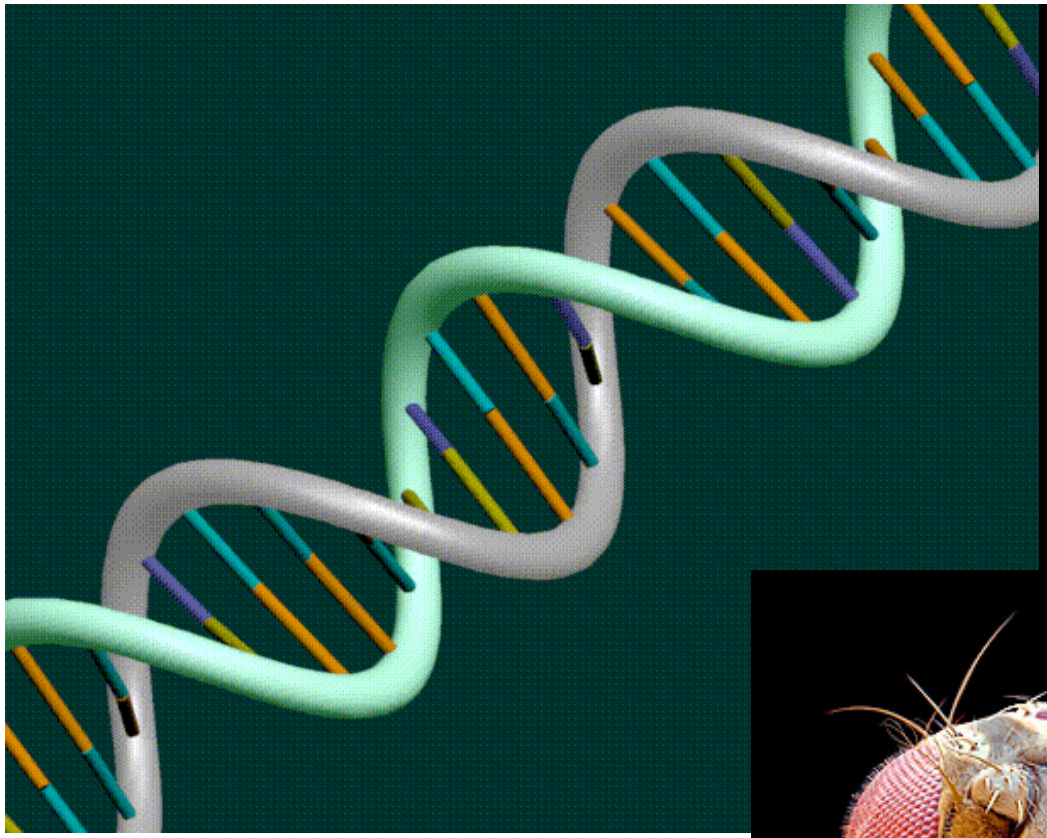
Genes, Brains and Behaviour
memory traces

Karl-Friedrich Fischbach, Neurogenetics, Freiburg



learning is the
adaptive reprogramming of the nervous system

1. non-associative learning
   - habituation
   - sensitization

2. associative learning

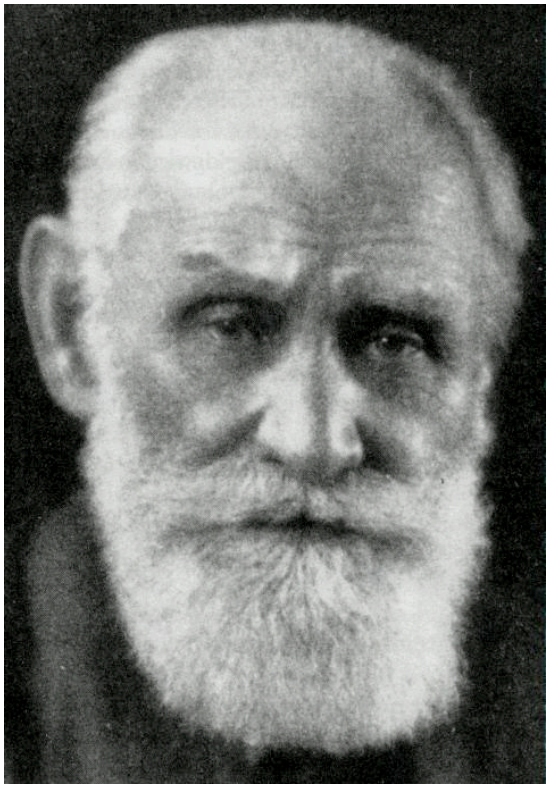
associative learning

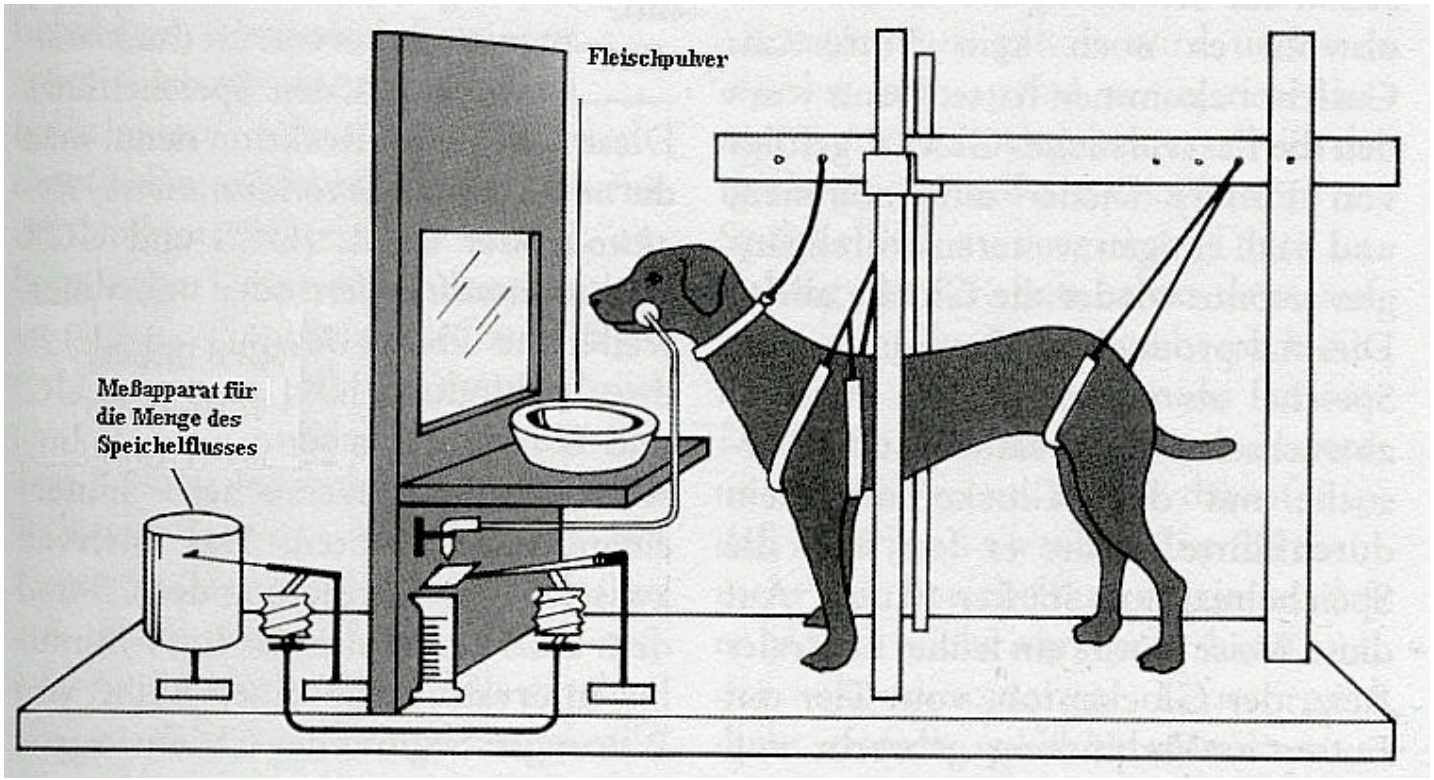
1. **classical conditioning**

2. **operant conditioning**

3. **higher kinds of learning**
   (learning by watching, learning by insight etc.)

classical conditioning (Pawlow)

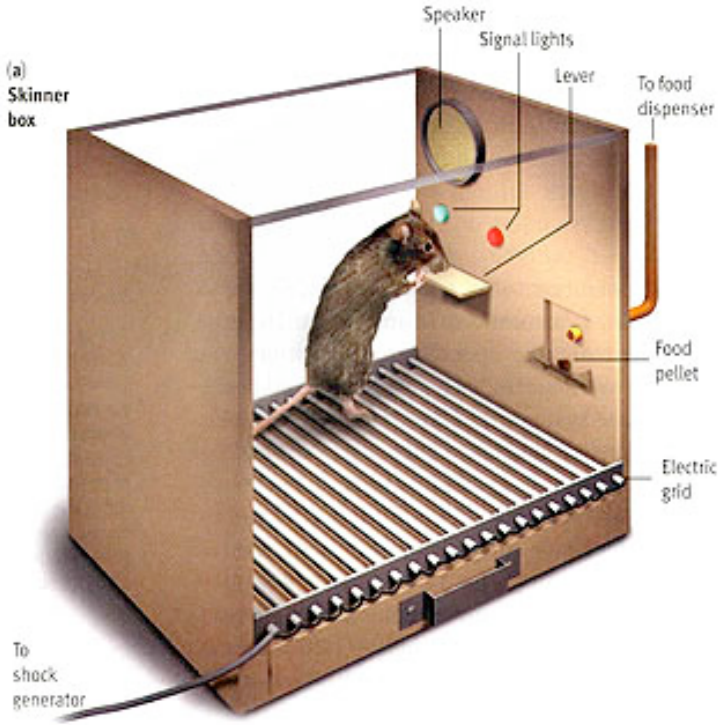




UCS + CS => UCR

food + bell => salivation

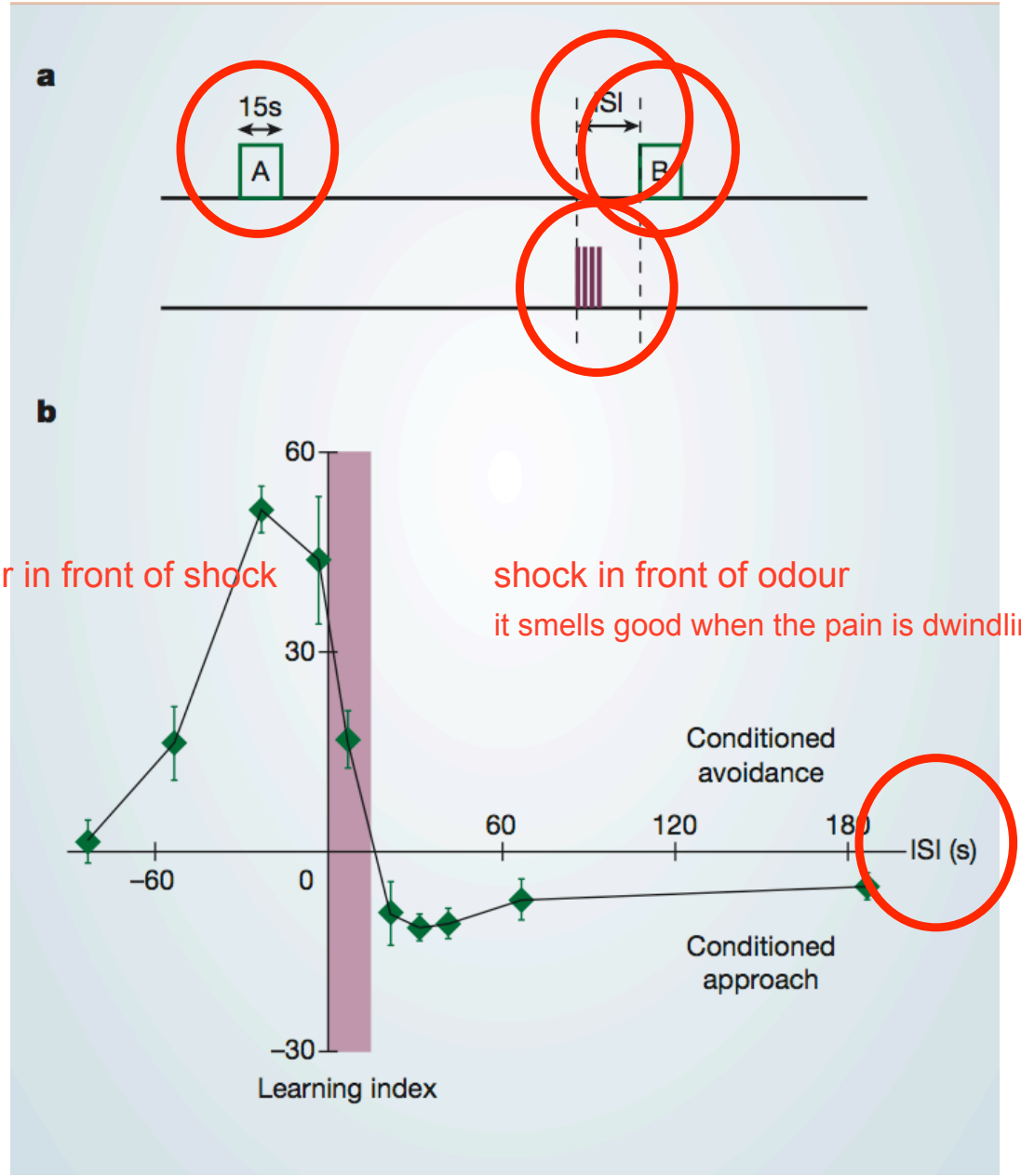
operant conditioning (Skinner)



common features of associative learning

- „instinctive“ (automated) making of a new connection (association) between two events
- requirement for contiguity of the events (the two events have to occur in a fixed sequence inside a narrow time window)
- The unconditioned stimulus, reward or punishment, has always to be given after the conditoned stimulus or behavior
- If the conditions are right, learning is inevitable

The importance of timing for learning:
Event timing turns punishment to reward



odour in front of shock

shock in front of odour

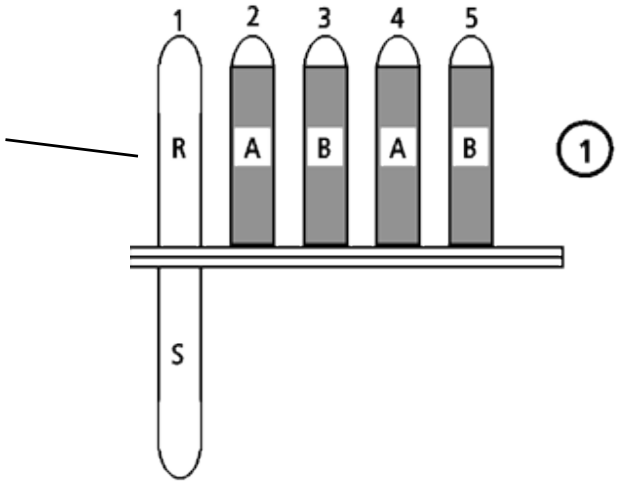
it smells good when the pain is dwindling

Does associative behaviour exist in Drosophila? Can genes of importance for learning be identified?

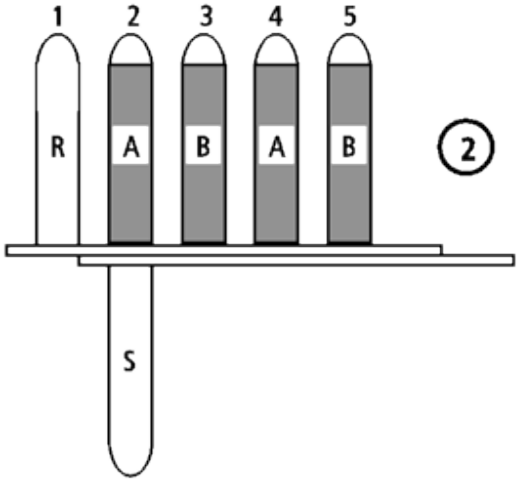
This question was asked in the early seventieth at the California Institute of Technology by Seymour Benzer, who at that time was already a famous molecular geneticist.

original learning apparatus of Benzer

rest tube

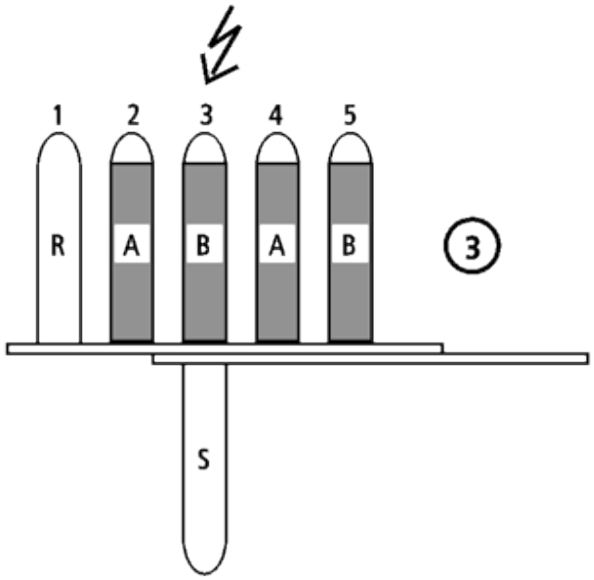


original learning apparatus of Benzer



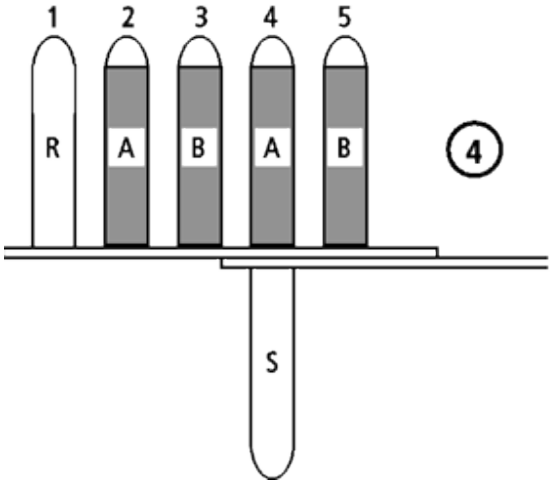
Training A
(not shocked odour)

original learning apparatus of Benzer



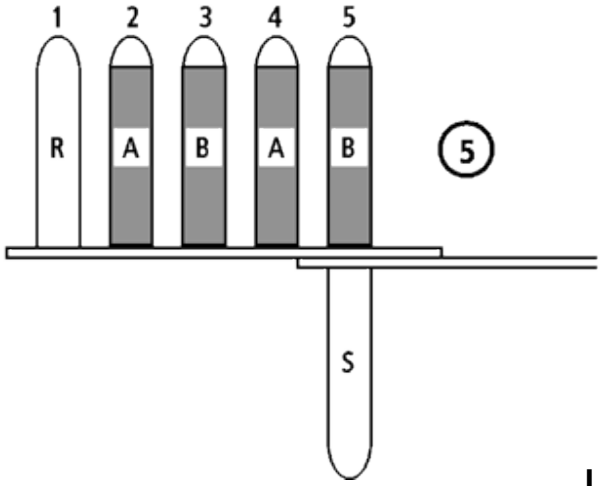
Training B
(shocked odour)

original learning apparatus of Benzer



Test A

original learning apparatus of Benzer



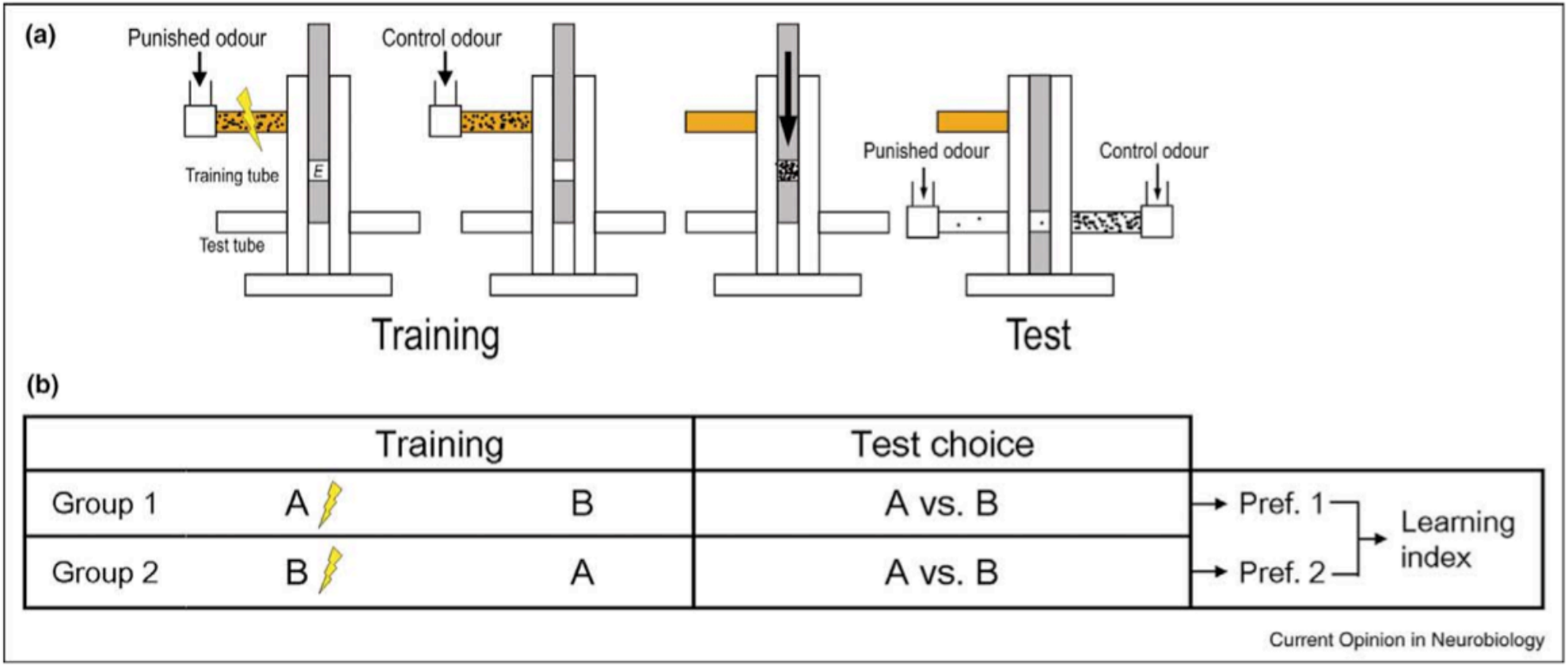
Procedure is repeated with shock given at A

Test B

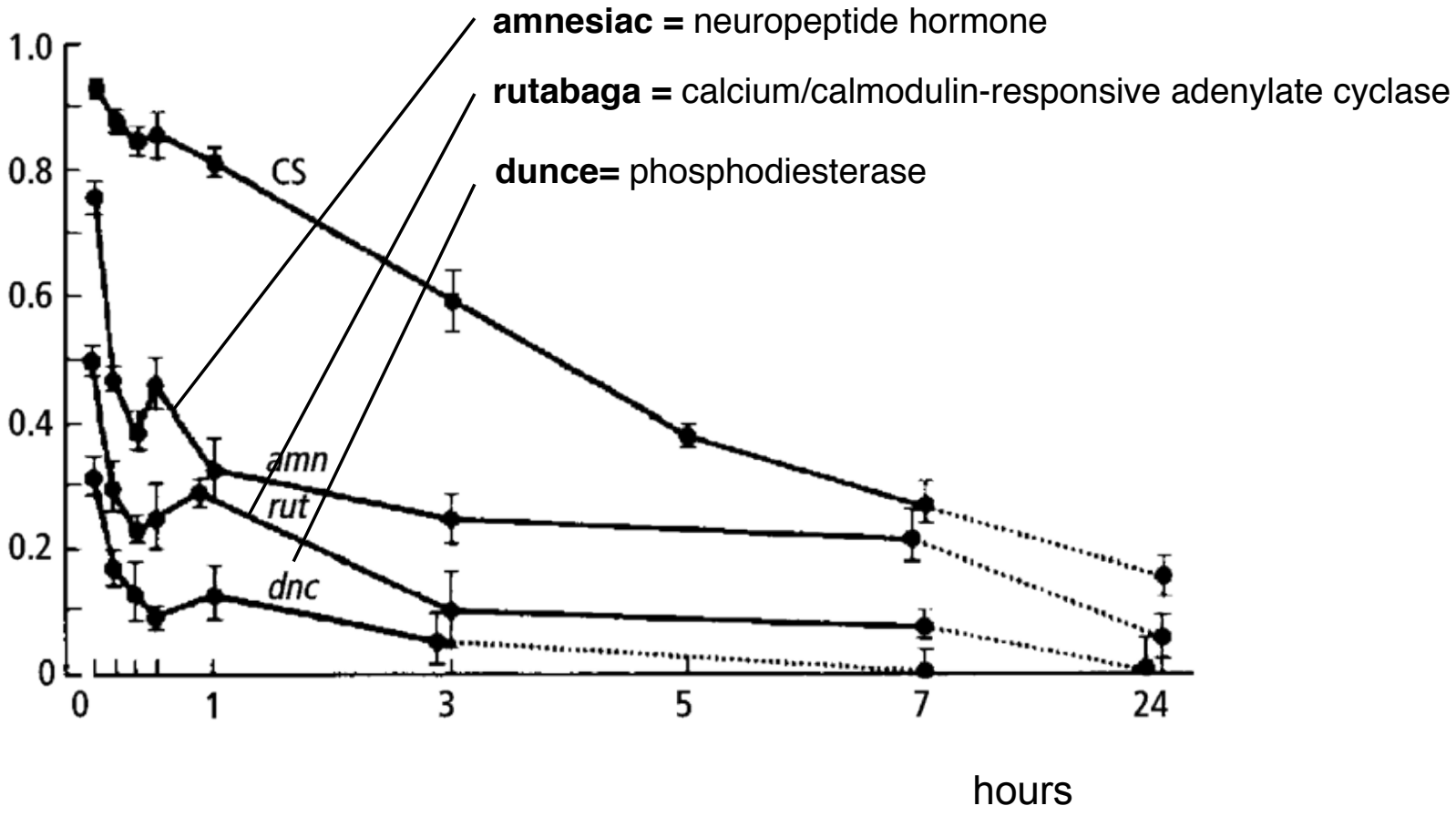
Learning index

$$\frac{\text{unshocked ordor} - \text{shocked order}}{\text{unshocked order} + \text{shocked order}}$$

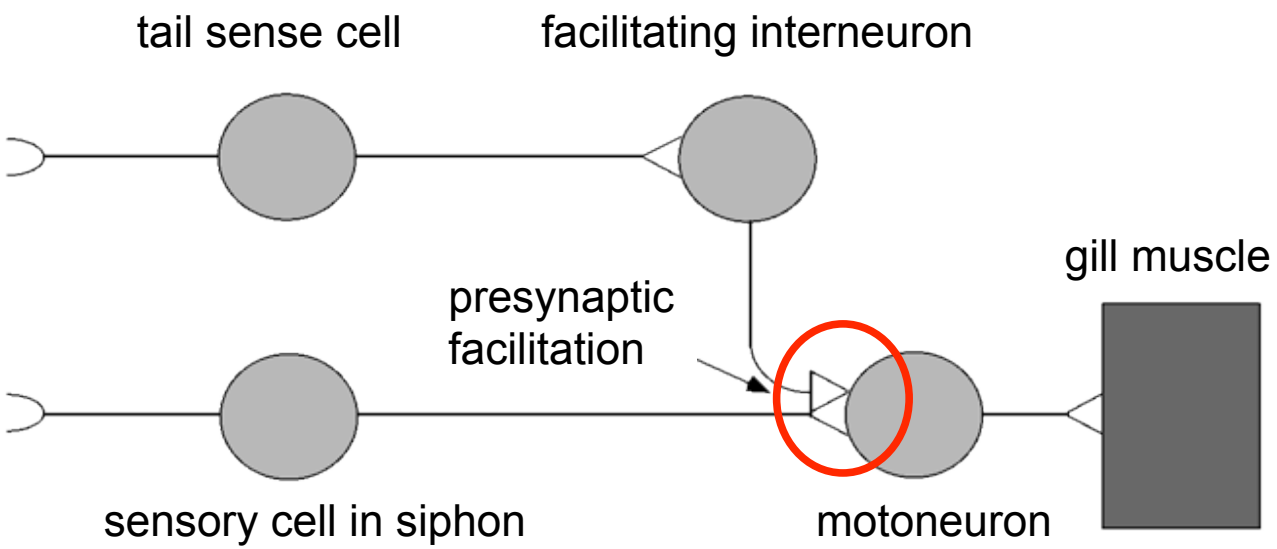
modern olfactory learning apparatus



The first memory-, learning mutants of Drosophila

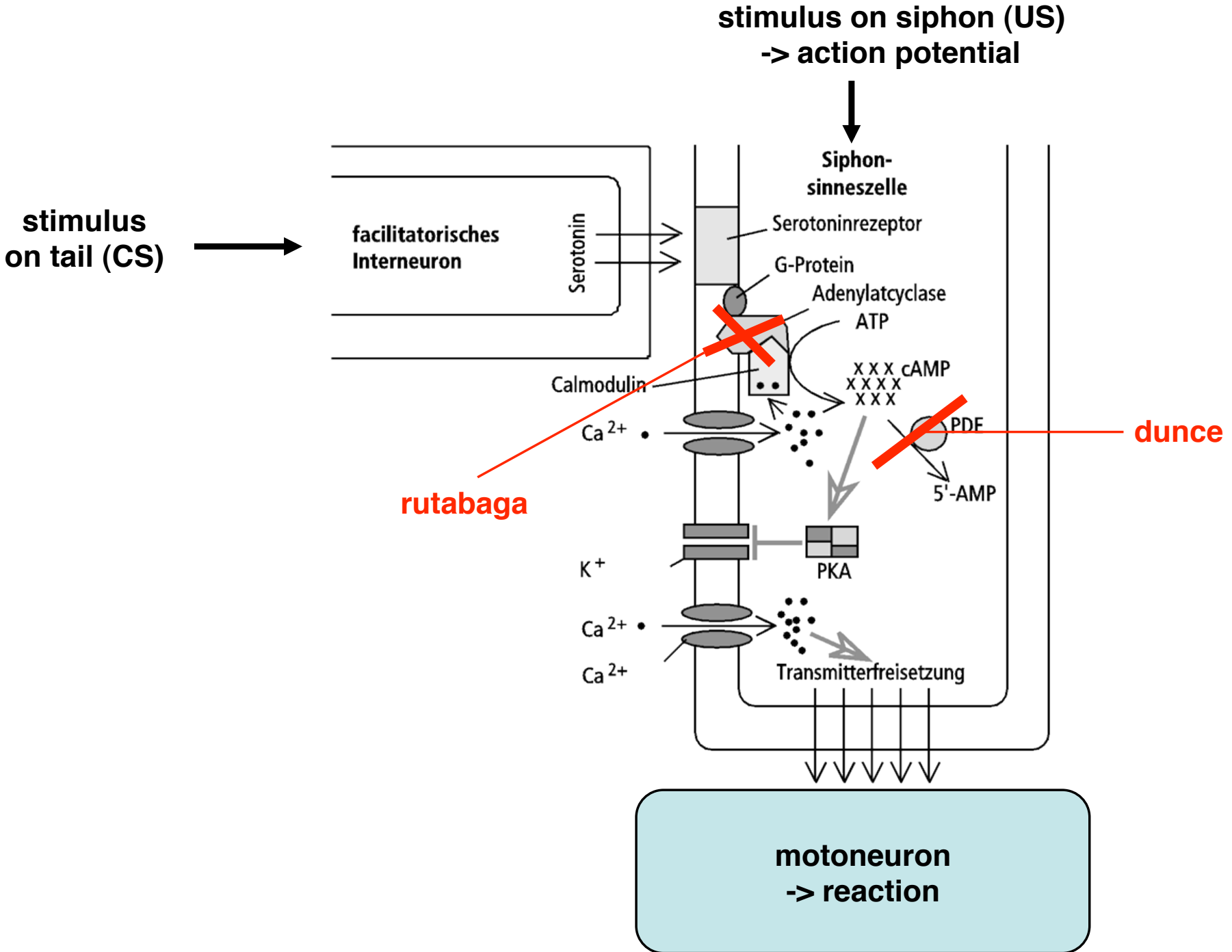


gill withdrawal reflex of Aplysia



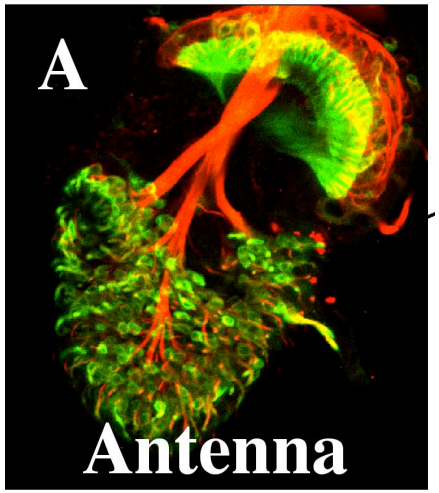
Eric Kandel

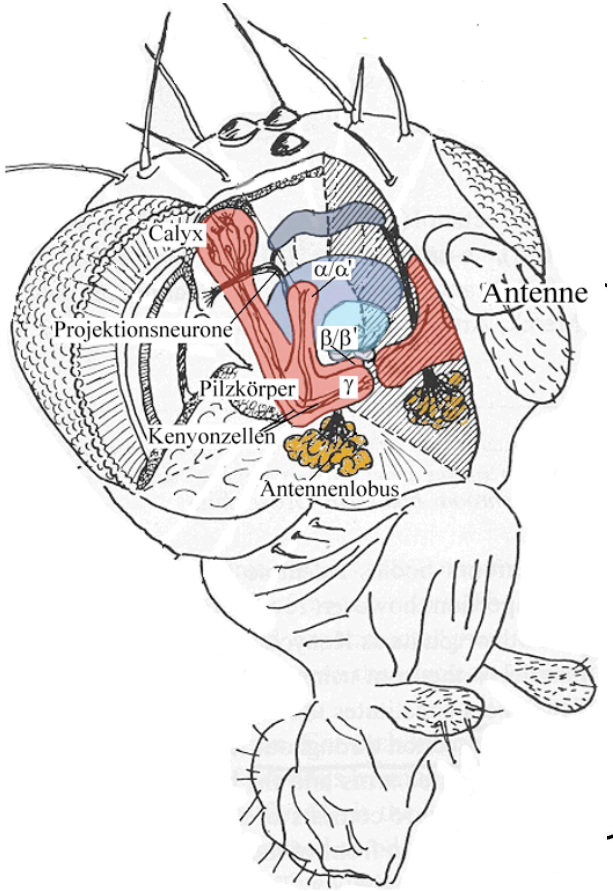
cAMP-mediated associative learning of Alysia

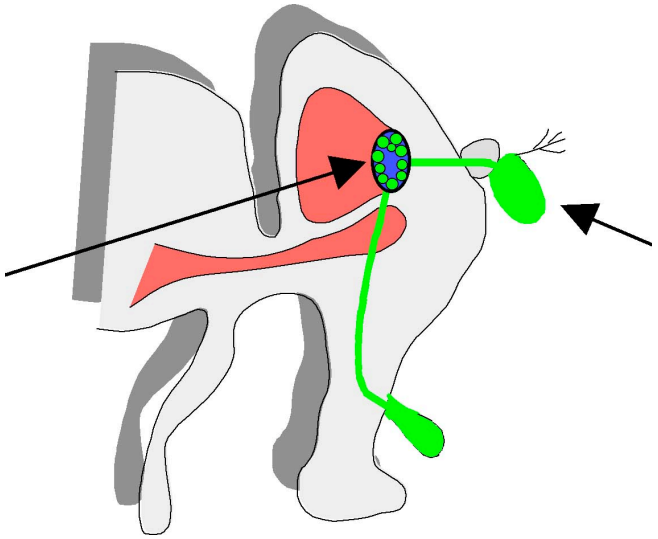


localization of the olfactory learning centers in Drosophila

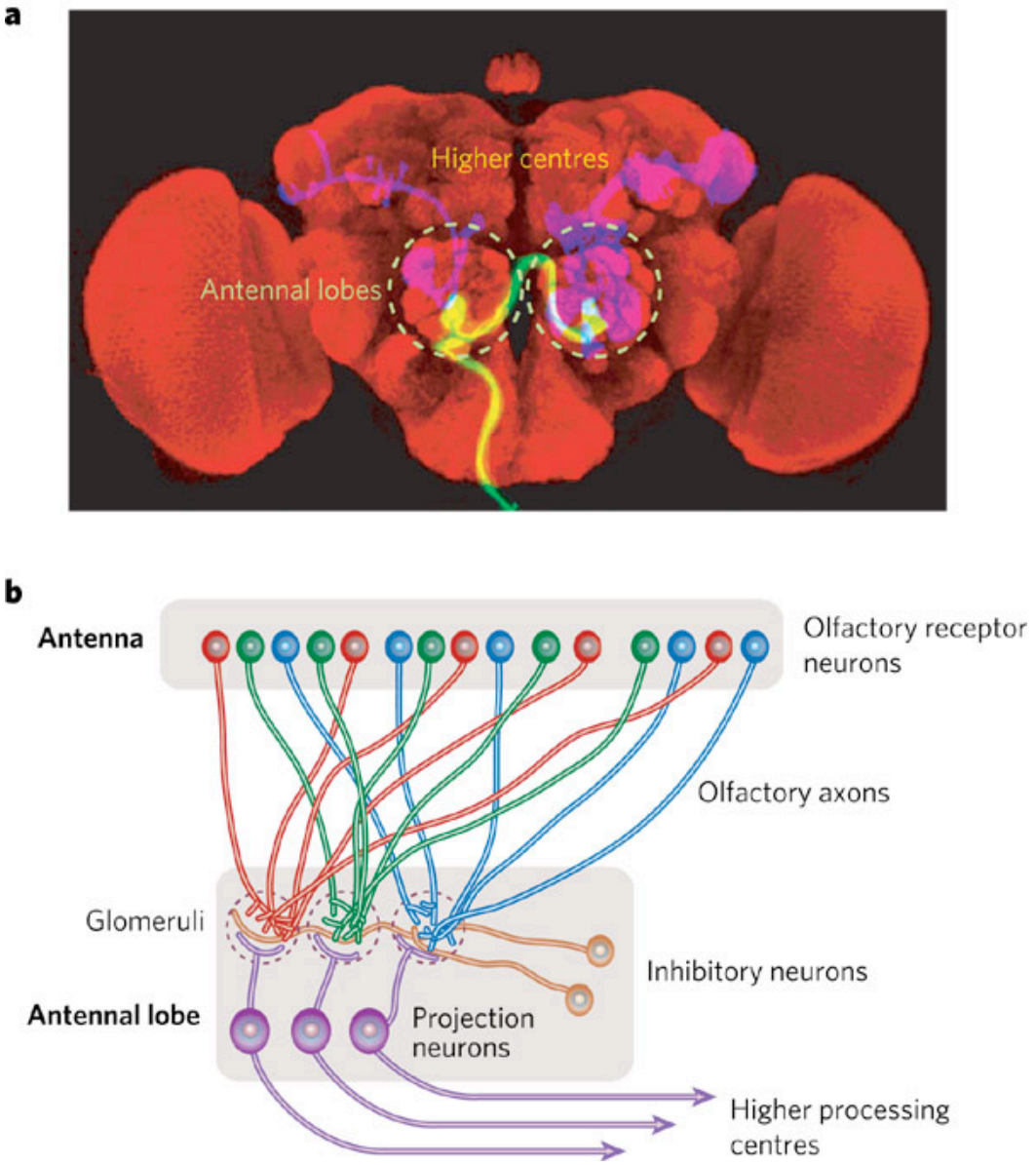
Olfaction pathways

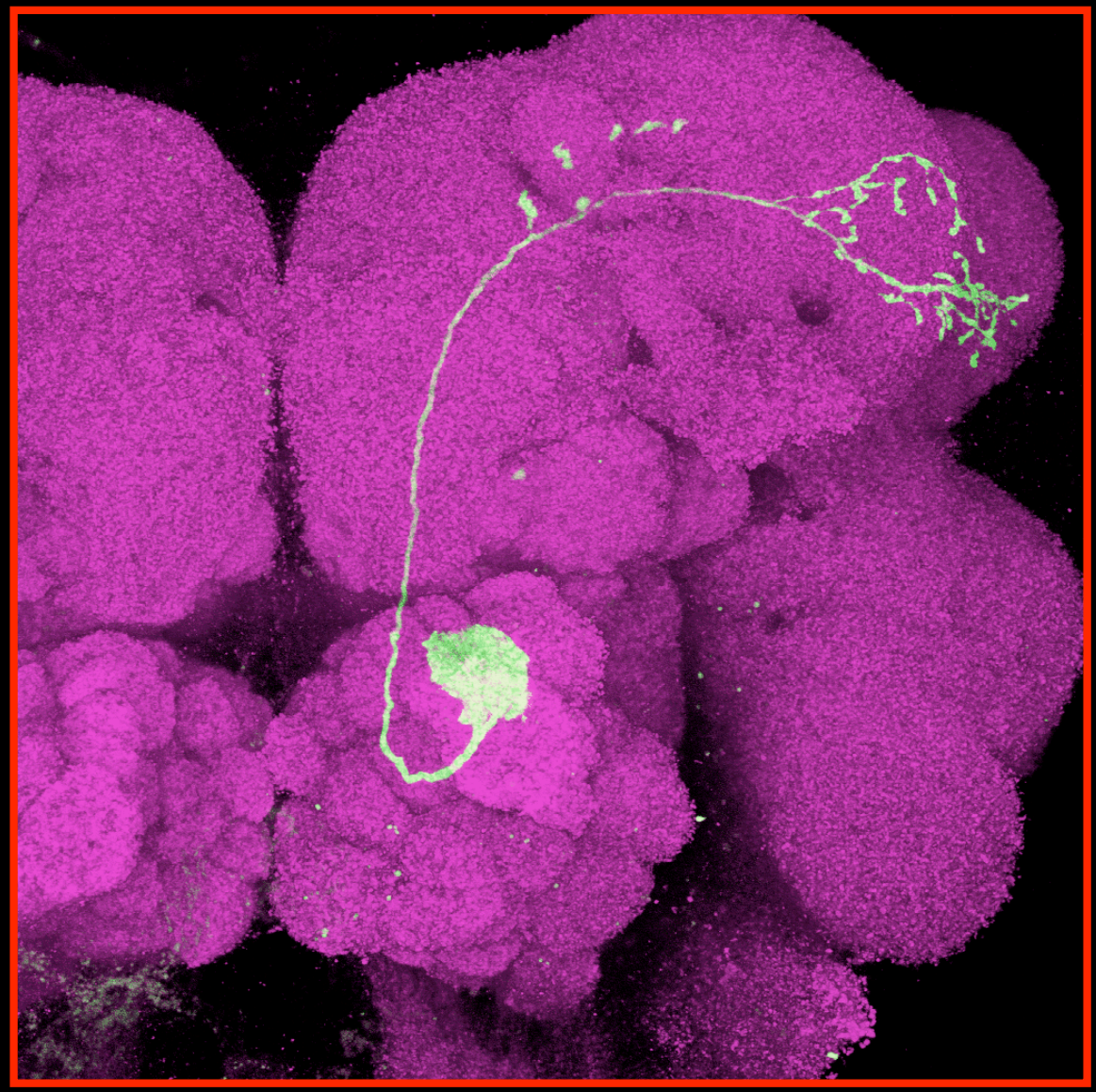






Olfaction pathways



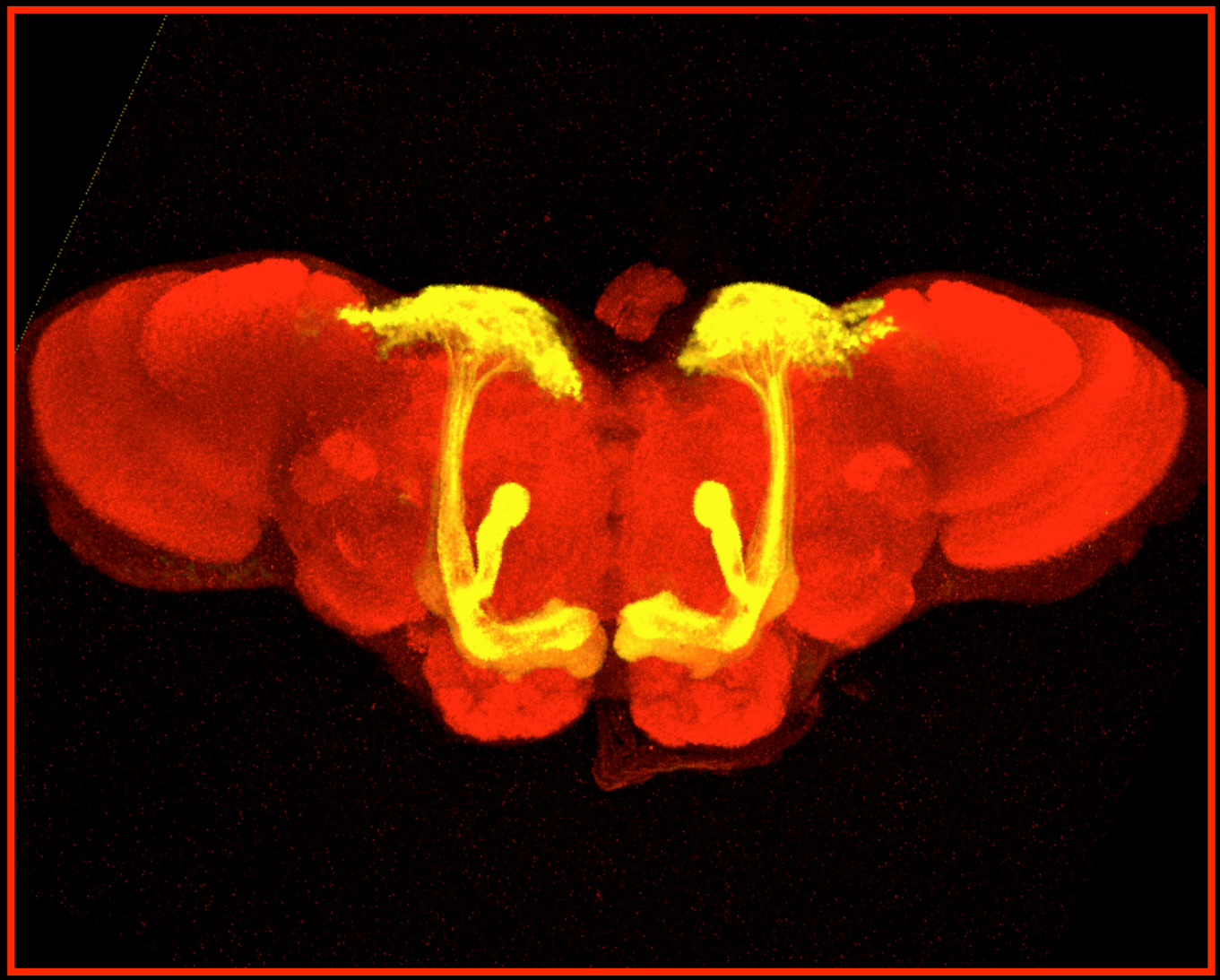


Single projection neuron
background: synaptic neuropil

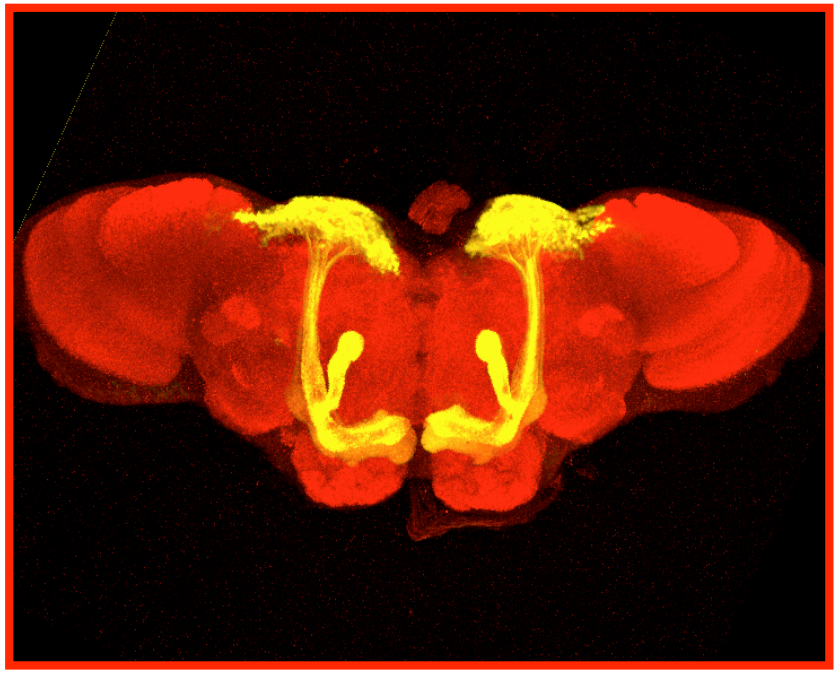
(modified after Luo, 2007)

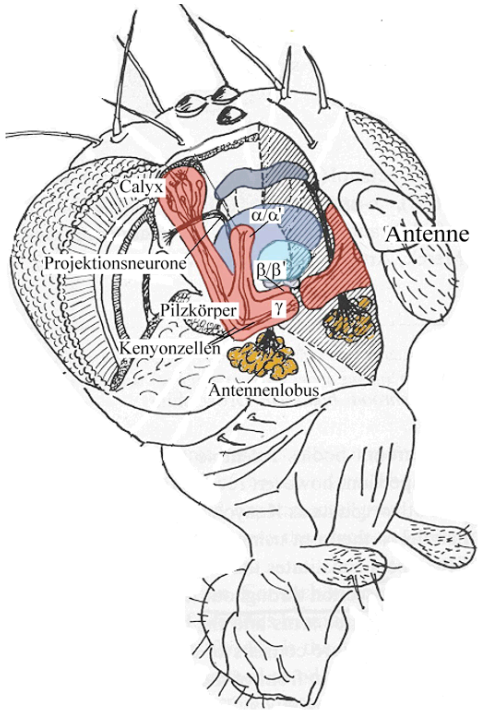
All projection neurons

mushroom bodies (Kenyon cells)



Mutants of the mushroom bodies:
The higher olfactory brain centers



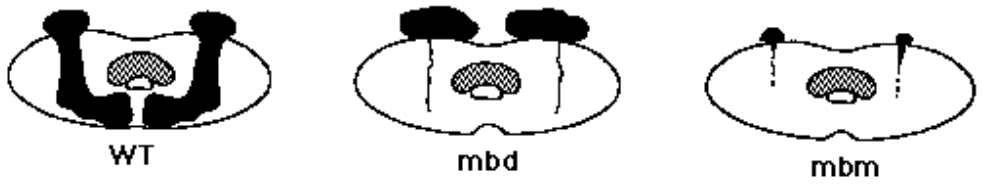


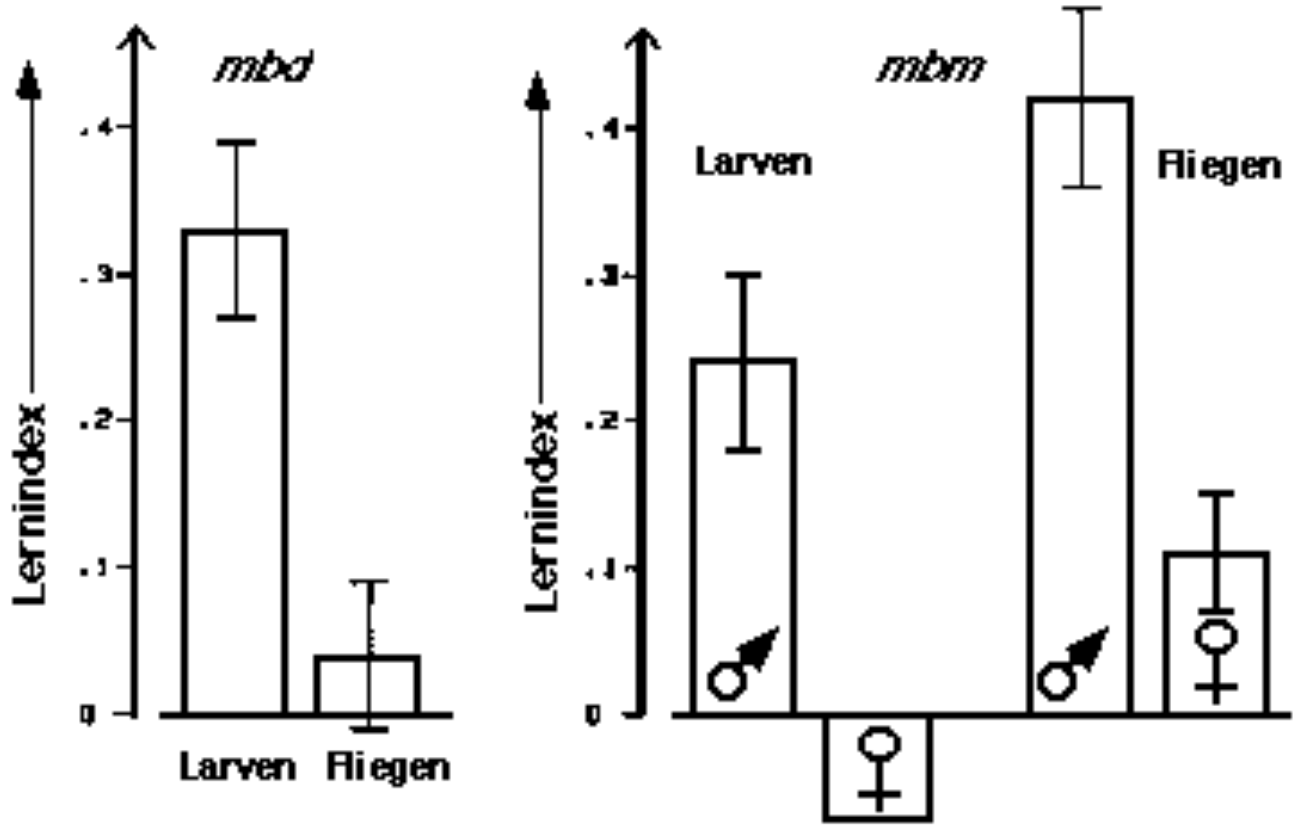
Martin Heisenberg

WT

mbd

mbm


WT
mbd
mbm


mbd
Lernindex
.4
.3
.2
.1
0
Larven
Fliegen
mbm
Lernindex
.4
.3
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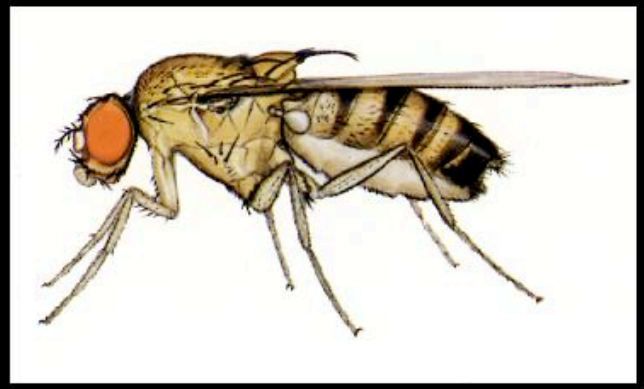
0
Larven
Fliegen

Technique used: The basic Gal4/UAS tool box



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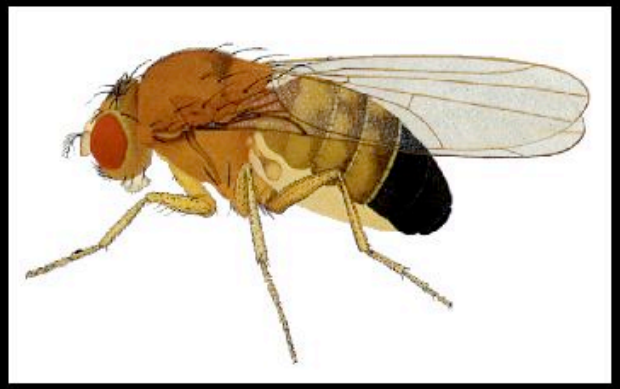
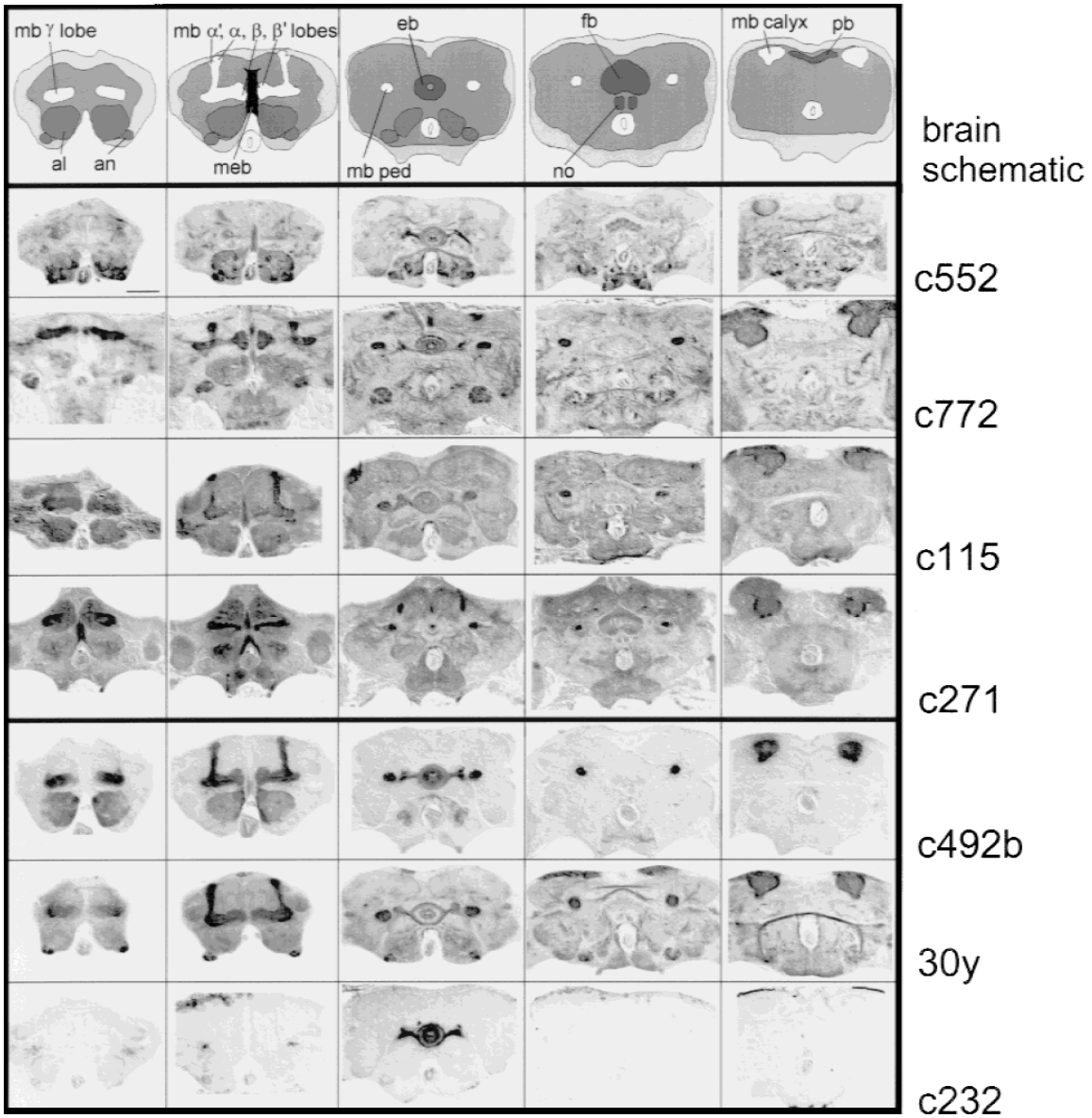


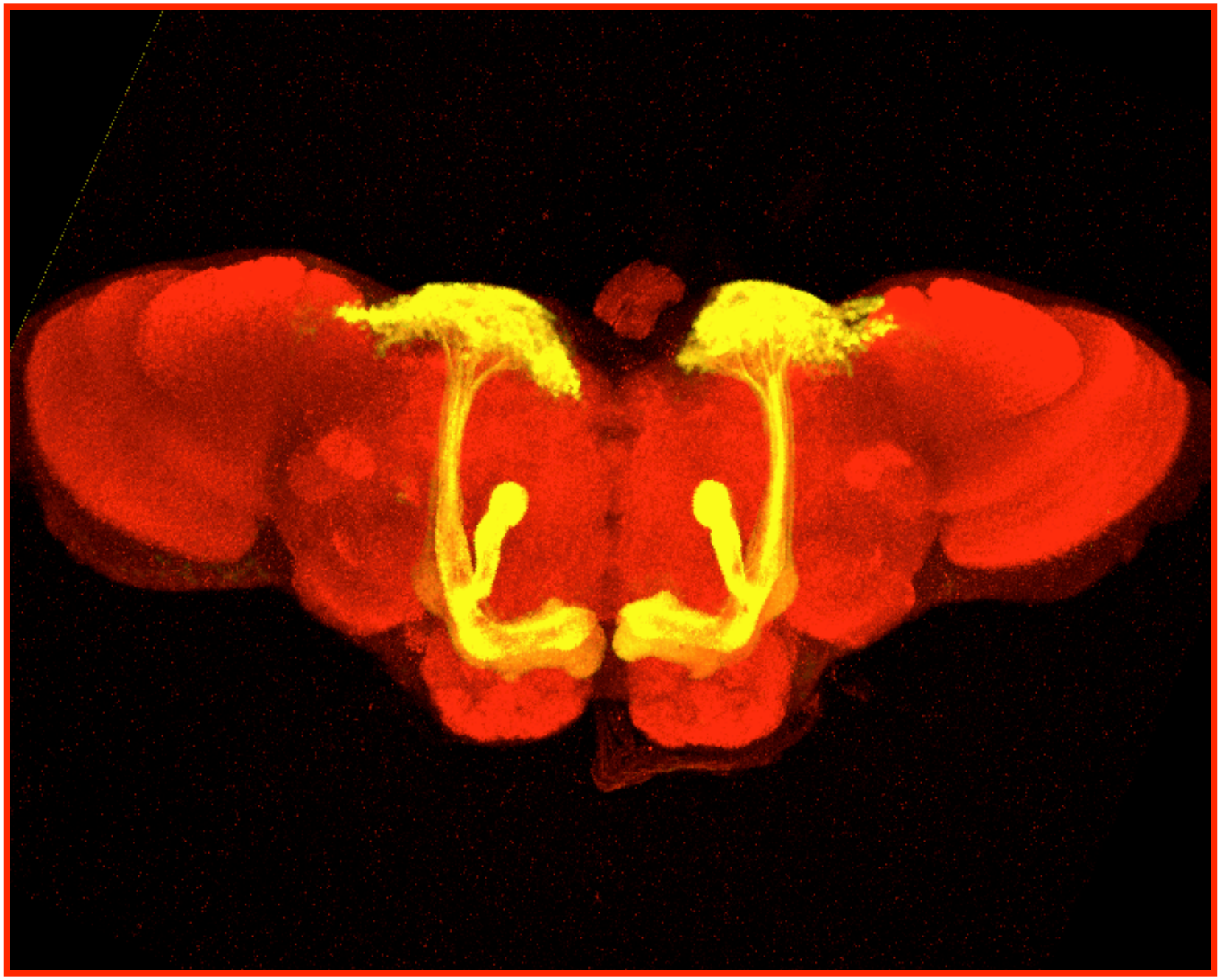
Gal4 driver line

UAS line

Brand and Perrimon, 1993

expression pattern of some Gal4-driver lines



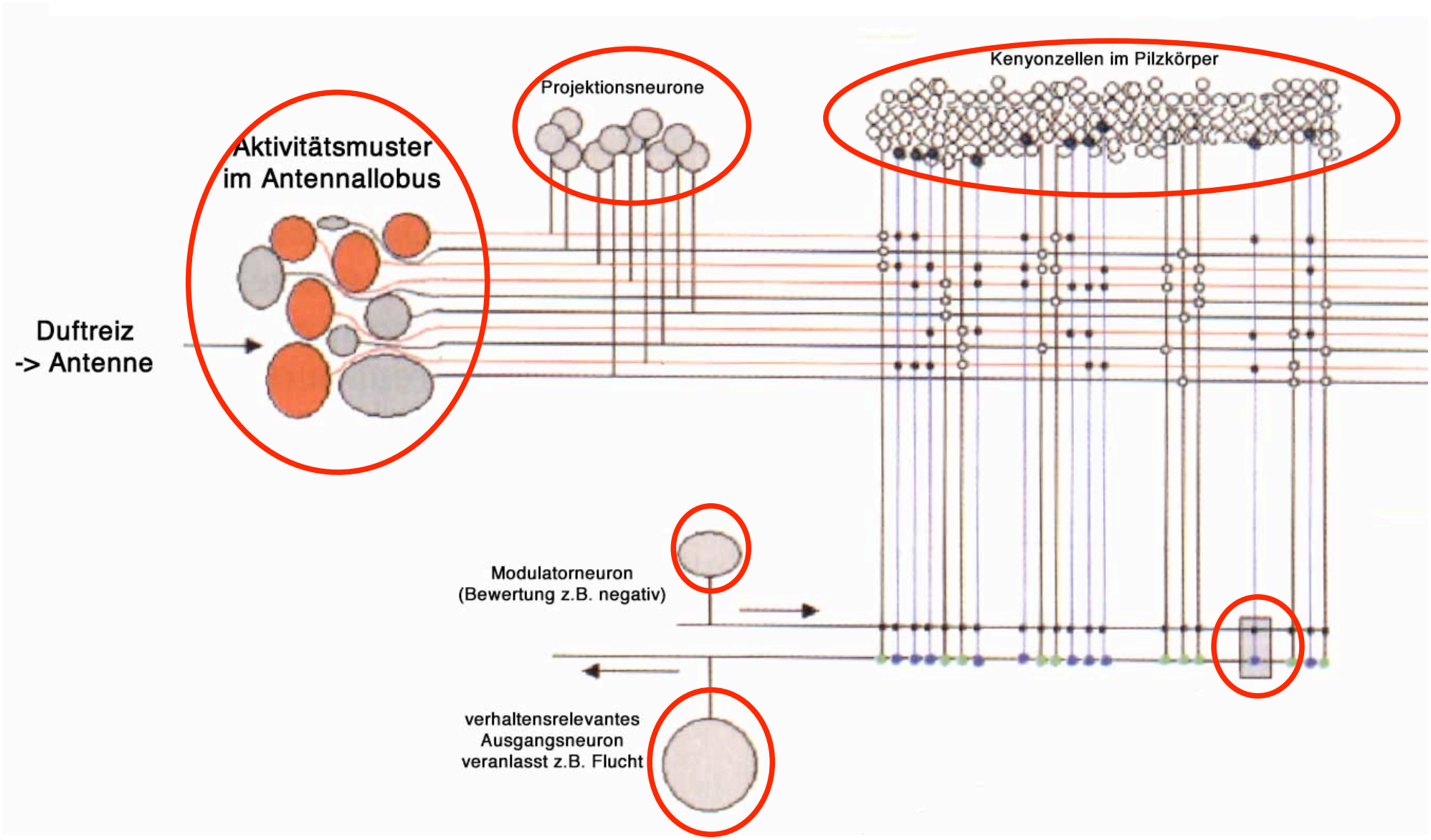


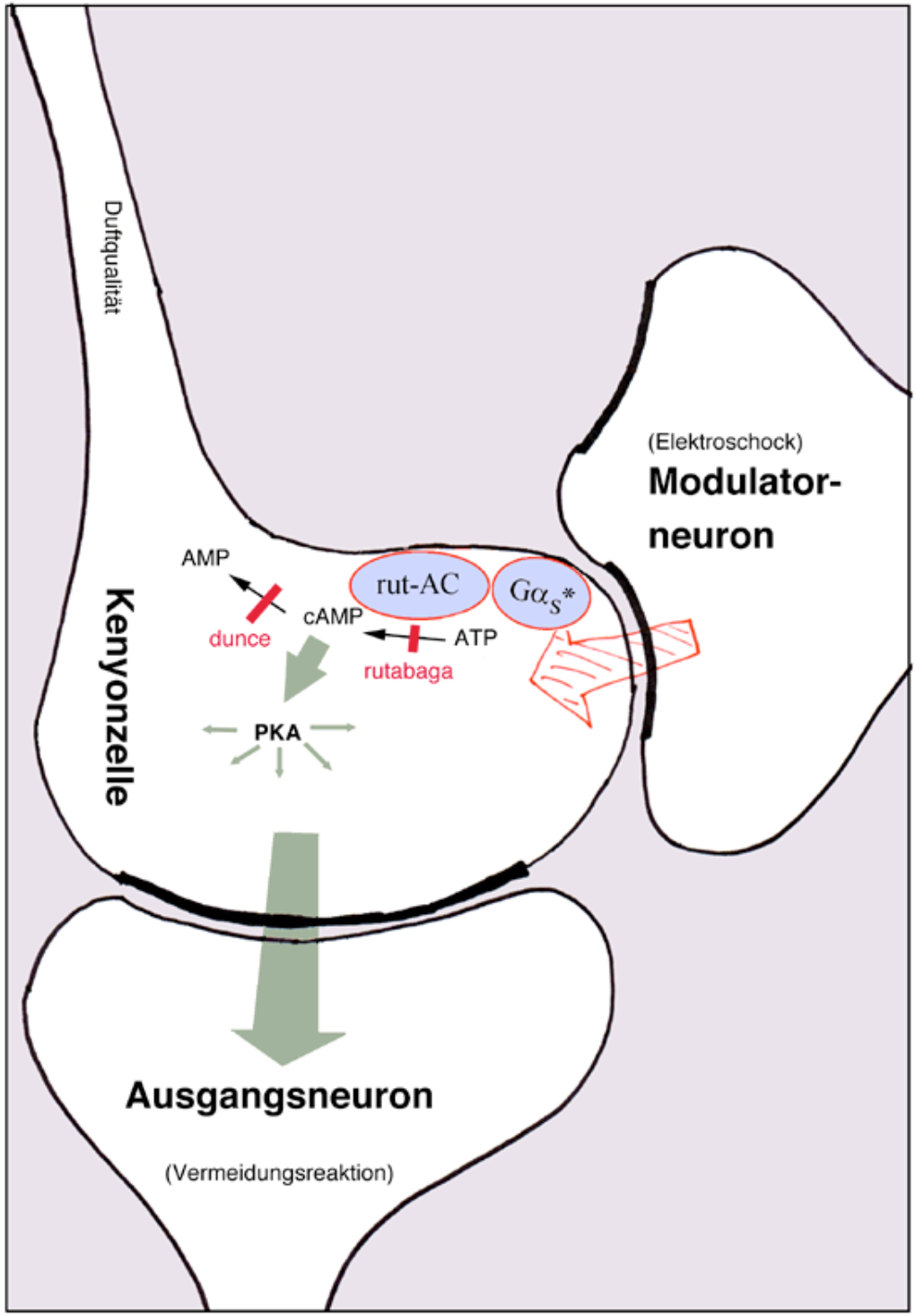
With the Gal4/ UAS-system a calmodulin-dependent adenylatcyclase can be reintroduced into a rutabaga-mutant.

In which cell types is rutabaga required for learning to occur?

In mushroom bodies!

Mushroom bodies as learning matrix

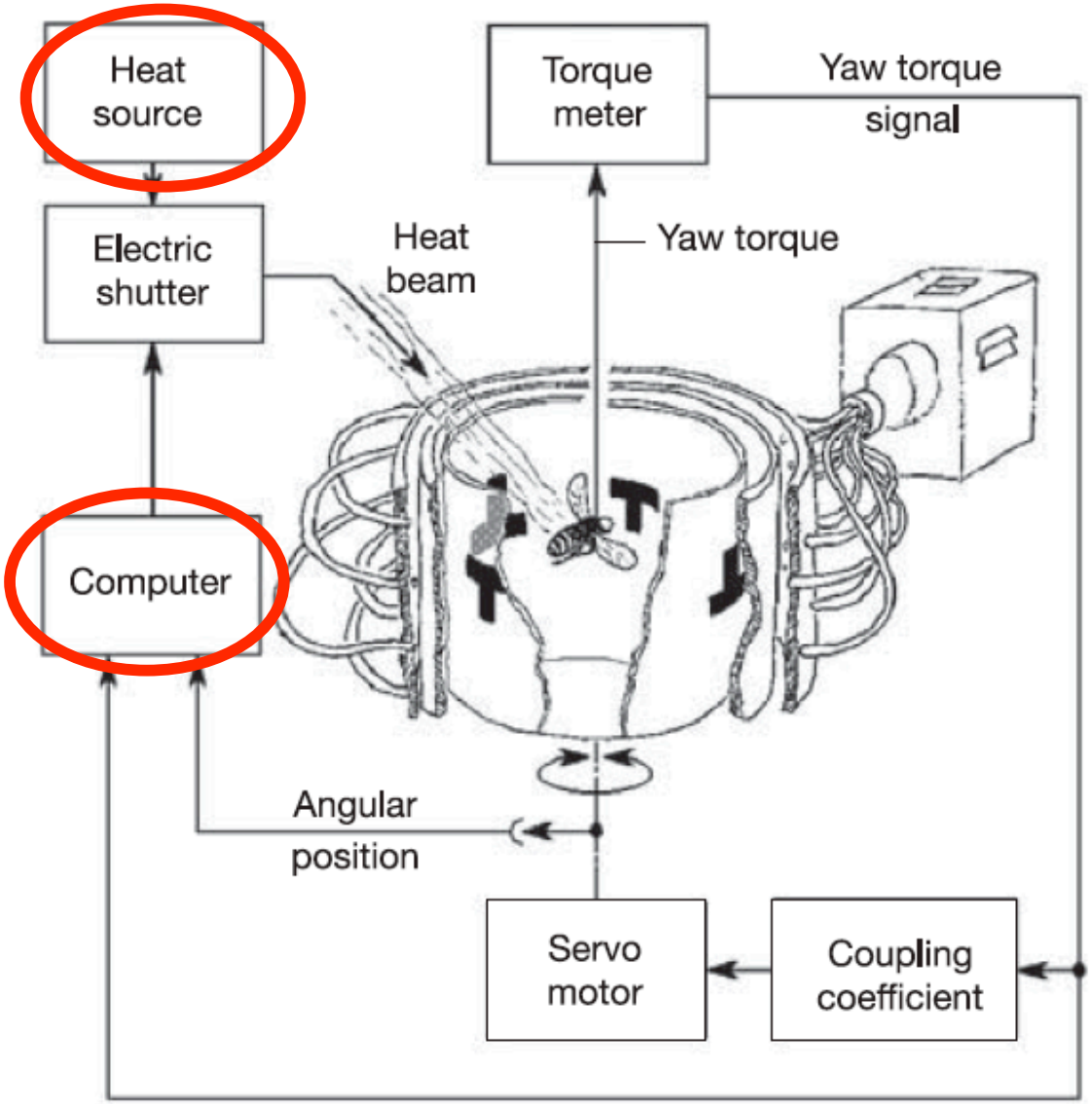




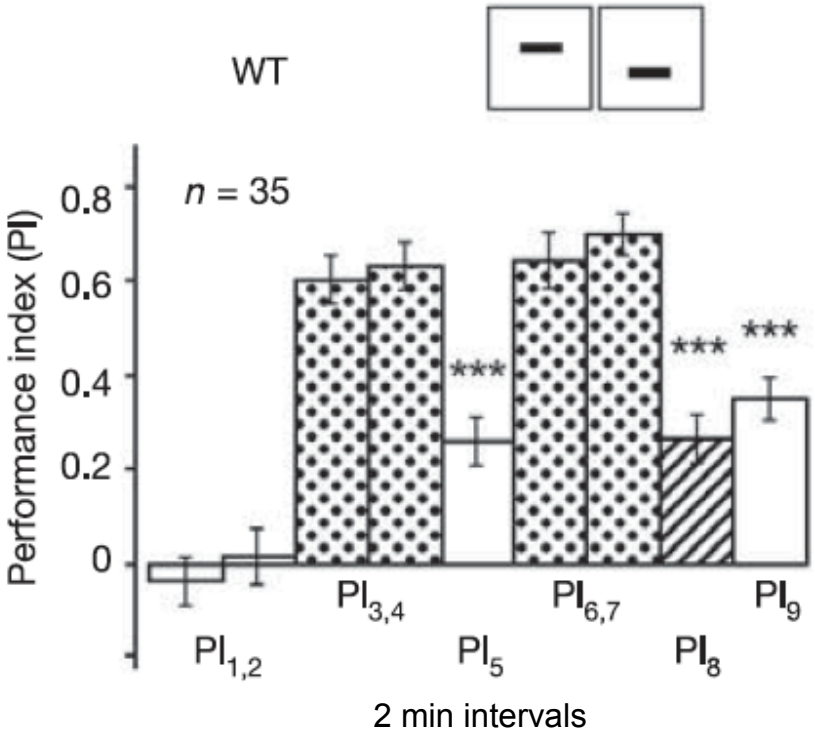
learning at the level of the synapses

associative
visual learning

learning paradigma at the torque compensator (closed loop)



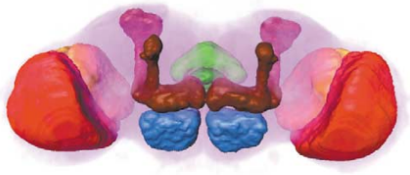
experimental procedure

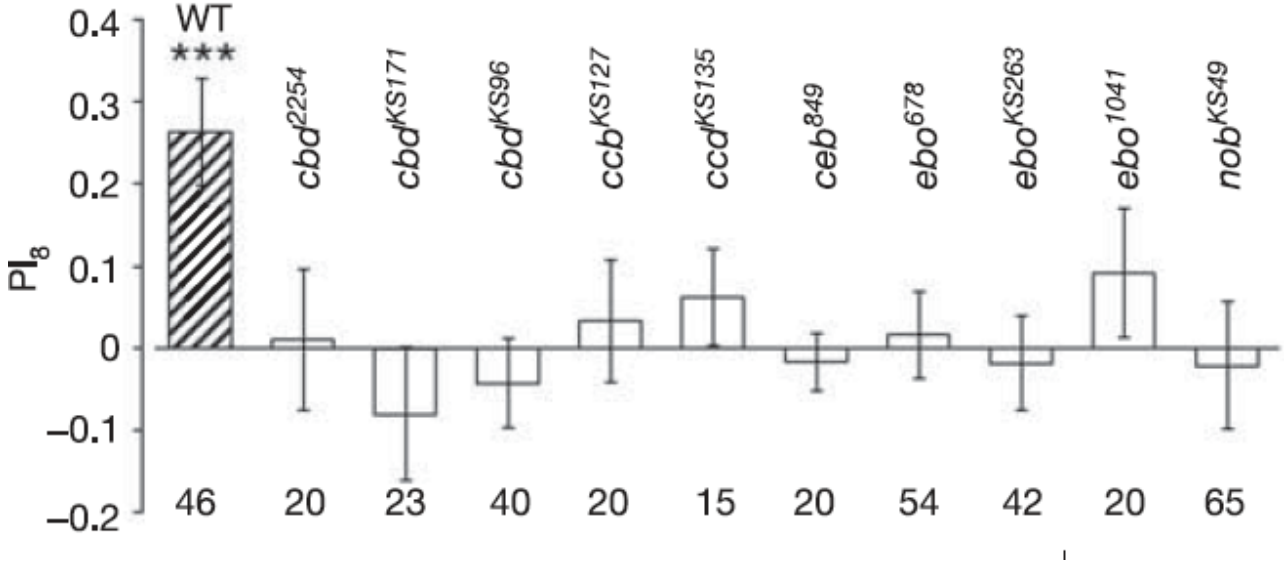


Definition PI: $(t_A - t_B)/(t_A + t_B)$

A = unpunished pattern
B = pattern correlated with punishment
t = duration of flight towards pattern

mutants of the central complex with visual memory defects





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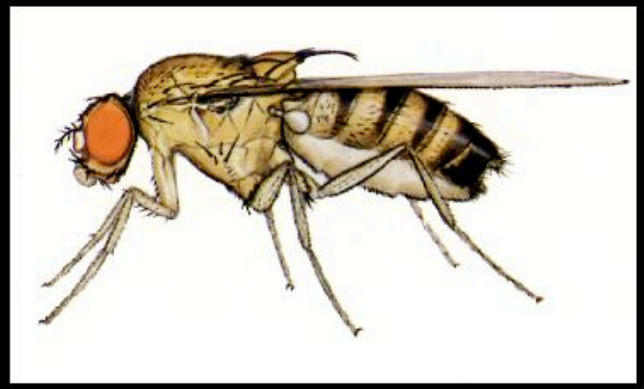
Technique used: The basic Gal4/UAS tool box



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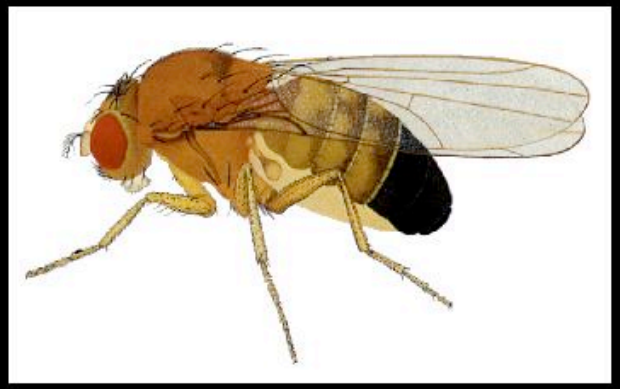
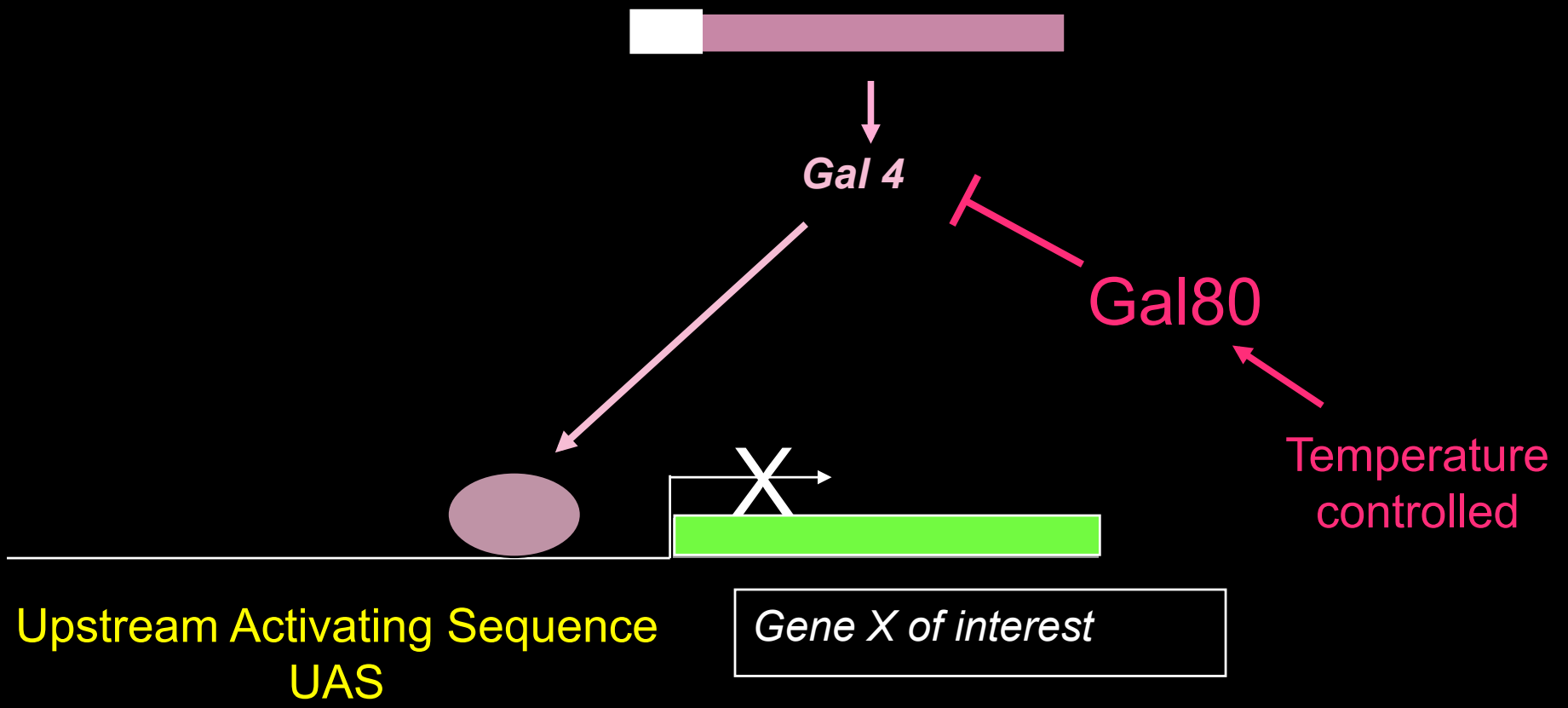


Gal4 driver line

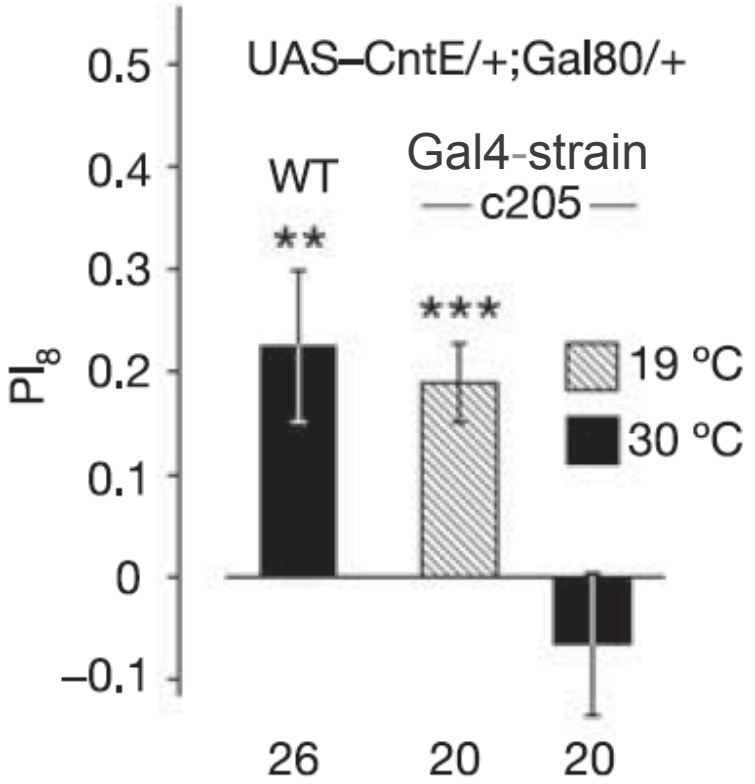
UAS line

Brand and Perrimon, 1993

Adding a temporal control of cell type specific expression

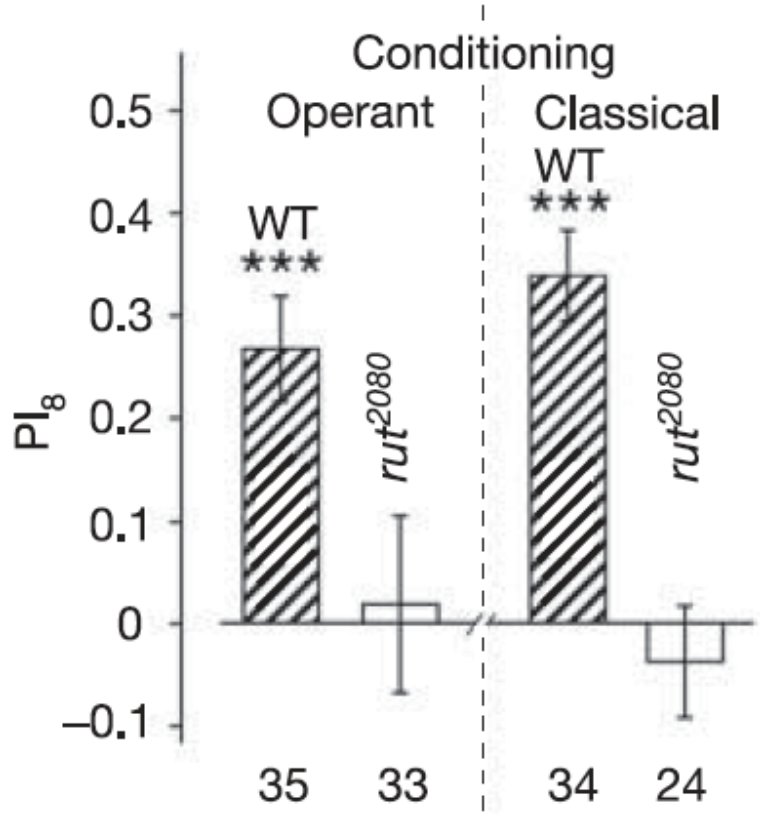


The light chain of **tetanus toxin** blocks the synaptic vesicle in neurons.
Its Gal4 driven expression eliminates visual memory only in central complex neurons

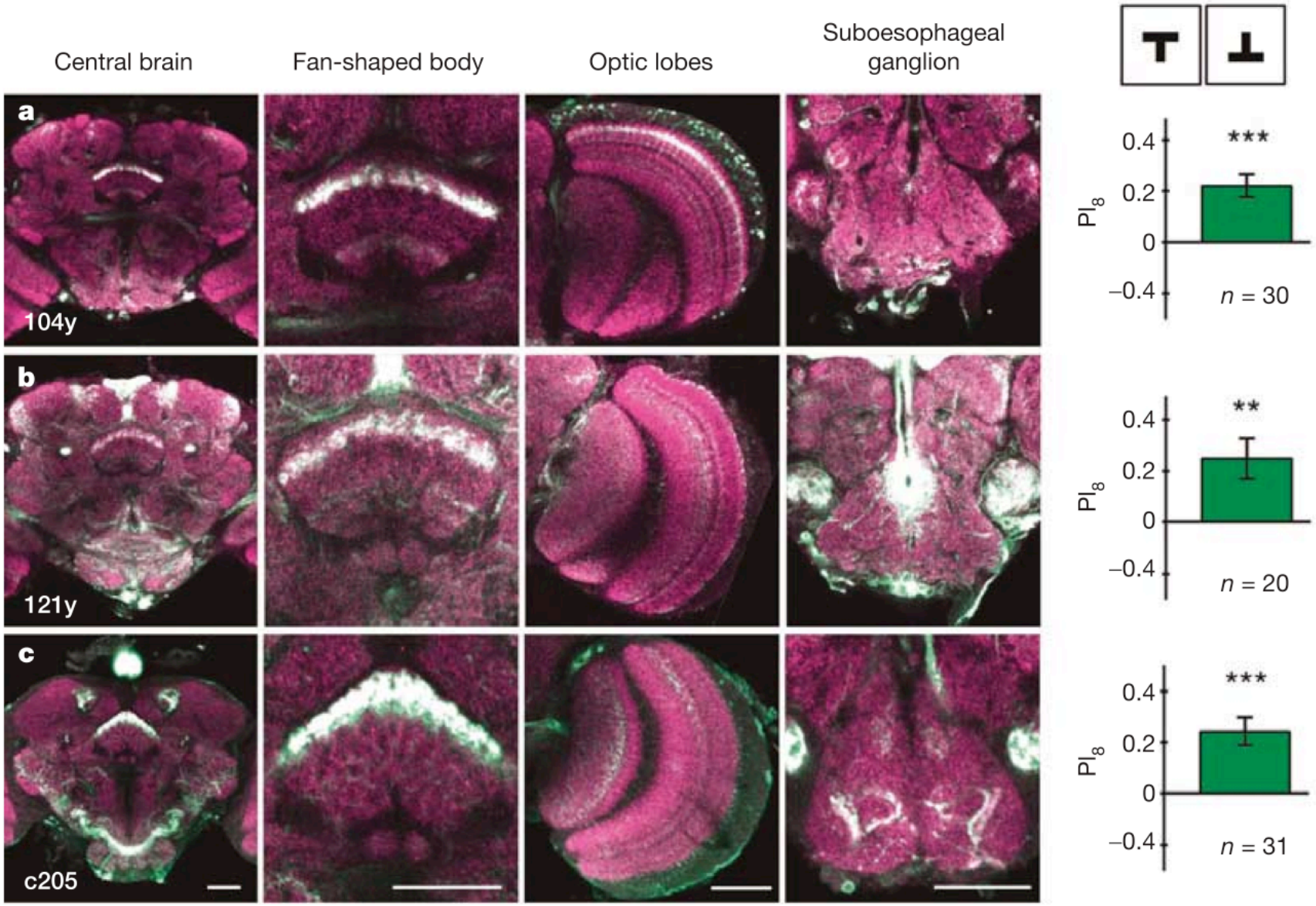


temperatursensitive Gal80 was used to inhibit Gal4 function

A mutation in the *rutabaga* adenylatcyclase-gene inhibits visual memory

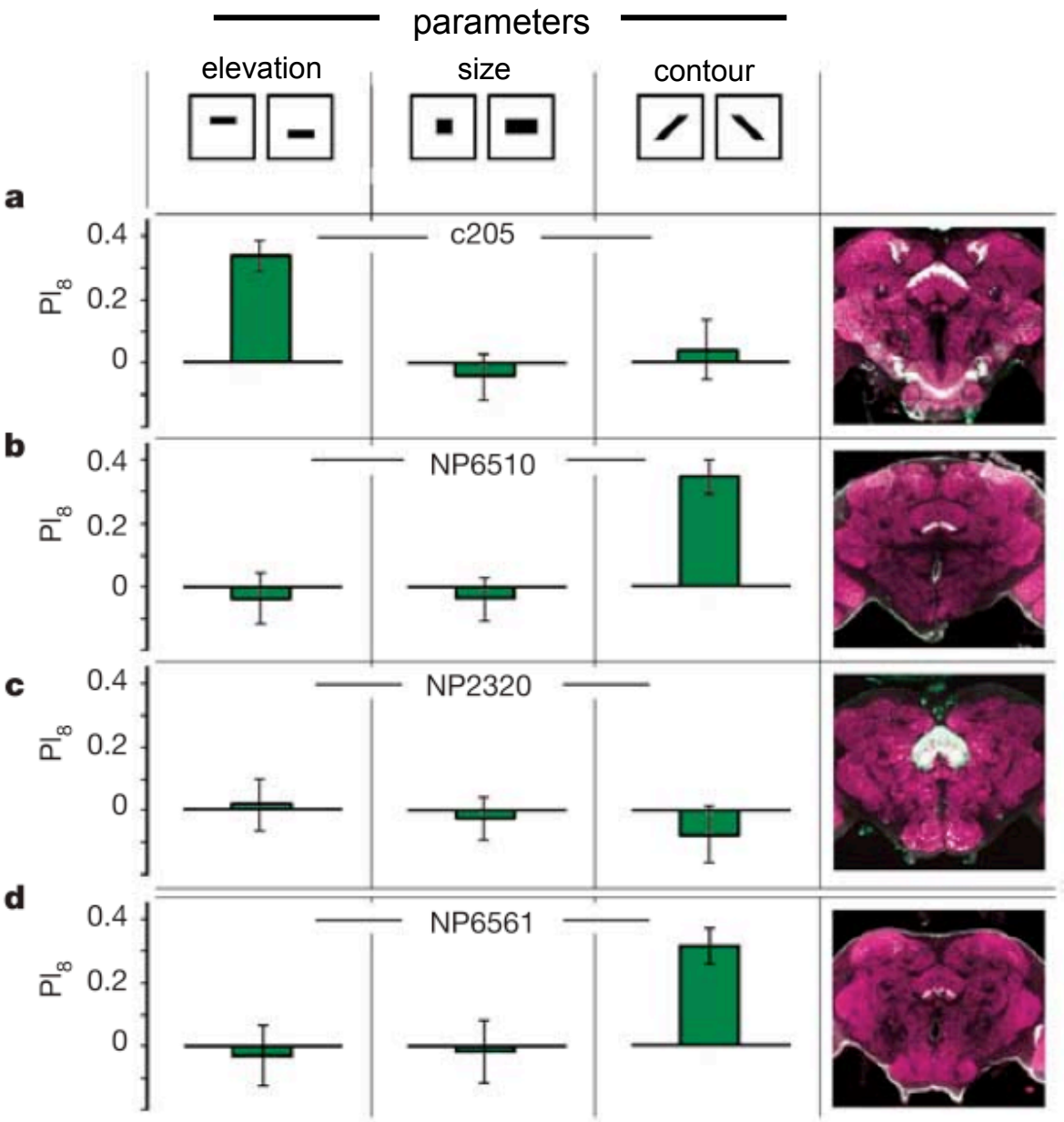


In which neurons visual learning in *rutabaga*-mutants can be restored by a *rut*$^{+}$-transgen? --> rescue-experiment



Memory traces for visual pattern parameters are spatially separated

Pattern specific rescue of learning by expression of *rut*$^{+}$ in tangential neurons of the fan shaped body of the central complex



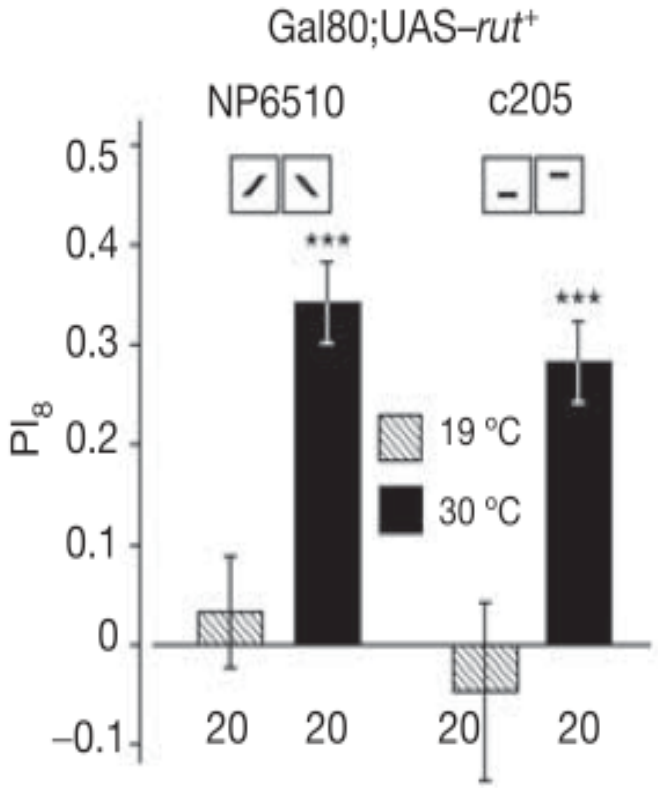
tangential neurons
in the **dorsal**
fan-shaped body

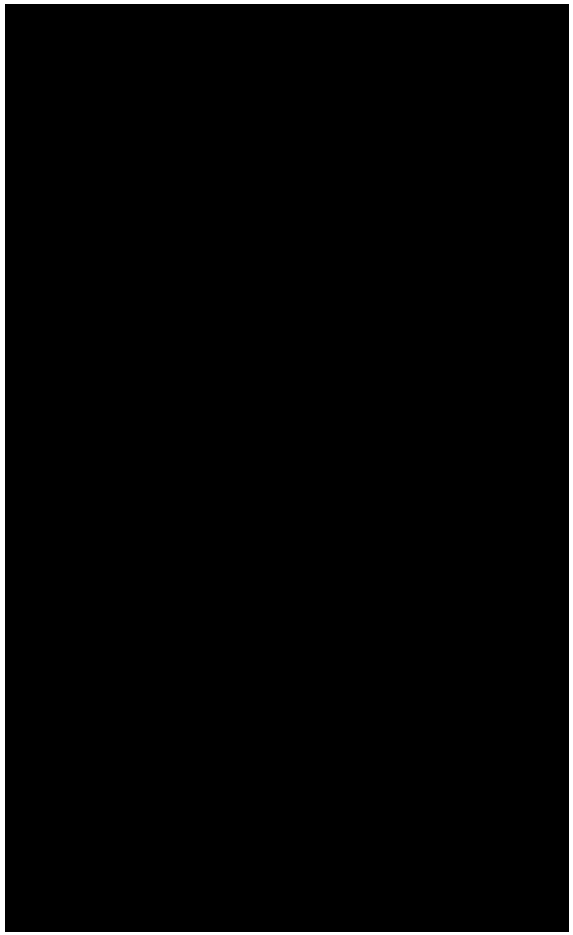
tangential neurons
in the **ventral**
fan-shaped body

only (!) columnar neurons
spanning the
fan-shaped body

tangential neurons
in the **ventral**
fan-shaped body

What is rescued? Performance in the adult or a developmental defect?





Again the heat shock controlled Gal4-inhibitor Gal80 was used

Take home message:

there is no central memory storage unit in the brain.
Different modalities use different neurons.

- Rutabaga, a calmodulin- and G-protein dependent adenylatcyclase, links at a molecular level US and CS by producing cAMP
- This adenylatcyclase is sufficient in Kenyon cells of the mushroom body for memory formation in olfaction
- In visual learning rutabaga is sufficient in horizontal neurons of the fan-shaped body (part of the central complex)
- Such memory traces are located in different neuronal cell types of the fan shaped body for different visual parameters learned


thank you!!