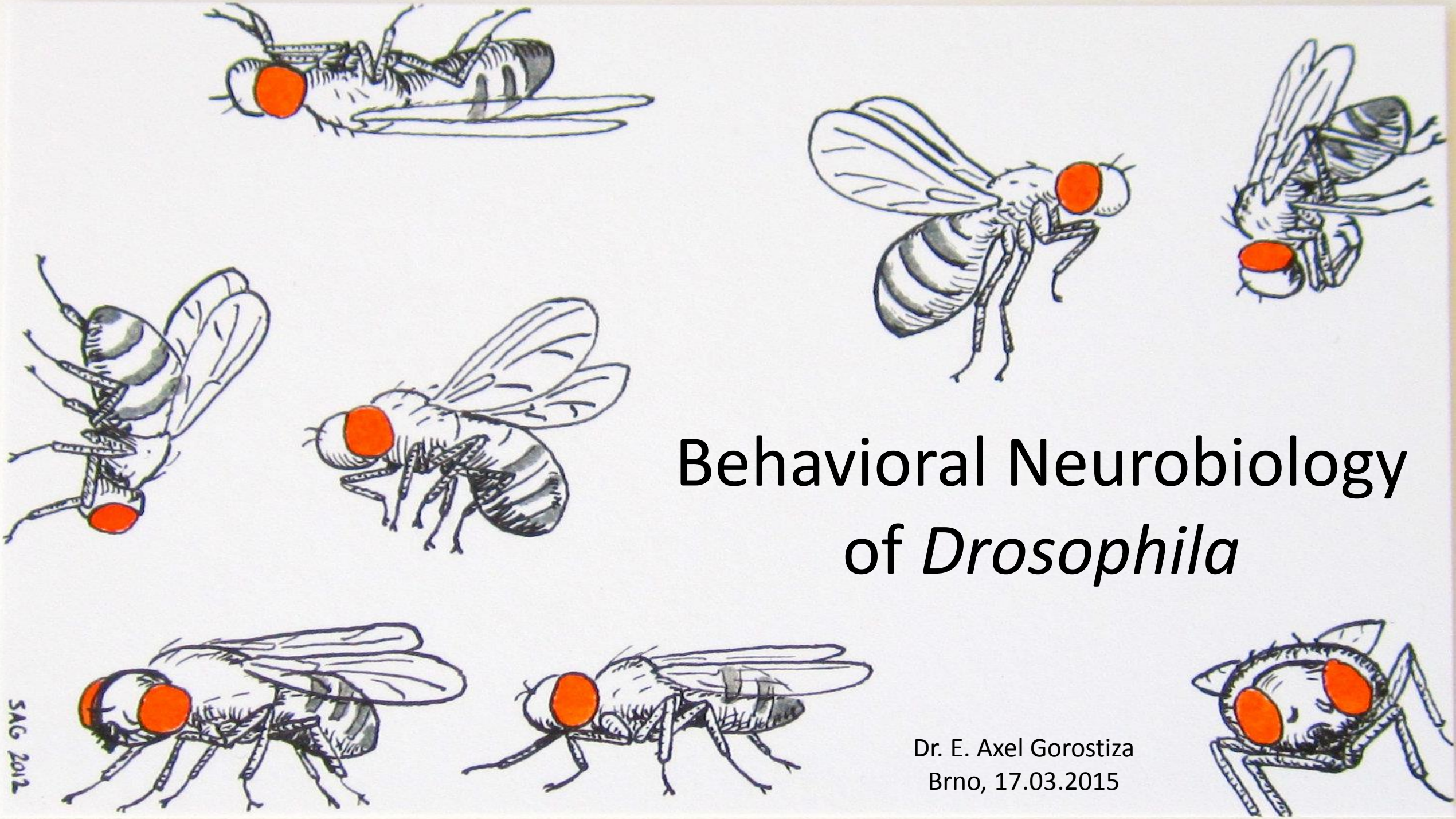
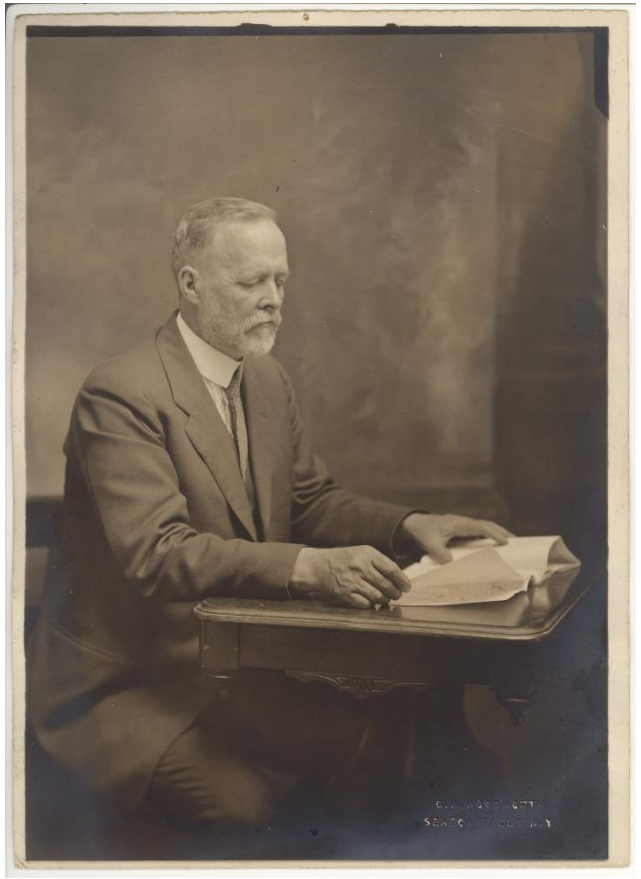


Behavioral Neurobiology of *Drosophila*

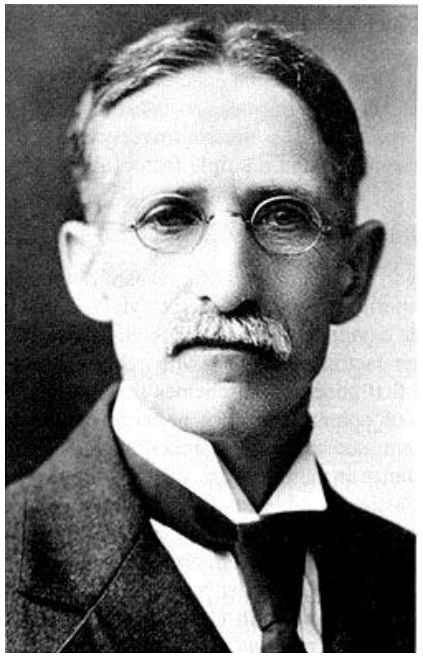
Dr. E. Axel Gorostiza

Brno, 17.03.2015

A little bit of history.



Charles W. Woodworth (USA)
Entomologist
(April 28, 1865 – November 19, 1940)



William Ernest Castle (USA)
Embryologist and geneticist
(October 25, 1867 – June 3, 1962)

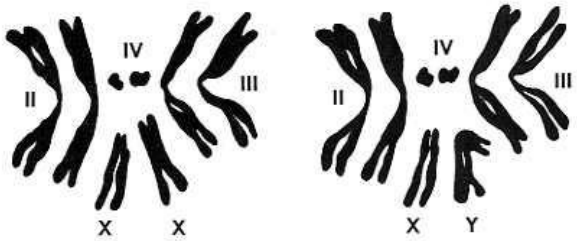
Thomas Hunt Morgan (USA)
evolutionary biologist, geneticist and embryologist
(September 25, 1866 – December 4, 1945)

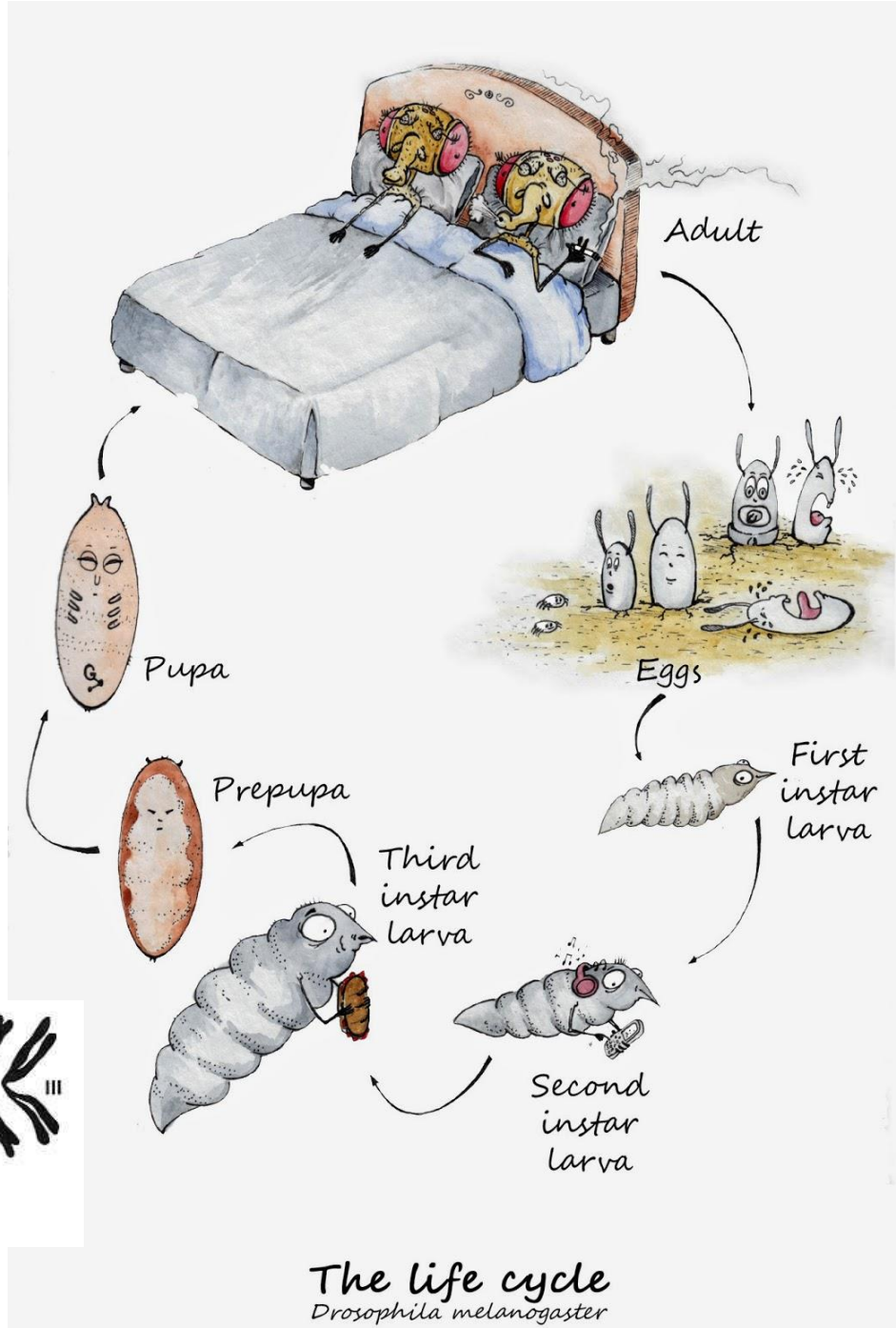
The Nobel Prize in Physiology or Medicine 1933 was awarded to Thomas H. Morgan *"for his discoveries concerning the role played by the chromosome in heredity"*.

Why *Drosophila*?

http://www.theflyroom.com/

Fly Food Ingredients	Amounts (ml or g)
Water	1000 ml
Yeast (dry)	20 g
Agar	10 g
Sucrose	40 g
Corn Flour	65 g
Propionic acid	4.4 ml
10 % Nipagin in 95% EtOH	14 ml





http://drosophiladrawings.blogspot.de/

But, what about behavior?

THE REACTIONS OF THE POMACE FLY (*DROSOPHILA AMPELOPHILA* LOEW) TO LIGHT, GRAVITY, AND MECHANICAL STIMULATION.

FREDERIC W. CARPENTER.

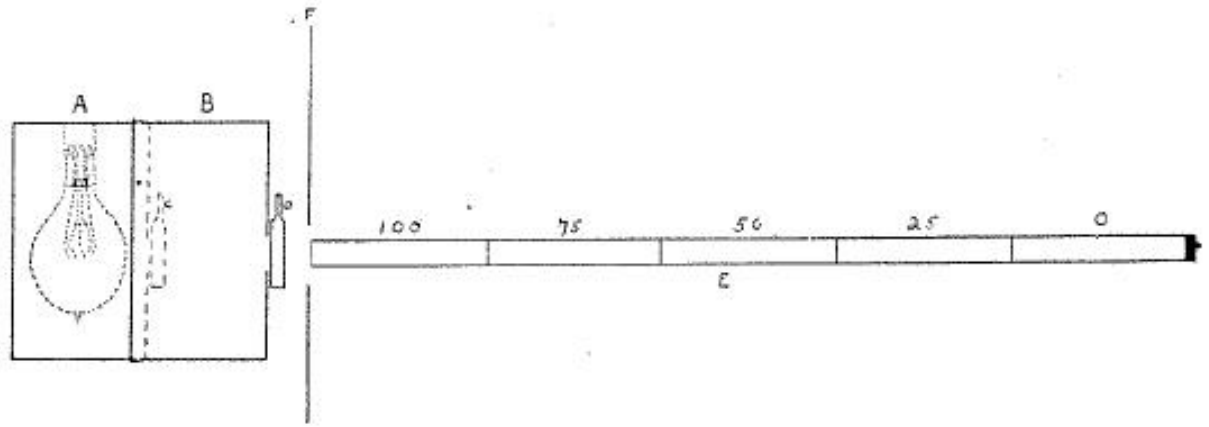
The American Naturalist, Mar., **1905**, pp. 157-171

THE REACTIONS TO LIGHT AND TO GRAVITY IN DROSOPHILA AND ITS MUTANTS

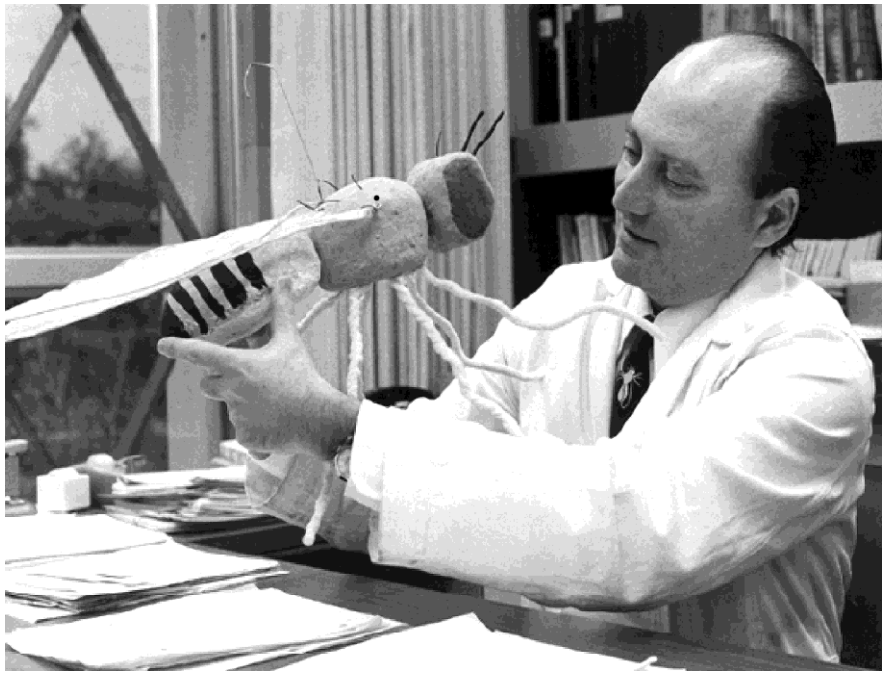
ROBERT STANLEY McEWEN

Columbia University, New York City

J. Exptl. Zool., **1918**, 49–106.



The father of Neurogenetics



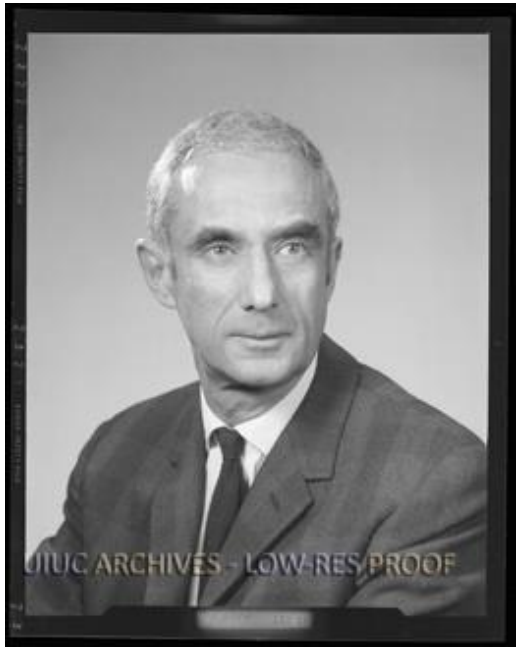
Seymour Benzer
Physicist, molecular biologist and behavioral geneticist
(October 15, 1921 – November 30, 2007)

OPEN ACCESS Freely available online PLoS BIOLOGY

Obituary

Seymour Benzer 1921–2007
The Man Who Took Us from Genes to Behaviour

William A. Harris



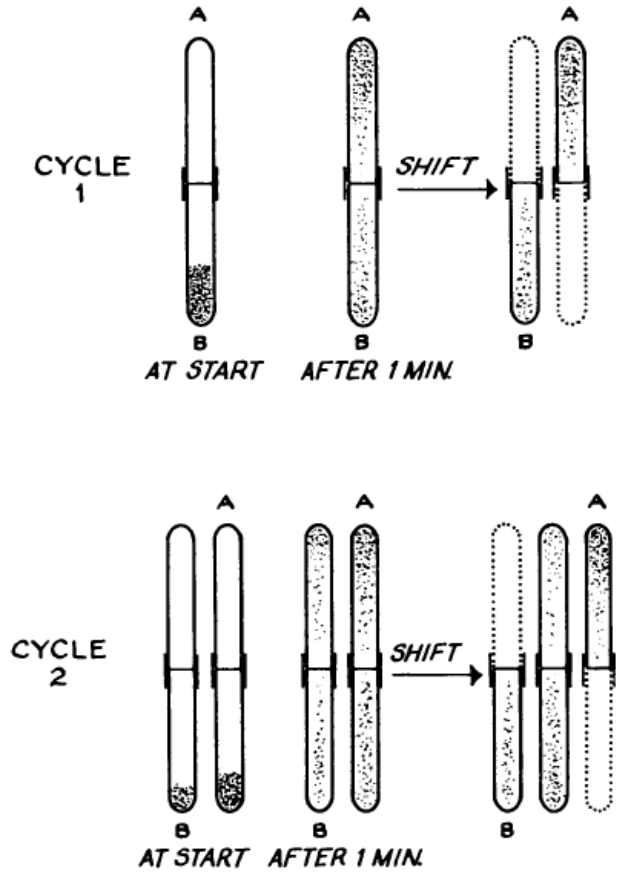
Jerry Hirsch
Behavioral geneticist
(September 20, 1922 – May 3, 2008)

BEHAVIORAL MUTANTS OF DROSOPHILA ISOLATED BY COUNTERCURRENT DISTRIBUTION

By Seymour Benzer

DIVISION OF BIOLOGY, CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA

Communicated June 28, 1967



Clock Mutants of *Drosophila melanogaster*

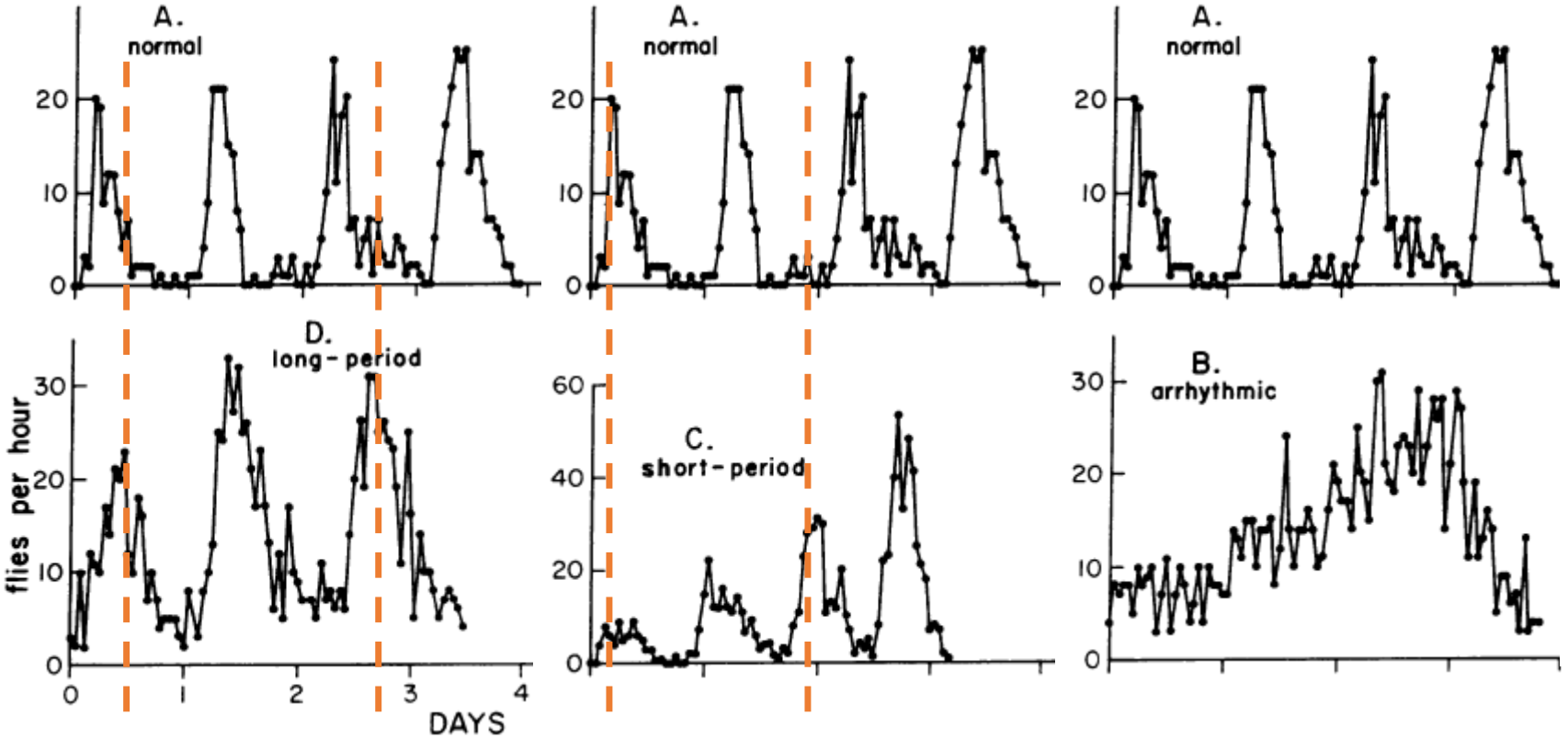
(eclosion/circadian/rhythms/X chromosome)

RONALD J. KONOPKA AND SEYMOUR BENZER

Division of Biology, California Institute of Technology, Pasadena, Calif. 91109

Contributed by Seymour Benzer, July 2, 1971

period



per^{long} *per*^{short} *per*^{0}

Table 1. *Free-running period of locomotor activity*

Genotype				
First X chromosome	Second X chromosome	N	Period ± SD	Phenotype
normal (C-S)	normal (FM 7)	4	24.4 ± 0.5	normal
arrhythmic	arrhythmic	4	arrhythmic	arrhythmic
short-period	short-period	5	19.5 ± 0.4	short-period
long-period	long-period	4	28.6 ± 0.5	long-period
arrhythmic	normal (FM 7)	8	25.2 ± 0.4	~ normal
short-period	normal (FM 7)	5	21.9 ± 0.4	intermediate
long-period	normal (FM 7)	5	25.5 ± 0.5	~ normal
short-period	arrhythmic	6	19.5 ± 0.4	short-period
long-period	arrhythmic	5	30.6 ± 1.3	long-period
short-period	long-period	6	22.9 ± 0.4	~ normal

Drosophila as a model for neurodegenerative diseases

Neuron, Vol. 10, 839–850, May, 1993, Copyright © 1993 by Cell Press

Defective Glia in the Drosophila Brain Degeneration Mutant *drop-dead*

Robert L. Buchanan and Seymour Benzer
California Institute of Technology
Division of Biology
Pasadena, California 91125

***Spongecake* and *eggroll*: two hereditary diseases in *Drosophila* resemble patterns of human brain degeneration**

Kyung-Tai Min and Seymour Benzer

Current Biology 1997, 7:885–888
http://biomednet.com/elecref/0960982200700885

Drosophila as a model for neurodegenerative diseases

1) To model human diseases.

Nature. 2000 Mar 23;404(6776):394-8.

A Drosophila model of Parkinson's disease.

Feany MB[1], Bender WW.

J Vis Exp. 2014 Aug 17;(90). doi: 10.3791/51625.

Methods to characterize spontaneous and startle-induced locomotion in a rotenone-induced Parkinson's disease model of Drosophila.

Liao J[1], Morin LW[1], Ahmad ST[2].

2) To find genes involved in neurodegeneration or diseases.

PLoS One. 2008 Oct 8;3(10):e3332. doi: 10.1371/journal.pone.0003332.

A functional misexpression screen uncovers a role for enabled in progressive neurodegeneration.

Rezával C[1], Berni J, Gorostiza EA, Werbajh S, Fagilde MM, Fernández MP, Beckwith EJ, Aranovich EJ, Sabio y García CA, Ceriani MF.

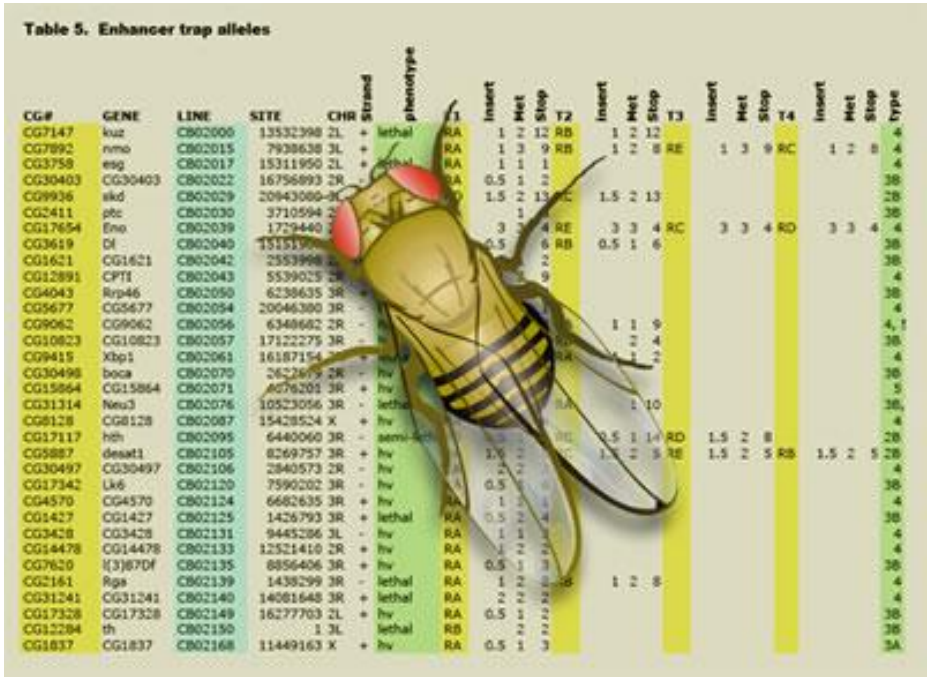
3) To find modulators, interacting genes or treatments related to diseases.

Neuroscience. 2015 Mar 6. pii: S0306-4522(15)00207-9. doi: 10.1016/j.neuroscience.2015.02.048. [Epub ahead of print]

Attenuation of Neuromotor Deficits by Natural Antioxidants of Decalepis hamiltonii in Transgenic Drosophila Model of Parkinson's Disease.

Jahromi SR[1], Haddadi M[2], Shivanandappa T[1], Ramesh SR[3].

Again, why *Drosophila*?

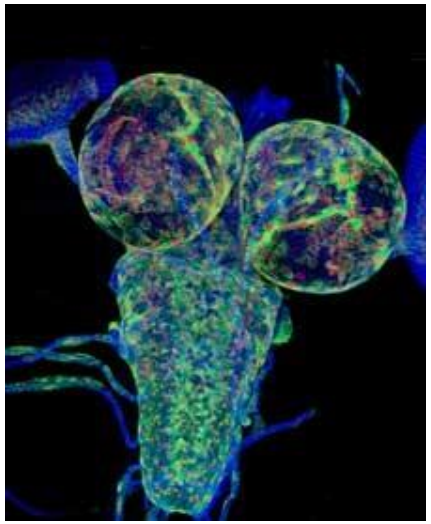


Genome Res. 2001 Jun;11(6):1114-25.

A systematic analysis of human disease-associated gene sequences in Drosophila melanogaster.

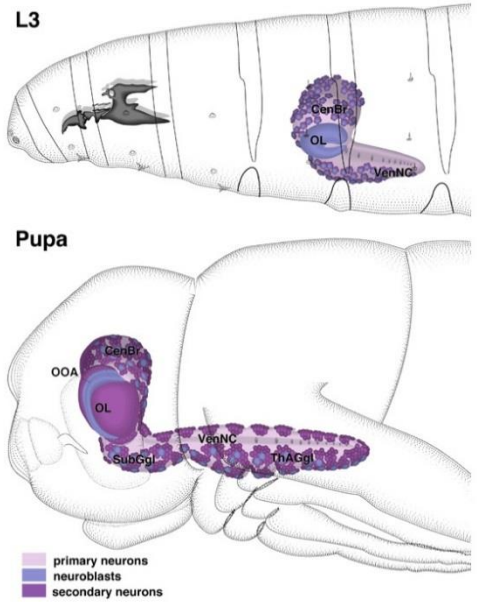
Reiter LT[1], Potocki L, Chien S, Gribskov M, Bier E.

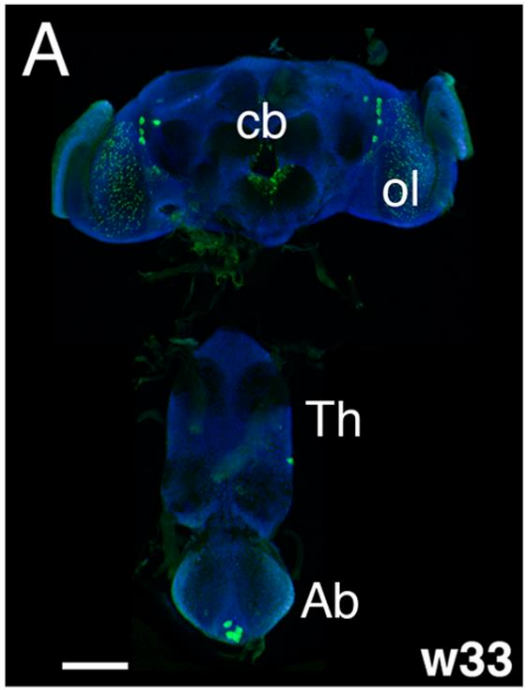
Again, why *Drosophila*?



Schmidt I. *et al*, The Journal of Neuroscience, 2012

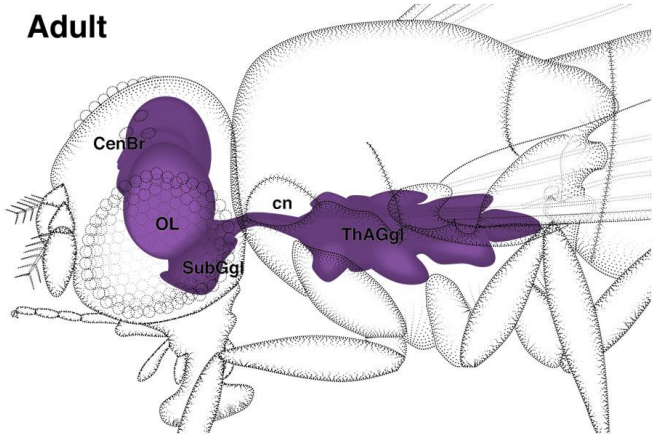
L1: 10000 neurons

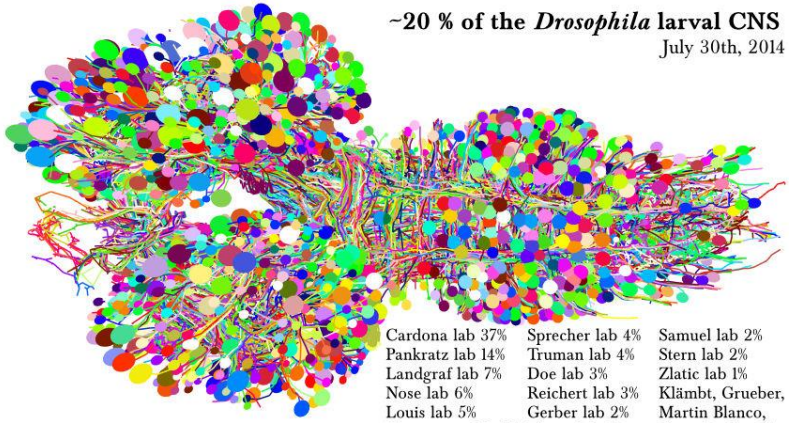




Shafer OT, Taghert PH, PLoS ONE, 2009

100000 neurons

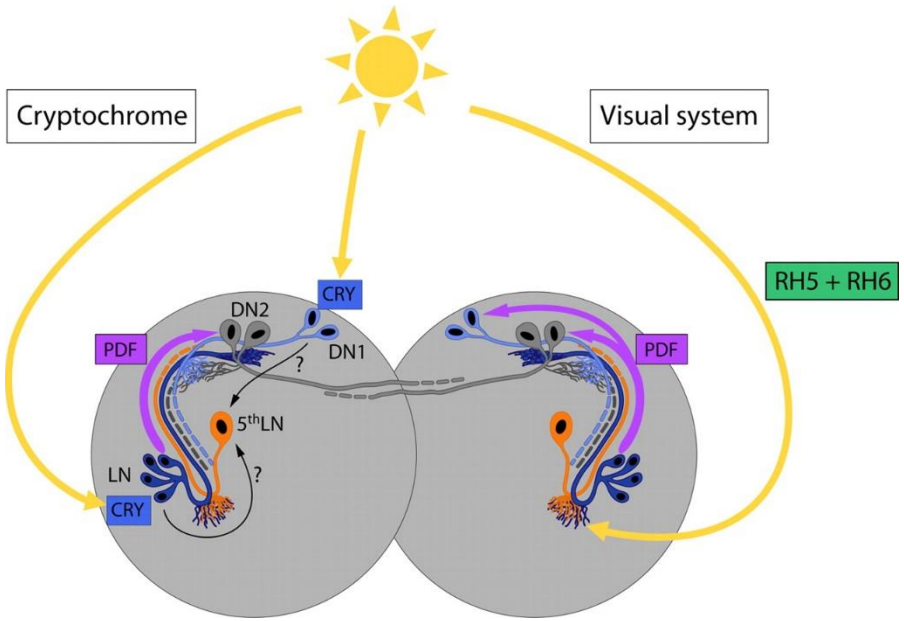




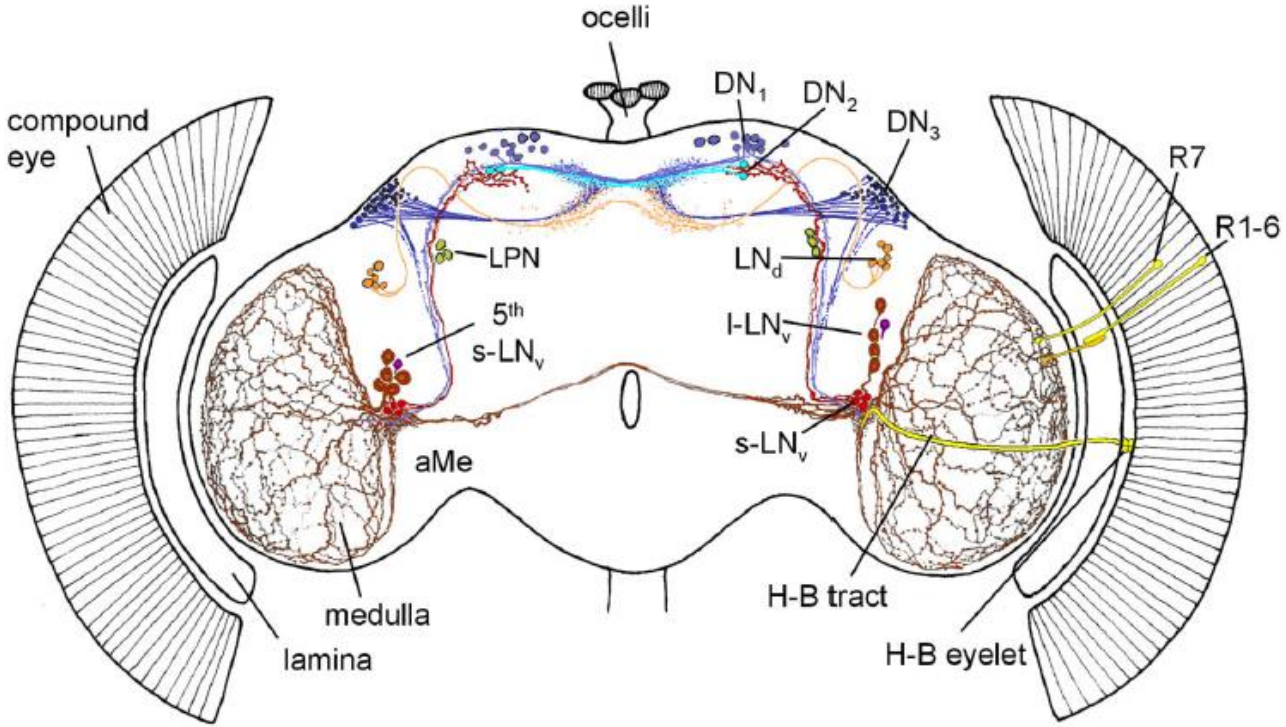
L1: 3 million synapses estimated

http://albert.rierol.net/lab.html

Metamorphosis: new body, new neurons, new behaviors



André Klarsfeld et al., The Journal of Neuroscience 2011



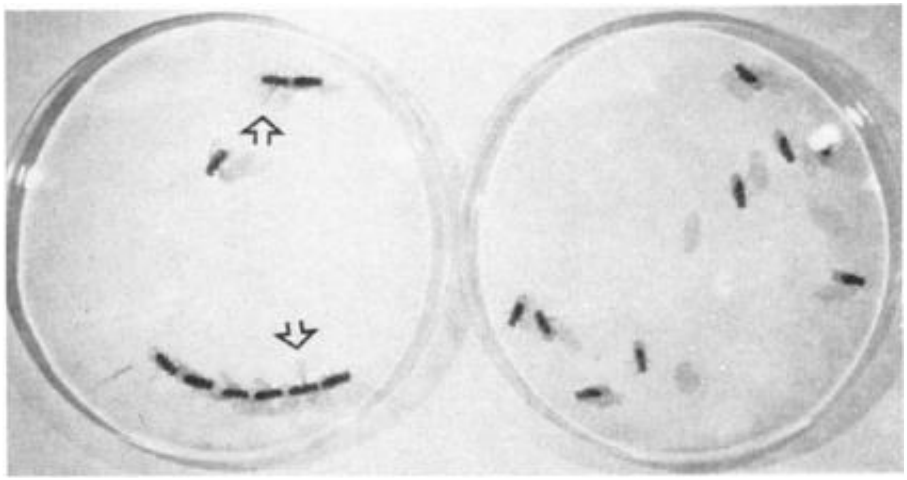
C. Helfrich-Förster et al., The Journal of Comparative Neurology 2007

Drosophila's toolbox

Genetic tools: balancers

fruitless

- ✓ Sex determination
- ✓ Development structures necessary for courtship:
  - Muscle development
  - Neurons
- ✓ Aggressive behavior
- ✓ Male courtship behavior:
  - wing vibration
  - song production
  - mating
  - etc.
- ✓ etc.



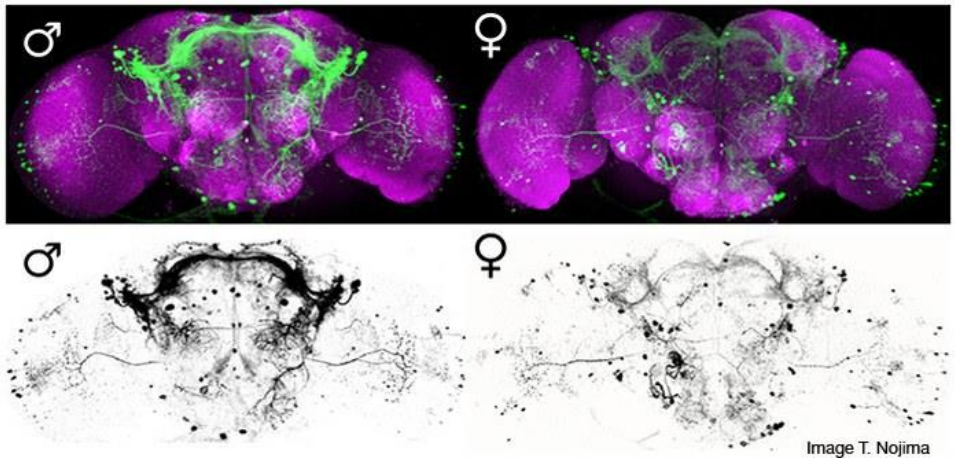
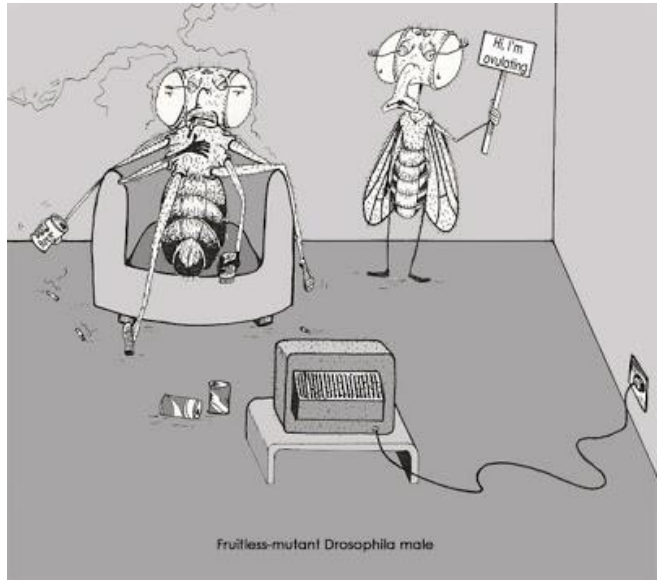
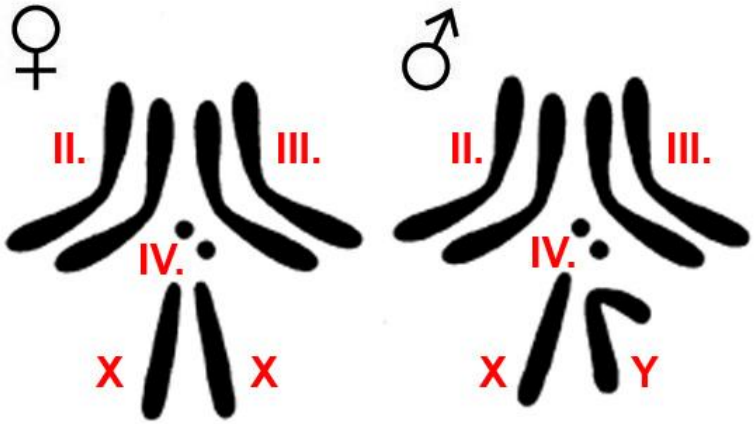


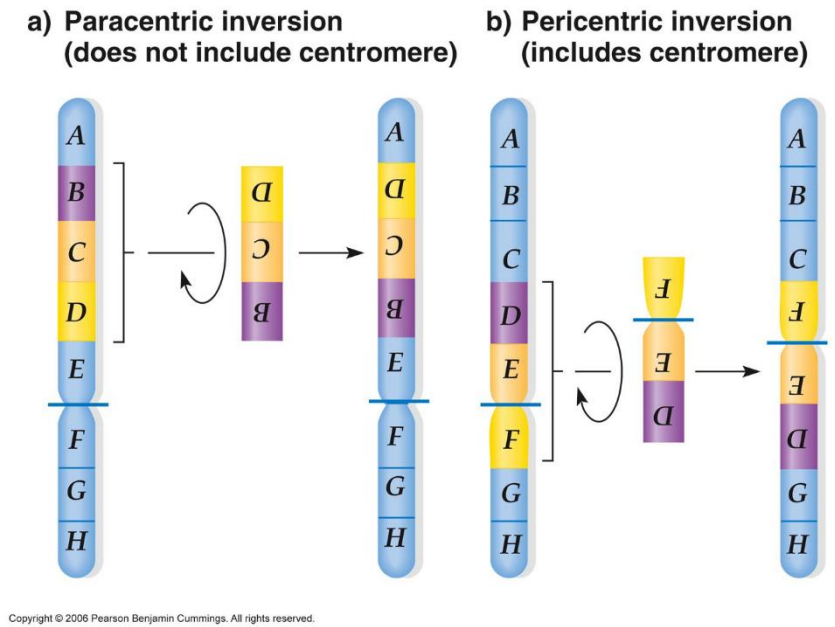
Image T. Nojima

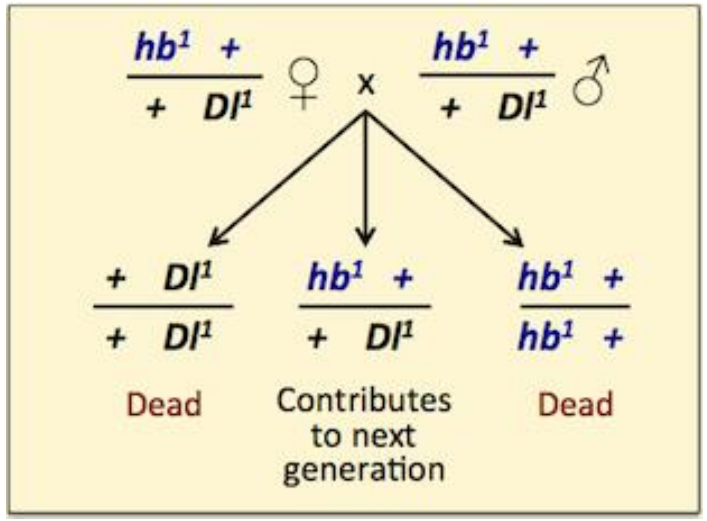


Fruitless-mutant Drosophila male

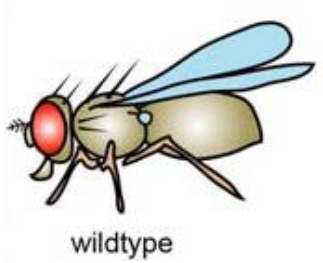
Genetic tools: balancers

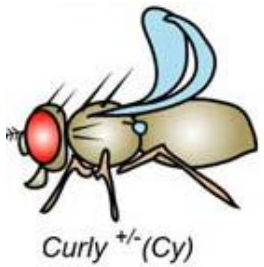


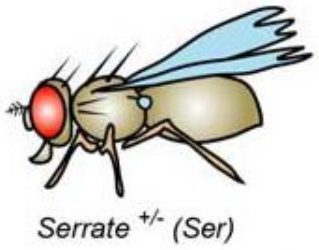


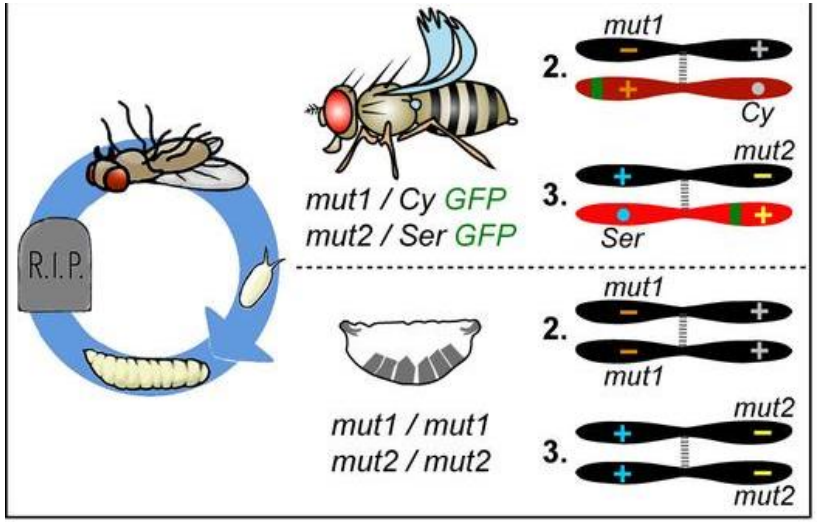


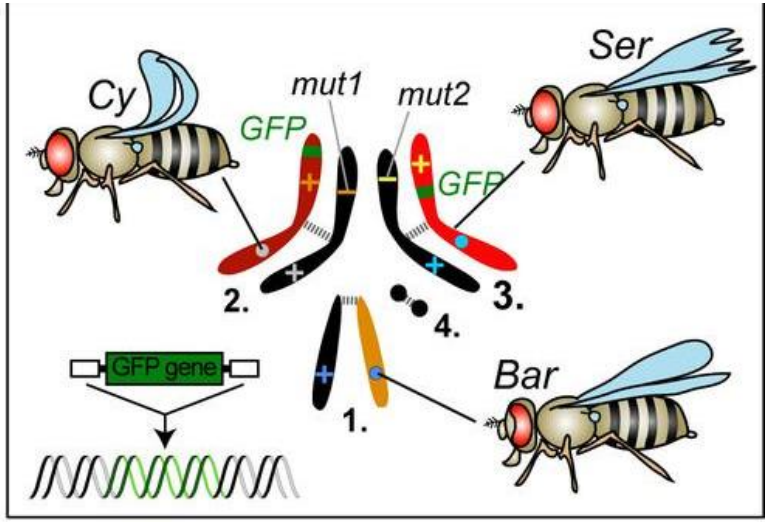
Genetic tools: balancers

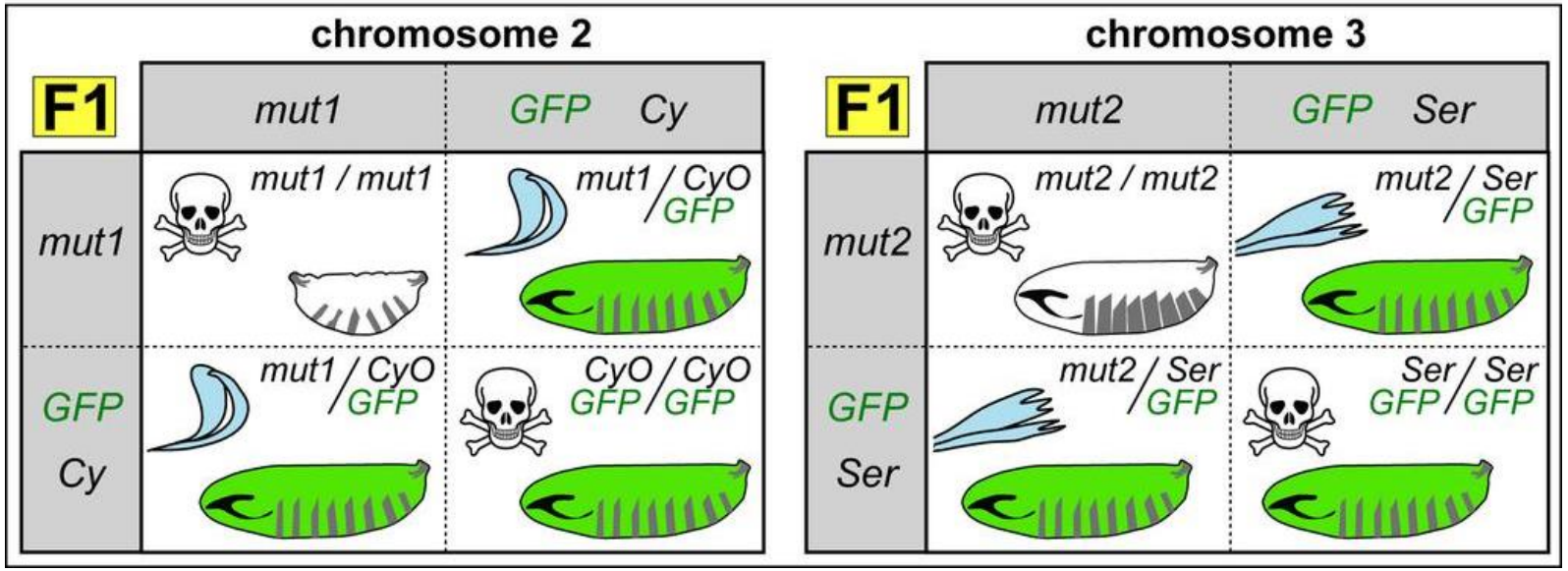












Genetic tools: transgenic flies

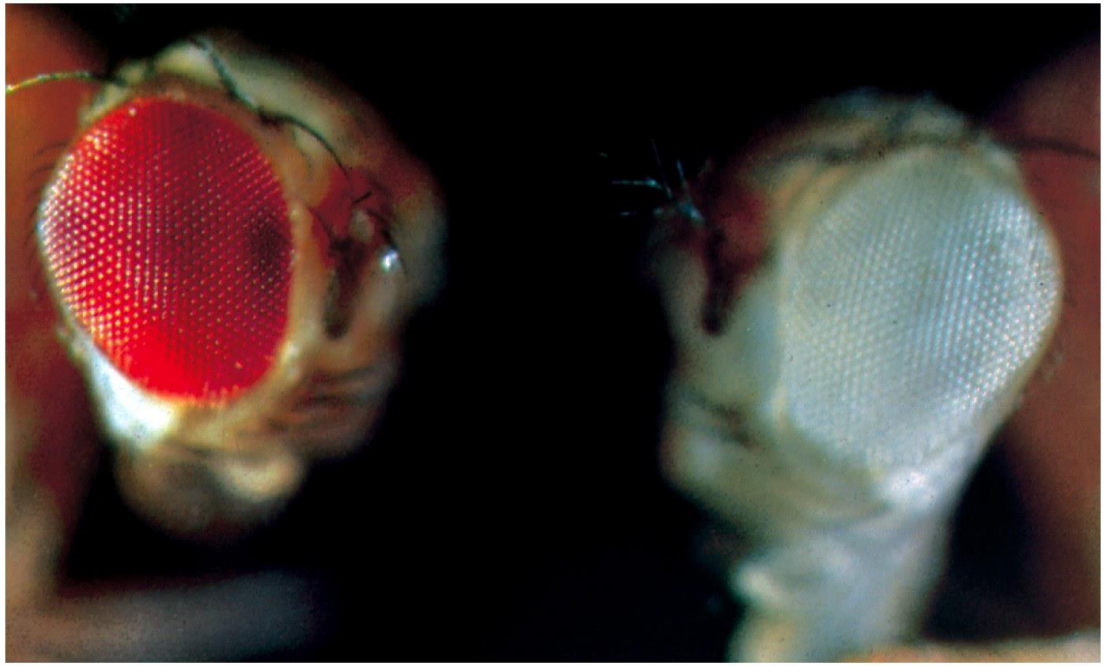
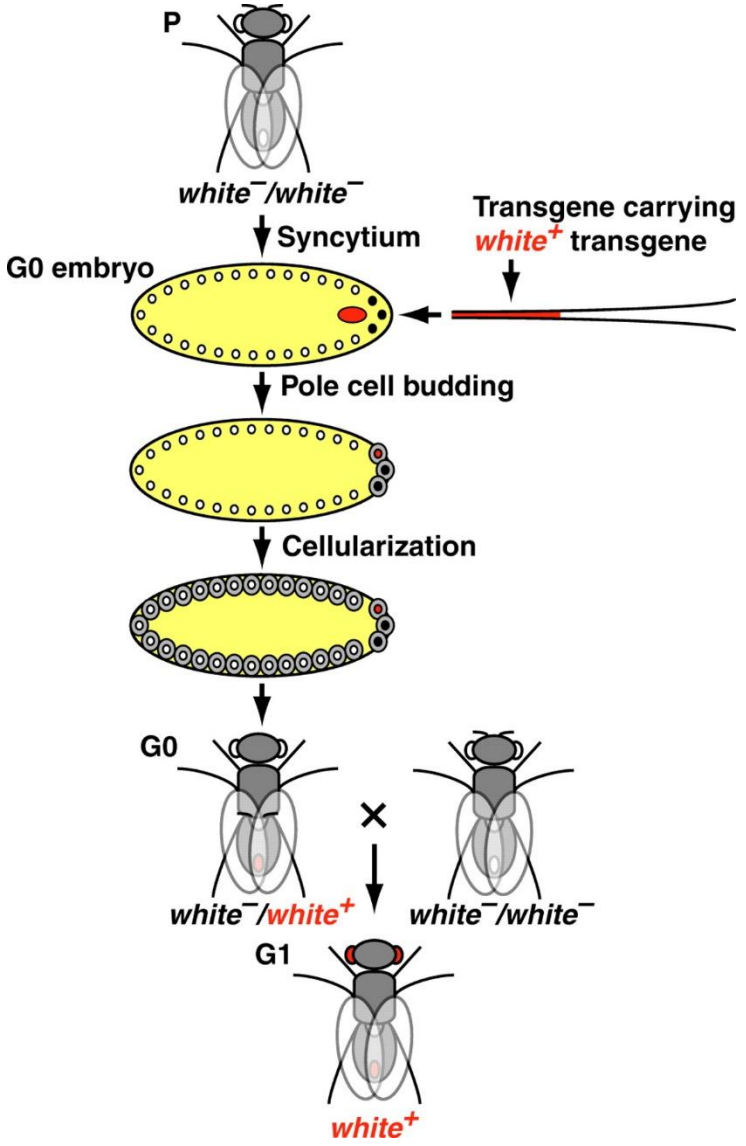


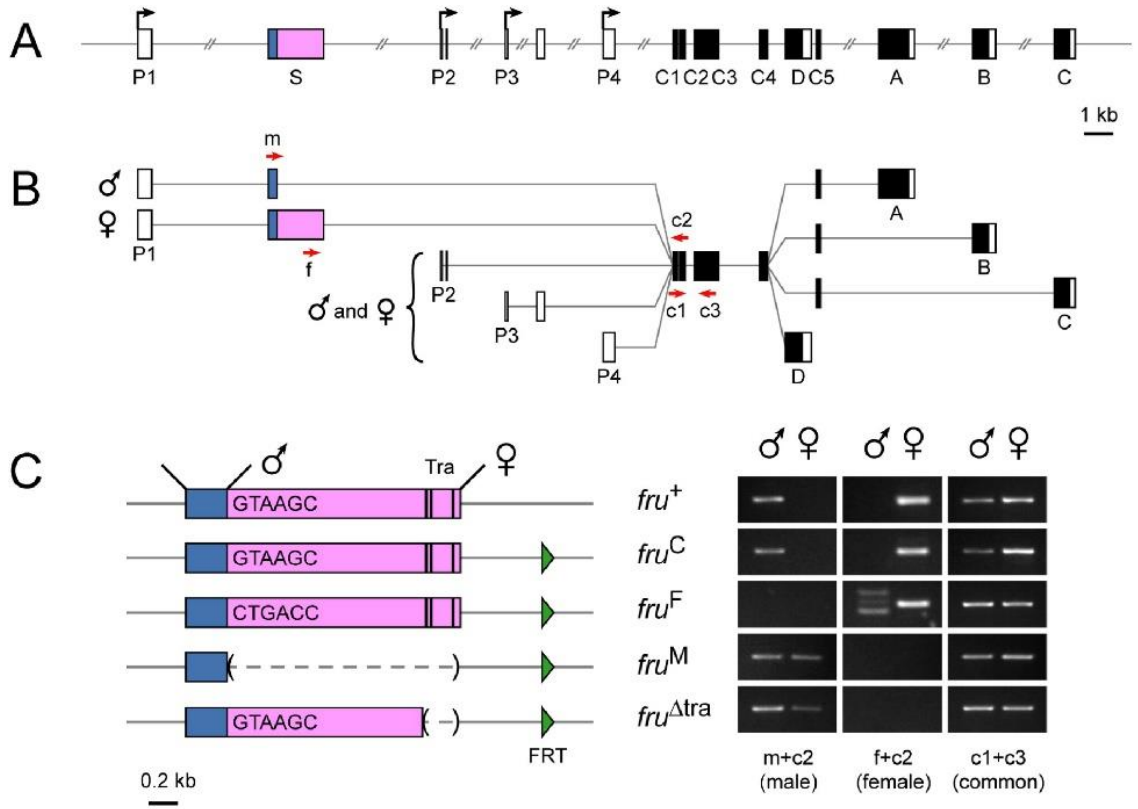
Figure 2-18
Introduction to Genetic Analysis, Tenth Edition

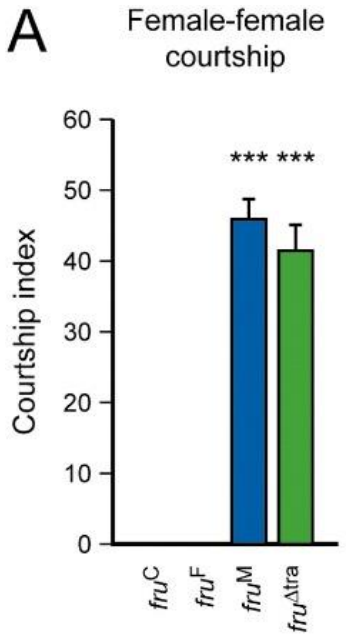


Drosophila transgenesis: *white*+ transgene DNA (red) is injected into generation zero *Drosophila* embryos (G0) of less than 1 hour old, which have been obtained from a parental (P) generation.

Koen J. T. *et al*, Development 2007

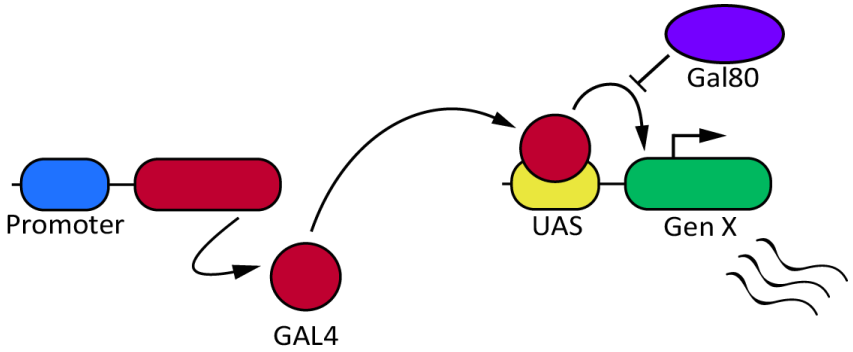
Genetic tools: transgenic flies

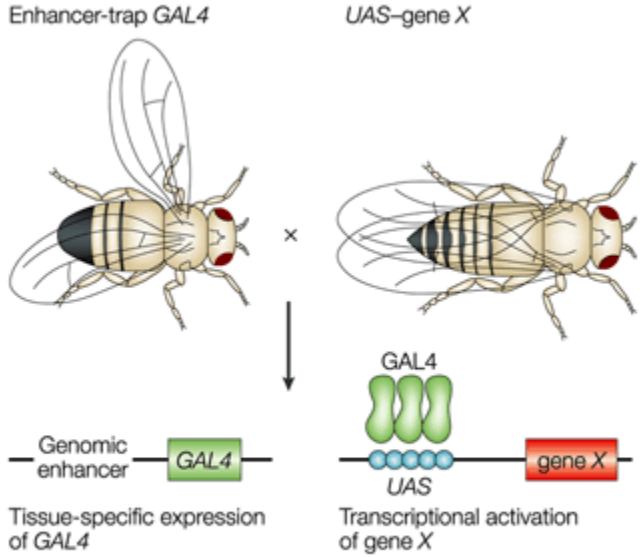


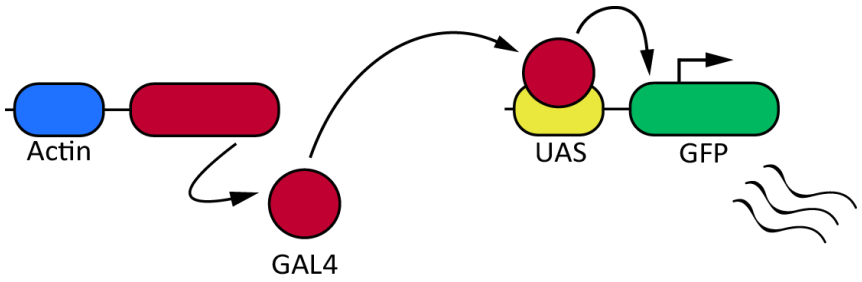


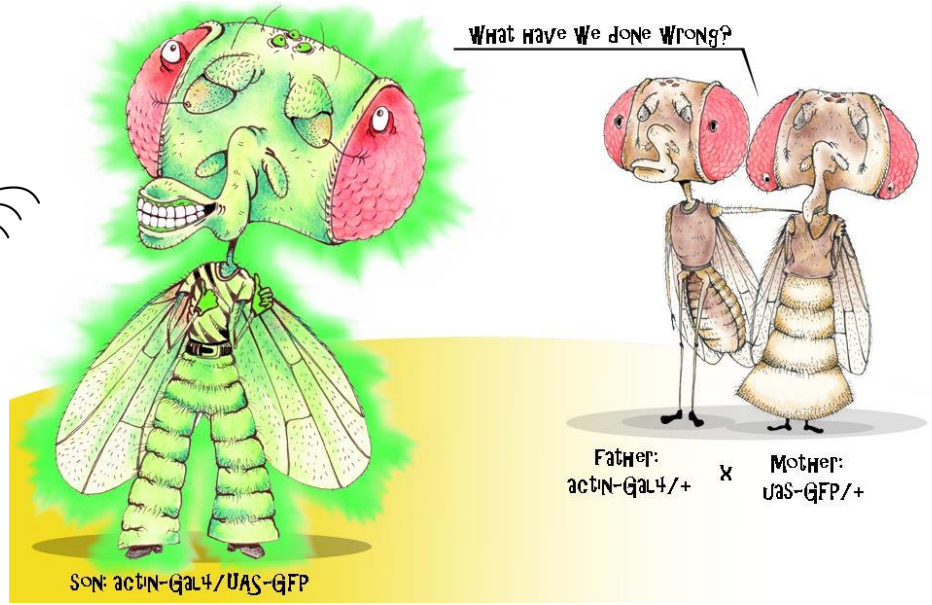
Demir E. & Dickson B, Cell 2005

Genetic tools: GAL4/UAS and other tools



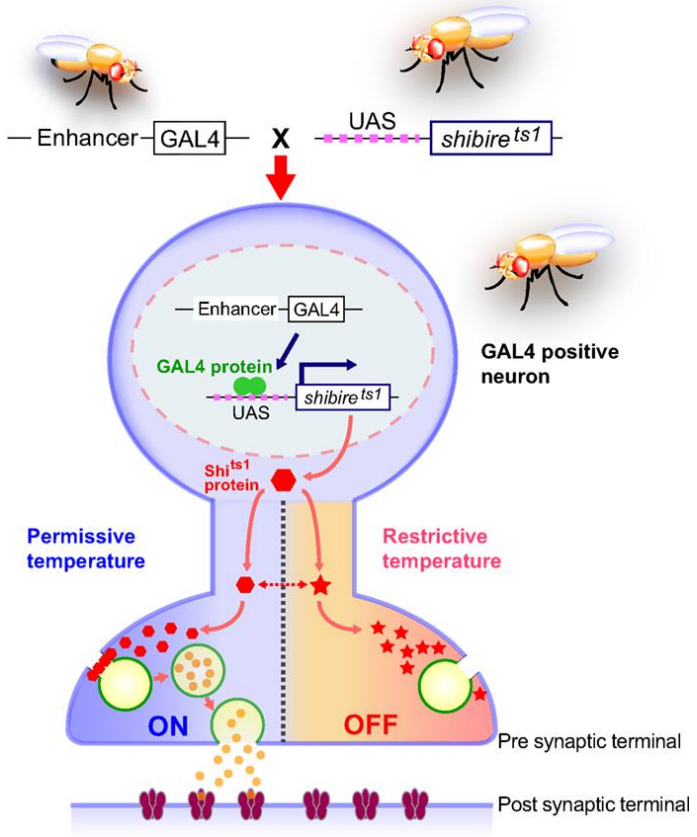


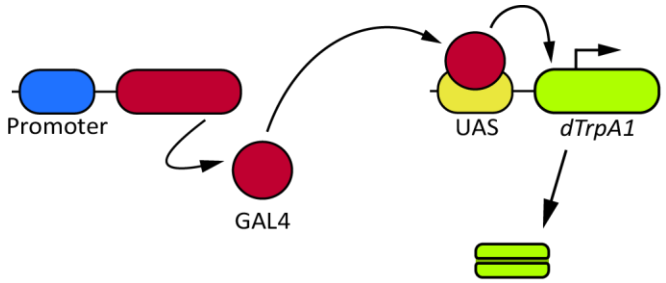


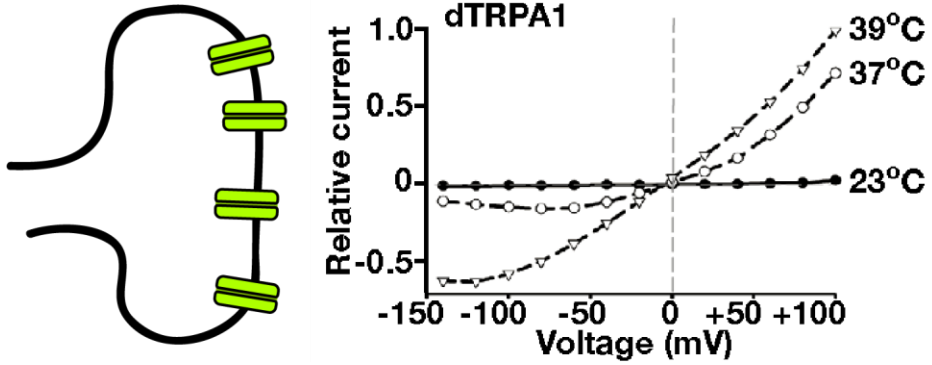


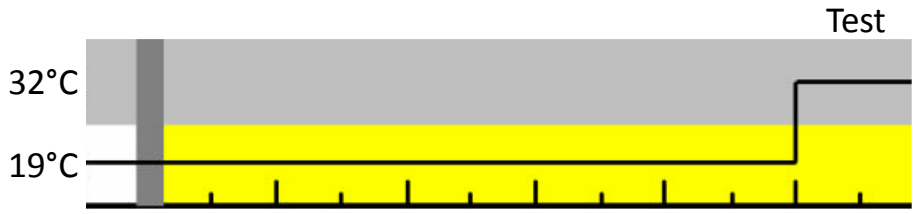
Genetic tools: GAL4/UAS and other tools

Neuronal inhibition and activation

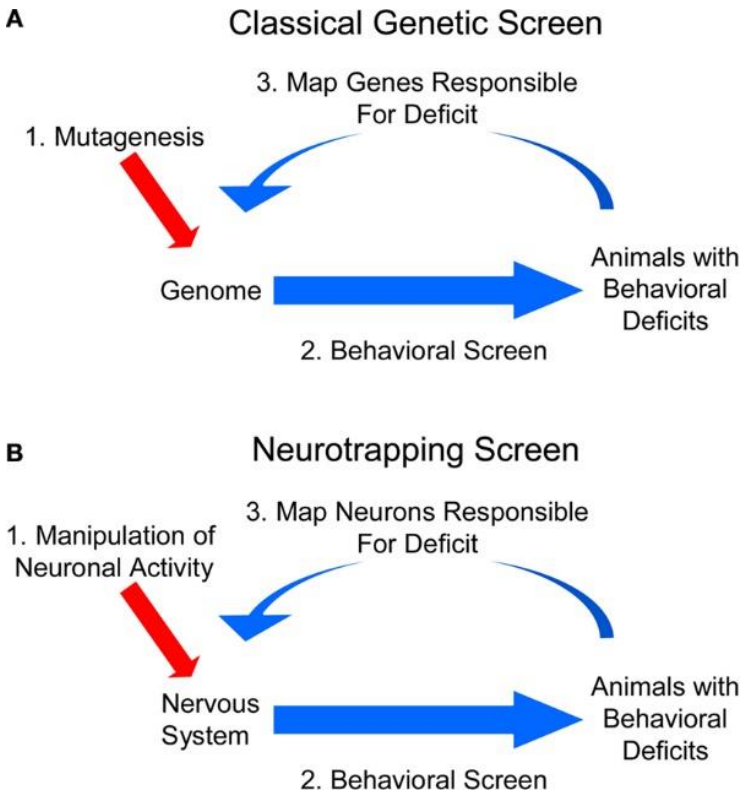








Genetic tools: GAL4/UAS and other tools

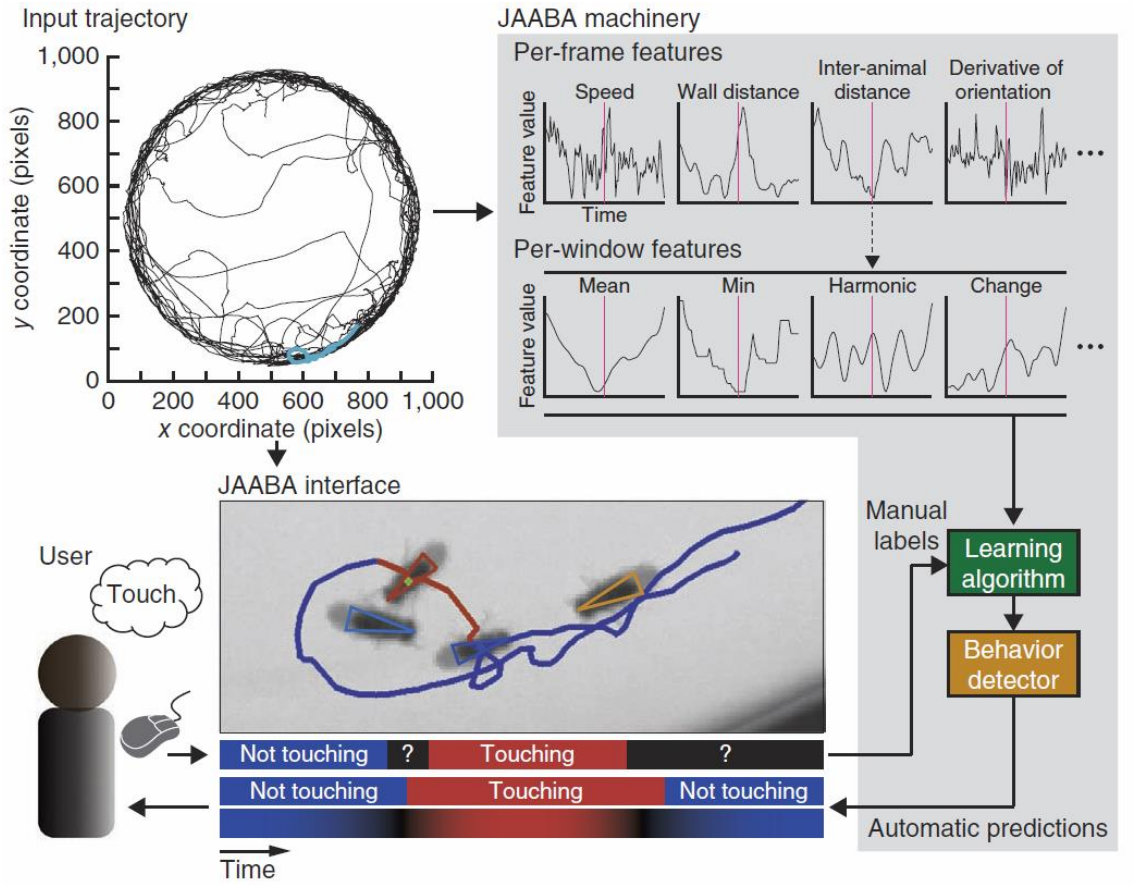


JAABA: interactive machine learning for automatic annotation of animal behavior

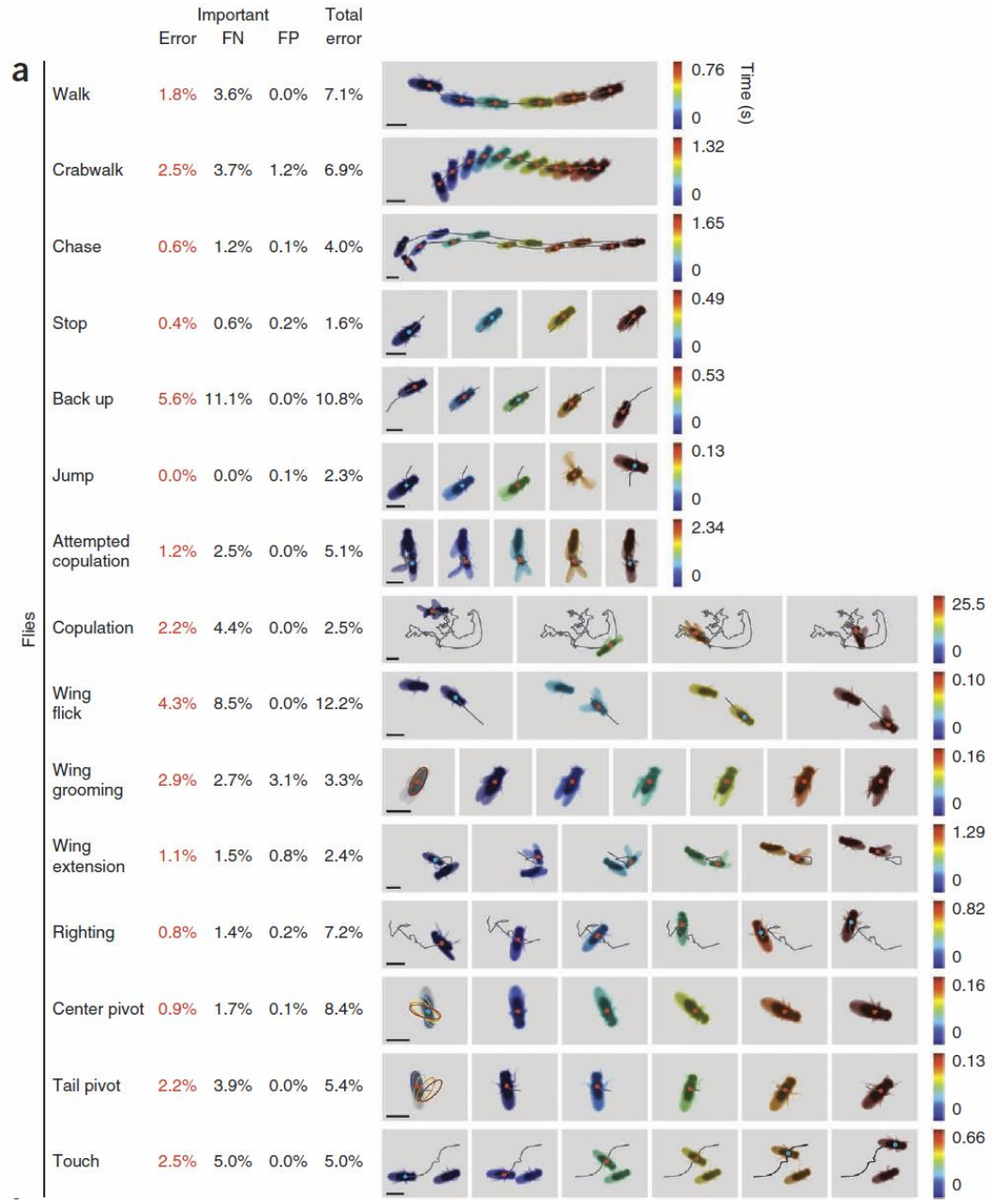
Mayank Kabra[1,4], Alice A Robie[1,4], Marta Rivera-Alba[1,2], Steven Branson[1,3] & Kristin Branson[1]

GAL4 collection + UAS-*dTrpA1*

Genetic tools: GAL4/UAS and other tools

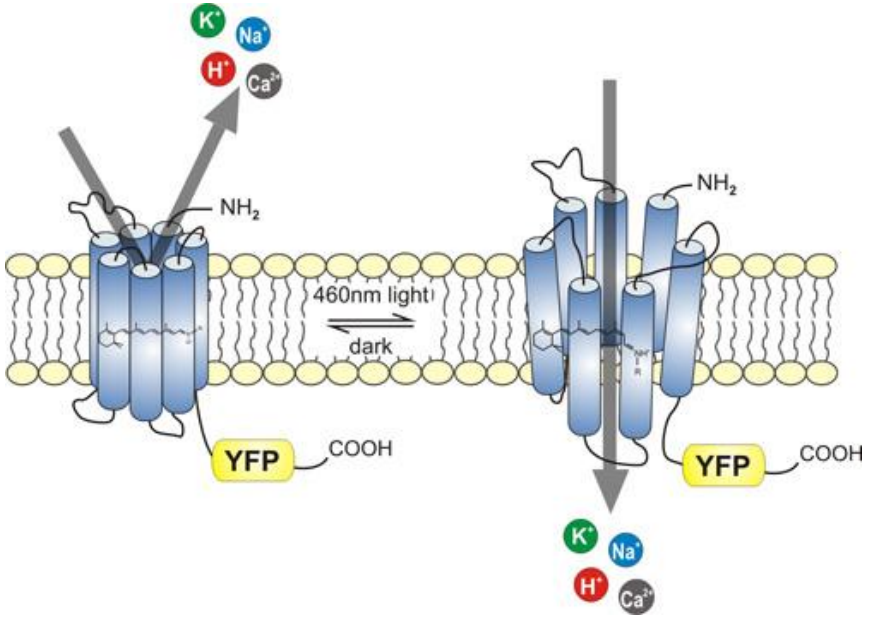


Genetic tools: GAL4/UAS and other tools

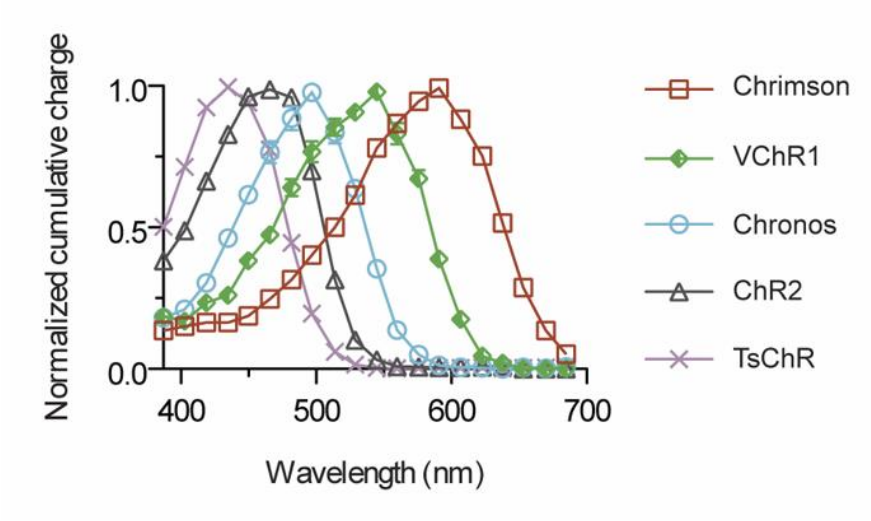


Genetic tools: GAL4/UAS and other tools

Optogenetics: Channelrodopsin & others



UAS-ChR2
UAS-ReaChR
UAS-Chrimson
UAS-Chronos



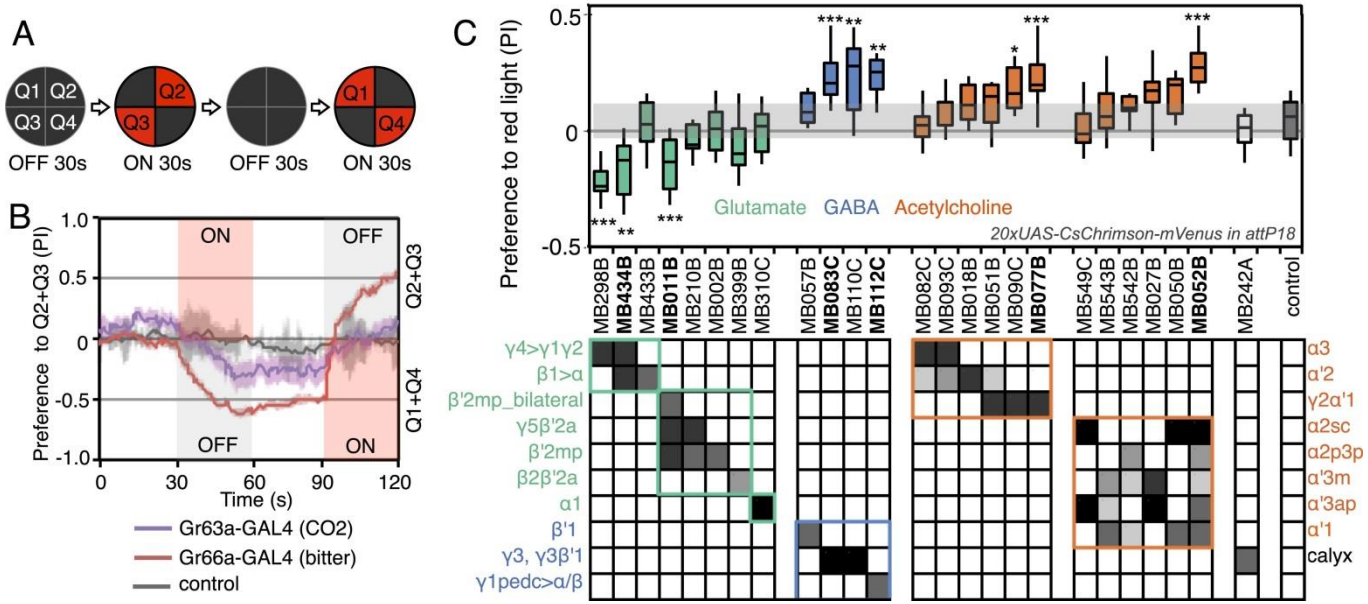
Proboscis extension reflex

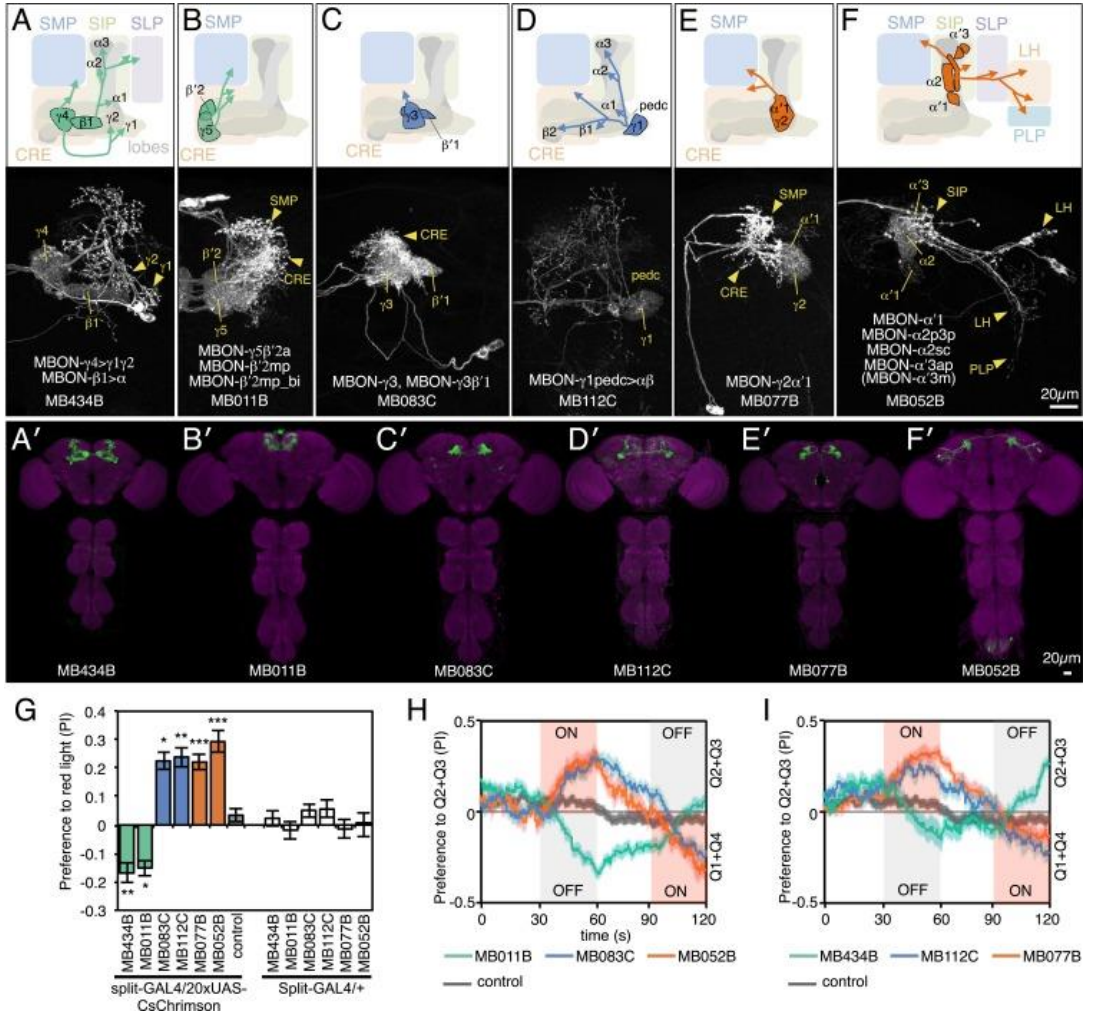
sugar-sensing gustatory receptor neurons (GRNs)

Genetic tools: GAL4/UAS and other tools

Mushroom body output neurons encode valence and guide memory-based action selection in *Drosophila*

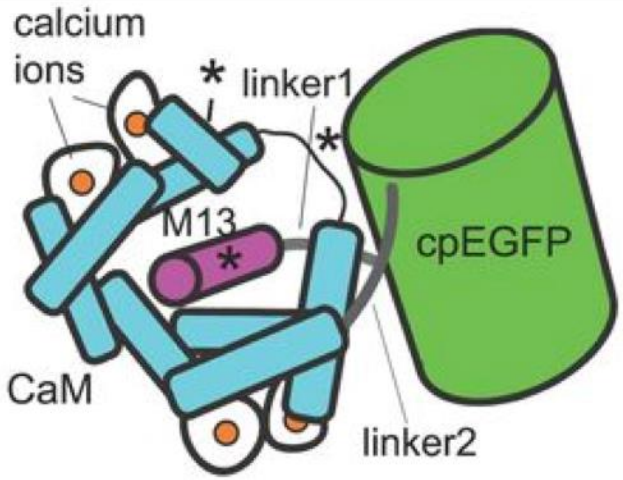
Yoshinori Aso[1]*, Divya Sitaraman[1,2,6,7†], Toshiharu Ichinose[3,4], Karla R Kaun[1‡], Katrin Vogt[3], Ghislain Belliart-Guérin[5], Pierre-Yves Plaçais[5], Alice A Robie[1], Nobuhiro Yamagata[3,4], Christopher Schnaitmann[3§], William J Rowell[1], Rebecca M Johnston[1], Teri-T B Ngo[1], Nan Chen[1], Wyatt Korff[1], Michael N Nitabach[1,2,6,7], Ulrike Heberlein[1], Thomas Preat[5], Kristin M Branson[1], Hiromu Tanimoto[3,4], Gerald M Rubin[1]*

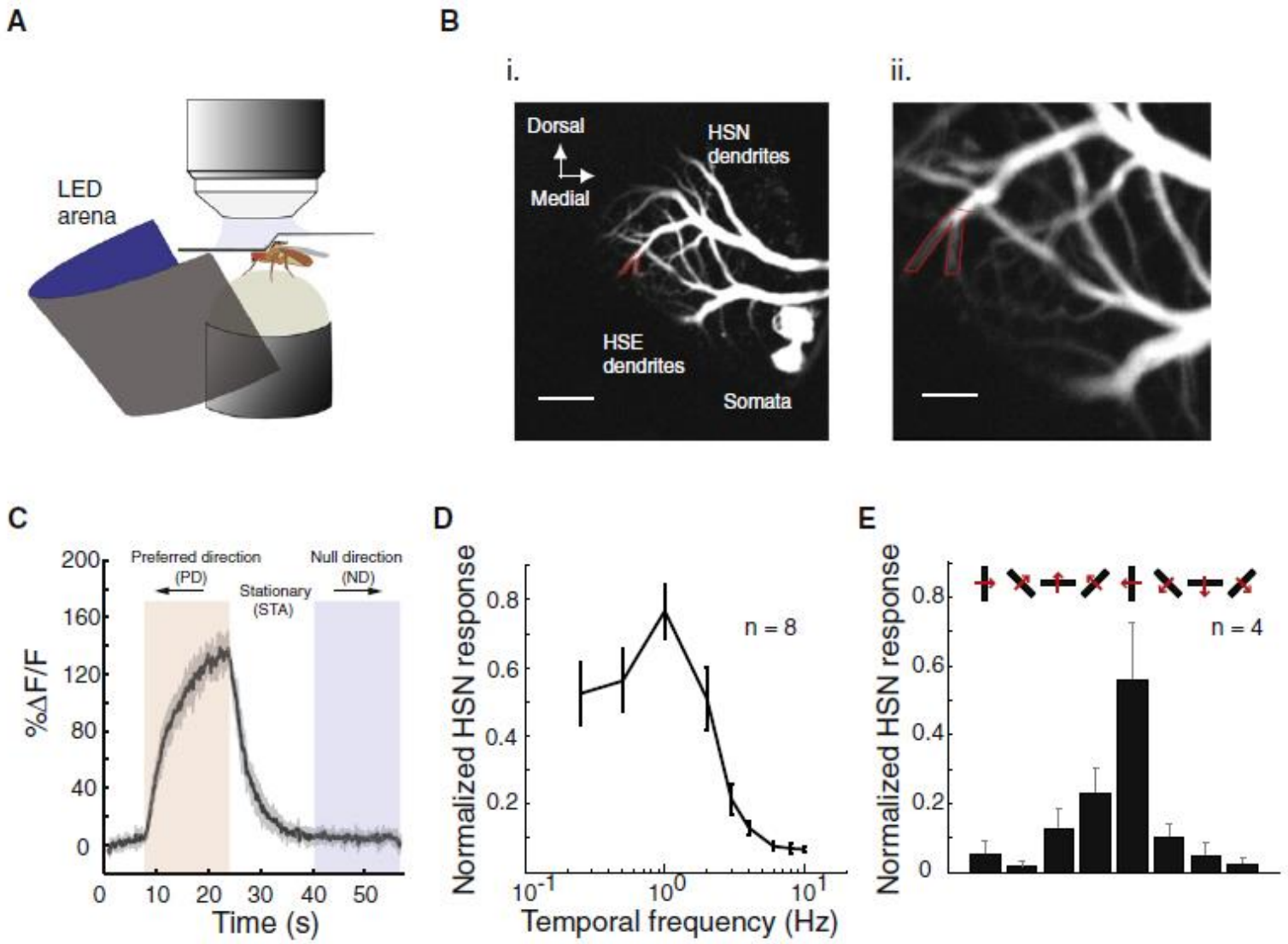




Genetic tools: GAL4/UAS and other tools

Calcium activity sensors: GCaMP





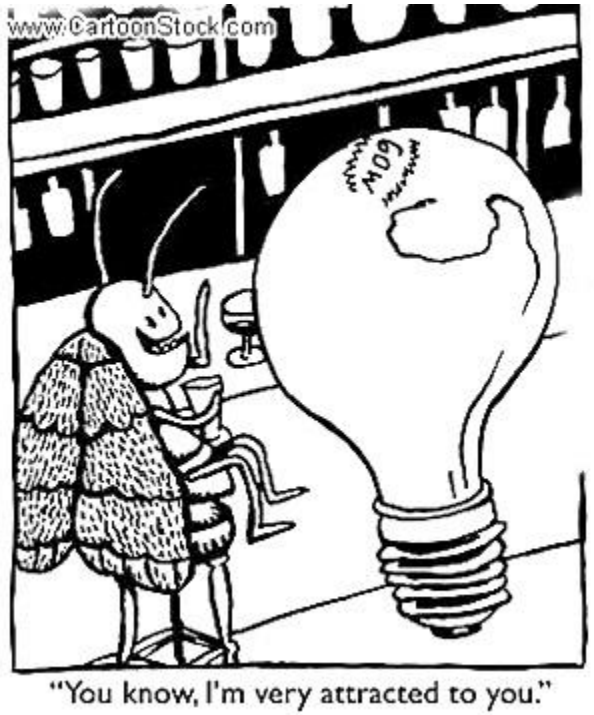
Chiappe M.E. *et al*, Current Biology 2010

Behavioral paradigms

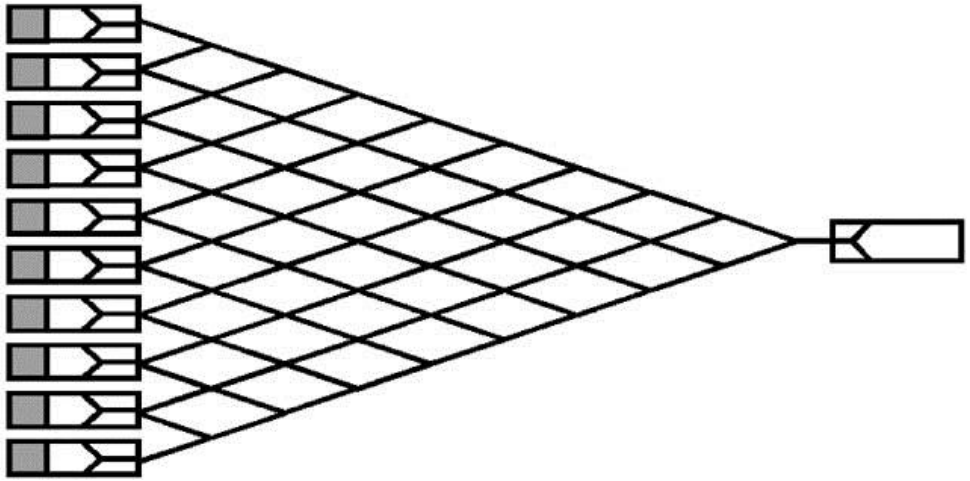
Behavioral paradigms: Taxis

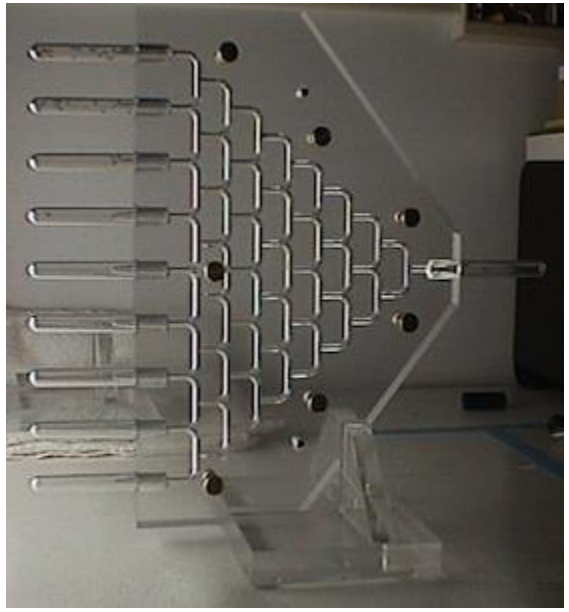
Phototaxis

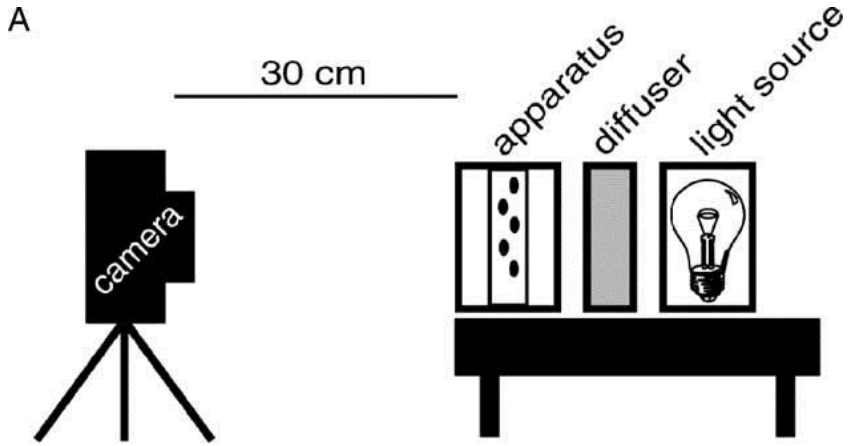
Geotaxis

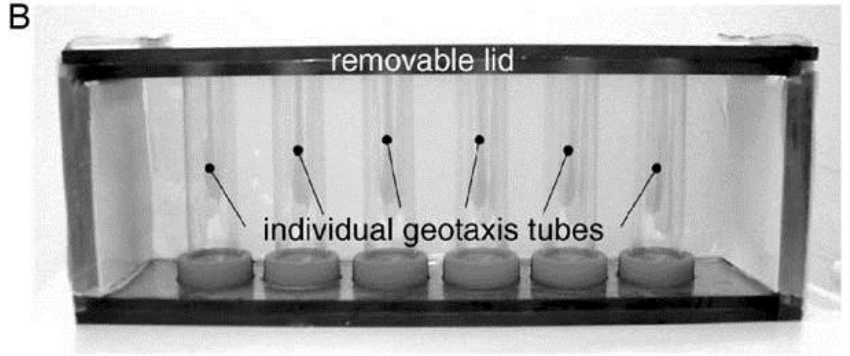


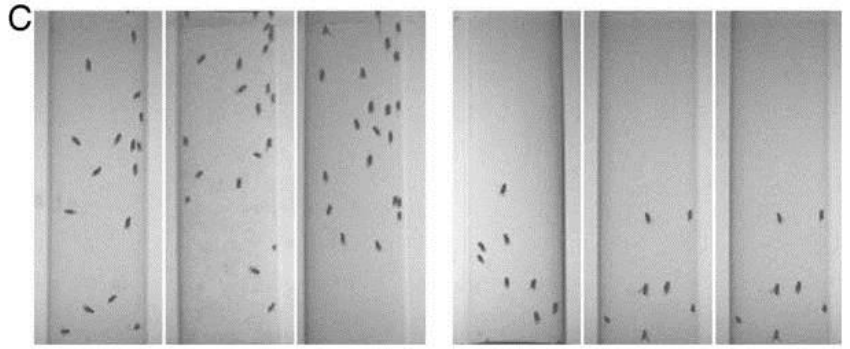
Behavioral paradigms: geotaxis



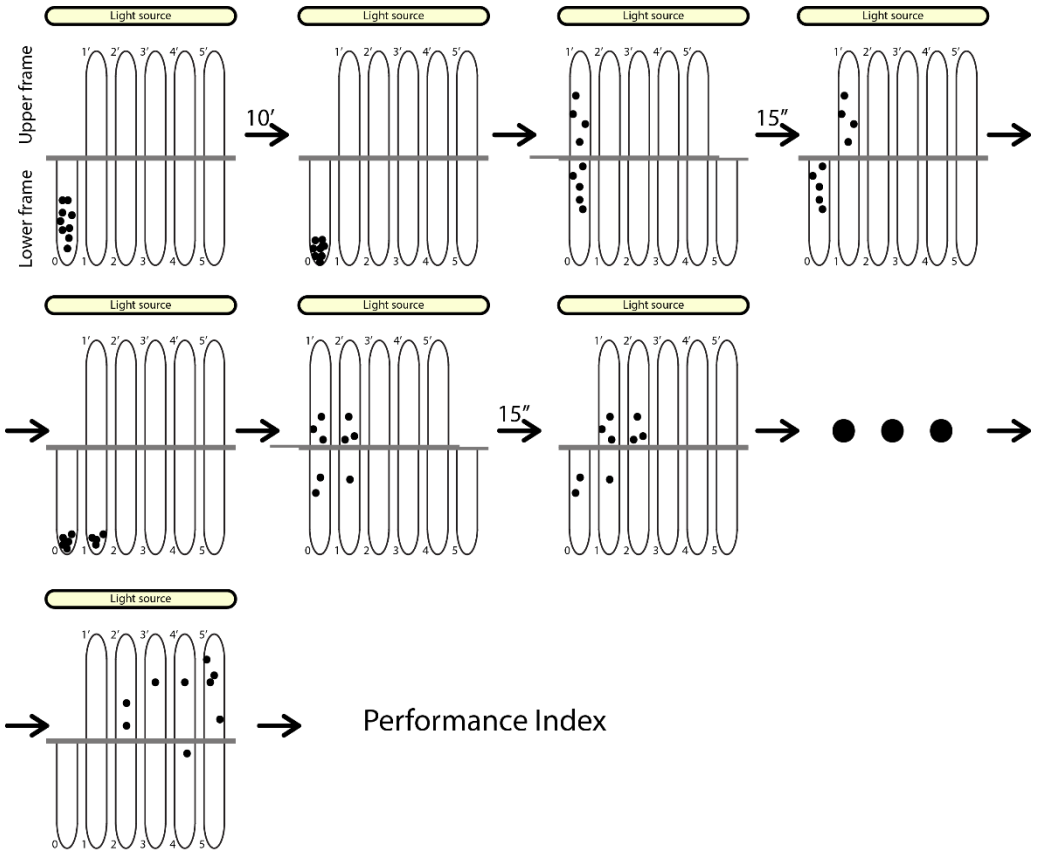


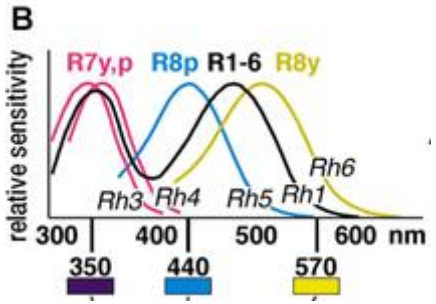


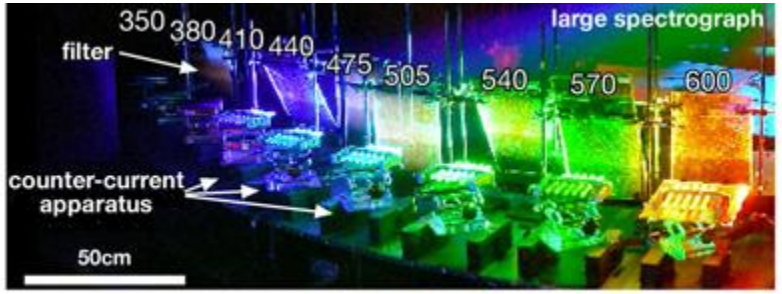




Behavioral paradigms: phototaxis



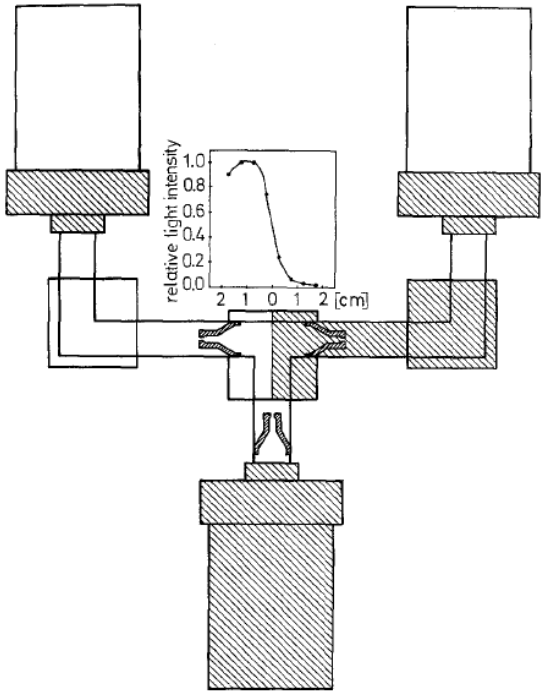


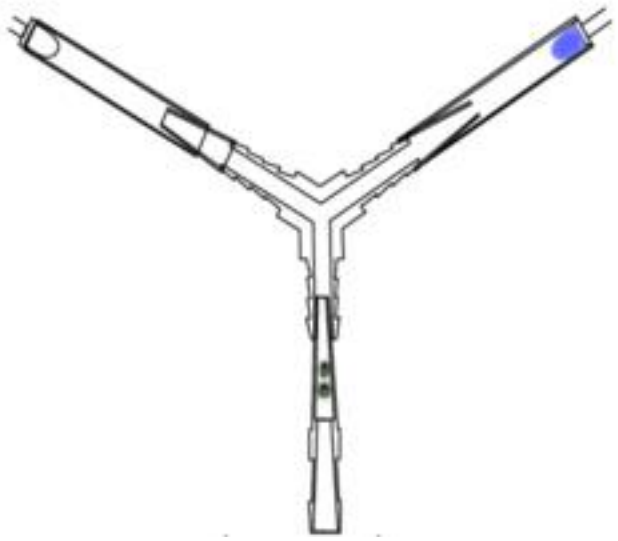


Otsuna H. et al, Front. Neural Circuits, 2014

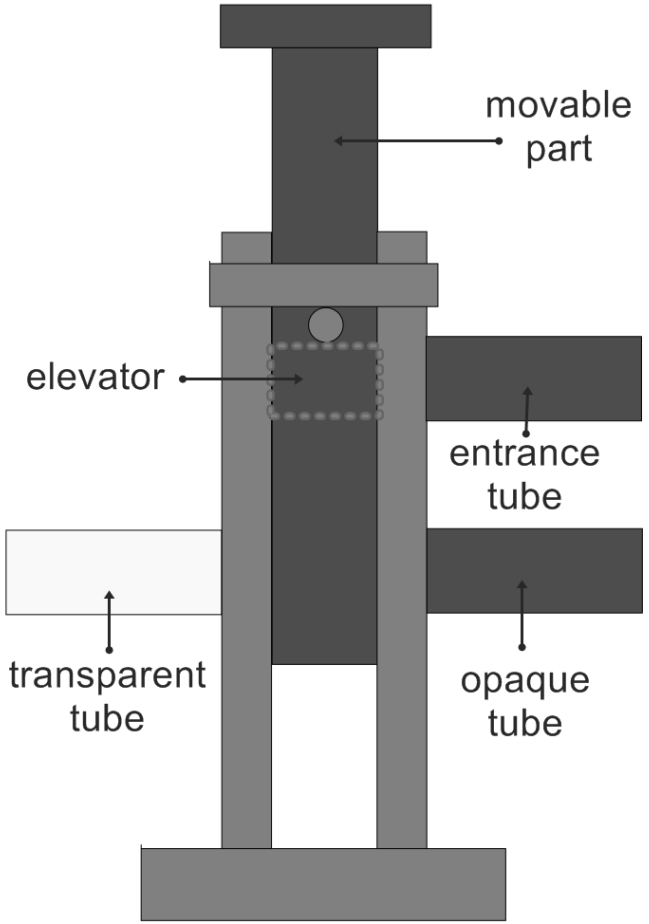
Behavioral paradigms: phototaxis

Single fly assay

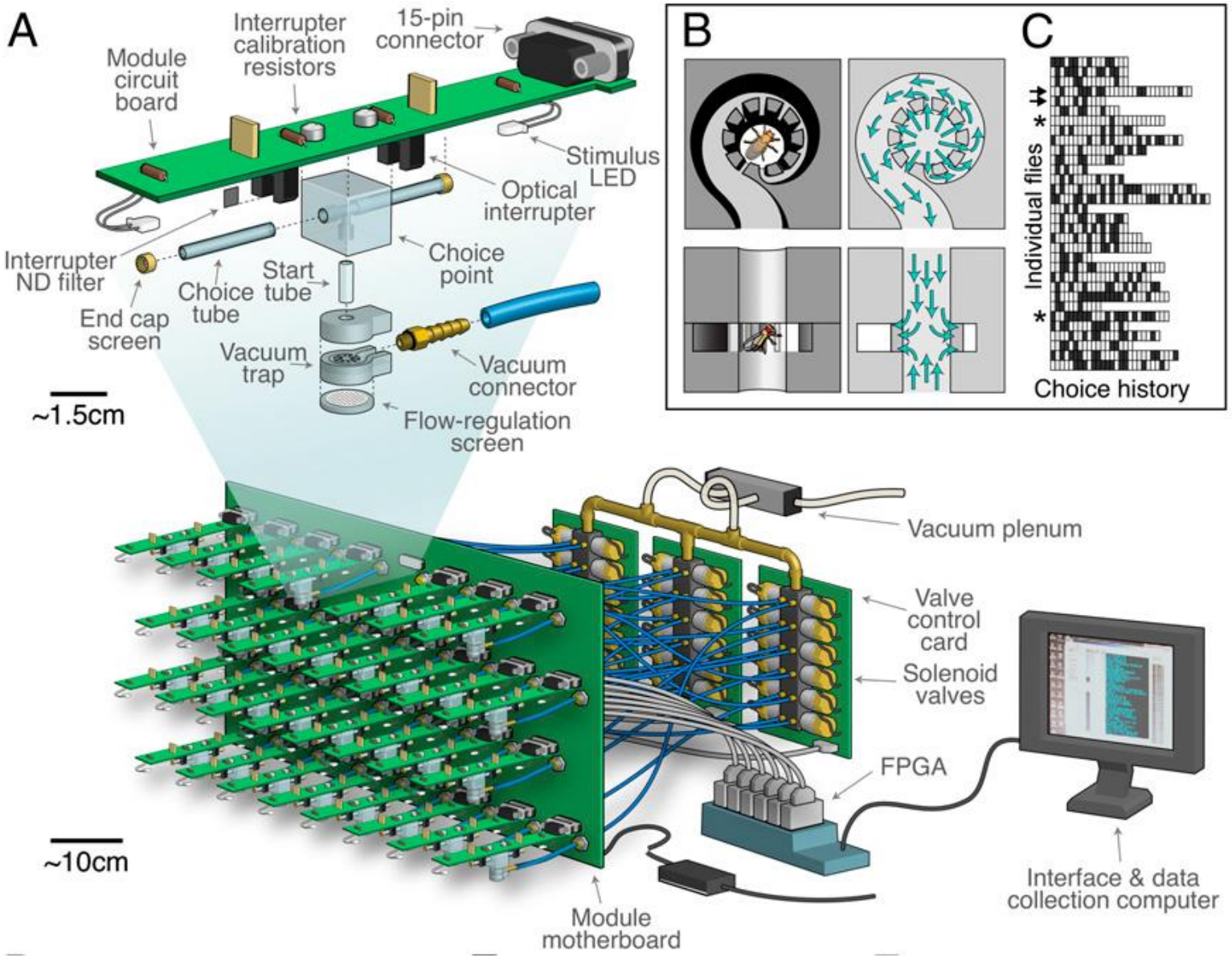




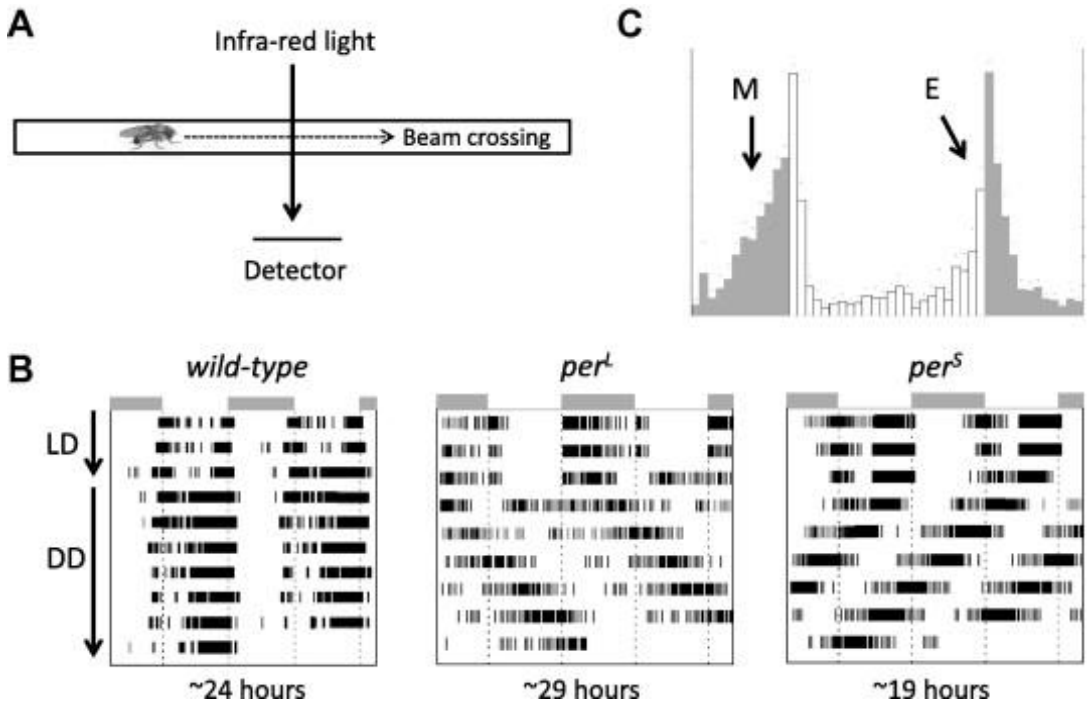
Population assay



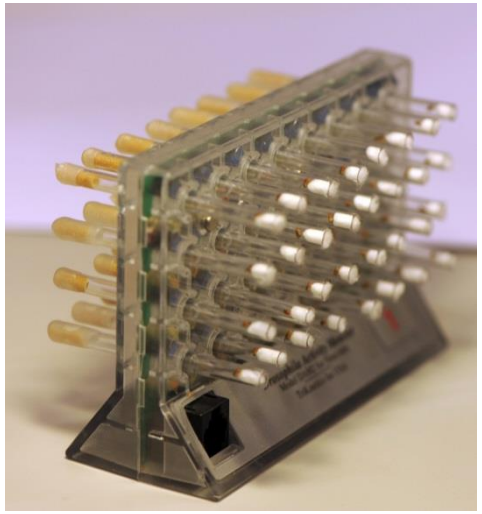
Behavioral paradigms: phototaxis

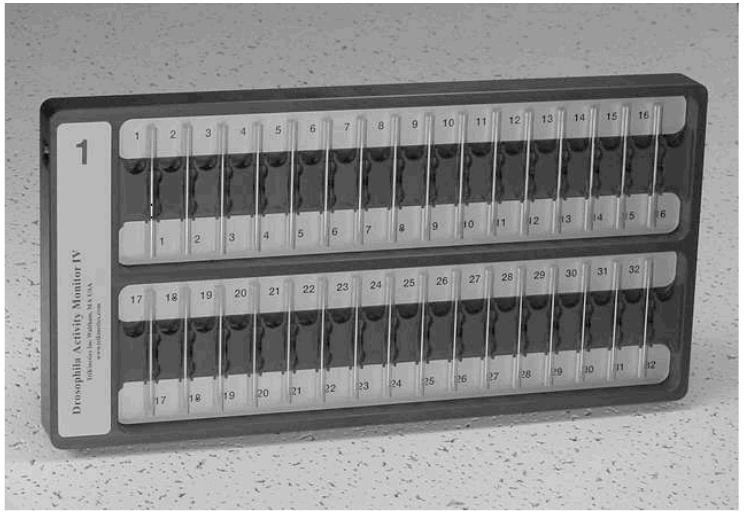


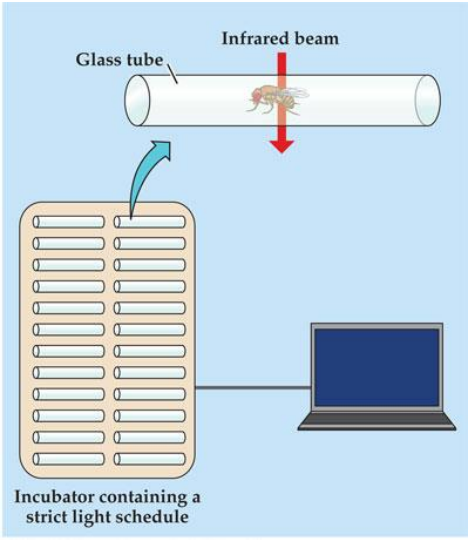
Behavioral paradigms: circadian rhythms & sleep



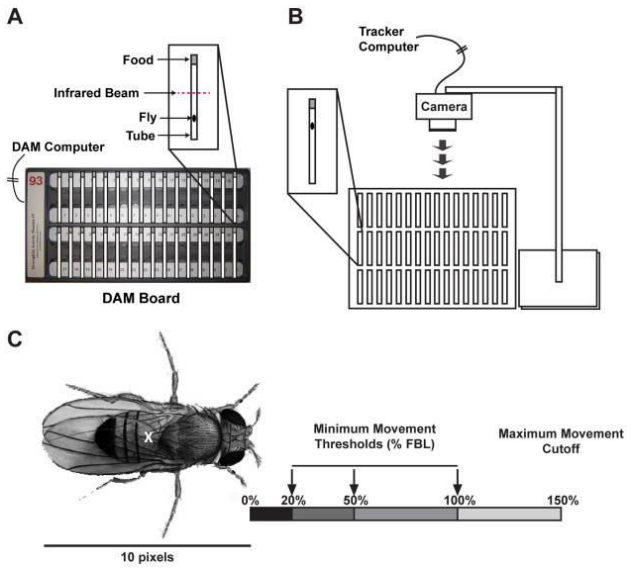
Ozgur Tataroglu & Patrick Emery, Methods, 2014, 140 - 150

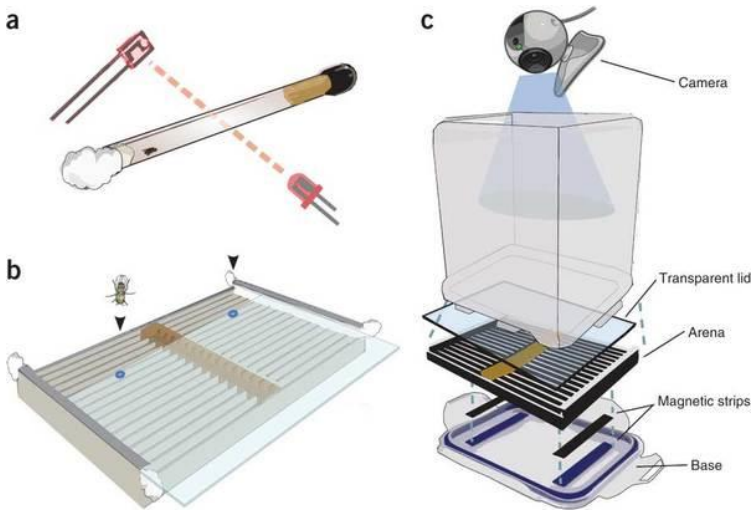


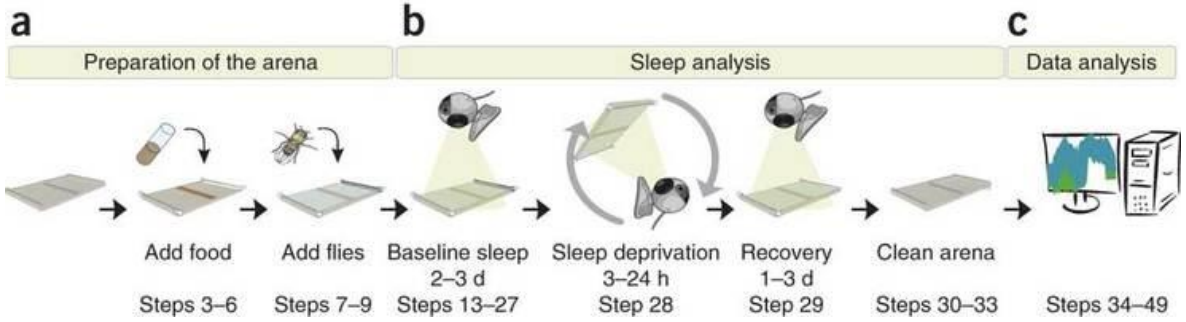




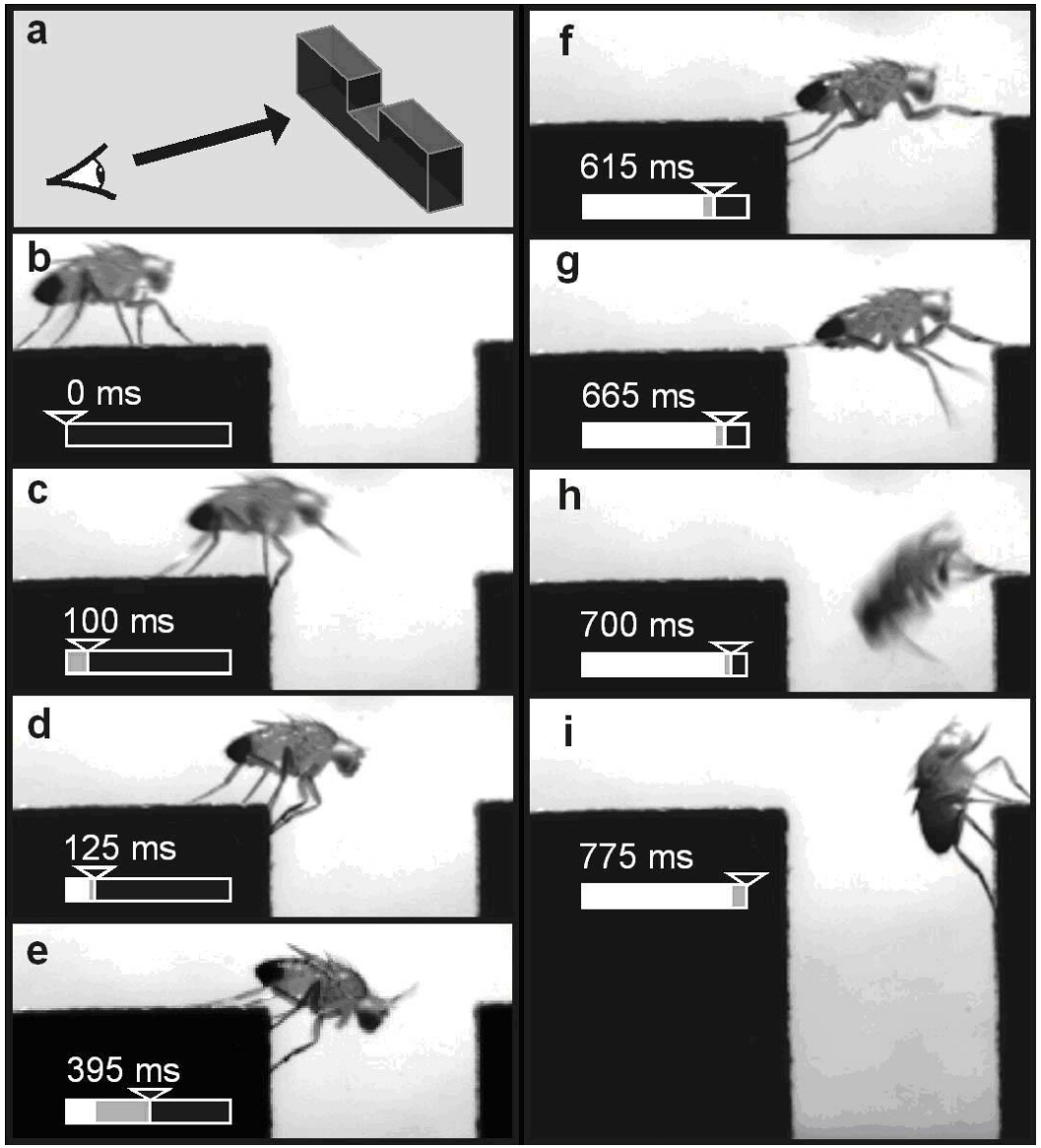
Behavioral paradigms: circadian rhythms & sleep

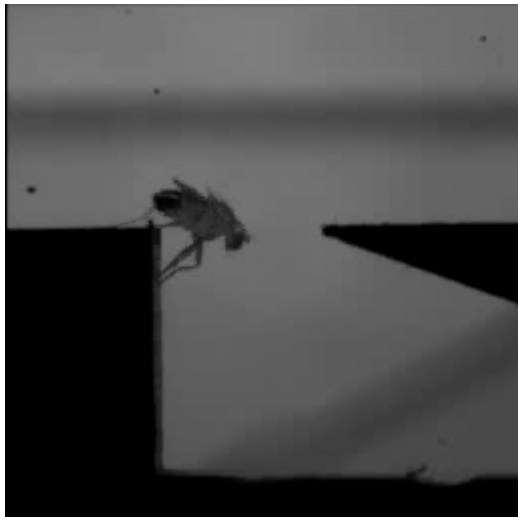


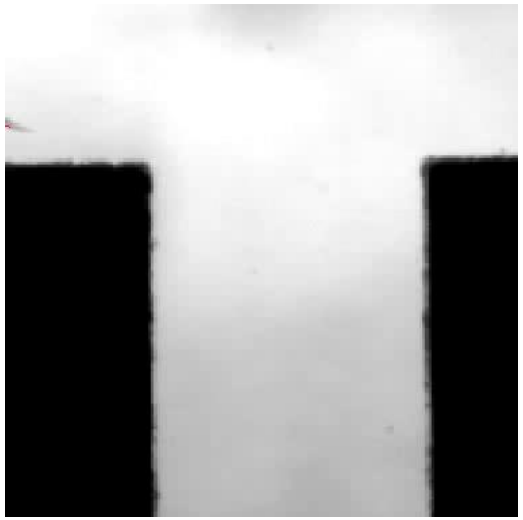




Behavioral paradigms: gap



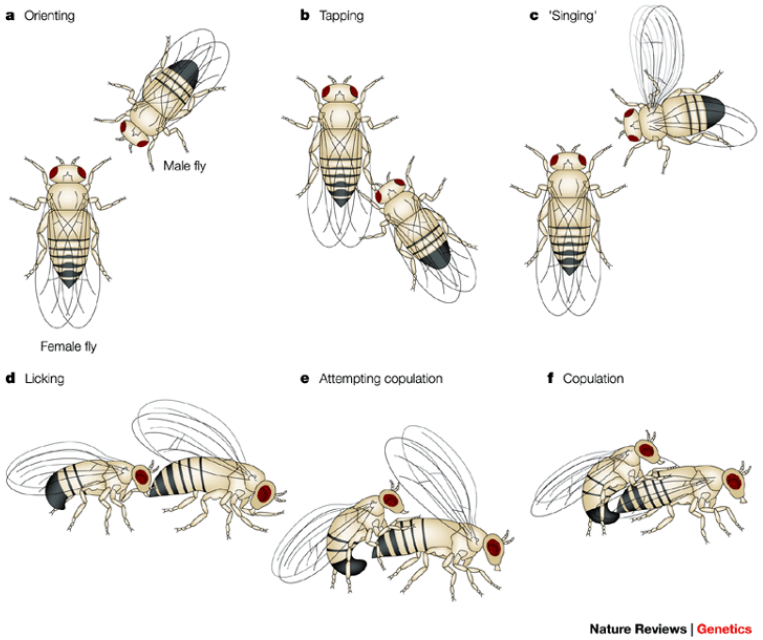


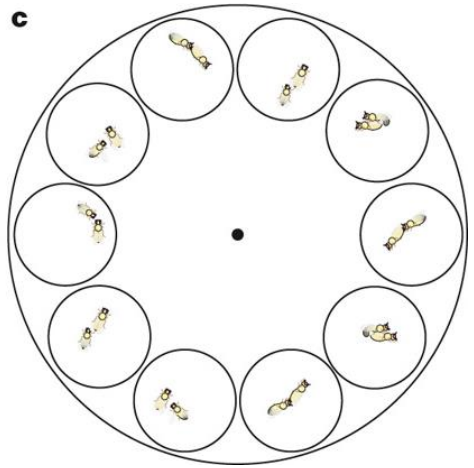


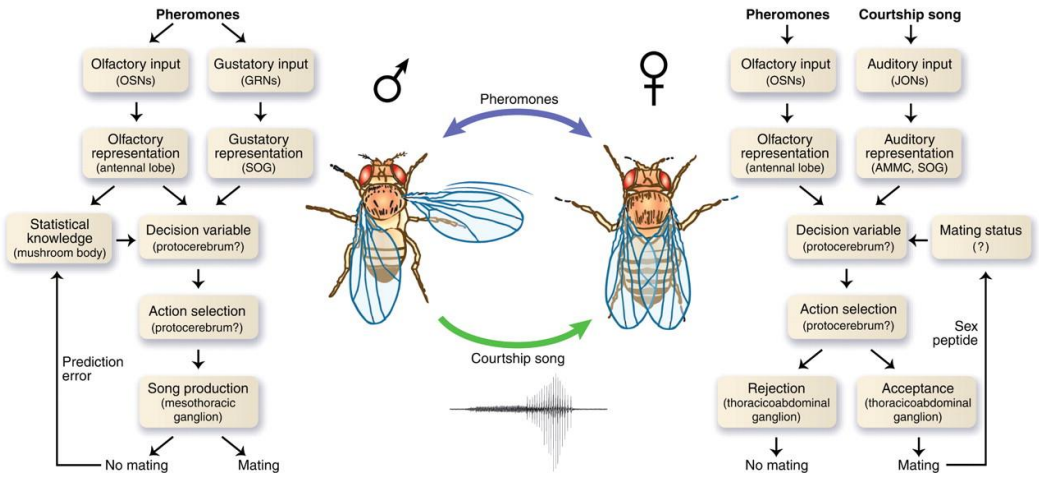
Motor coordination

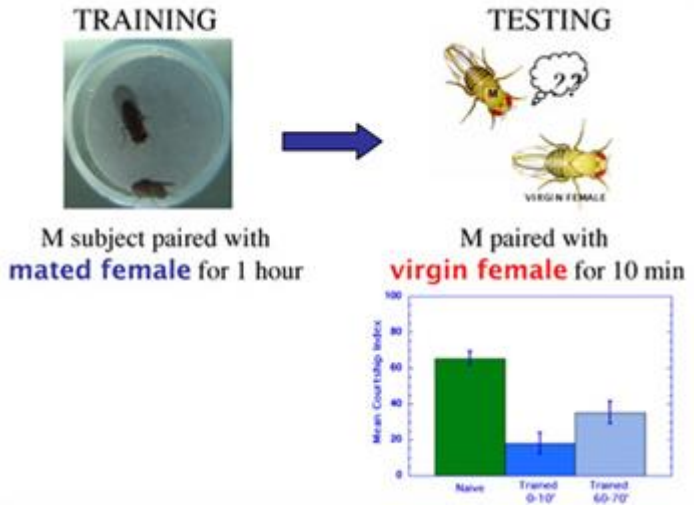
Goal-directed actions

Behavioral paradigms: courtship

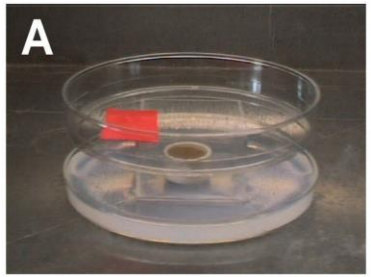


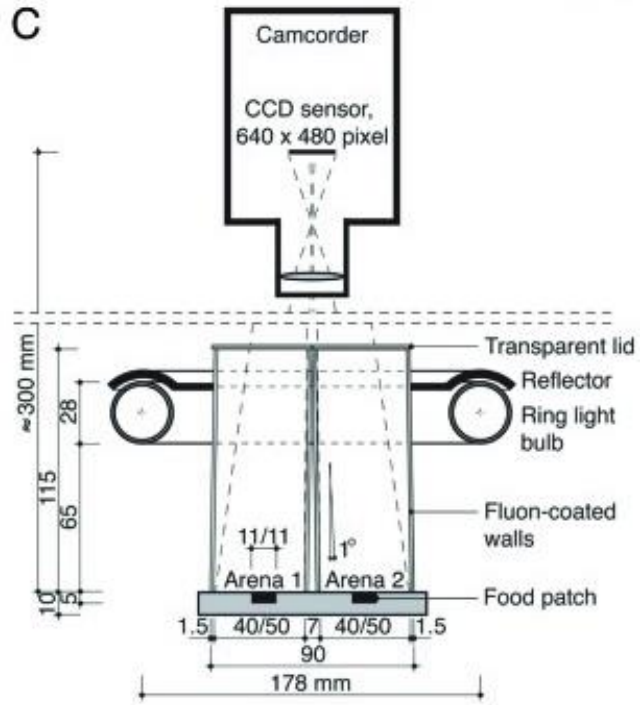


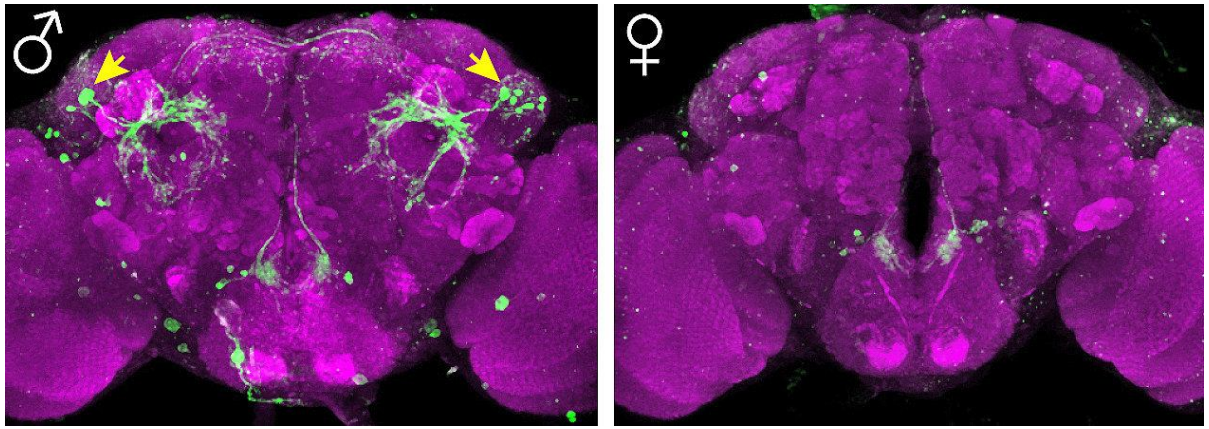




Behavioral paradigms: aggression

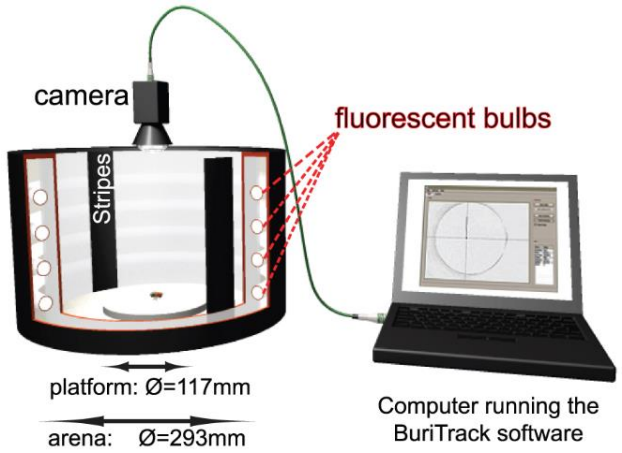


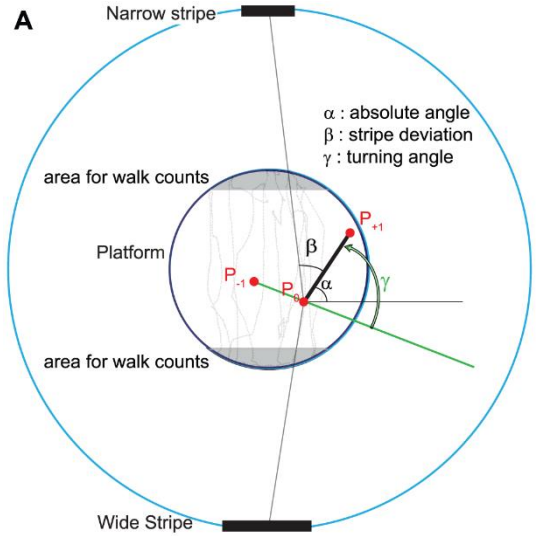


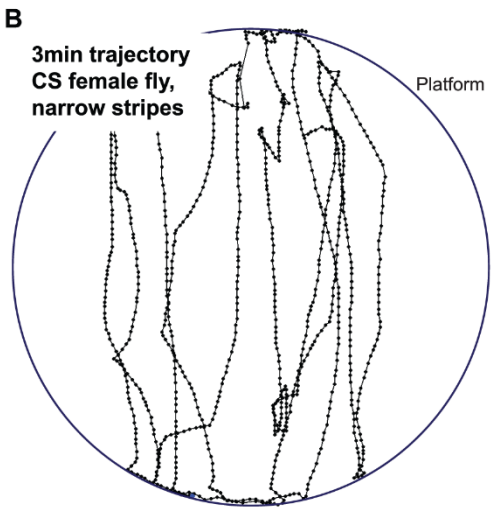


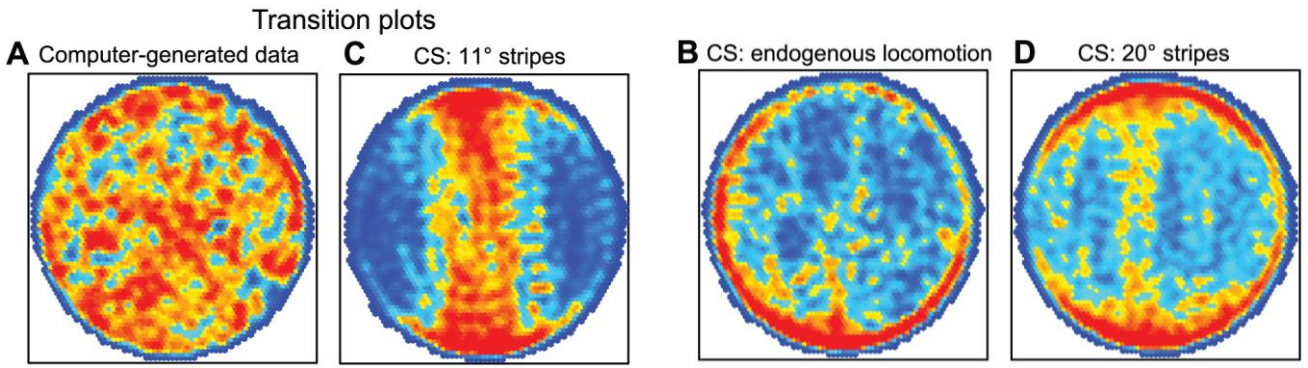
Tachykinin-expressing neurons

Behavioral paradigms: Buridan

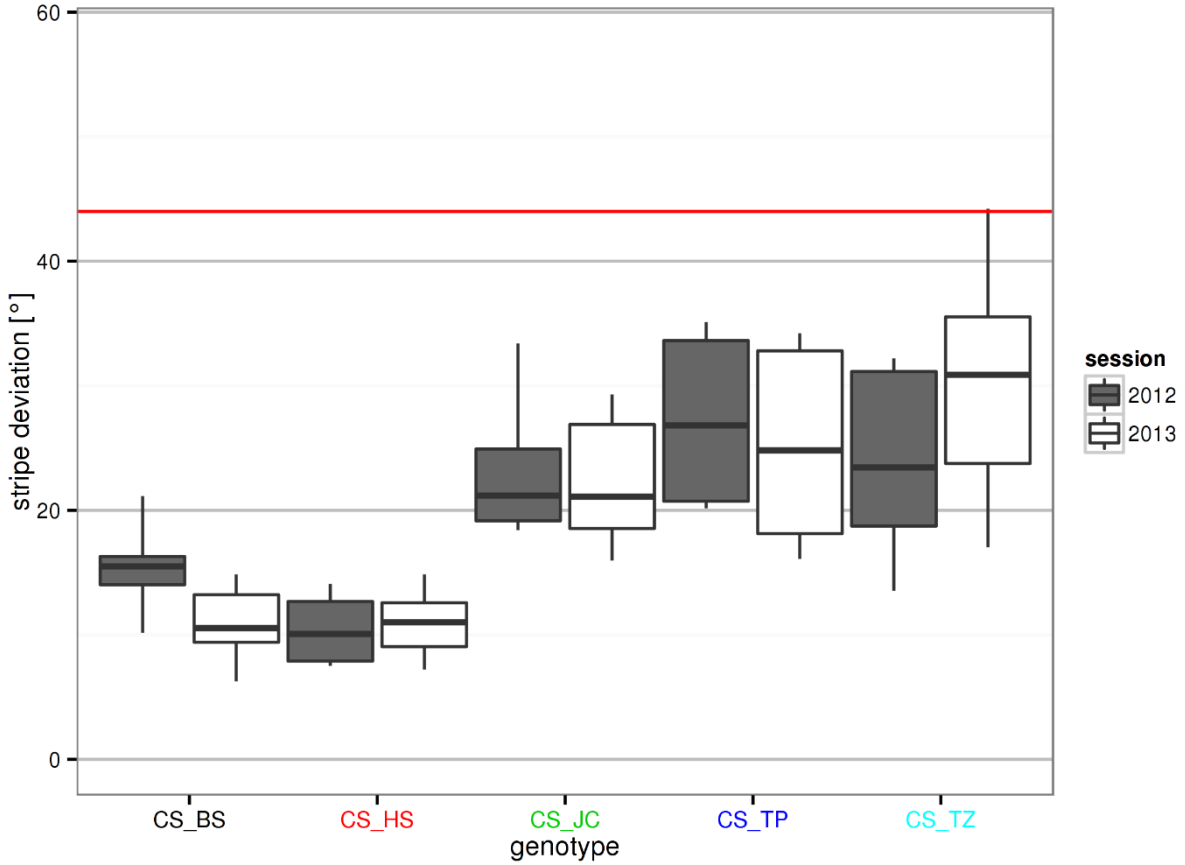


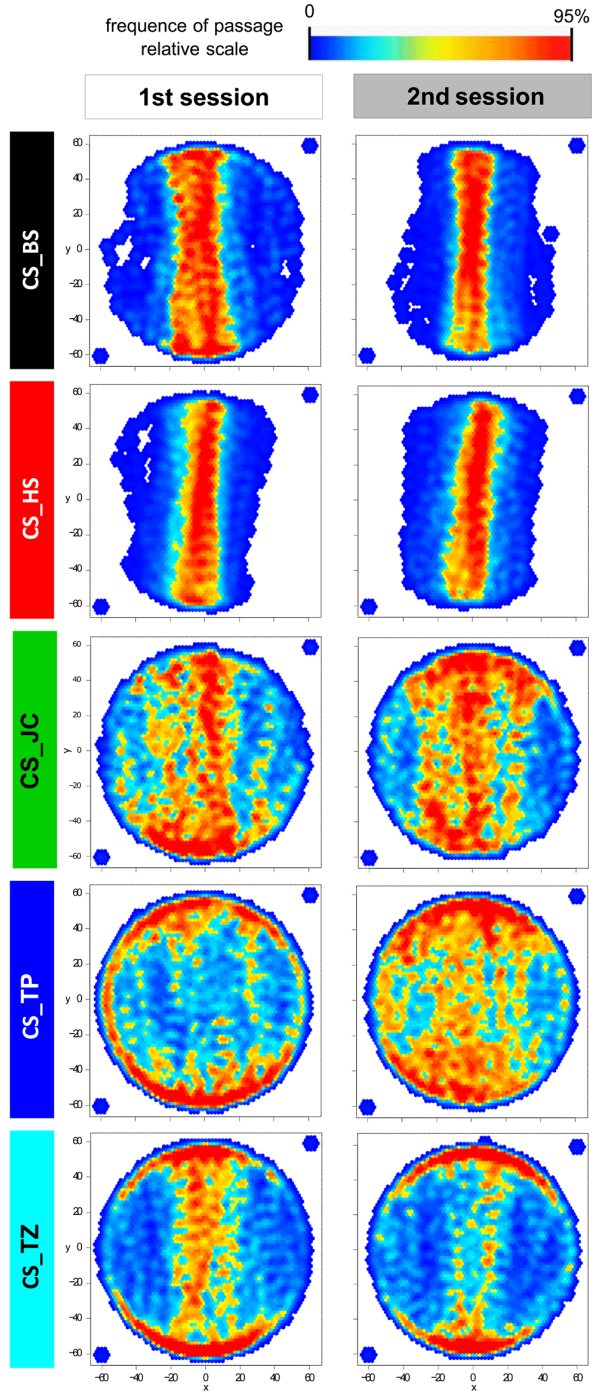






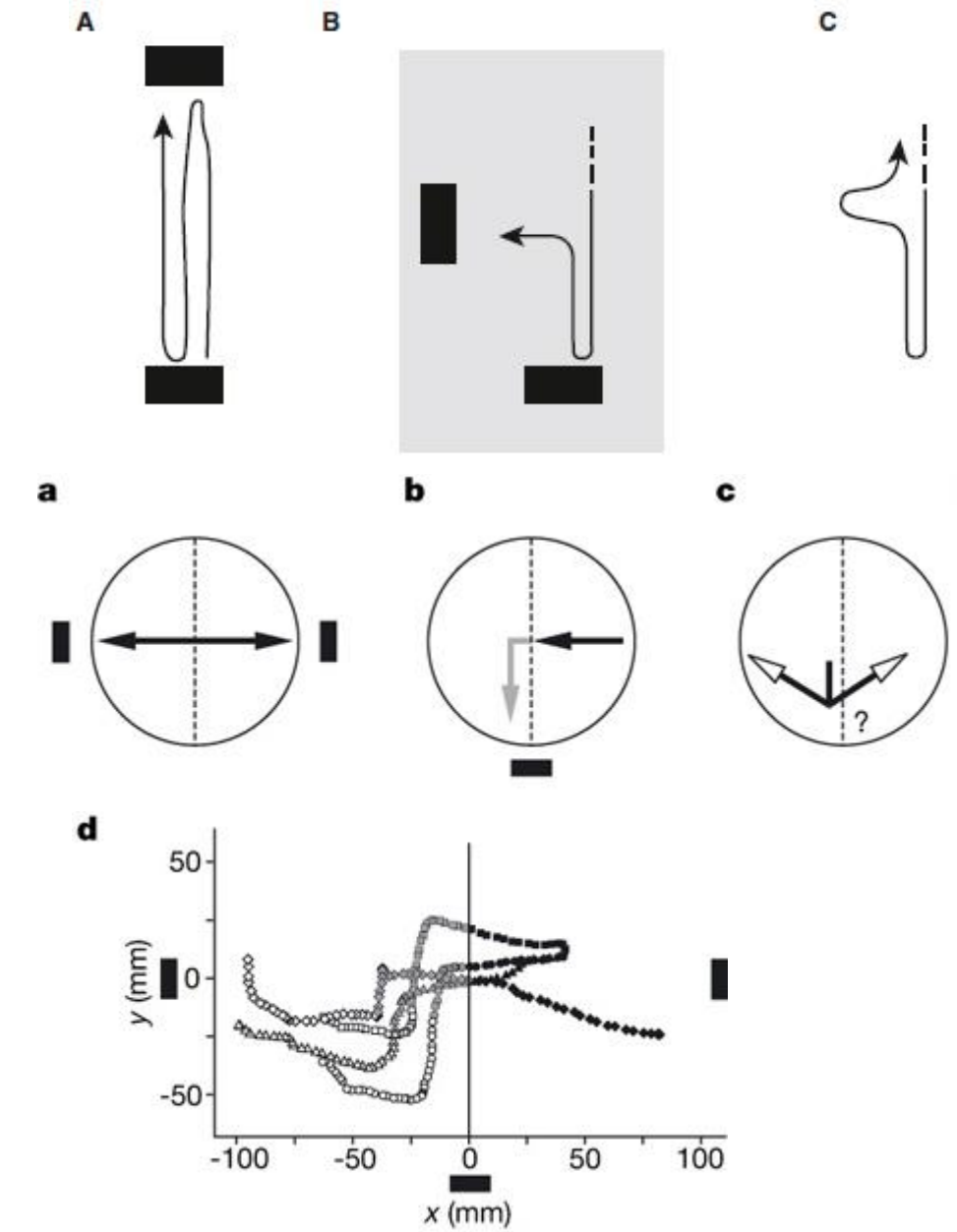
Behavioral paradigms: Buridan

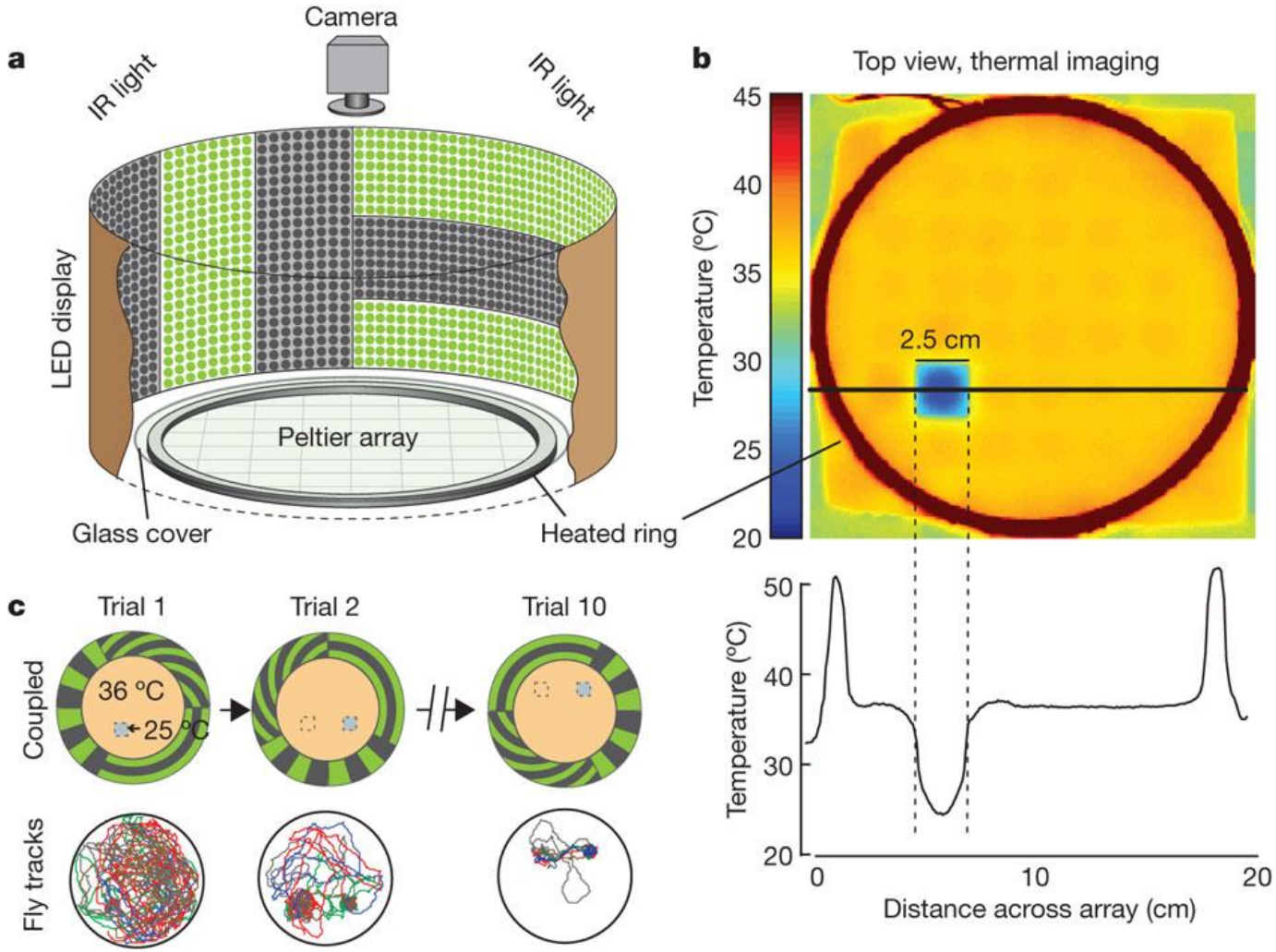




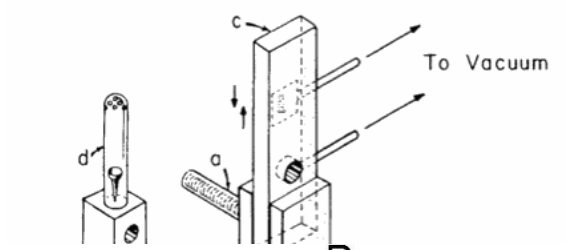
Colomb J and Brembs B, F1000Research 2014

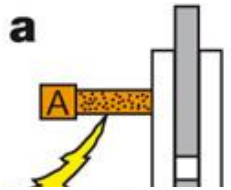
Behavioral paradigms: detour & visual place learning

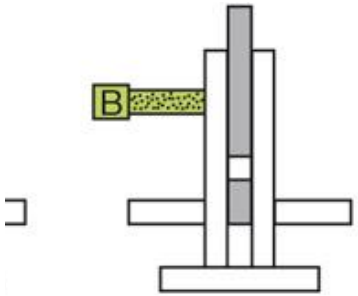


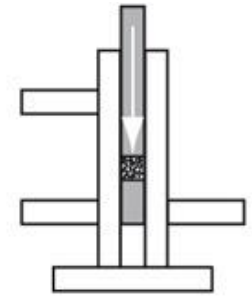


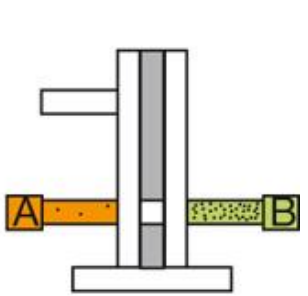
Behavioral paradigms: olfactory learning











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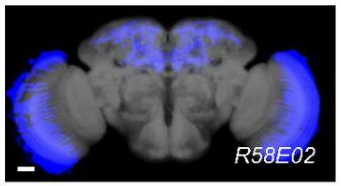

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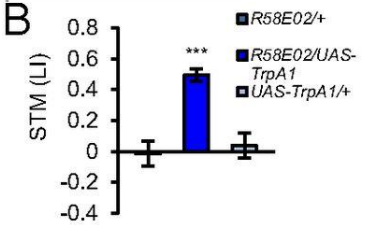

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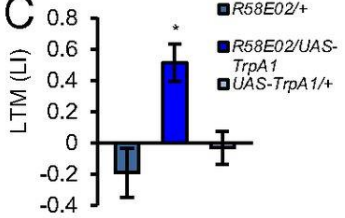

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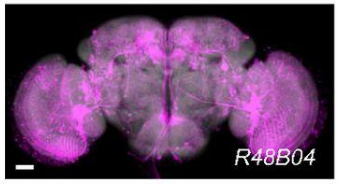

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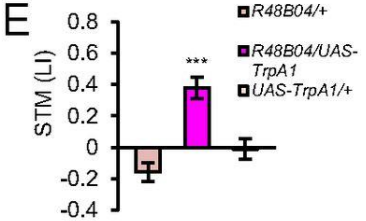

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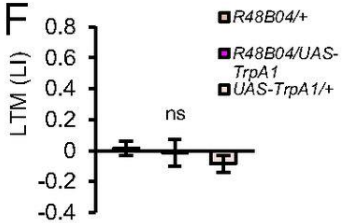

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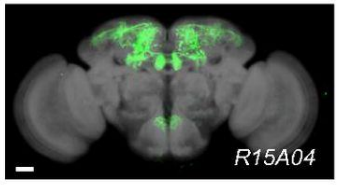

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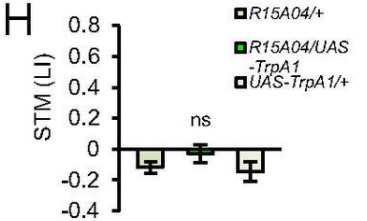

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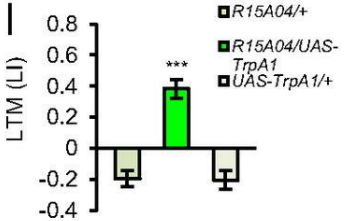

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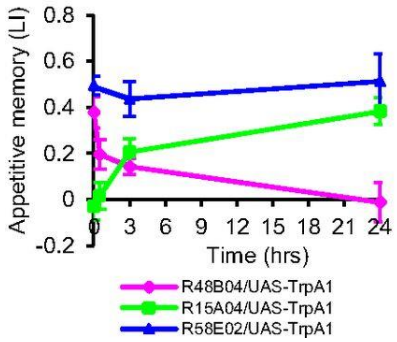

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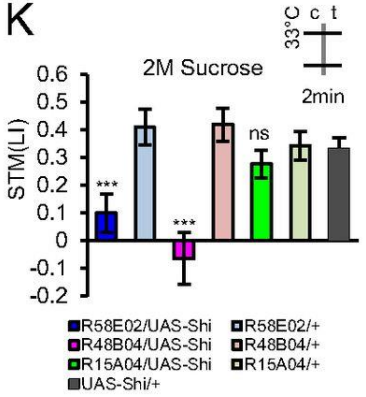

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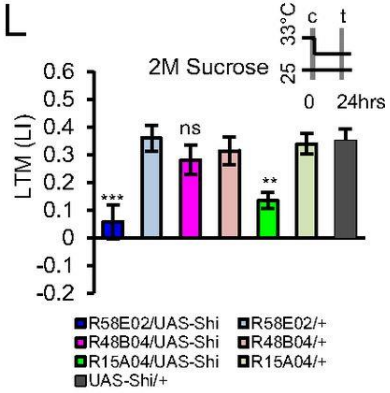
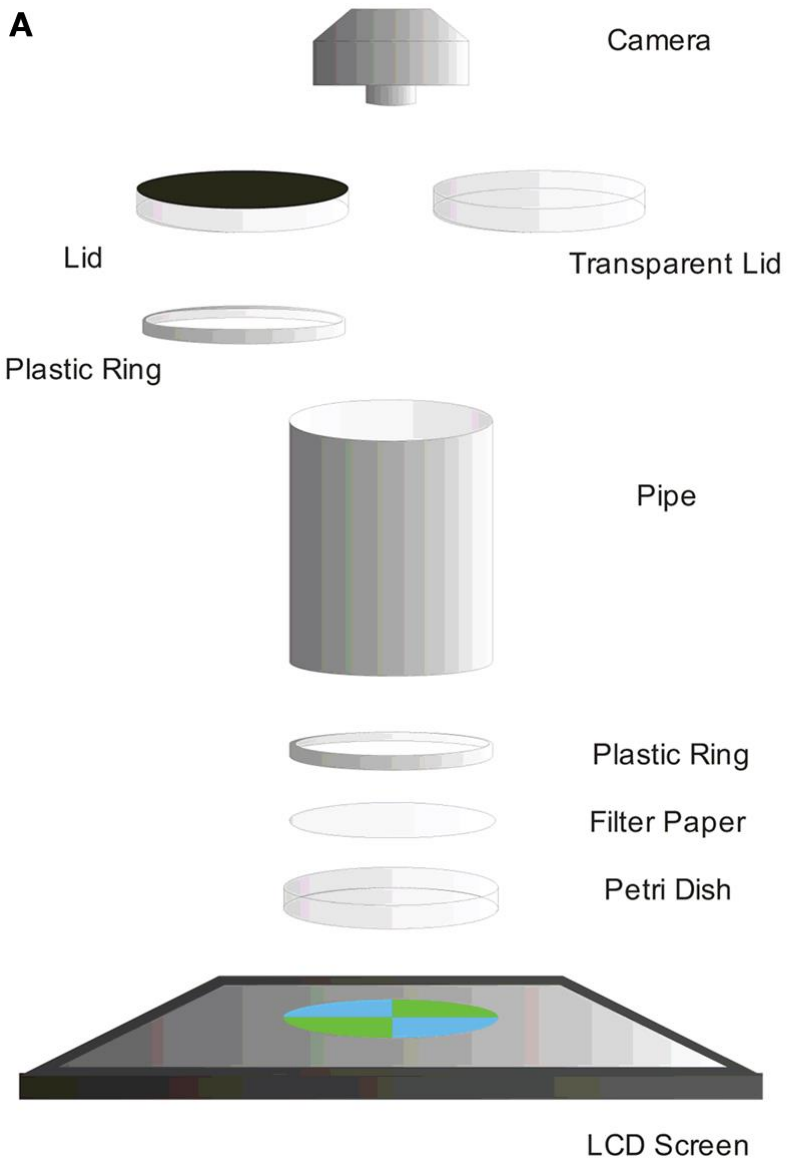
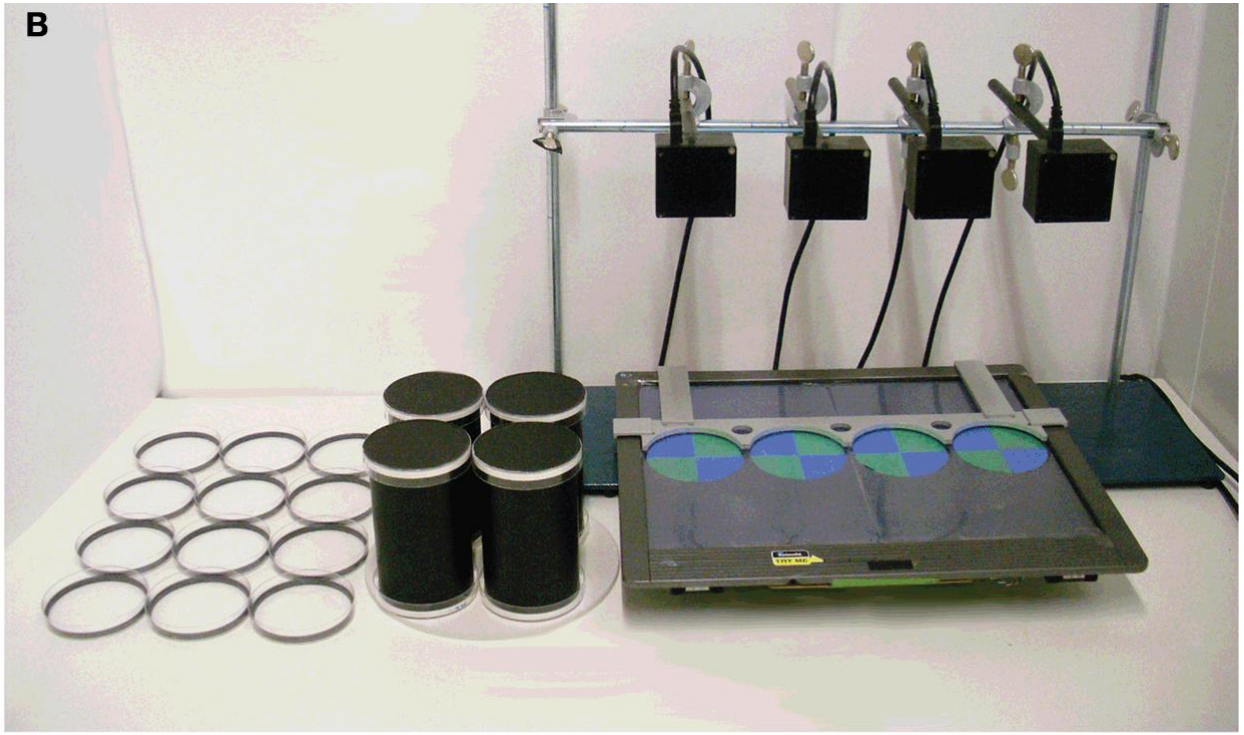
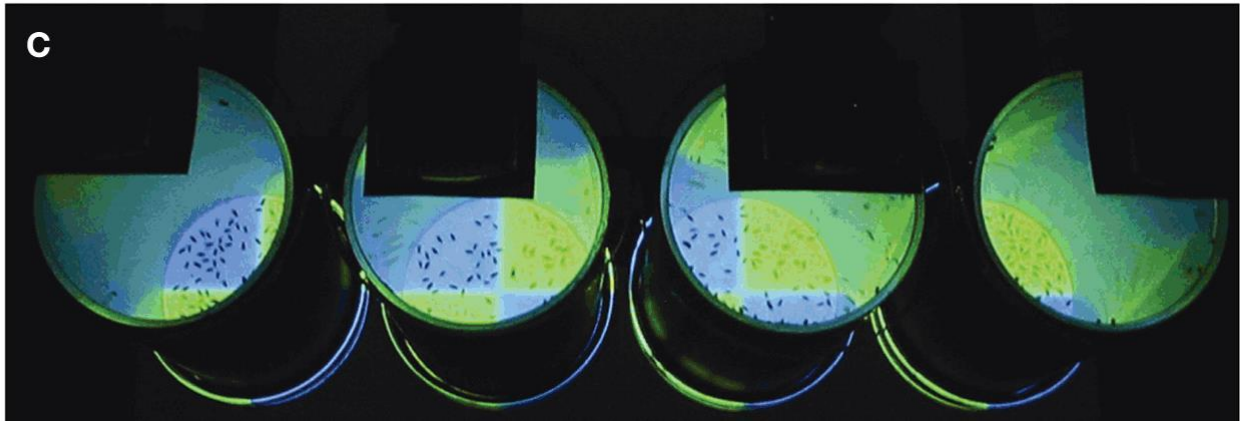


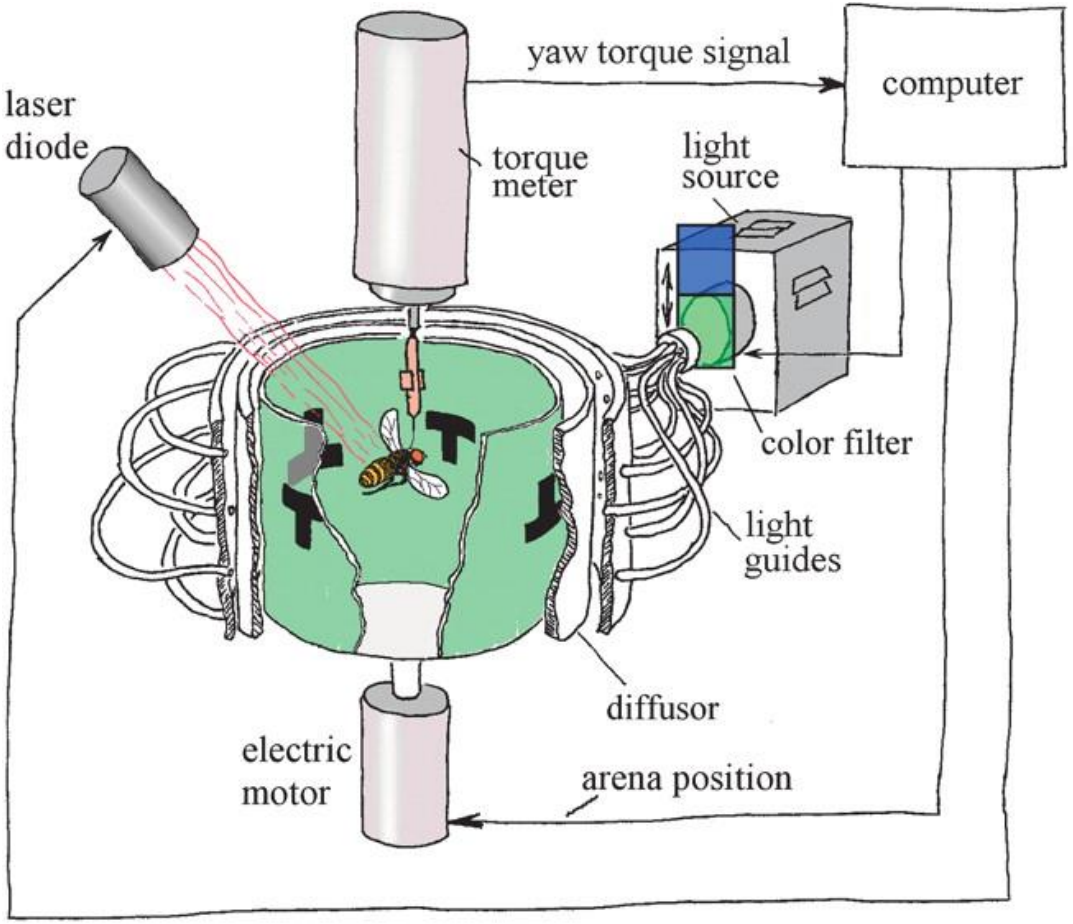
Behavioral paradigms: visual learning

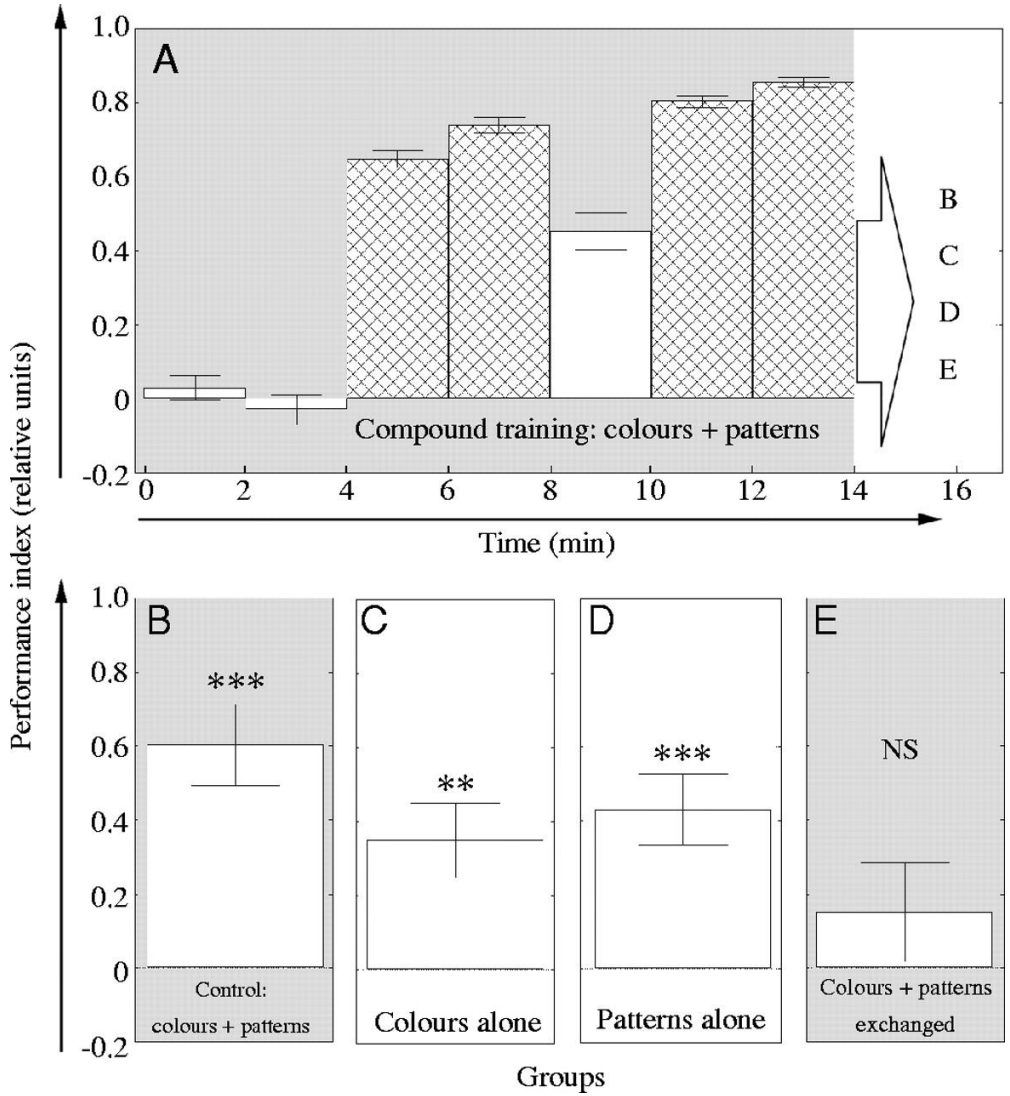






Behavioral paradigms: flight simulator





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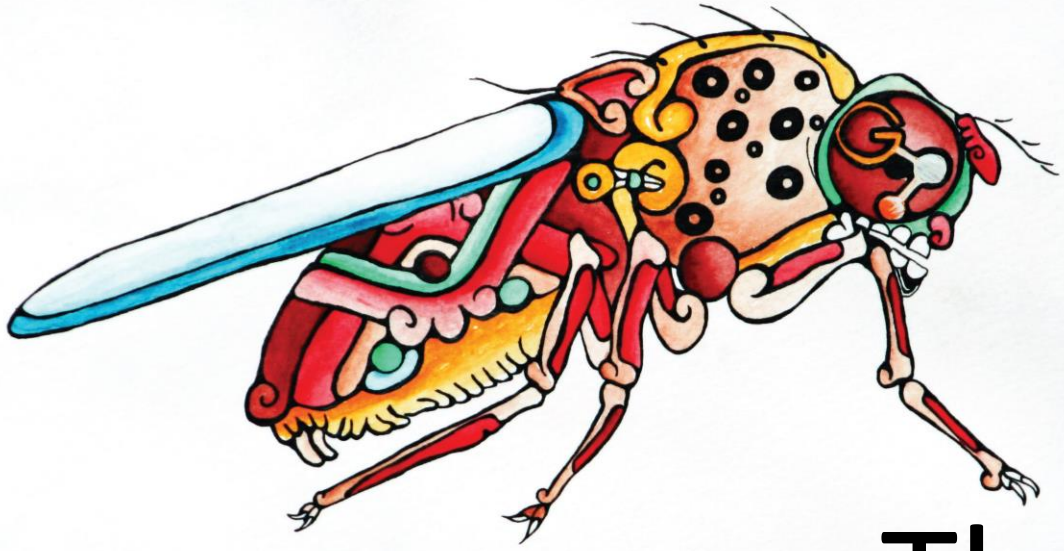

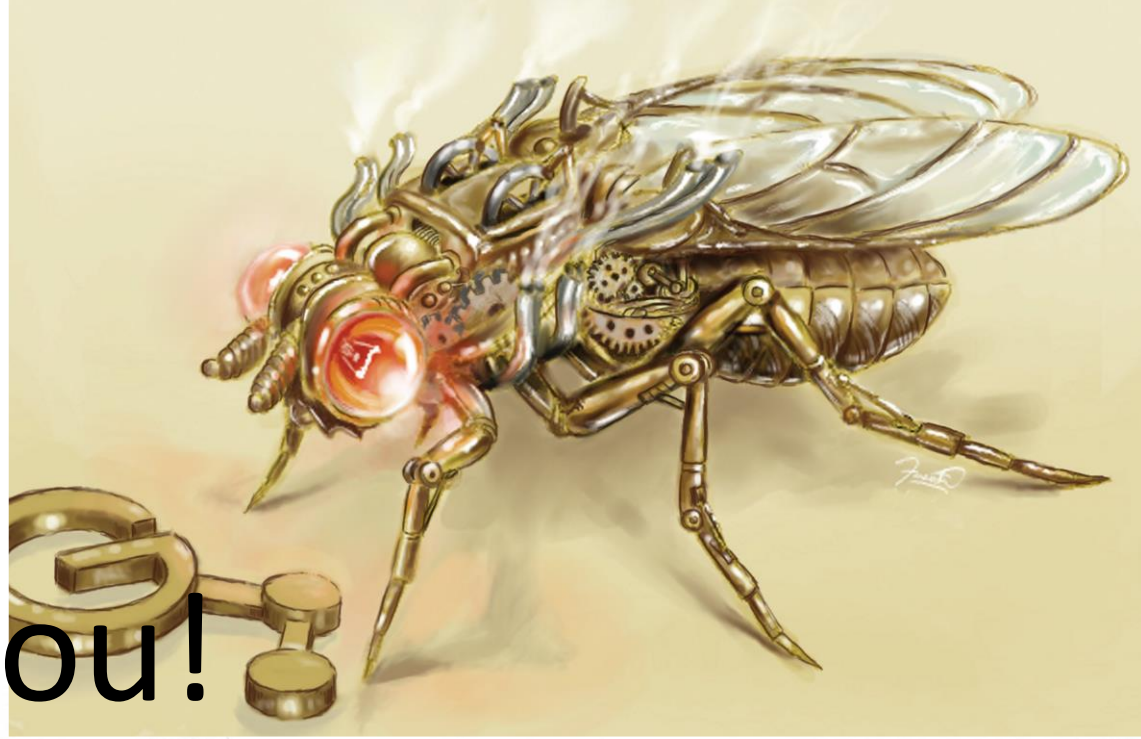

Thank you!