Ways of exploring:

Key and new techniques that have advanced the research in neural circuits of Drosophila and other model animals

Sun MS, Zhao H, Chen J

Feburary 22th, 2019

season 1

Part I. Animal models in neurobiology research and genetic & molecular techniques in neural circuits research.

Part II. The way of Recording neuronal activity.

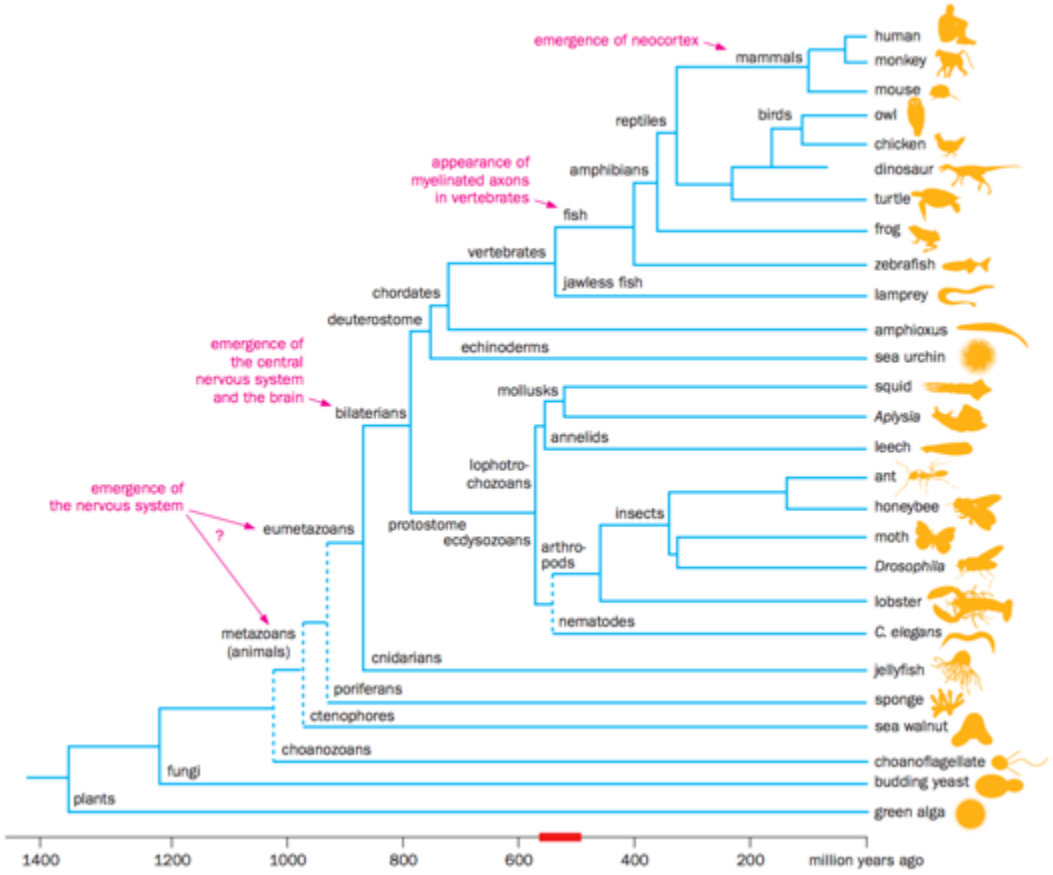
Part III. Manipulating neuronal activity and behavioral analyses.

Part I. Animal models in neurobiology research and genetic & molecular techniques in neural circuits research

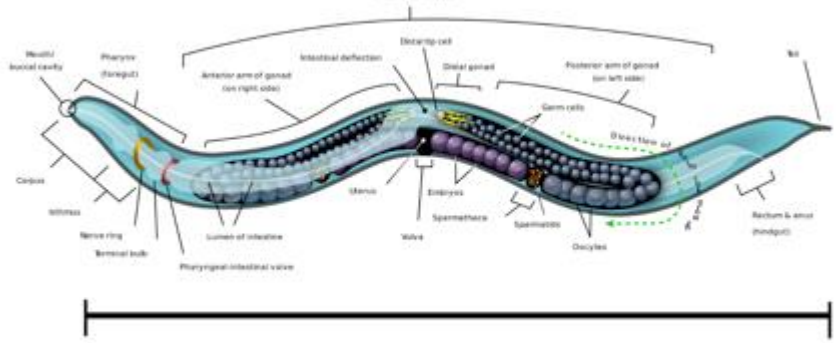
Sun Mengshi

I. Animal models in neurobiology research

‘ideal’ animal models:
A simple genome and short generation time;
Complex brain functions and behaviors to extrapolate findings more easily to humans;
Large and easily identifiable neurons.



- *Drosophila* and *C. elegans* allow sophisticated genetic manipulations



In 1963, Sydney Brenner proposed research into C. elegans .
It is one of the simplest organisms with a nervous system .
In the wild: lives in the soil and eats bacteria.

In 2002, the Nobel Prize in Physiology or Medicine was awarded to Sydney Brenner, H. Robert Horvitz, and John Sulston for their work on the genetics of organ development and programmed cell death in C. elegans.

The 2006 Nobel Prize in Physiology or Medicine was awarded to Andrew Fire and Craig C. Mello for their discovery of RNA interference in C. elegans.

In 2008, Martin Chalfie shared a Nobel Prize in Chemistry for his work on green fluorescent protein

https://wormbase.org

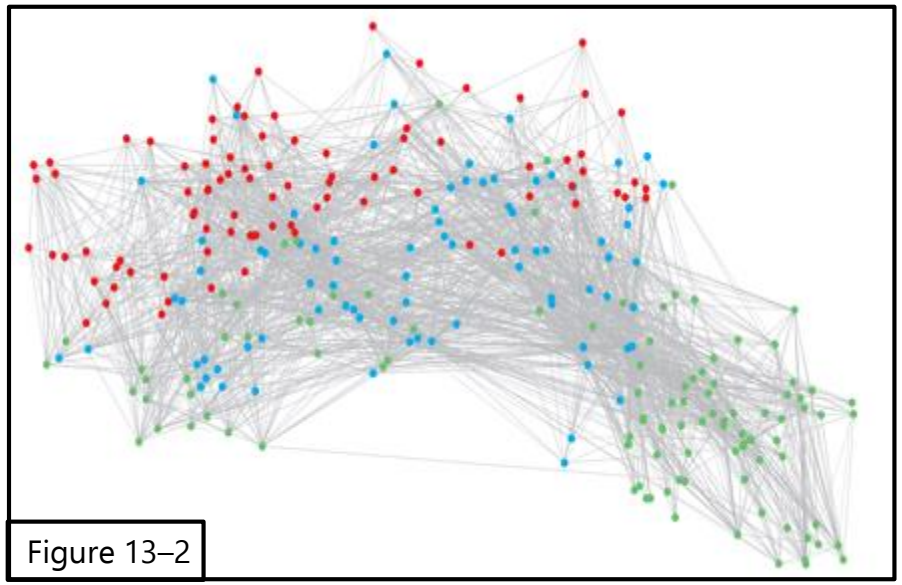


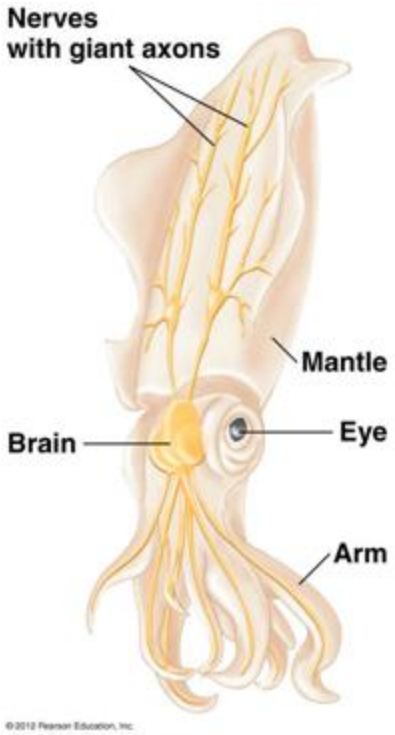
Figure 13–2

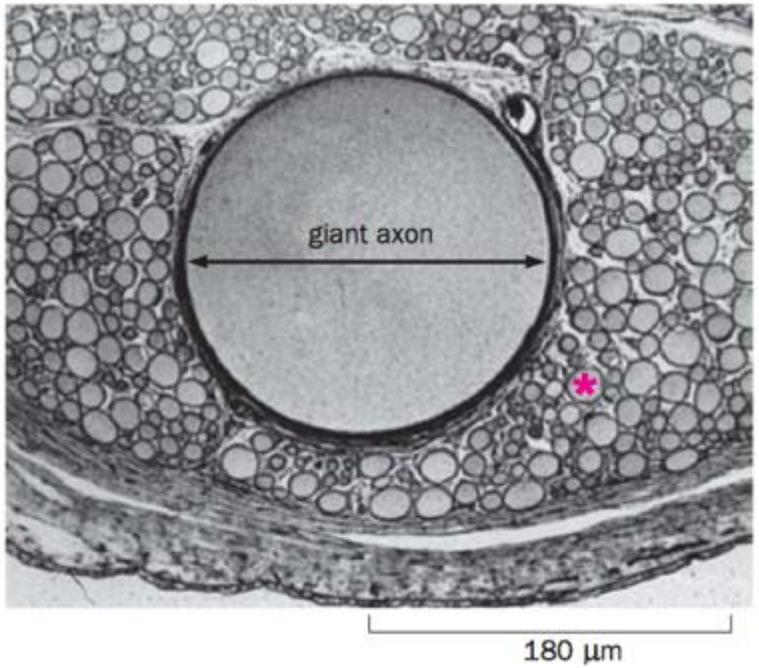
Red:
sensory neurons;

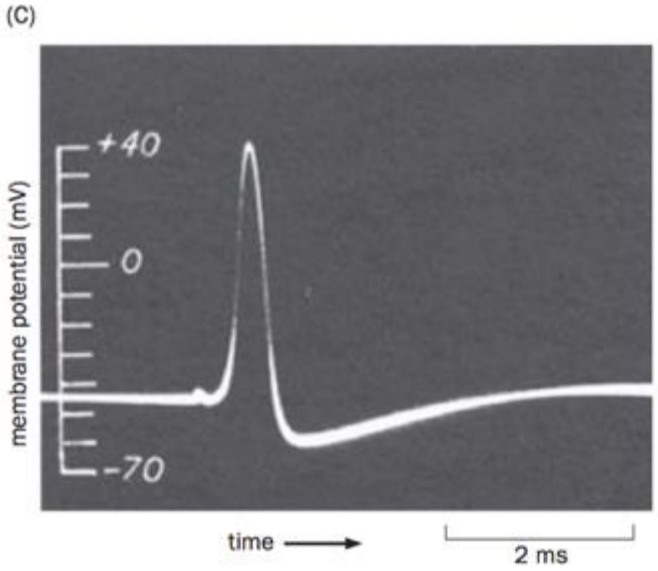
blue:
interneurons;

green:
motor neurons.

- Some invertebrates provide large, identifiable neurons for electrophysiological investigations



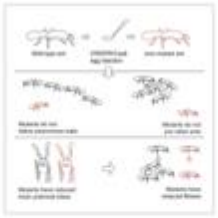




- squid *Loligo* giant axon.

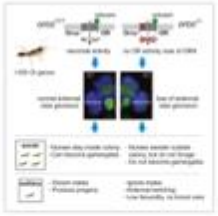
Principles of neurobiology, 2015

- New tools, new insights — probing social behavior in ants



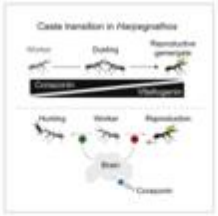
orco Mutagenesis Causes Loss of Antennal Lobe Glomeruli and Impaired Social Behavior in Ants

Waring Trible, Leonora Olivos-Cisneros, Sean K. McKenzie, Jonathan Saragosti, Ni-Chen Chang, Benjamin J. Matthews, Peter R. Oxley, Daniel J.C. Kronauer
Cell, Vol. 170, Issue 4, p727–735.e10
Published in issue: August 10, 2017
Open Archive
In Brief | Full-Text HTML | PDF



An Engineered *orco* Mutation Produces Aberrant Social Behavior and Defective Neural Development in Ants

Hua Yan, Comzit Opachaloemphan, Giacomo Mancini, Huan Yang, Matthew Gallitto, Jakub Mlejnek, Alexandra Leibholz, Kevin Haight, and others
Cell, Vol. 170, Issue 4, p736–747.e9
Published in issue: August 10, 2017
Open Archive
In Brief | Full-Text HTML | PDF

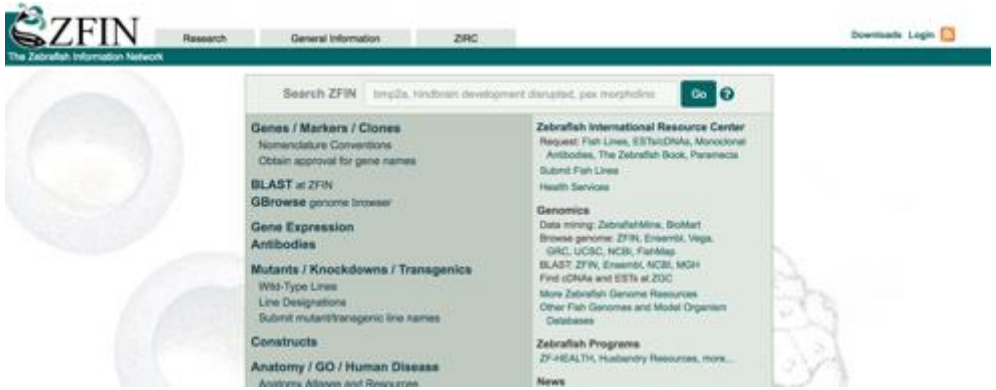


The Neuropeptide Corazonin Controls Social Behavior and Caste Identity in Ants

Janko Gospocic, Emily J. Shields, Karl M. Glastad, Yanping Lin, Clint A. Penick, Hua Yan, Alexander S. Mikheyev, Timothy A. Linksvayer, and others
Cell, Vol. 170, Issue 4, p748–759.e12
Published in issue: August 10, 2017
Open Archive
In Brief | Full-Text HTML | PDF

the ant Harpegnathos saltator

- Diverse vertebrate animals offer technical ease or special faculties



https://zfin.org/

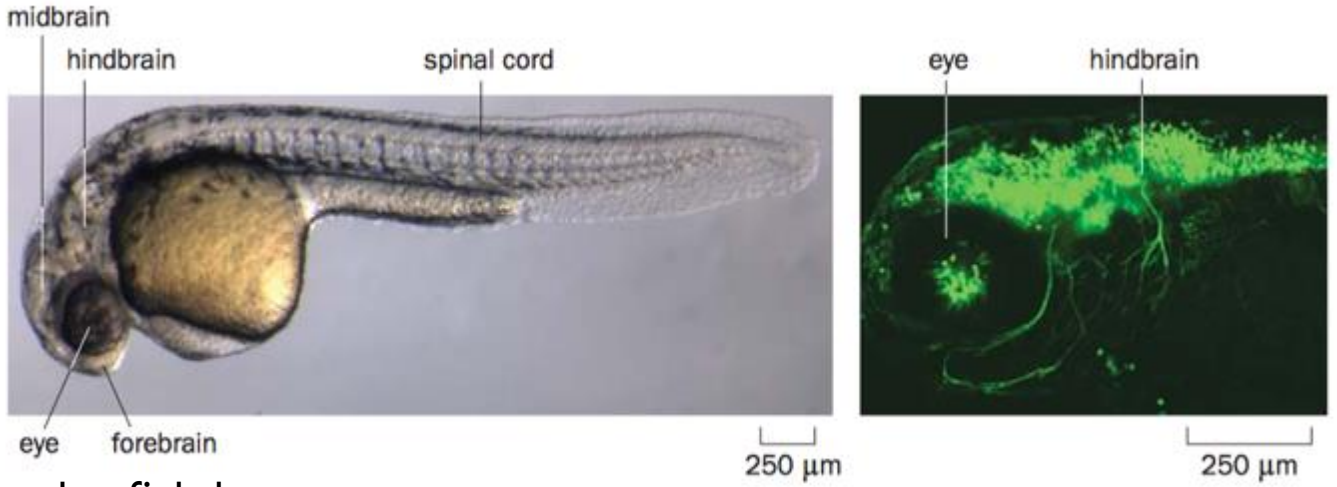
http://www.zfish.cn/

The use of zebrafish (Danio rerio) as a model organism began in the 1960s.

Its embryonic development is very rapid, and its embryos are nearly transparent;

As a vertebrate, the zebrafish has the same major organs and tissues as humans.

Zebrafish have the ability to regenerate their heart, hair cells, photoreceptor cells and retinal neurons.



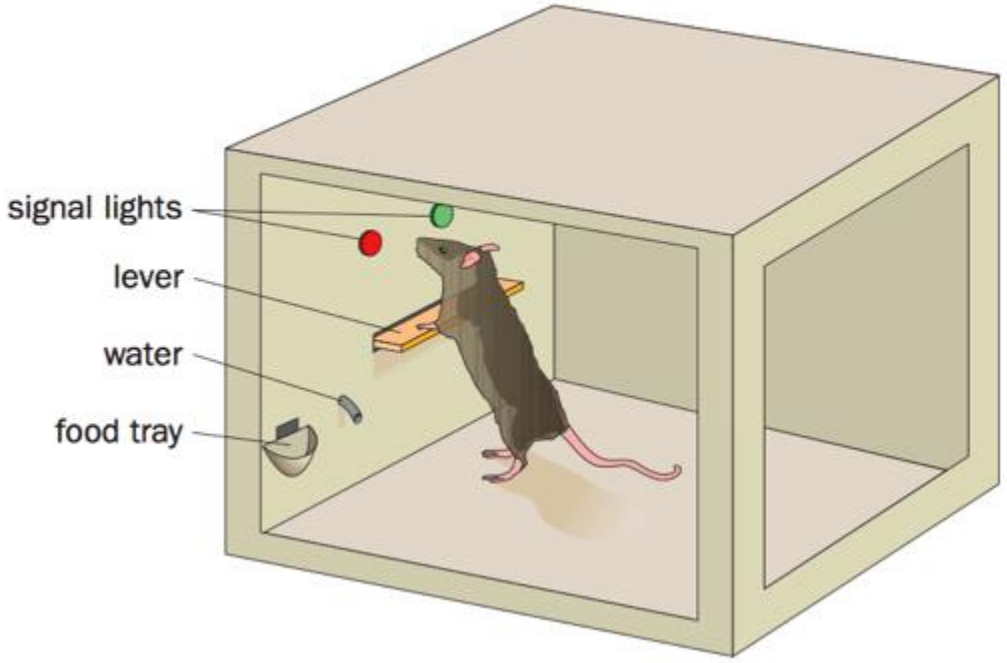
zebrafish larvae

Songbirds: communication neuroscience, to study vocalization and learning

Barn owls: to study audition because of their superb ability to locate sounds

Figure 1–5 Barn owls use their auditory system to locate prey in complete darkness. The image was constructed by superimposing a series of photographs taken with an infrared camera. (Courtesy of Masakazu Konishi.)

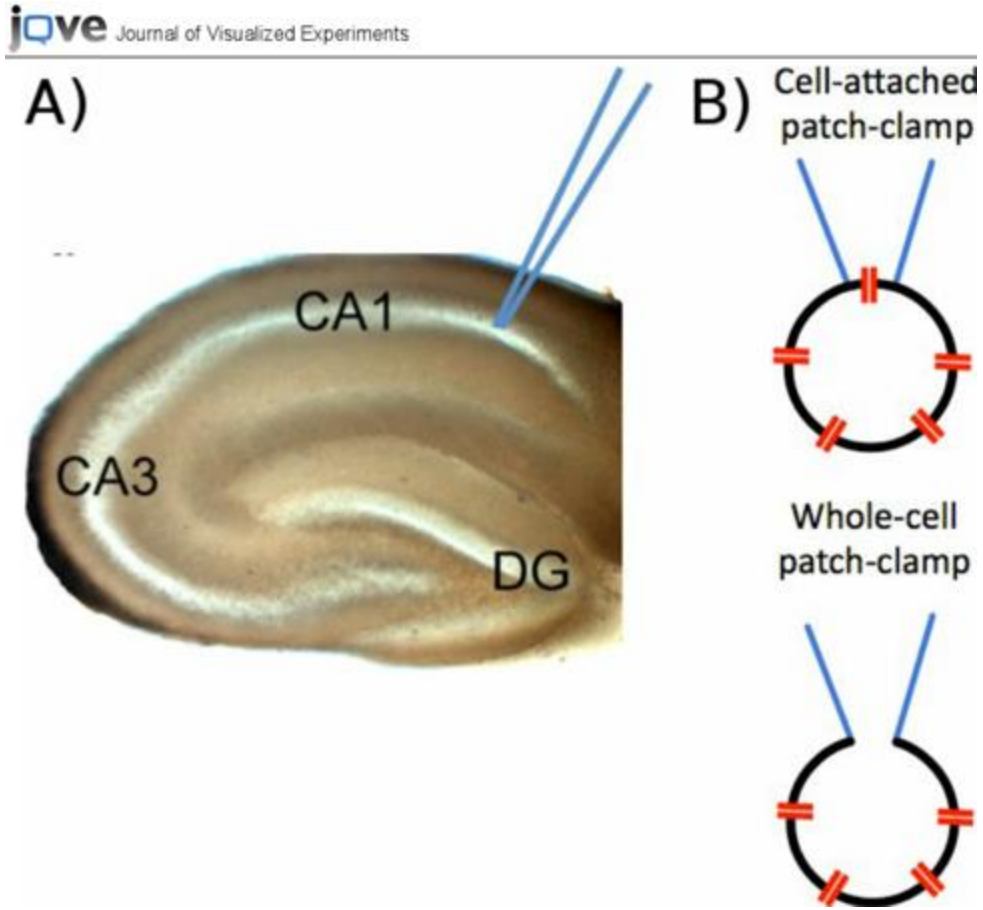
- Mice, rats, and nonhuman primates are important models for mammalian neurobiology research



operant conditioning (also called instrumental conditioning)

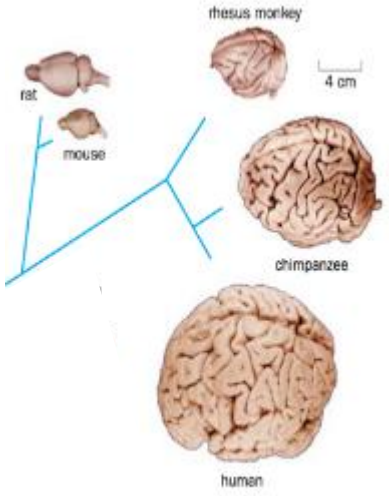
Figure 10–22

See Skinner BF [1938] The Behavior of Organisms. B.F. Skinner Foundation

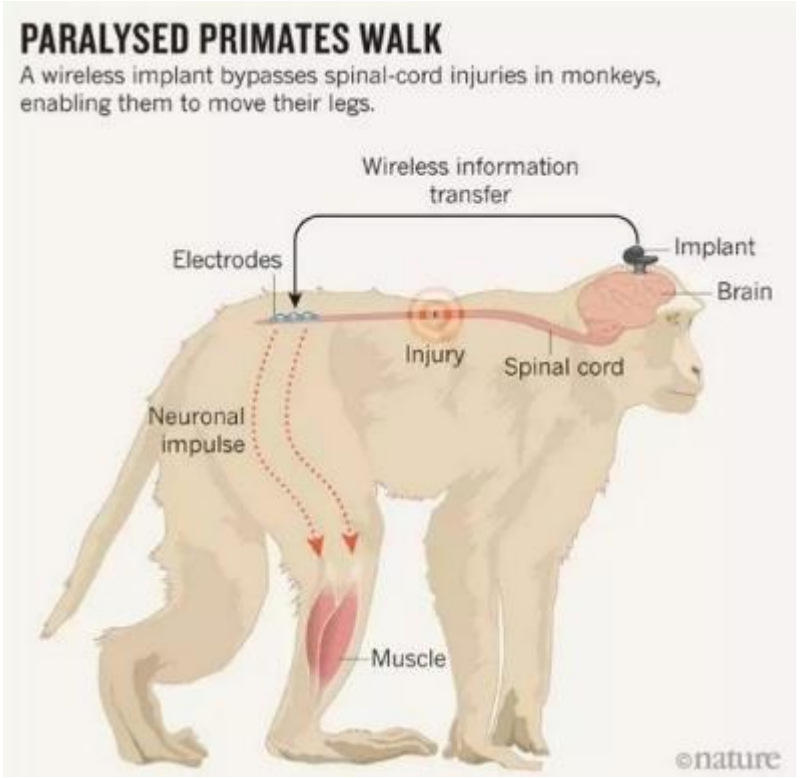


Rat hippocampal brain slice

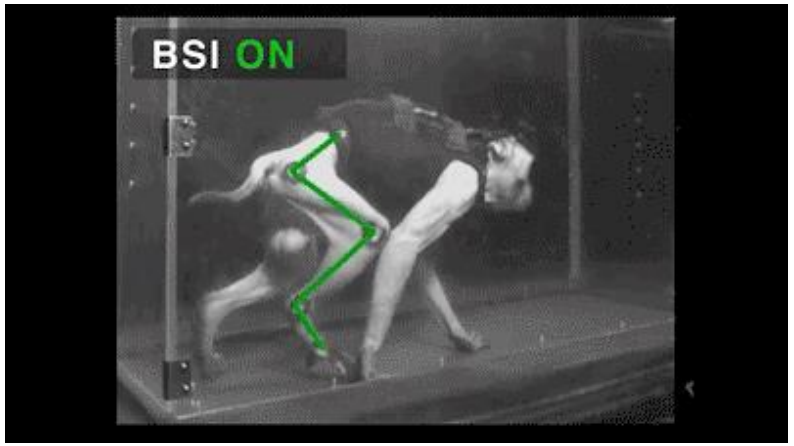
- Mice, rats, and nonhuman primates are important models for mammalian neurobiology research



http://www.brainmuseum.org/

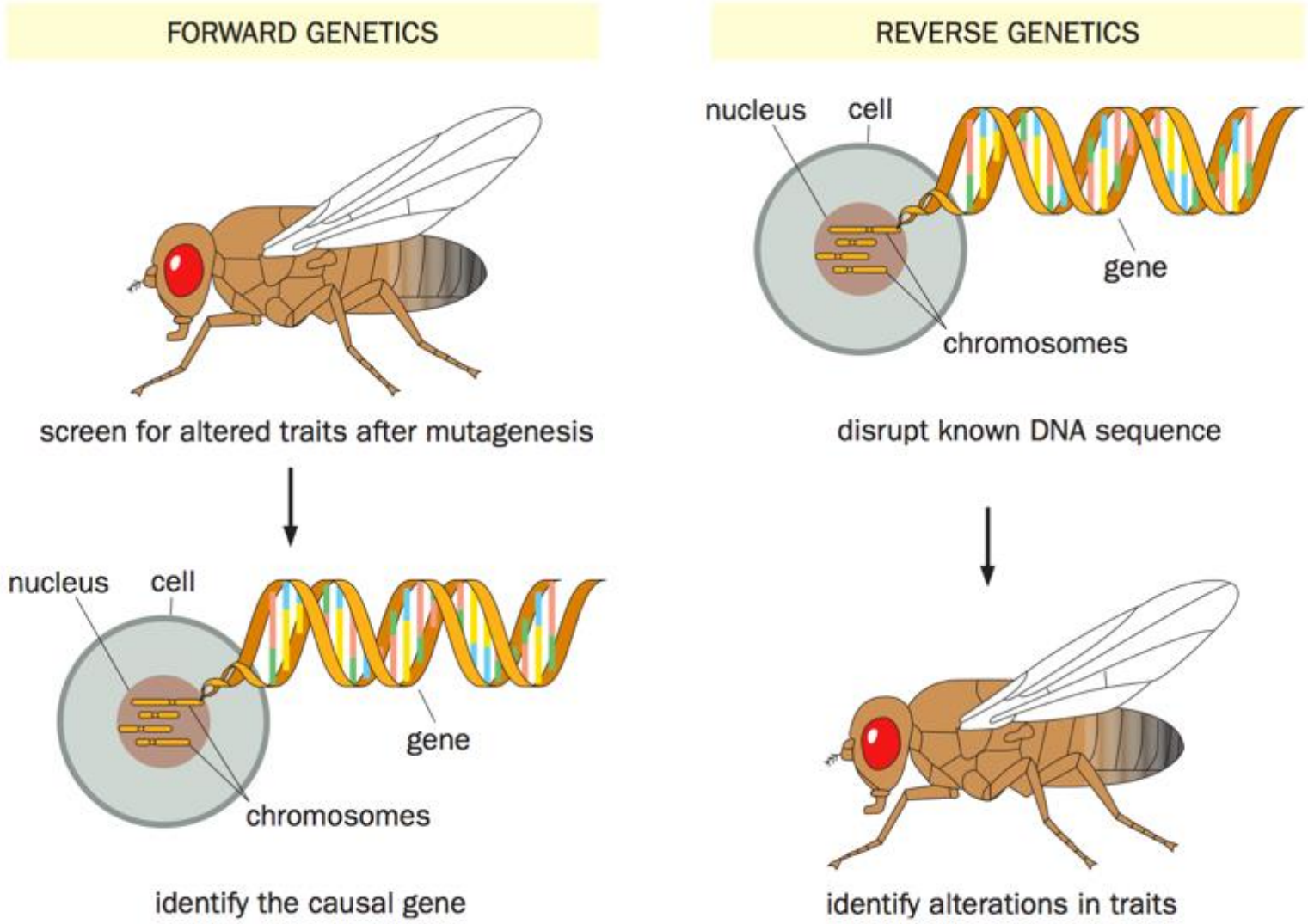


These cloned macaque monkeys are almost genetically identical, and share a mutation that disrupts their sleep cycle.



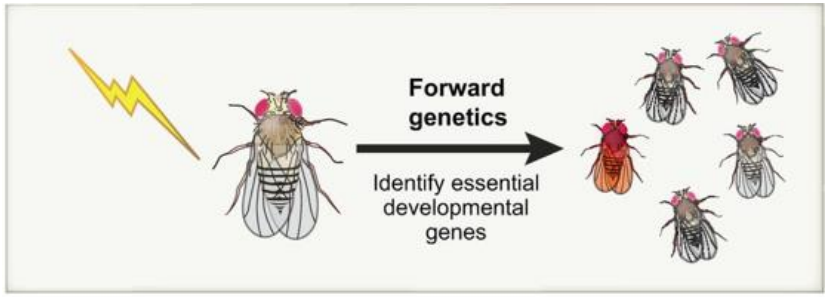
II. genetic & molecular techniques

To disrupt the function of an individual gene—**loss-of-function mutation**



Principles of neurobiology, 2015

- Forward genetics

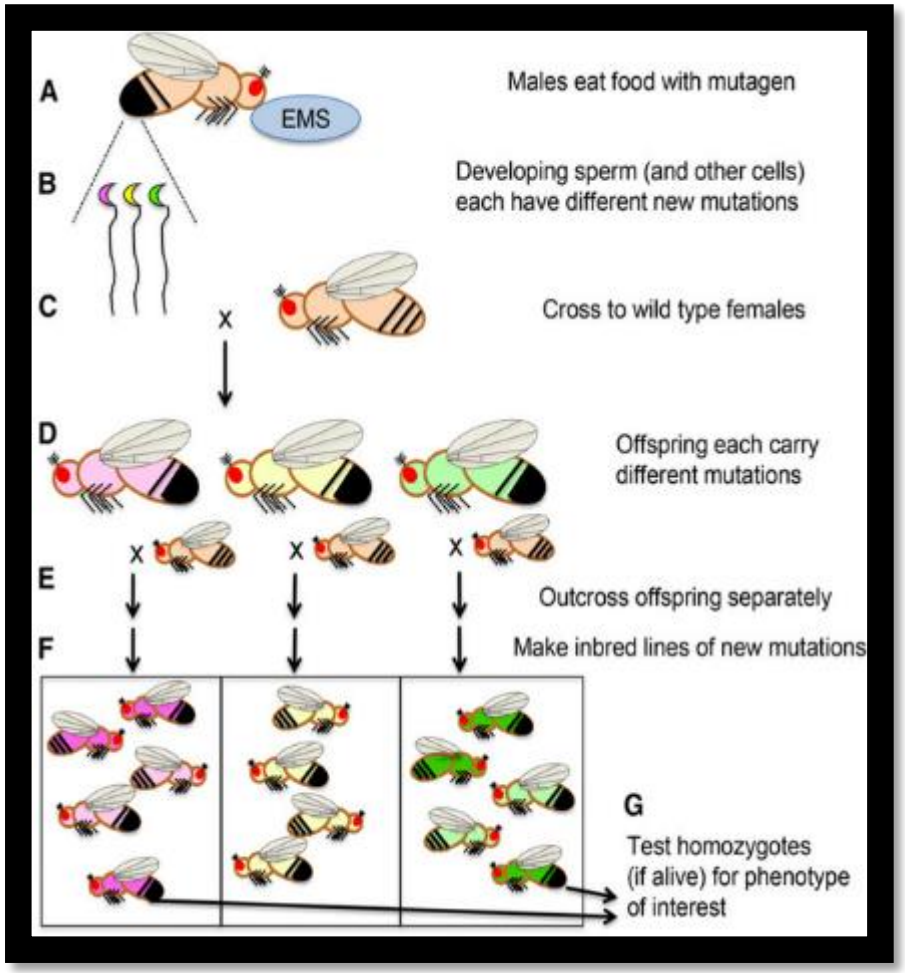


ex. *Drosophila fruitless* gene (derived from X-ray mutagenesis),

Drosophila Period gene and mouse _Clock_ gene

random mutagenesis：

chemical mutagens: EMS
radiation: X rays
transposon insertion: P-element

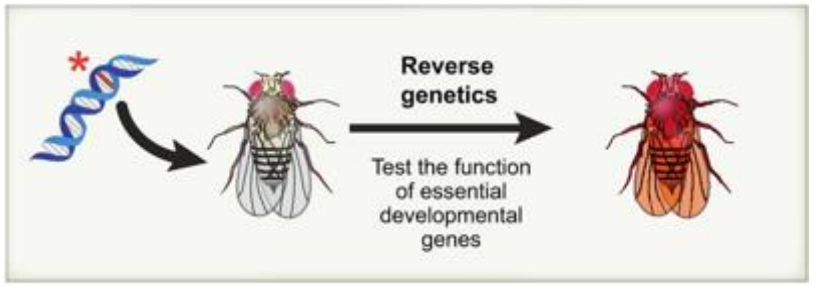


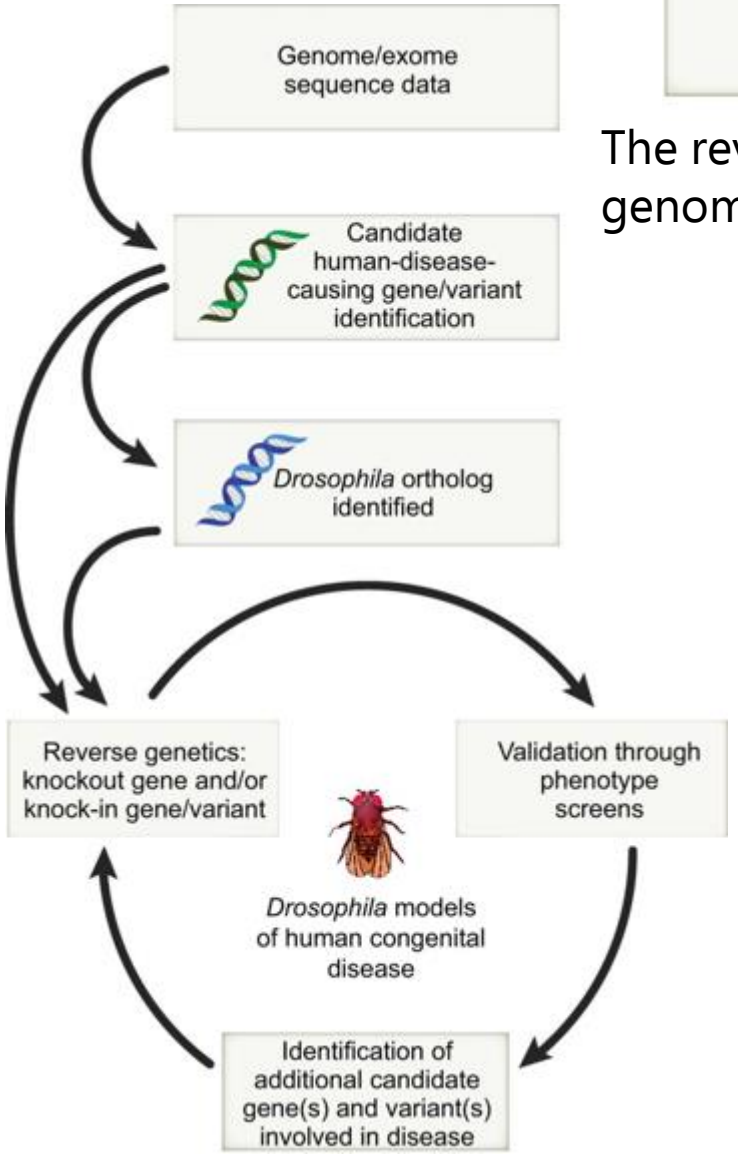
screen for dominant phenotypes;
screen males for X-linked recessive phenotypes

screen for recessive phenotypes

Hales, K. et al. 2015.

- Reverse genetics





The reverse approach became much more common only after the *D. melanogaster* genome was sequenced.

Knock-out

homologous recombination (Rong,2000)

zinc-finger nuclease (ZFN) and the transcription activator-like

effector nuclease (TALEN)

CRISPR/Cas9

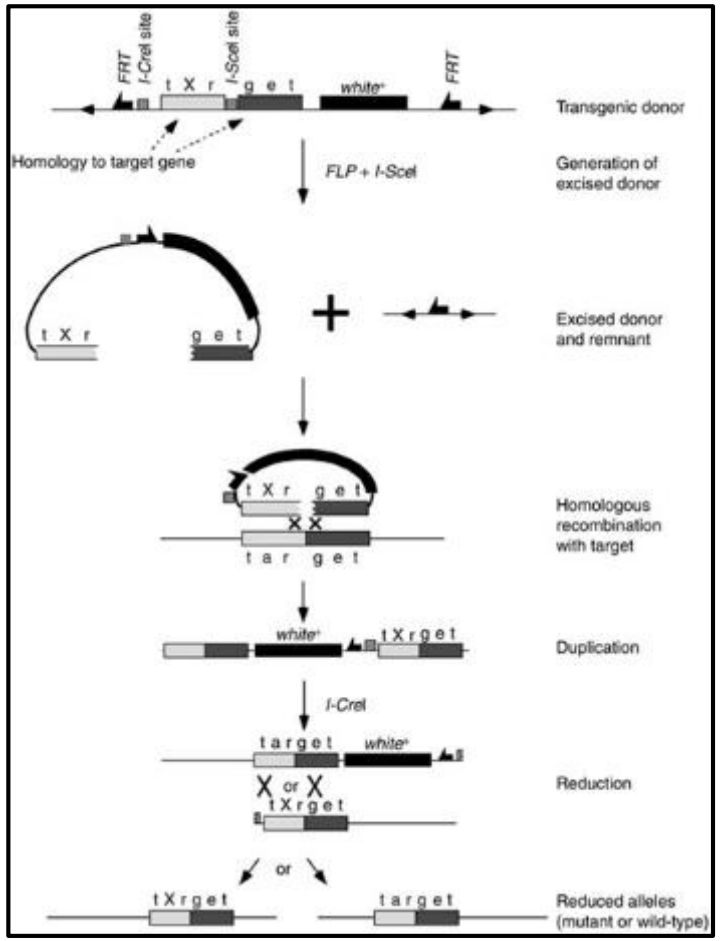
Knock-down

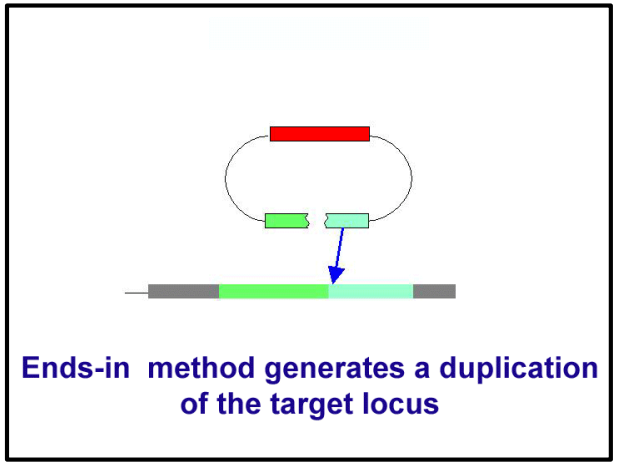
RNA interference

Matthew J. et al.2016.

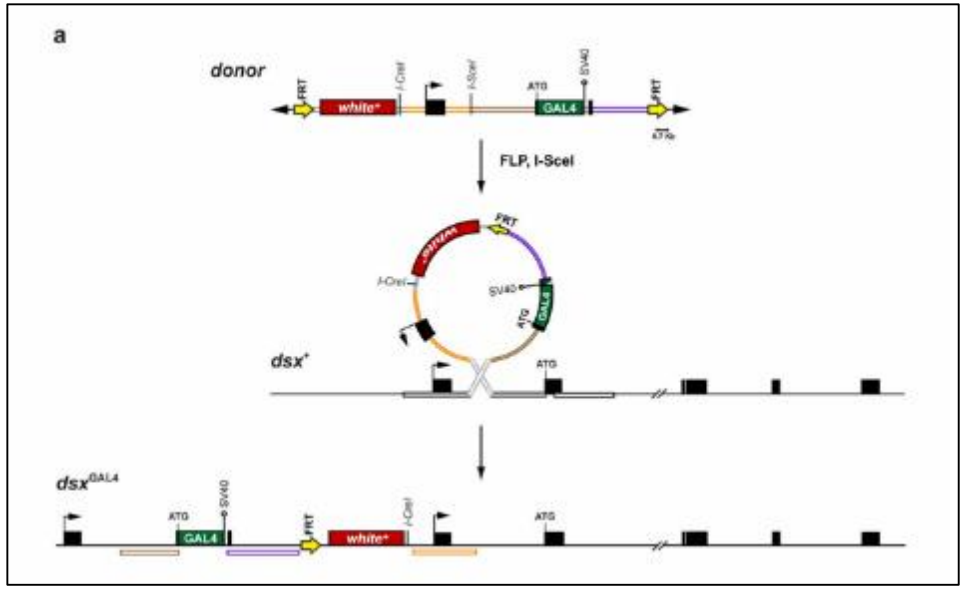
Hales, K. et al. 2015.

homologous recombination



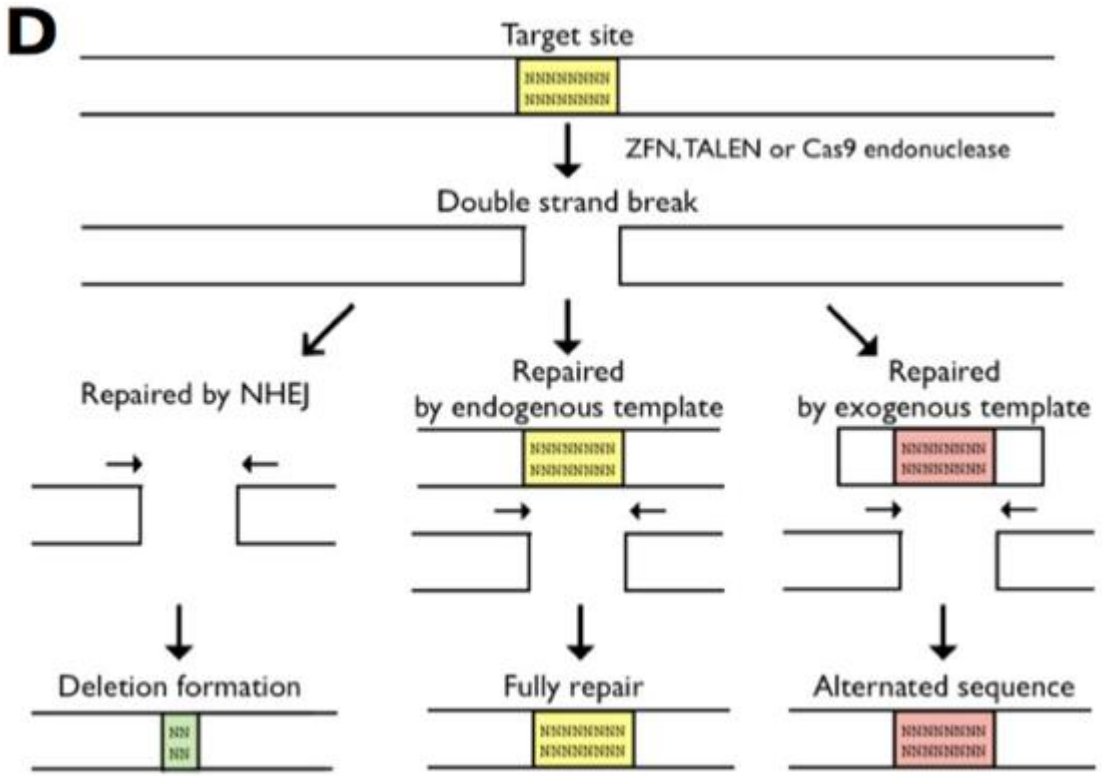


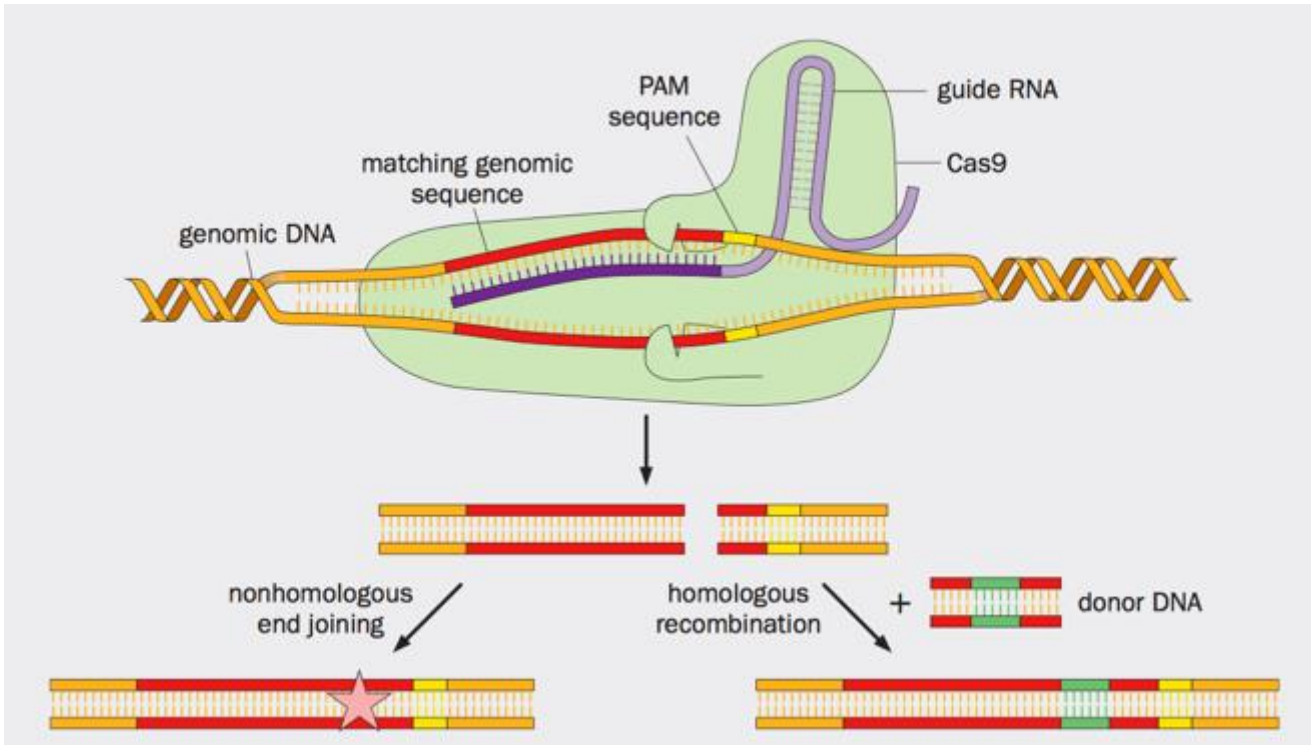
Ends-in method generates a duplication of the target locus



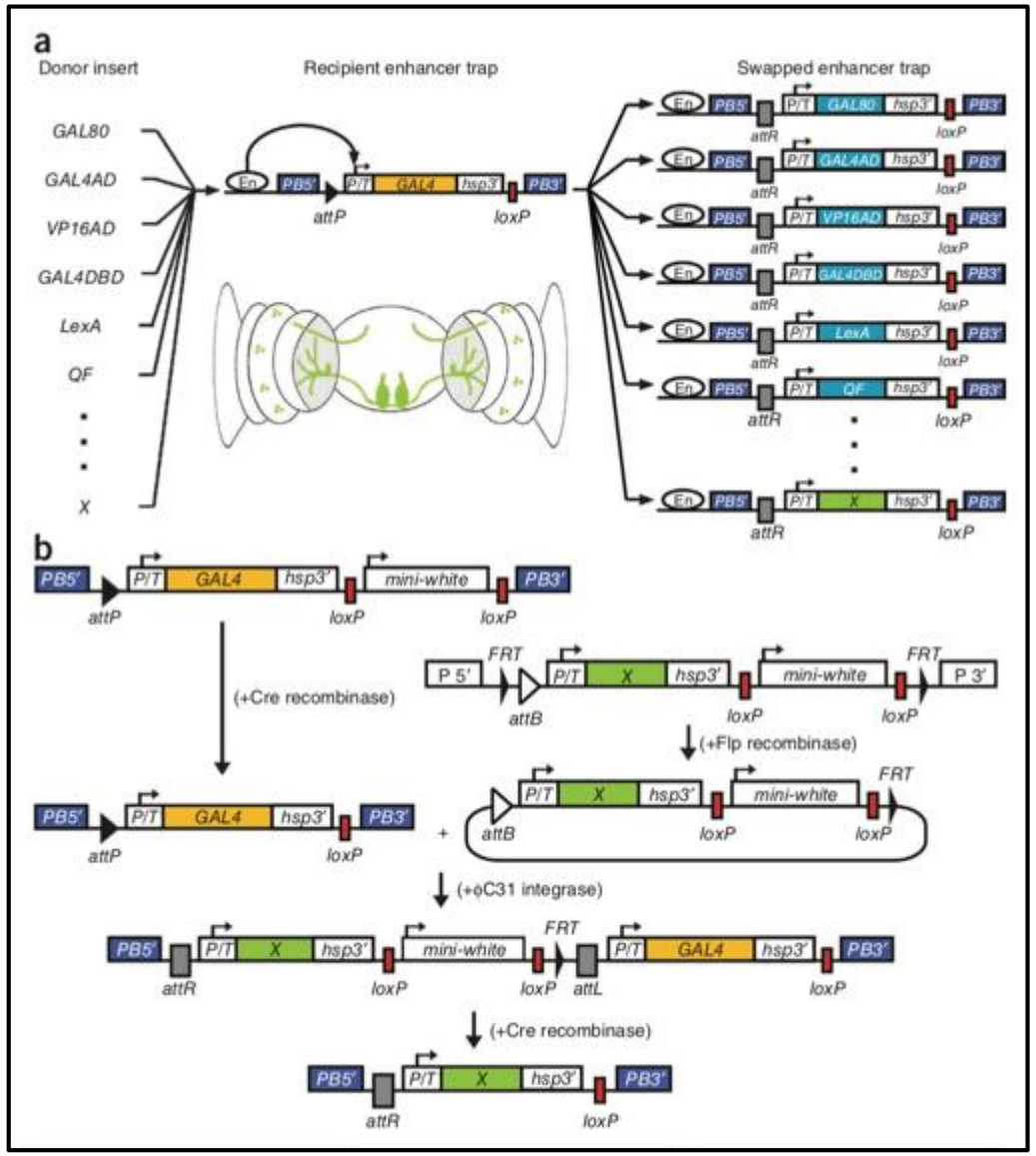
Maggert, K. et al. 2008

- zinc-finger nuclease (ZFN) and the transcription activator-like effector nuclease (TALEN), CRISPR/Cas9



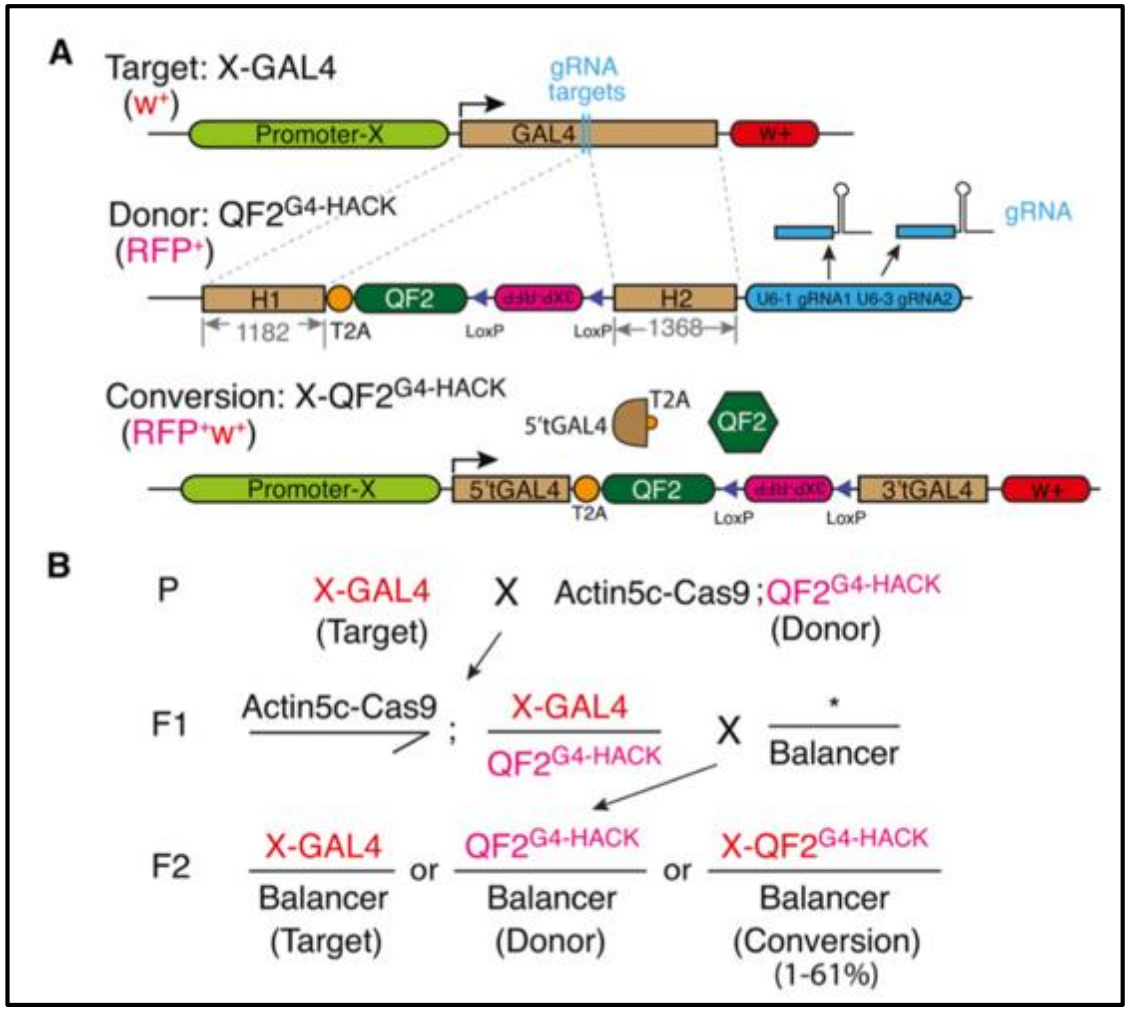


the integrase swappable in vivo targeting element (InSITE) system



Gohl, D. et al. 2011

homology assisted CRISPR knock-in (HACK)



Lin, C.-C. and Potter, C. 2016

To misexpress the gene of interest at different levels or with different spatiotemporal patterns—**gain-of-function**

misexpress fru^{M} in female

Binary expression systems: GAL4/UAS, LexA/LexAop and QF/QUAS systems.

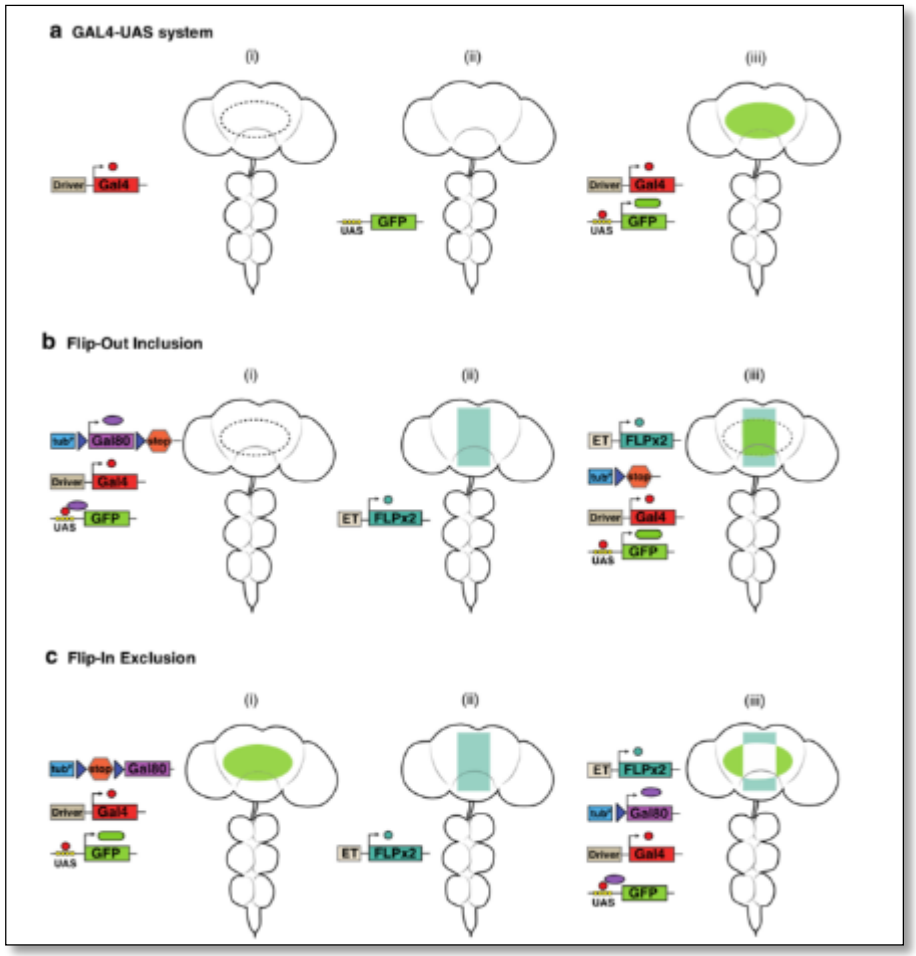
Ternary expression systems: GAL80, QS, split GAL4 and split LexA.

Flp-out: flipase (Flp) and its recognition target sequence (FRT)

Quaternary expression system: Killer Zipper (KZip+), a suppressor of split Gal4

Sivanantharajah, L. and Zhang, B. 2015.

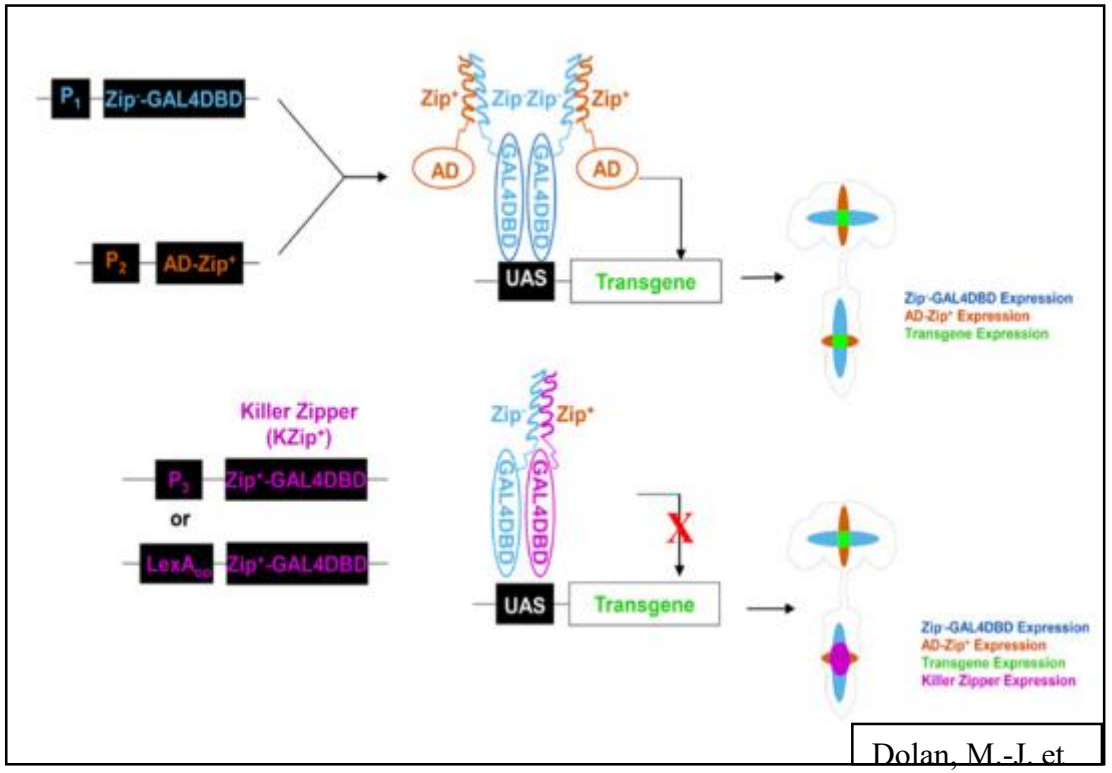
Demir, E. and Dickson, B. 2005



otd-Flpl;Tub^{p}>Gal80>stop

otd-Flpl;Tub^{p}>stop>Gal80

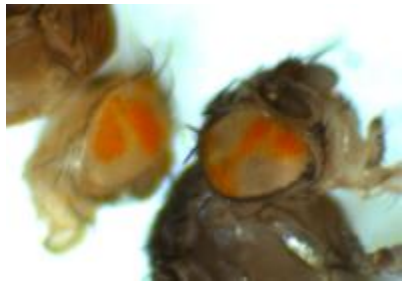
Killer Zipper

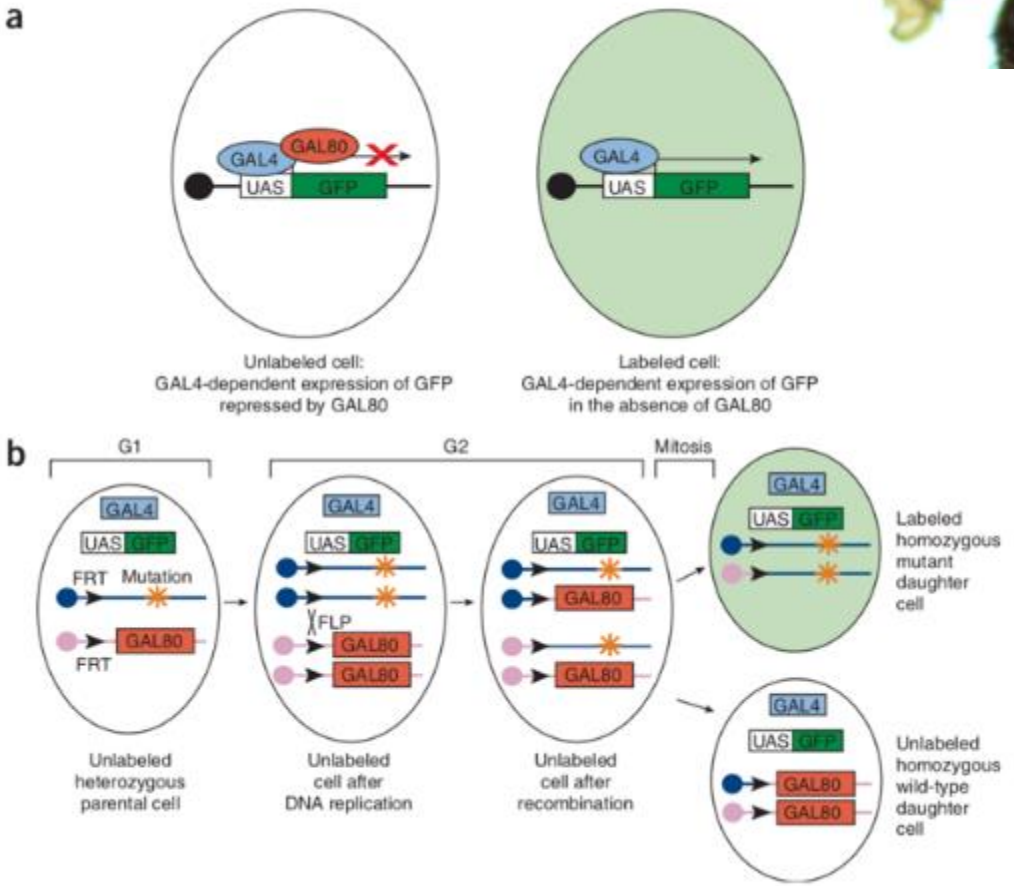


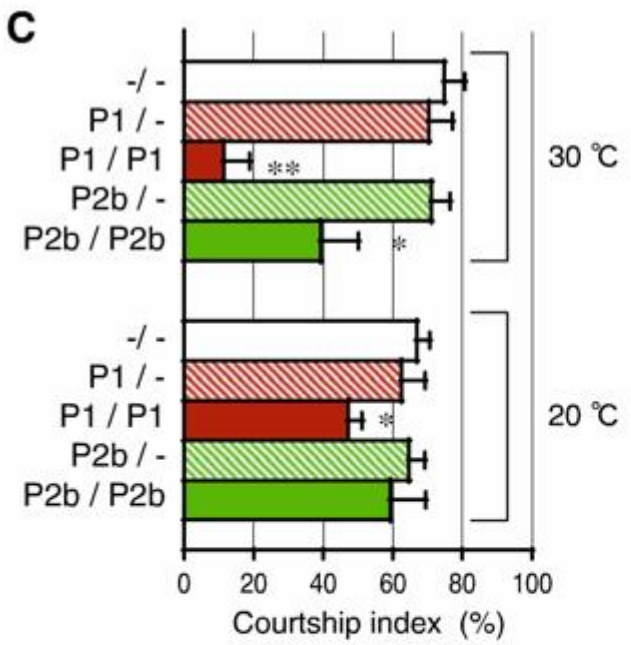
Dolan, M.-J. et al. 2017.

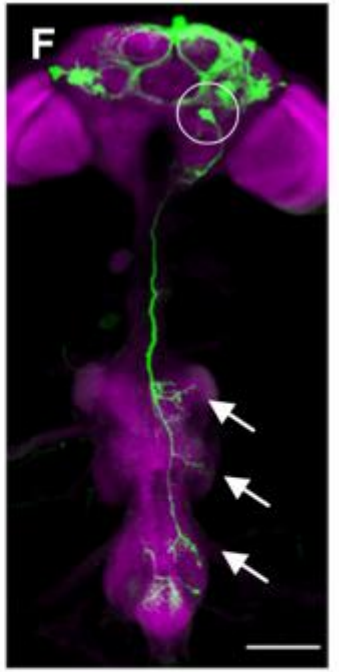
The mosaic analysis with a repressible cell marker (MARCM) technique

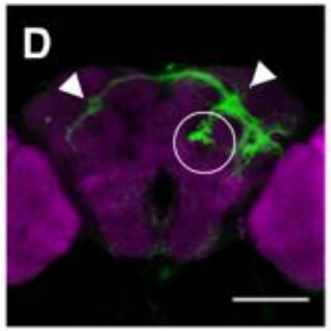
Genetic mosaics are individuals composed of cells with at least two different genotypes.

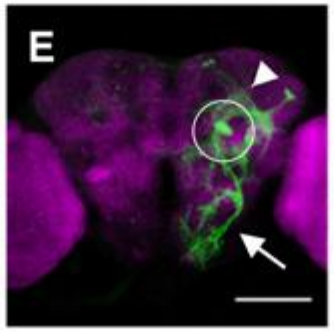


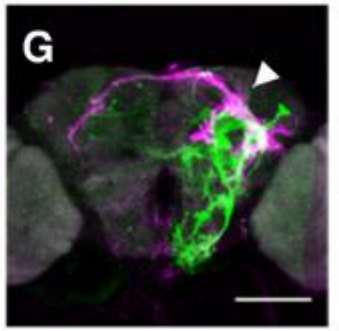






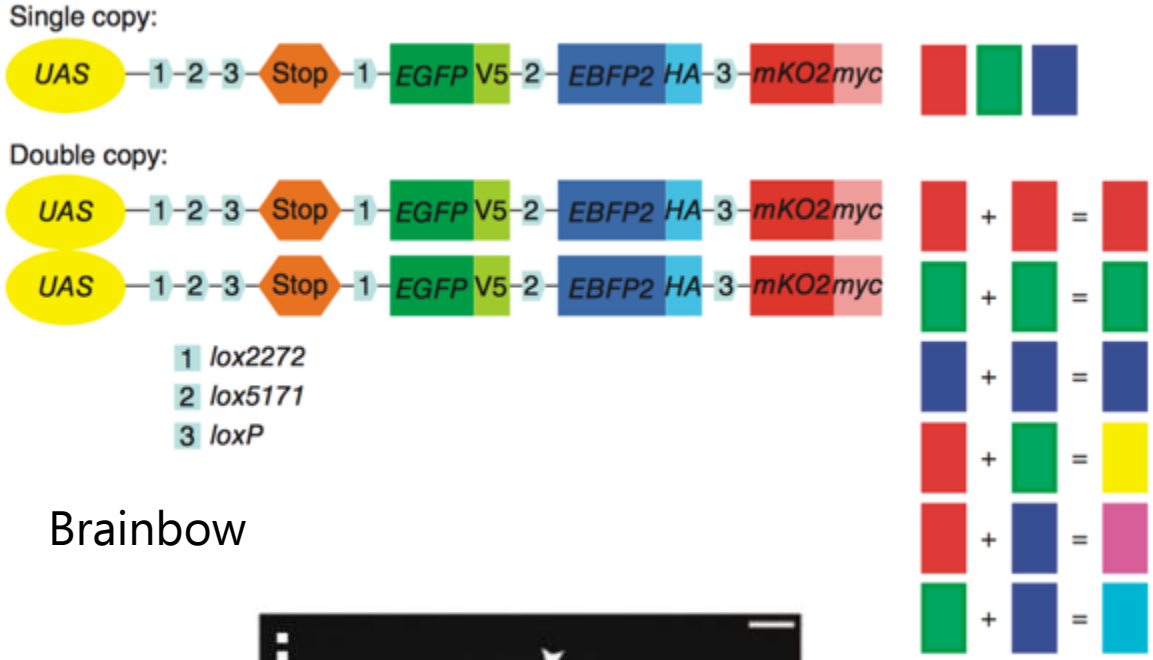




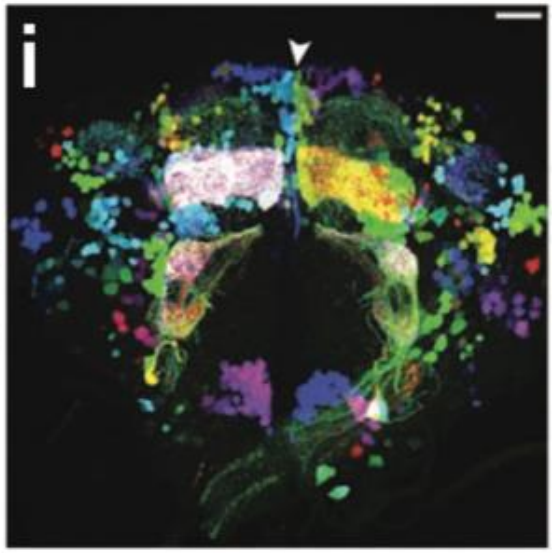


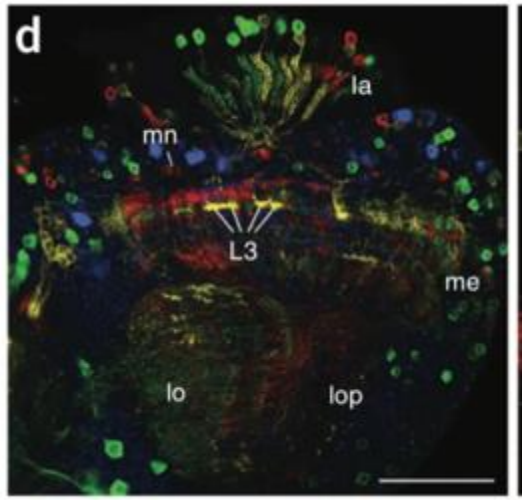
$$\frac{\text{hs-flp}}{+} ; \frac{\text{FRTG13 tub-Gal80}}{\text{FRTG13 UAS-mCD8::GFP}} ; \frac{\text{fru}^{\text{NP21}}}{\text{UAS-shi}^{\text{ts}}}$$

Multicolor system: Drosophila Brainbow , Flybow

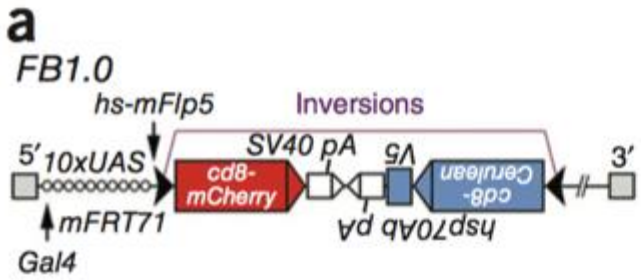


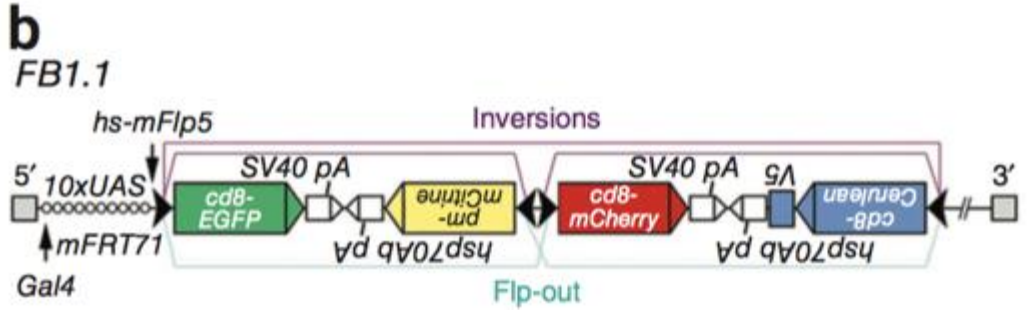
Brainbow

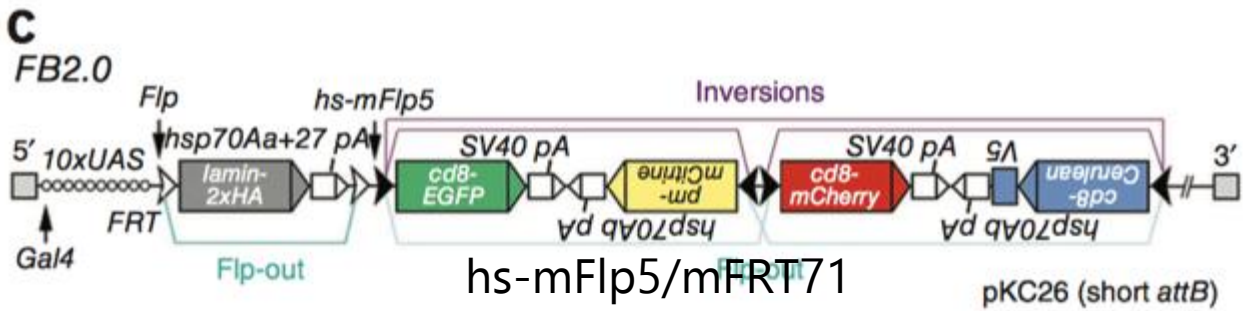




adult optic lobe







hs-mFlp5/mFRT71

Flybow

Ways to determine gene expression patterns

proteins:
- immunostaining
- western blot

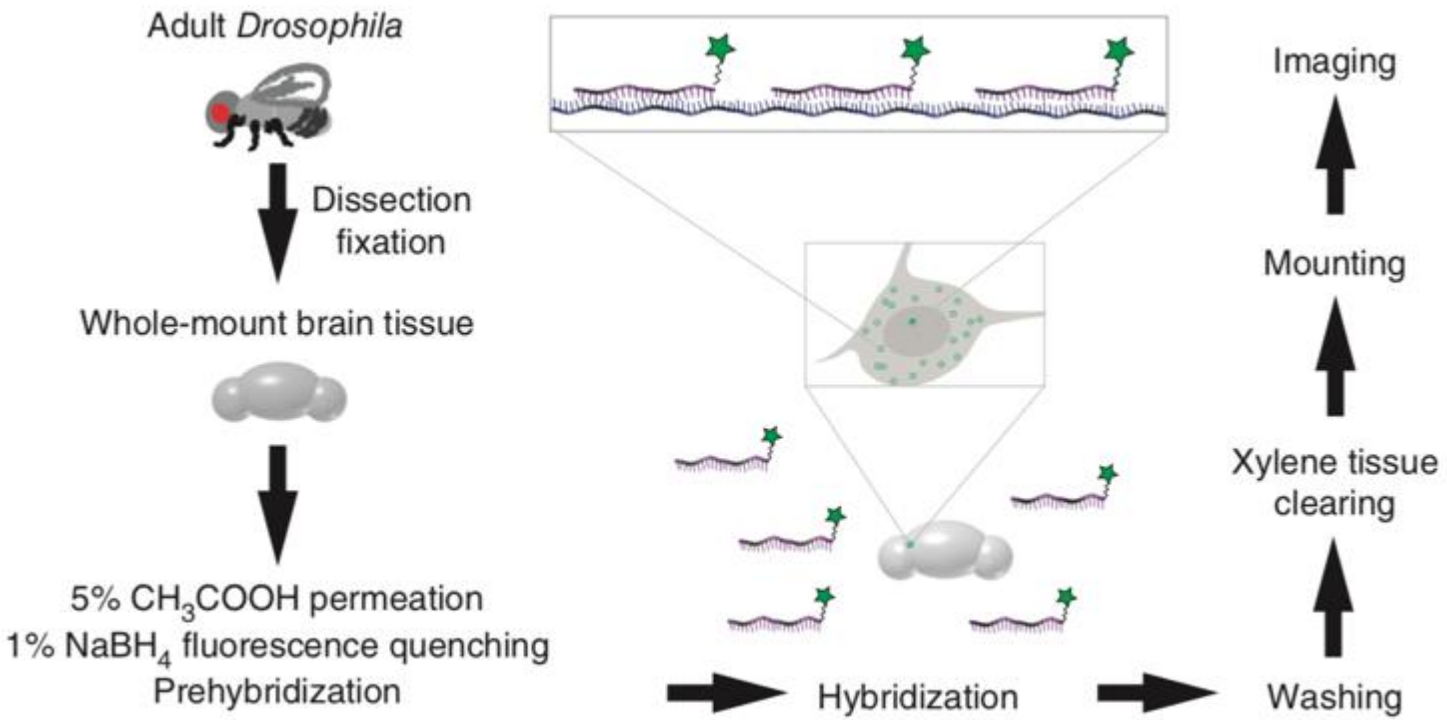
mRNA:
- in situ hybridization
- northern blot

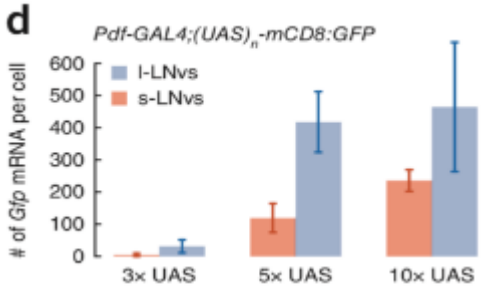
nature methods

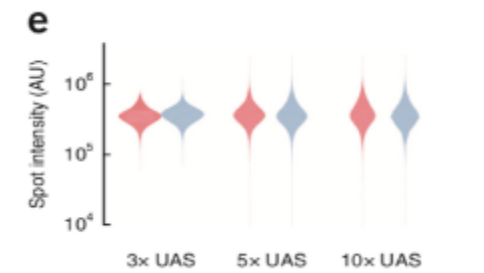
Brief Communication | Published: 05 June 2017

Quantitative mRNA imaging throughout the entire *Drosophila* brain

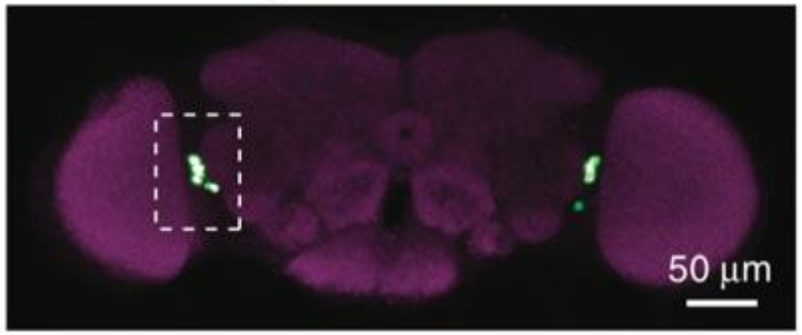
Xi Long ✉, Jennifer Colonell, Allan M Wong, Robert H Singer & Timothée Lionnet ✉

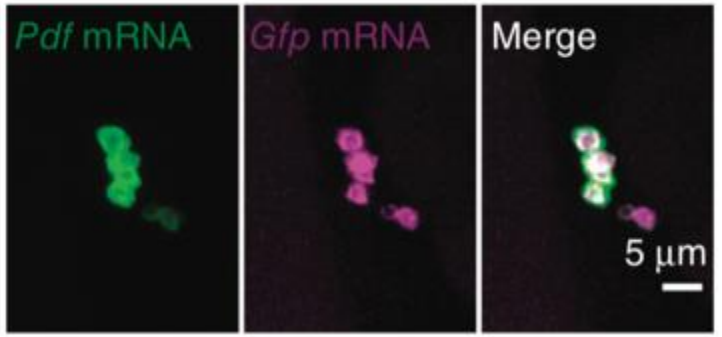






Pdf-Gal4;(UAS)$_5$-IVS-mCD8::GFP





- Reference

[1] Hales, K. et al. 2015. Genetics on the Fly: A Primer on the Drosophila Model System. *Genetics*. 201, 3 (2015), 815–842.

[2] Del Rodríguez, A. et al. 2012. Power tools for gene expression and clonal analysis in Drosophila. *Nature Methods*. 9, 1 (2012), 47–55.

[3] Sivanantharajah, L. and Zhang, B. 2015. Current techniques for high-resolution mapping of behavioral circuits in Drosophila. *Journal of Comparative Physiology A*. 201, 9 (2015), 895–909.

[4] Dolan, M.-J. et al. 2017. Facilitating Neuron-Specific Genetic Manipulations in Drosophila Using a Split GAL4 Repressor. *Genetics*. 206, 2 (2017), 775–784.

[5] Long, X. et al. 2017. Quantitative mRNA imaging throughout the entire Drosophila brain.*Nature Methods*. 14, 7 (2017), 703–706.

[6] Meissner, G. et al. 2018. Mapping Neurotransmitter Identity in the Whole-Mount Drosophila Brain Using Multiplex High-Throughput Fluorescence in Situ Hybridization.*Genetics*. (2018), genetics.301749.2018.

[7] Lin, C.-C. and Potter, C. 2016. Editing Transgenic DNA Components by Inducible Gene Replacement in Drosophila melanogaster.*Genetics*. 203, 4 (2016), 1613–1628.

[8] Gohl, D. et al. 2011. A versatile in vivo system for directed dissection of gene expression patterns. *Nature Methods*. 8, 3 (2011), 231.

[9] Maggert, K., Gong, W. and Golic, K. 2008.*Drosophila, Methods and Protocols*. springer.

[10] Pfeiffer, B., Ngo, T.-T., Hibbard, K., Murphy, C., Jenett, A., Truman, J. and Rubin, G. 2010. Refinement of Tools for Targeted Gene Expression in Drosophila. *Genetics*. 186, 2 (2010), 735–755.

- Reference

[11] Lin, S.-C., Chang, Y.-Y. and Chan, C.-C. 2014. Strategies for gene disruption in Drosophila. *Cell & Bioscience*. 4, 1 (2014), 63.

[12] Gospocic, J. et al. 2017. The Neuropeptide Corazonin Controls Social Behavior and Caste Identity in Ants. *Cell*. 170, 4 (2017), 748–759.e12.

[13] Yan, H. et al. 2017. An Engineered orco Mutation Produces Aberrant Social Behavior and Defective Neural Development in Ants.*Cell*. 170, 4 (2017), 736–747.e9.

[14] Trible, W. et al. 2017. orco Mutagenesis Causes Loss of Antennal Lobe Glomeruli and Impaired Social Behavior in Ants. *Cell*. 170, 4 (2017), 727–735.e10.

[15] Kohatsu, S., Koganezawa, M. and Yamamoto, D. 2011. Female Contact Activates Male-Specific Interneurons that Trigger Stereotypic Courtship Behavior in Drosophila. *Neuron*. 69, 3 (2011), 498–508.

[16] 2015. Principles of Neurobiology. taylorfrancis.

Part II. The way of Recording neuronal activity.

Zhao Huan

- Neuronal activity:
  - Firing of neurons
    - Electrophysiological methods
    - Optical imaging GCamp
  - Synaptic connections between neurons
    - Electrophysiological methods
    - Anatomical methods
    - activity-dependent Calcium imaging

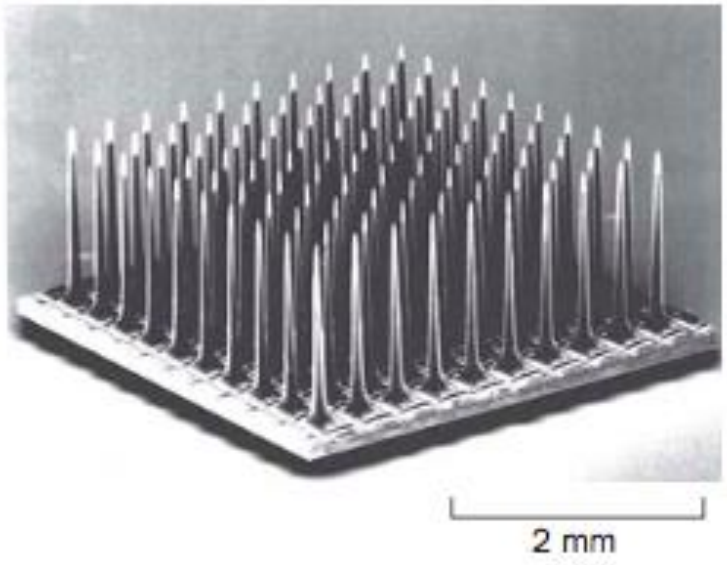
Firing of neurons

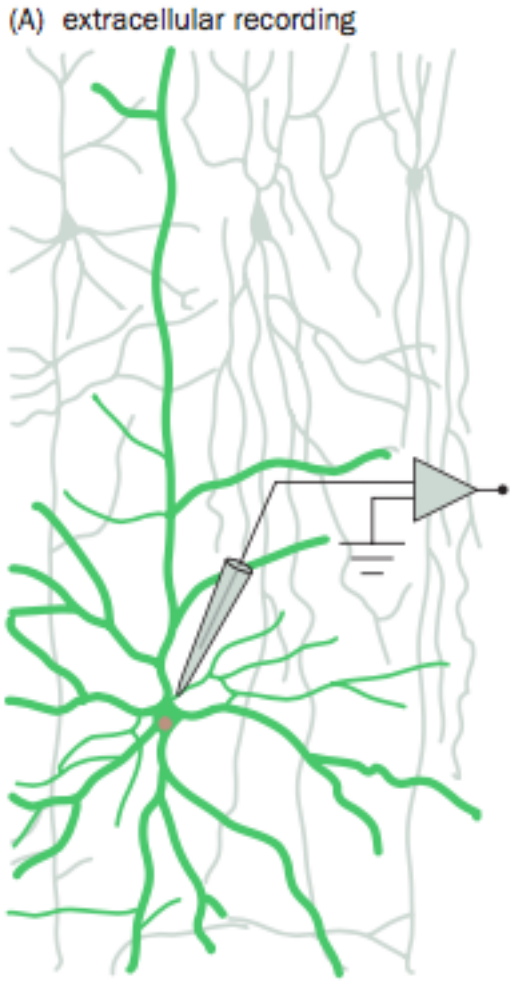
- individual neuron

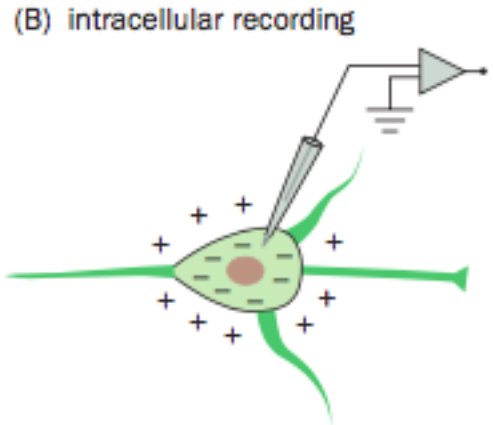
Extracellular recording

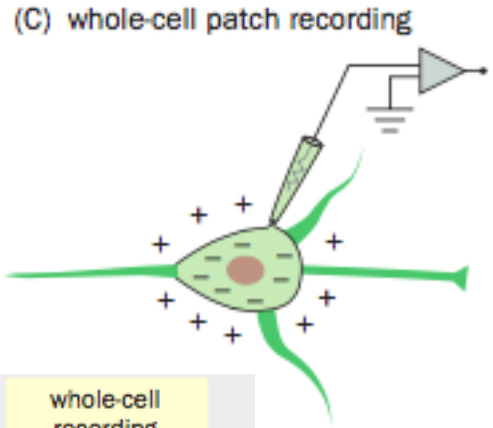
- synaptic input and firing patterns

Intracellular and whole-cell patch r



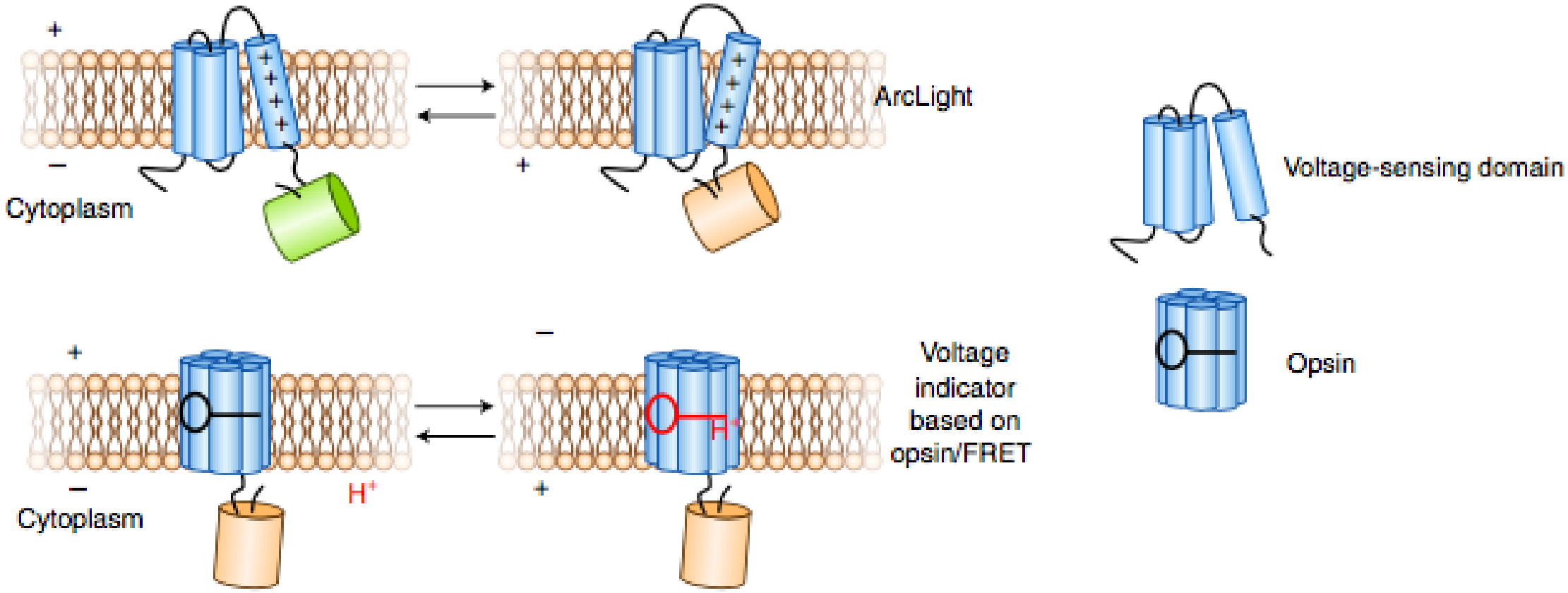




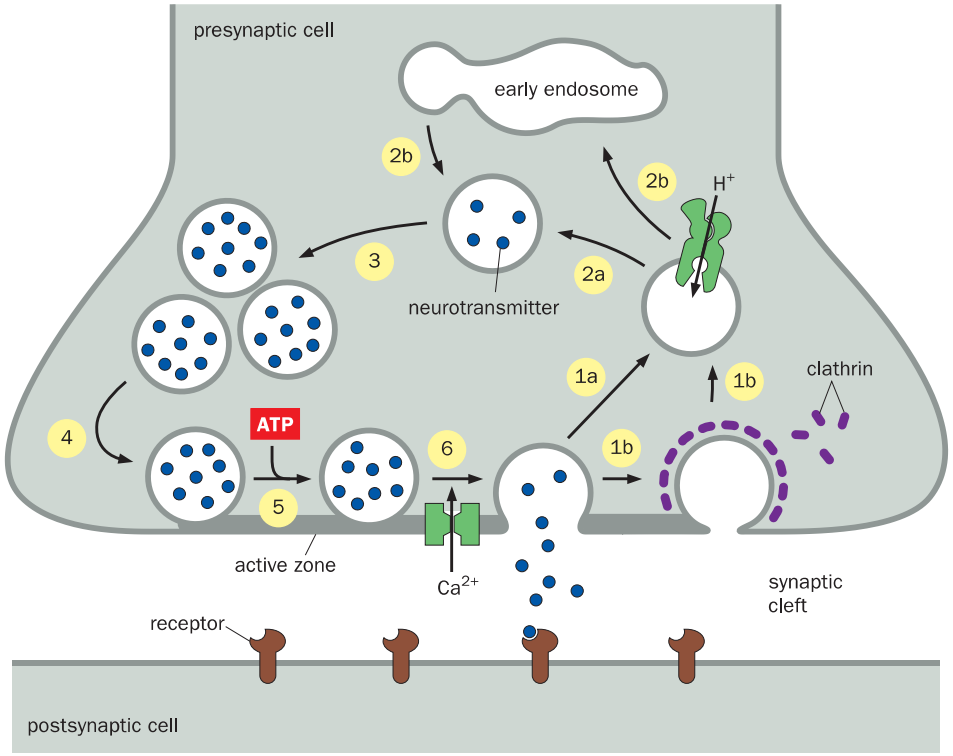


Neuroscience. 3rd edition

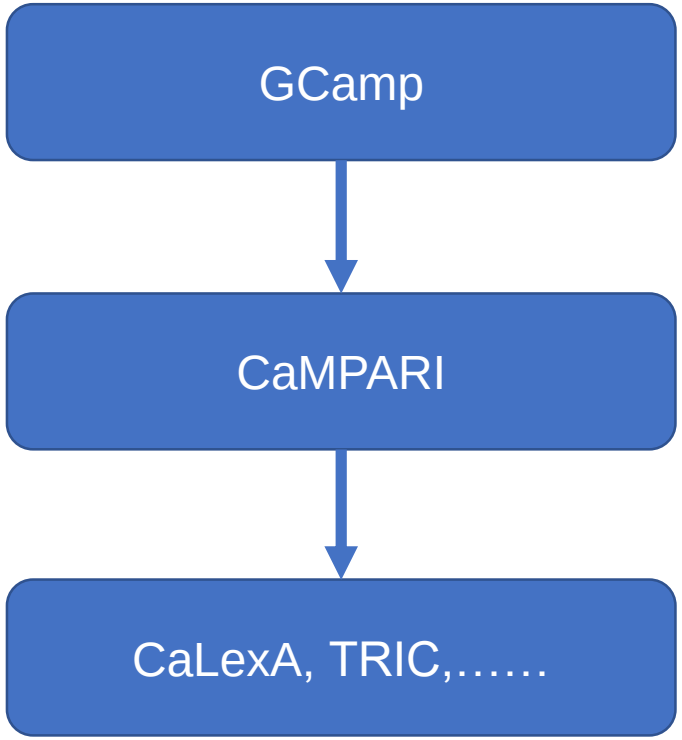
Genetically encoded voltage indicator (GEVI)



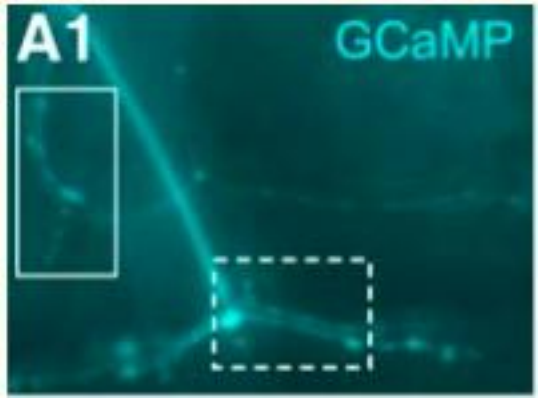
- Activity-Dependent Methods

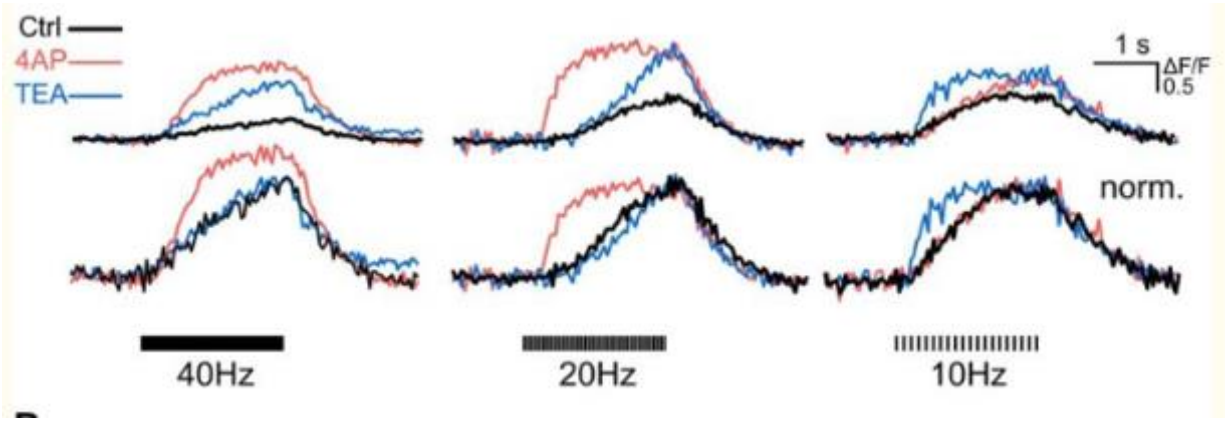


Neuroscience. 3rd edition

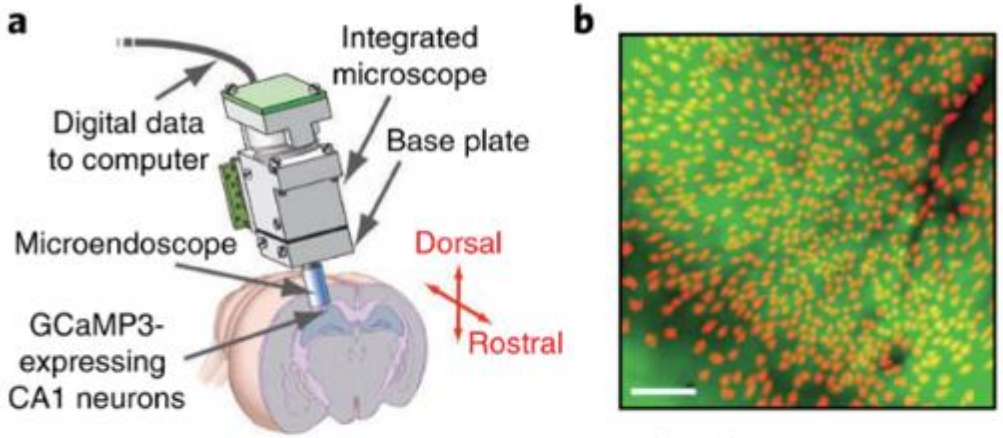


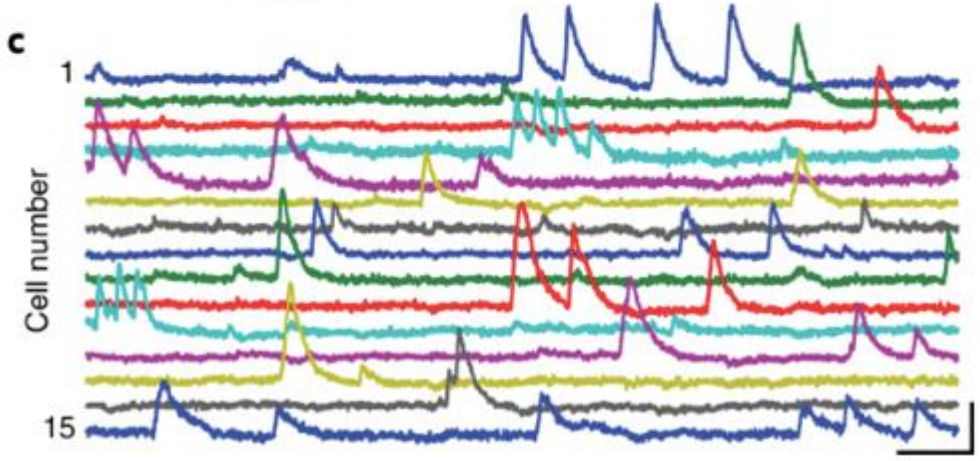
Activity of many neurons simultaneously-- Optical imaging GCamp





Xiaomin Xing et al. eNeuro.2018





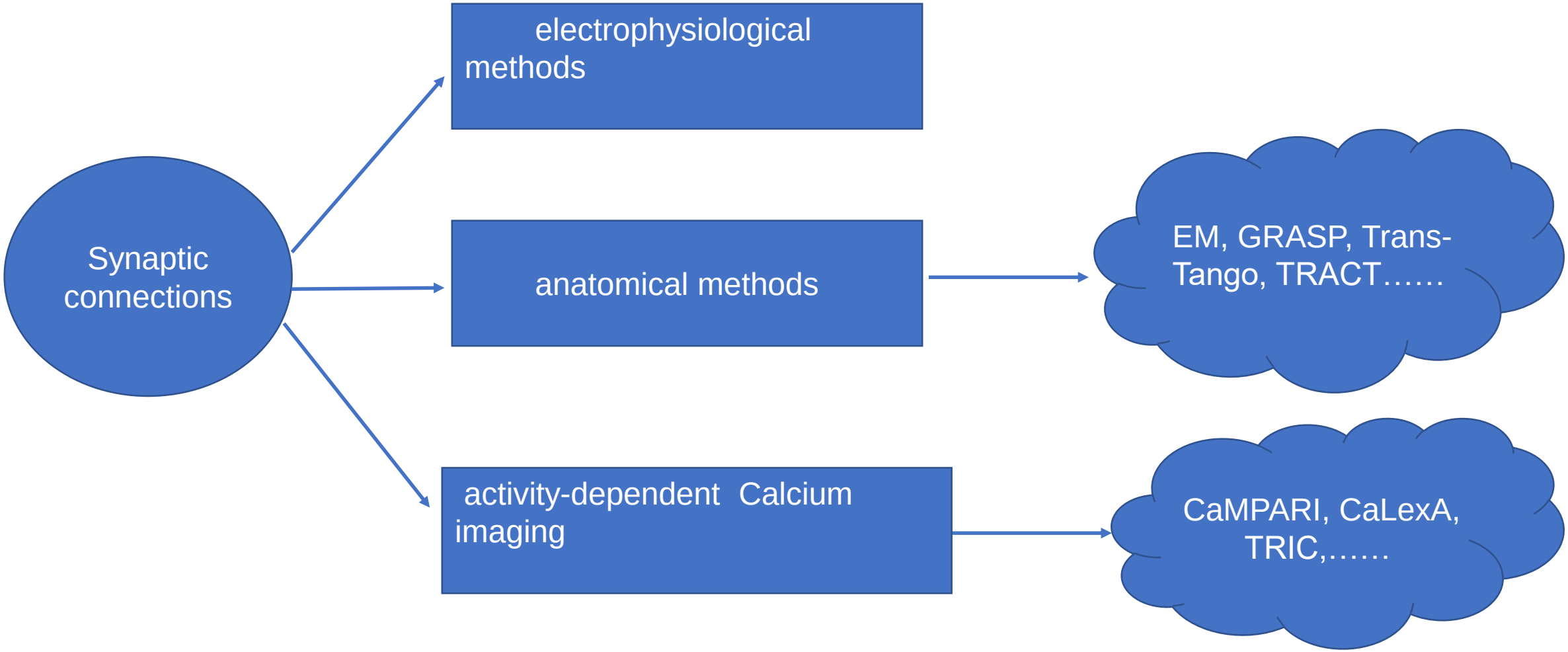
Wenjing Wang et al. Nature Chemical Biology.2015

Comparison of electrophysiological and optical imaging methods for recording neuronal activity

Property	Electrophysiology		Optical imaging with Ca^{2+} indicators[1]
	Extracellular recording	Intracellular recording	
Sensitivity to electrical signal	spikes	spikes and sub-threshold activity	generally less sensitive[2]
Spatial resolution	cellular to network	cellular to subcellular[3]	cellular and subcellular
Temporal resolution	<1 millisecond	<1 millisecond	10s to 100s of milliseconds for a single imaging plane
Number of neurons recorded simultaneously	up to hundreds	at most a few	thousands or more
Stability during movement	good	poor	poor
Depth of recording	any depth	easier superficially	limited[4]
Duration of recording	days to weeks	10s of minutes	hours with chemical indicators; months with protein indicators
Cell-type-specific recording	poor	good	excellent with protein indicators
Biases	active neurons; dominant cell types	large cells	cells that take up or express the indicators well

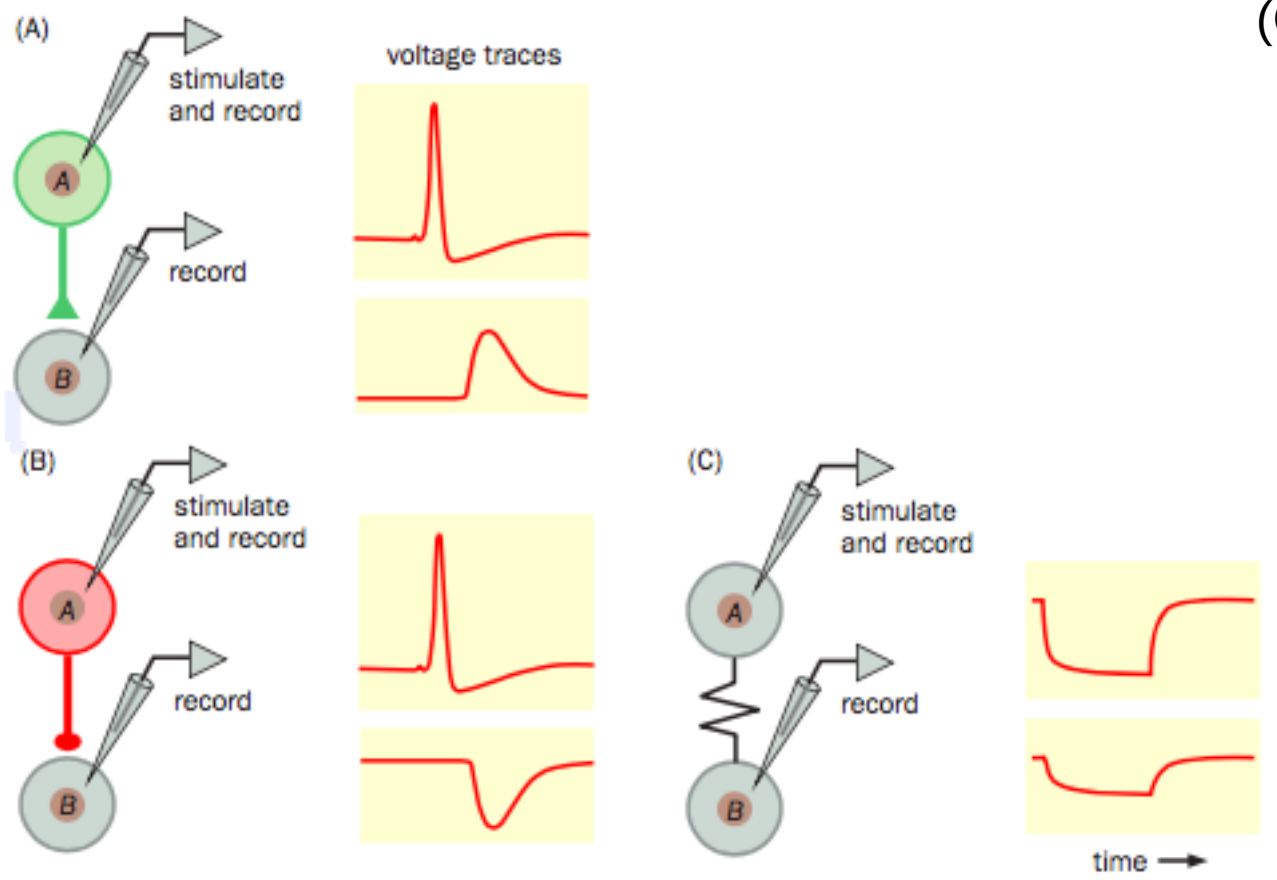
Neuroscience. 3rd edition

Synaptic connections between neurons

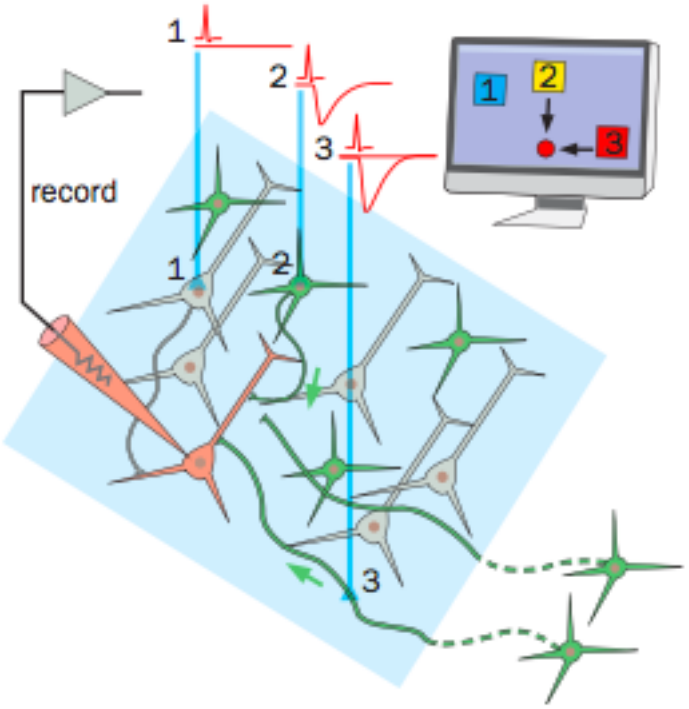


Synaptic connections between neurons

- physiological methods



- A widely used method for CRACM (ChR2-assisted circuit mapping)

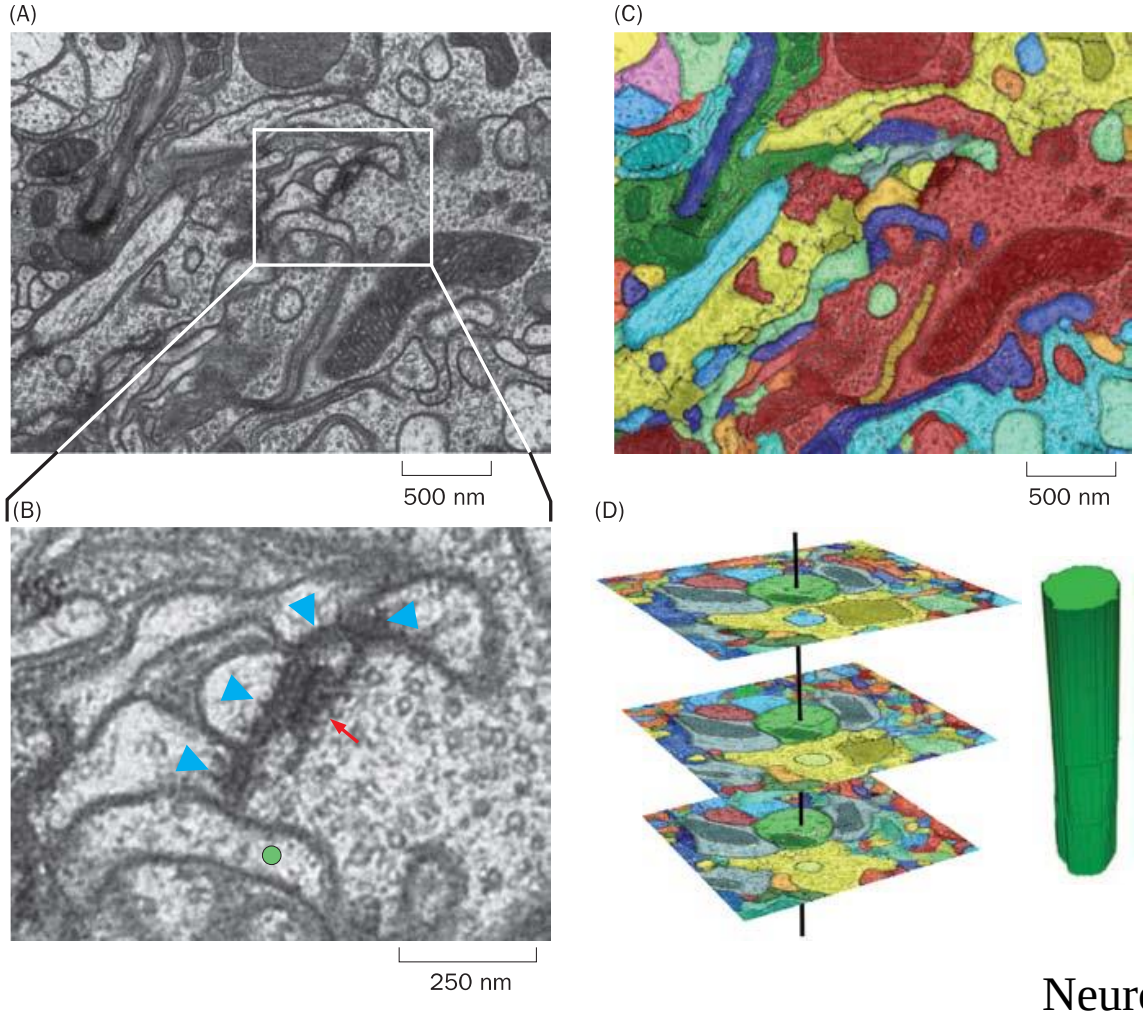


Neuroscience. 3rd edition

Synaptic connections between neurons

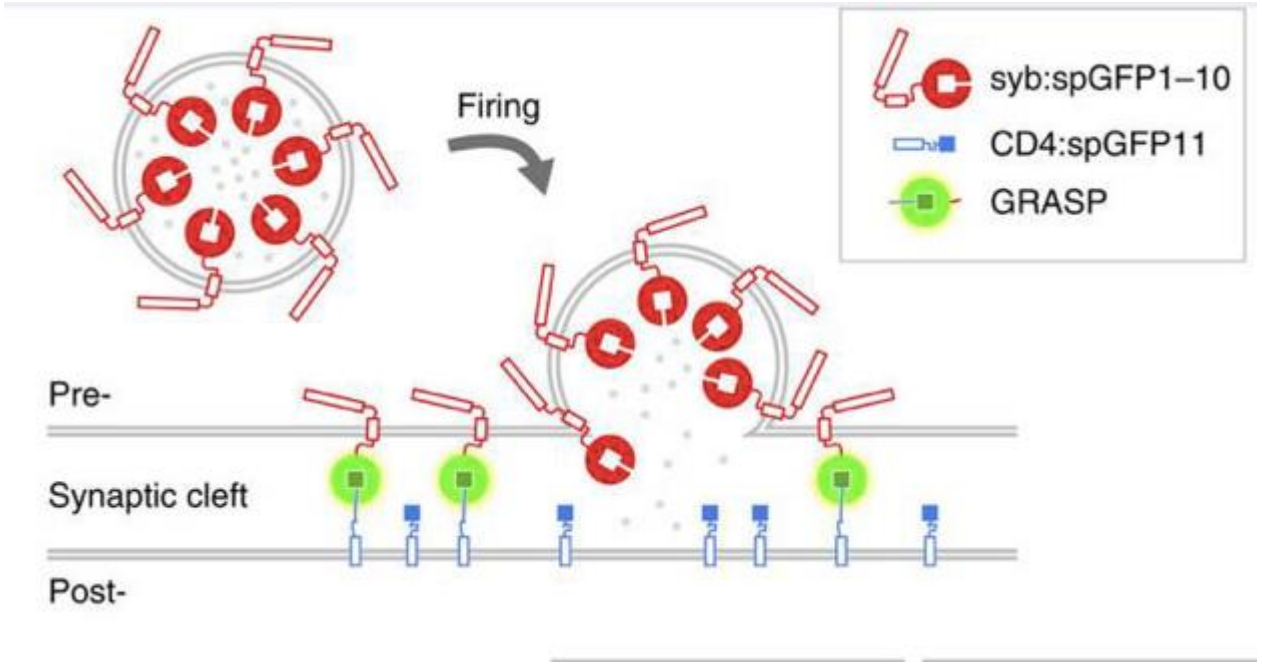
- anatomical method

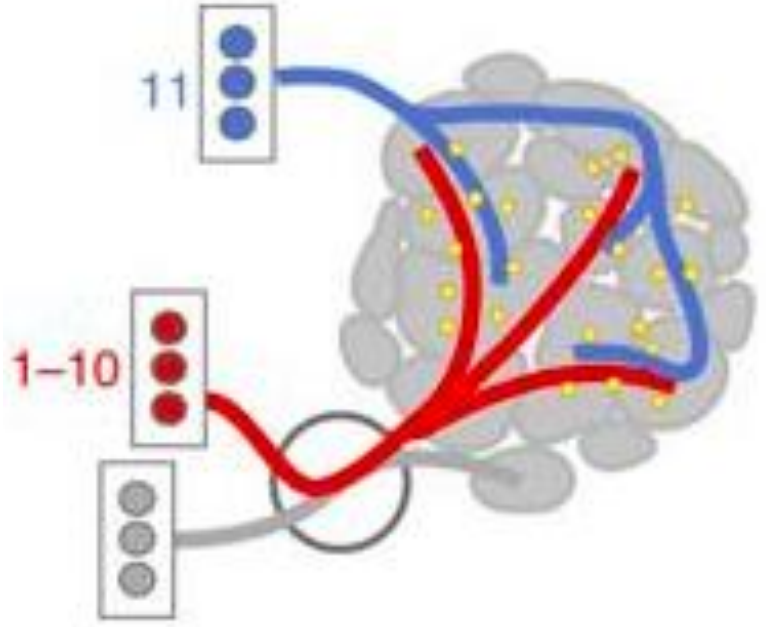
The most reliable anatomical method to determine whether or not two neurons form synaptic connections is EM(electron microscopy).



Neuroscience. 3rd edition

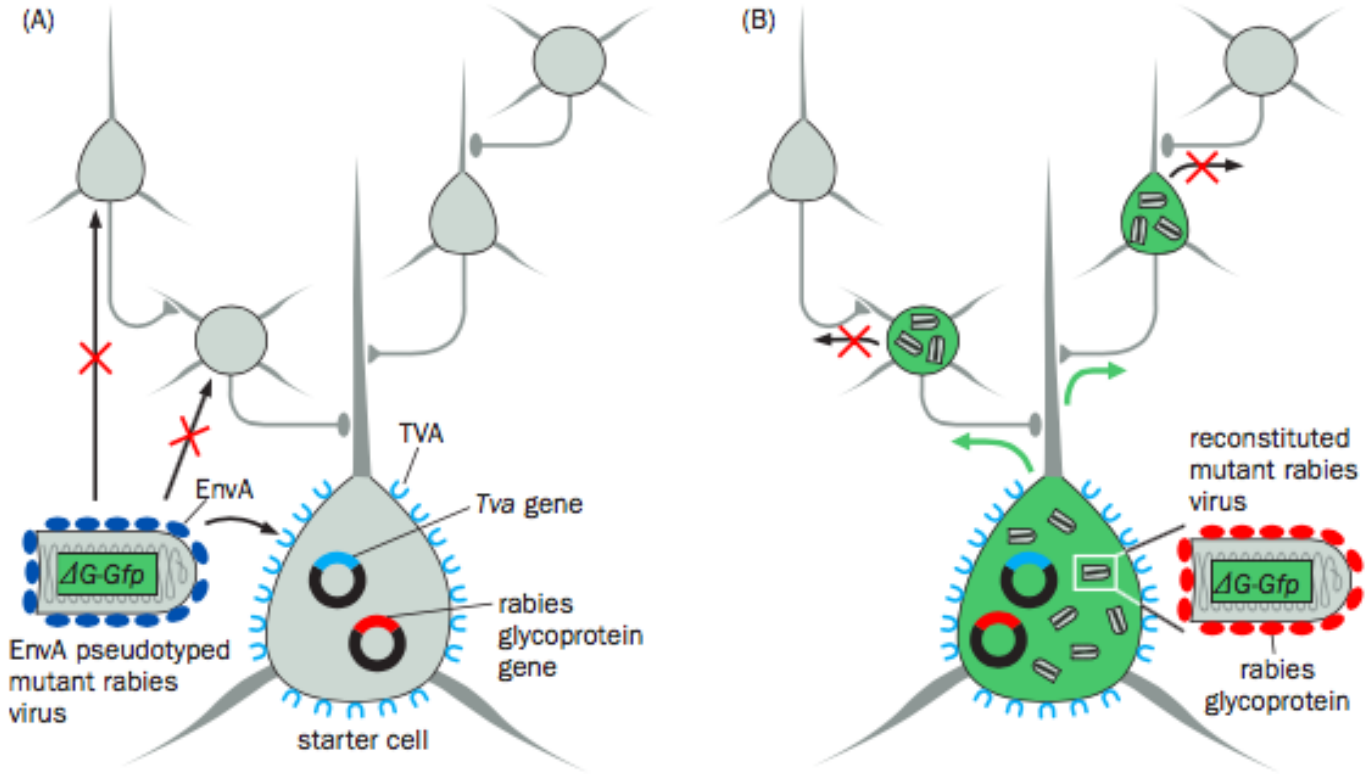
- GRASP uses complementary split-GFP fragments (sp-GFP1–10 and sp-GFP11) expressed on the extracellular membranes of different neurons to reconstitute a functional fluorescent GFP reporter at the points of contact.





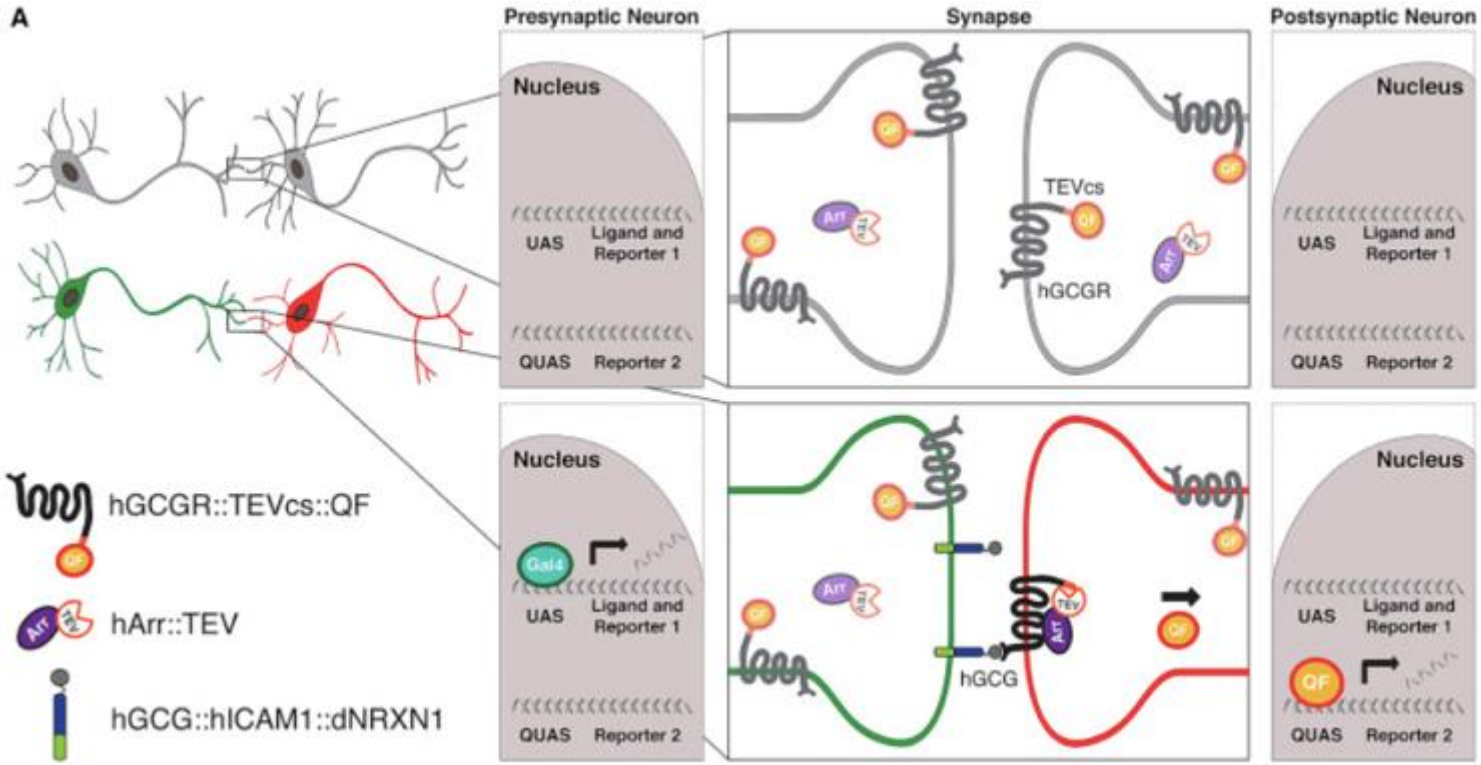
Lindsey J Cacpherson et al. Nature Comunication.2015

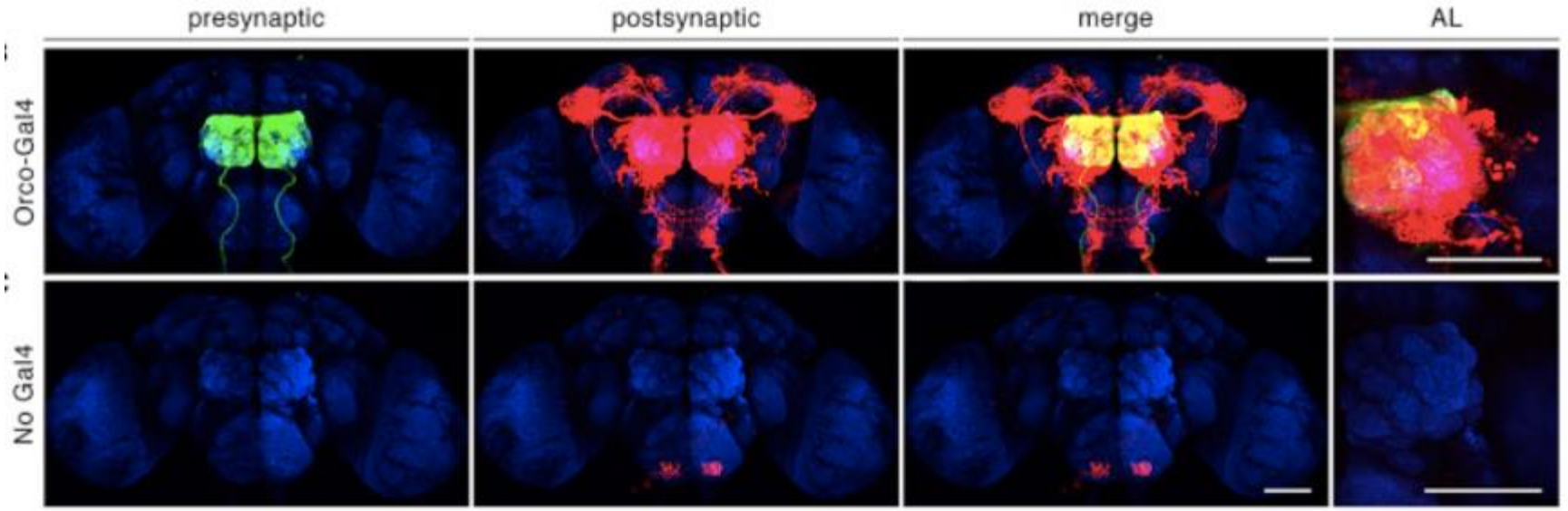
- trans-synaptic tracing： rabies virus and herpes simplex virus spread within the nervous systems of their hosts naturally by crossing synapses.



Neuroscience. 3rd edition

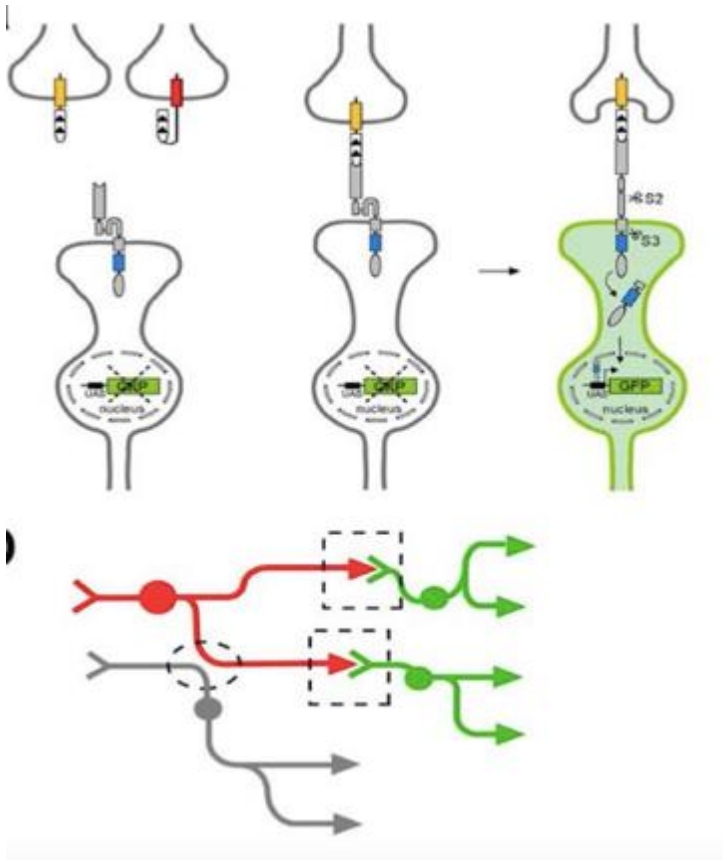
- Trans-Tango: a technique for anterograde transsynaptic circuit tracing and manipulation

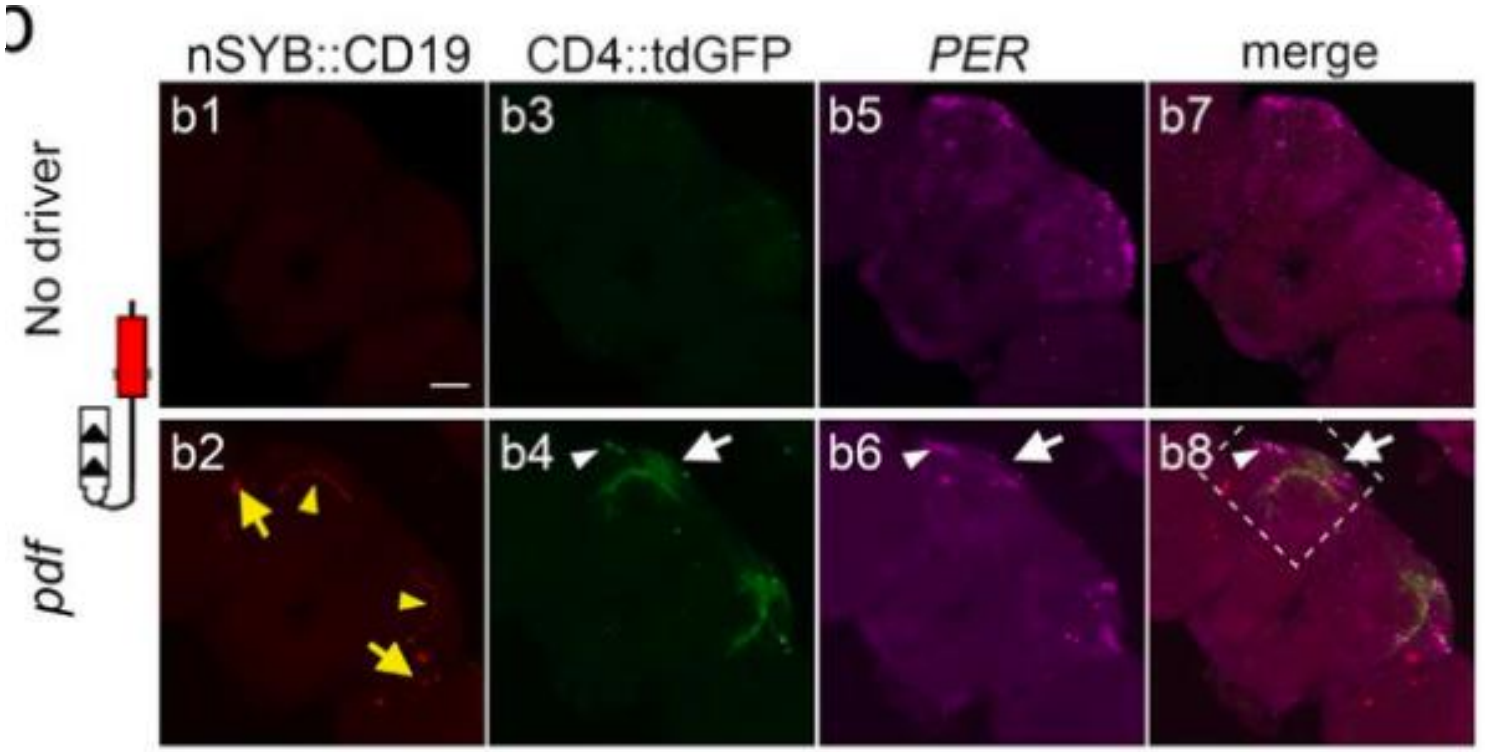




Mustafa Talay et al.Neuron.2017

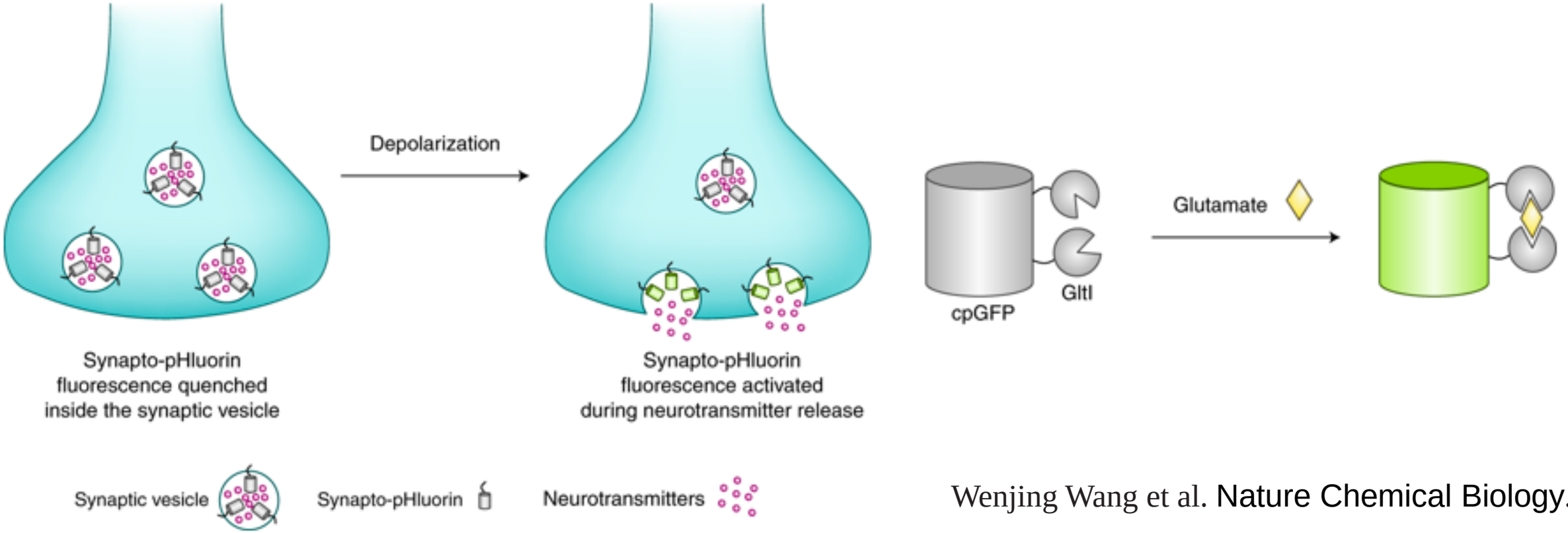
- TRACT: ligand-induced intramembrane proteolysis to reveal monosynaptic connections arising from genetically labeled neurons of interest





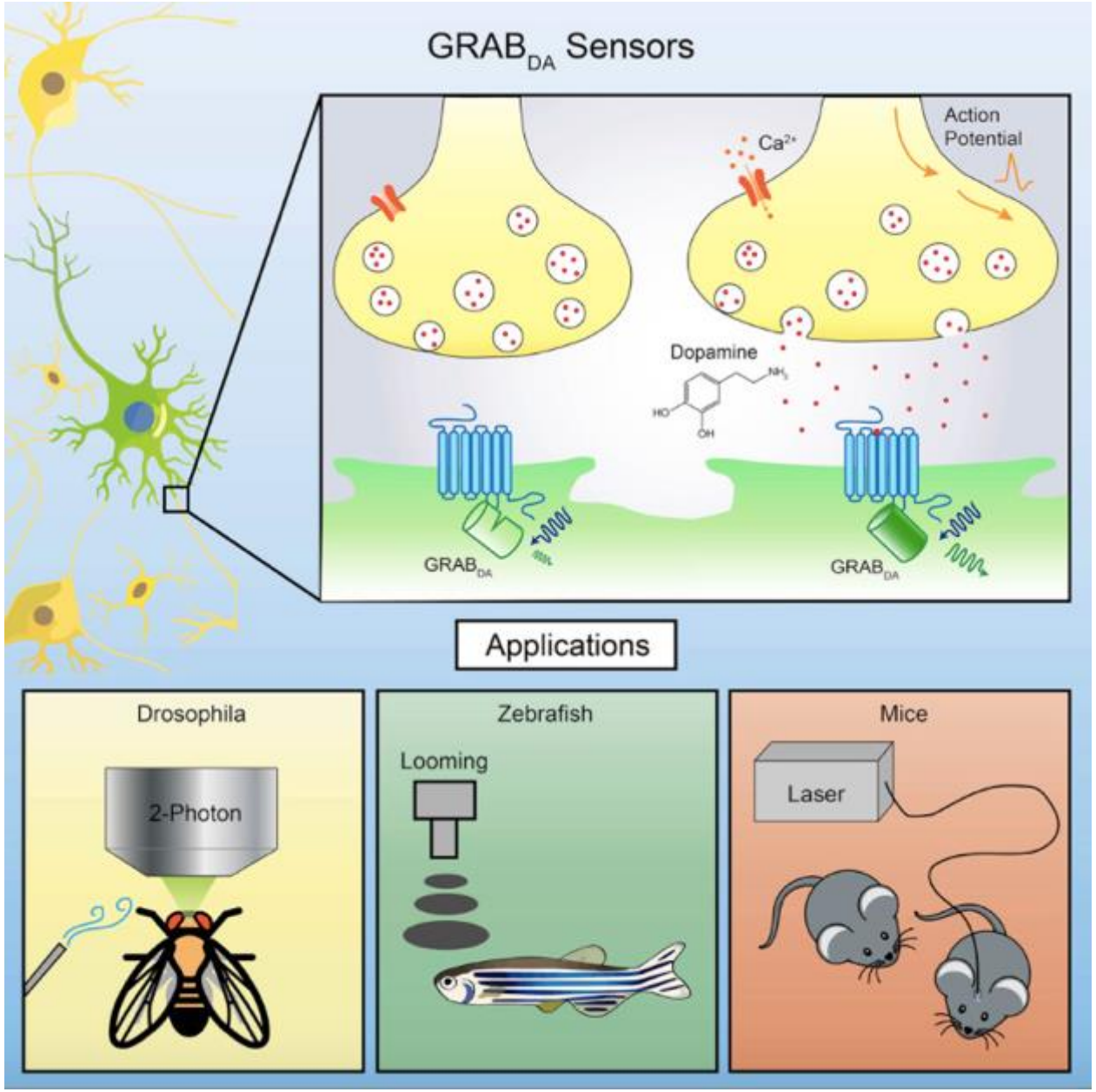
Ting-hao Huang et al. eLife.2017

- pH sensors and neurotransmitter sensors



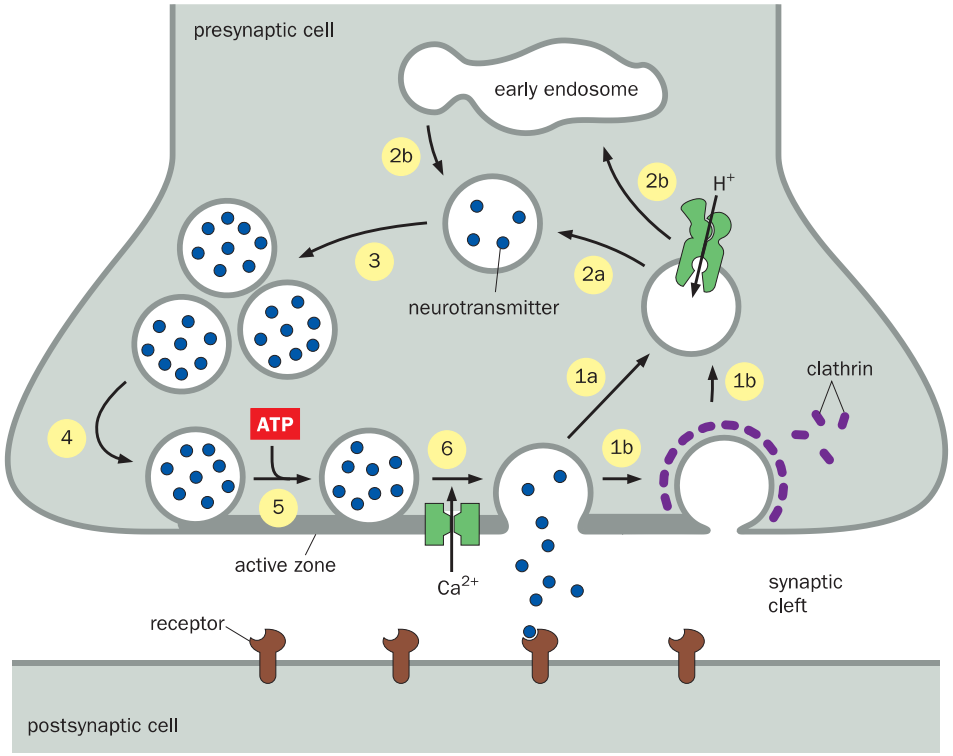
Wenjing Wang et al. Nature Chemical Biology.2015

- GPCR-activation-based-DA ($GRAB_{DA}$) sensors are genetically encoded dopamine (DA) sensors based on GPCR

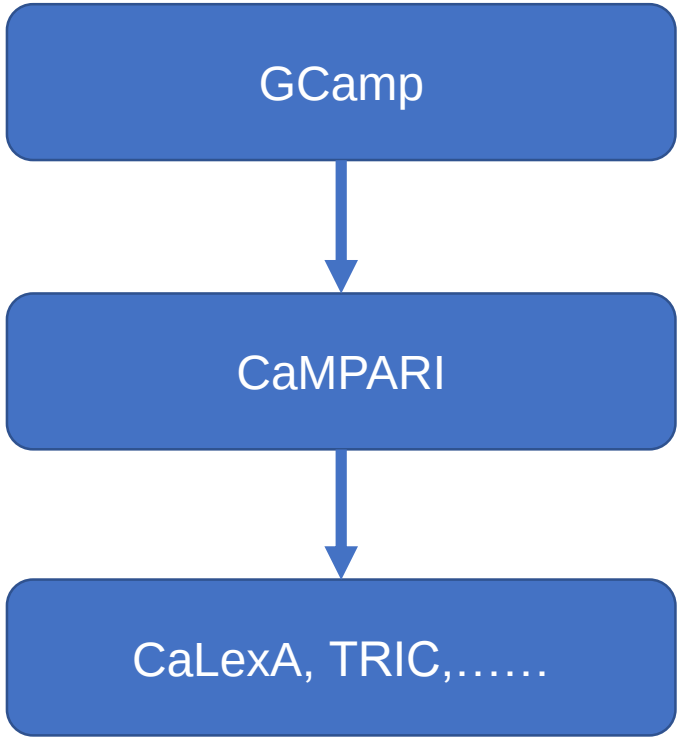


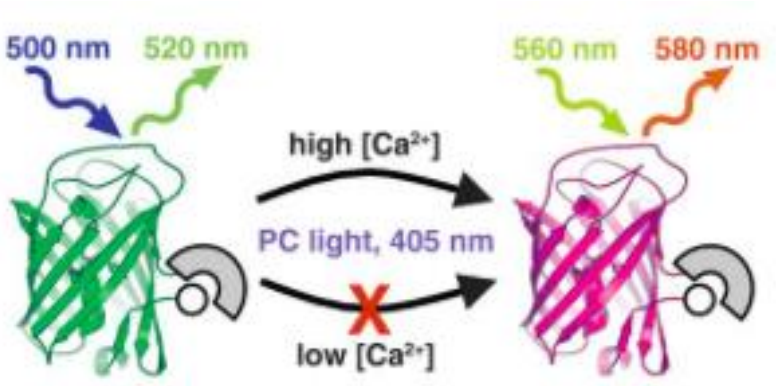
Fangmiao Sun et al. Cell.2018

- Activity-Dependent Methods



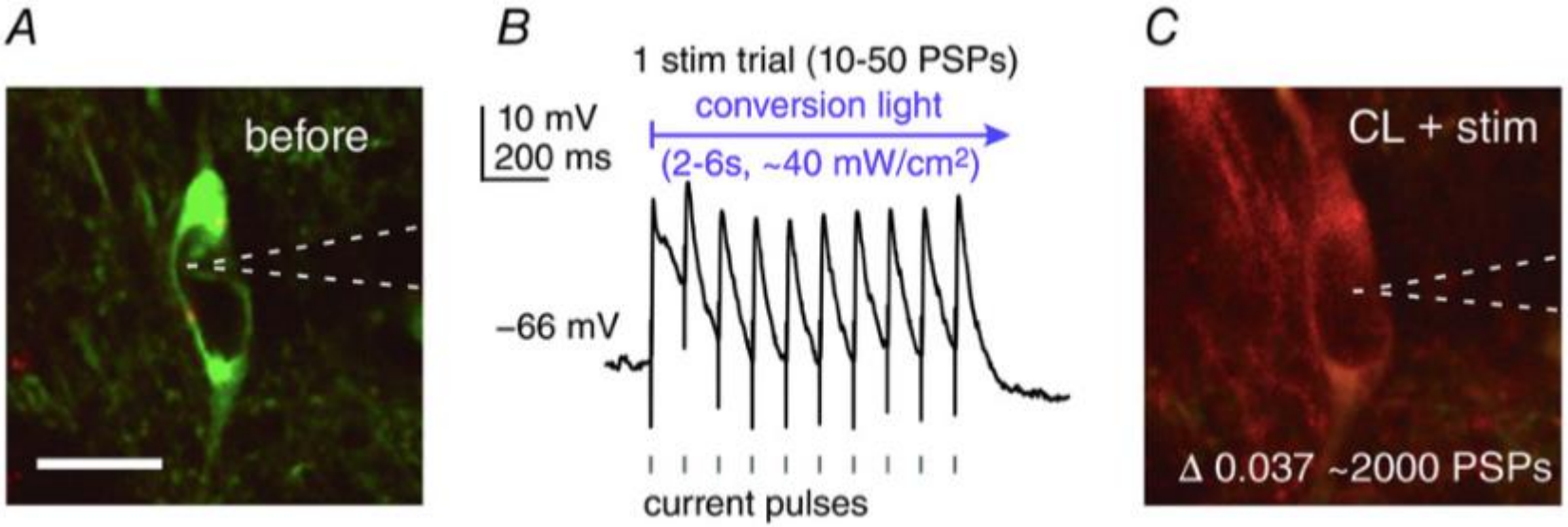
Neuroscience. 3rd edition





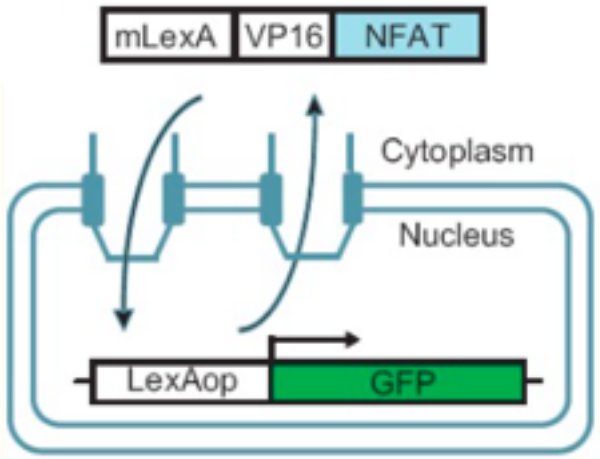
CaMPARI: The genetically encoded fluorescent calcium integrator calcium-modulated photoactivatable ratiometric integrator

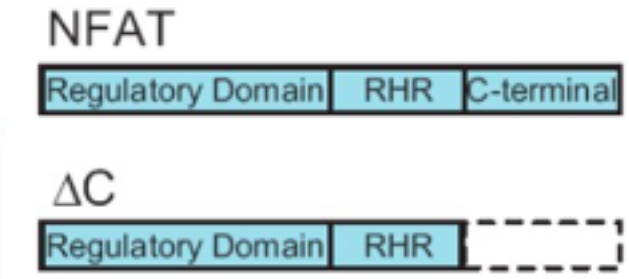
Benjiamin F. et al. Science.2015

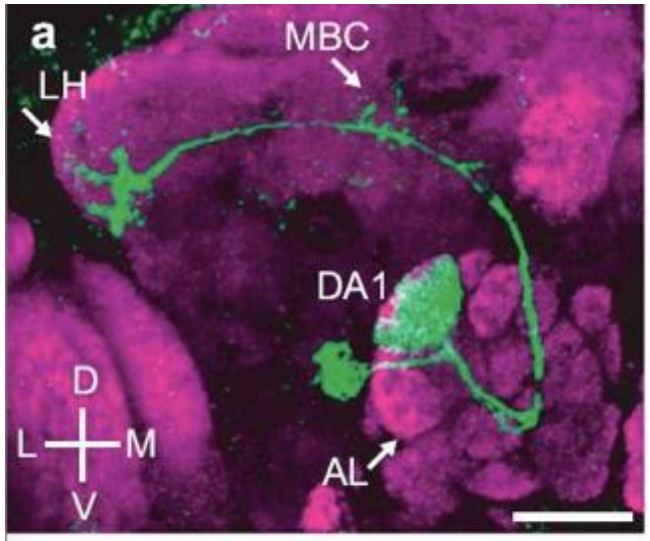


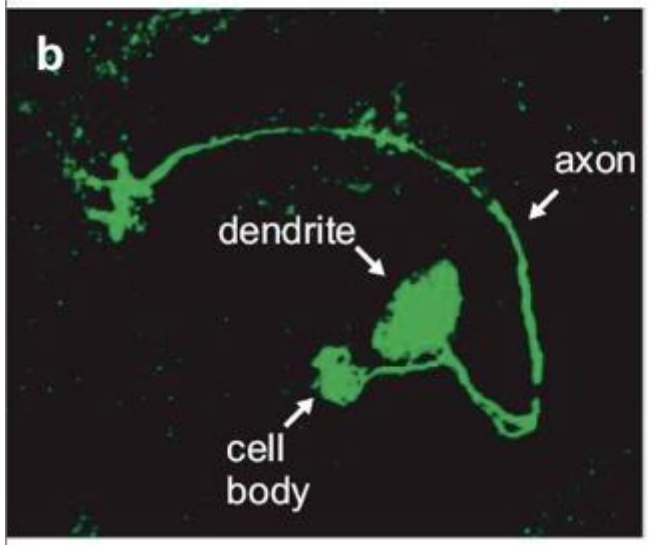
Timothy A.Zolnik et al. The Journal Of Physiology.2016

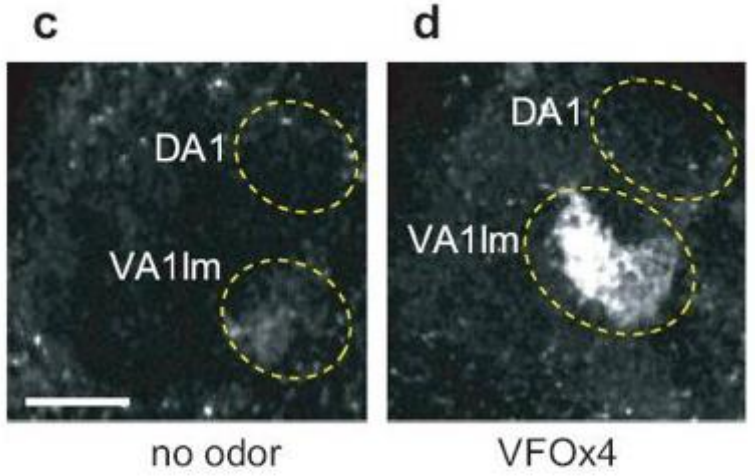
CaLexA

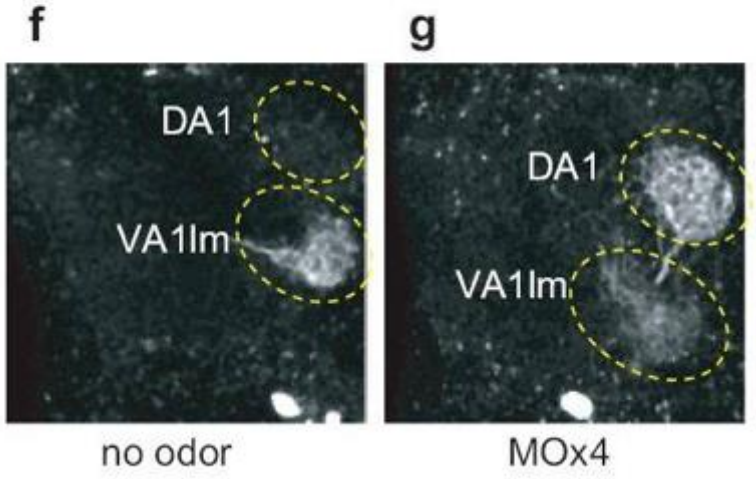






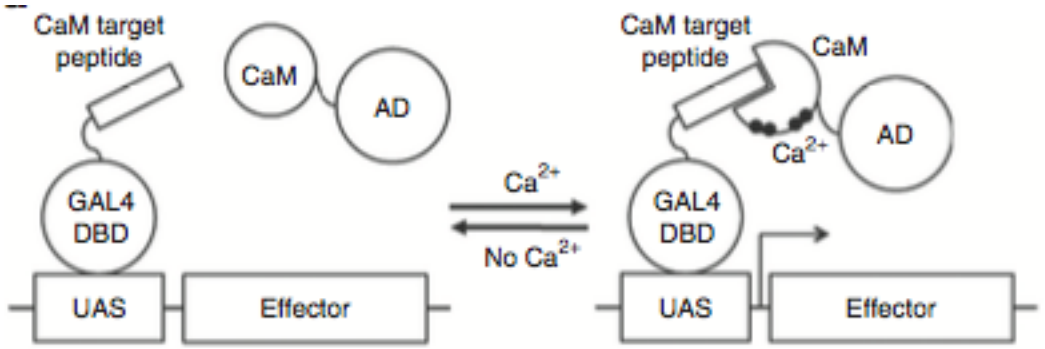


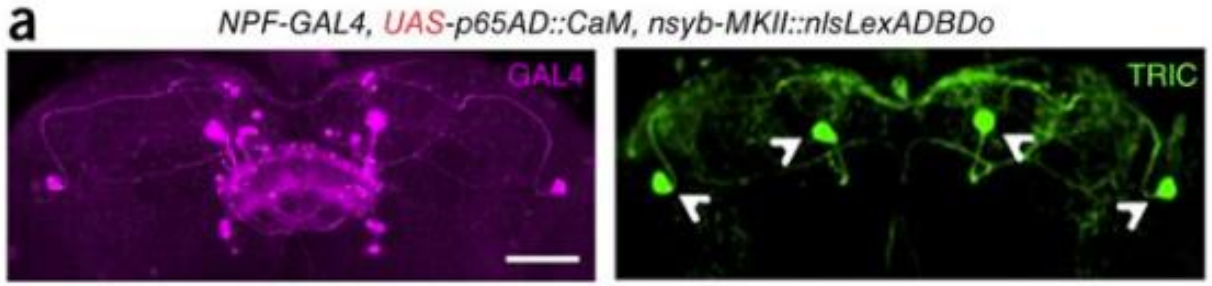


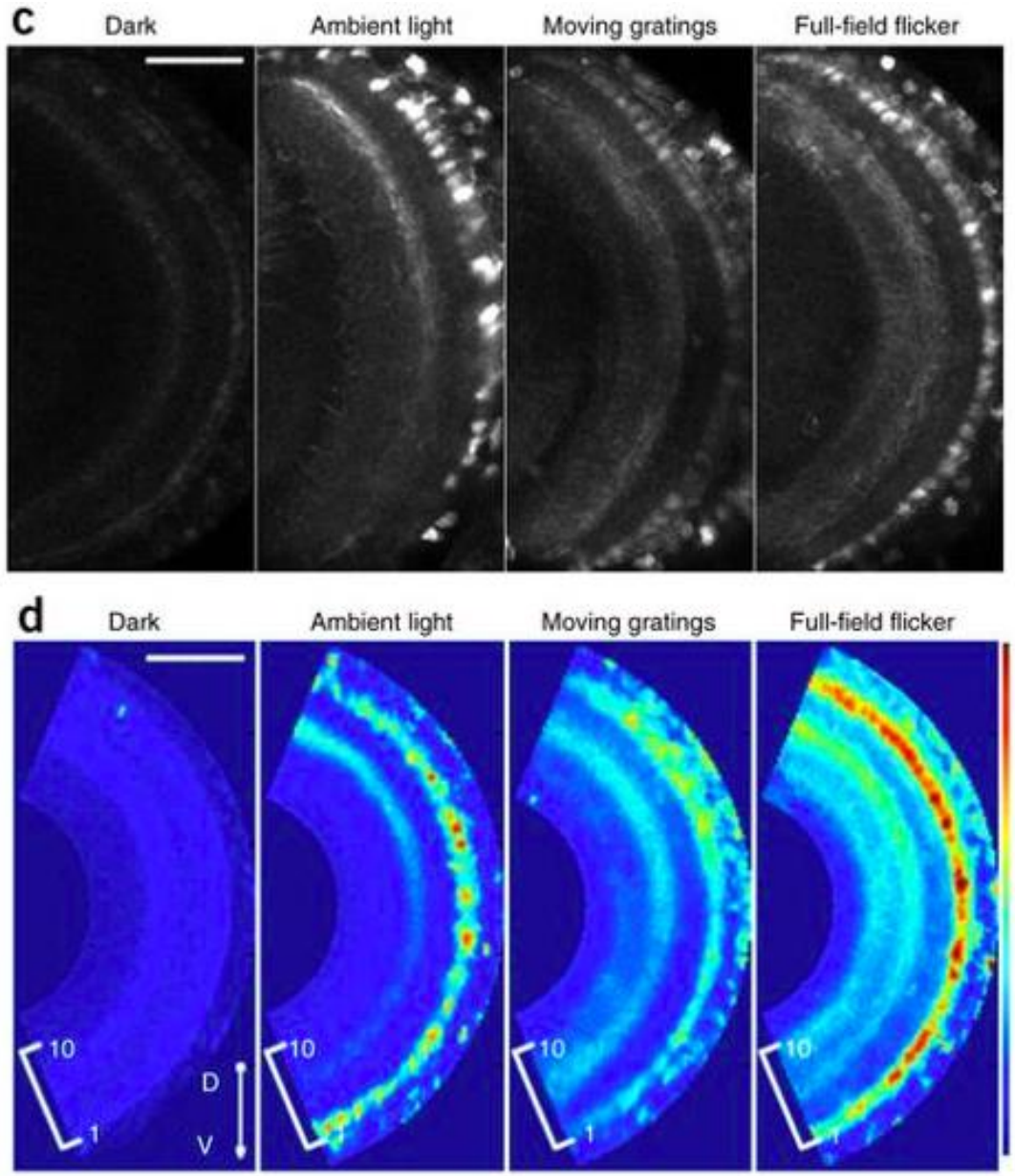


Kaoru Masuyama et al. Journal of Neurogenetics.201

TRIC







Xiaojing J Gao et al. Nature neuroscience.2015

Part III. Manipulating neuronal activity and behavioral analyses

Chen Jie

Manipulating neuronal activity

Inactivation of neurons

- Lesion

  Ablate using a high-intensity laser

- Genetic approaches

  Tetanus toxin

  Kir2.1

  Shibire protein(inactivate target neurons transiently)

- Chemogenetic approaches

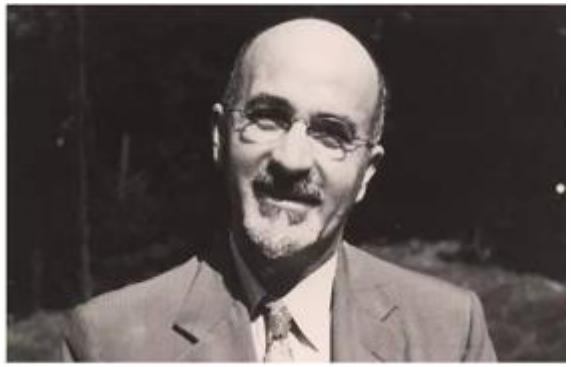
  DREADD

  PSEM

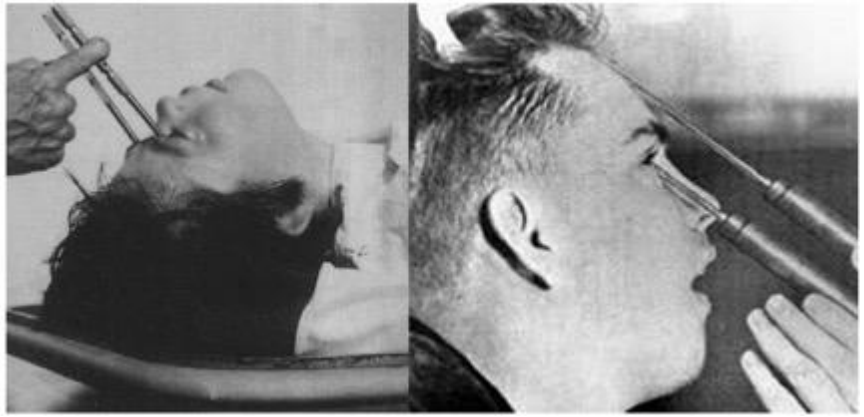
Inactivation of neurons

- Lesion

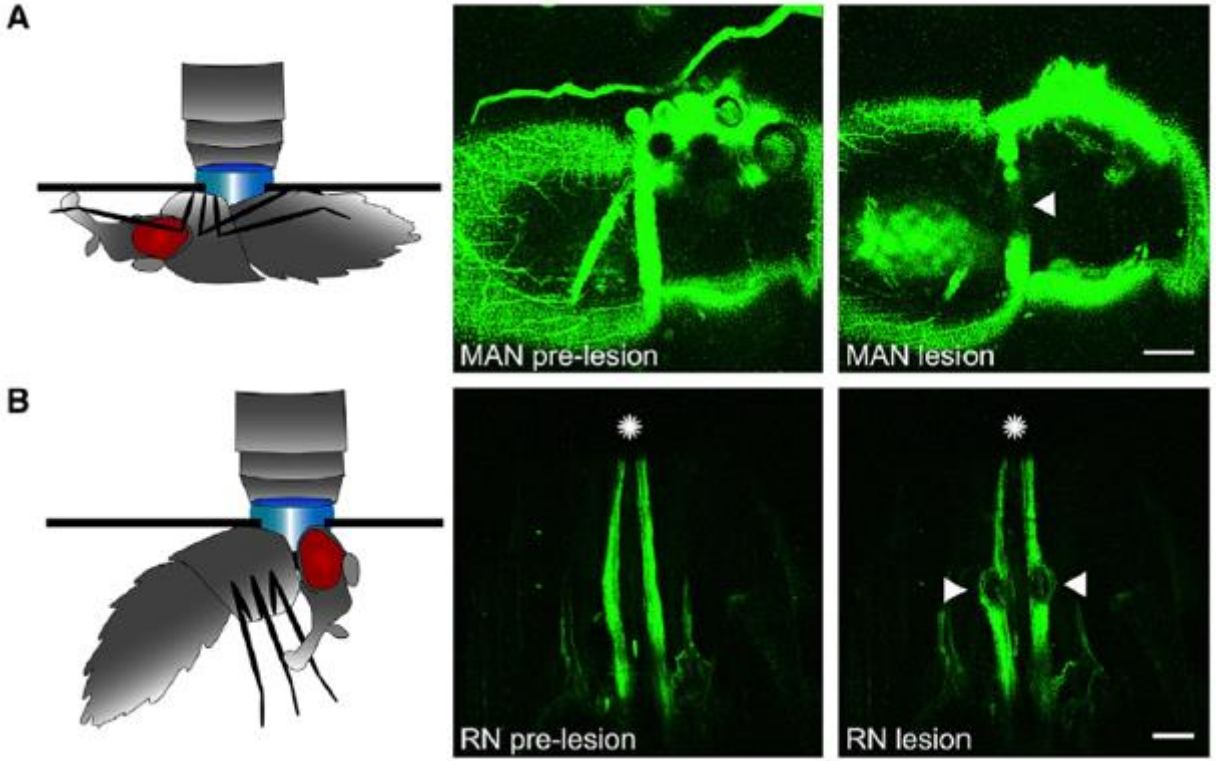
António Egas Moniz



Walter Jackson Freeman II



Ablate using a high-intensity laser



Allan-Hermann Pool et al. Neuron.2014

Inactivation of neurons

- Genetic approaches

  Tetanus toxin

  Shibire protein(inactivate target neurons transiently)

  Kir2.1

  Reaper

Tetanus toxin

Tetanus toxin

A heavy chain

binds to dissialogangliosides (GD2 and GD1b) on the neuronal membrane and contains a translocation domain which aids the movement of the protein across that membrane and into the neuron

A light chain

1.present in the cytosol

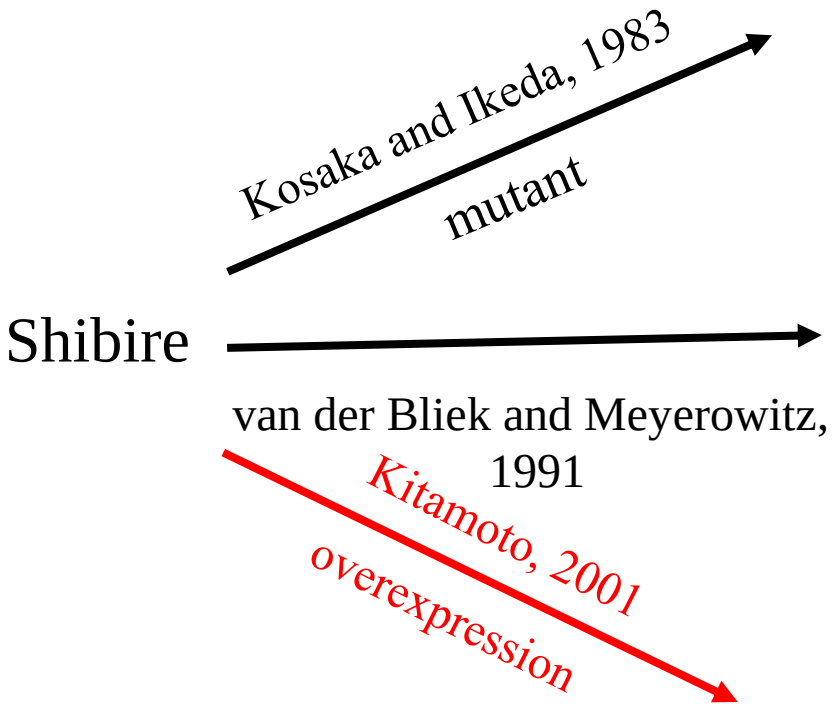
2.can cleave synaptobrevin (an intrinsic membrane protein localized on synaptic vesicles)

Sweeney et al., 1995

TeTxLC

(Such as UAS-TNT)

Shibire protein (inactivate target neurons transiently)



is essential for synaptic vesicle recycling

encodes the protein dynamin

- A powerful tool to inactivate target neurons transiently
- Using the GAL4/UAS system (Brand and Perrimon, 1993)

（Such as UAS-Shits）

Kir2.1

Synaptic activity was blocked TeTxLC or shibire protein.

But how about the electrical phenotype of these neurons?

They are abnormal

Kir2.1 —Baines et al., 2001→

1. is potassium channel
2. hyperpolarizes neurons, thereby efficiently blocking action potential generation
3. is electrical silencing
4. can block neuronal activity regardless of the synapse type

（UAS-Kir2.1）

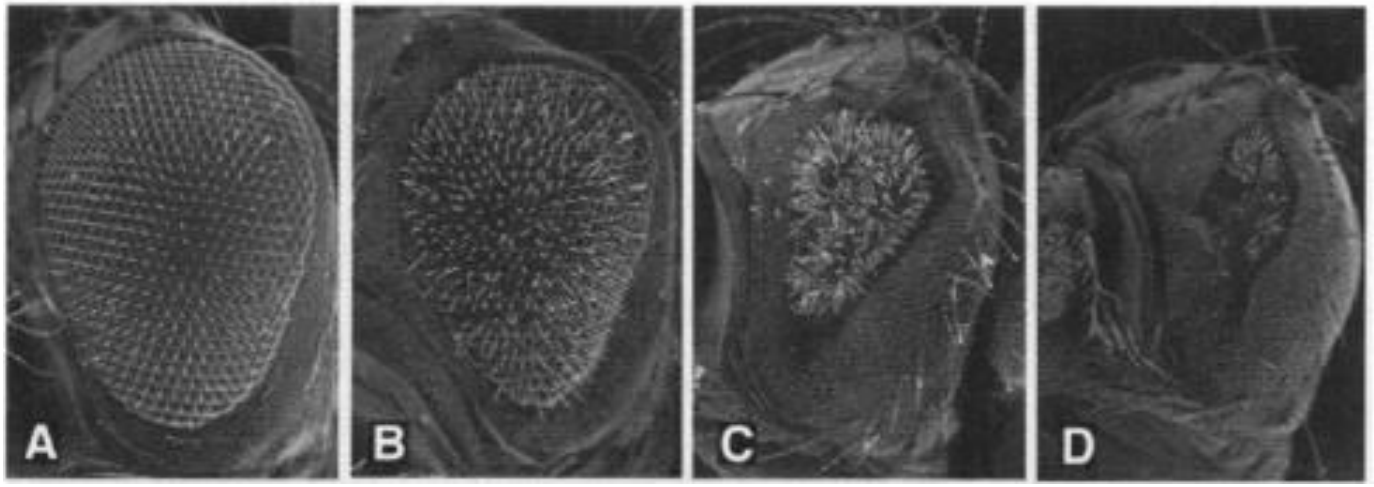
Reaper

Science
AAAS

Cell Killing by the *Drosophila* Gene *reaper*

Kristin White, Elvan Tahaoglu, Hermann Steller

The *reaper* gene (*rpr*) is important for the activation of apoptosis in *Drosophila*



（ Such as UAS-rpr ）

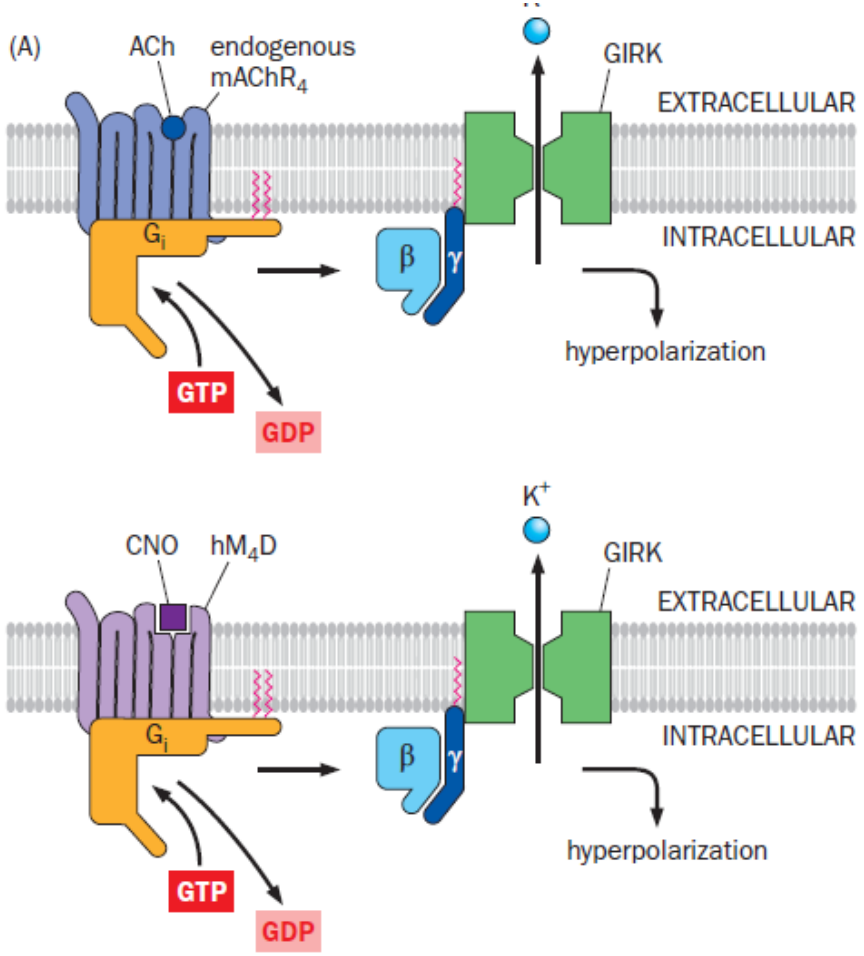
White et al. Science.1996

Inactivation of neurons

➢Chemogenetic approaches

DREADD

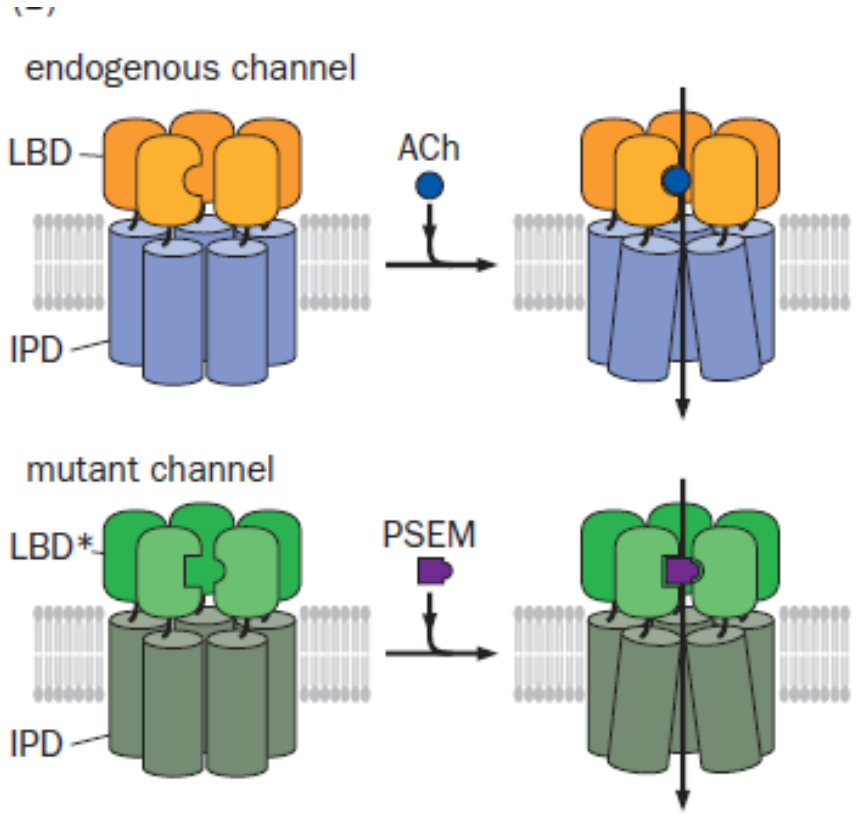
(for designer receptors exclusively activated by a designer drug)



CNO 氯氮平

PSEM

(pharmacologically selective effector molecule)



Manipulating neuronal activity

Activation of neurons

Electrical stimulation

A temperature-gated TrpA1 channel

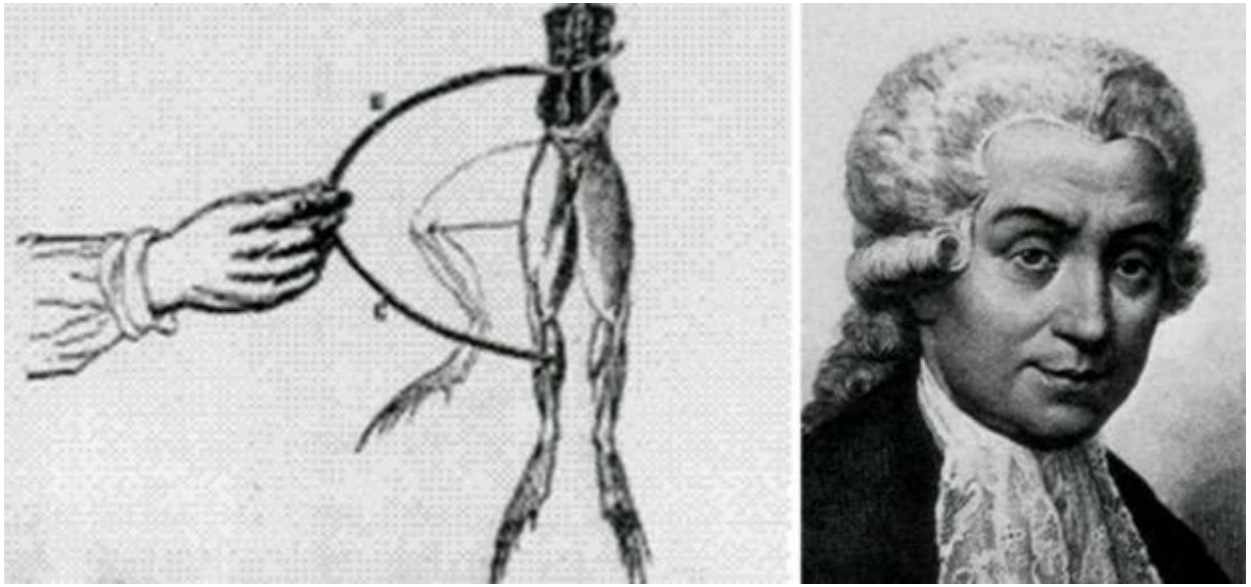
A mammalian ATP-gated P2X2 channel

Optogenetics

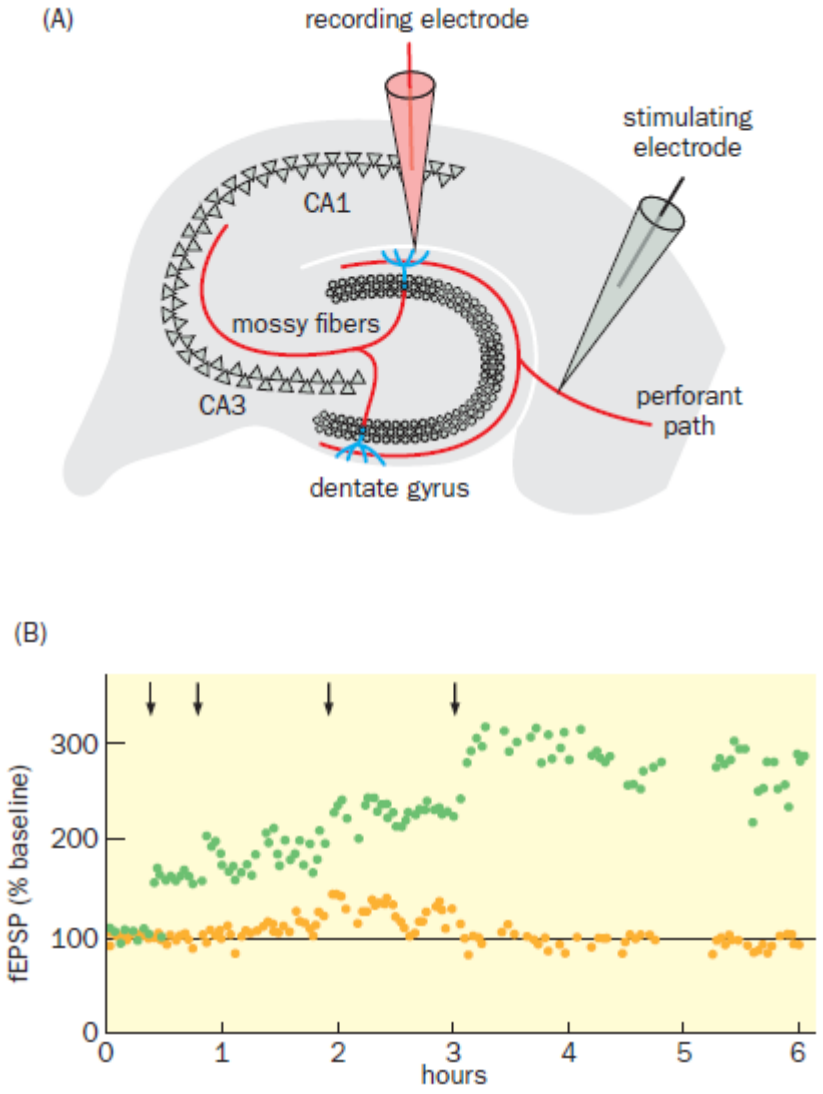
Chemogenetic approaches

Activation of neurons

Electrical stimulation



Luigi Galvani



Neuroscience. 3rd edition

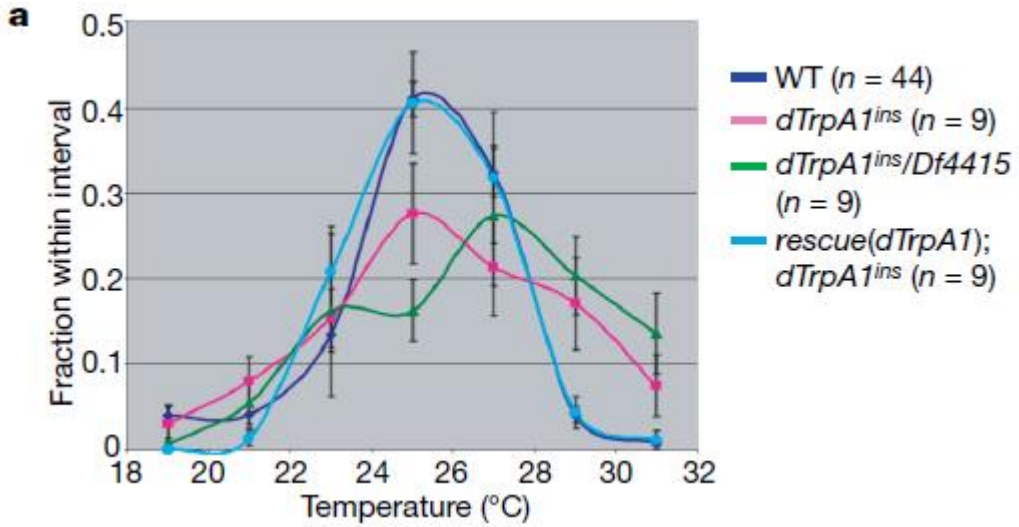
Activation of neurons

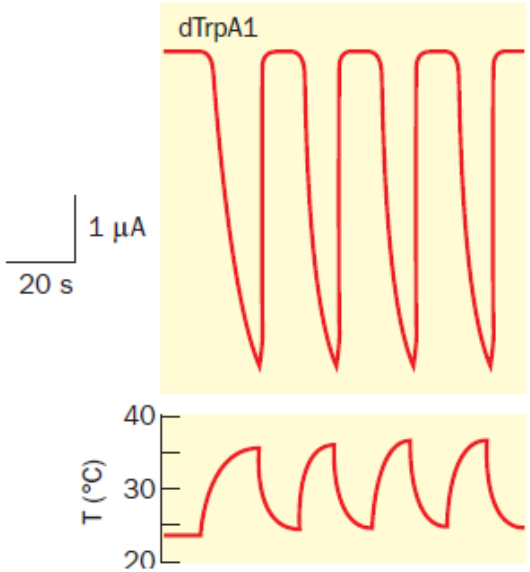
A temperature-gated TrpA1 channel

Trp: Transient receptor potential (TRP) family (thermos TRPs)

Vol 454|10 July 2008|doi:10.1038/nature07001 nature

An internal thermal sensor controlling temperature preference in *Drosophila*





Turning heat into depolarization

（ Such as UAS-TrpA1 ）

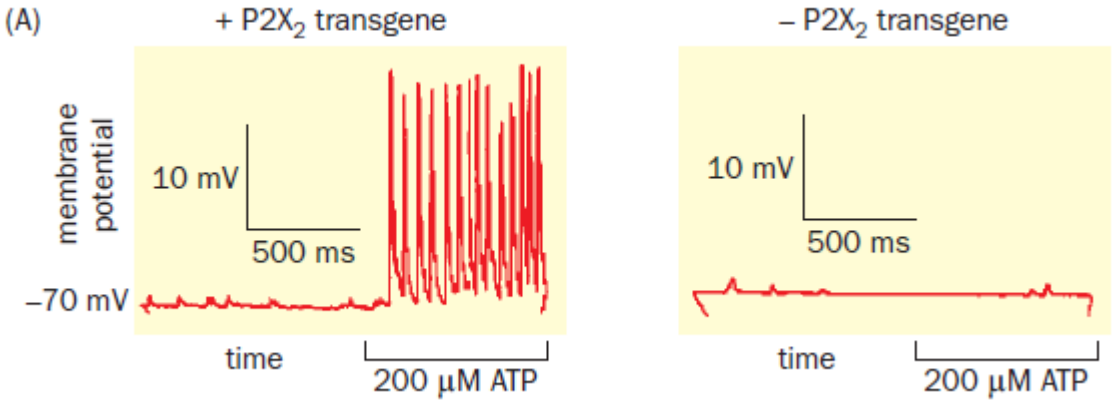
Activation of neurons

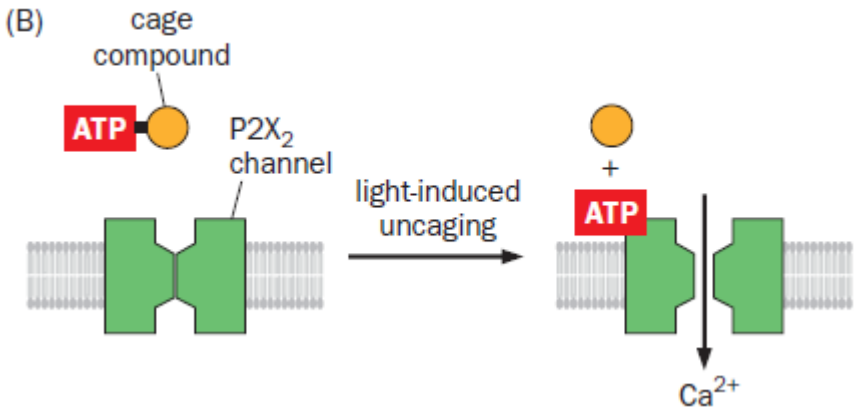
A mammalian ATP-gated P2X2 channel

Cell, Vol. 121, 141–152, April 8, 2005, Copyright ©2005 by Elsevier Inc. DOI 1(

Remote Control of Behavior through Genetically Targeted Photostimulation of Neurons

Susana Q. Lima and Gero Miesenböck*



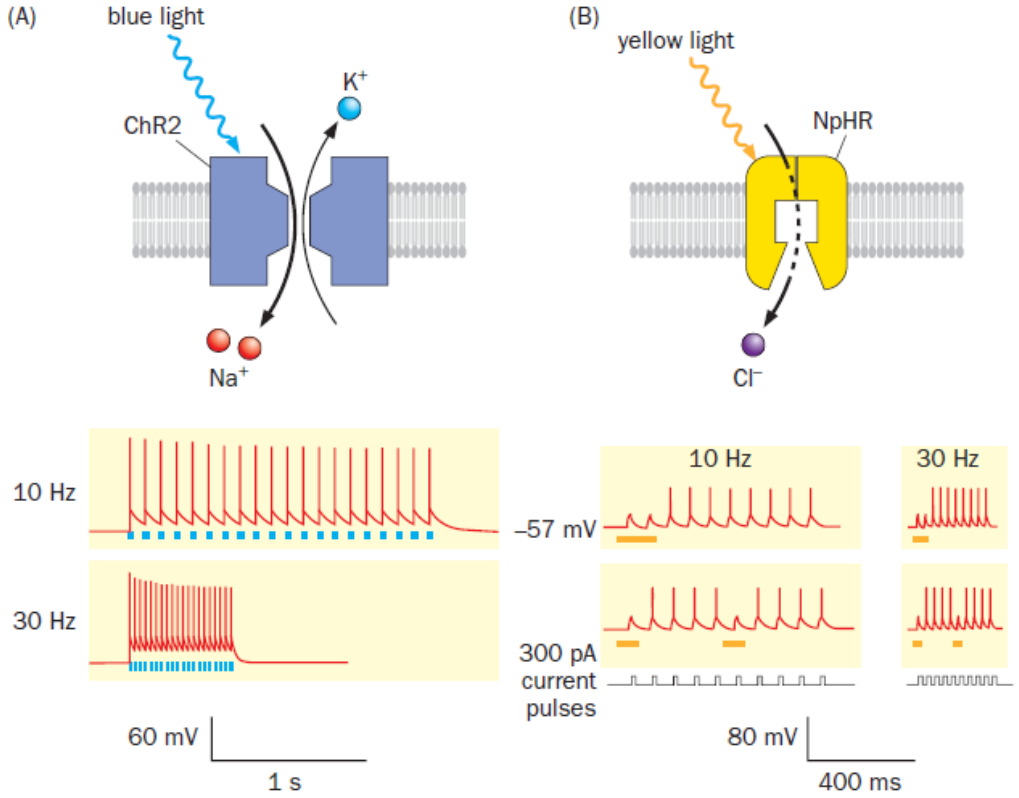


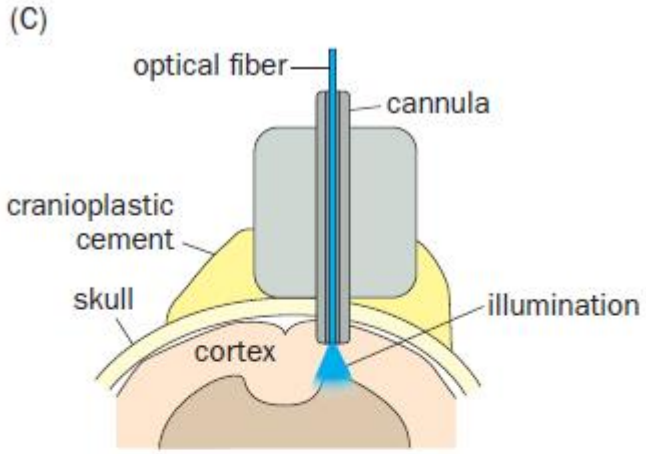
（ Such as UAS-P2X2 ）

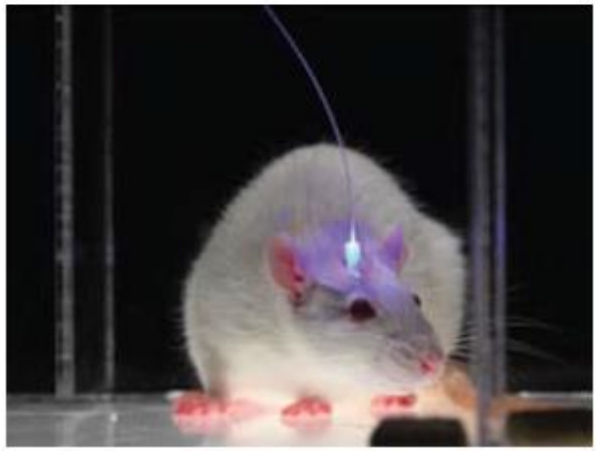
Neuroscience. 3rd edition

Activation of neurons

Optogenetics







ChR2:*Chlamydomonas reinhardtii* Channelrhodopsin-2
NpHR: *Natronomonas pharaonis* halorhodopsin

（ Such as UAS-Chrimson ）

Neuroscience. 3rd edition

Behavioral analyses

Three purposes

- Behavioral analyses aim to explain the behavior itself

in natural environments

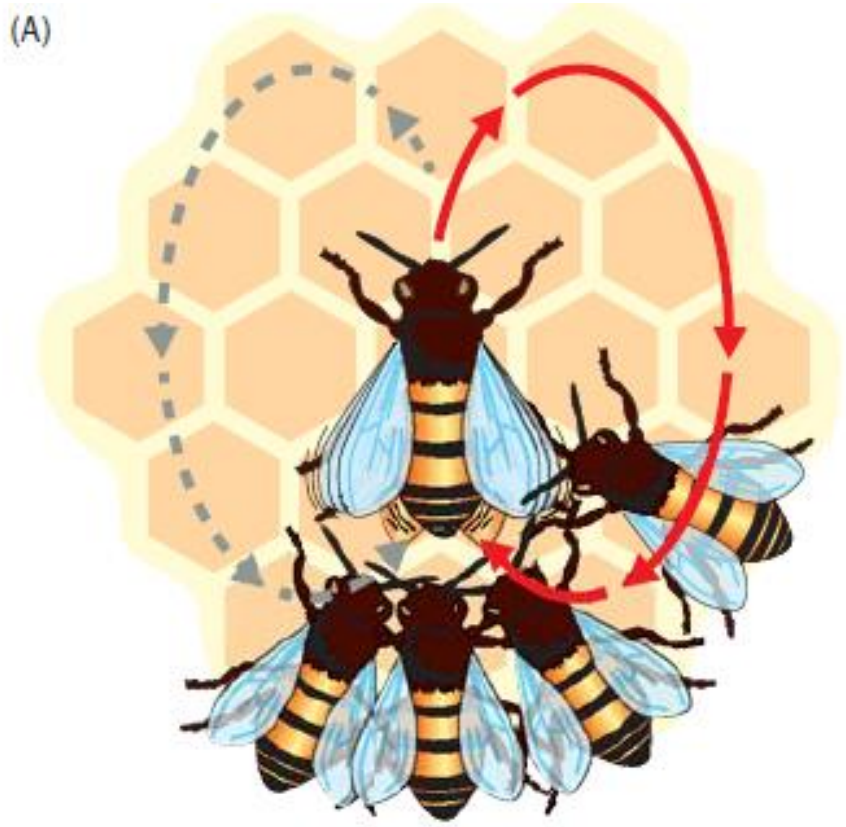
- Behavioral analyses are used as quantitative assays for the functions of brain regions, circuits, and neurons in specific neurobiological processes being investigated
  (such as sensory perception or learning and memory)

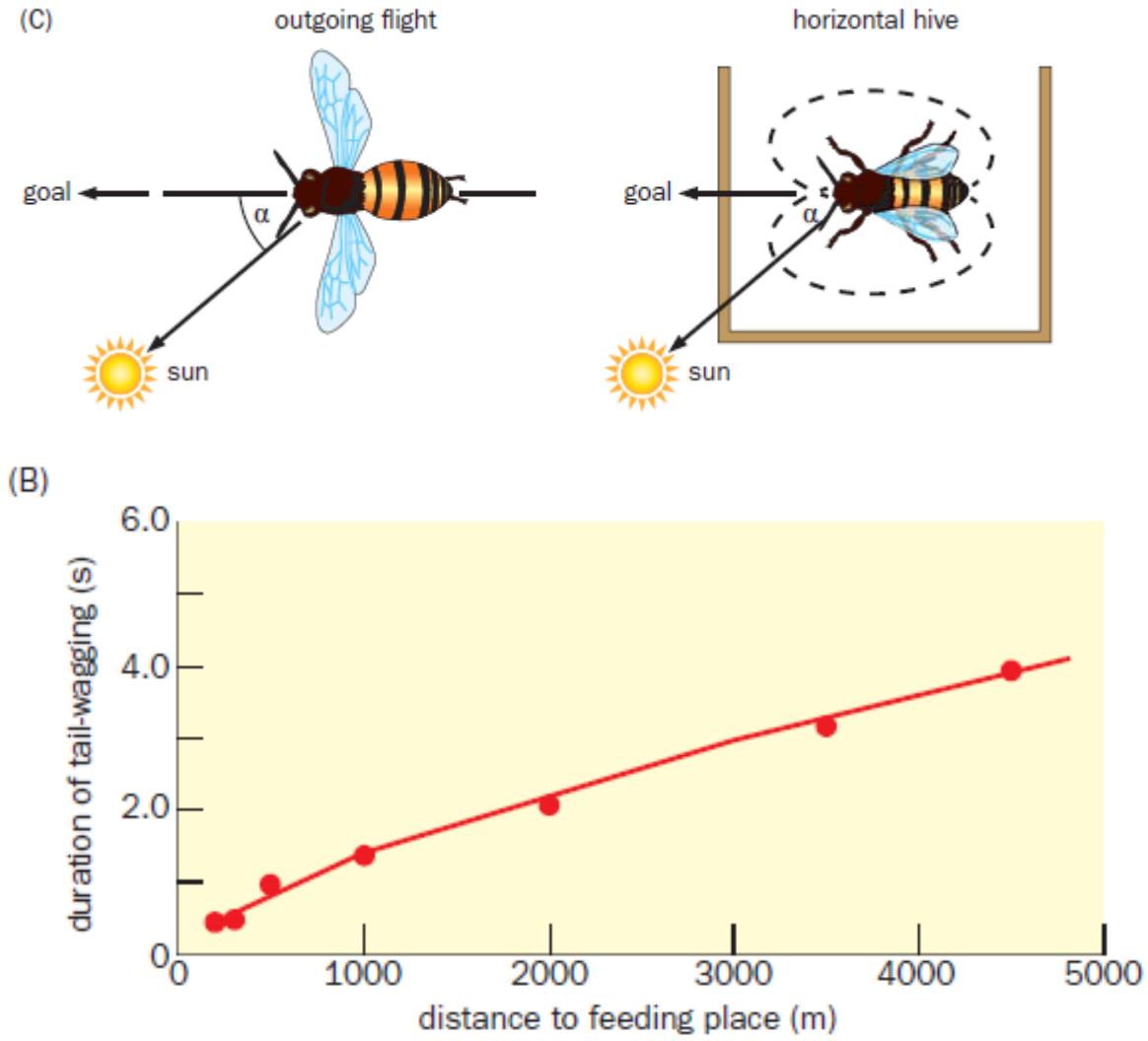
- Behavioral analyses are used to test the effects of manipulating specific genes or to assess animal models of human brain disorders

in controlled conditions

- Behavioral analyses aim to explain the behavior itself

Honeybee foraging behavior

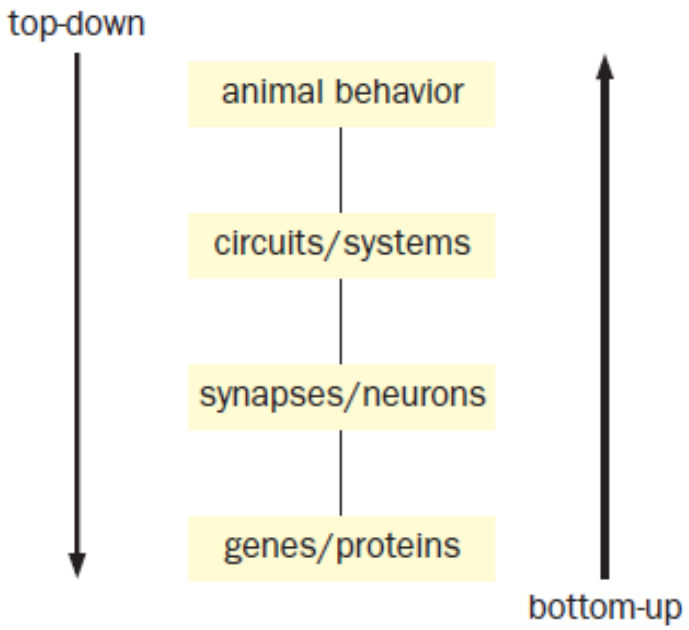




Neuroscience. 3rd edition

- Behavioral analyses are used as quantitative assays for the functions of brain regions, circuits, and neurons

- Behavioral analyses are used to test the effects of manipulating specific genes or to assess animal models of human brain disorders



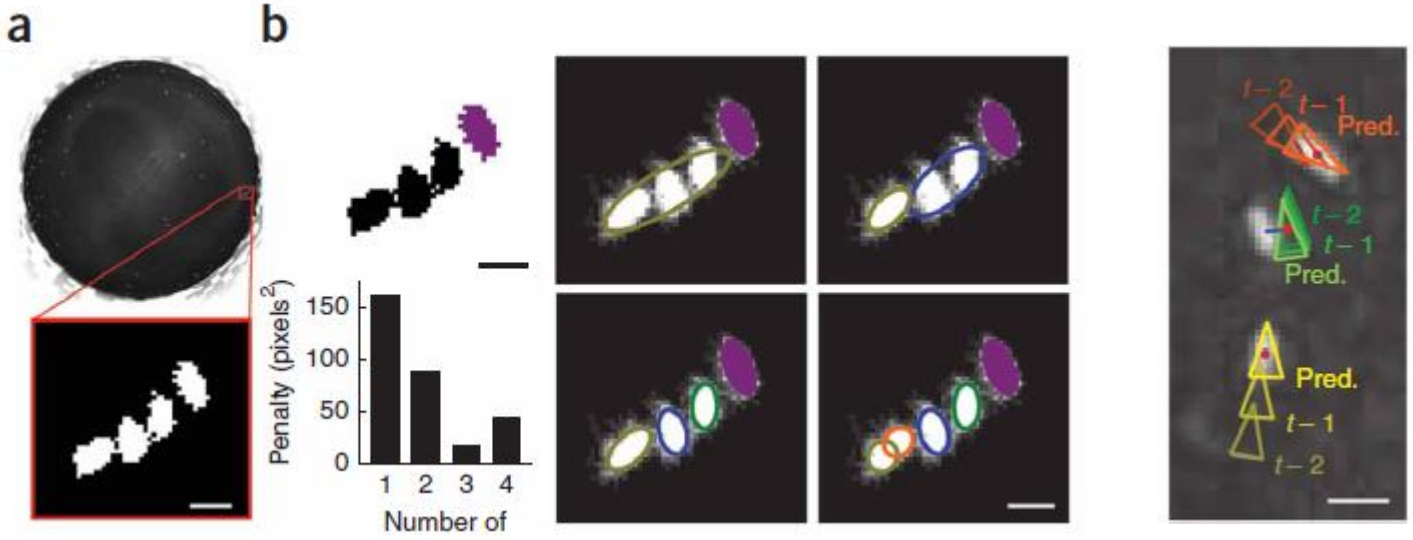
Neuroscience. 3rd edition

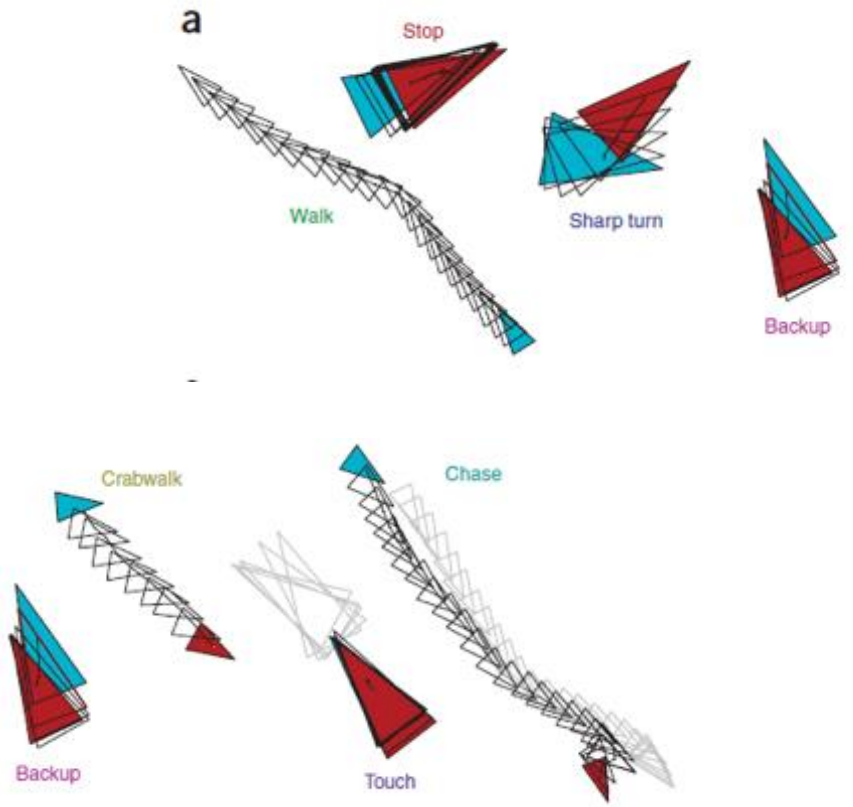
Some new ways of behavioral analyses

Individual and social behaviors

High-throughput ethomics in large groups of *Drosophila*

Kristin Branson[1], Alice A Robie[1], John Bender[2], Pietro Perona[1] & Michael H Dickinson[1]

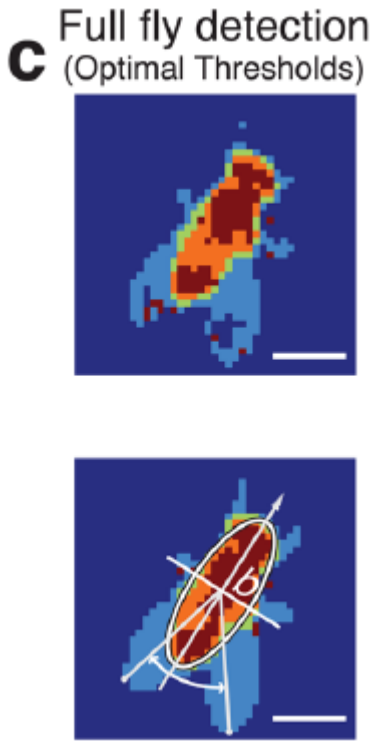


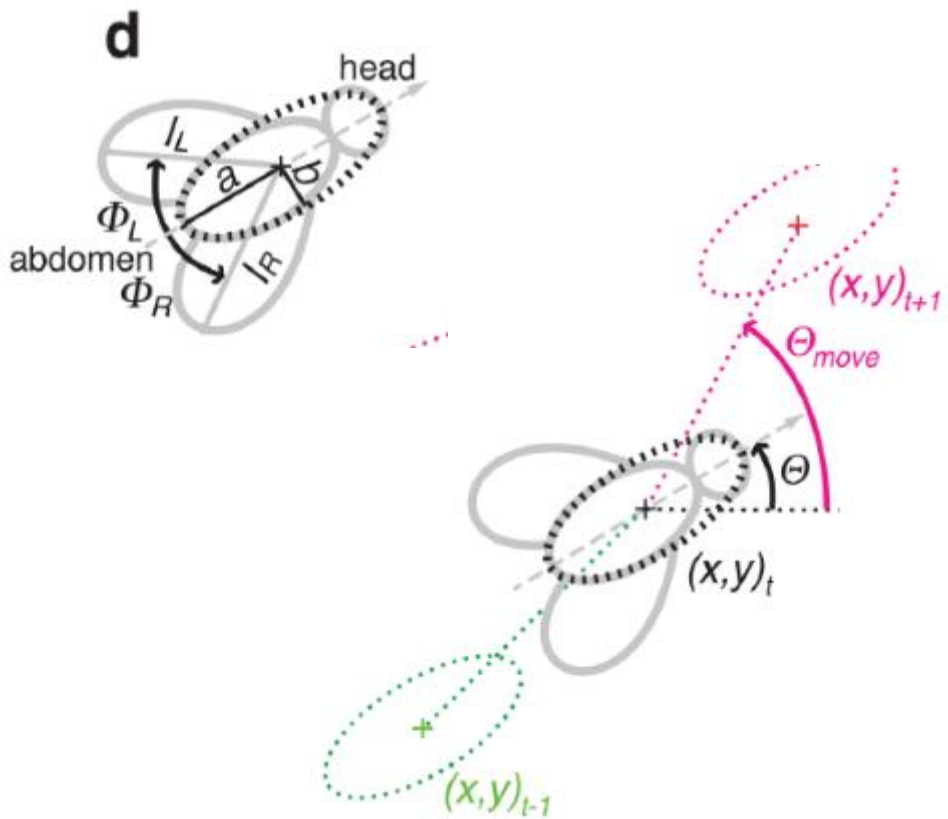


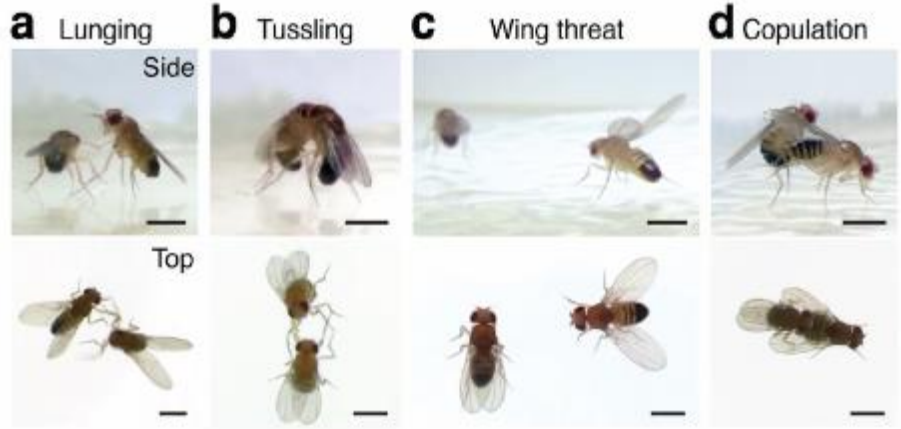
https://dickinsonlab.caltech.edu/techniques/

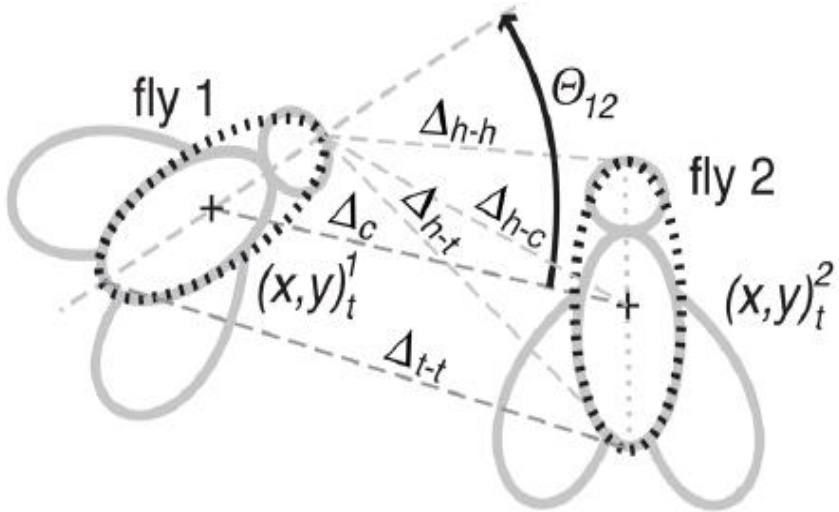
Automated Monitoring and Analysis of Social Behavior in *Drosophila*

Heiko Dankert[1,2], Liming Wang[2], Eric D. Hoopfer[2], David J. Anderson[2], and Pietro P





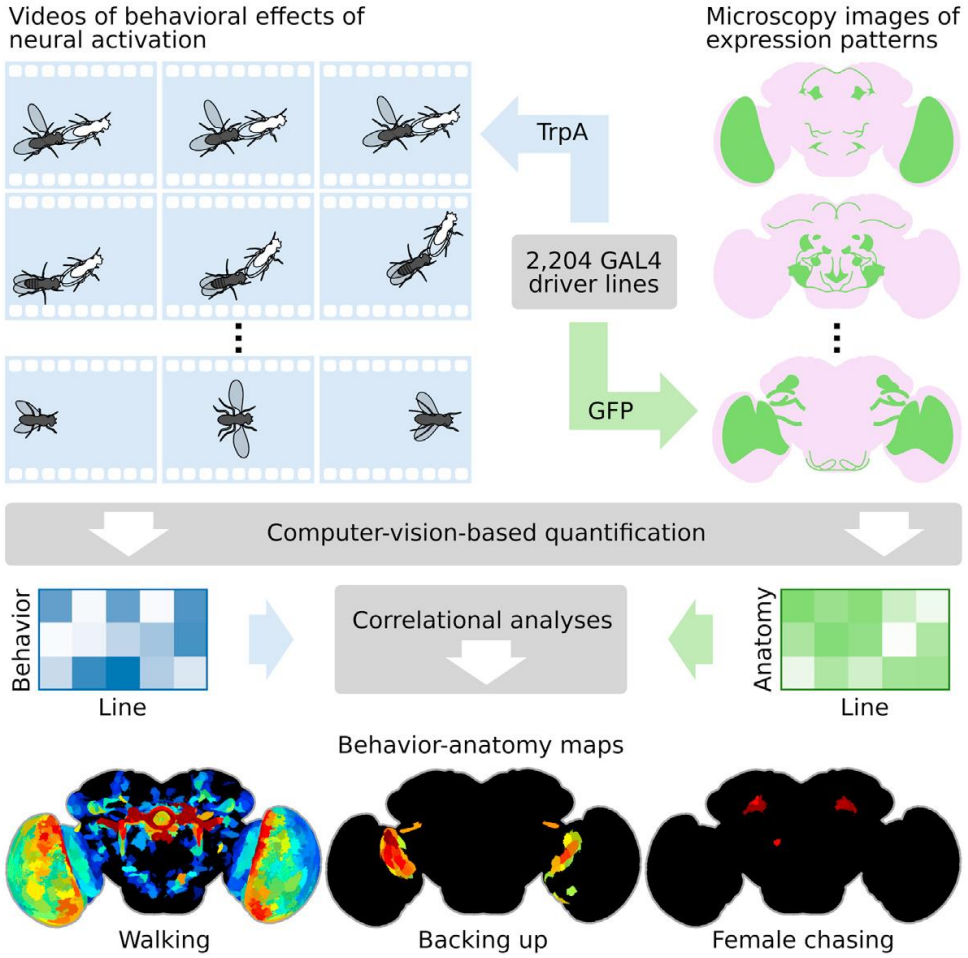


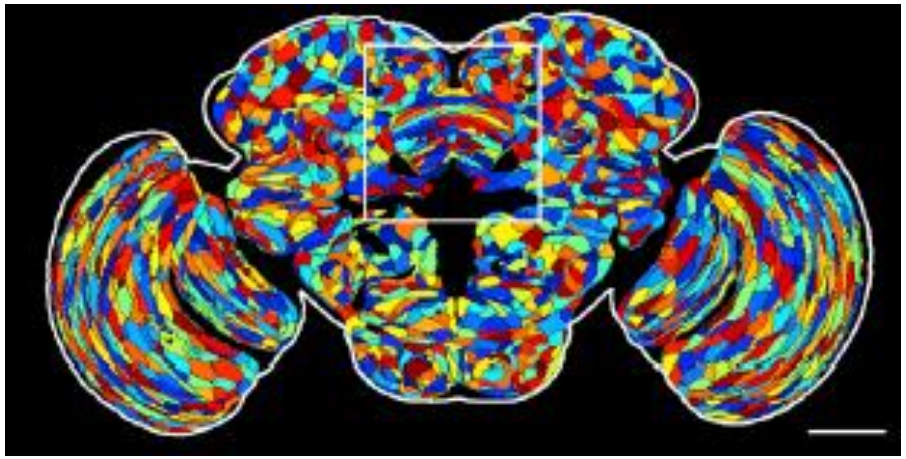


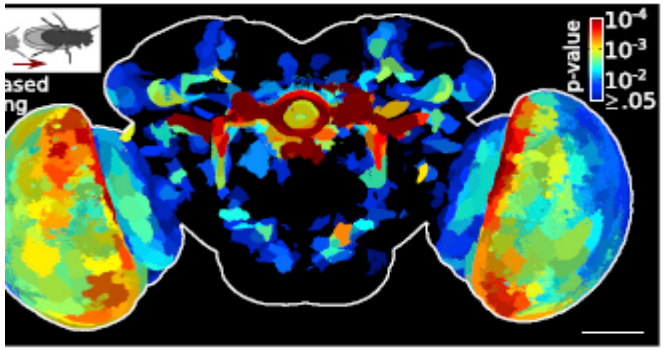
https://www.nature.com/articles/nmeth.1310

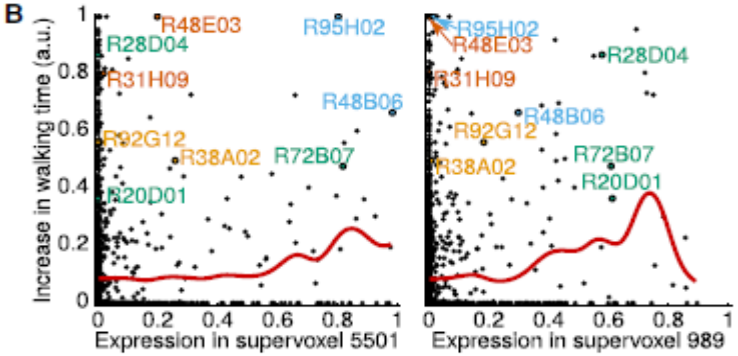
Cell

Mapping the Neural Substrates of Behavior





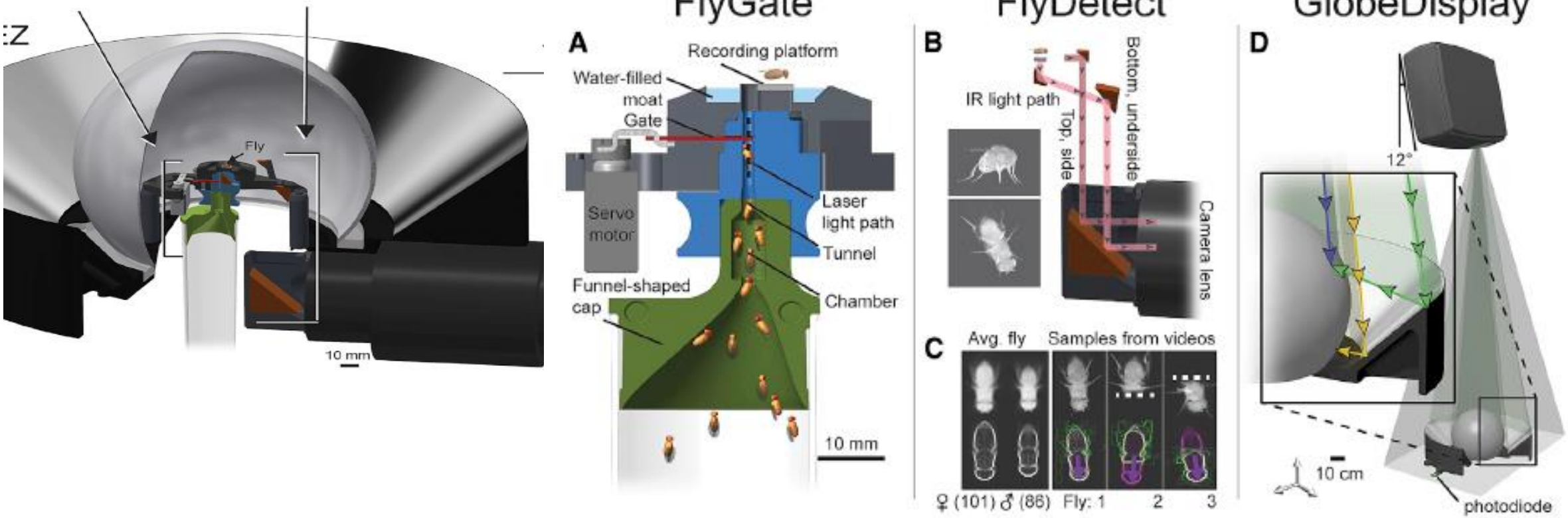




http://research.janelia.org/bransonlab/FlyBowl/BehaviorResults/

Cell Reports

Tools for Rapid High-Resolution Behavioral Phenotyping of Automatically Isolated *Drosophila*



References

1. Aso Y, Siwanowicz I, Bracker L, Ito K, Kitamoto T, Tanimoto H. Specific dopaminergic neurons for the formation of labile aversive memory. Current biology : CB. 2010;20(16):1445-51.
2. Chang HY, Grygoruk A, Brooks ES, Ackerson LC, Maidment NT, Bainton RJ, et al. Overexpression of the Drosophila vesicular monoamine transporter increases motor activity and courtship but decreases the behavioral response to cocaine. Molecular psychiatry. 2006;11(1):99-113.
3. Claridge-Chang A, Roorda RD, Vrontou E, Sjulson L, Li H, Hirsh J, et al. Writing memories with light-addressable reinforcement circuitry. Cell. 2009;139(2):405-15.
4. Friggi-Grelin F, Coulom H, Meller M, Gomez D, Hirsh J, Birman S. Targeted gene expression in Drosophila dopaminergic cells using regulatory sequences from tyrosine hydroxylase. Journal of neurobiology. 2003;54(4):618-27.
5. Honjo K, Furukubo-Tokunaga K. Distinctive neuronal networks and biochemical pathways for appetitive and aversive memory in Drosophila larvae. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2009;29(3):852-62.
6. Inagaki HK, Ben-Tabou de-Leon S, Wong AM, Jagadish S, Ishimoto H, Barnea G, et al. Visualizing neuromodulation in vivo: TANGO-mapping of dopamine signaling reveals appetite control of sugar sensing. Cell. 2012;148(3):583-95.
7. Keleman K, Vrontou E, Kruttner S, Yu JY, Kurtovic-Kozaric A, Dickson BJ. Dopamine neurons modulate pheromone responses in Drosophila courtship learning. Nature. 2012;489(7414):145-9.
8. Liu T, Dartevelle L, Yuan C, Wei H, Wang Y, Ferveur JF, et al. Increased dopamine level enhances male-male courtship in Drosophila. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2008;28(21):5539-46.

References

9. Marella S, Mann K, Scott K. Dopaminergic modulation of sucrose acceptance behavior in Drosophila. Neuron. 2012;73(5):941-50.
10. Nutt DJ, Lingford-Hughes A, Erritzoe D, Stokes PR. The dopamine theory of addiction: 40 years of highs and lows. Nature reviews Neuroscience. 2015;16(5):305-12.
11. Pimentel D, Donlea JM, Talbot CB, Song SM, Thurston AJF, Miesenbock G. Operation of a homeostatic sleep switch. Nature. 2016;536(7616):333-7.
12. Ueno T, Tomita J, Tanimoto H, Endo K, Ito K, Kume S, et al. Identification of a dopamine pathway that regulates sleep and arousal in Drosophila. Nature neuroscience. 2012;15(11):1516-23.
13. Waddell S. Dopamine reveals neural circuit mechanisms of fly memory. Trends in neurosciences. 2010;33(10):457-64.
14. Wise RA. Dopamine, learning and motivation. Nature reviews Neuroscience. 2004;5(6):483-94.