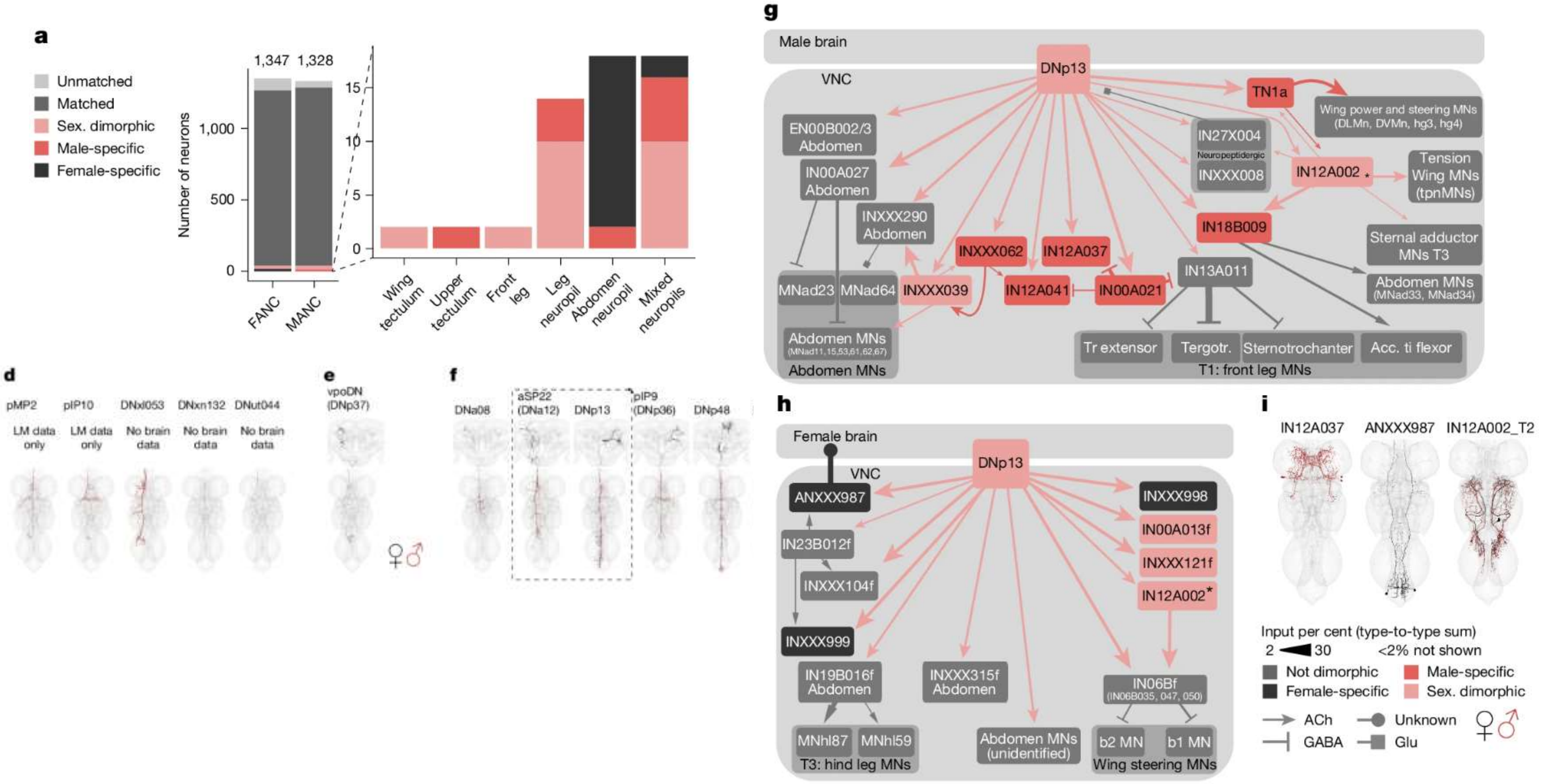
Sexually dimorphic and sex-specific DNs.



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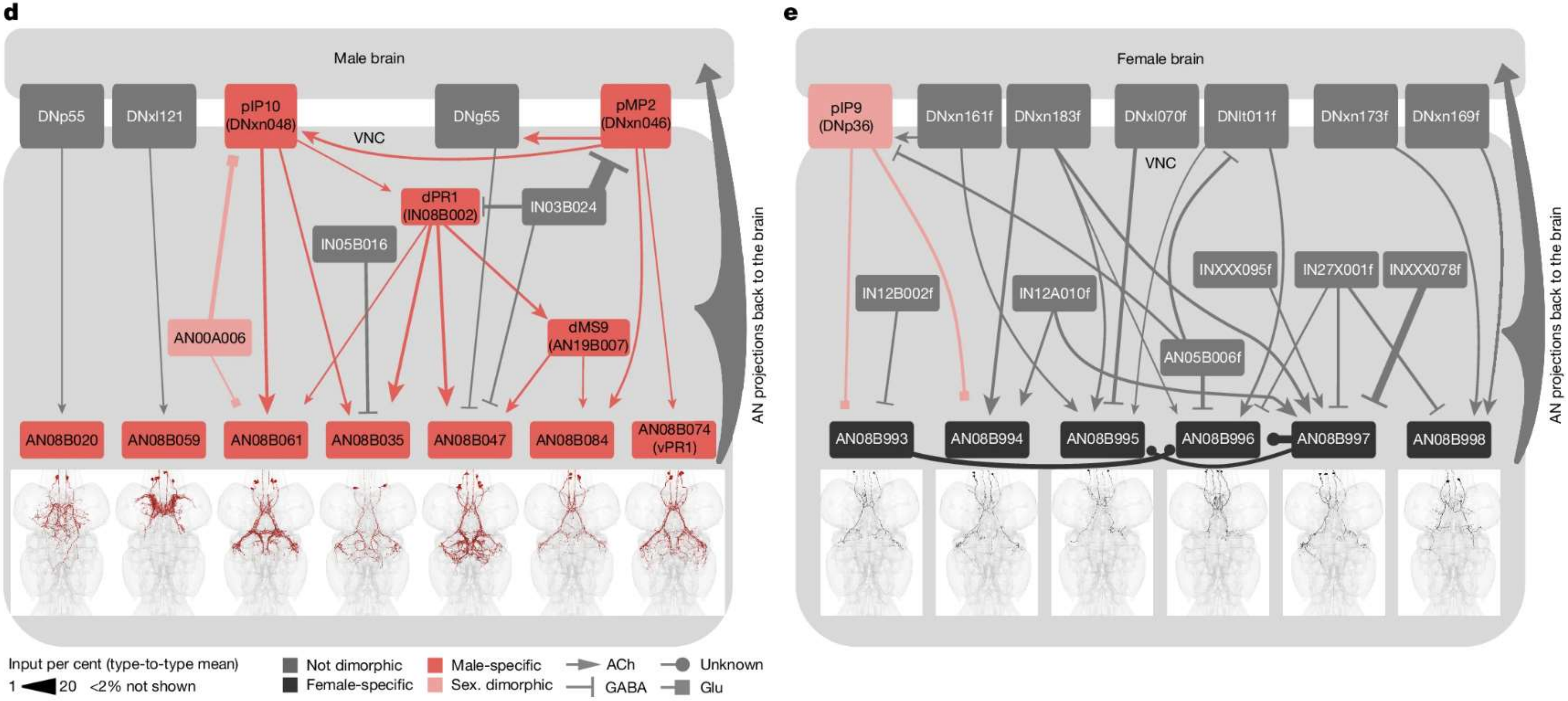
Sexually dimorphic and sex-specific ANs



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Article

A *Drosophila* computational brain model reveals sensorimotor processing

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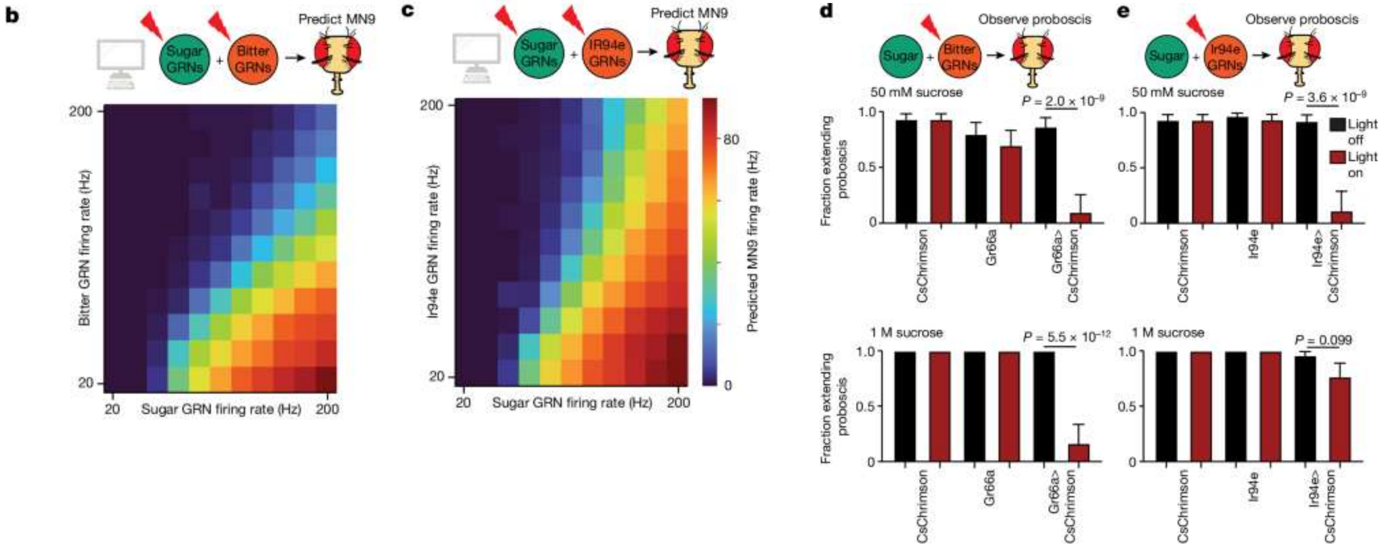
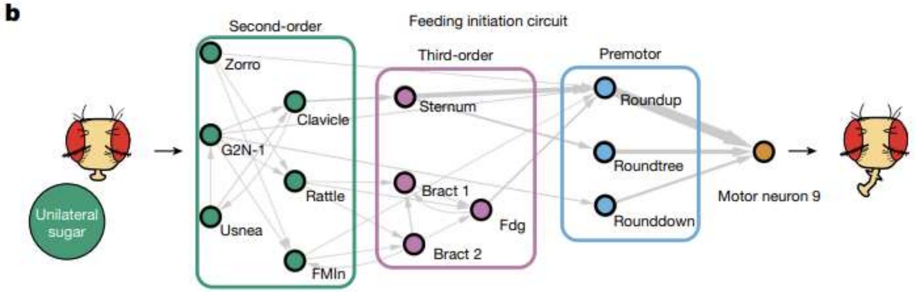
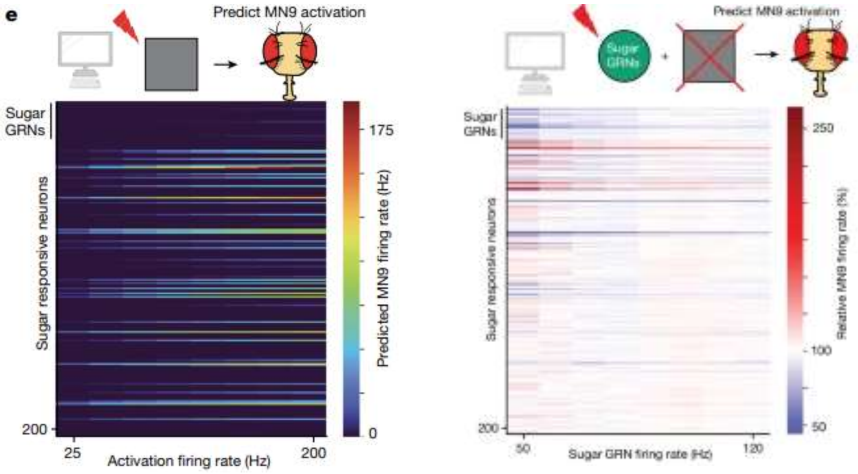
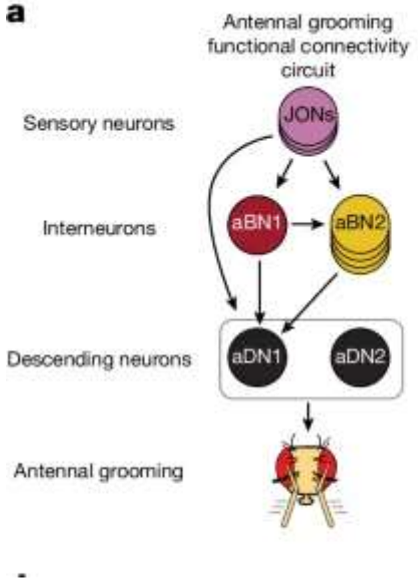
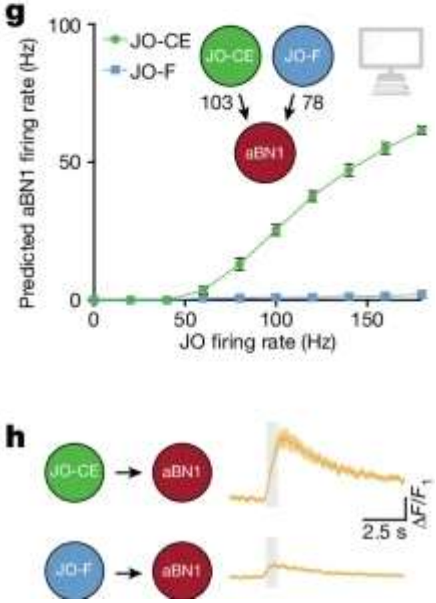


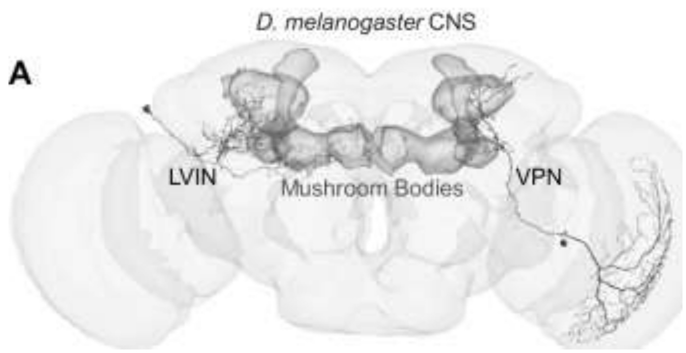


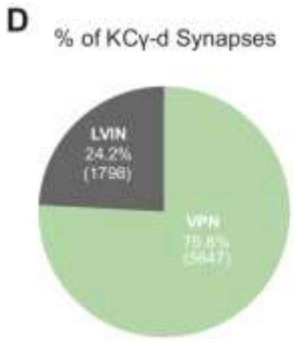


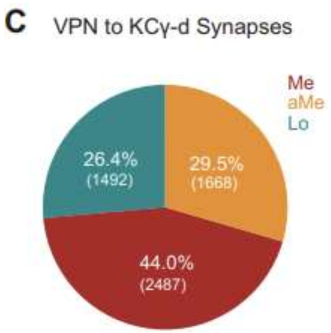


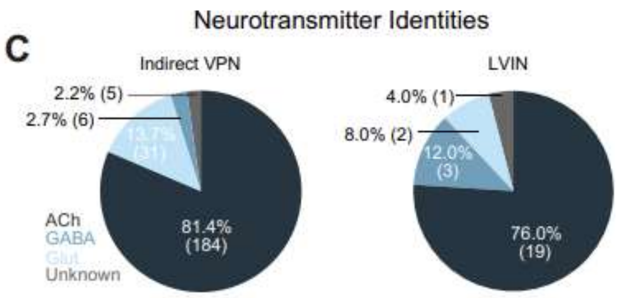


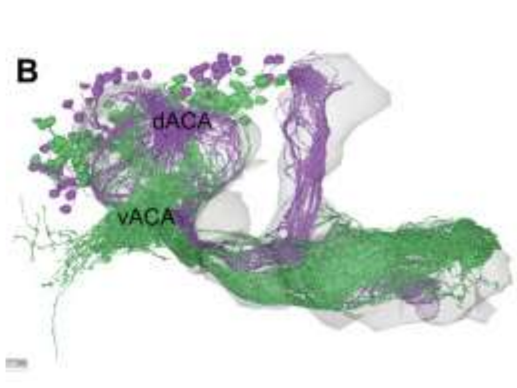
Diversity of visual inputs to Kenyon cells of the *Drosophila* mushroom body

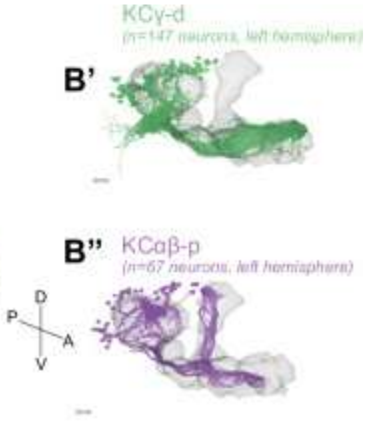


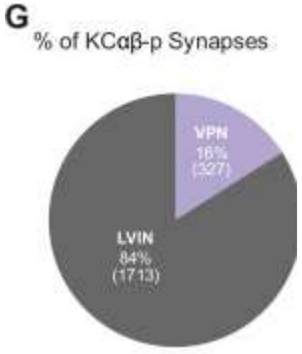


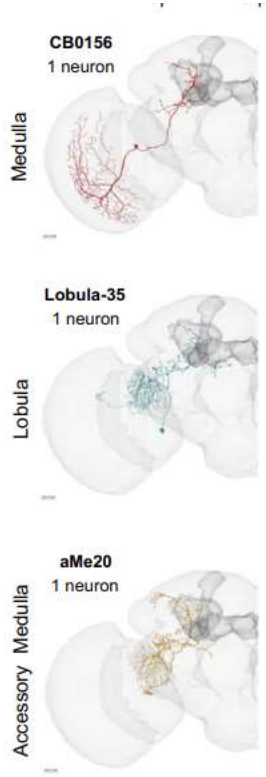


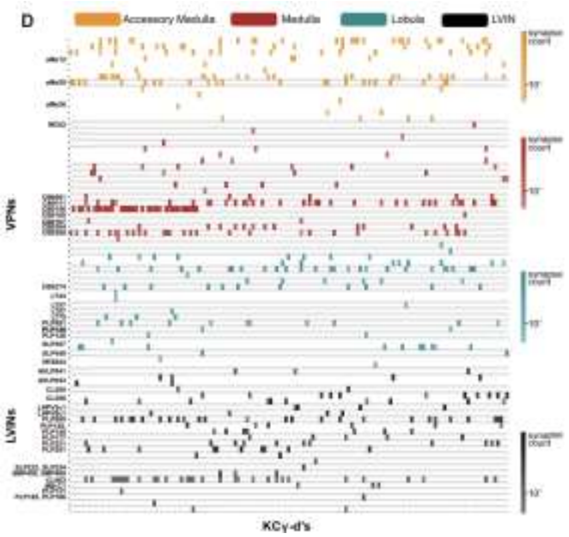












1. Identify inputs to visual Kenyon cells using the flywire adult whole-brain connectome.
2. Visual coding in the mushroom body, like olfactory coding, is sparse, distributed, and combinatorial.
3. The specific input repertoire to the smaller population of visual Kenyon cells

Ganguly I. *et al.Nat Commun*.2024

Conclusions：

- FlyWire has been well applied in various research fields, such as courtship, sleep rhythms, etc.
- The application of FlyWire has largely facilitated the search for potential neurons and the exploration of the connections in neural circuits.
- The use of FlyWire should be rational, as it is based on neural connection mechanisms and the brain structure of female.

Thanks

25.5.29