
小さな脳を俯瞰する
Tetsuya Tabata
University of Tokyo
＊山本雅敏氏提供

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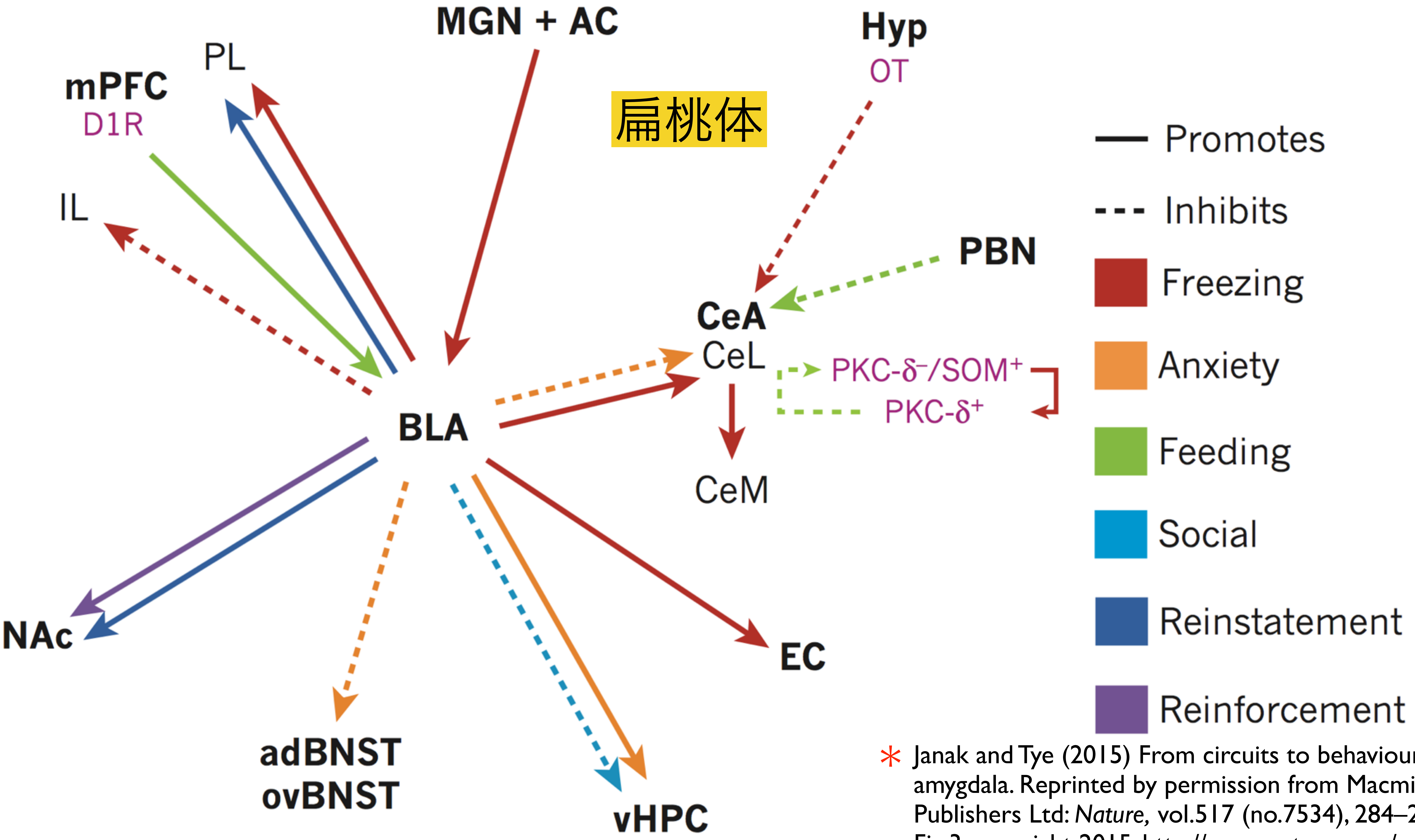
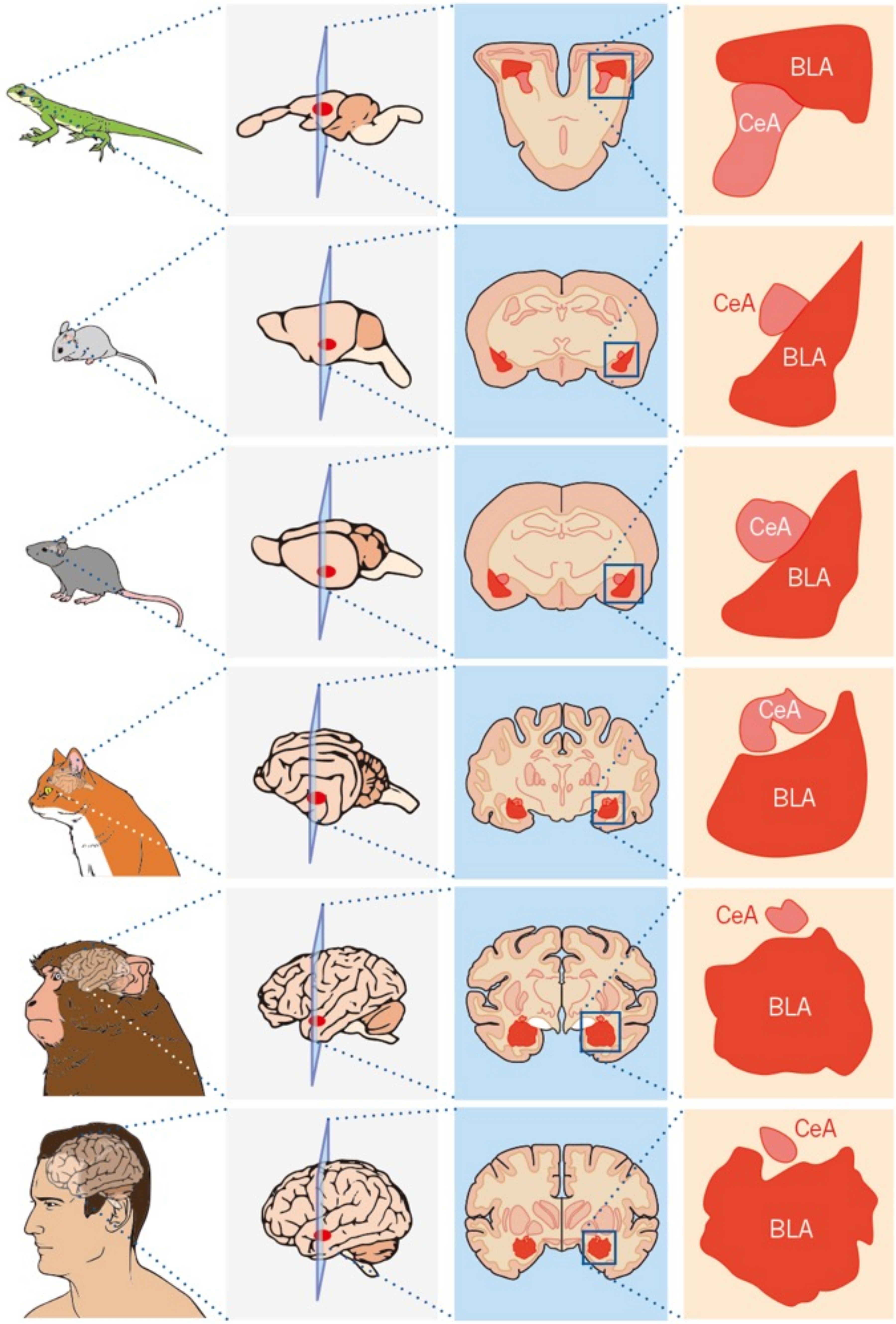
映画『インサイド・ヘッド』
（ディズニー／ピクサー、2015年）
日本版ポスター
http://www.allcinema.net/prog/image_large.php?i=351369



* Janak and Tye (2015) From circuits to behaviour in the amygdala. Reprinted by permission from Macmillan Publishers Ltd: *Nature*, vol.517 (no.7534), 284–292, p.287 Fig.3, copyright 2015. http://www.nature.com/nature/



扁桃体

it is clear that he no longer clearly understands the meaning of the sounds, sights, and other impressions that reach him. In addition, Brown and Schäfer, and later Klüver and Bucy, reported reduced aggression, fear and defensive behaviours.

An Investigation into the Functions of the Occipital and Temporal Lobes of the Monkey's Brain

By Sanger Brown and E. A. Schafer

Philosophical Transactions of the Royal Society of London B, vol.179, 1888, pp. 303–327
http://rstb.royalsocietypublishing.org/content/179/303

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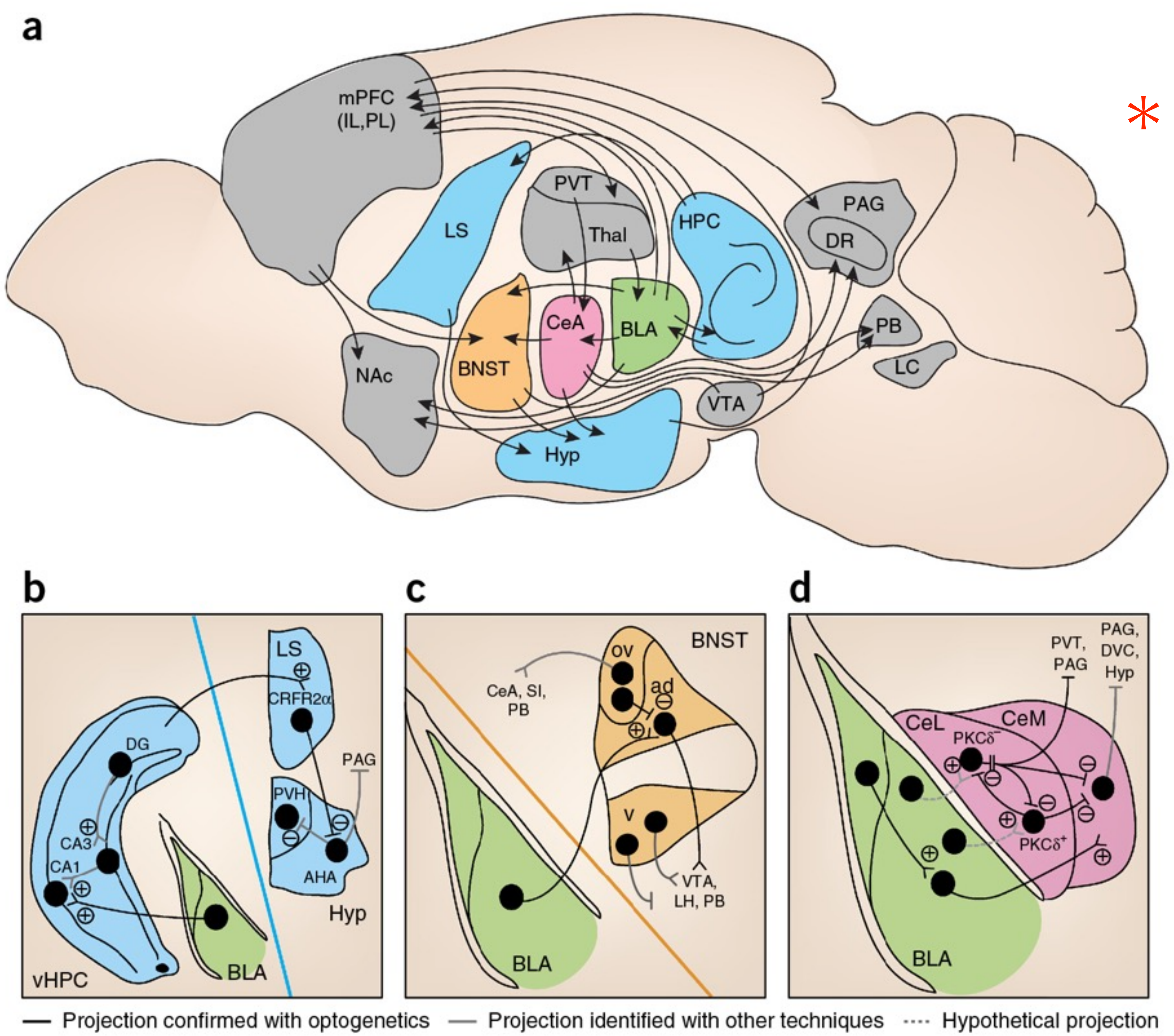
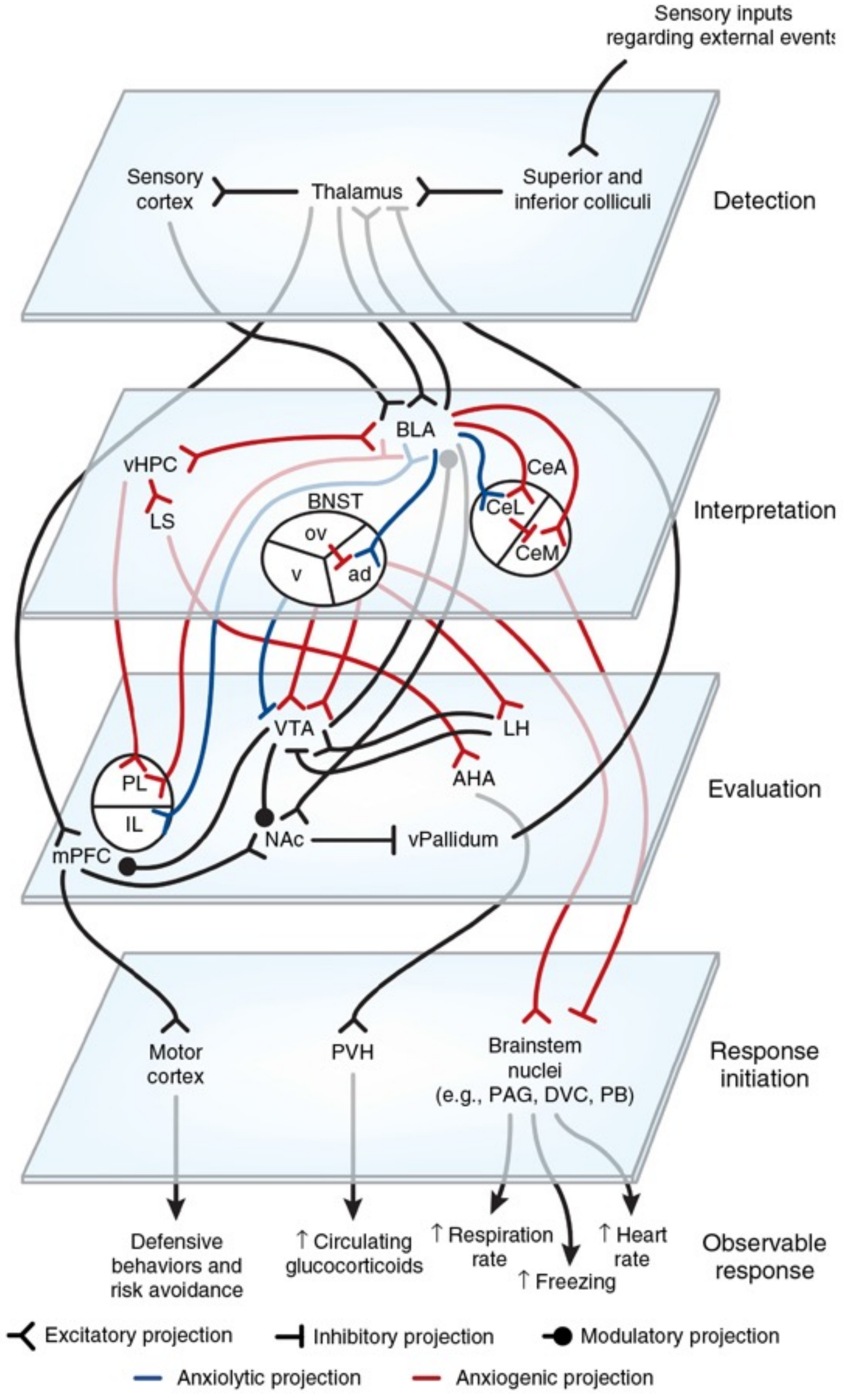
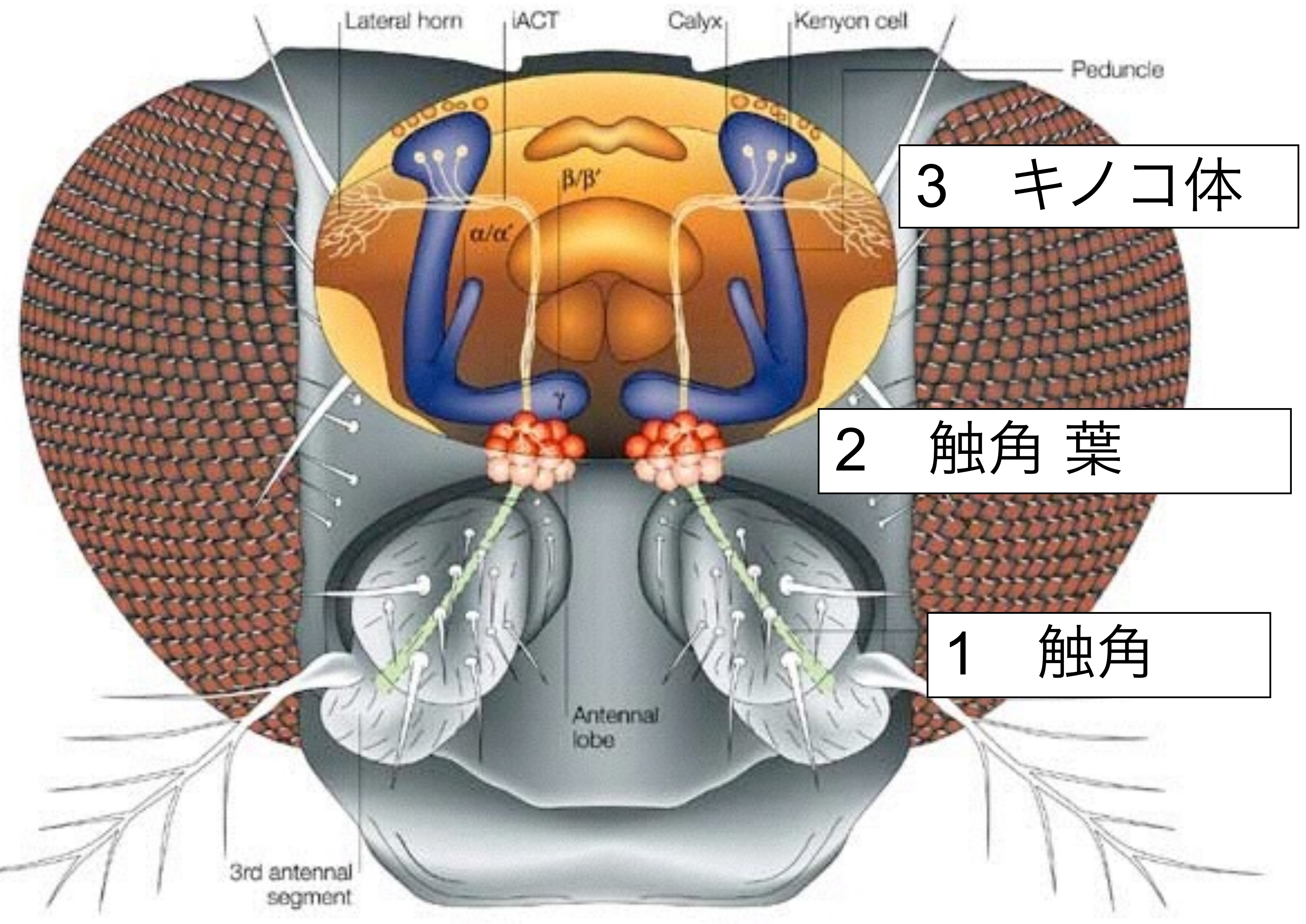


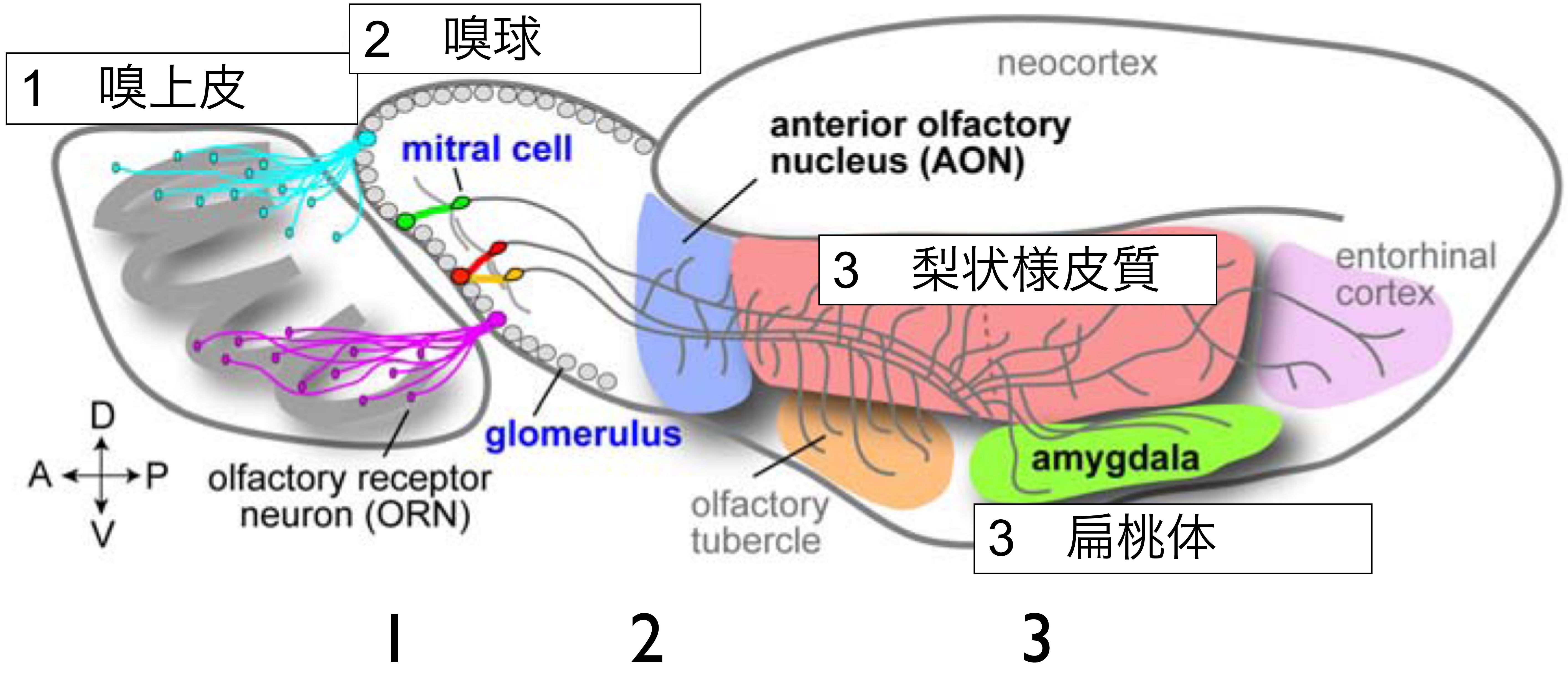


Calhoon and Tye (2015) Resolving the neural circuits of anxiety. Reprinted by permission from Macmillan Publishers Ltd: *Nature Neuroscience*, vol.18 (no.10): 1394-1404, [left] p.1398 Fig.3 and [right] p.1401 Fig.4, copyright 2015. http://www.nature.com/neuro/

Circuit-based intervention: the future of anxiety therapy

嗅覚神経系の構造はショウジョウバエと脊椎動物間で良く保存されている





＊ Martin Heisenberg (2003) Mushroom body memoir: from maps to models. Reprinted by permission from Macmillan Publishers Ltd: *Nature Reviews Neuroscience*, vol.4 (no.4): 266-275, p.267 Fig. 2, copyright 2003. http://www.nature.com/nrn/

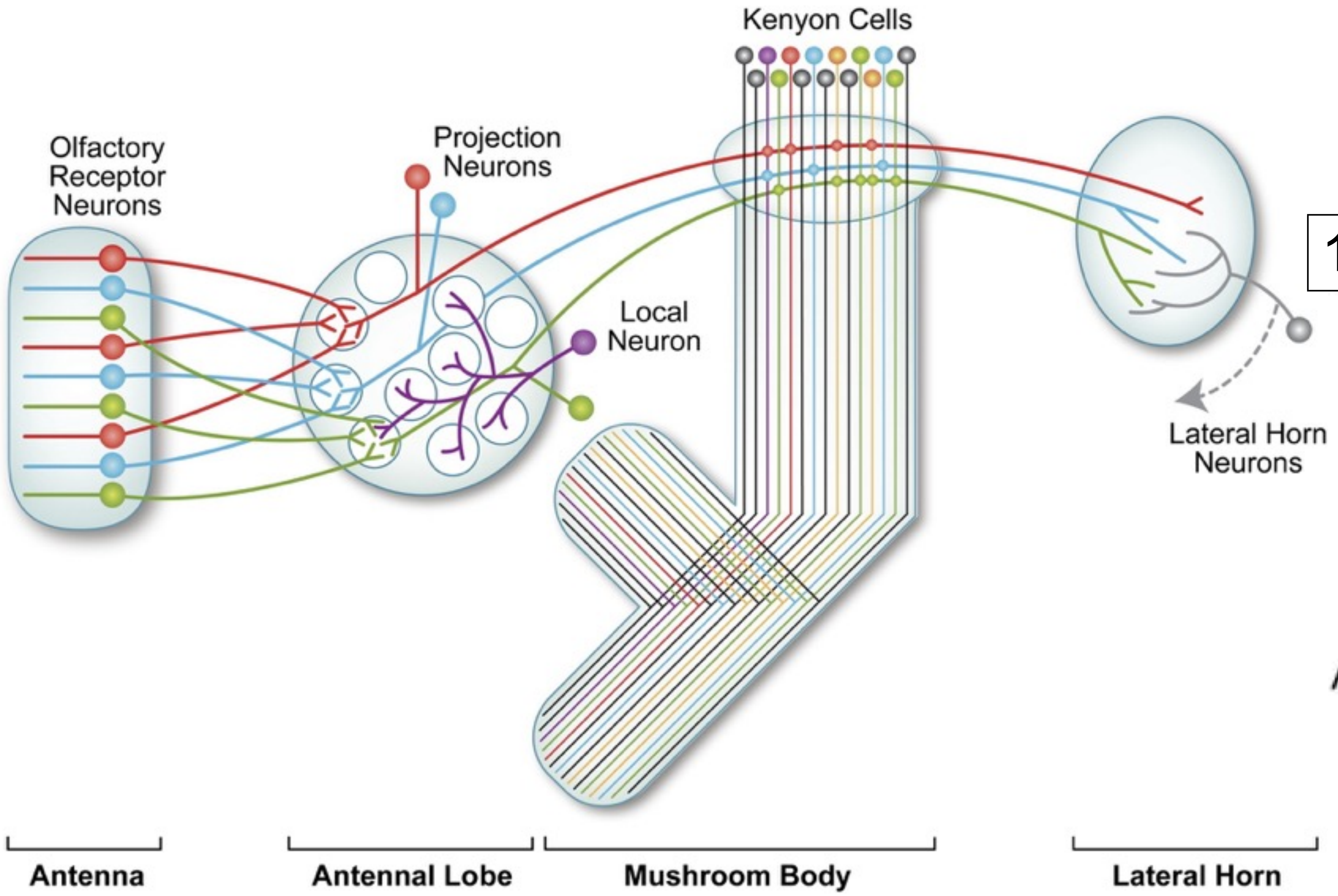
＊ Miyamichi et al. (2011) Cortical representations of olfactory input by transsynaptic tracing. Reprinted by permission from Macmillan Publishers Ltd: *Nature*, vol.472 (no.7342): 191-196, Supplementary Fig.1a, copyright 2011. http://www.nature.com/nature/

ショウジョウバエ　　マウス

mouse brain by courtesy of Yuki Imaizumi and Yukio Goto

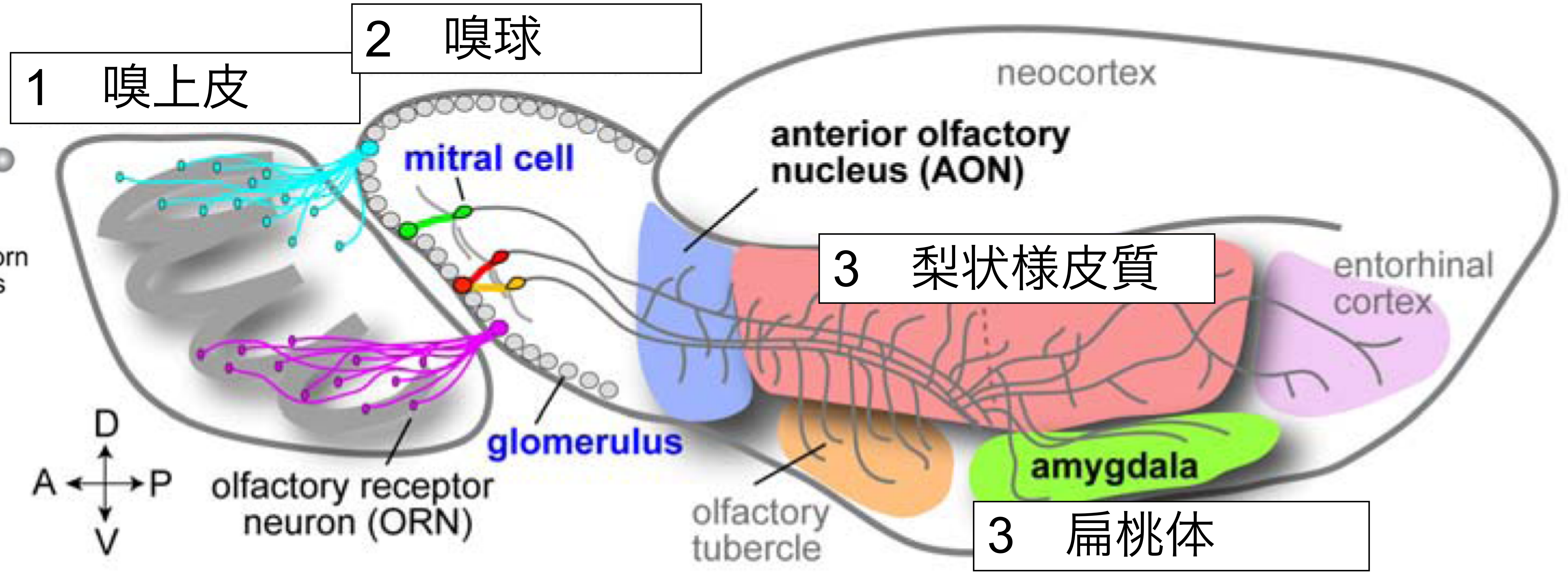
嗅覚神経系の構造はショウジョウバエと脊椎動物間で良く保存されている

1400　　150　　2000



1　　2　　3

ショウジョウバエ

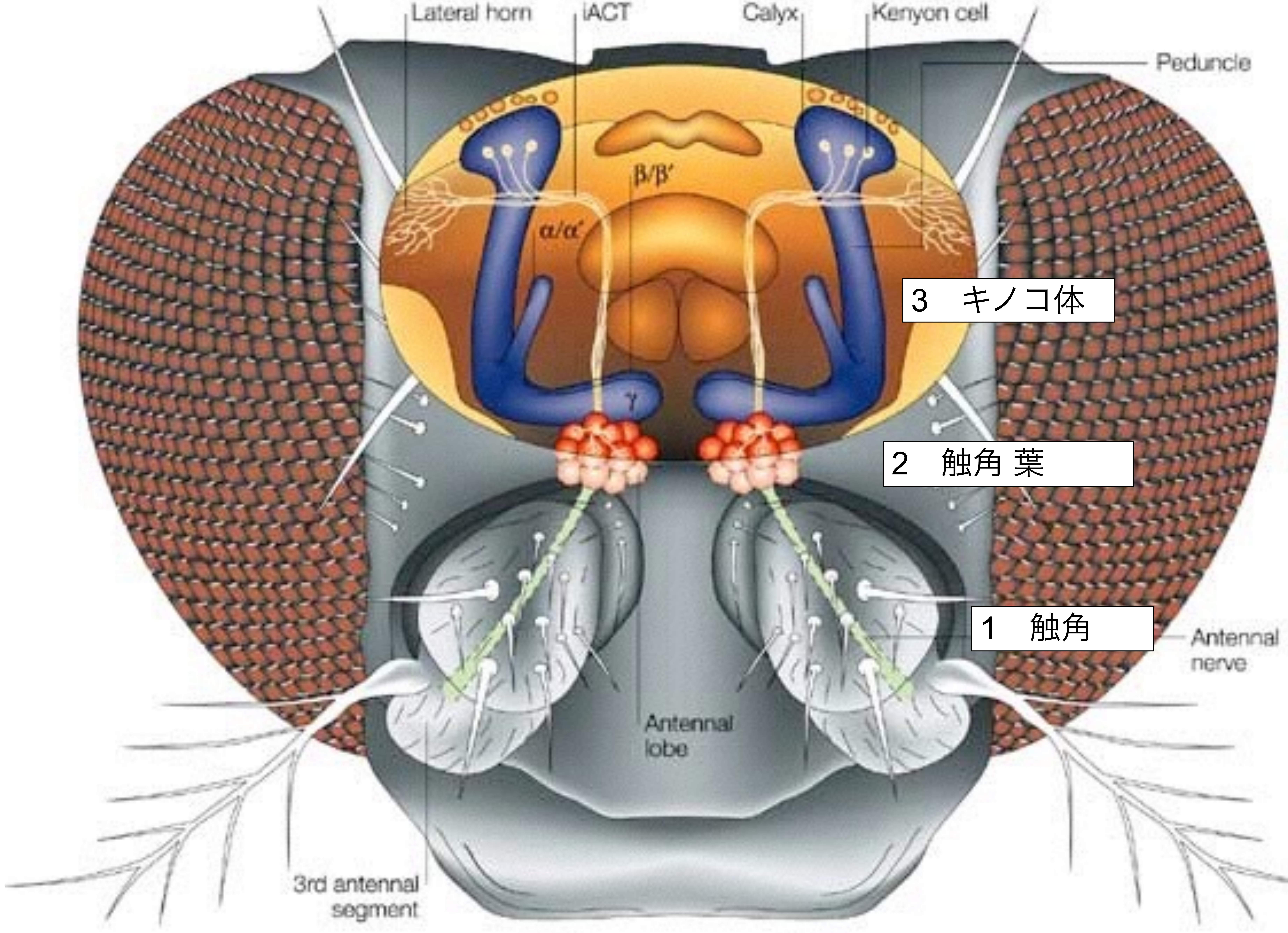


1　　2　　3

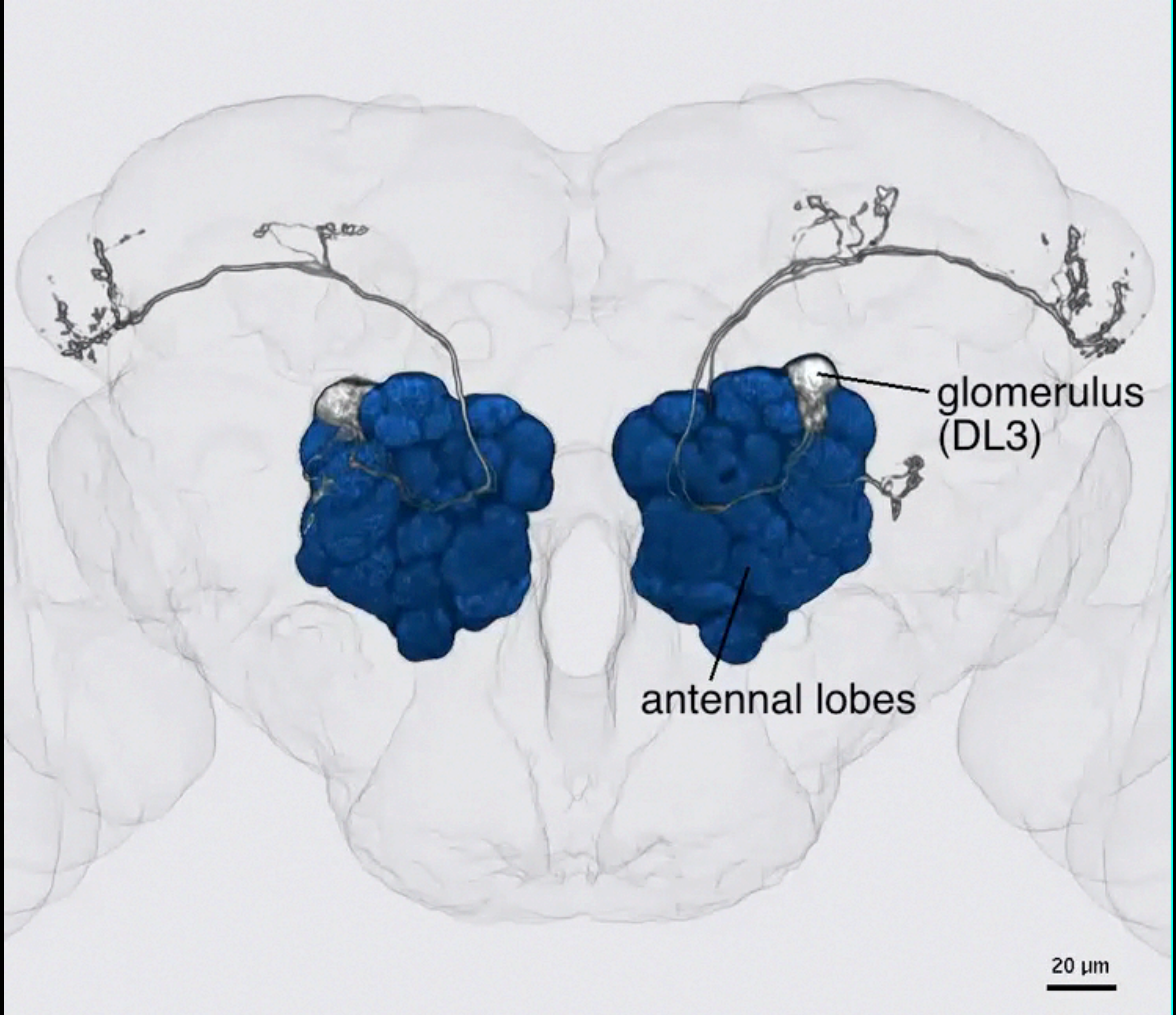
マウス

＊ Cachero and Jefferis (2008) *Drosophila* Olfaction: The End of Stereotypy?, *Neuron* 59(6):843–845, p.844 Fig. 1. http://dx.doi.org/10.1016/j.neuron.2008.07.04

＊ Miyamichi et al. (2011) Cortical representations of olfactory input by transsynaptic tracing. Reprinted by permission from Macmillan Publishers Ltd: *Nature*, vol.472 (no.7342): 191-196, Supplementary Fig.1a, copyright 2011. http://www.nature.com/nature/

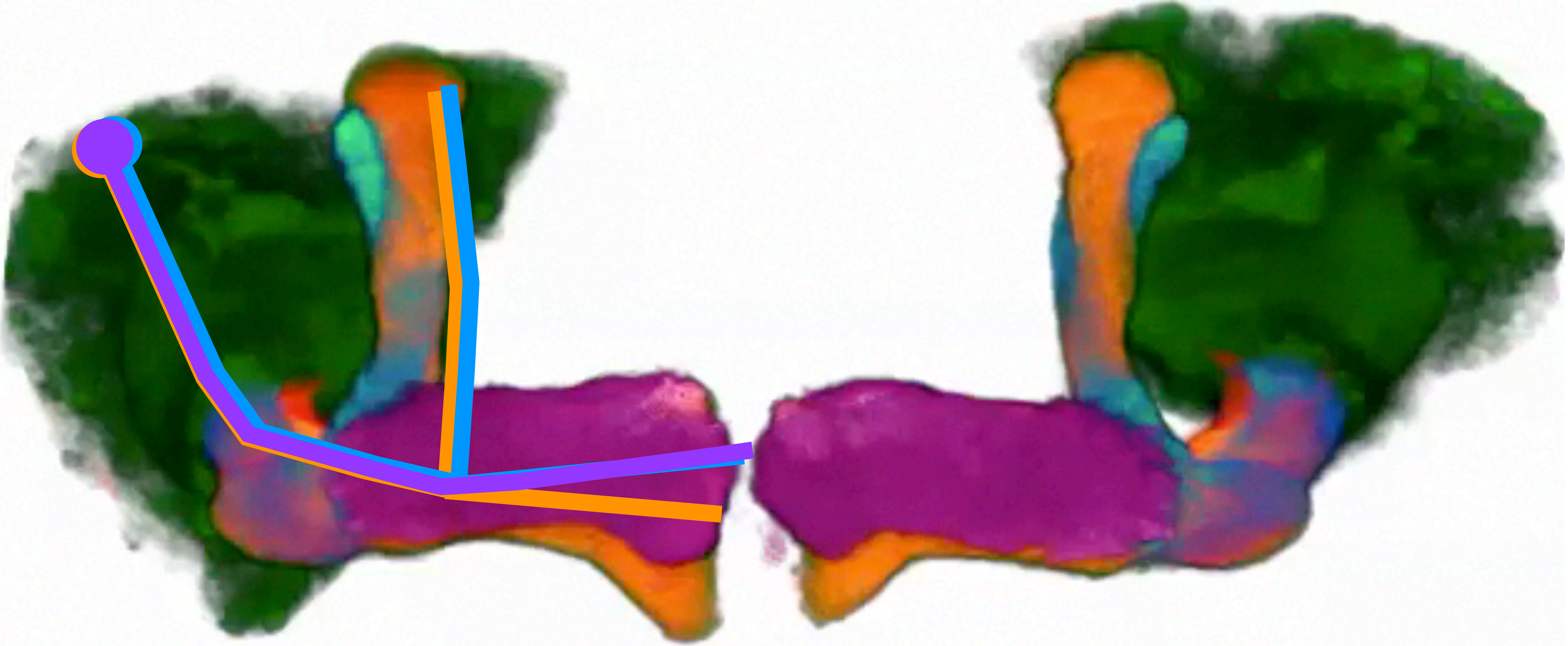


*
Martin Heisenberg (2003) Mushroom body memoir: from maps to models. Reprinted by permission from Macmillan Publishers Ltd: *Nature Reviews Neuroscience*, vol.4 (no. 4): 266-275, p.267 Fig.2, copyright 2003. http://www.nature.com/nrn/



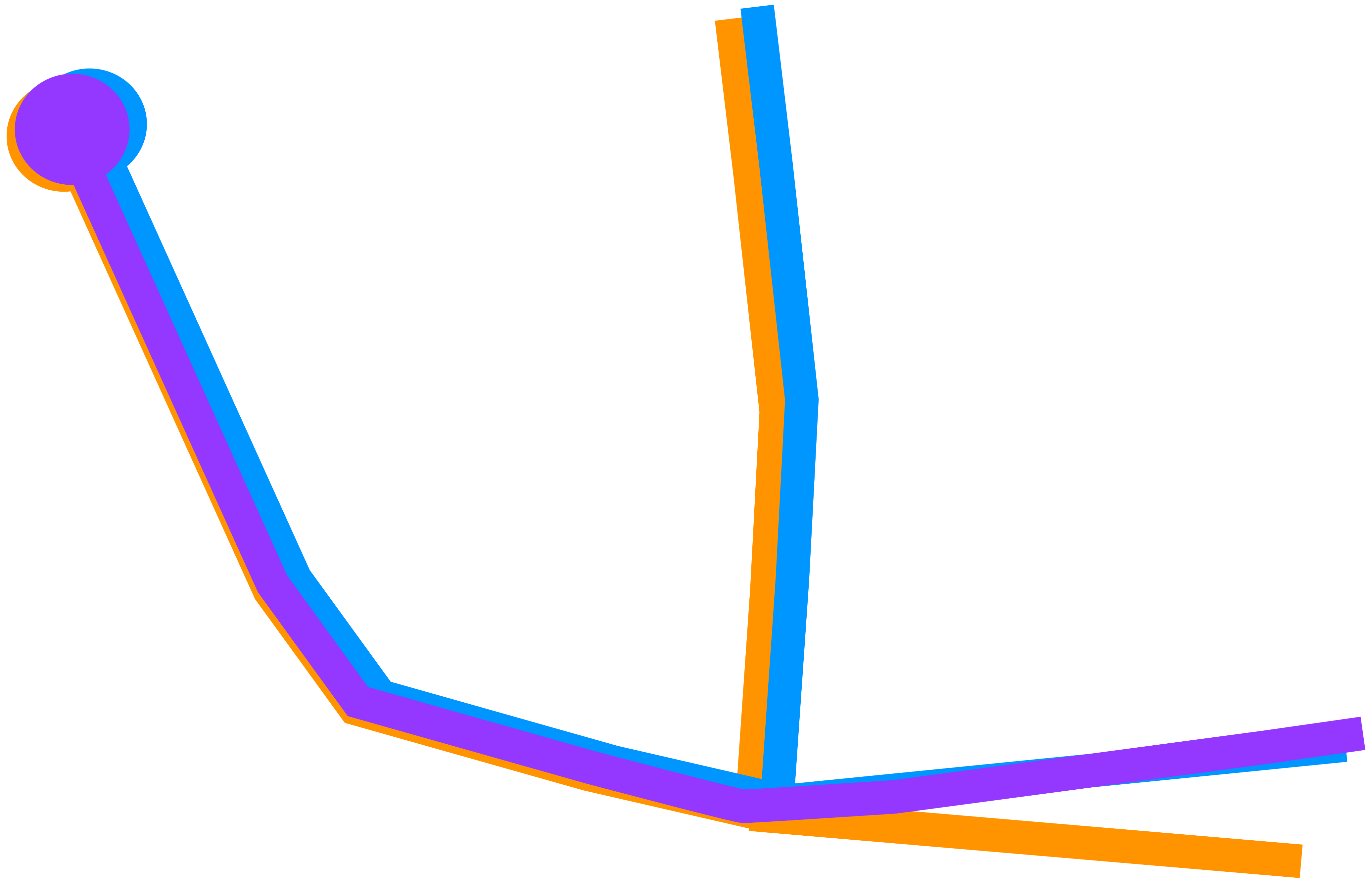
Olfactory sensory neurons expressing the same odorant receptor converge onto one of the 51 glomeruli of the antennal lobes, where they synapses on the projection neurons. Six projection neurons from the DL3 glomerulus are shown.

Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.4 Video 1 http://elifesciences.org/content/3/e04577



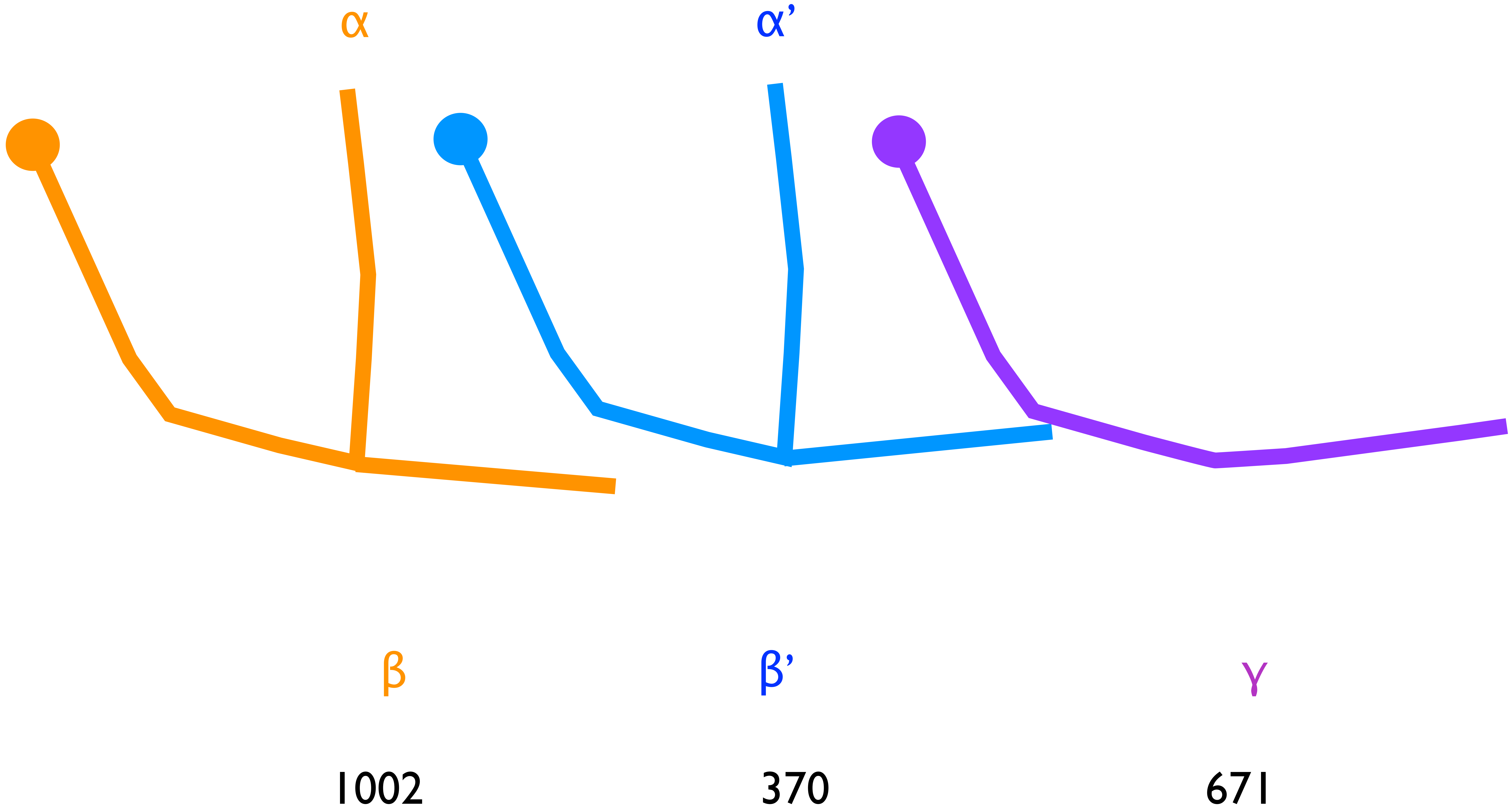
The Kenyon cells, the 2,000 intrinsic neurons of the mushroom body encode the olfactory code and their output synapses are responsible for plasticity underlying memory formation.

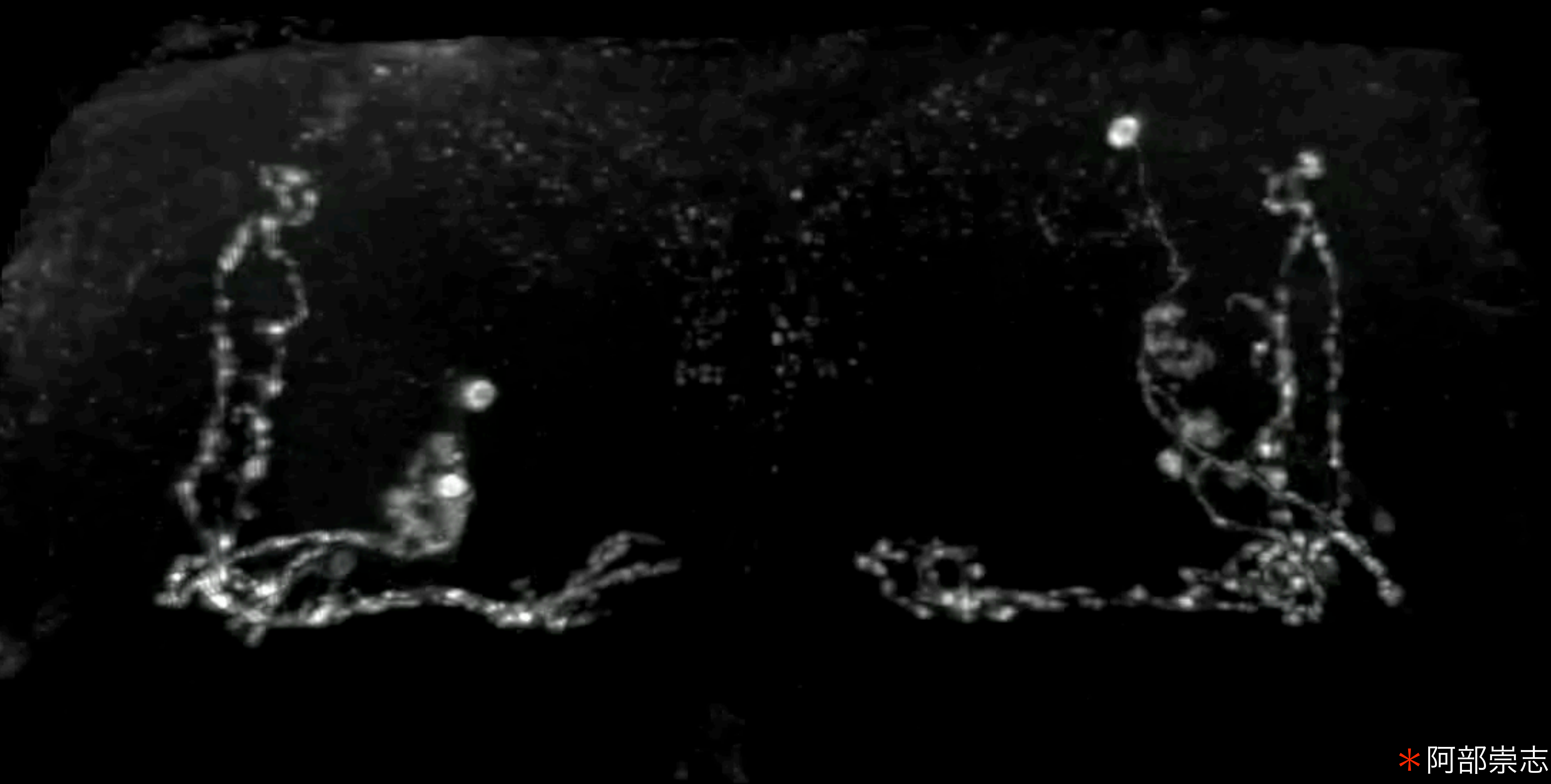
α α’



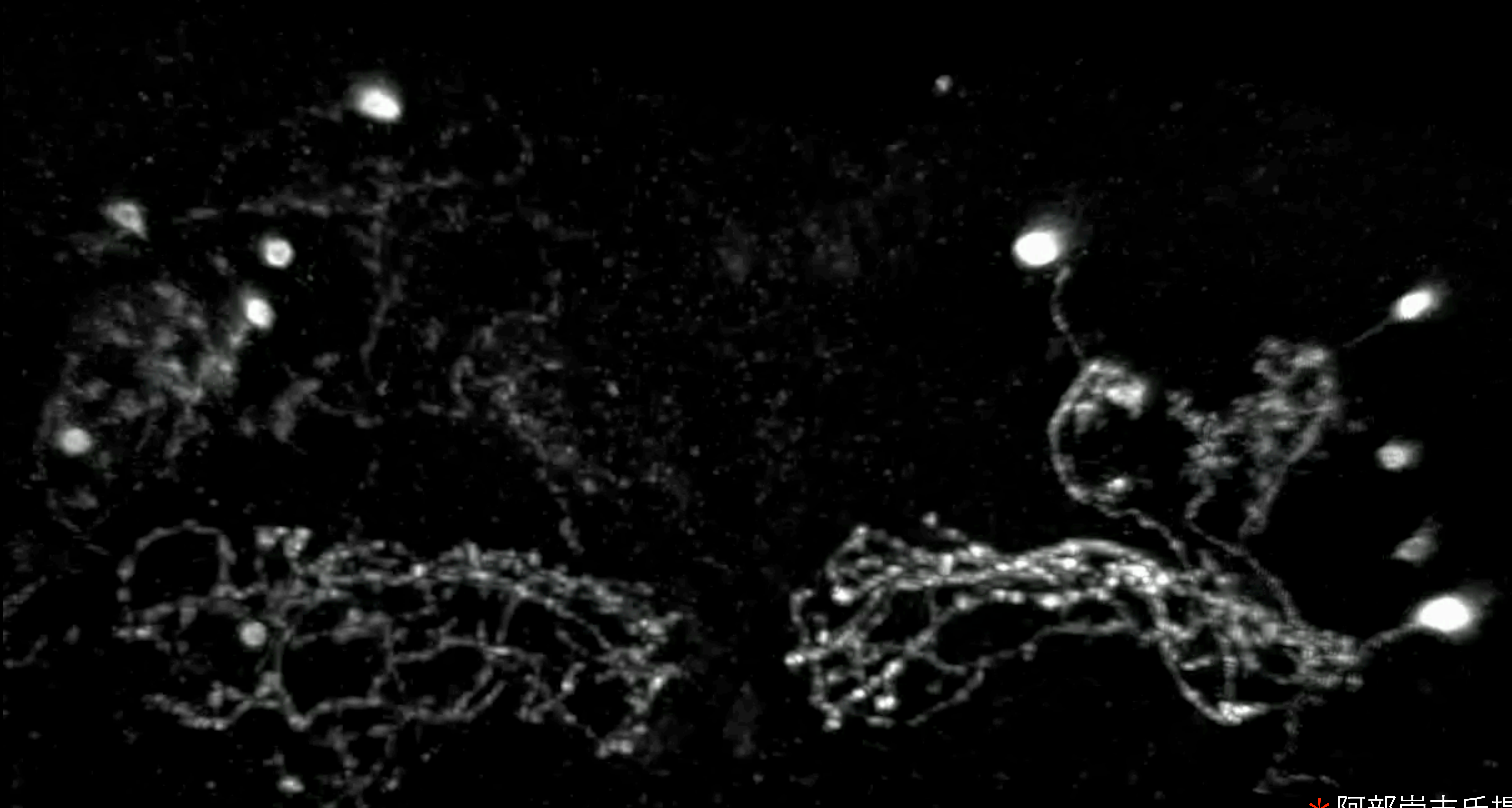
β β’ γ

1002 370 671

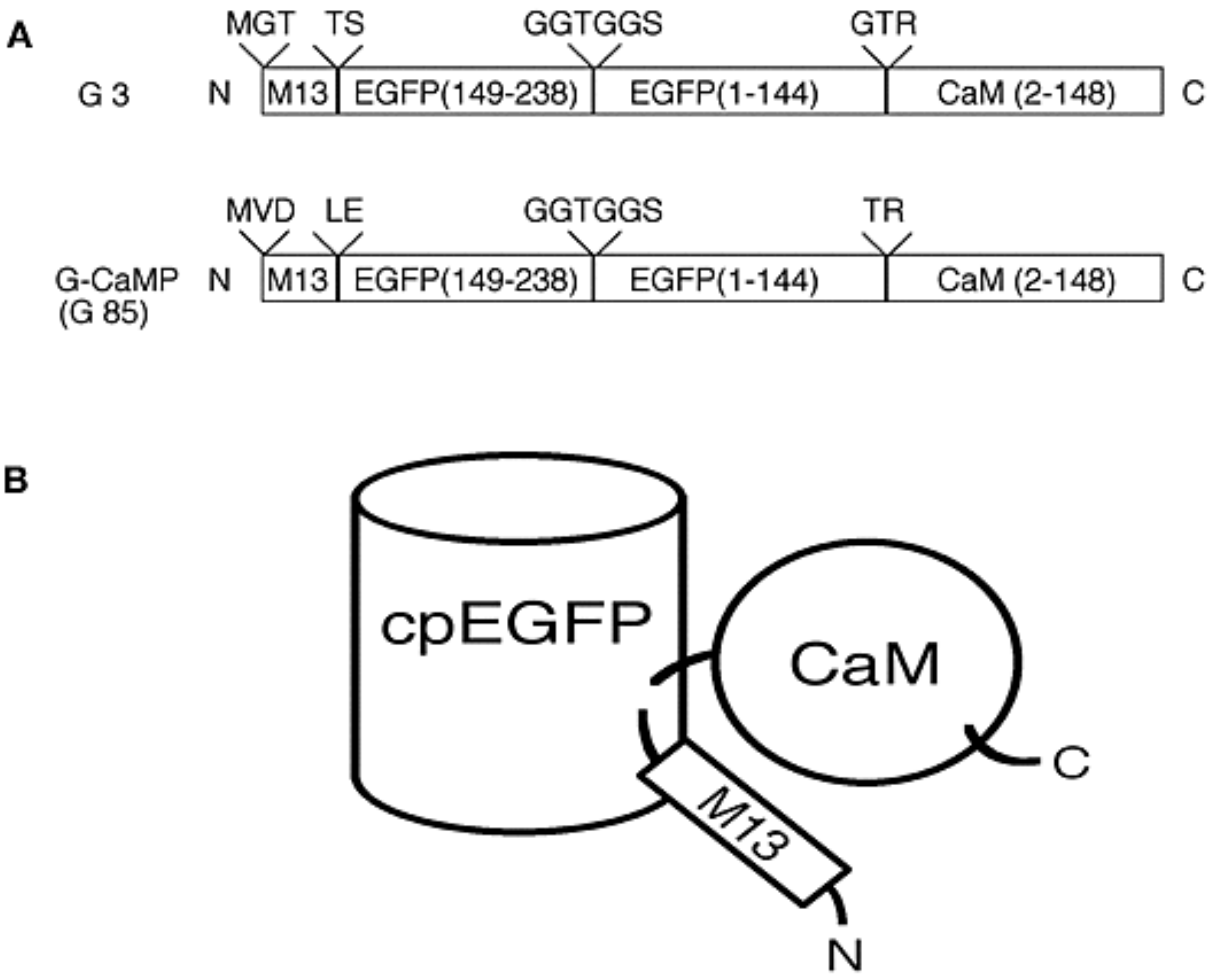

α
α'
β
β'
γ
1002
370
671



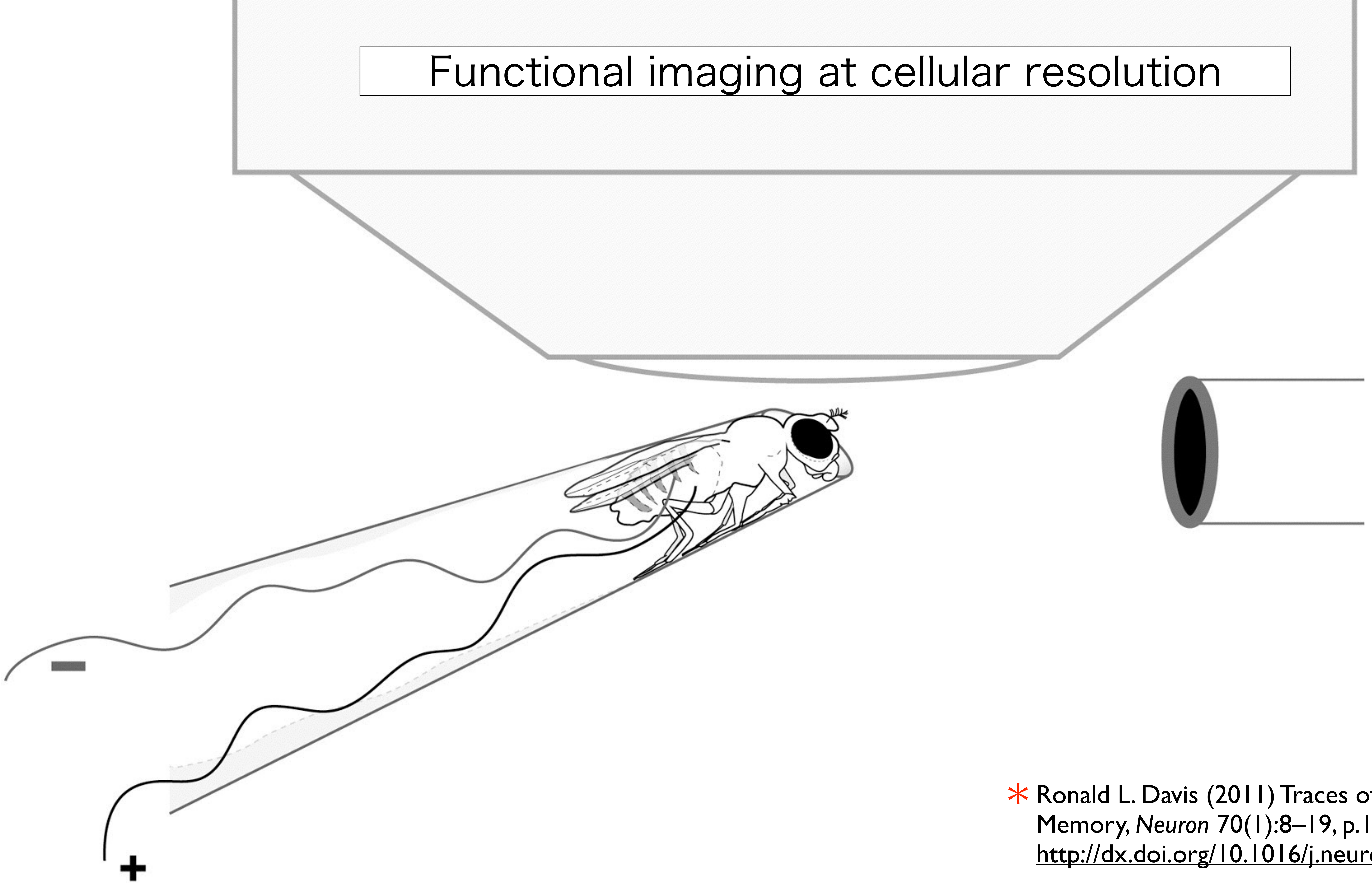
＊阿部崇志氏提供



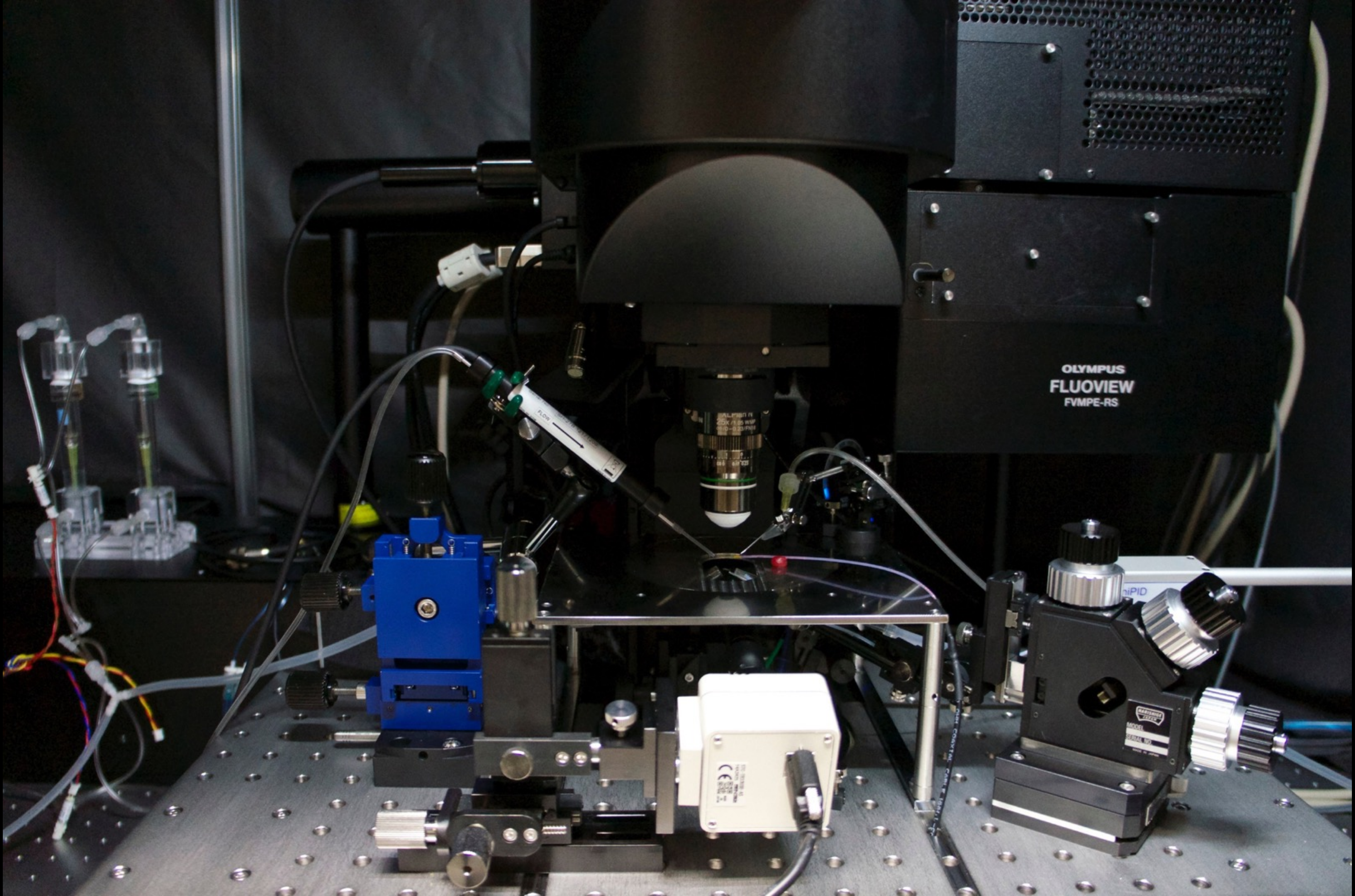
＊阿部崇志氏提供


A
MGT
TS
GGTGGS
GTR
G 3
N
M13
EGFP(149-238)
EGFP(1-144)
CaM (2-148)
C
MVD
LE
GGTGGS
TR
G-CaMP
(G 85)
N
M13
EGFP(149-238)
EGFP(1-144)
CaM (2-148)
C
B
cpEGFP
CaM
C
M13
N

Functional imaging at cellular resolution



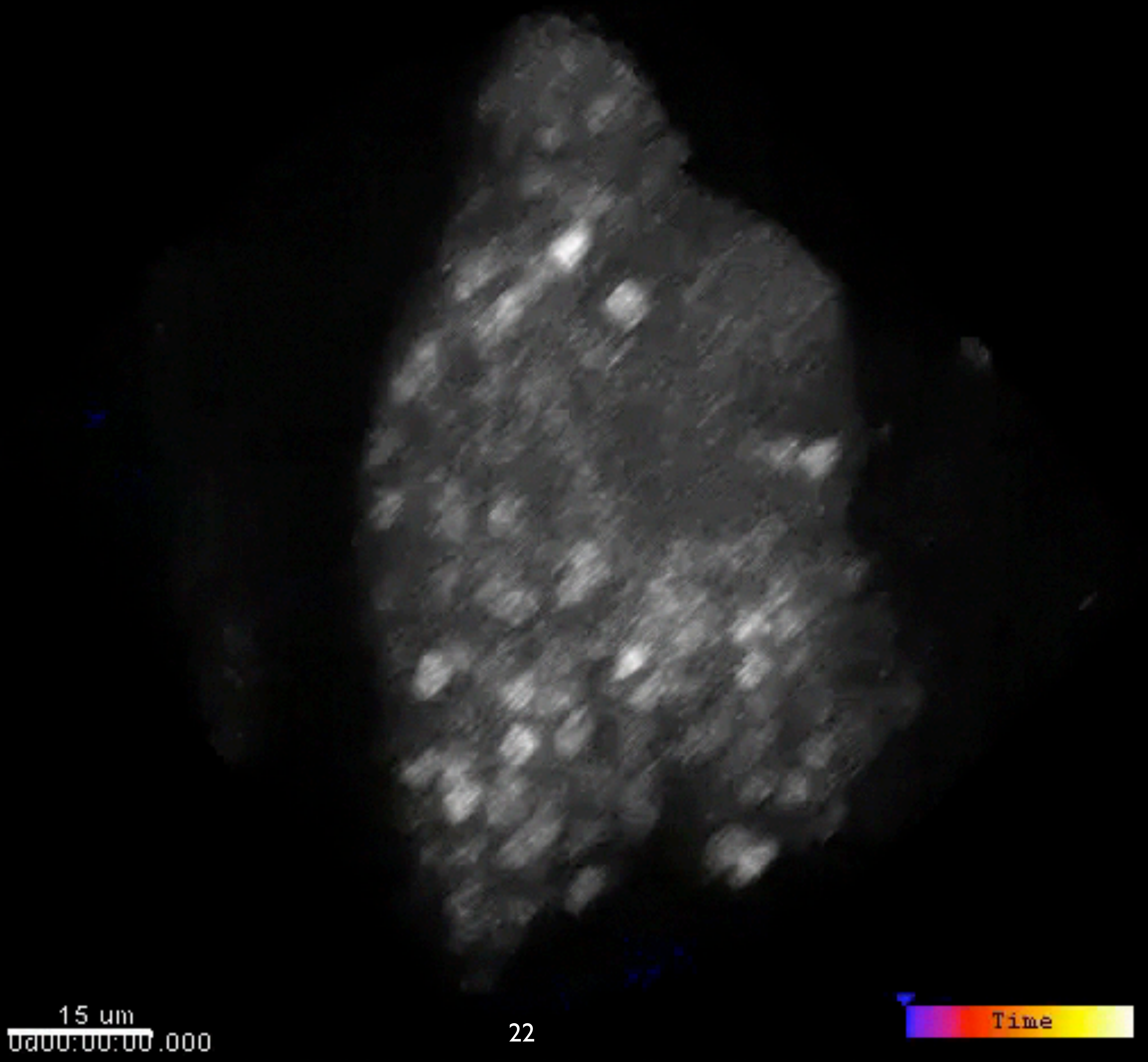
* Ronald L. Davis (2011) Traces of *Drosophila* Memory, *Neuron* 70(1):8–19, p.11 Fig.3.
http://dx.doi.org/10.1016/j.neuron.2011.03.012


OLYMPUS
FLUOVIEW
FVMPE-RS

Memory formation under the microscope

＊廣井誠氏提供

4次元イメージング　GCaMP シグナル



＊廣井誠氏提供

OK107 all KCs > GCaMP5

All KCs > DsRed

Oct 34ms 81slices 2.78sec

20 um

0d00:01:12.000

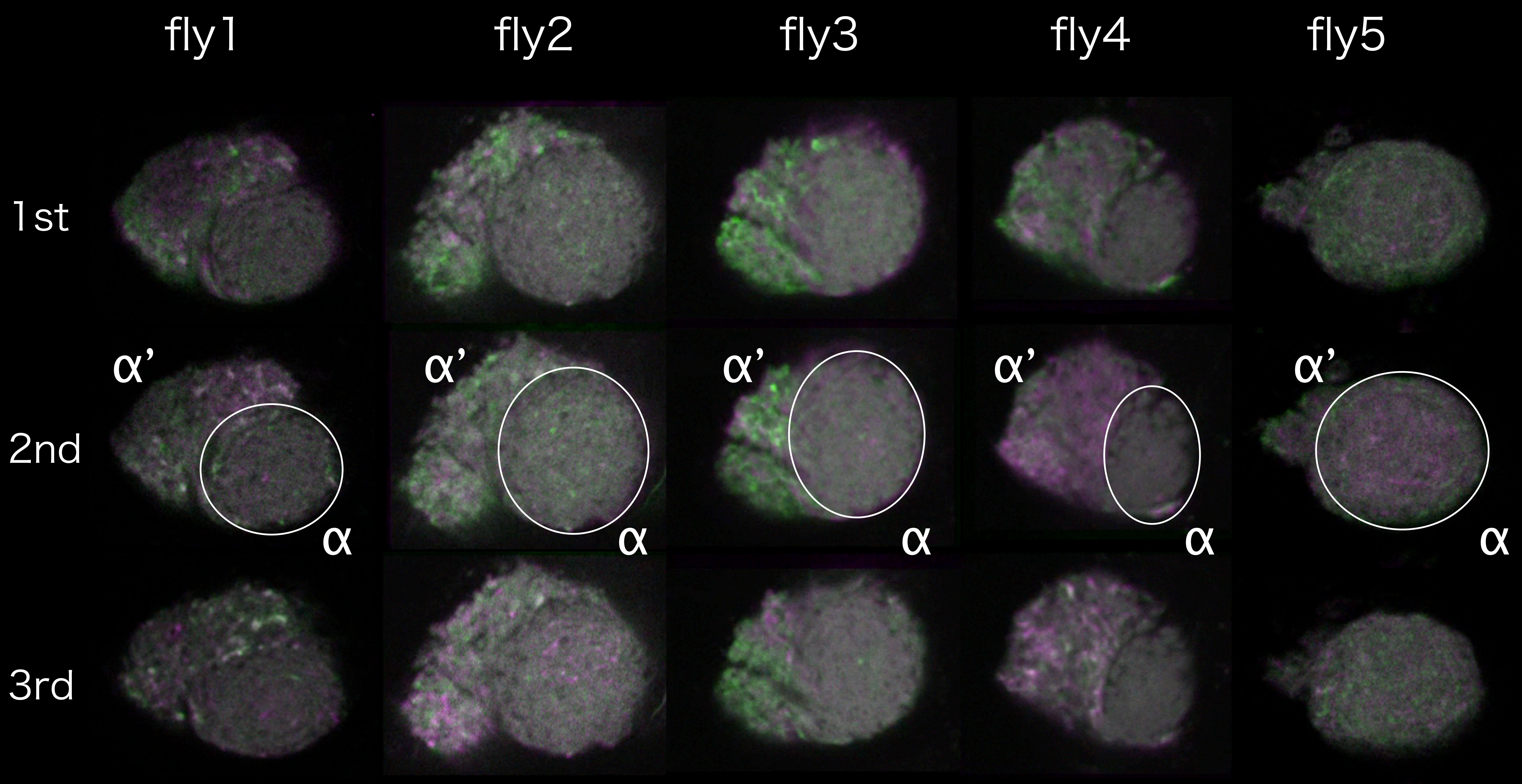
＊廣井誠氏提供

OK107 all KCs > GCaMP5

All KCs > DsRed

15 um

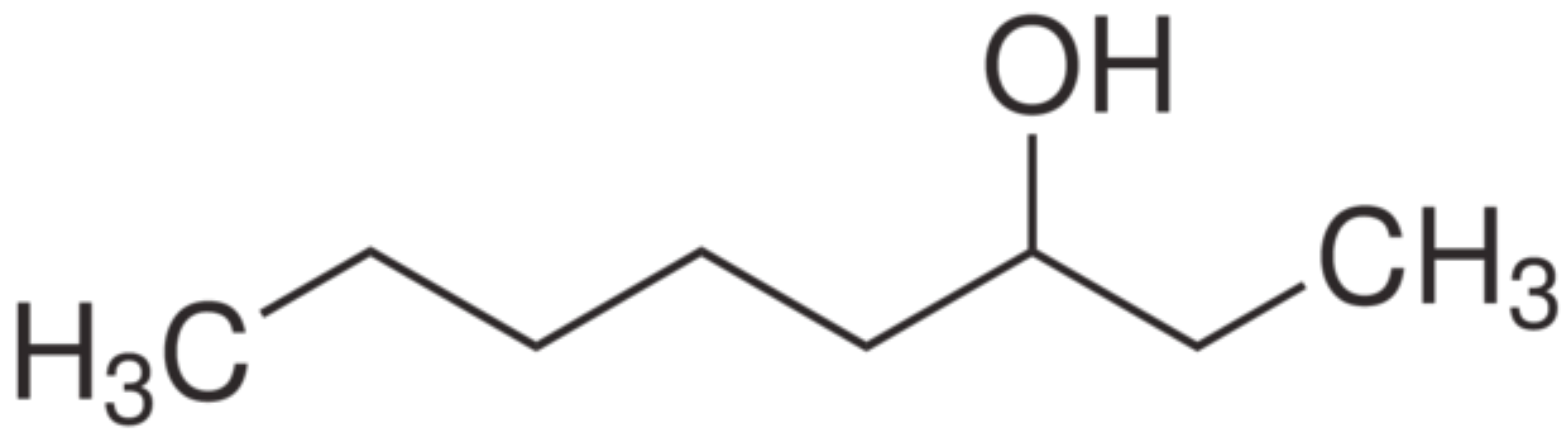
＊廣井誠氏提供



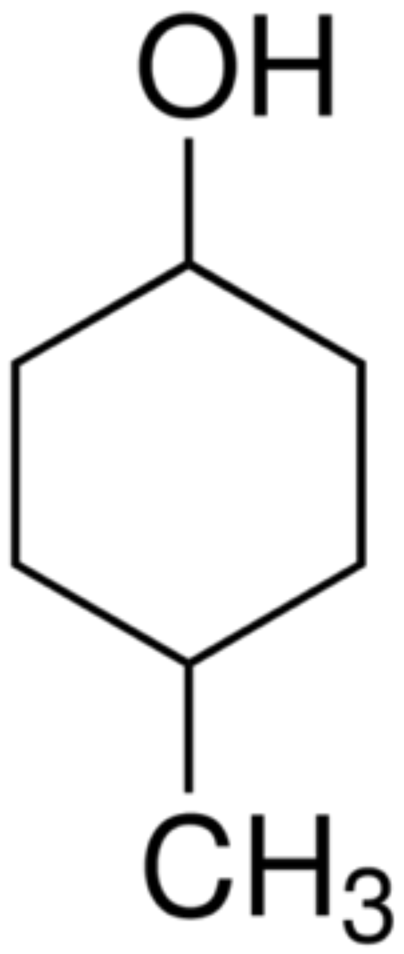
300ms / frame, 7f/s

MCH Oct

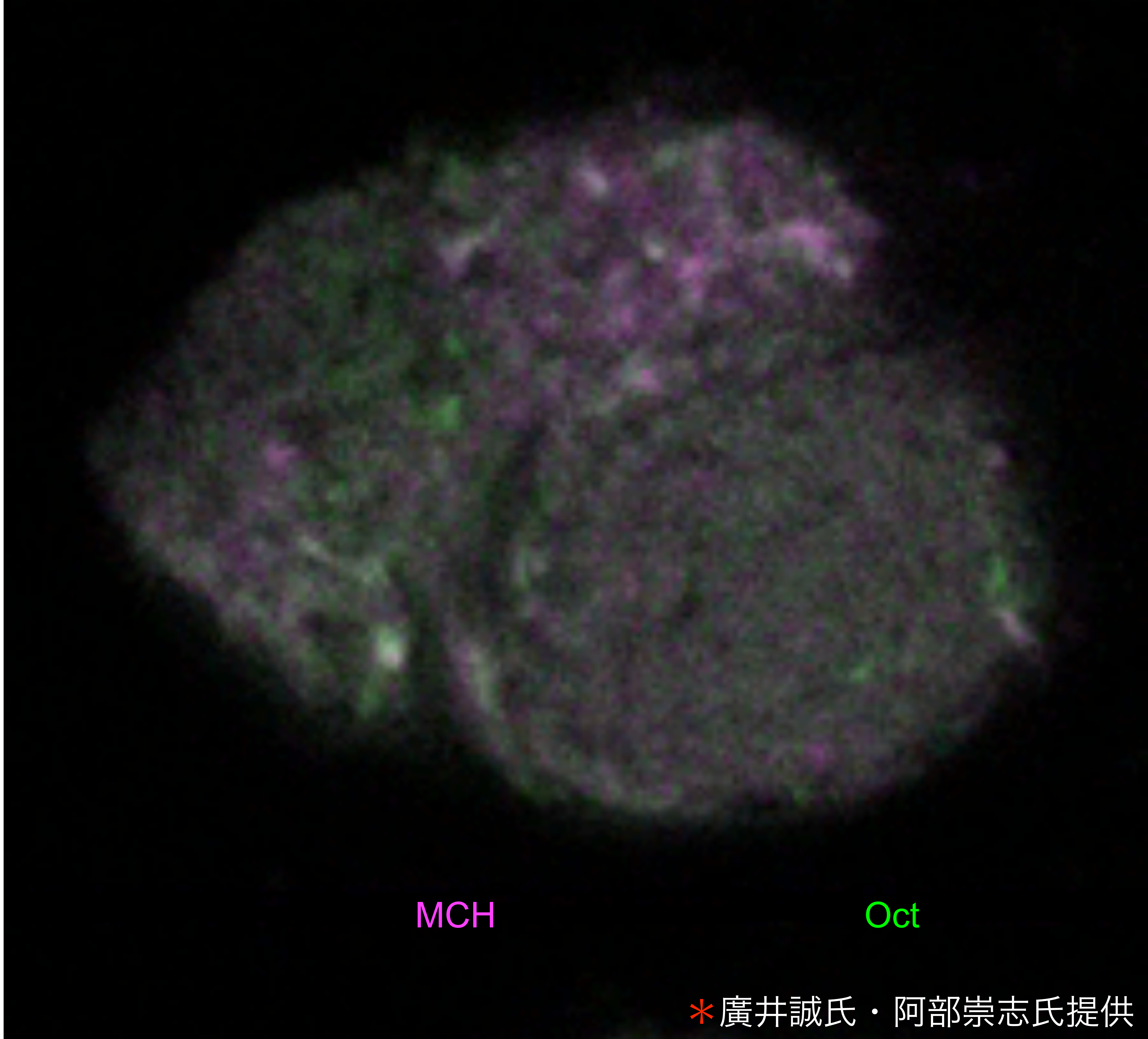
＊廣井誠氏・阿部崇志氏提供



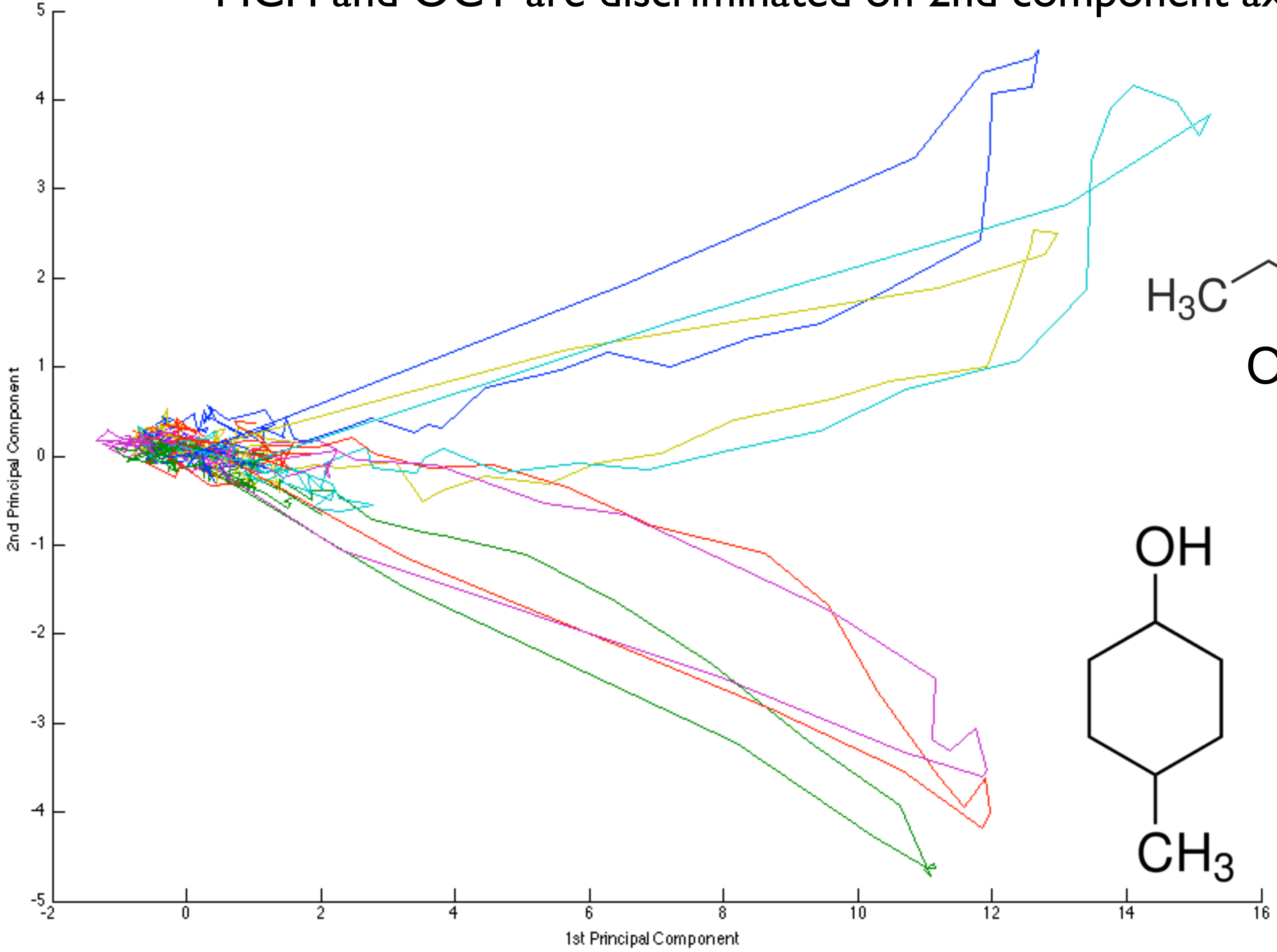
3-Octanol (OCT)

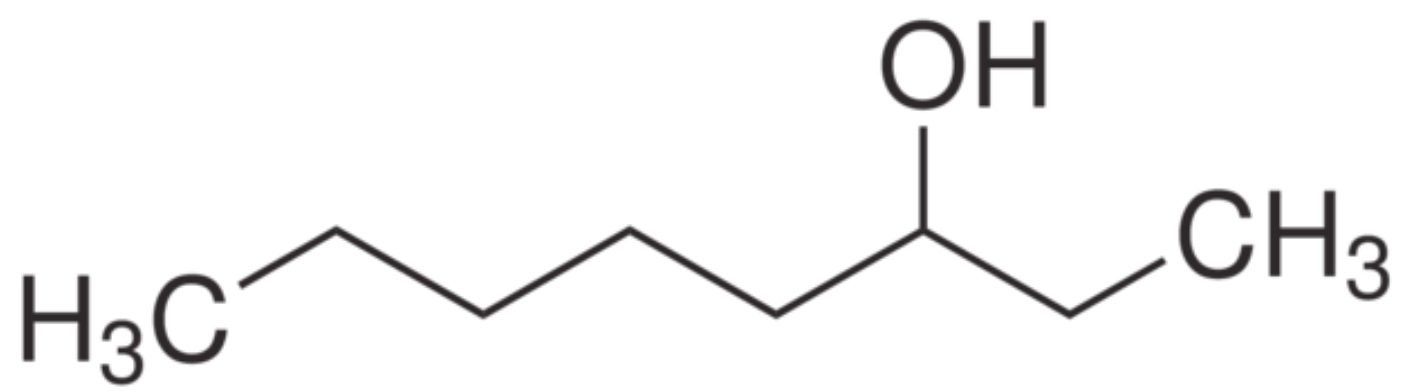


4-Methylcyclohexanol (MCH)



MCH and OCT are discriminated on 2nd component axis

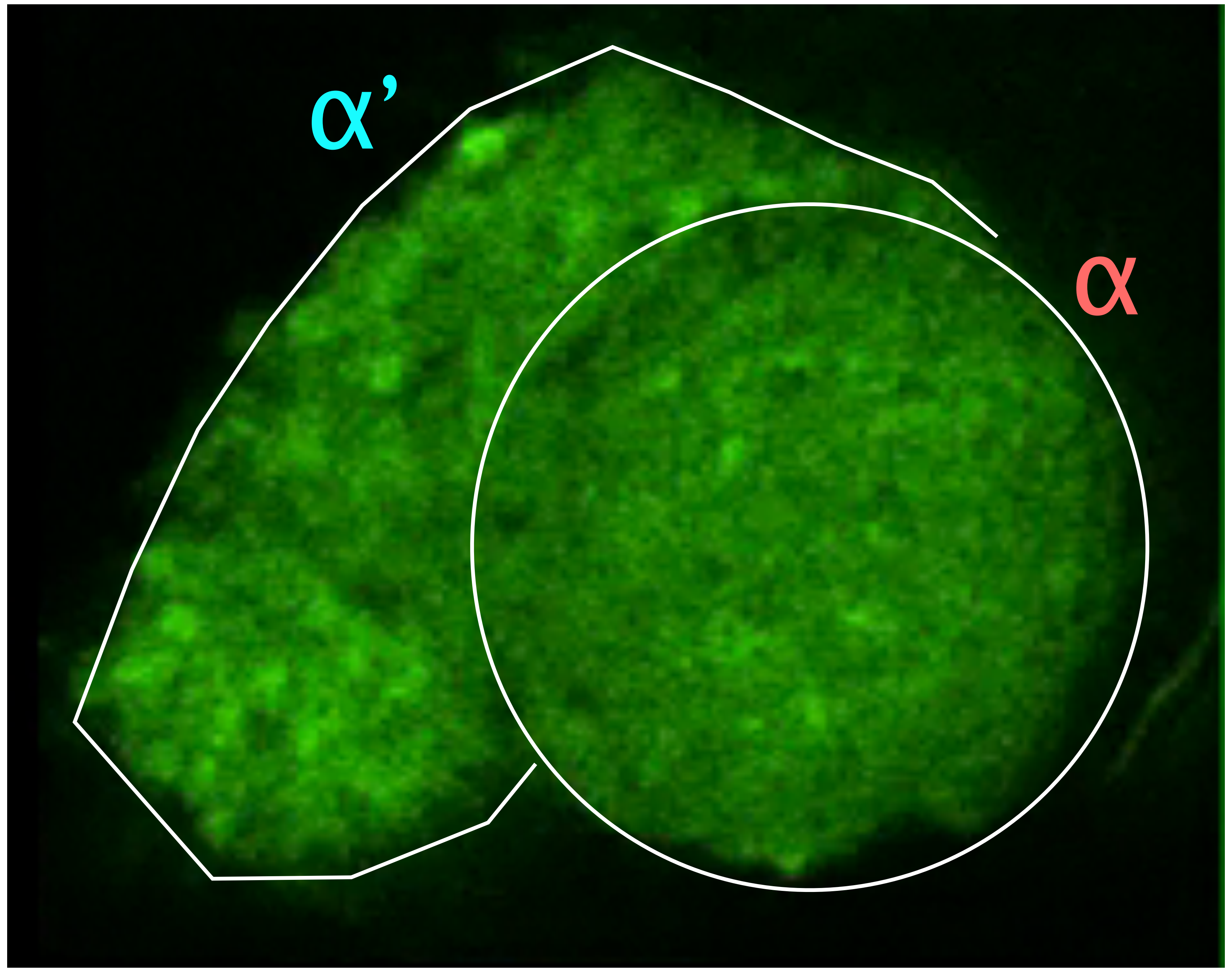




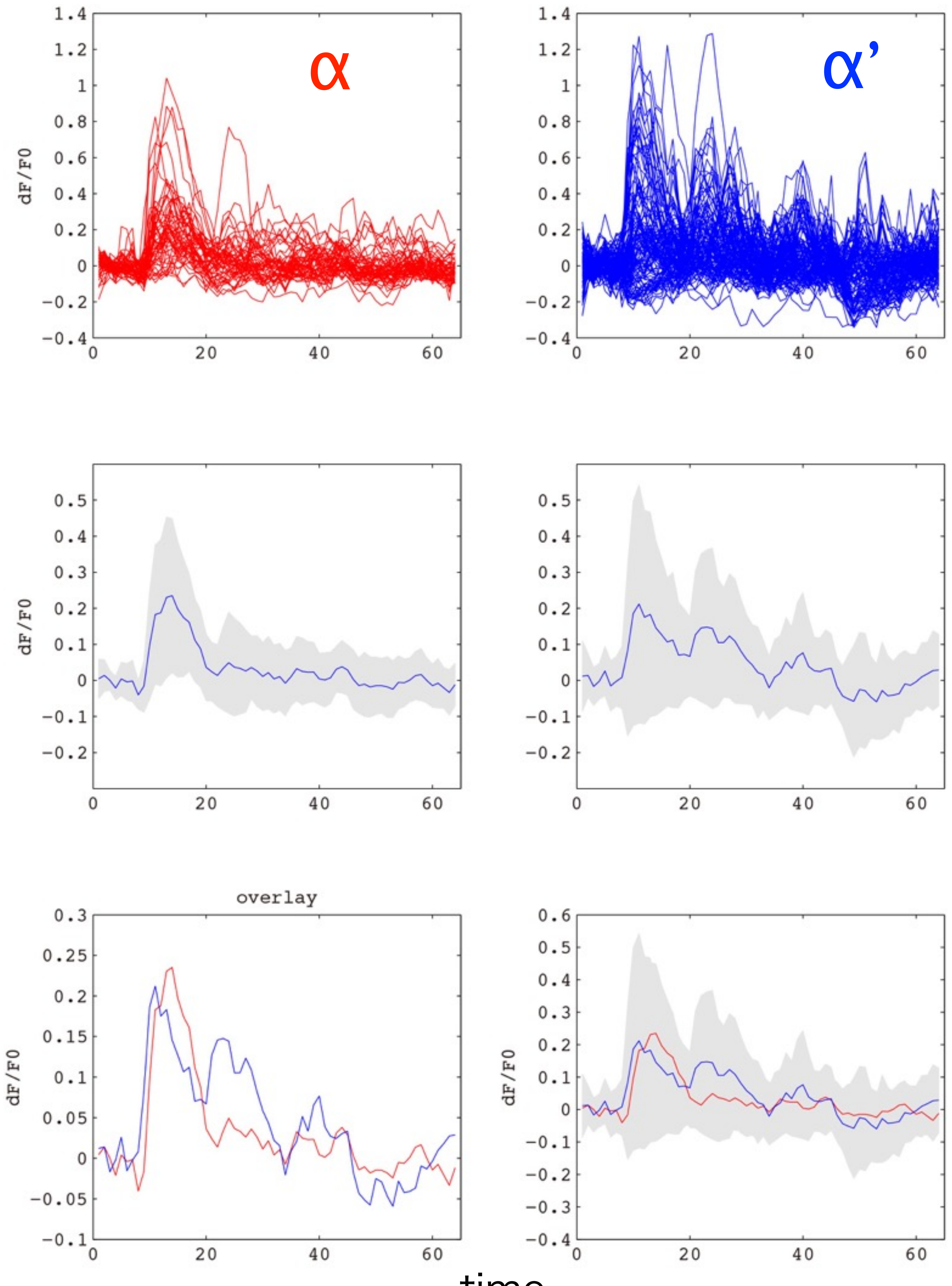
OCT

MCH

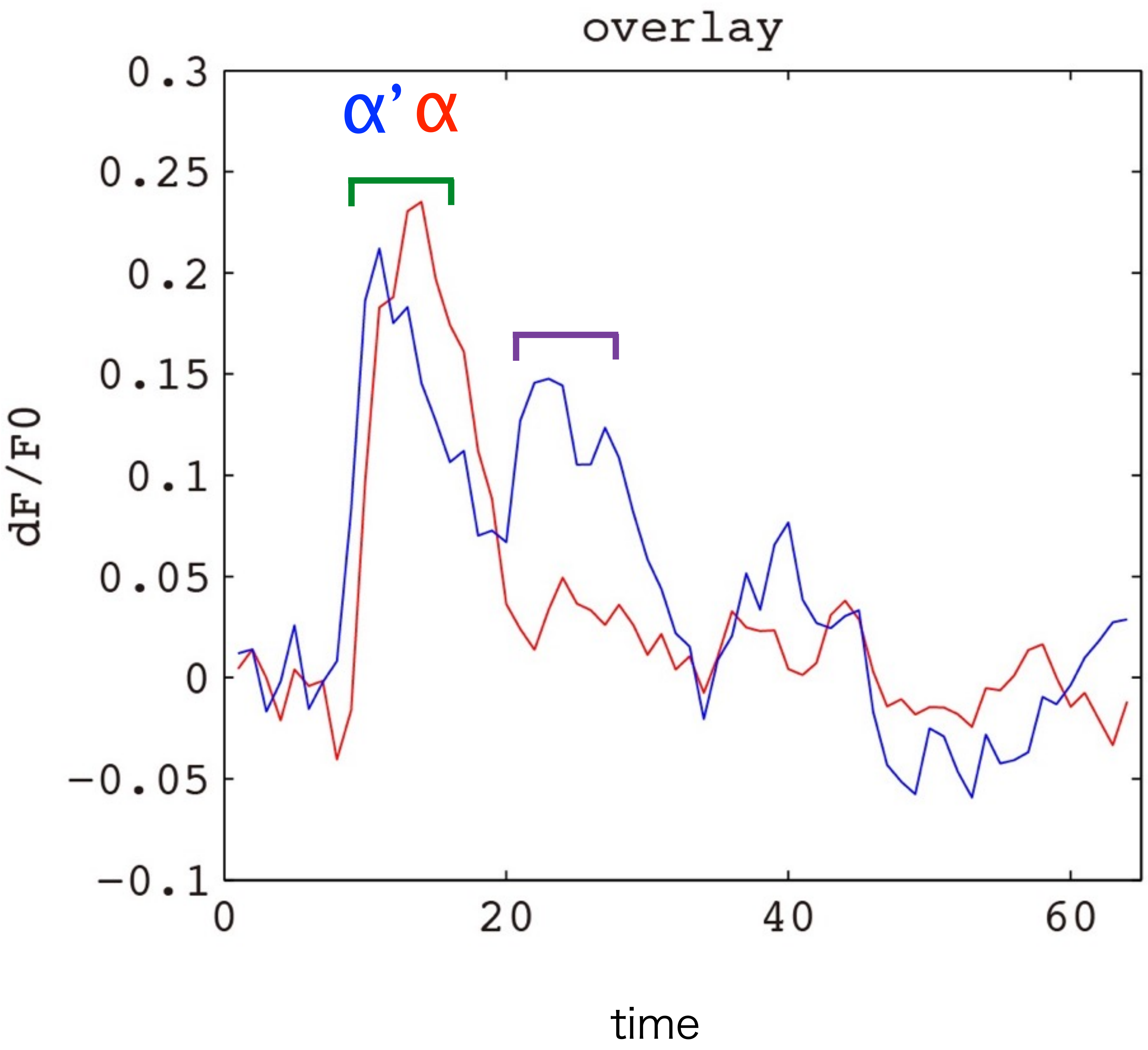
＊廣井誠氏提供

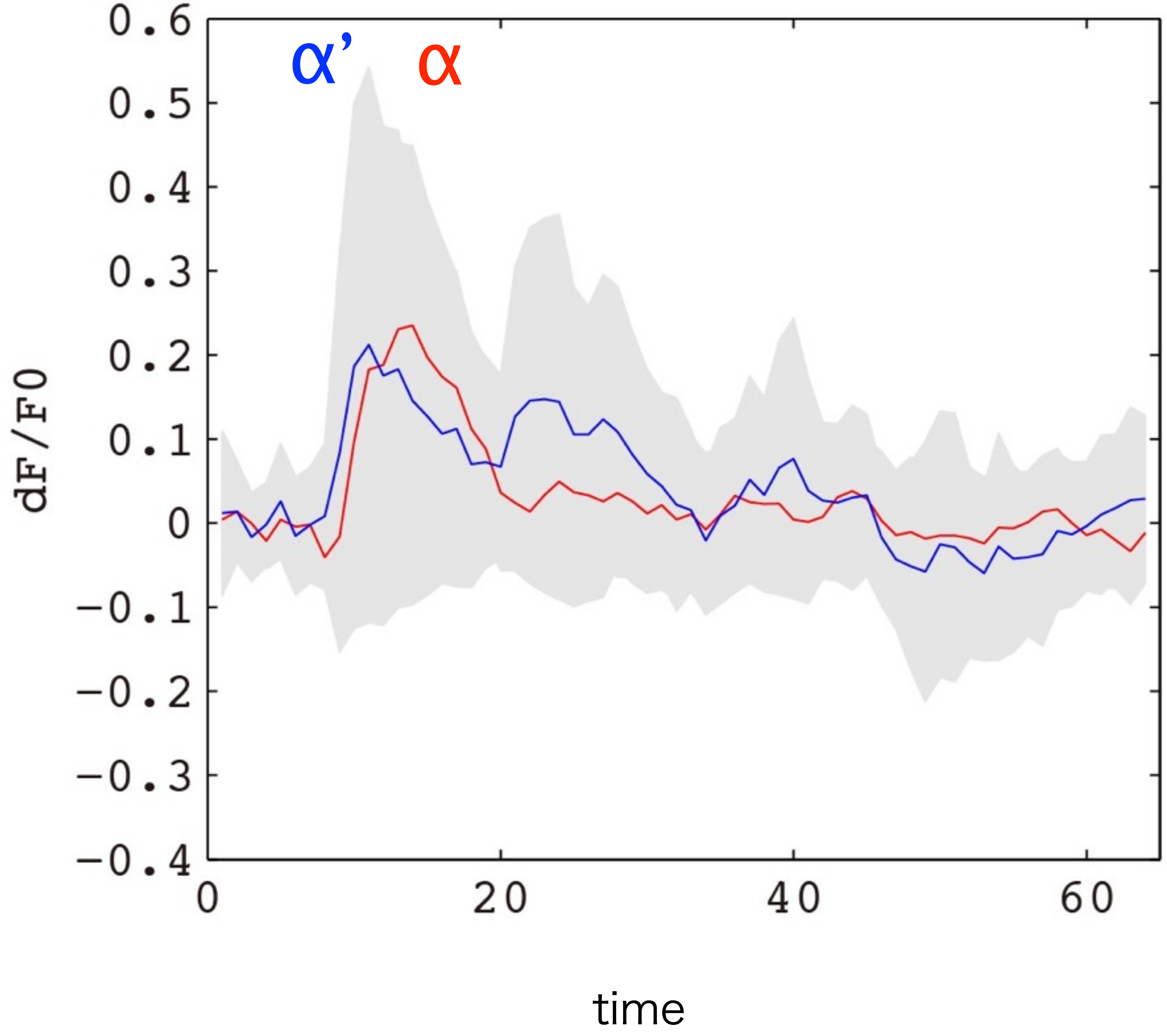


Oct



＊
廣井誠氏・
阿部崇志氏提供

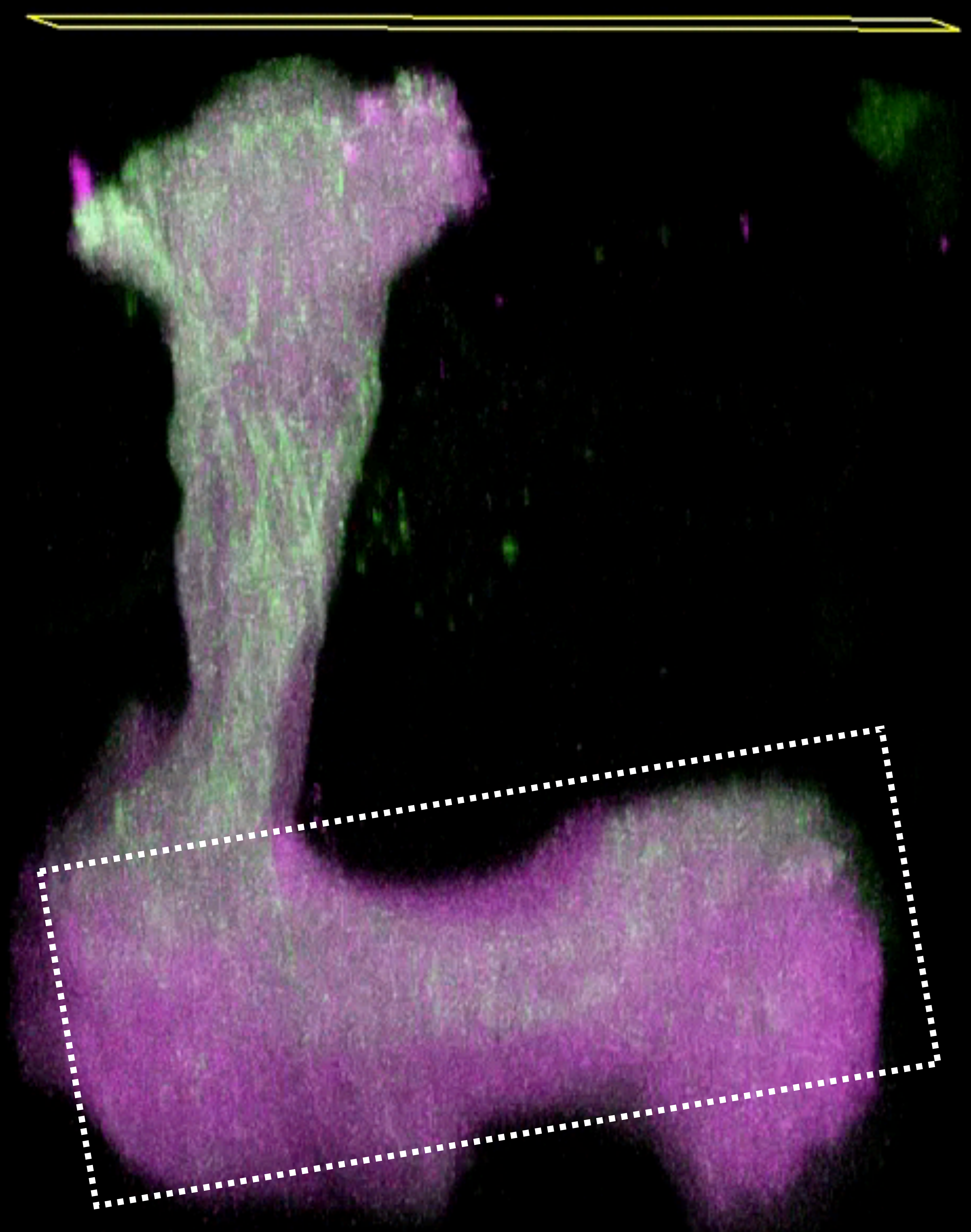




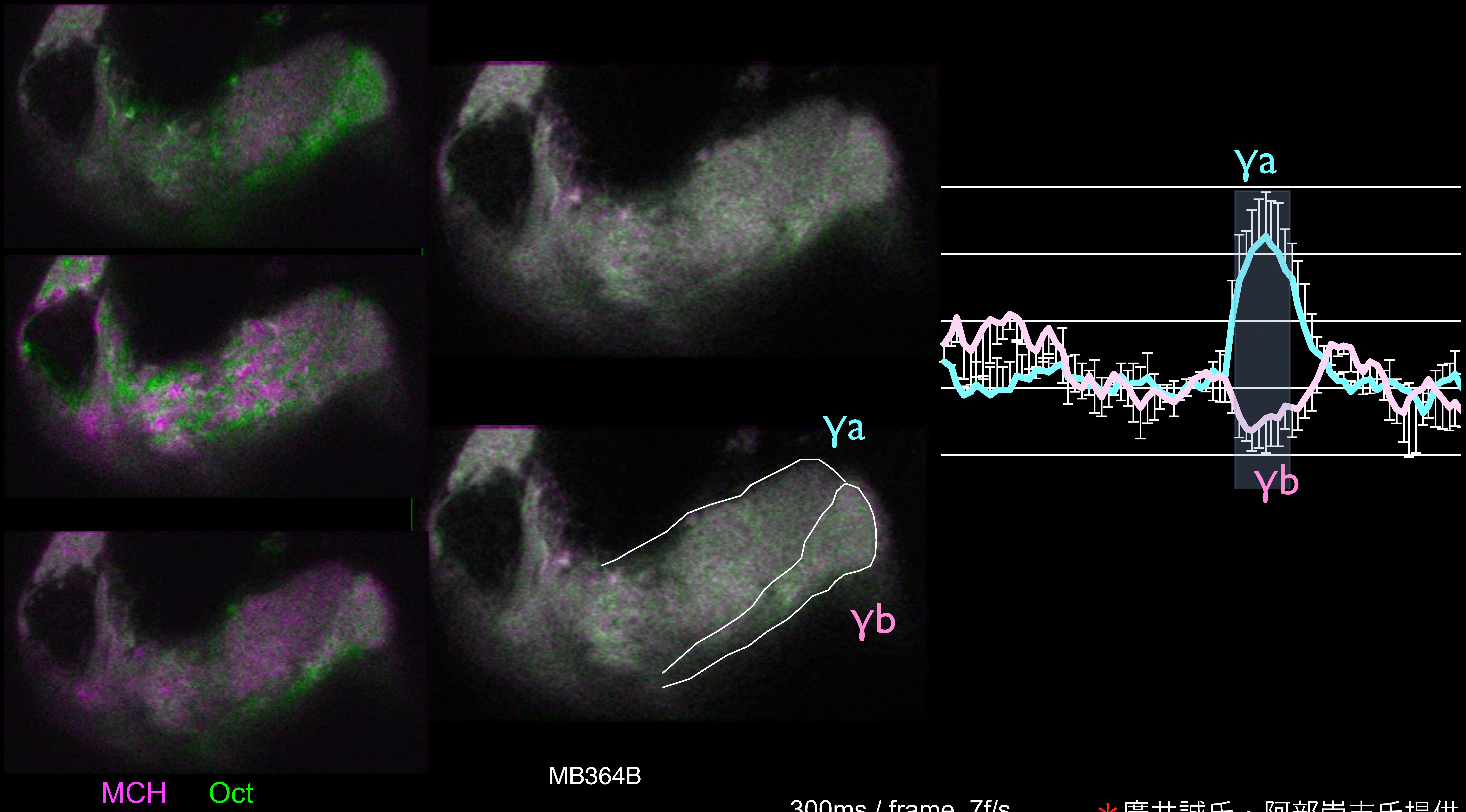
＊廣井誠氏・阿部崇志氏提供

OK107 all KCs > GCaMP5

All KCs > DsRed



＊廣井誠氏提供



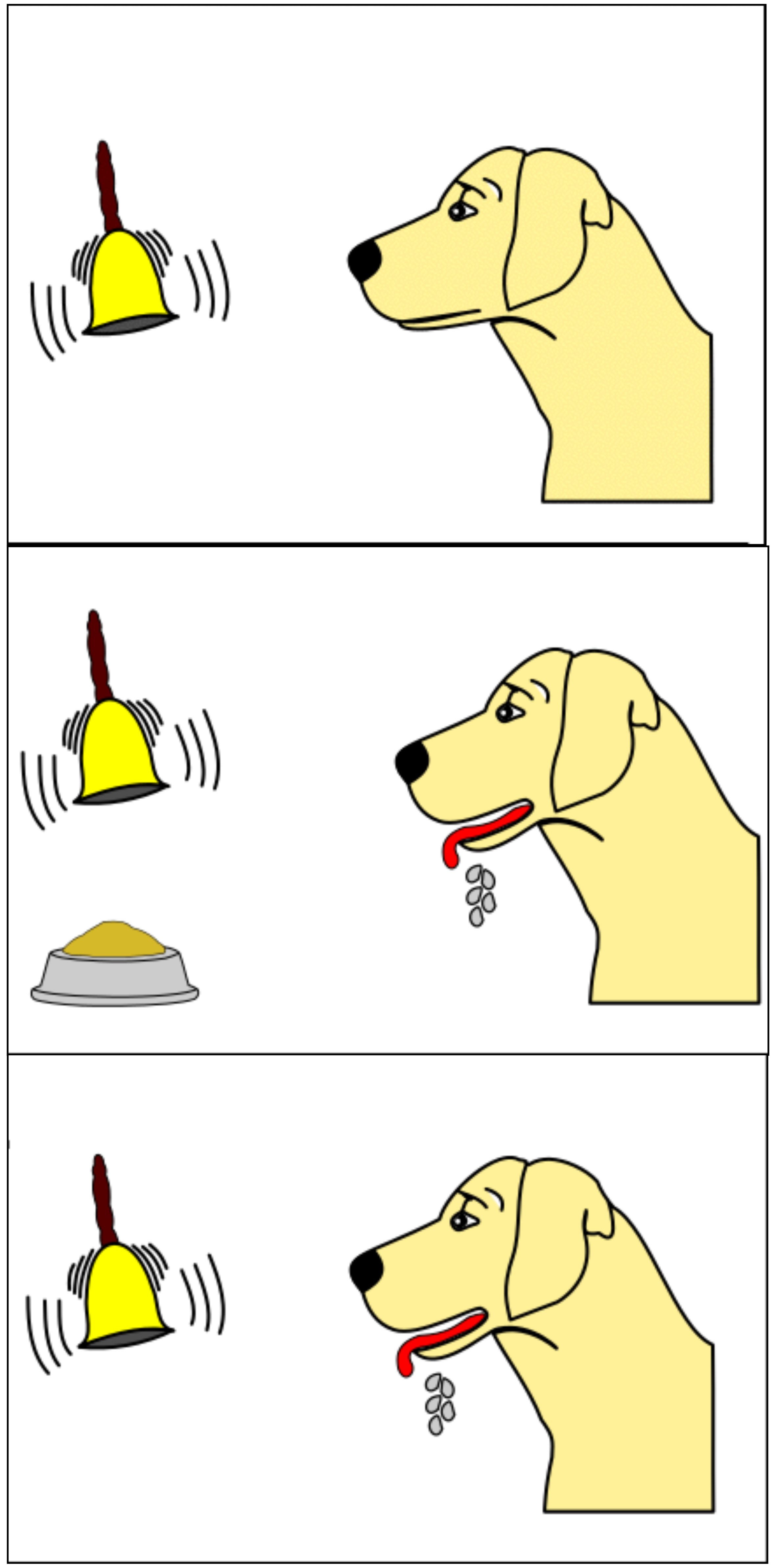
300ms / frame, 7f/s

＊廣井誠氏・阿部崇志氏提供

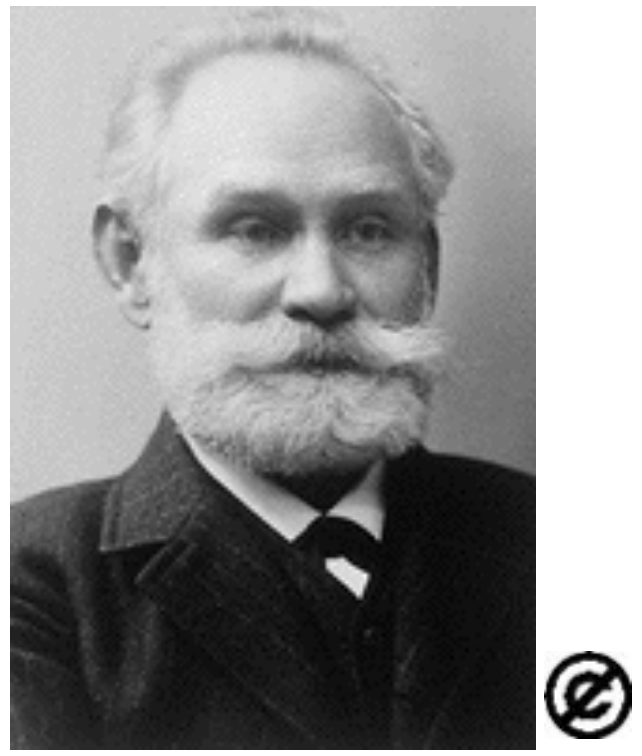
パブロフの犬

Conditional stimulus（条件刺激）: Bell ringing

Unconditional stimulus（非条件刺激）: Food



Adapted from image by MaxxL, from Wikimedia Commons
https://commons.wikimedia.org/wiki/File:Pavlov%27s_dog_conditioning.svg



Ivan Pavlov

におい学習記憶

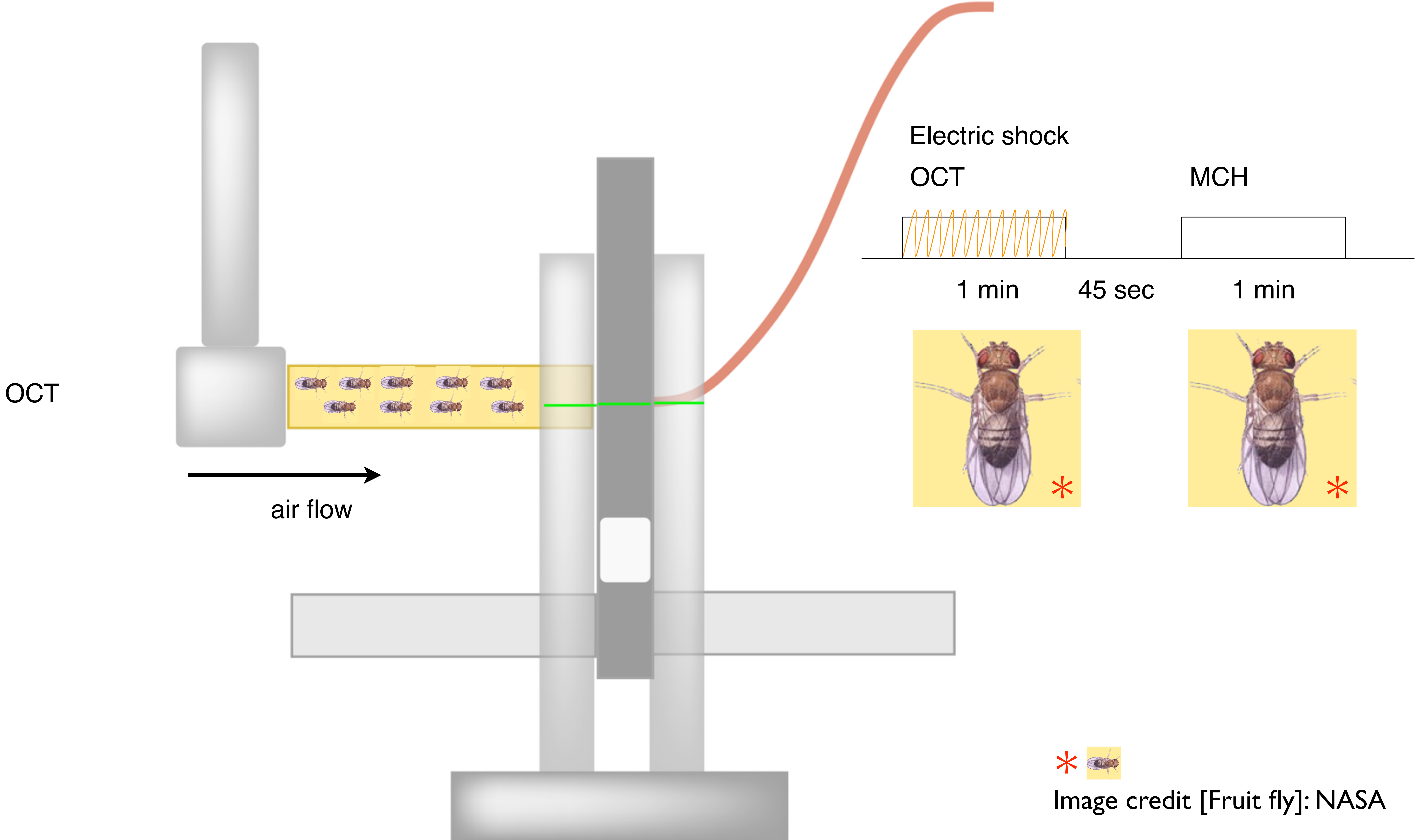
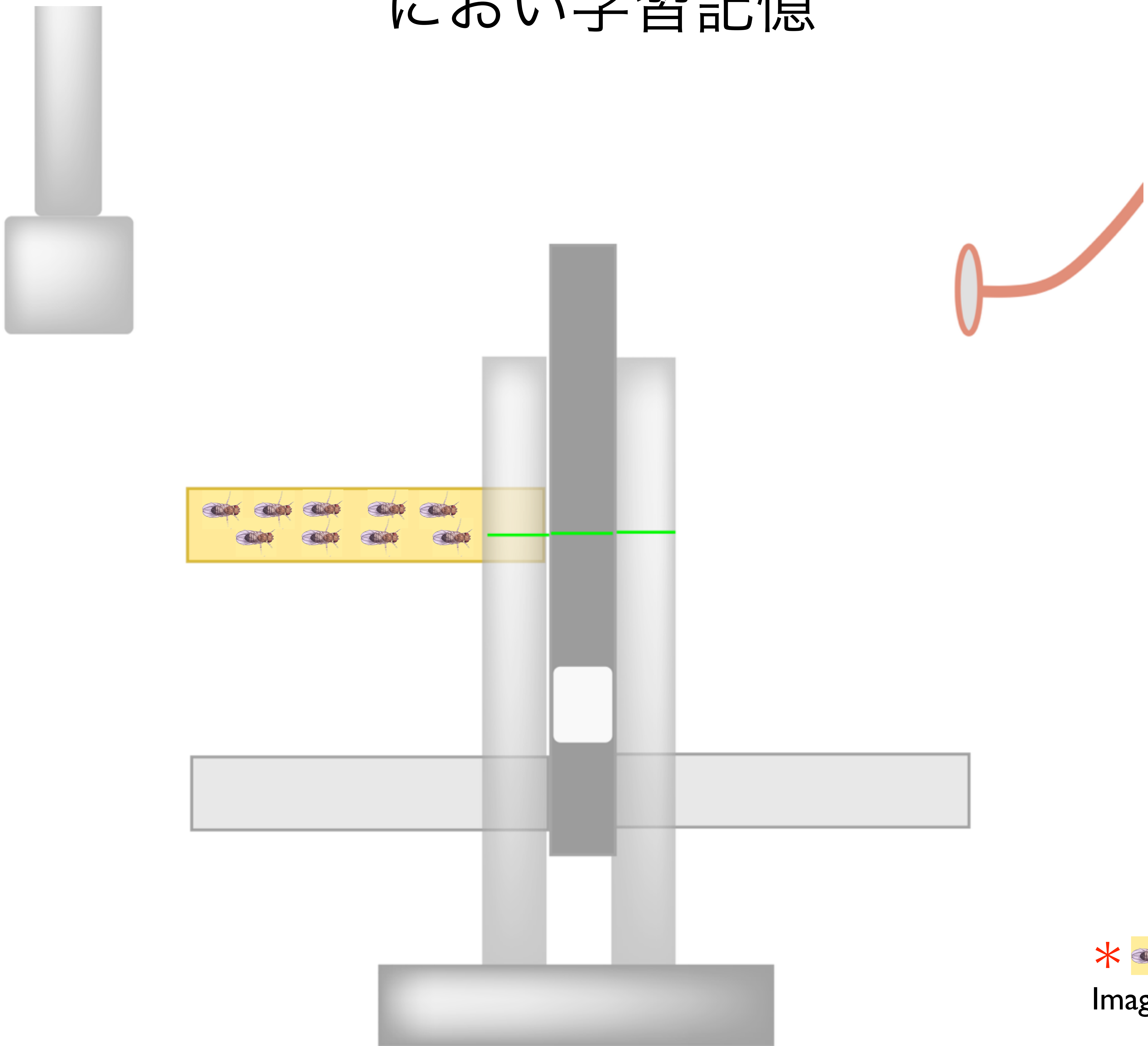


Image credit [Fruit fly]: NASA

においう学習記憶



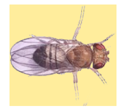
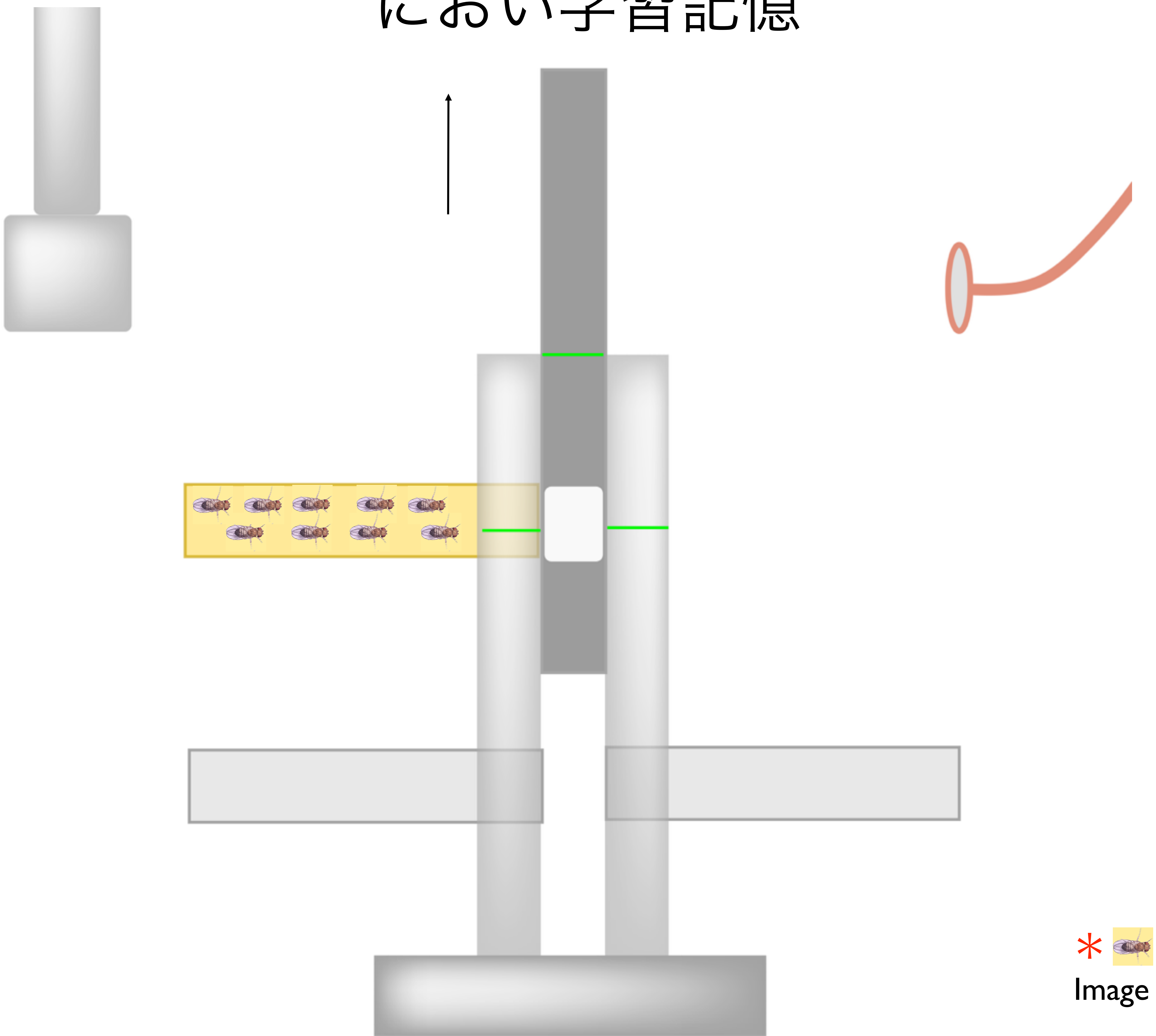


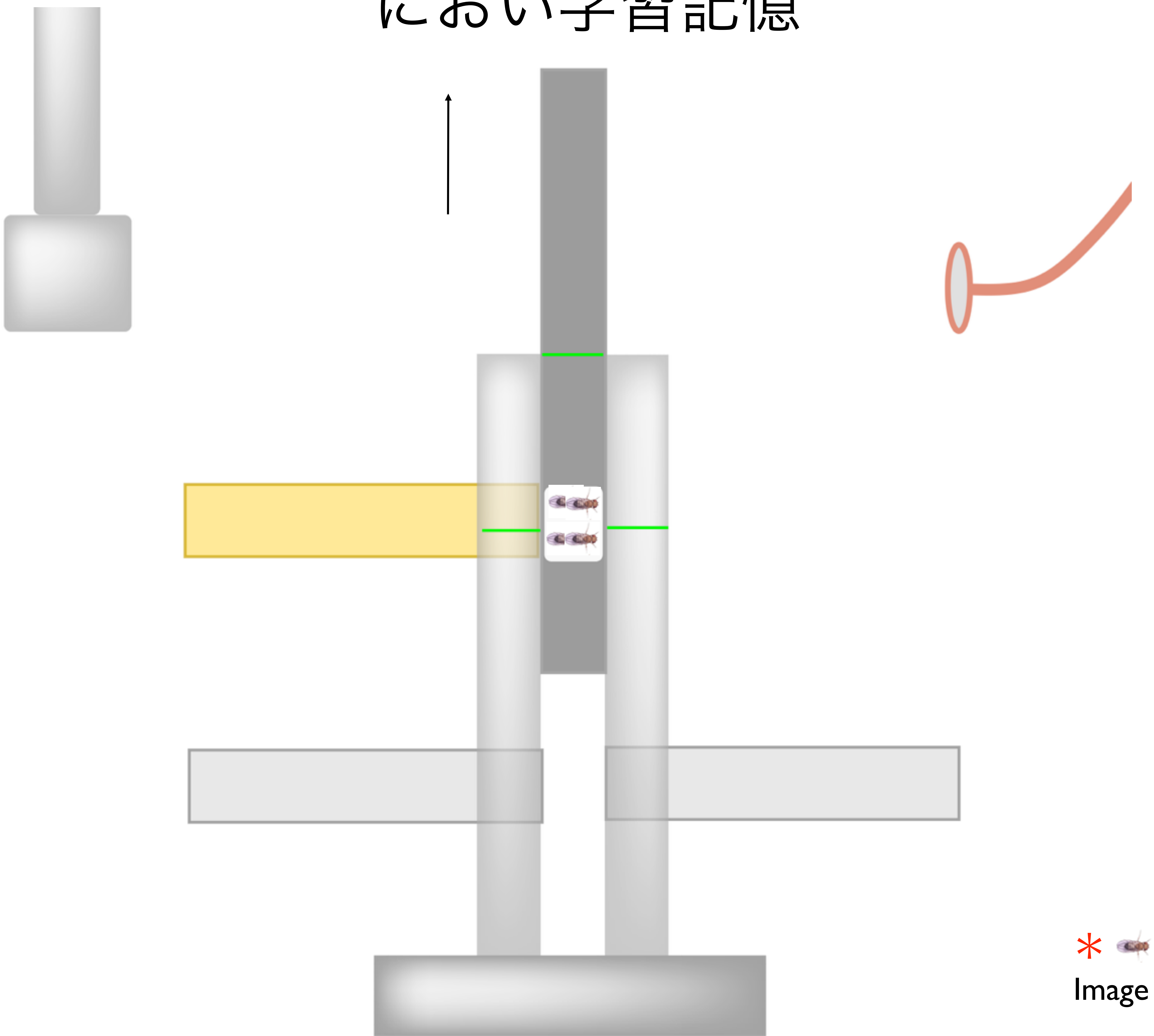
Image credit [Fruit fly]: NASA

におい学習記憶



＊ Image credit [Fruit fly]: NASA

におい学習記憶



*

Image credit [Fruit fly]: NASA

においし学習記憶

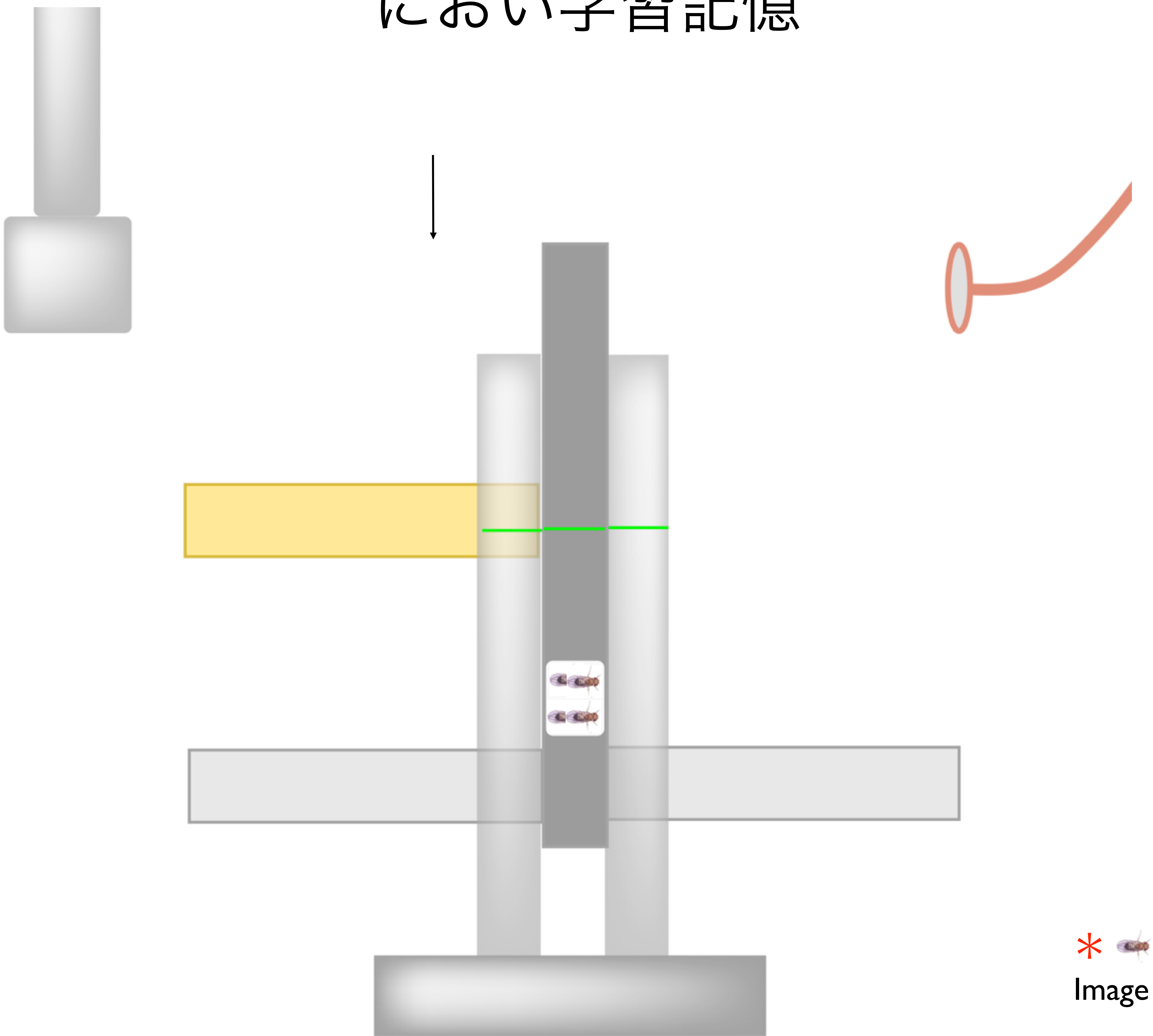
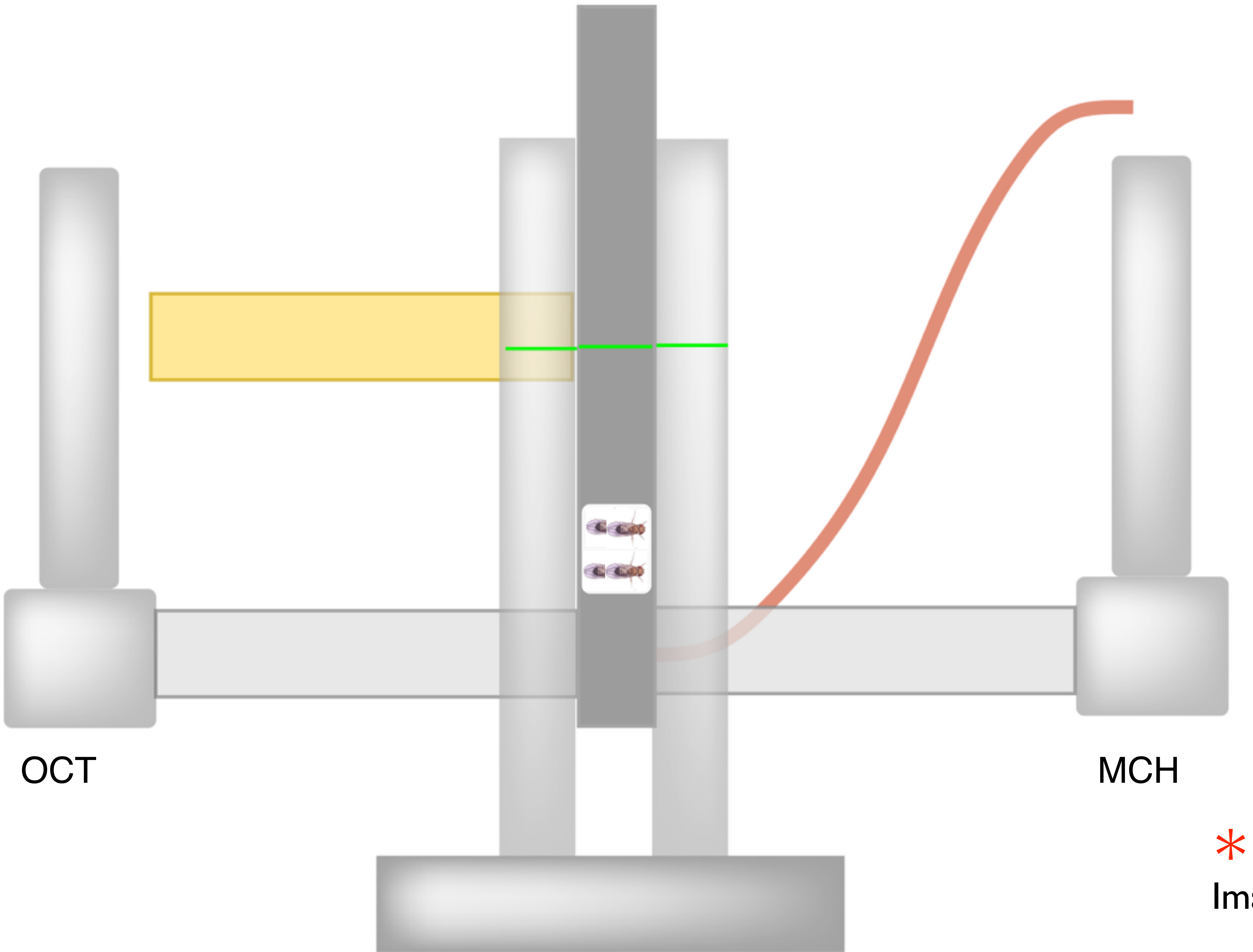


Image credit [Fruit fly]: NASA

におい学習記憶

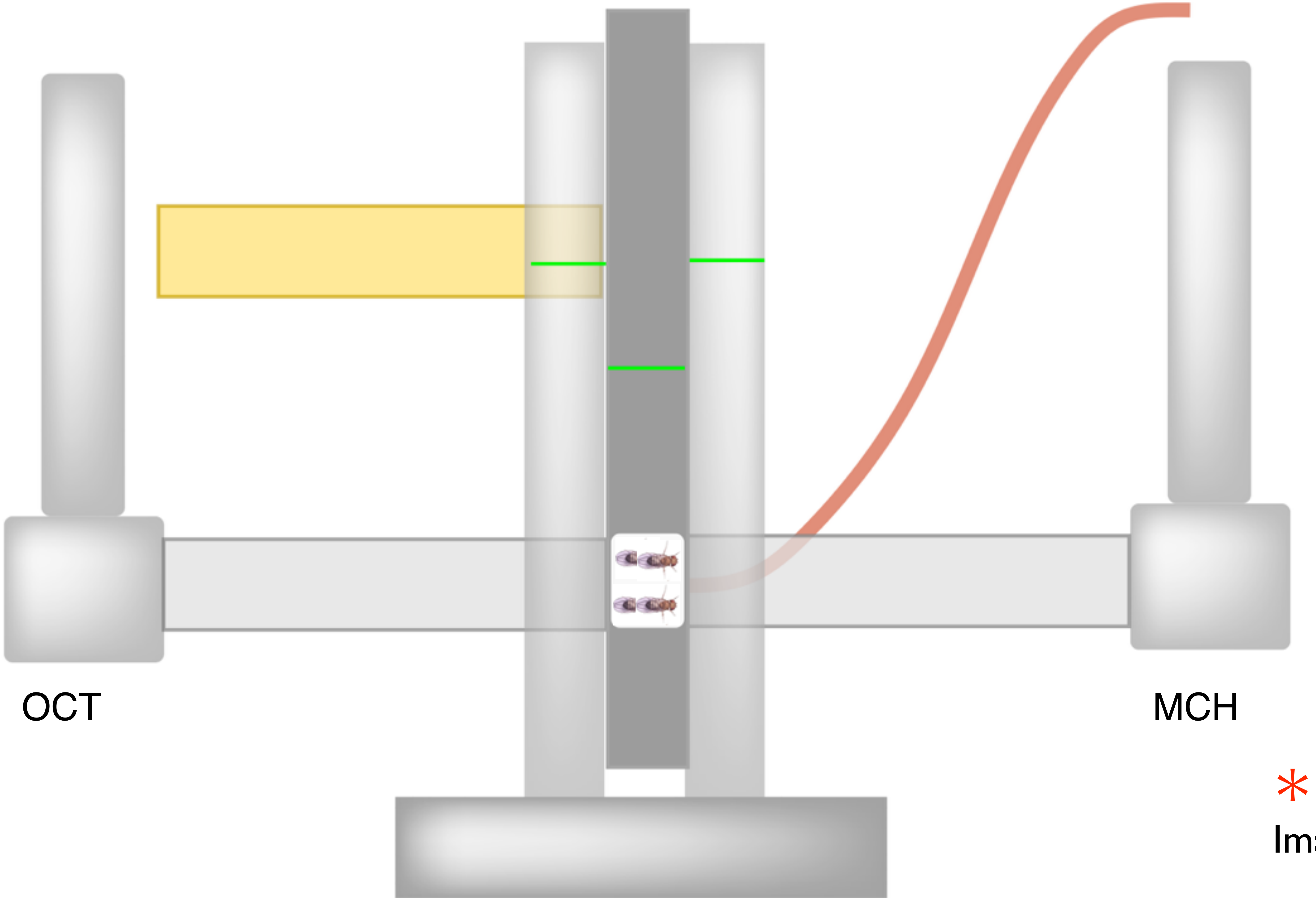


*

Image credit [Fruit fly]: NASA

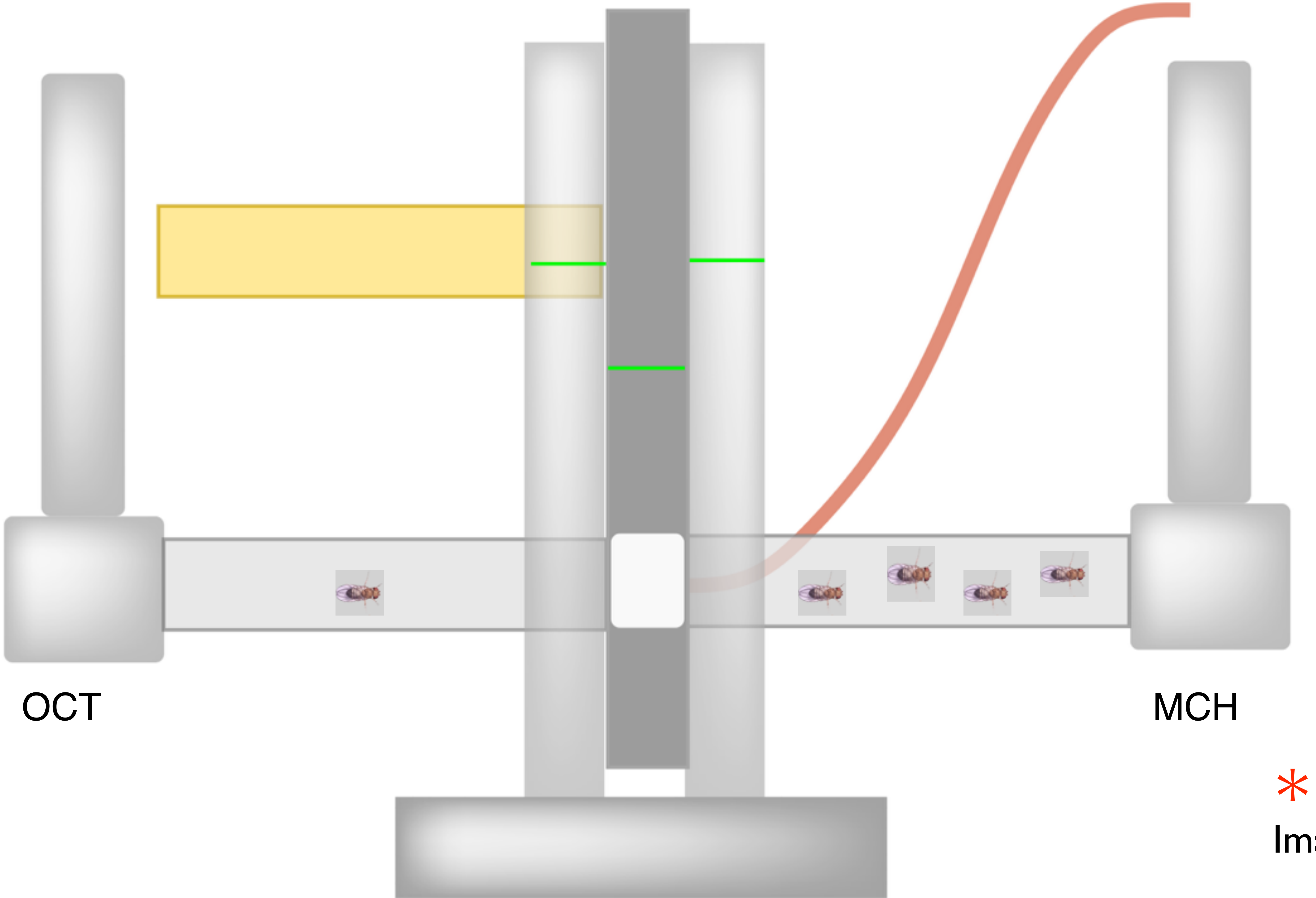
Olfactory memory

Choice to OCT or MCH



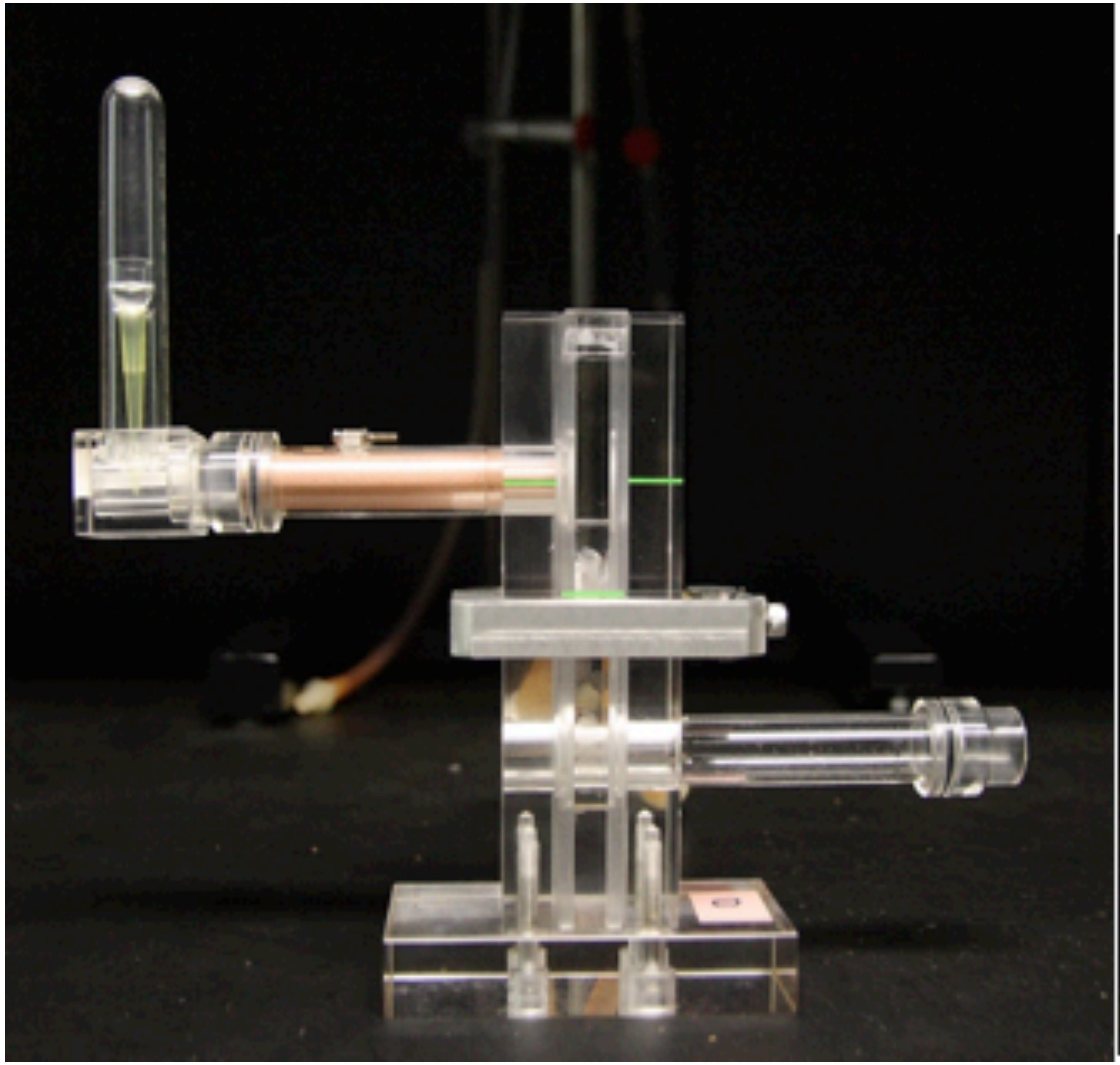
* Image credit [Fruit fly]: NASA

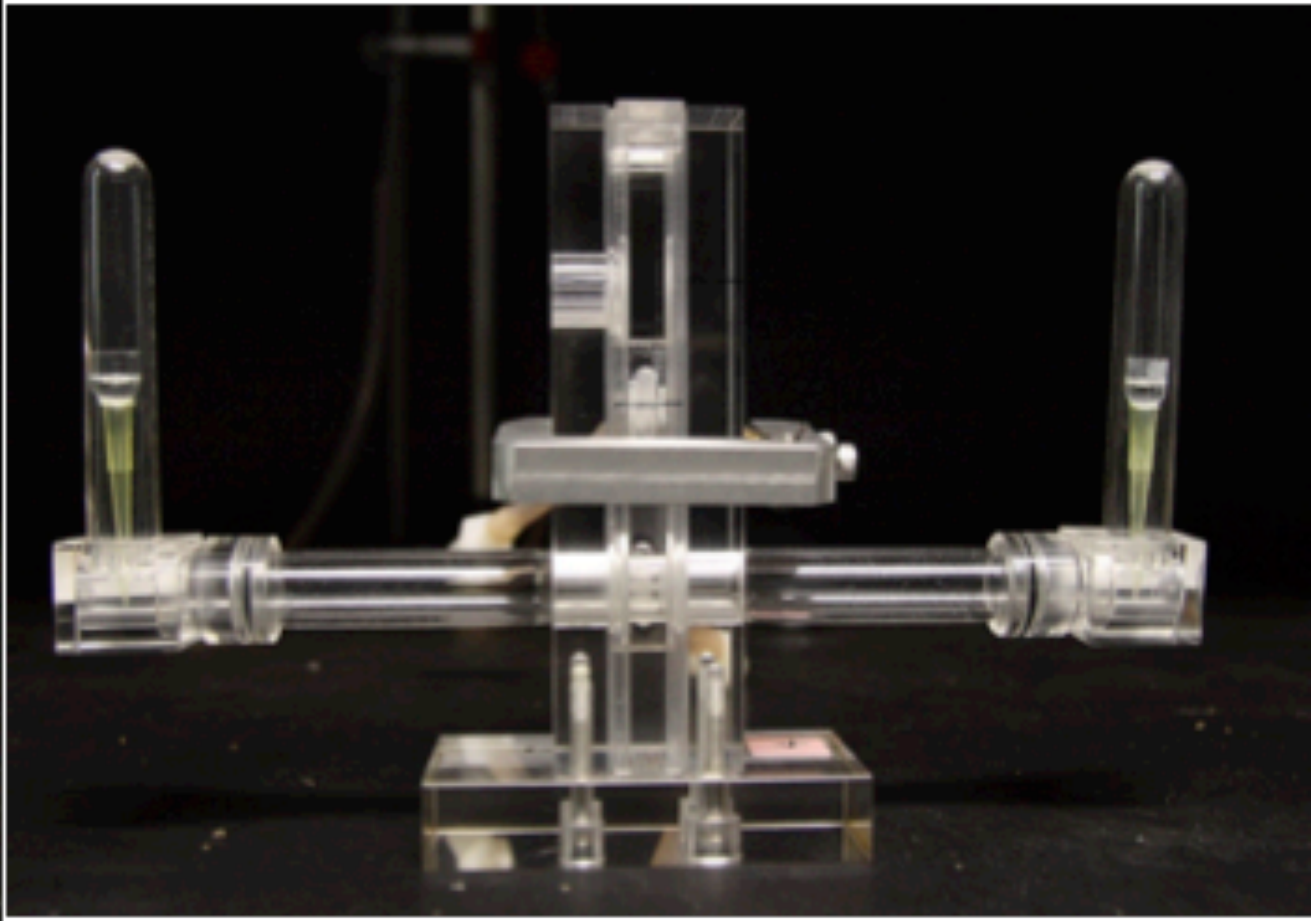
Olfactory memory

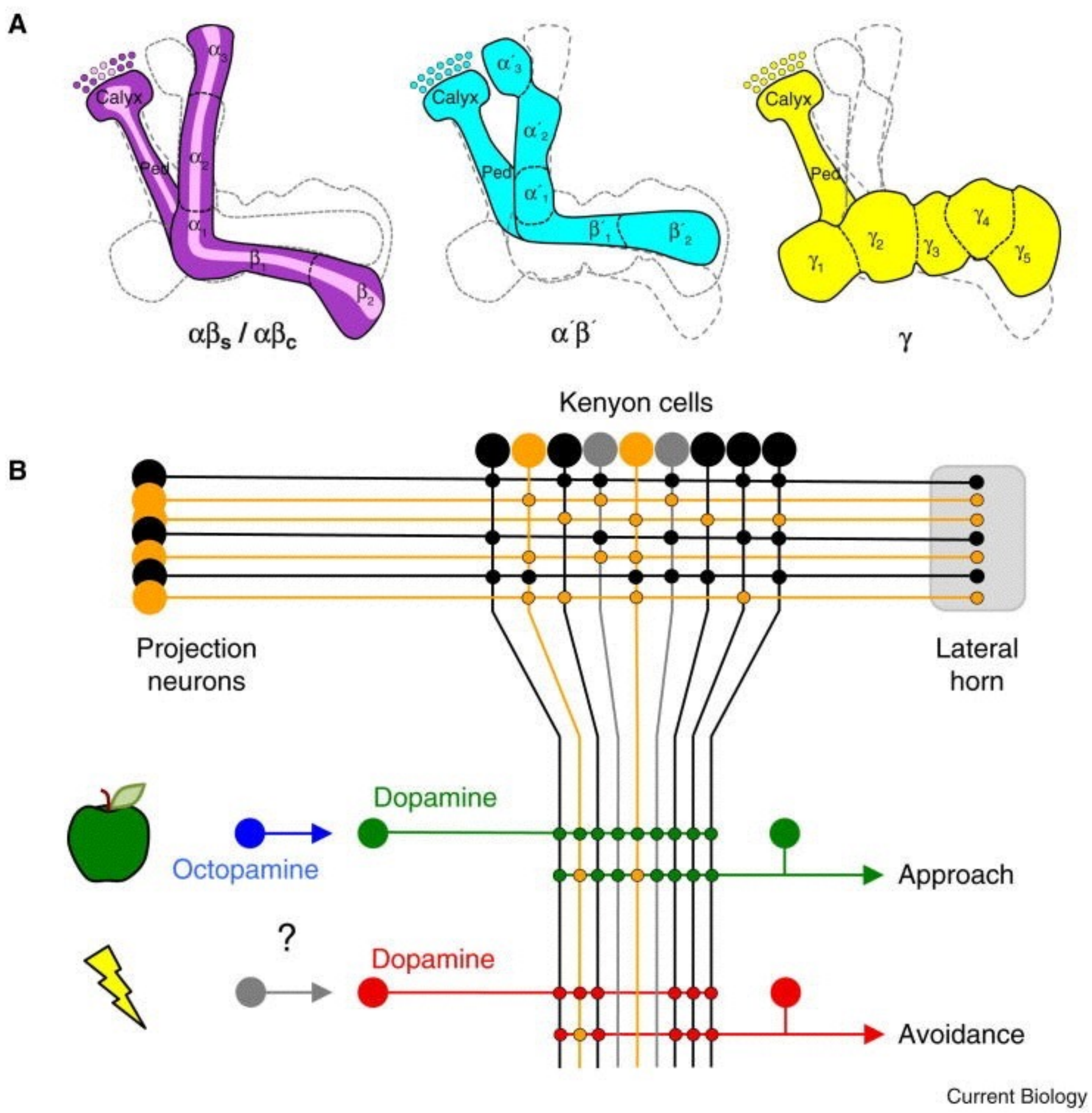


* Image credit [Fruit fly]: NASA

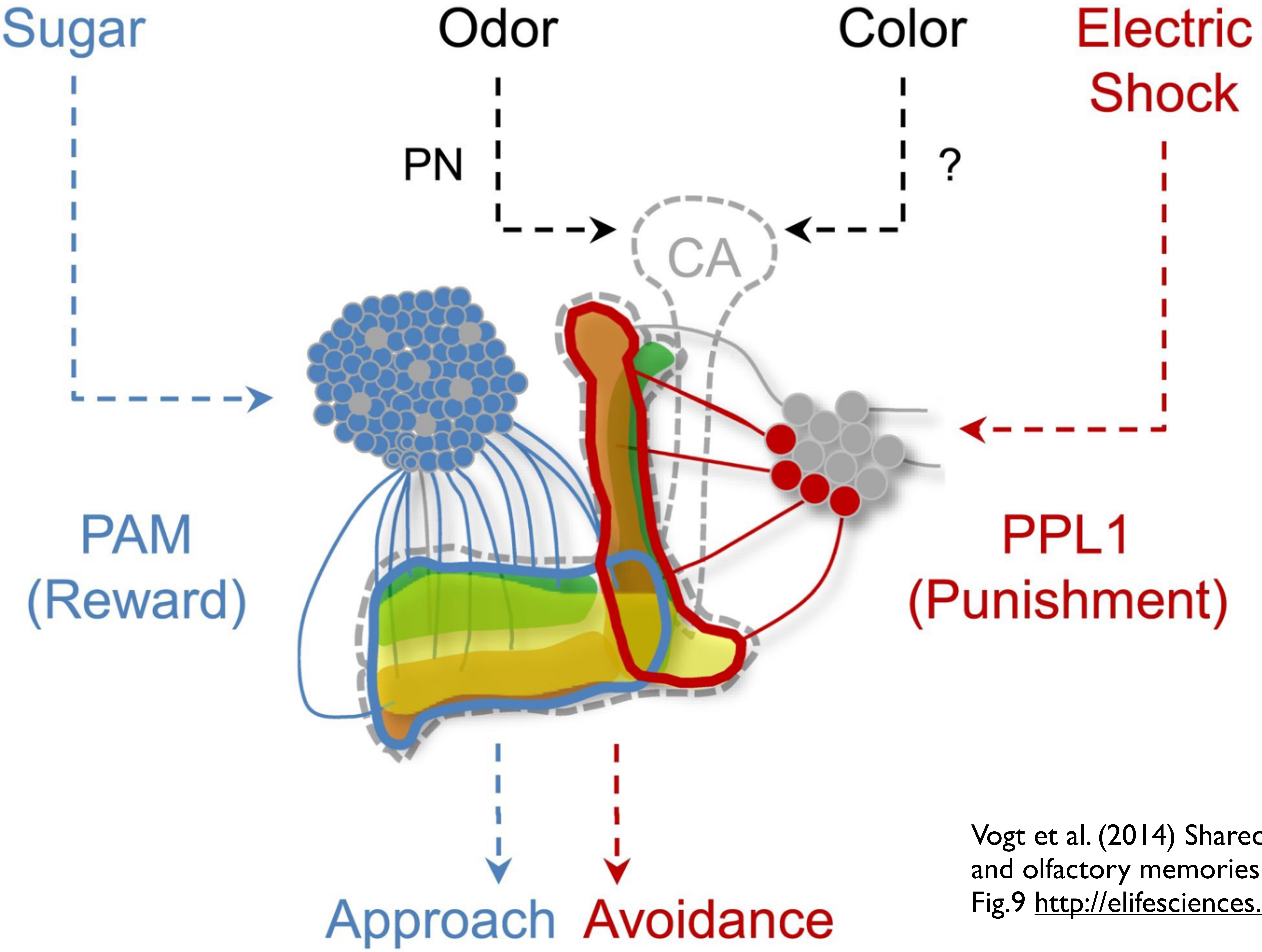
Olfactory memory

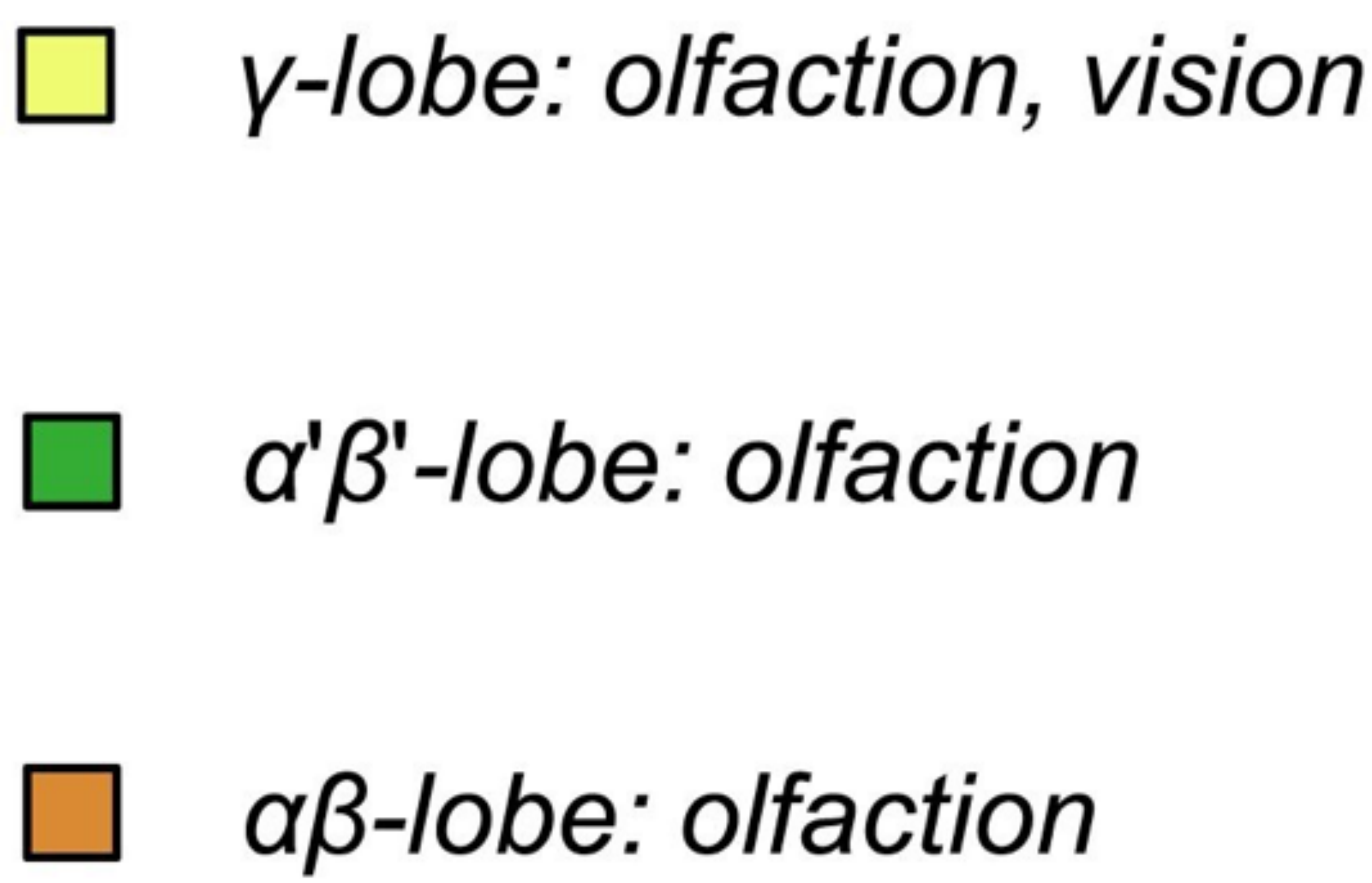




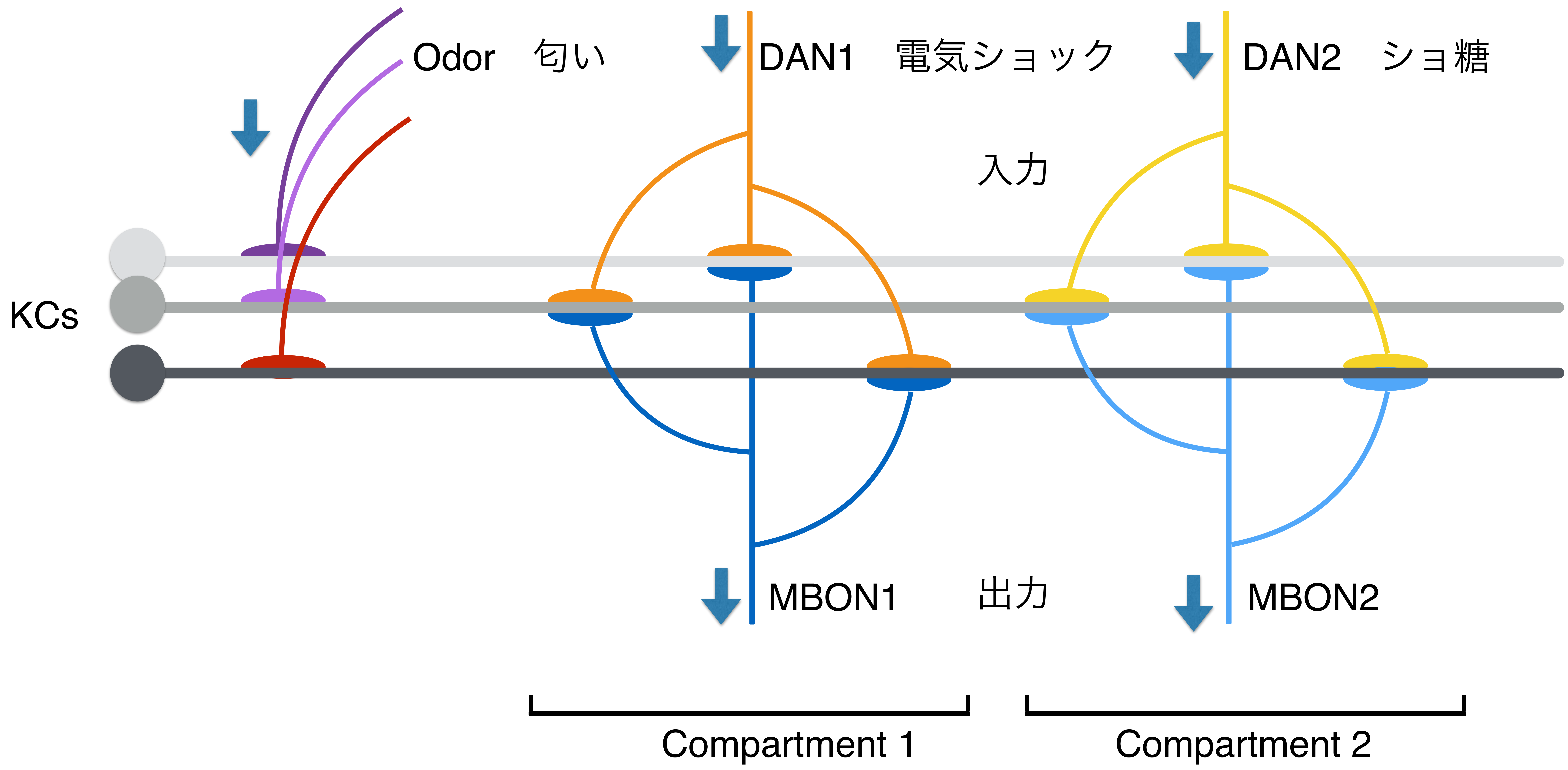


Perisse et al. (2013) Shocking Revelations and Saccharin Sweetness in the Study of *Drosophila* Olfactory Memory, *Current Biology* 23(17): R752–R763, p.R755 Fig.2. http://www.sciencedirect.com/science/article/pii/S0960982213009214

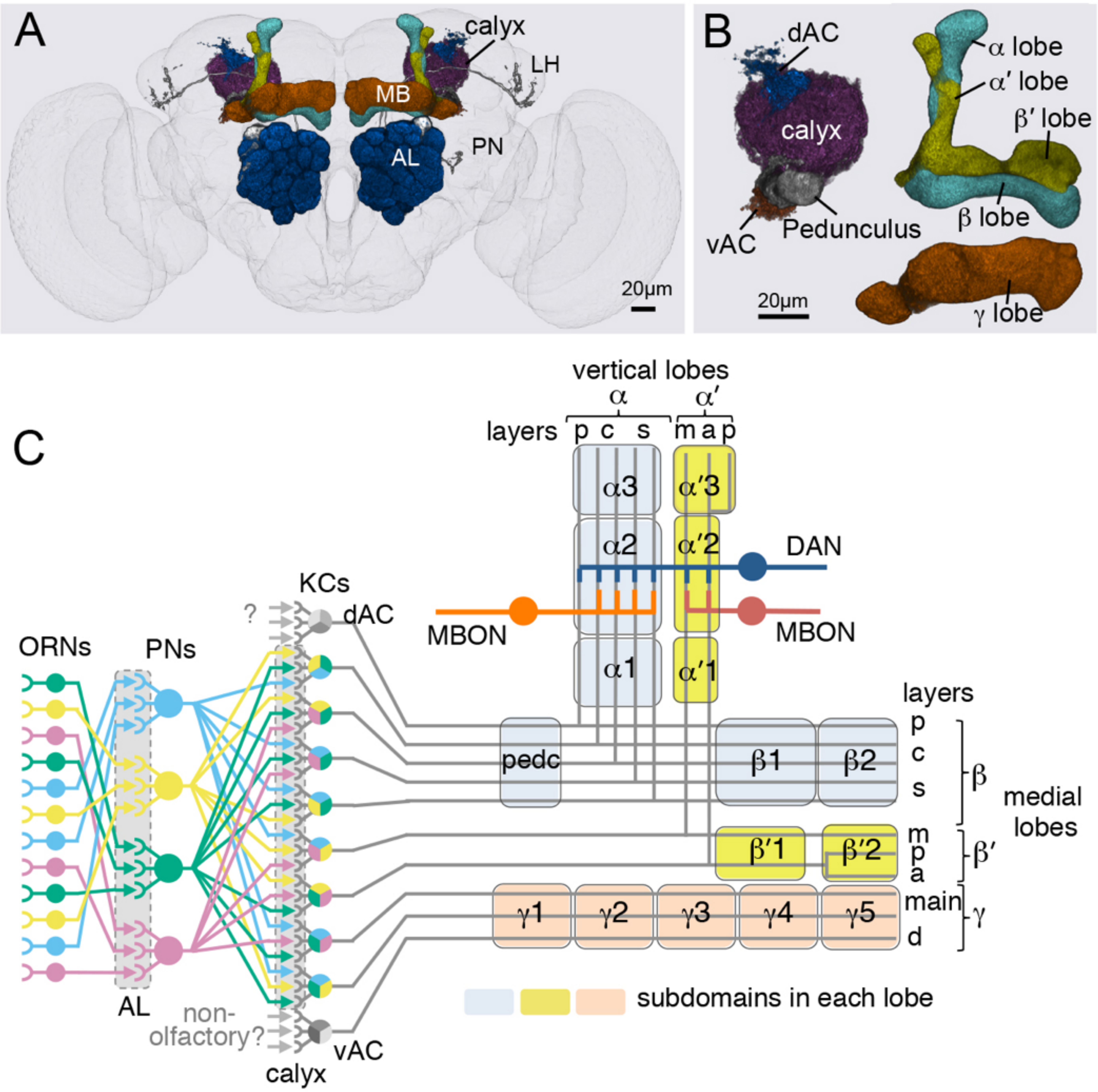




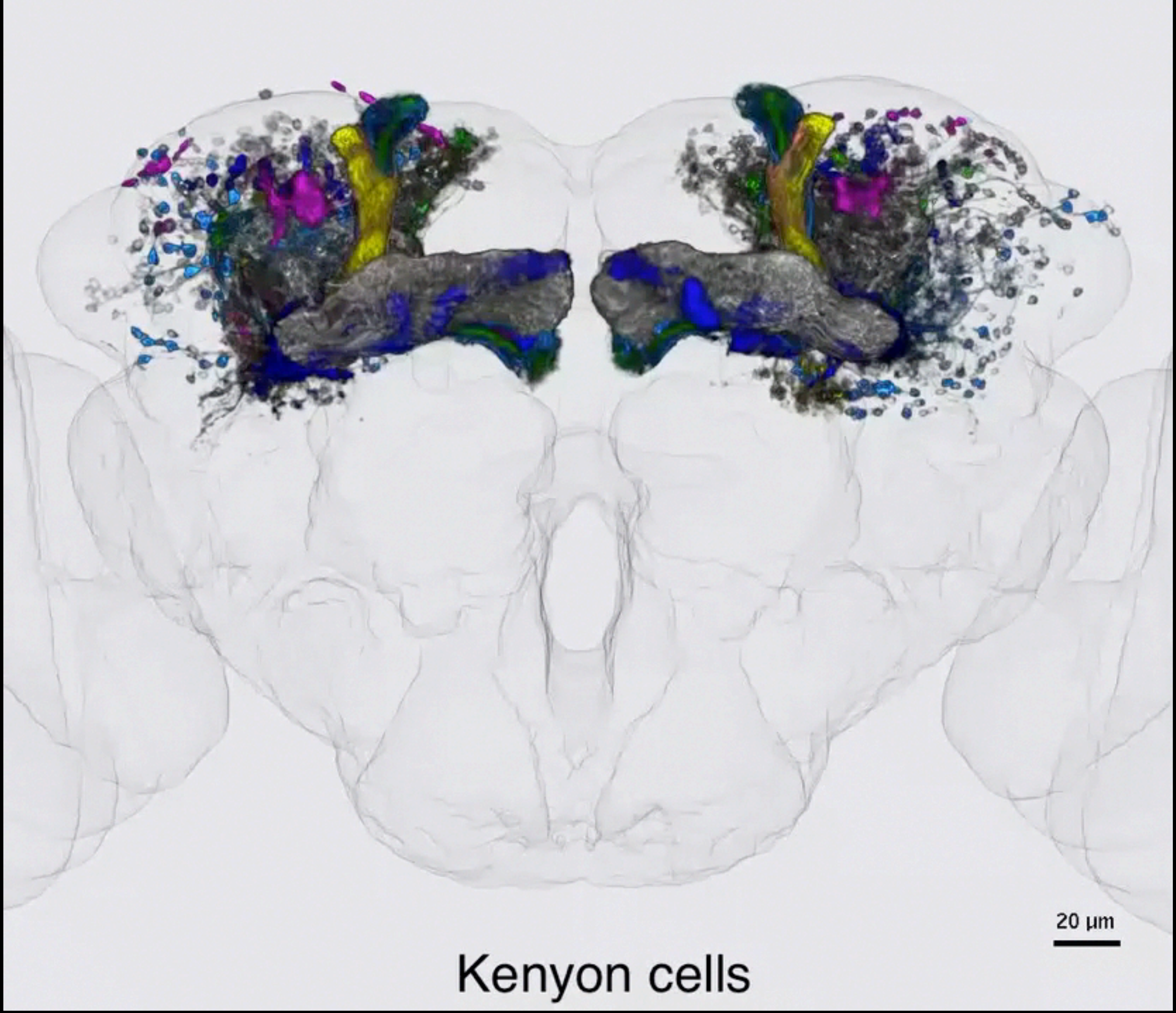
Vogt et al. (2014) Shared mushroom body circuits underlie visual and olfactory memories in *Drosophila*, *eLife* 2014;3:e02395, p.14 Fig.9 http://elifesciences.org/content/3/e02395


Odor　匂い
DAN1　電気ショック
DAN2　ショ糖
入力
KCs
MBON1
出力
MBON2
Compartment 1
Compartment 2

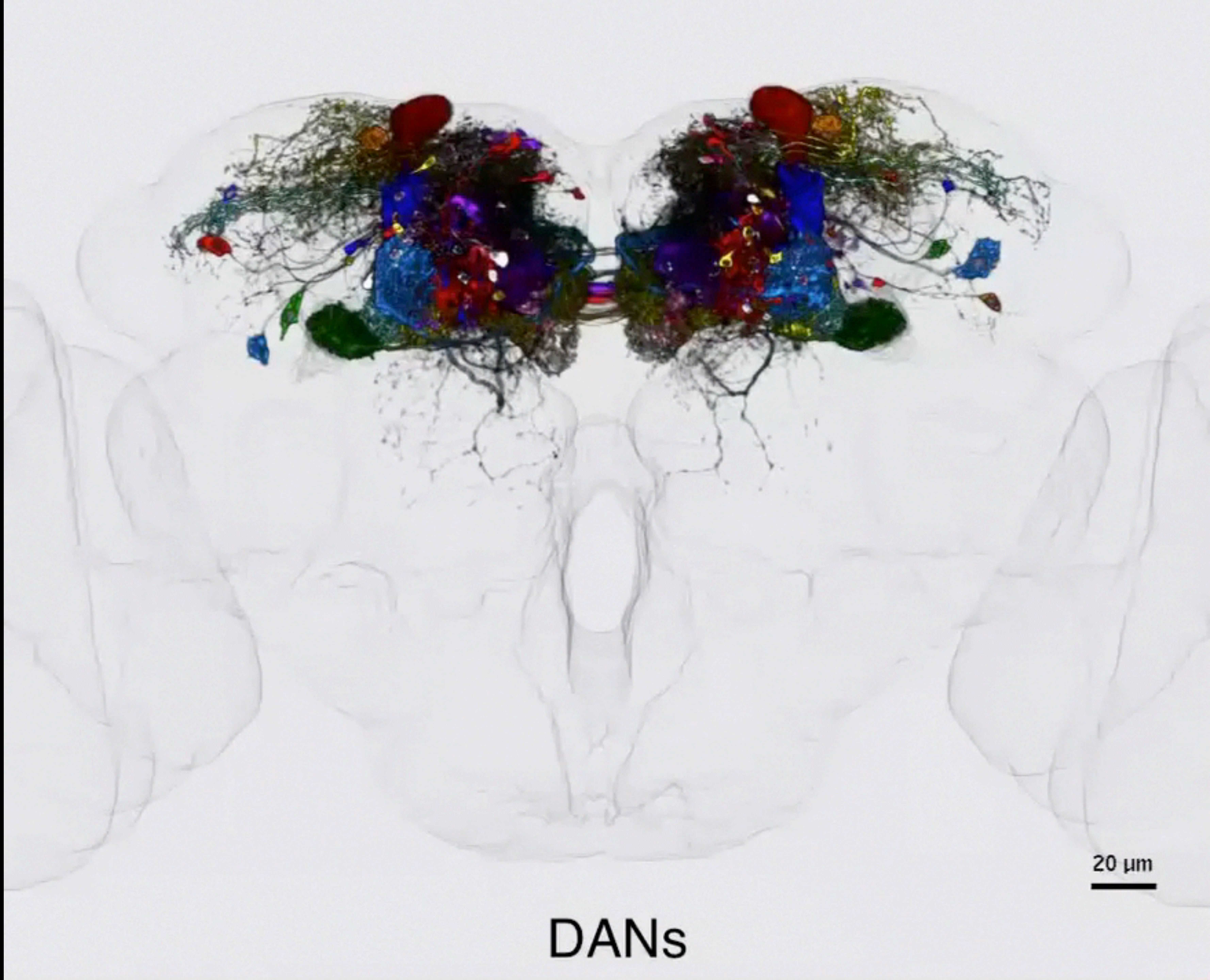
Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.22 Fig.10 http://elifesciences.org/content/3/e04577



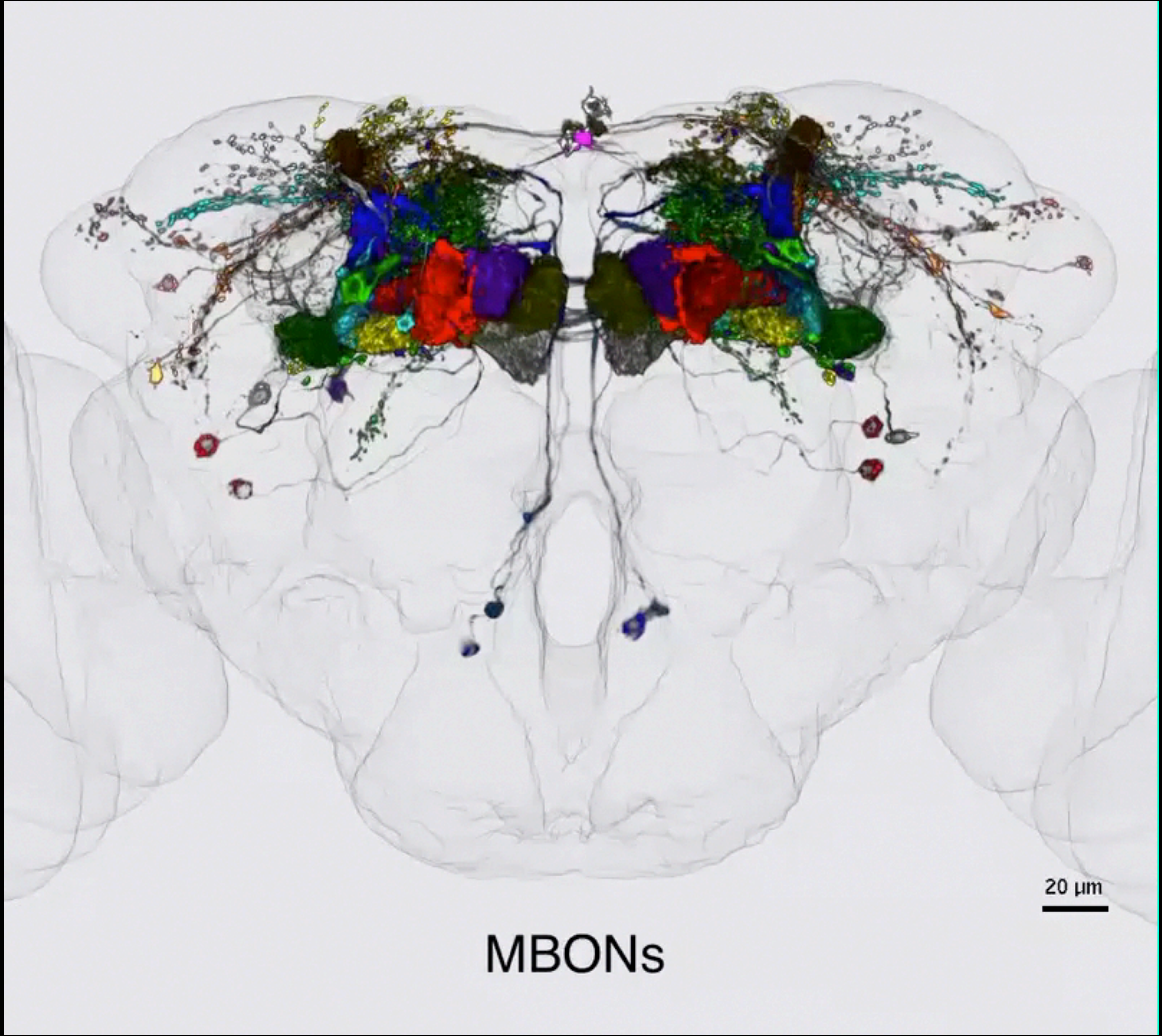
Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.3 Fig.1 http://elifesciences.org/content/3/e04577



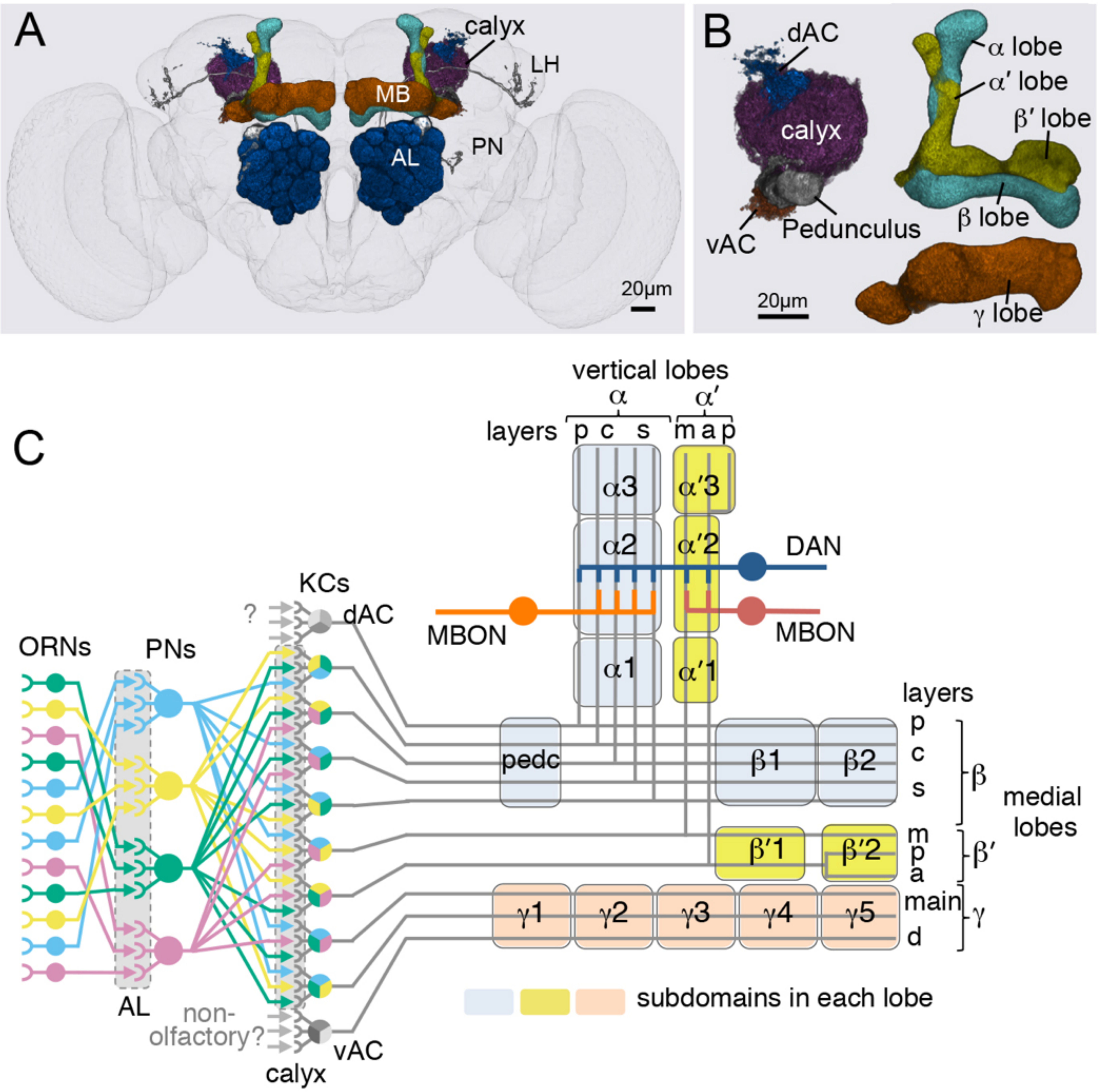
Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.7 Video 2 http://elifesciences.org/content/3/e04577



Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.8 Video 4 http://elifesciences.org/content/3/e04577



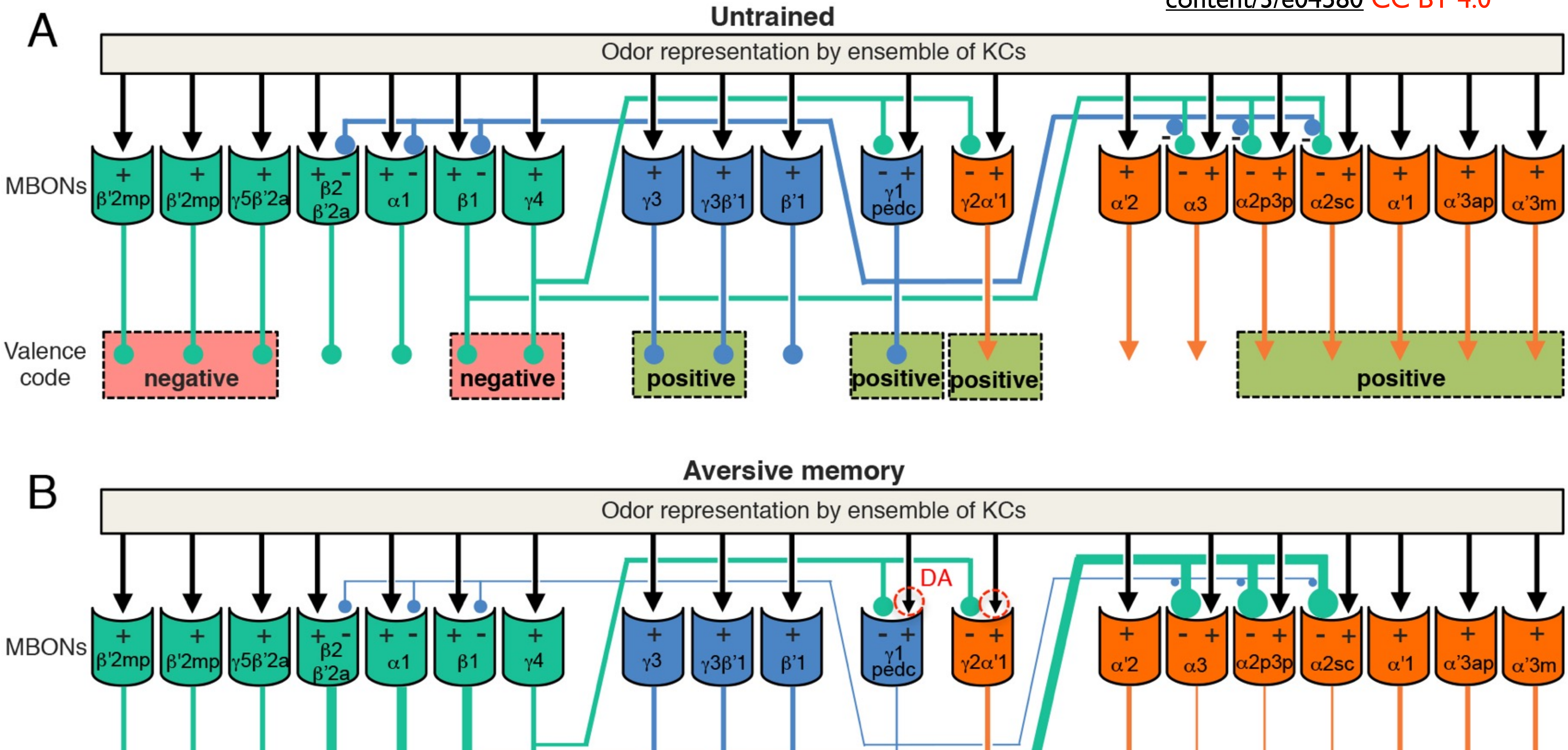
Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.8 Video 3 http://elifesciences.org/content/3/e04577



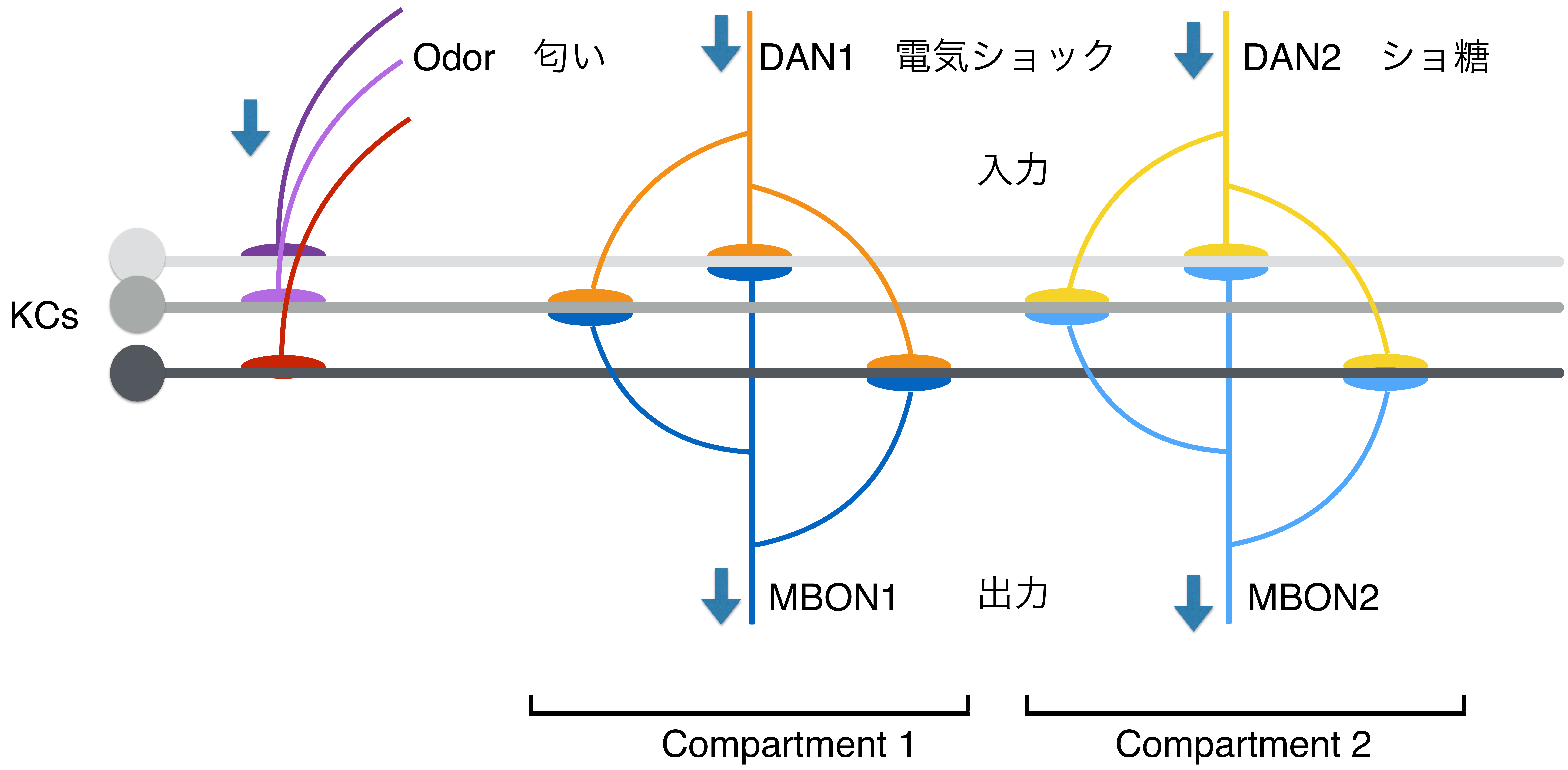
Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.3 Fig.1 http://elifesciences.org/content/3/e04577

Associative logic by Aso

Aso et al. (2014) Mushroom body output neurons encode valence and guide memory-based action selection in *Drosophila*, *eLife* 2014;3:e04580, p.25 Fig.14(A and B) http://elifesciences.org/content/3/e04580

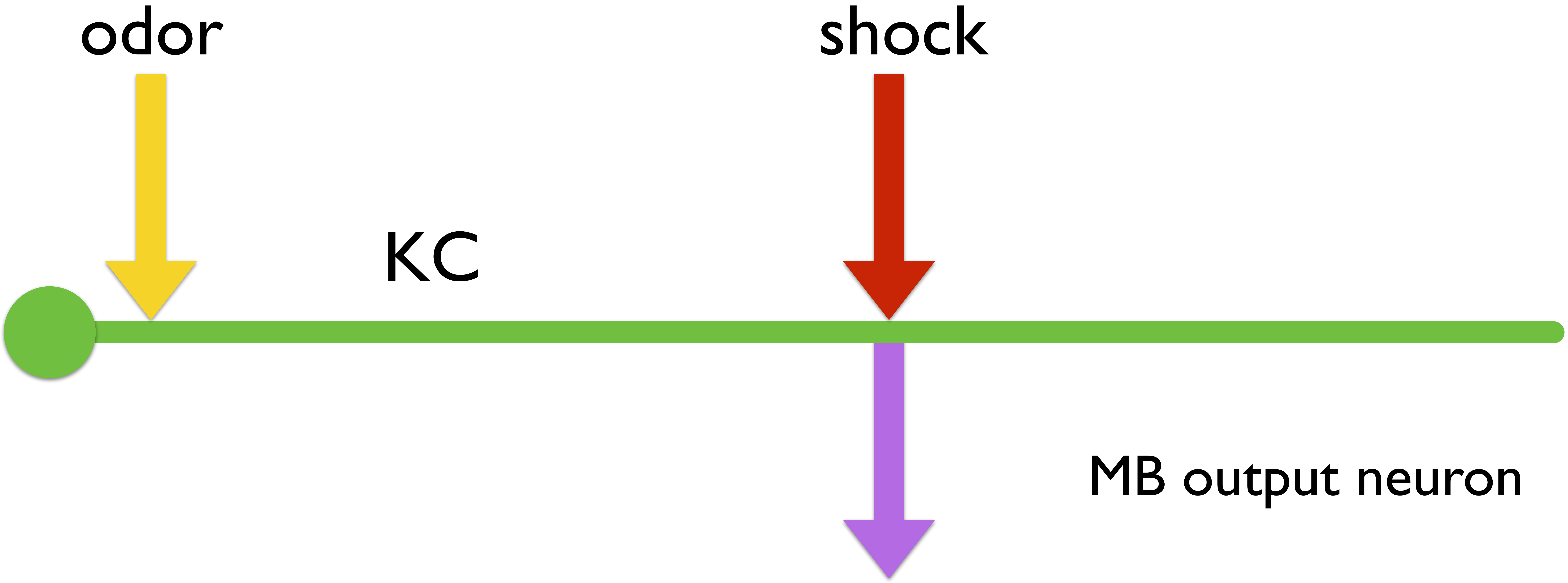



B
Aversive memory
Odor representation by ensemble of KCs
DA
MBONs
+ β'2mp
+ β'2mp
+ γ5β'2a
+ - β2 β'2a
+ - α1
+ - β1
+ γ4
+ γ3
+ γ3β'1
+ β'1
- + γ1 pedc
- + γ2α'1
+ α'2
- + α3
- + α2p3p
- + α2sc
+ α'1
+ α'3ap
+ α'3m
Valence code
negative
negative
positive
positive
positive
positive
C
Appetitive memory
Odor representation by ensemble of KCs
DA
MBONs
Valence code
negative
negative
positive
positive
positive
positive



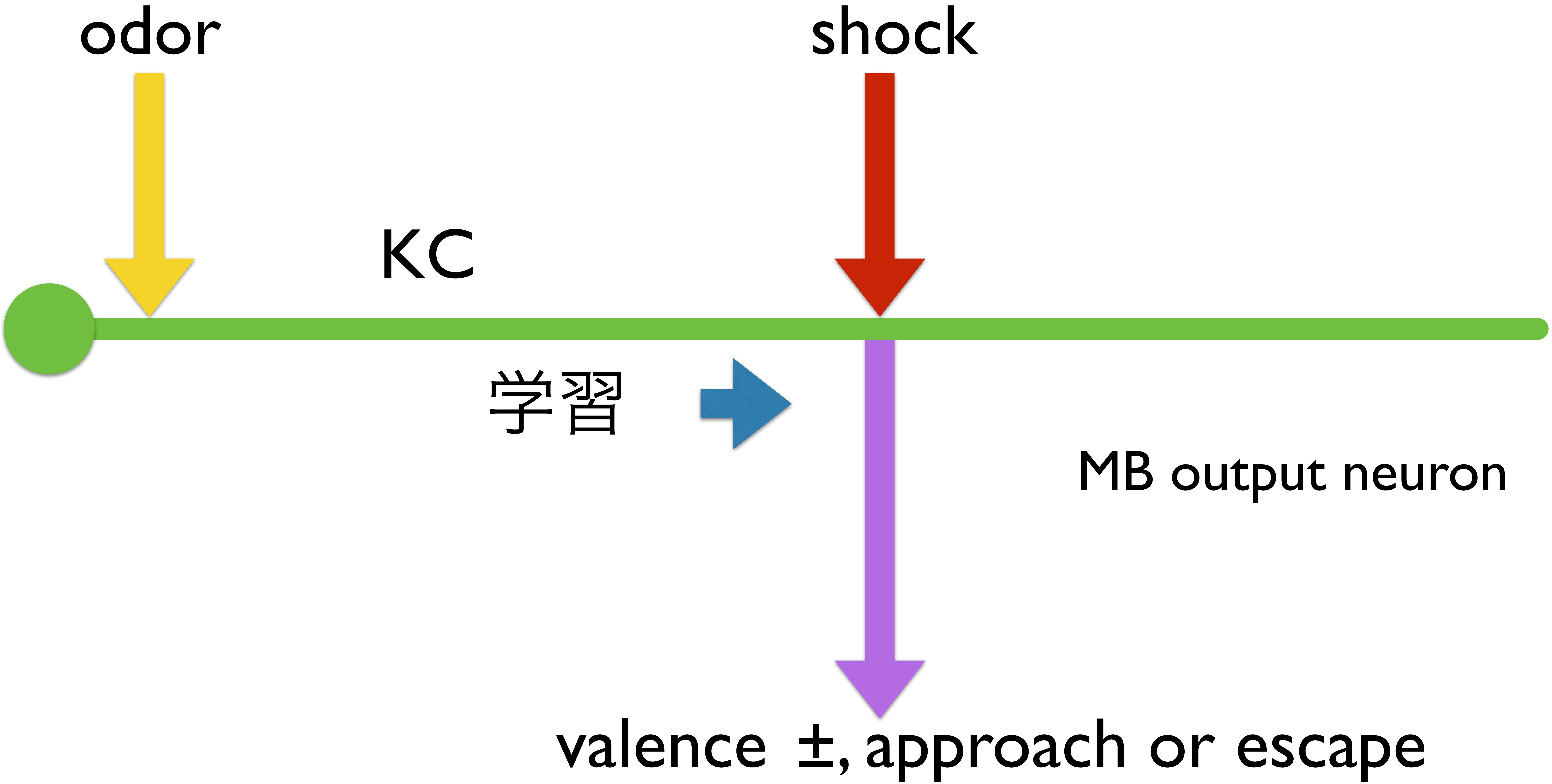
Odor　匂い
DAN1　電気ショック
DAN2　ショ糖
入力
KCs
MBON1
出力
MBON2
Compartment 1
Compartment 2

回路の模式図

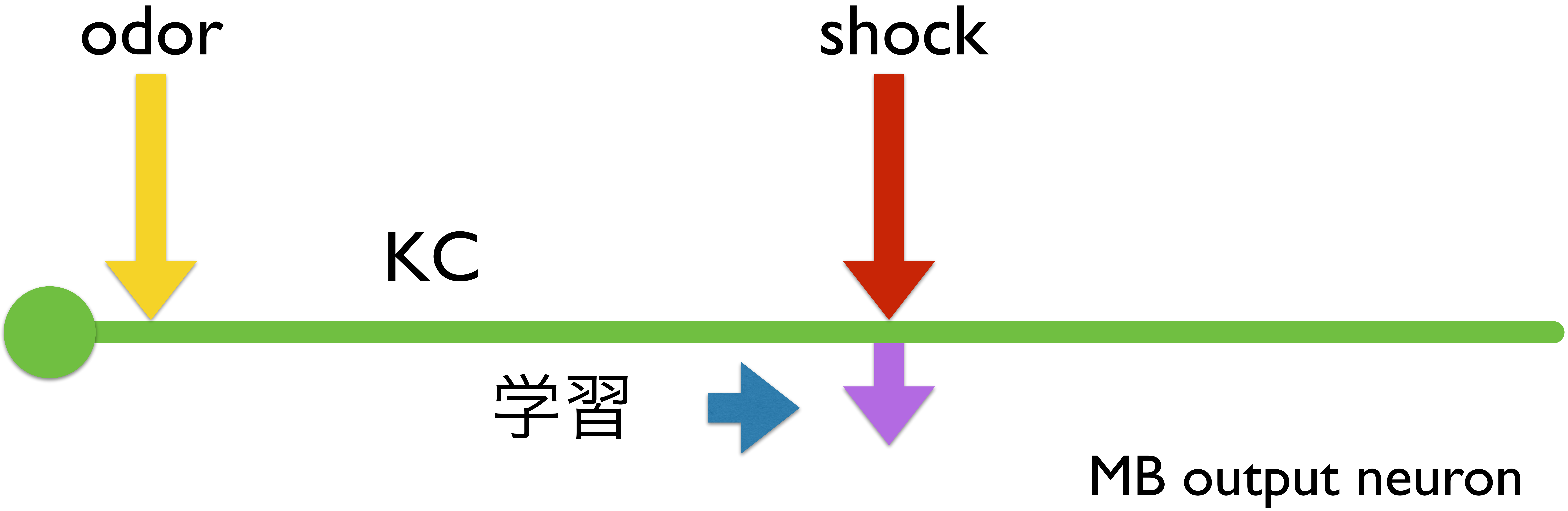


valence ±, approach or escape

回路の模式図

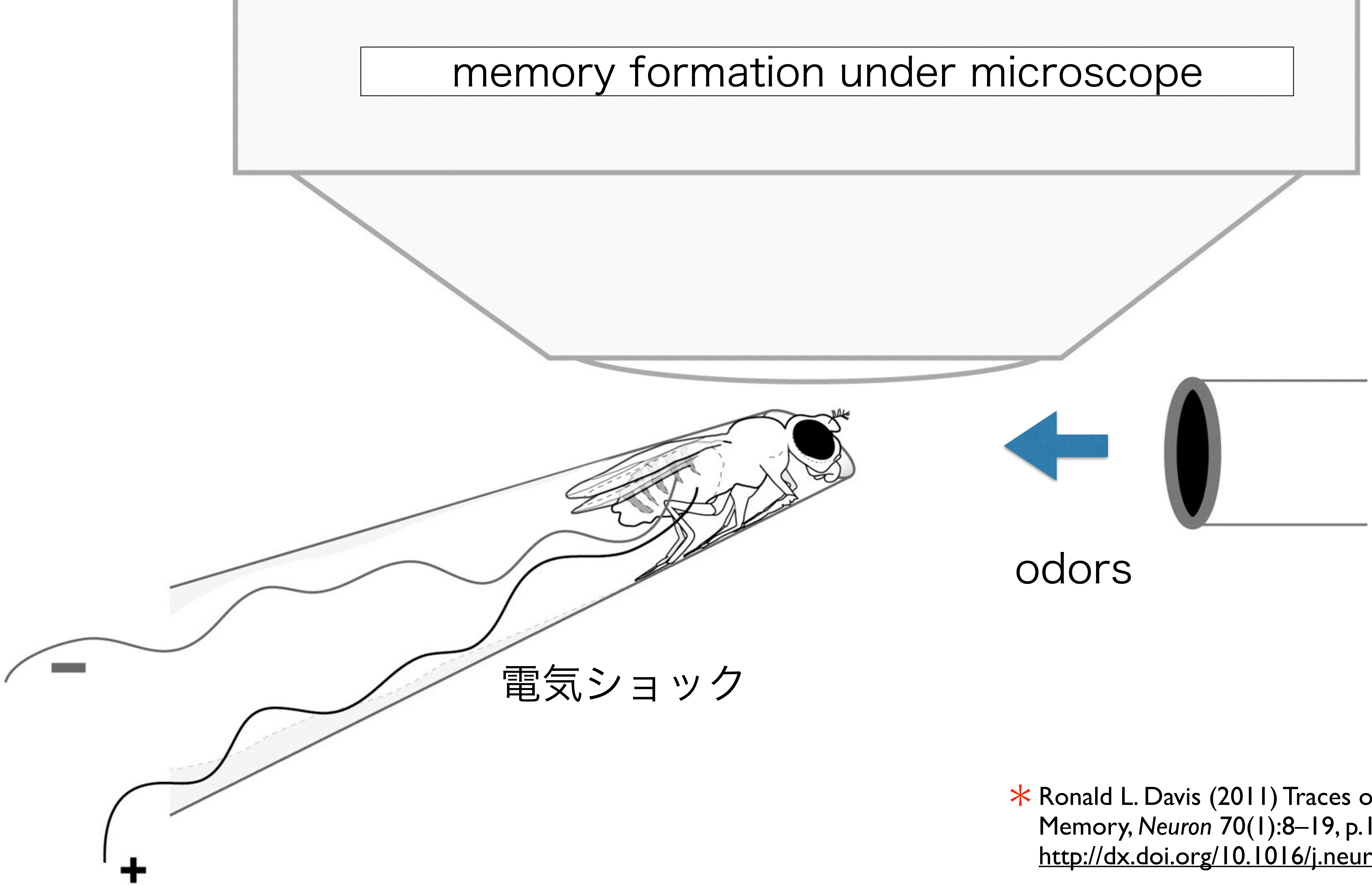

odor
shock
KC
学習
MB output neuron
valence ±, approach or escape

回路の模式図



valence ±, approach or escape

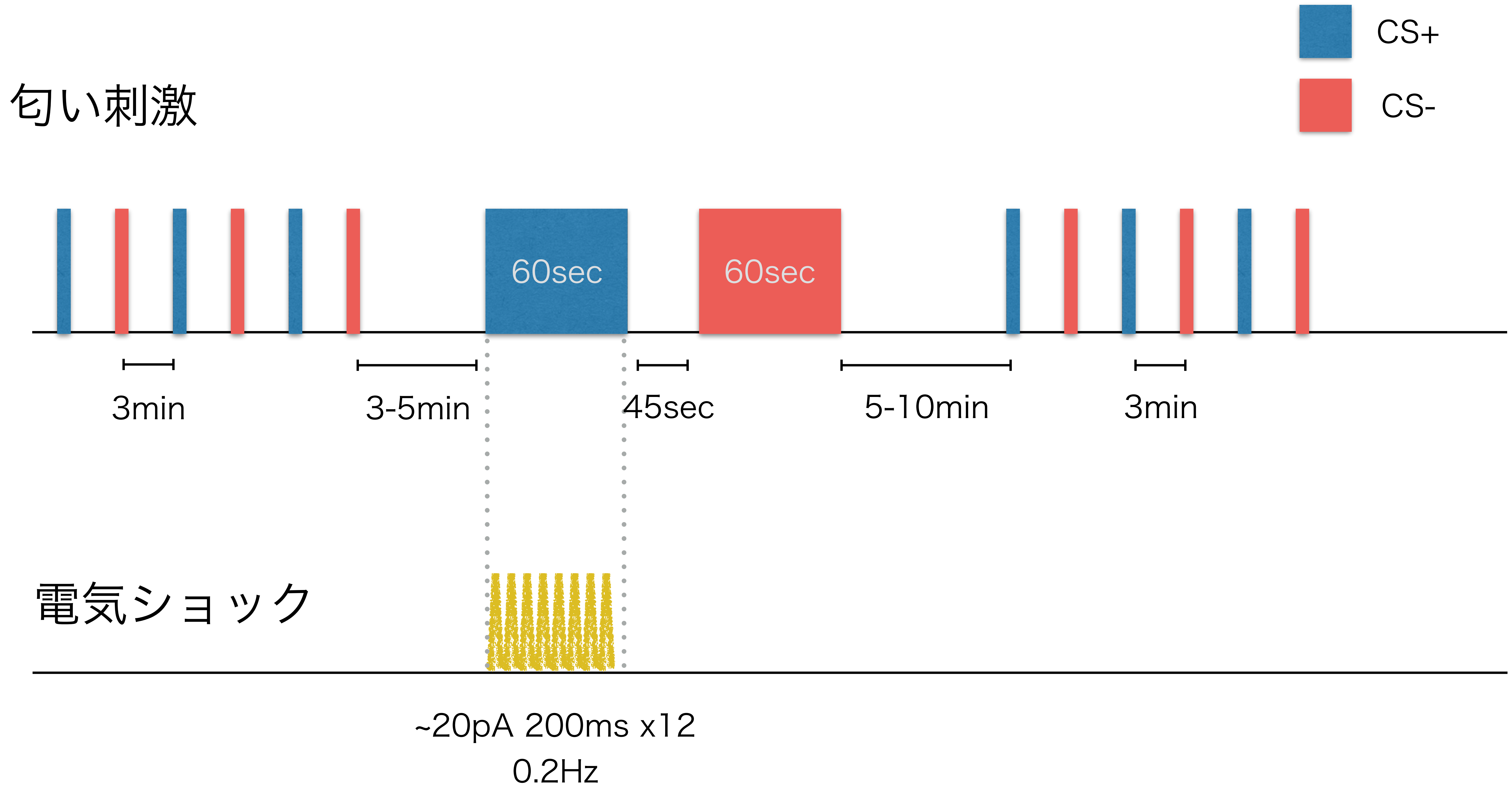
memory formation under microscope



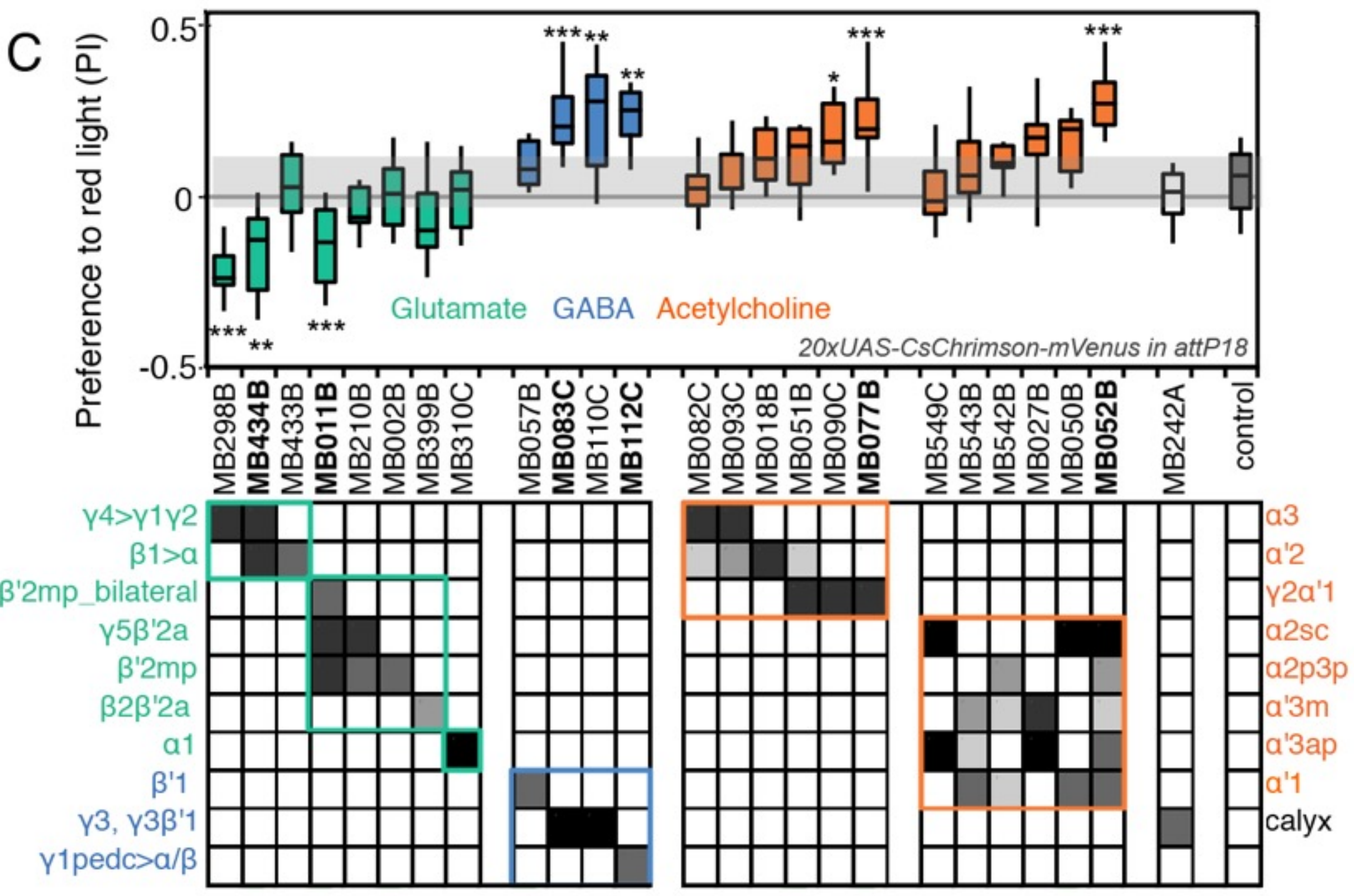
* Ronald L. Davis (2011) Traces of *Drosophila* Memory, *Neuron* 70(1):8–19, p.11 Fig.3.
http://dx.doi.org/10.1016/j.neuron.2011.03.012

条件付け

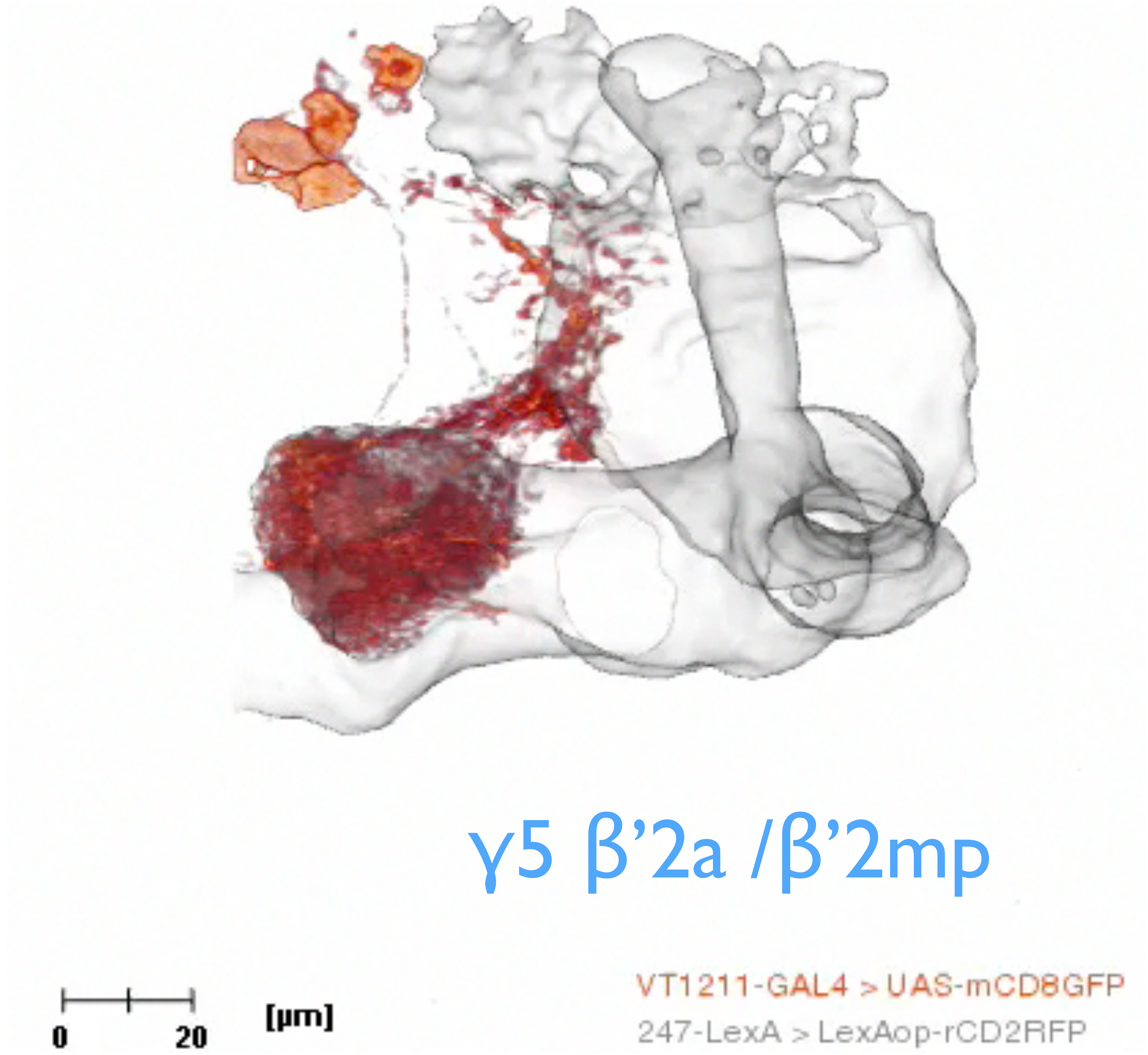
VT1211-Gal4>UAS-GCaMP5, mb247-dsRed



＊廣井誠氏提供



Aso et al. (2014) Mushroom body output neurons encode valence and guide memory-based action selection in *Drosophila*, *eLife* 2014;3:e04580, p.6 Fig.2C
http://elifesciences.org/content/3/e04580 CC BY 4.0

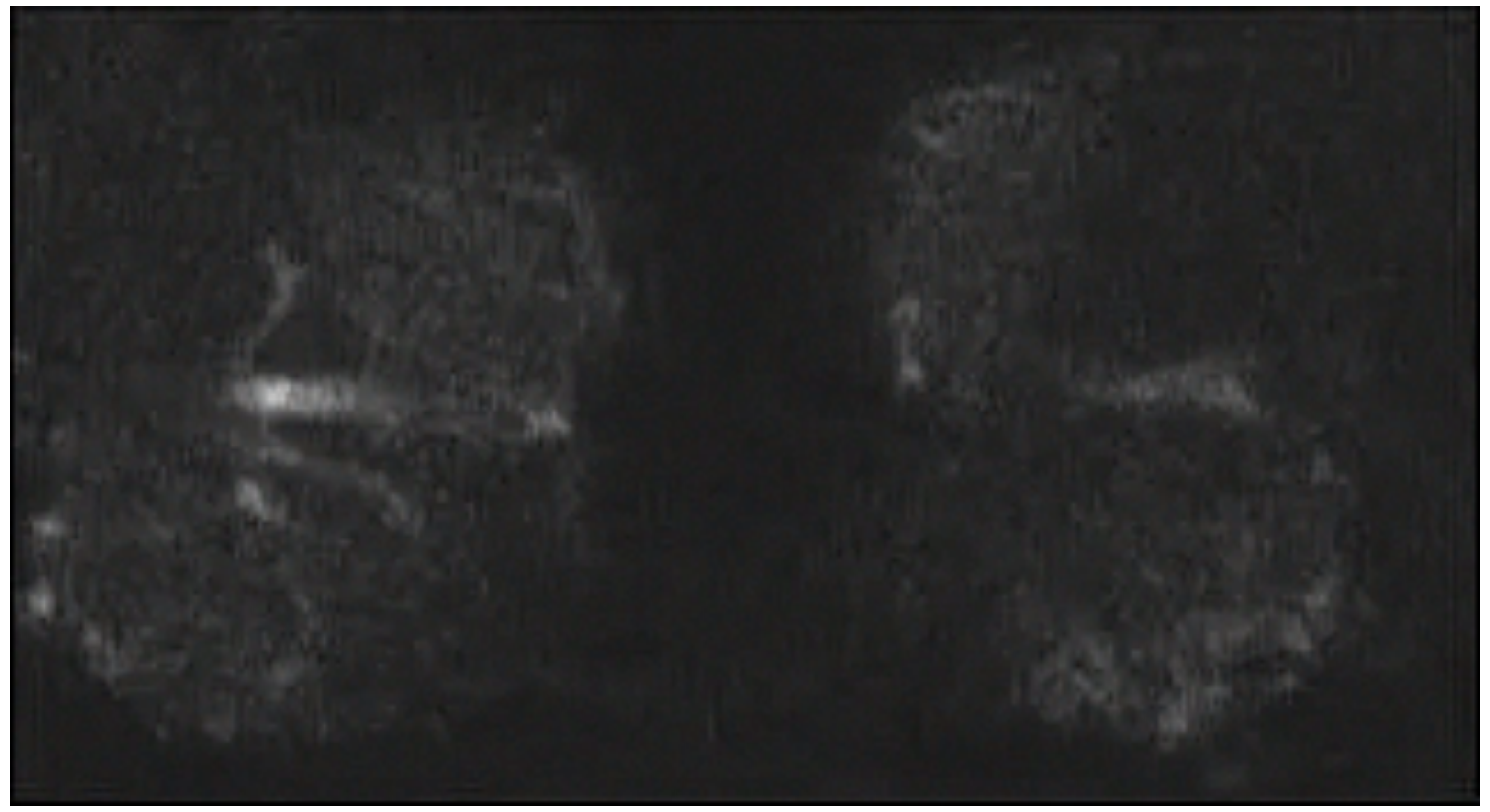


Oswald et al. (2015) Activity of Defined Mushroom Body Output Neurons Underlies Learned Olfactory Behavior in *Drosophila*, *Neuron* 86(2):417–427, Supplement Movie S2. http://www.cell.com/neuron/abstract/S0896-6273%2815%2900221-4 ©2015 The Authors CC BY 4.0

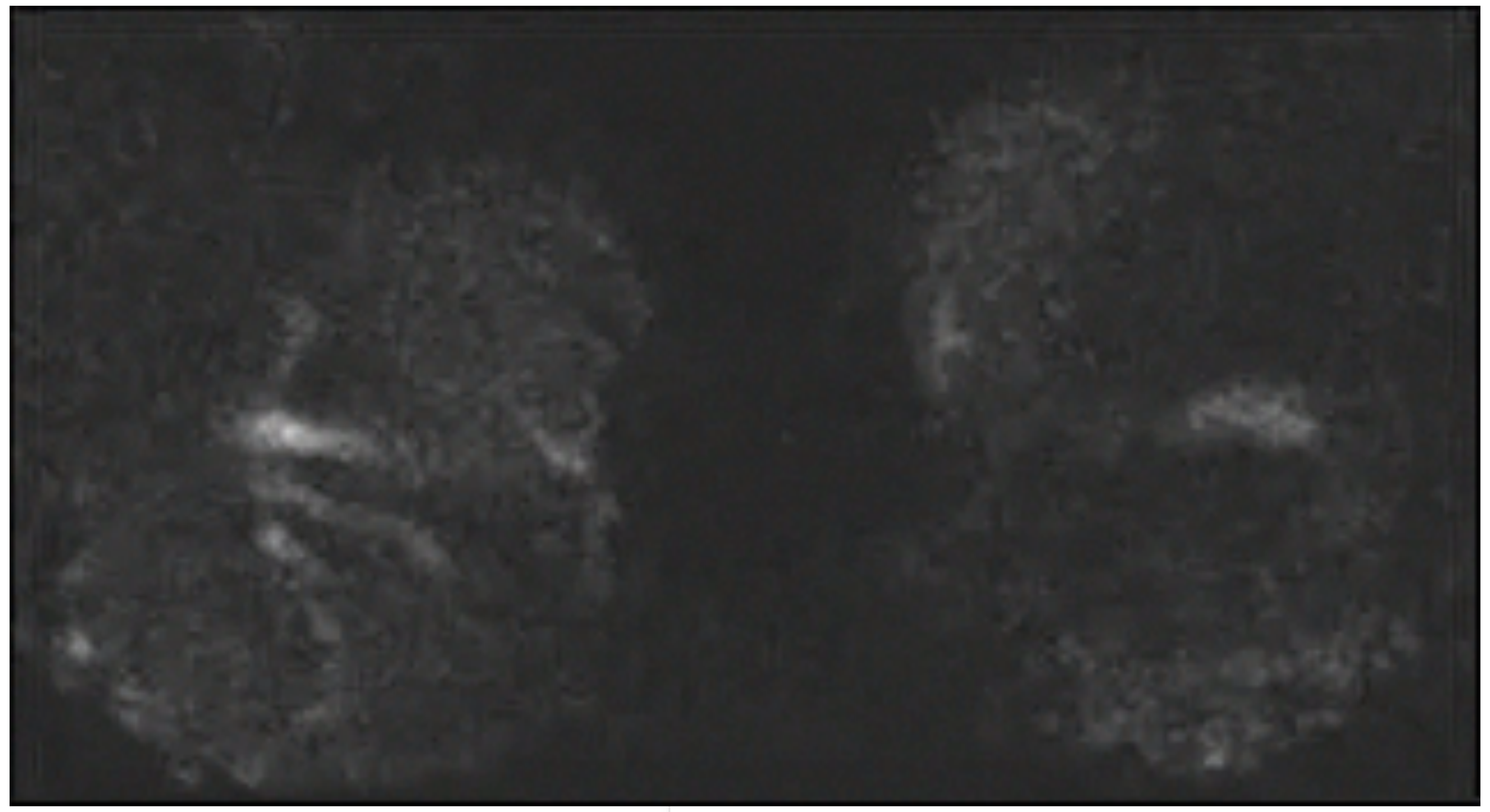
Under the microscope

β'2

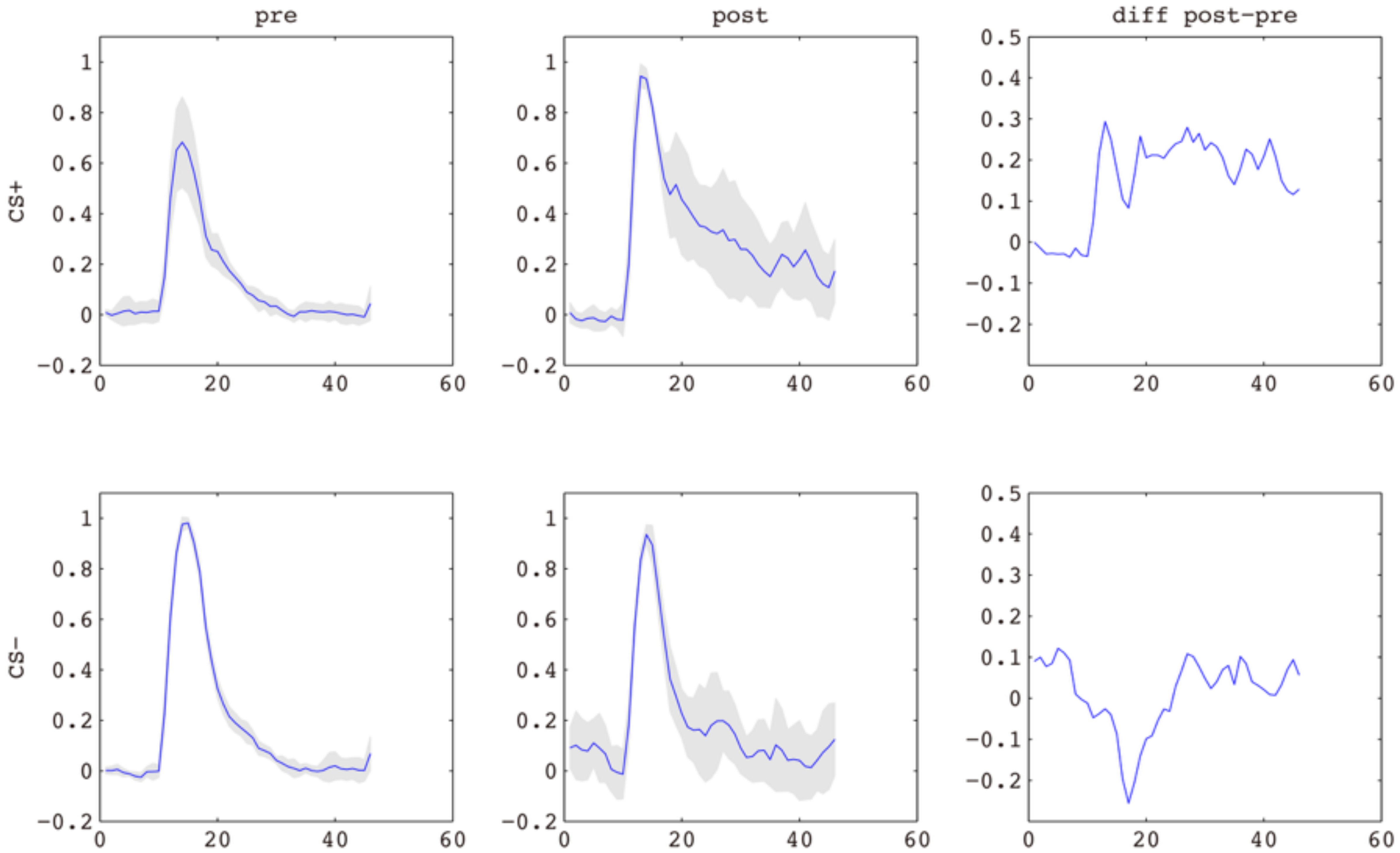
学習前

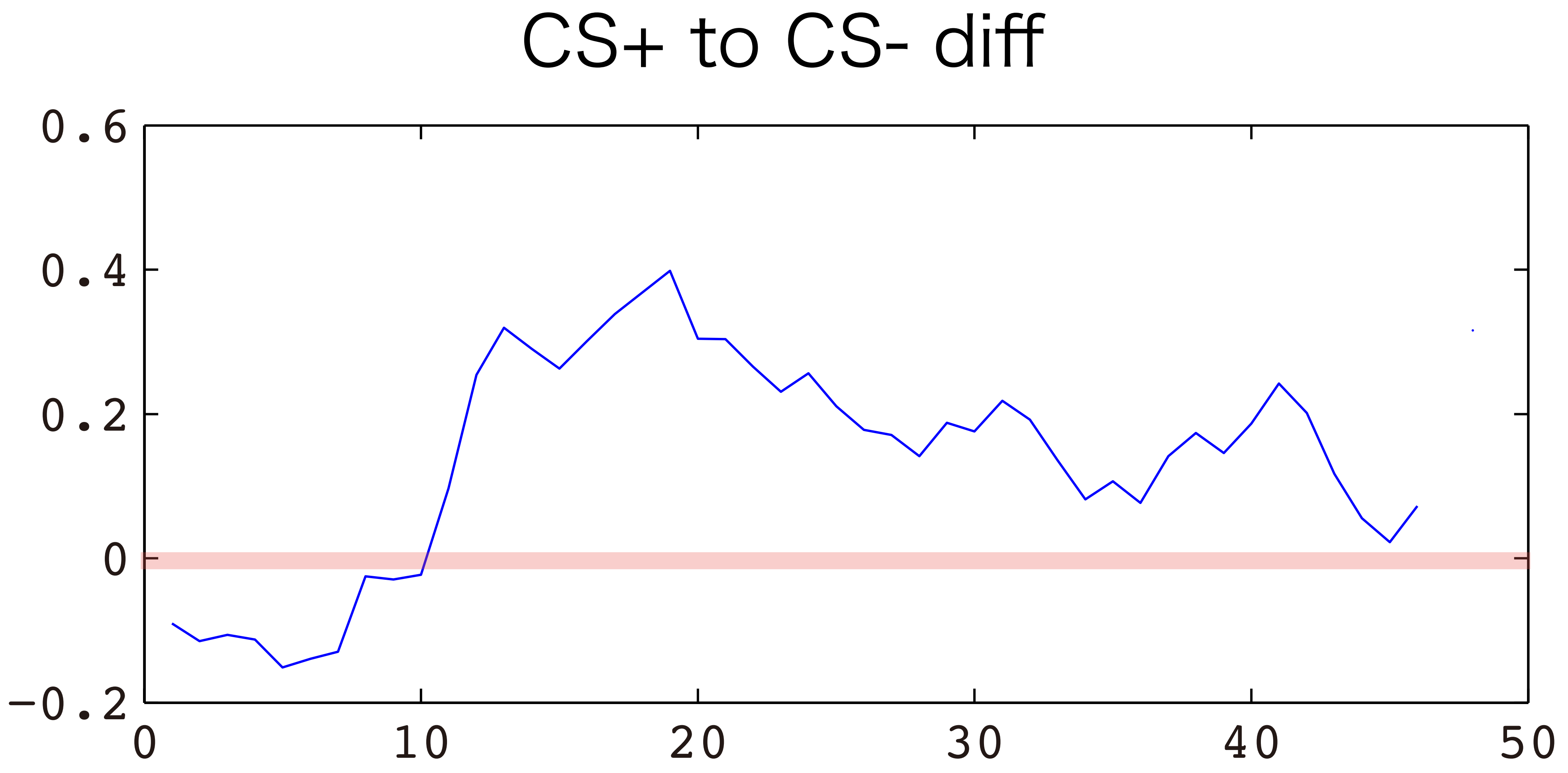


学習後

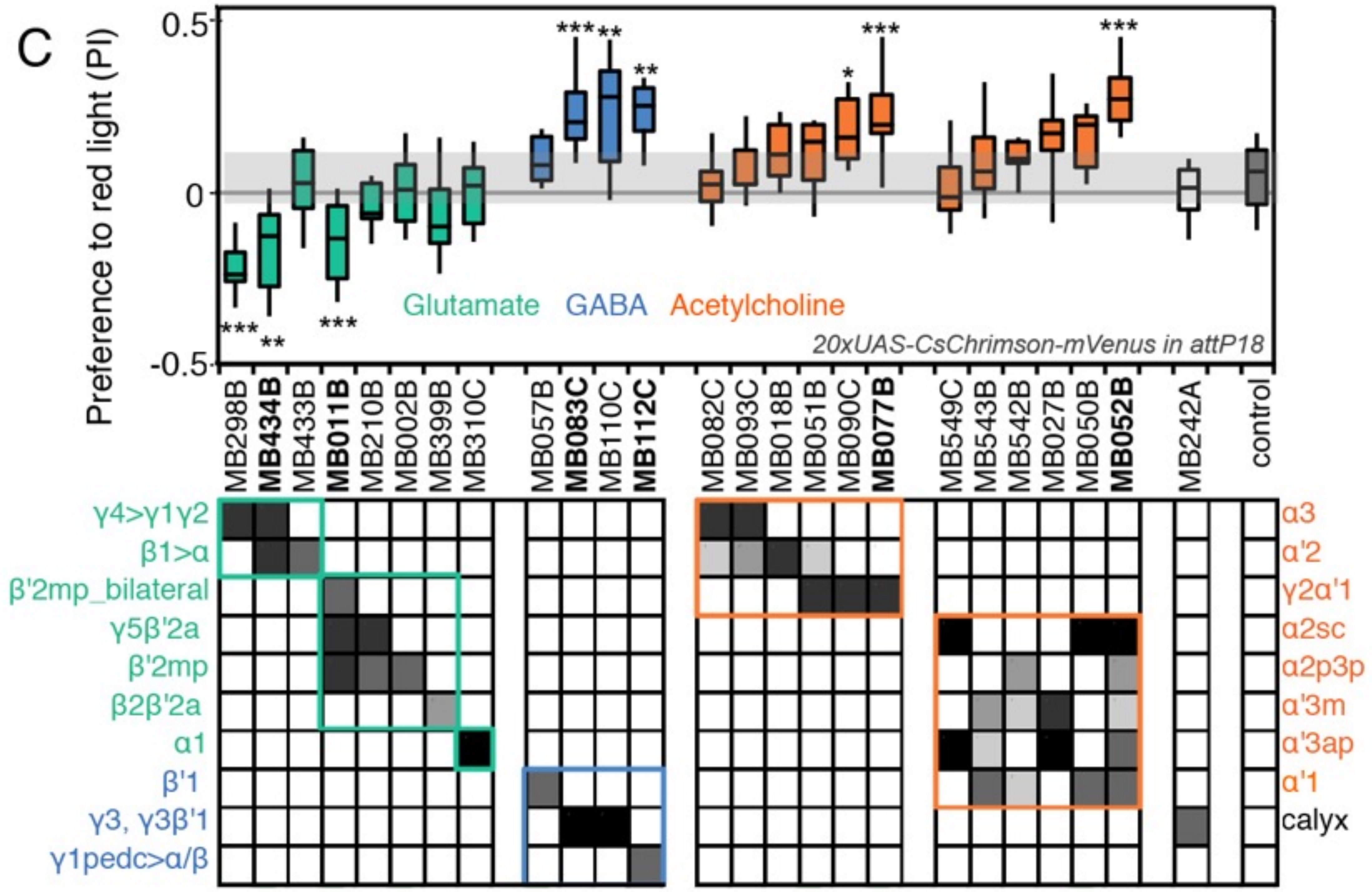


MCH Oct+

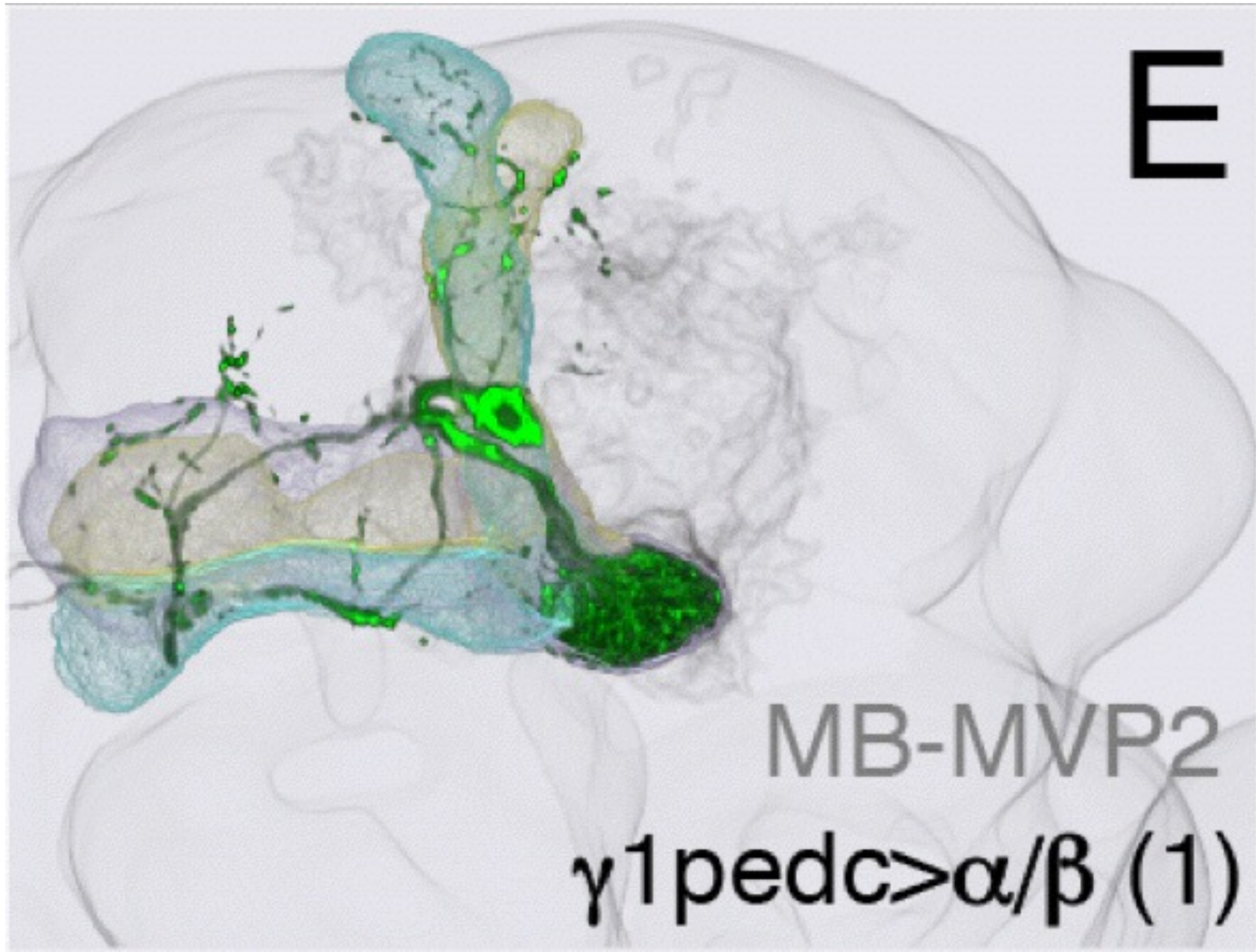




＊廣井誠氏提供



Aso et al. (2014) Mushroom body output neurons encode valence and guide memory-based action selection in *Drosophila*, *eLife* 2014;3:e04580, p.6 Fig.2C
http://elifesciences.org/content/3/e04580 CC BY 4.0

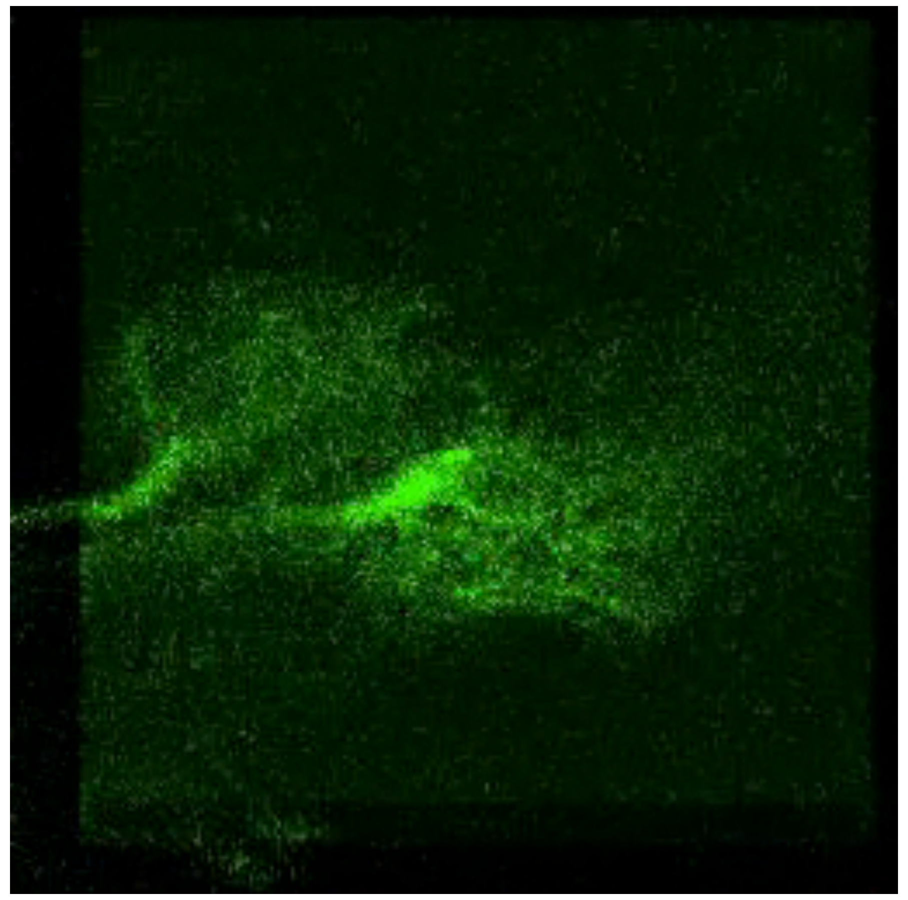


GABA

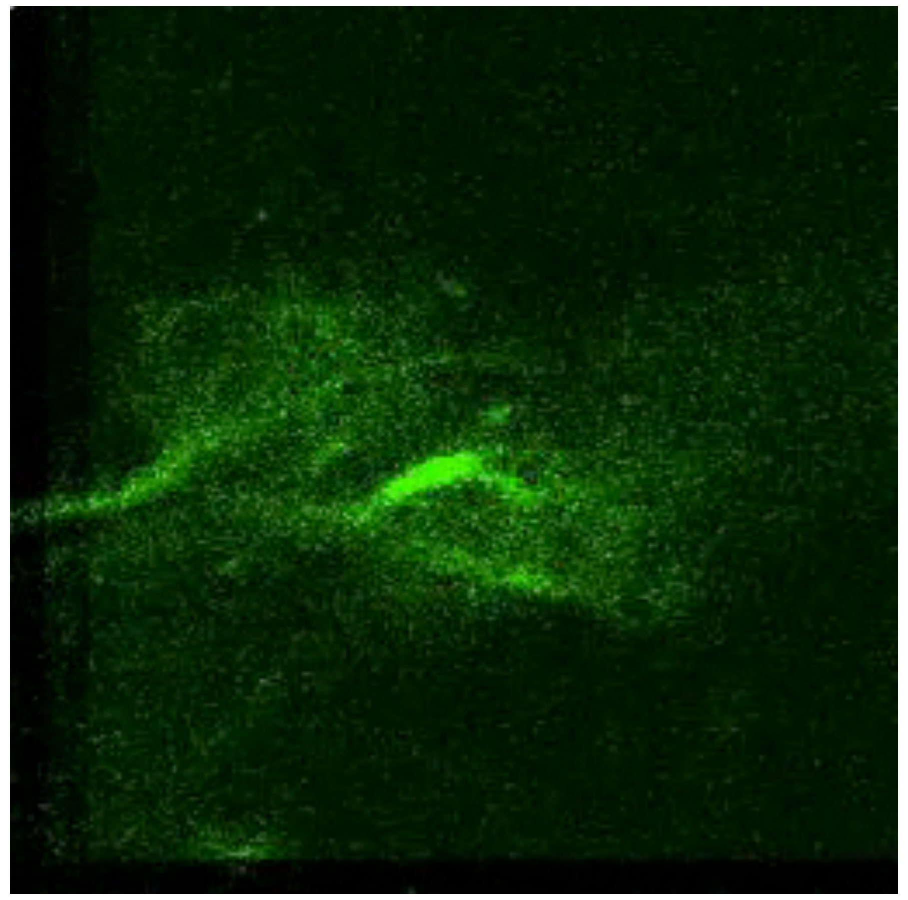
Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.28 Fig.15E http://elifesciences.org/content/3/e04577 CC BY 4.0

γl pedc

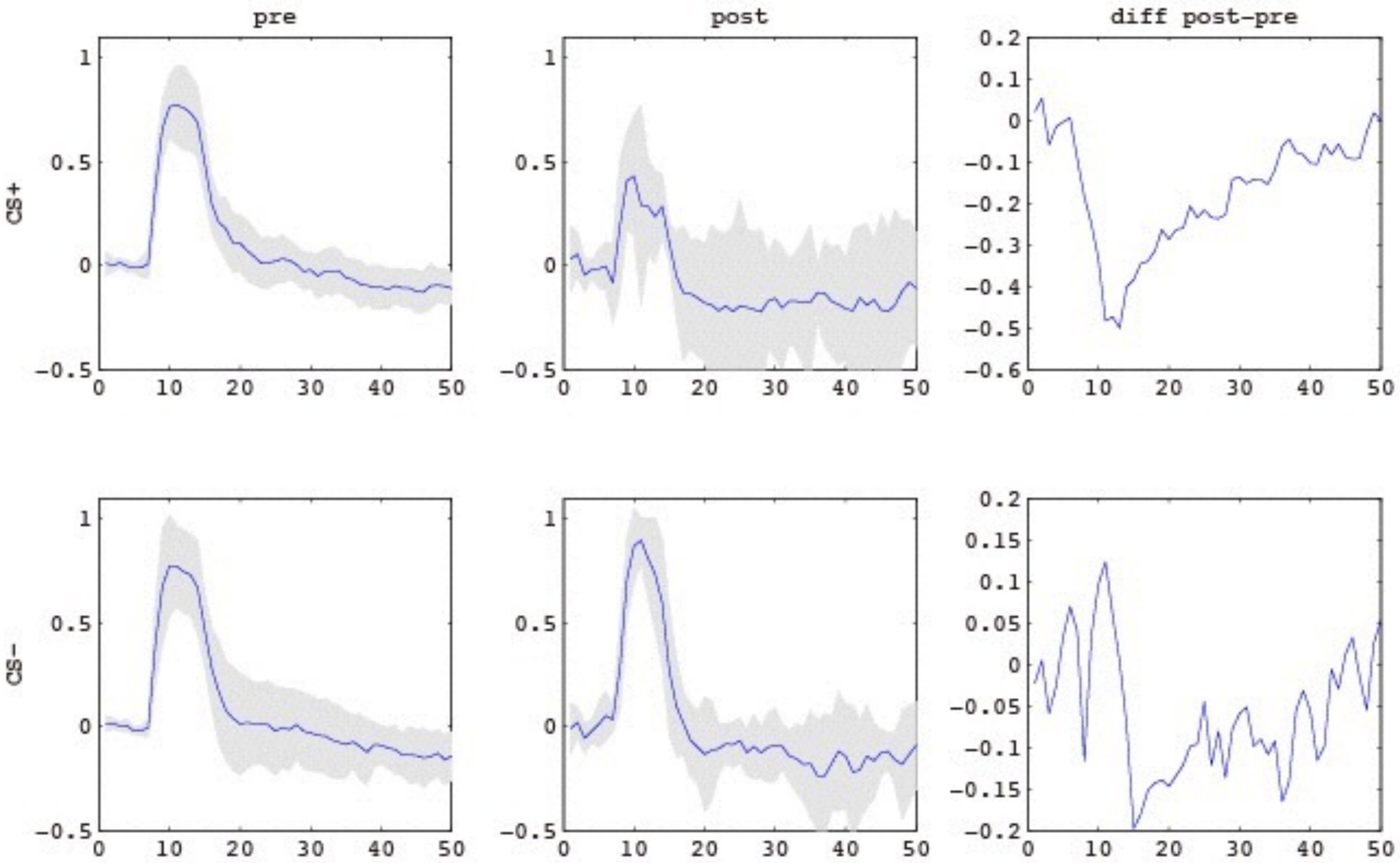
学習前



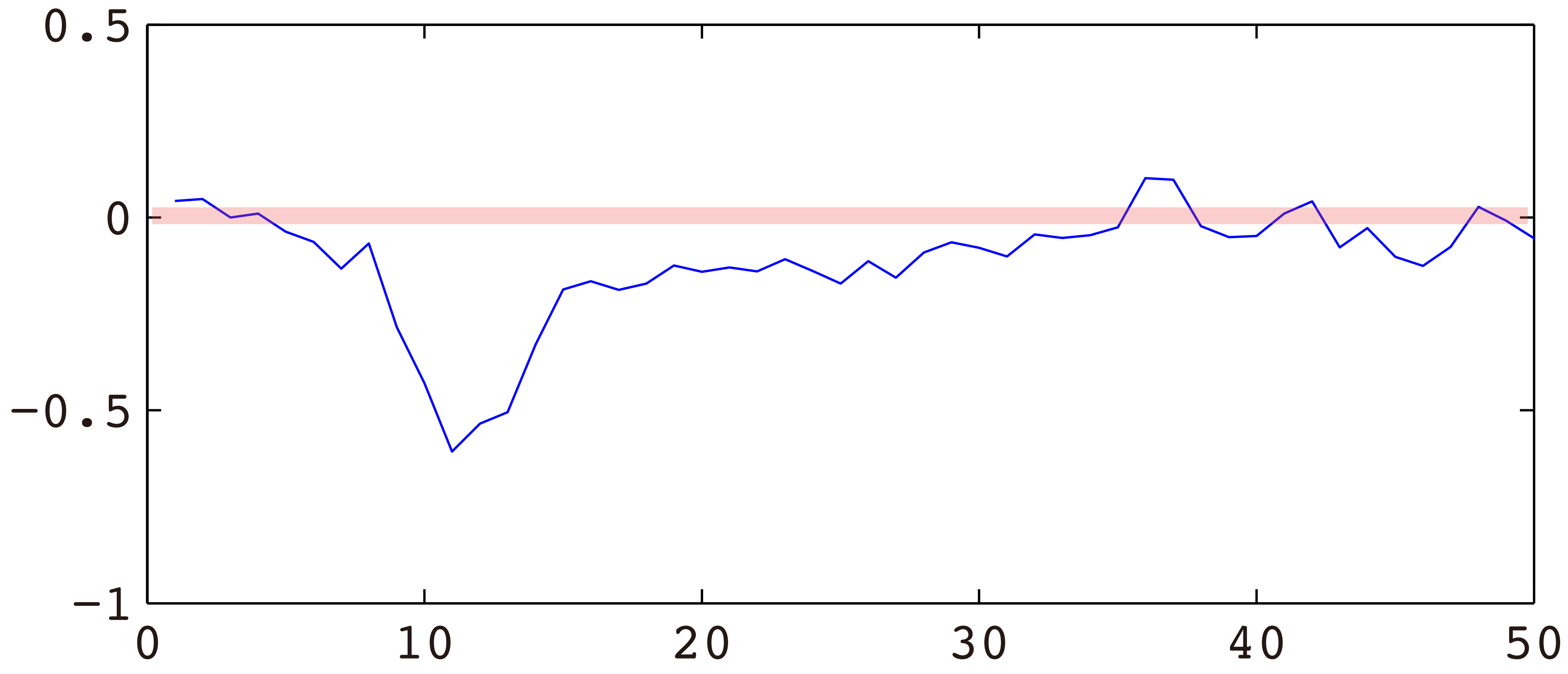
学習後



MCH Oct+

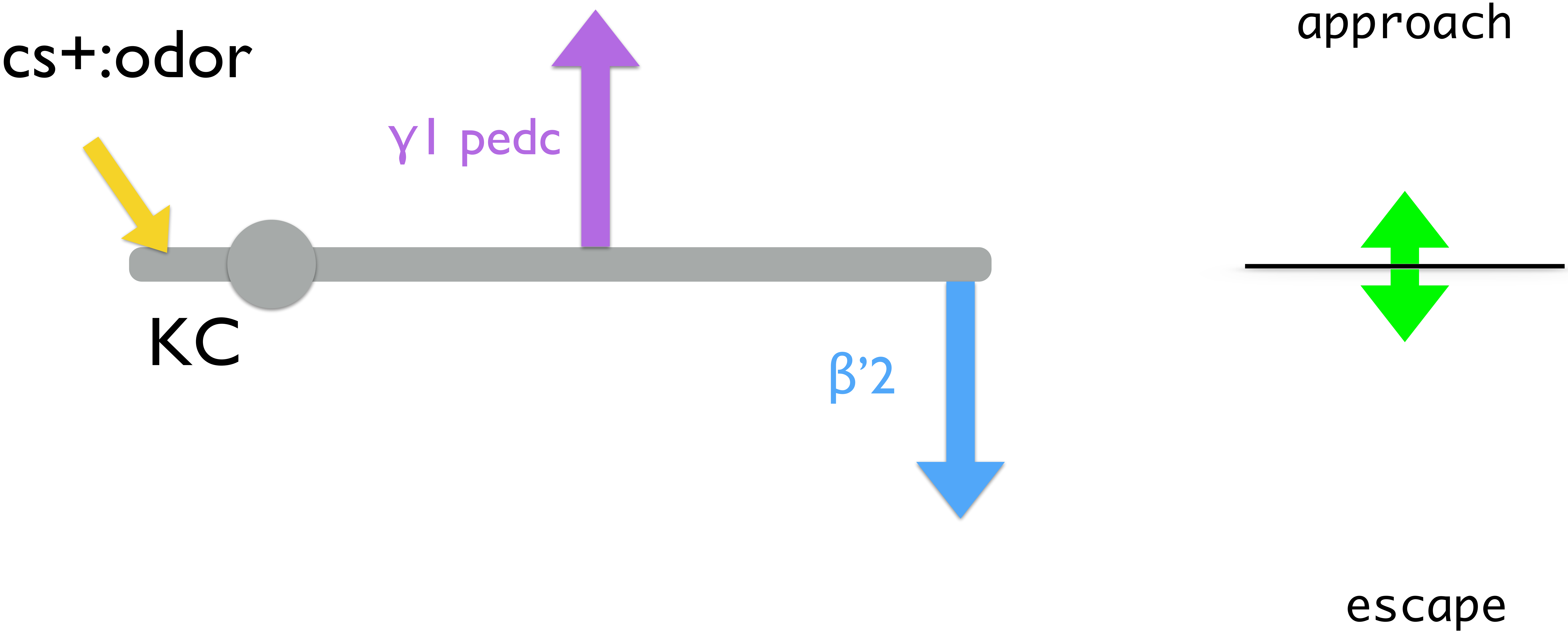


CS+ to CS- diff

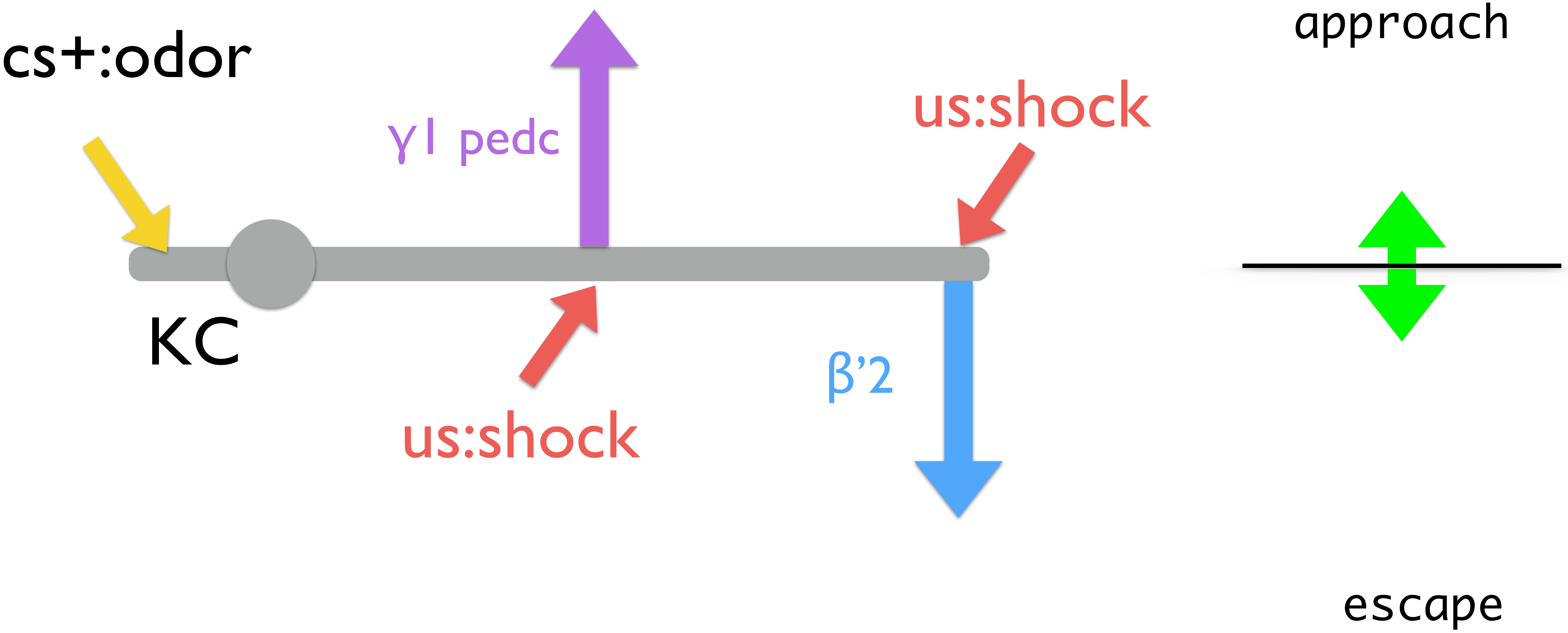


＊廣井誠氏・上岡雄太郎氏提供

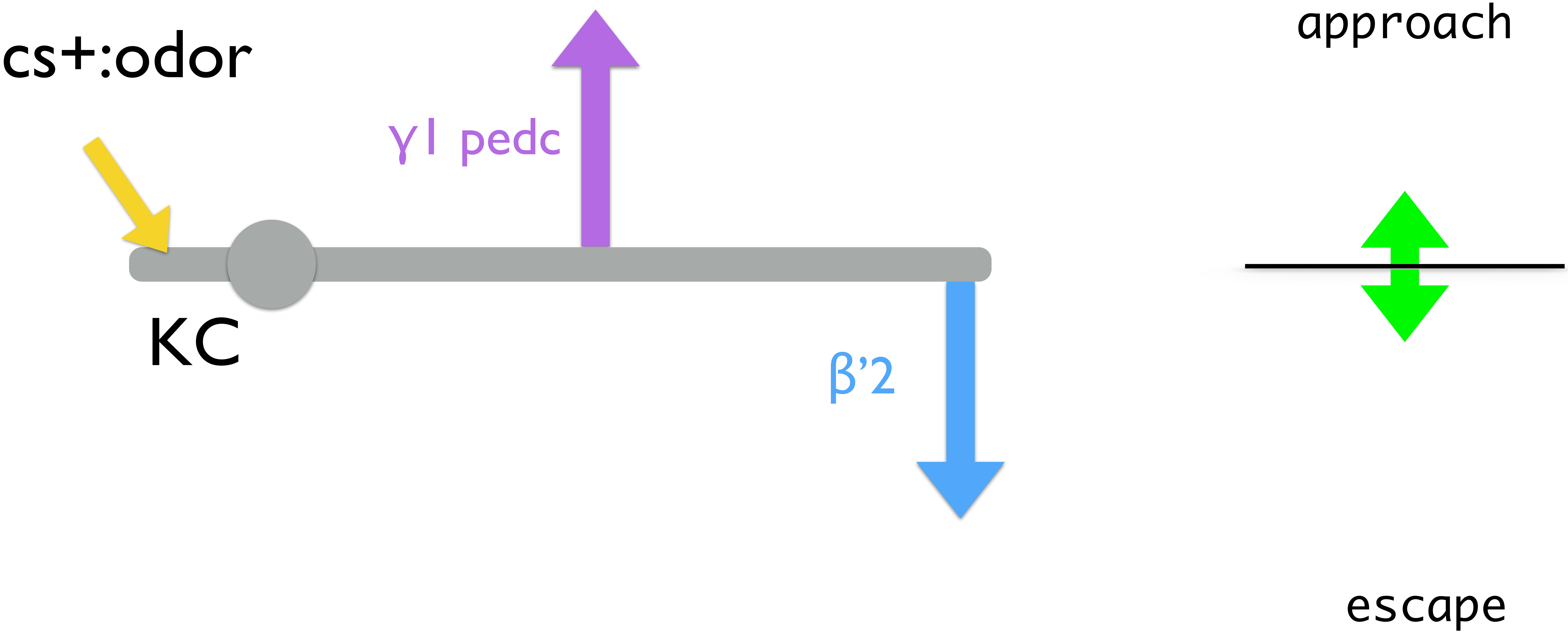
Valence



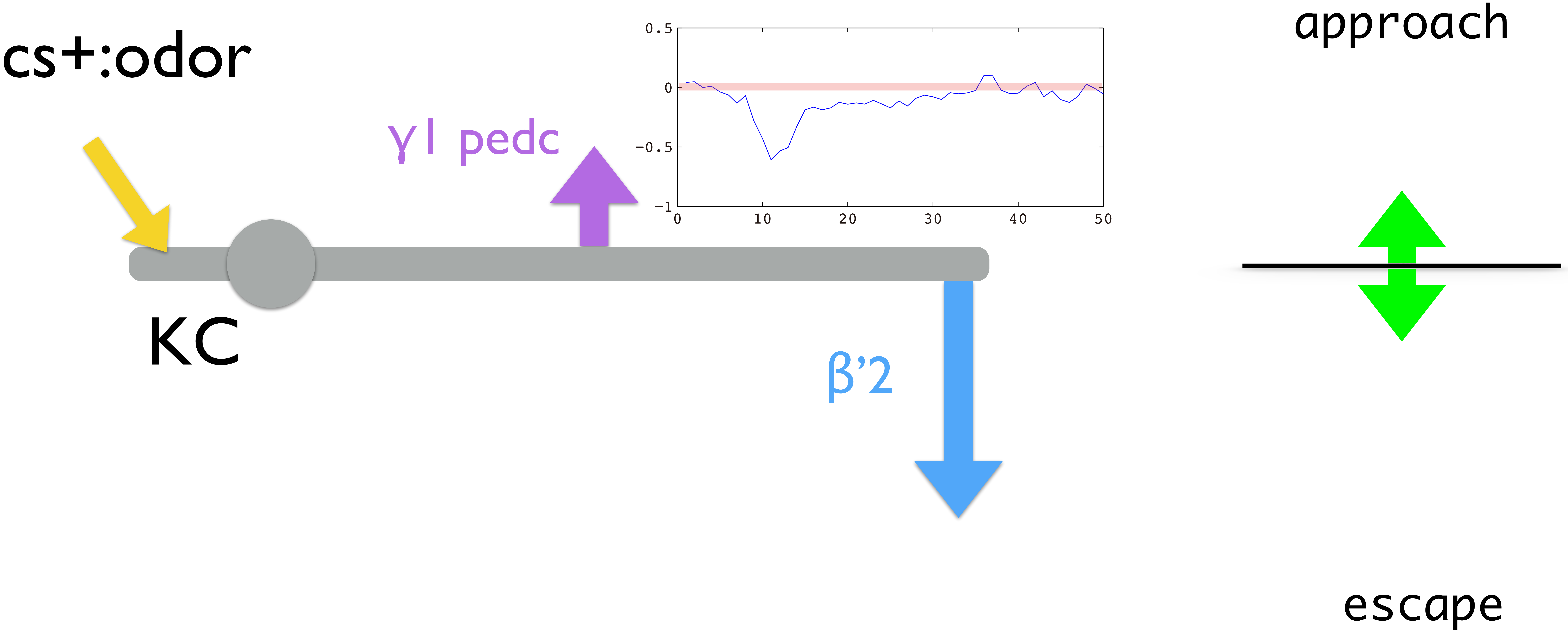
Valence

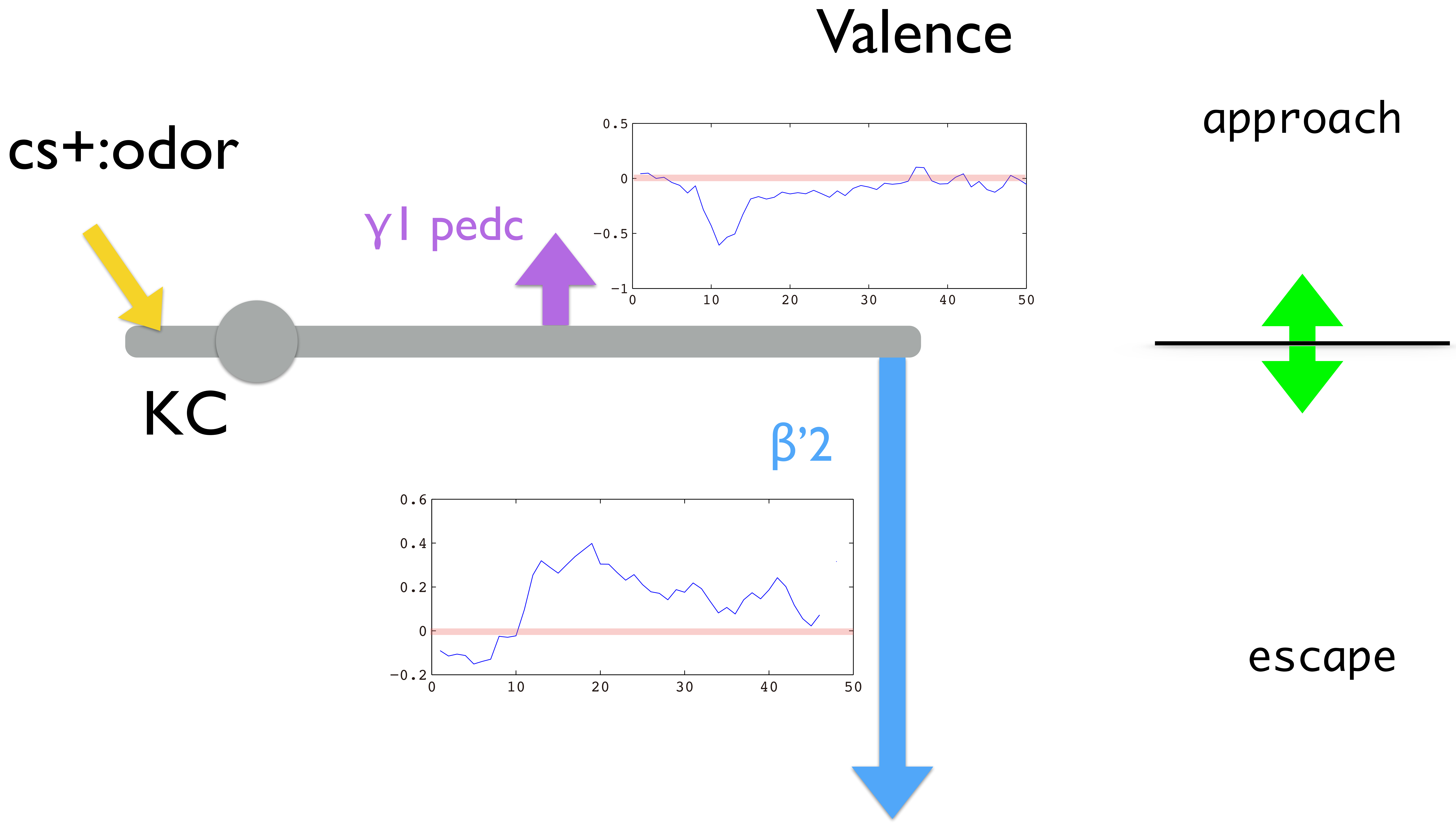


Valence



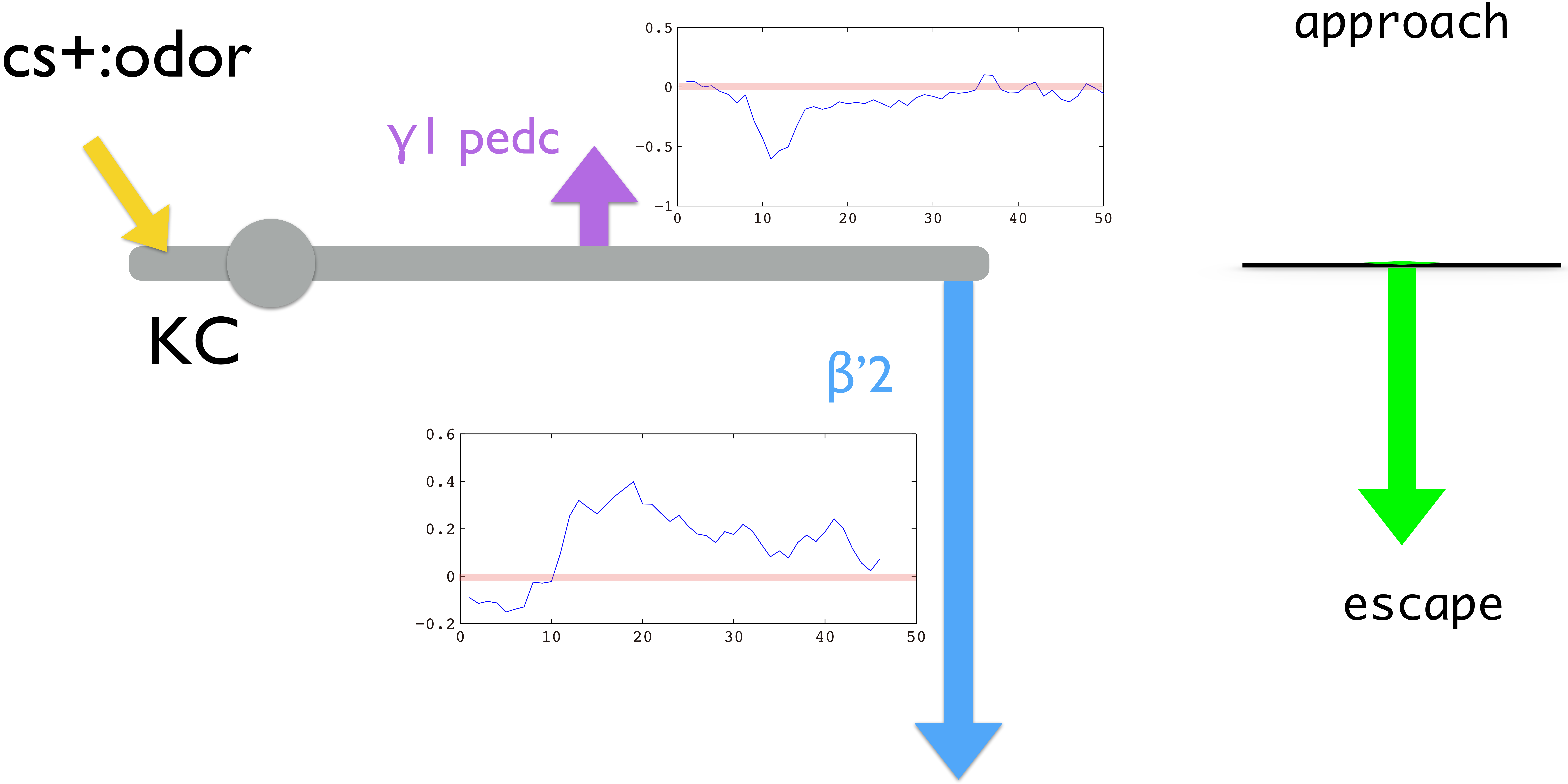
Valence

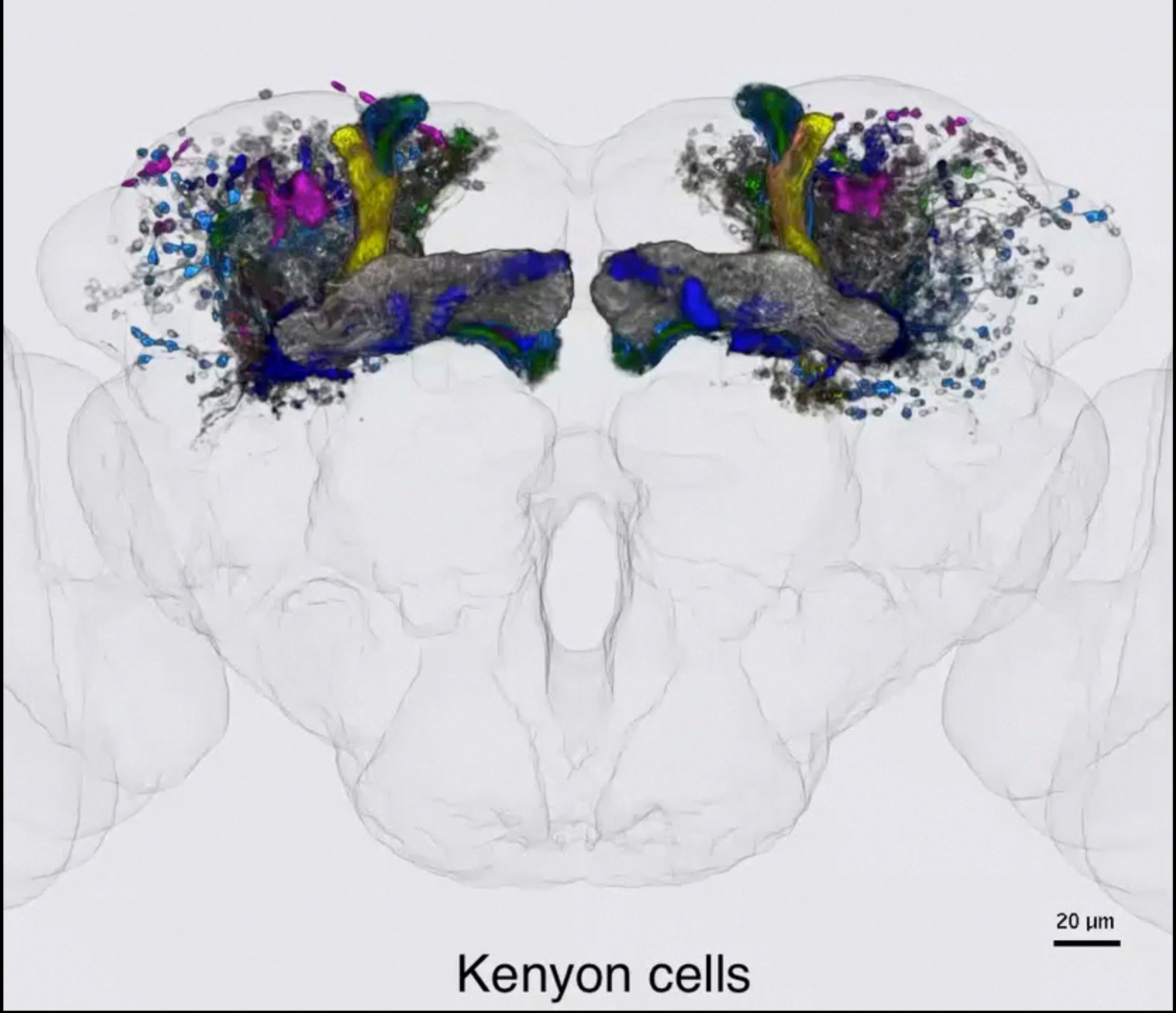




Valence
cs+:odor
γ1 pedc
approach
KC
β'2
escape
0.5
0
−0.5
−1
0 10 20 30 40 50
0.6
0.4
0.2
0
−0.2
0 10 20 30 40 50

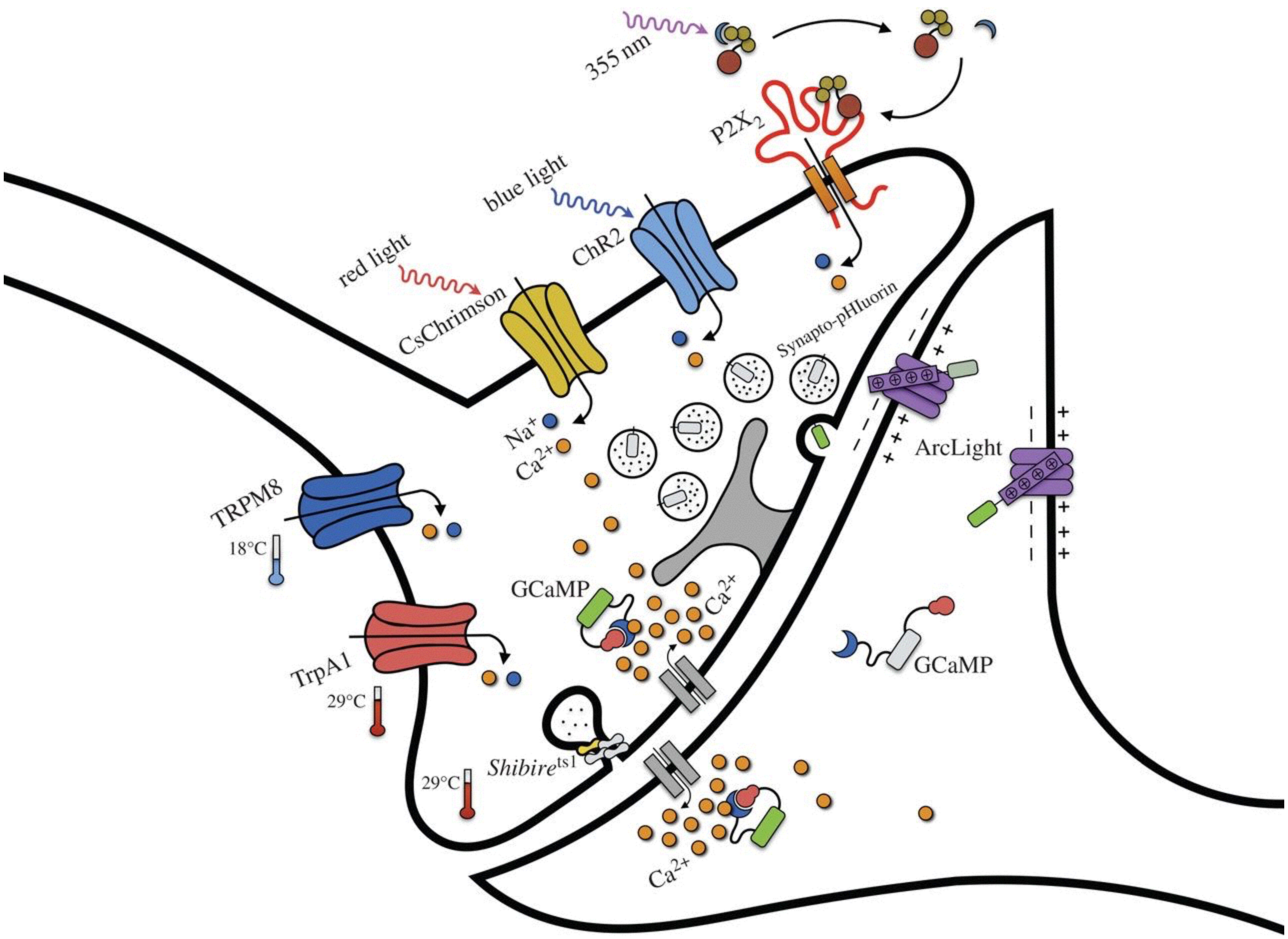
Valence



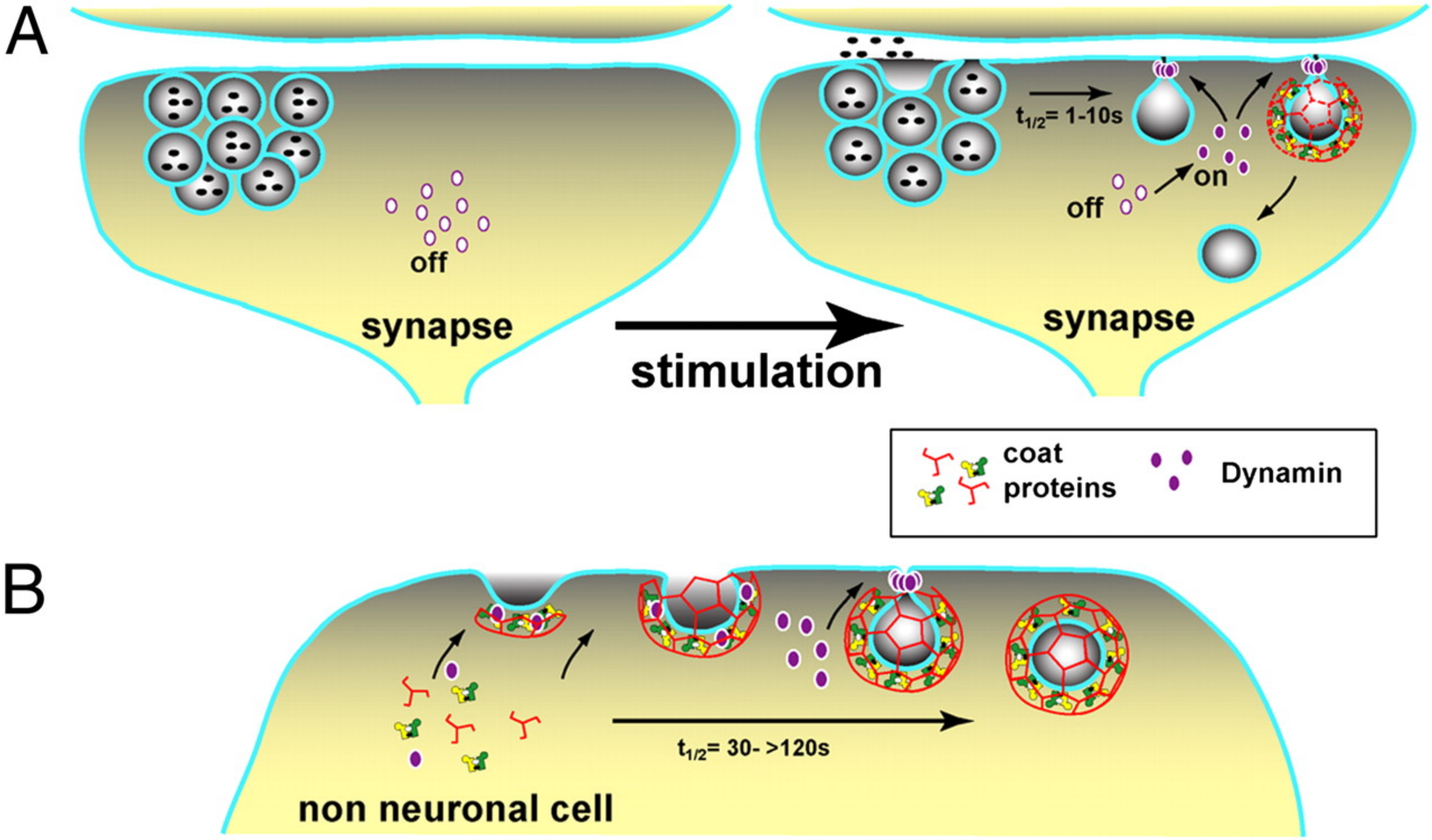


Aso et al. (2014) The neuronal architecture of the mushroom body provides a logic for associative learning, *eLife* 2014;3:e04577, p.7 Video 2 http://elifesciences.org/content/3/e04577


CRE-P
CRE-N

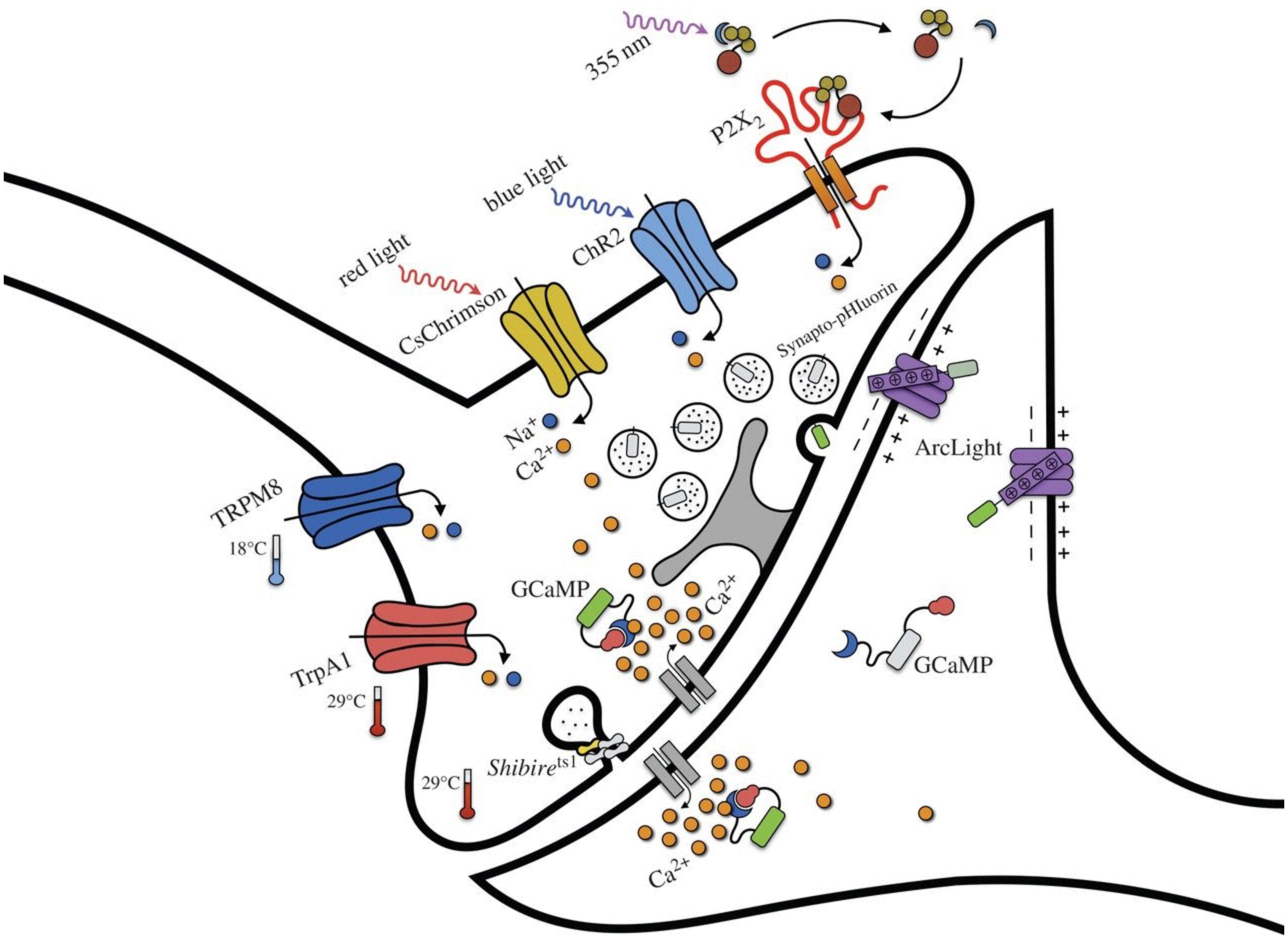


Owald et al. (2015) Light, heat, action: neural control of fruit fly behaviour, *Philosophical Transactions of the Royal Society B* 370:20140211, p.5 Fig.4 http://rstb.royalsocietypublishing.org/content/370/1677/20140211

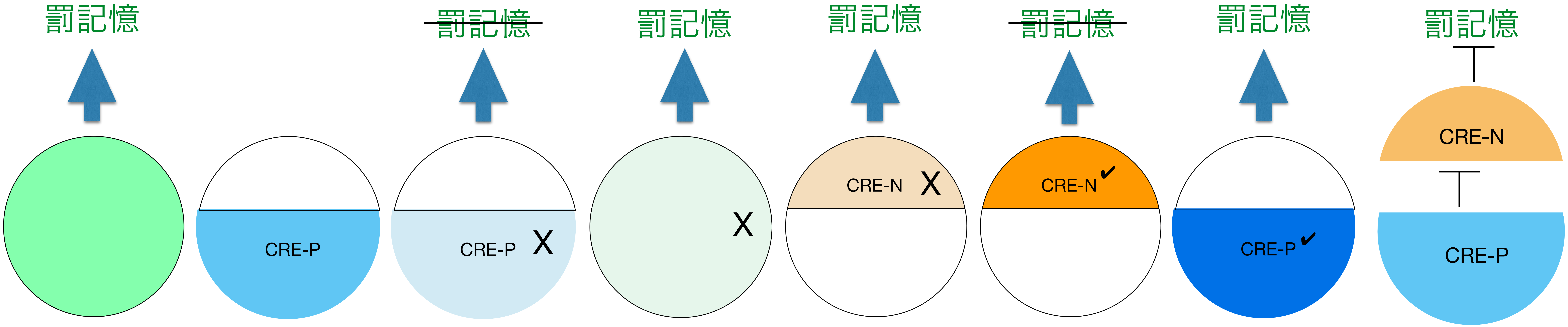


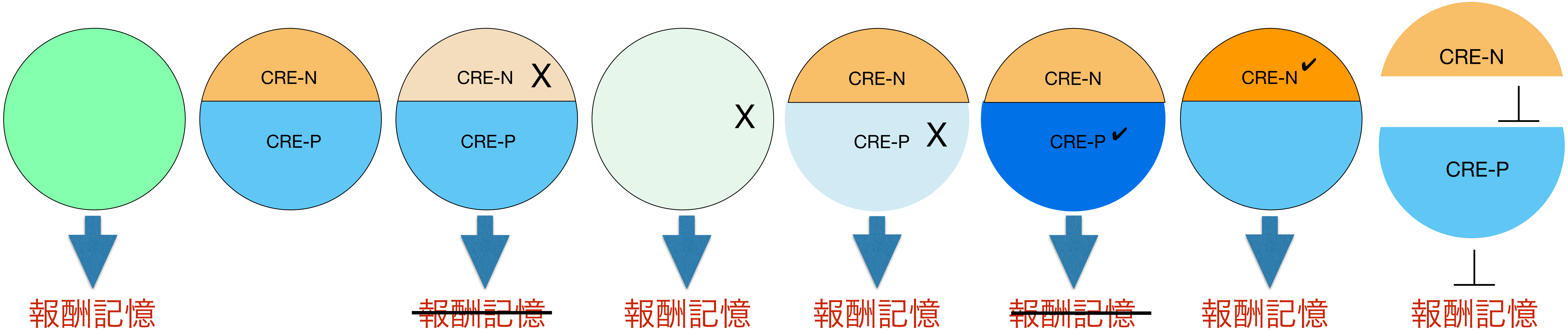
* Liu et al. (2011) Differential curvature sensing and generating activities of dynamin isoforms provide opportunities for tissue-specific regulation, PNAS 108(26):E234-E242, p.E240 Fig.7 http://www.pnas.org/content/108/26/E234.full

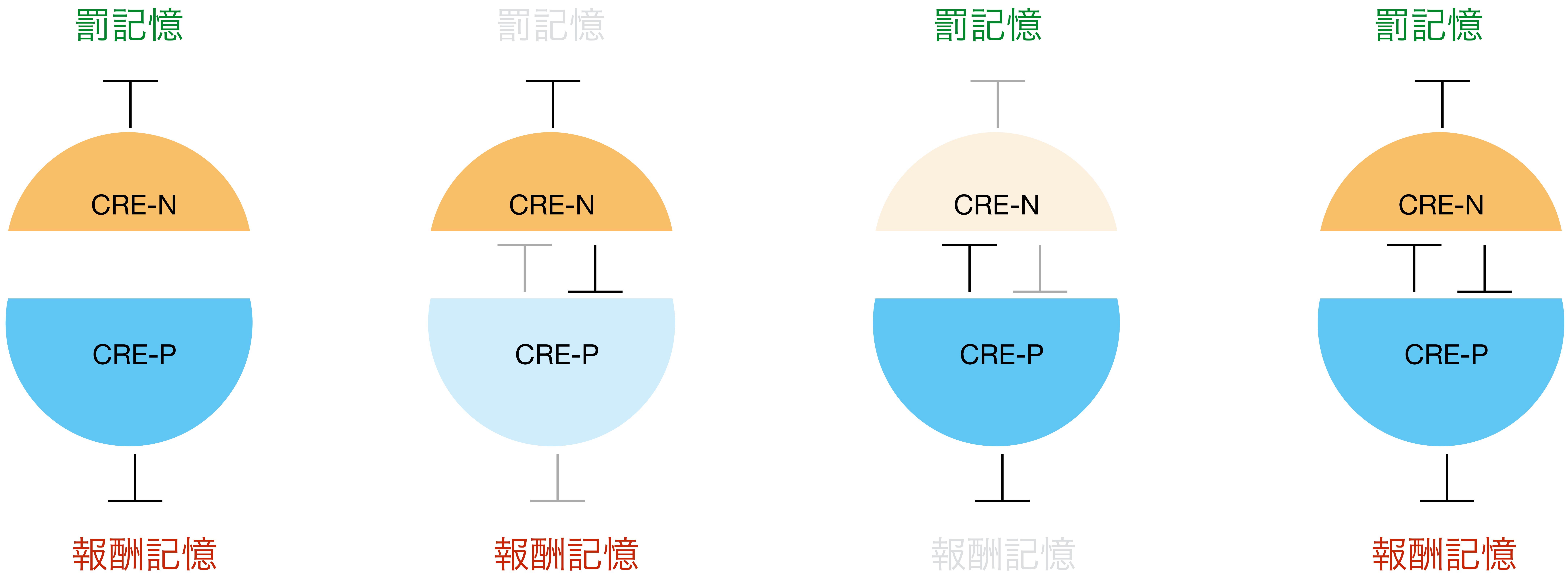
＊上岡雄太郎氏提供



Owald et al. (2015) Light, heat, action: neural control of fruit fly behaviour, *Philosophical Transactions of the Royal Society B* 370:20140211, p.5 Fig.4 http://rstb.royalsocietypublishing.org/content/370/1677/20140211

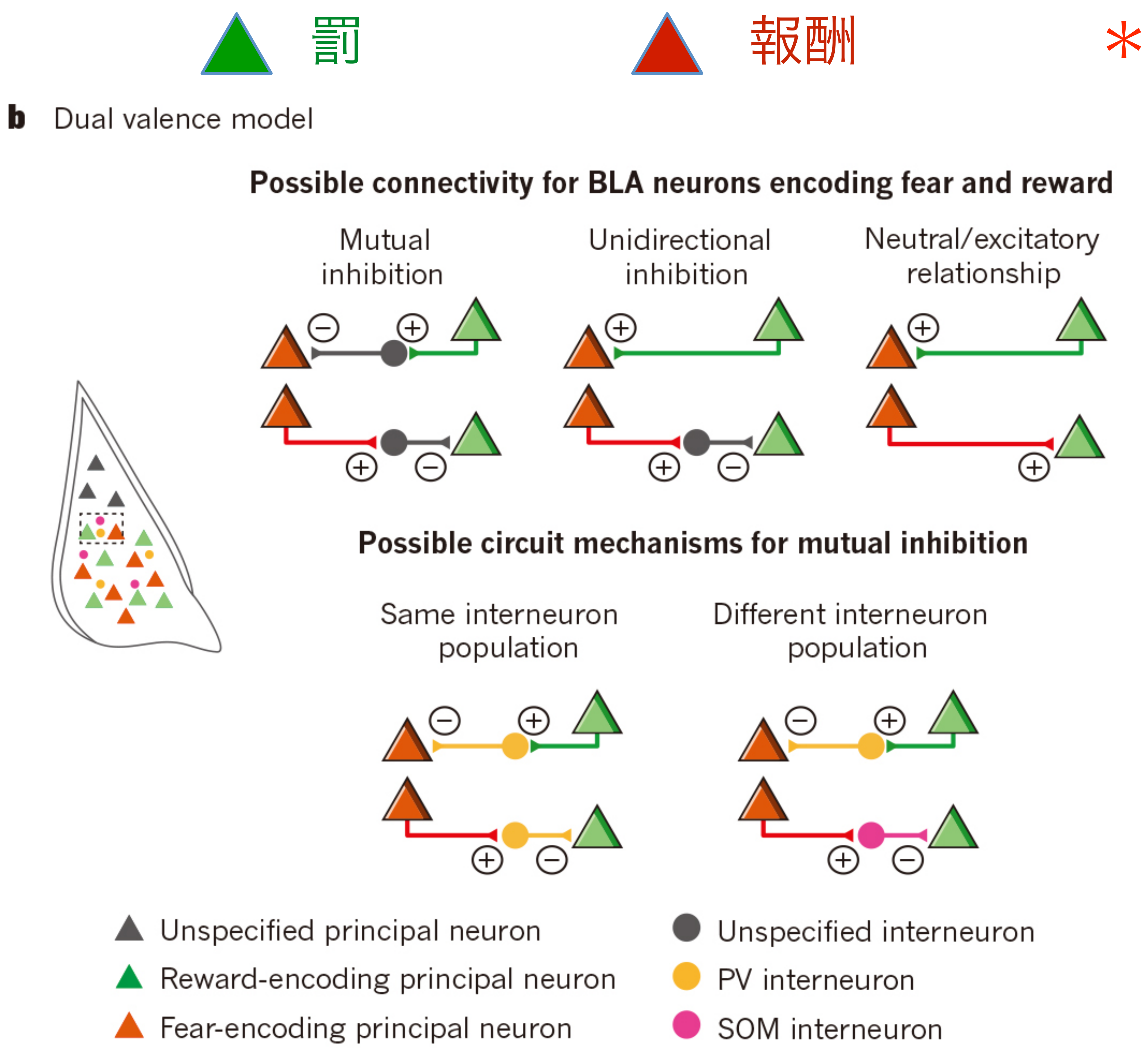

罰記憶
CRE-P
罰記憶
CRE-P X
罰記憶
X
罰記憶
CRE-N X
罰記憶
CRE-N ✔
罰記憶
CRE-P ✔
罰記憶
CRE-N
CRE-P


報酬記憶
CRE-N
CRE-P
CRE-N X
CRE-P
~~報酬記憶~~
X
報酬記憶
CRE-N
CRE-P X
報酬記憶
CRE-N
CRE-P ✔
~~報酬記憶~~
CRE-N ✔
報酬記憶
CRE-N
CRE-P
報酬記憶



罰記憶
CRE-N
CRE-P
報酬記憶
罰記憶
CRE-N
CRE-P
報酬記憶
罰記憶
CRE-N
CRE-P
報酬記憶
罰記憶
CRE-N
CRE-P
報酬記憶

扁桃体



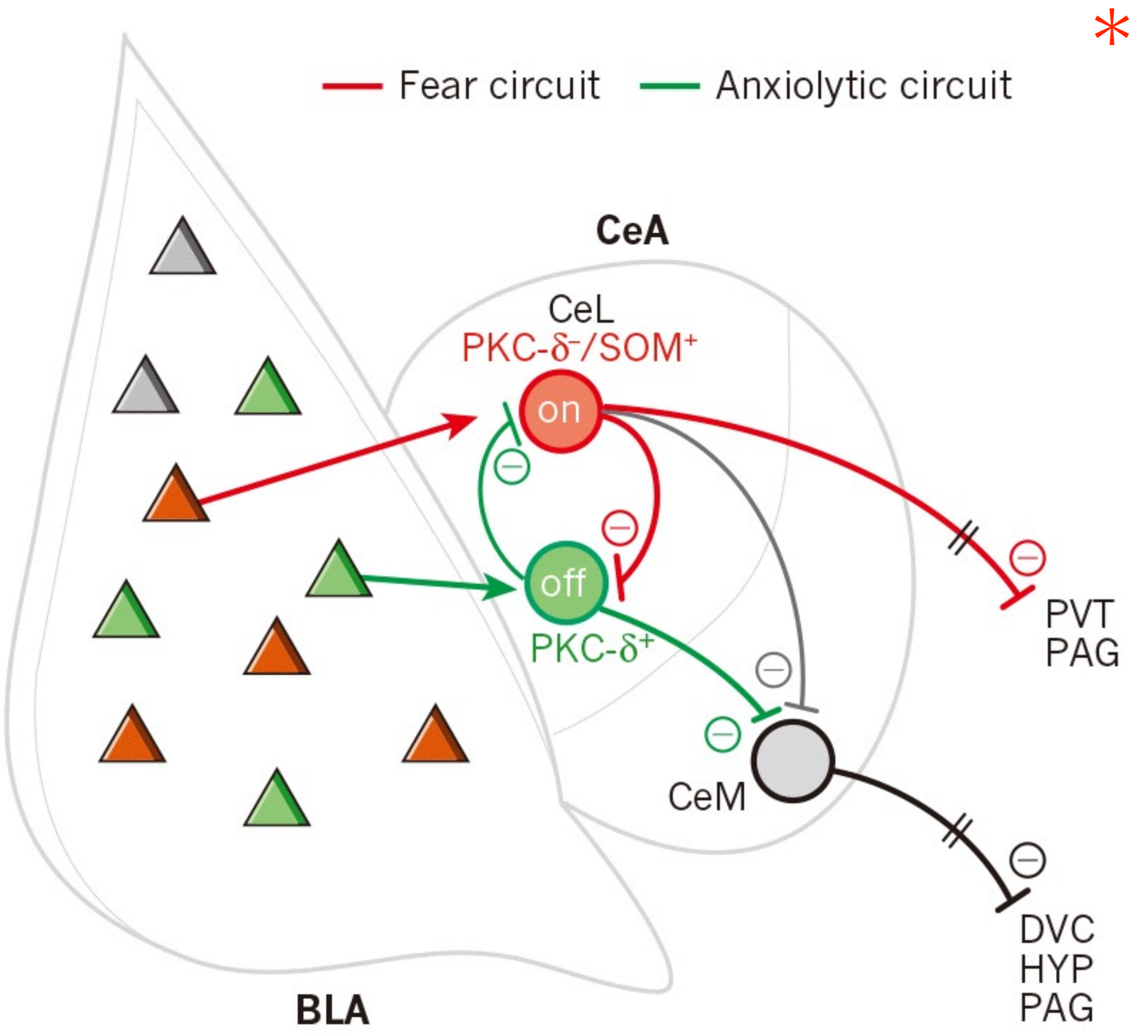
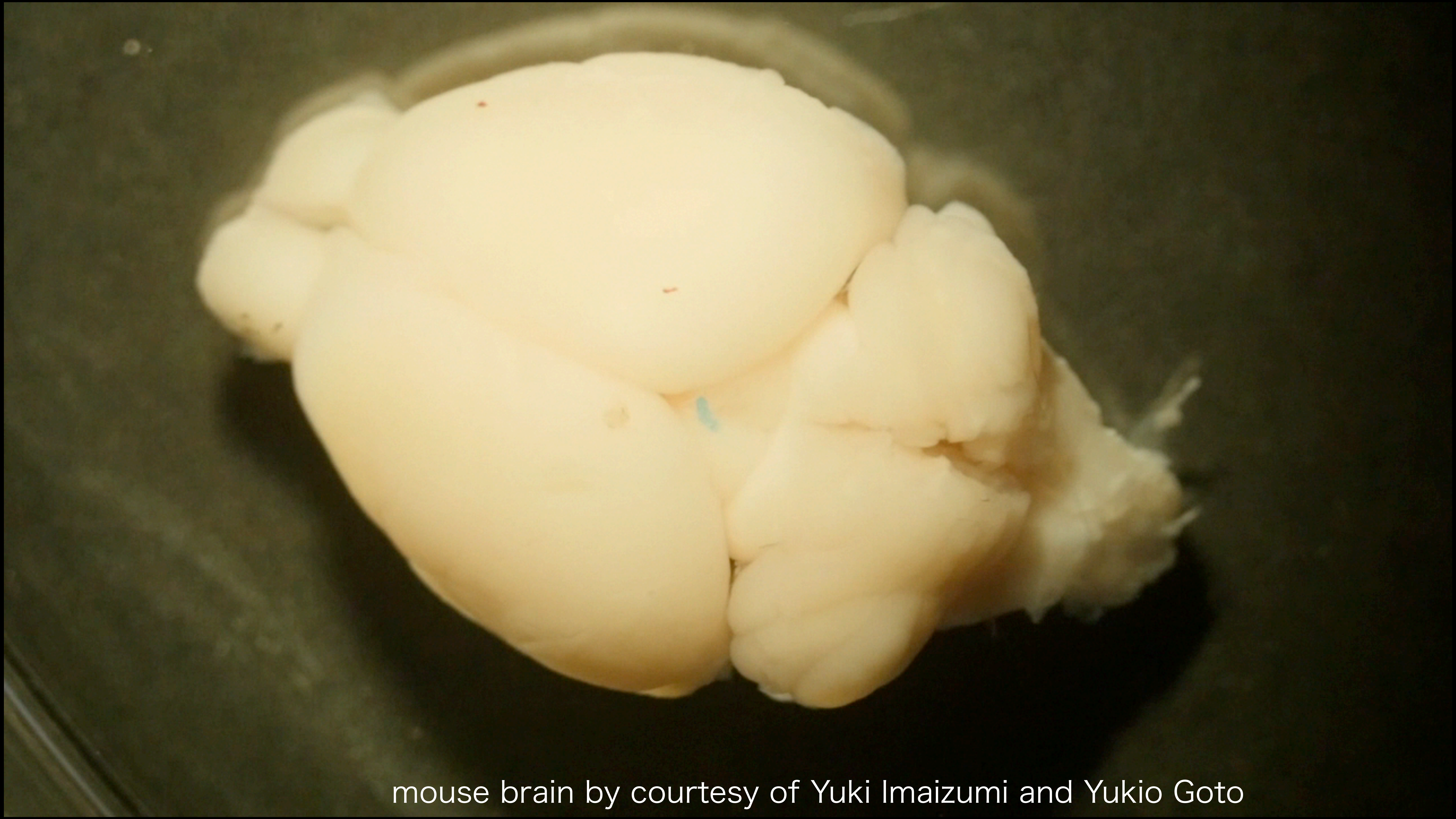


Figure 4 | Model of amygdala microcircuits that give rise to behaviour.

Approach ⊣⊢ **Escape**



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Takashi Abe
Yutaro Ueoka
Daisuke Yamazaki

Yohei Nitta
Kiichi Inoue
Yuko Kamoshida-Maeyama
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Mai Nakabayashi

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Yoshinori Aso
Gerry Rubin
Barret Pfeiffer
Tzumin Lee
Loren Looger

Tohoku University
Koichi Hashimoto