Sensory integration in the fly gustatory system

Accept or reject?

Craig Montell, UCSB

Sugars

Salts

Bitter compounds

pH

Aromas
& odors

Temperature

Color

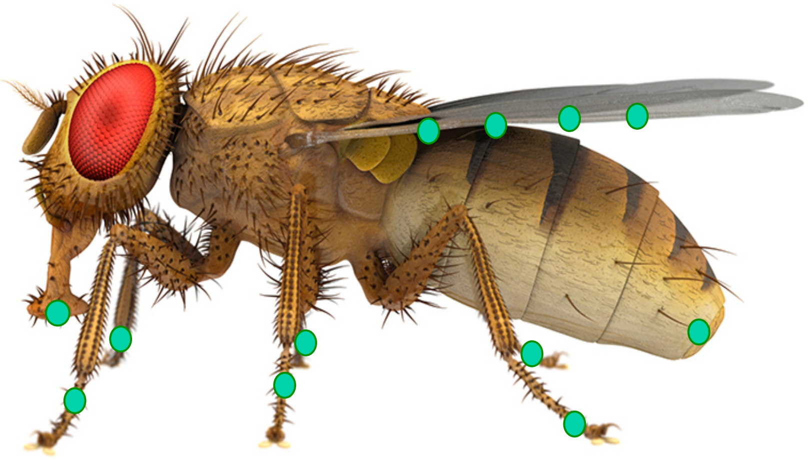
Texture

KITP SNav18, Aug 6, 2018

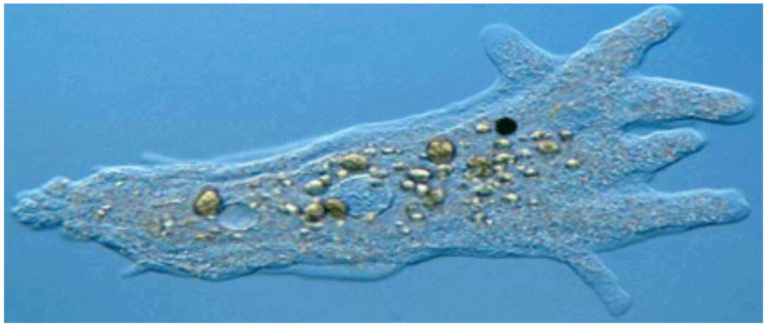
Where are sensory neurons?

Acclimate or Evacuate?

Sensory integration in the taste system?

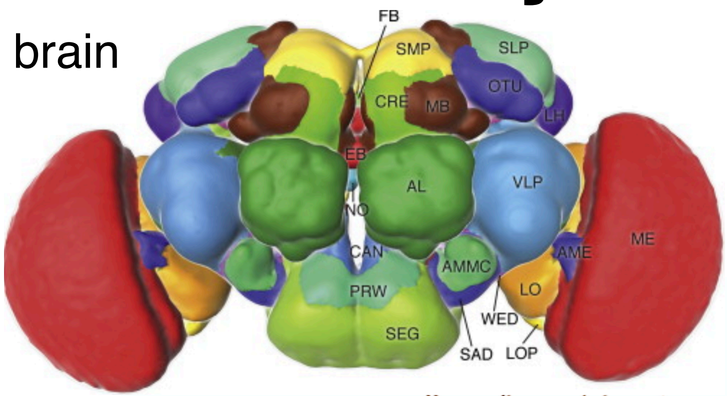


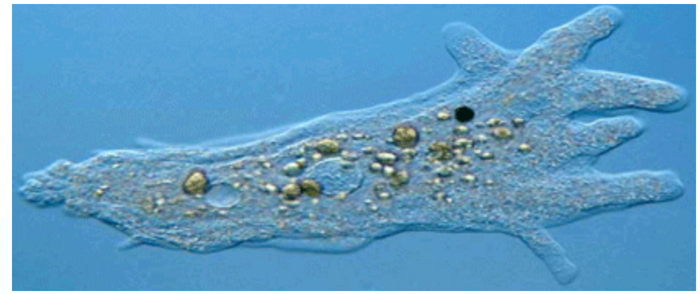
The Brain in Sensory Neurons, and Sensory Neurons in the Brain

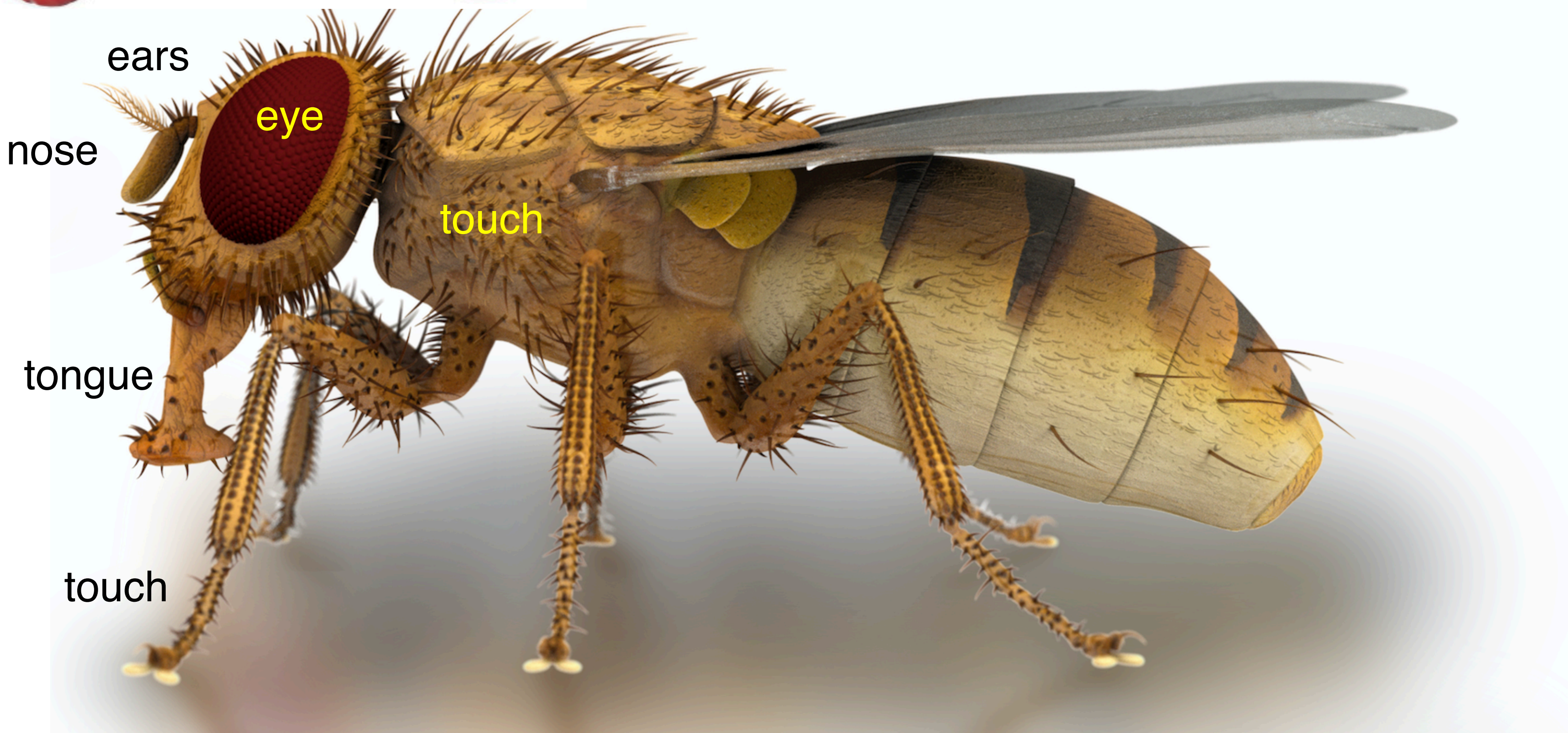


The Brain in Sensory Neurons, and Sensory Neurons in the Brain

Fly brain







Primary Sensory Neurons in the Fly Brain

Neurons in central brain
sense light with rhodopsin

Ni, Baik, Holmes and Montell. Nature (2017)

Neurons in brain sense rate of
temperature change via TRPA1

J. Luo, W. Shen and C. Montell. Nat. Neurosci. (2017)

Brain function in peripheral sensory neurons

Experience Affects Food Preferences

All cultures have preferred foods

Pungent cheese

Spicy Sichuan cuisine

Food preferences are acquired in part by upbringing or longterm exposure.

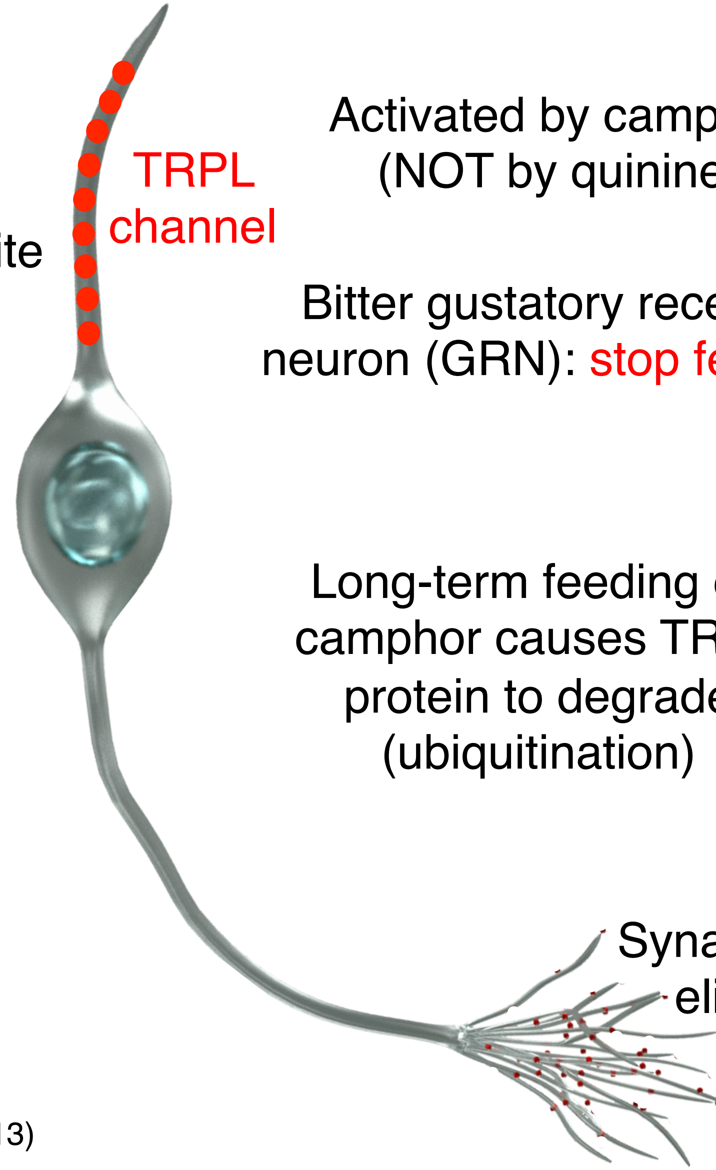
Some bitter foods are toxic.

Many bitter foods are nutritious and safe and avoided needlessly.

Taste experience encoded in peripheral sensor neurons

Animals will NOT learn to accept foods with toxic chemicals.
e.g. quinine

Animals WILL learn to accept foods with bad tasting but safe additives.
e.g. camphor



dendrite

TRPL channel

Activated by camphor (NOT by quinine)

Bitter gustatory receptor neuron (GRN): stop feeding

Long-term feeding on camphor causes TRPL protein to degrade (ubiquitination)

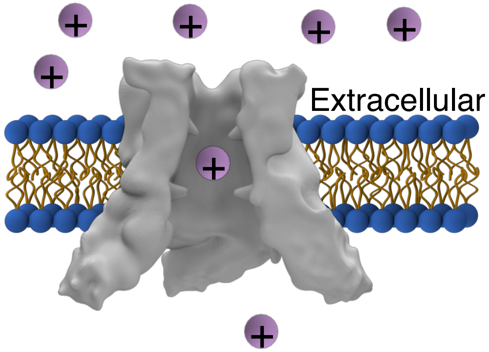
Synaptic bouton elimination

Zhang, Raghuwanshi, Shen and Montell. Nat. Neurosci. (2013)

Evacuate or Acclimate

Evacuate

High levels of stimulus



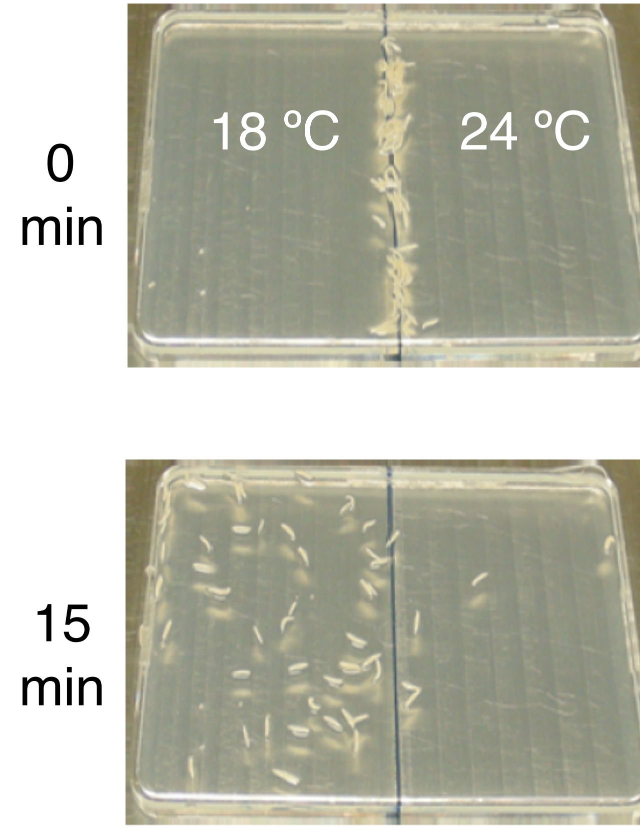
Thermally-activated
TRP channel

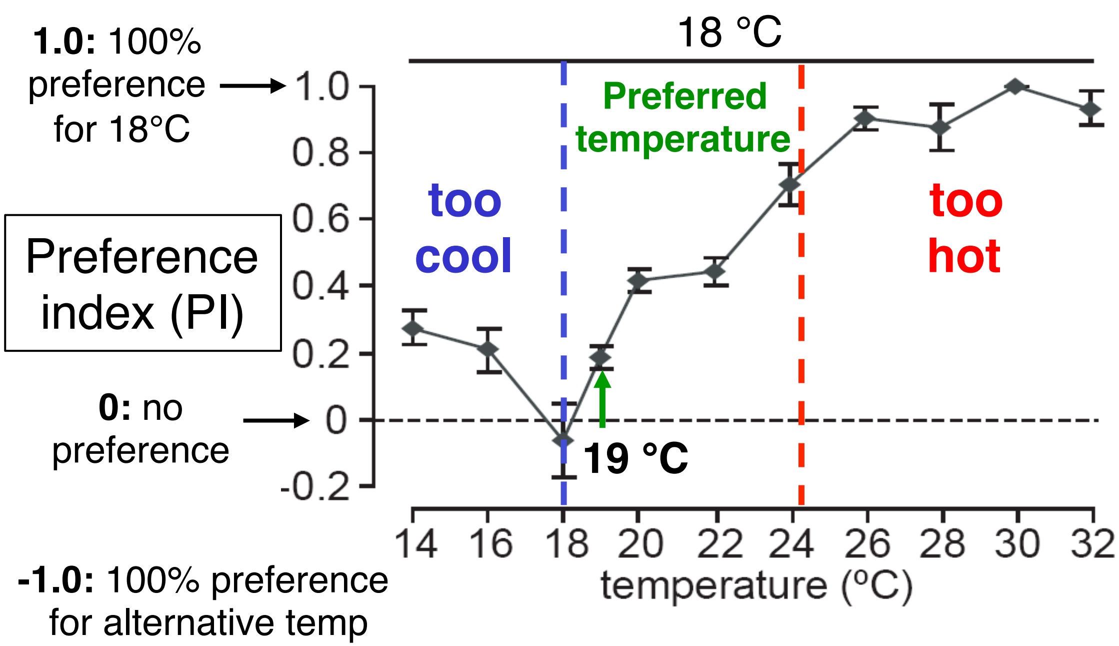
Acclimate

Low levels of stimulus

Choosing favorite comfortable temperature

Two way choice assay

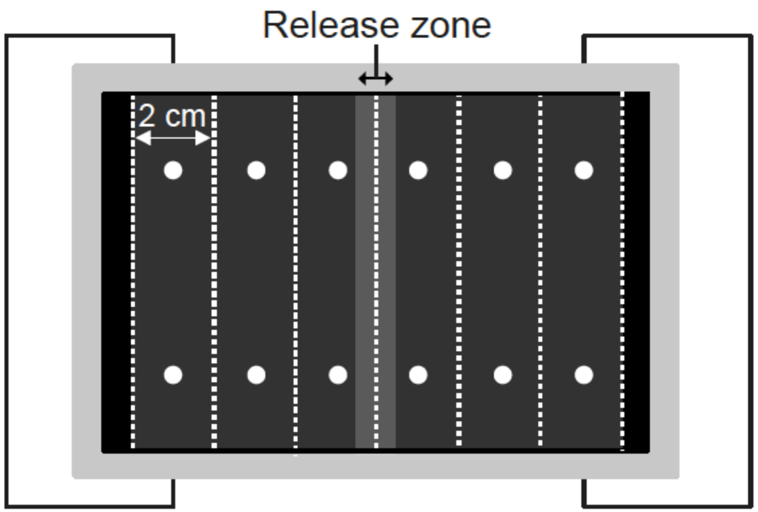


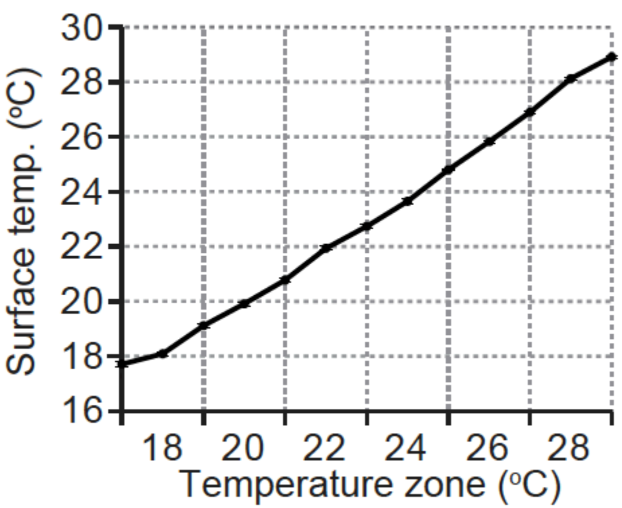


$$\text{Preference index} = \frac{(\#\text{ at } 18\ °C) - (\#\text{ at } 24\ °C)}{\#\text{ of larvae on both sides}}$$

Thermal gradient assay

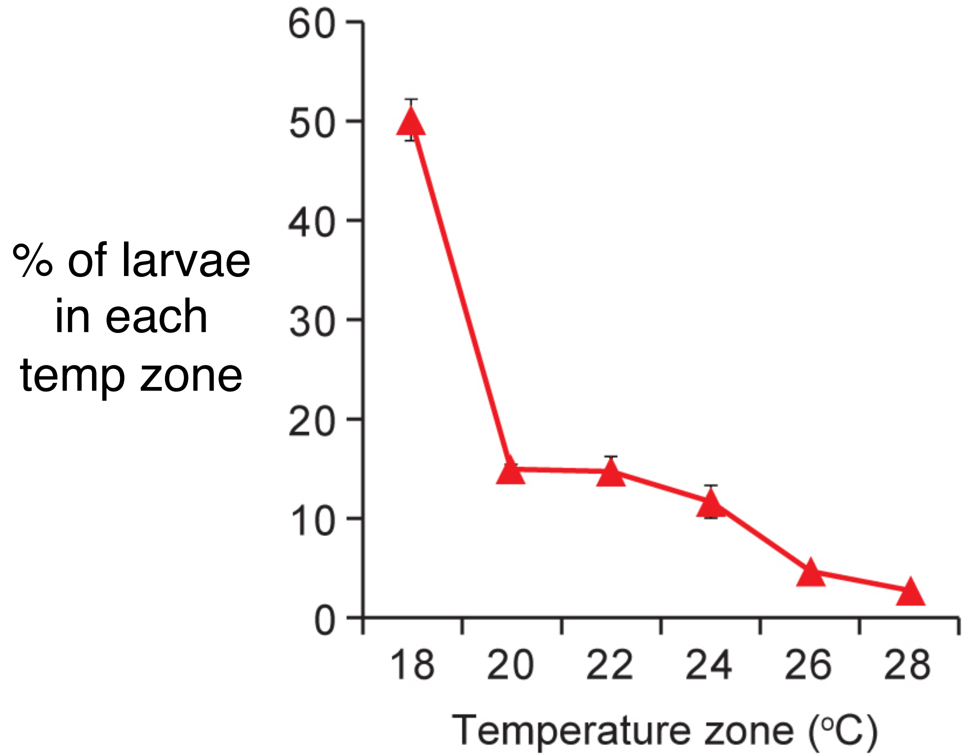
Thermal Gradient Assay





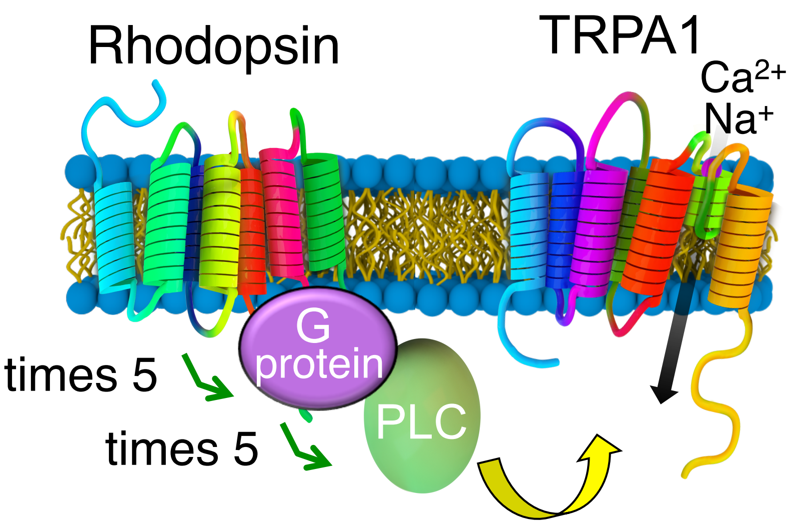
Late 3rd instar larvae

120 h AEL



Thermo signaling cascade in comfortable (18-24°C) range

TRPA1 activated ≥29°C



thermal amplification

thermal adaptation

Kwon, Shim, Wang & Montell. Nat. Neurosci. (2008)

Shen, Kwon, Adegbola, Luo, Chess & Montell. Science. (2011)

H.C. Chen , T. Sokabe & Montell Cell Rep. (2016)

Escape

Adapt

Unconventional Roles for Rhodopsins

Fly opsin	Classical photoreceptors	Non-classical function
● Rh1	yes	Thermosensation, taste, smell
Rh2	yes	
Rh3	yes	
● Rh4	yes	Taste
● Rh5	yes	Thermosensation, hearing
● Rh6	yes	Thermosensation, hearing
● Rh7	no	Taste, light sensaton in brain: circadian entrainment

Shen, Kwon, Adegbola, Luo, Chess & Montell. Science (2011)

Ni, Baik, Holmes & Montell. Nature (2017)

Sokabe, Chen & Montell Cell Rep. (2016)

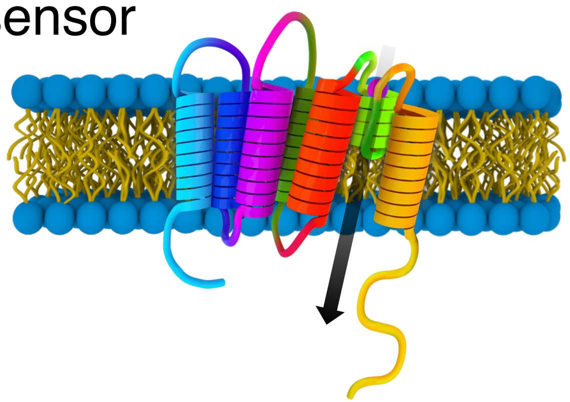
Leung, Kim, Gurav & Montell (in preparation)

Evacuate or Acclimate

Evacuate

High levels of stimulus

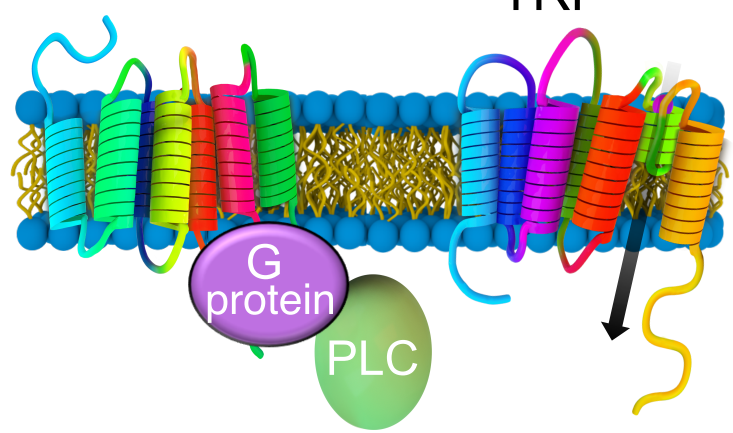
Direct sensor ➡ TRP



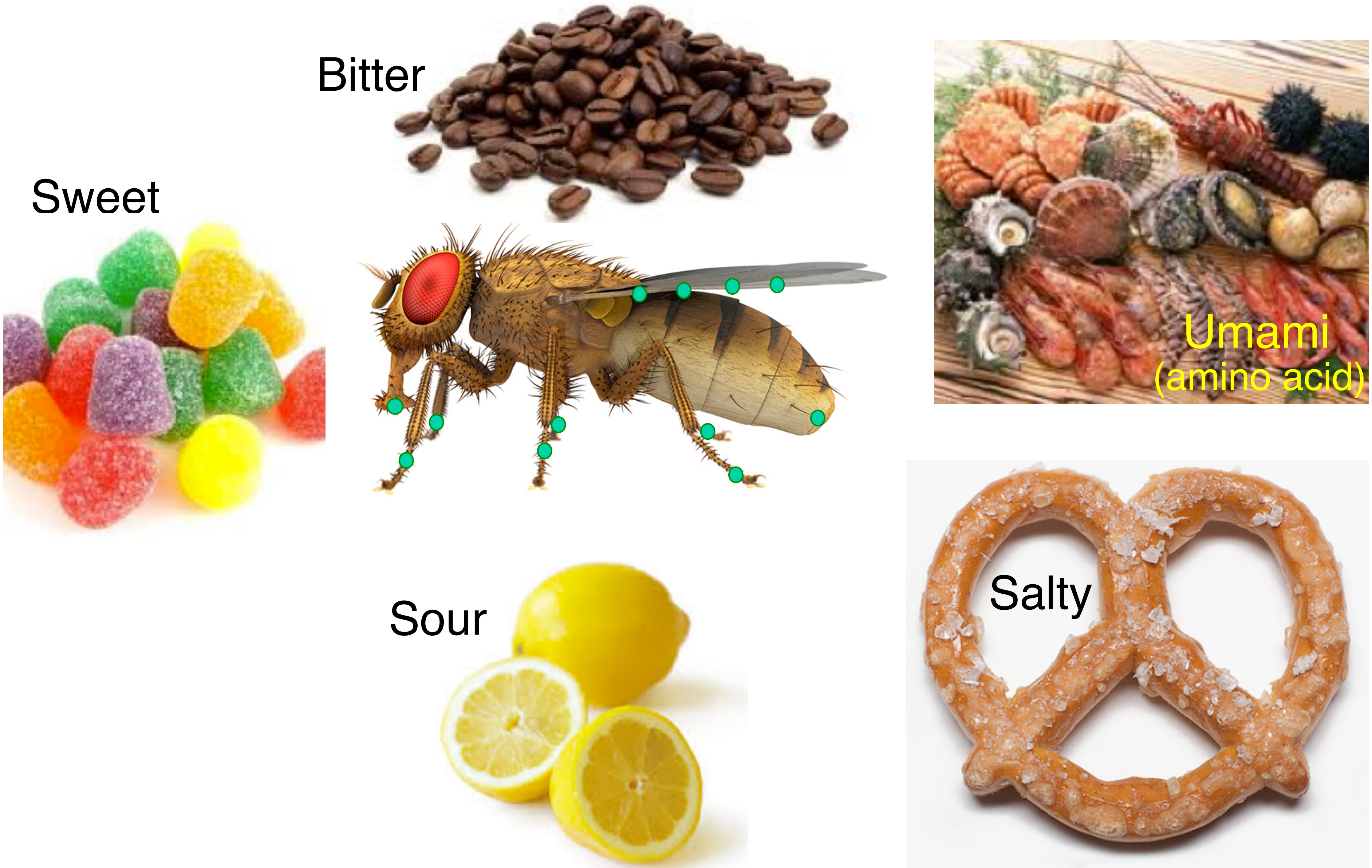
Acclimate

Low levels of stimulus

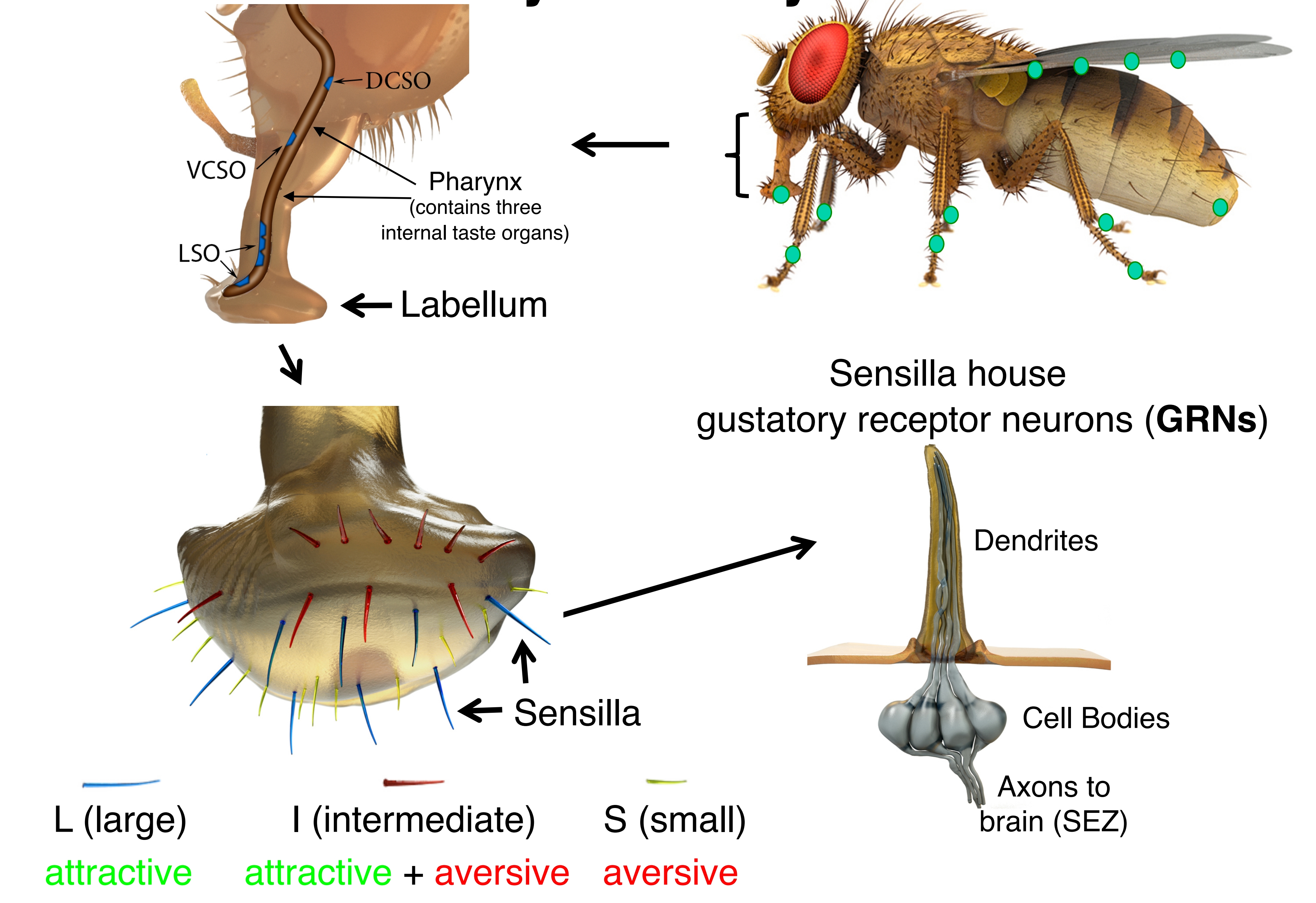
Rhodopsin TRP



Flies respond to the same tastes as we do!



Anatomy of the fly labellum



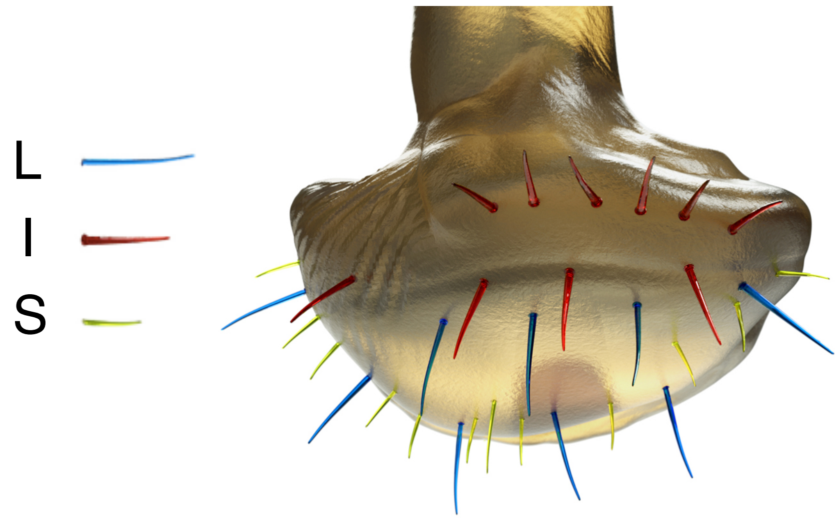
Assaying Taste Behavior in Flies

Two-way choice assay

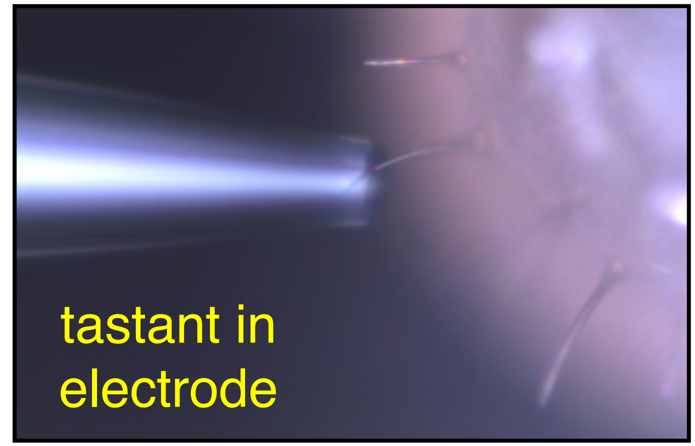
(Determine Preference Index)

Proboscis extension response

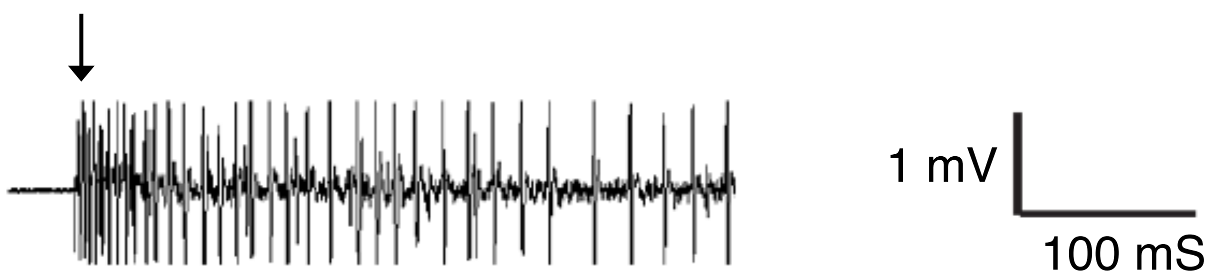
Assaying Tastant-Induced Action Potentials in Flies
(Tip recordings)



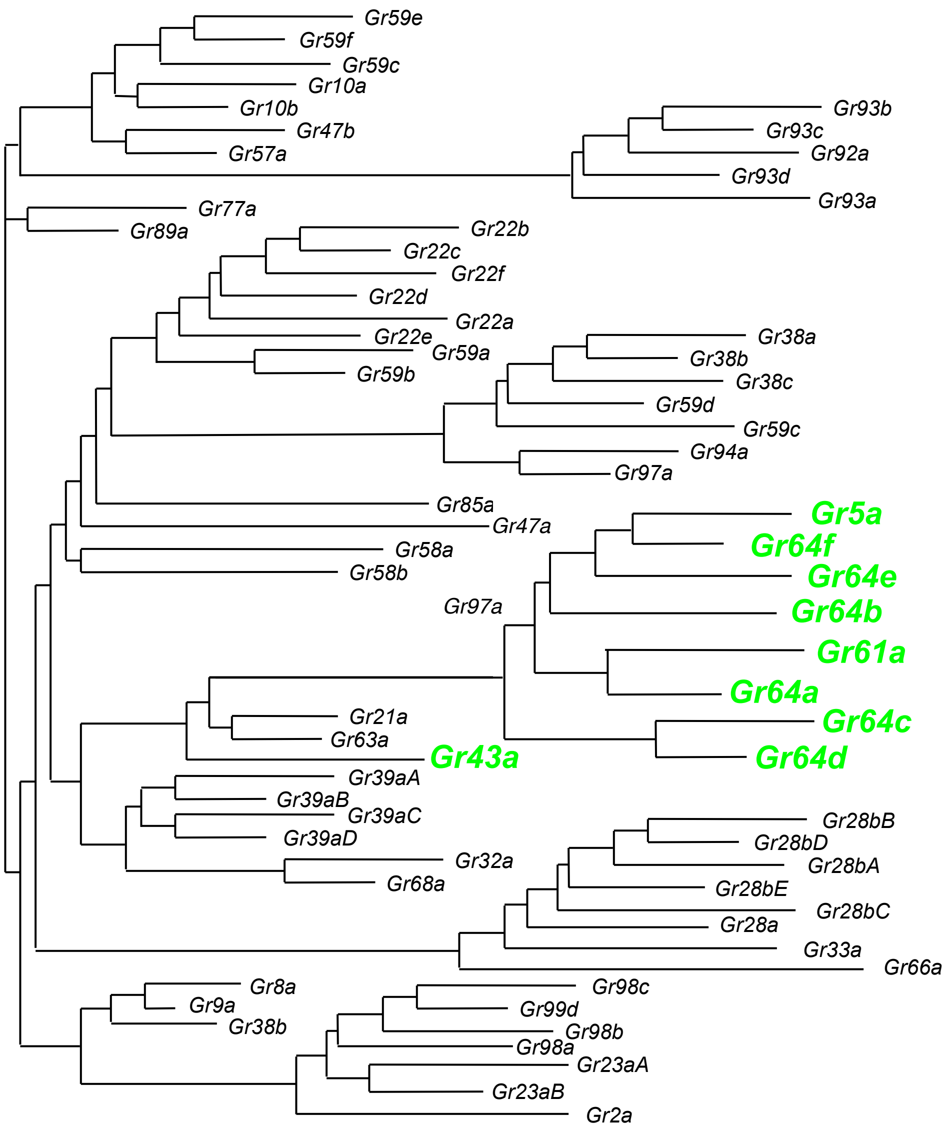
Performing tip recordings

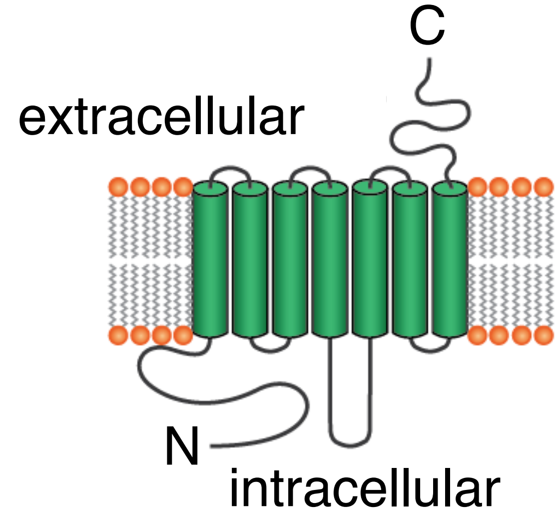


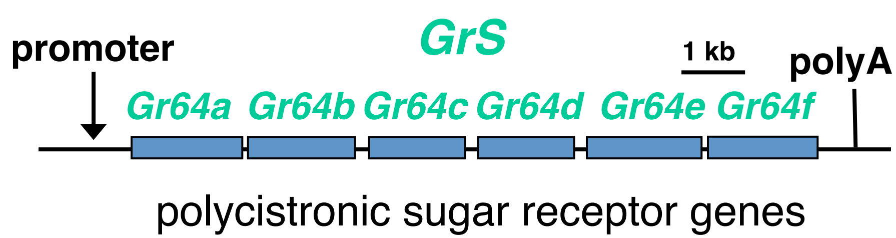
Tastant induced action potentials



Fly Gustatory Receptors: Sweet GRs (GR-S clade)







Jiao, Moon and Montell. PNAS. 2007

Dahanukar, Lei, Kwon and Carlson. Neuron. 2007

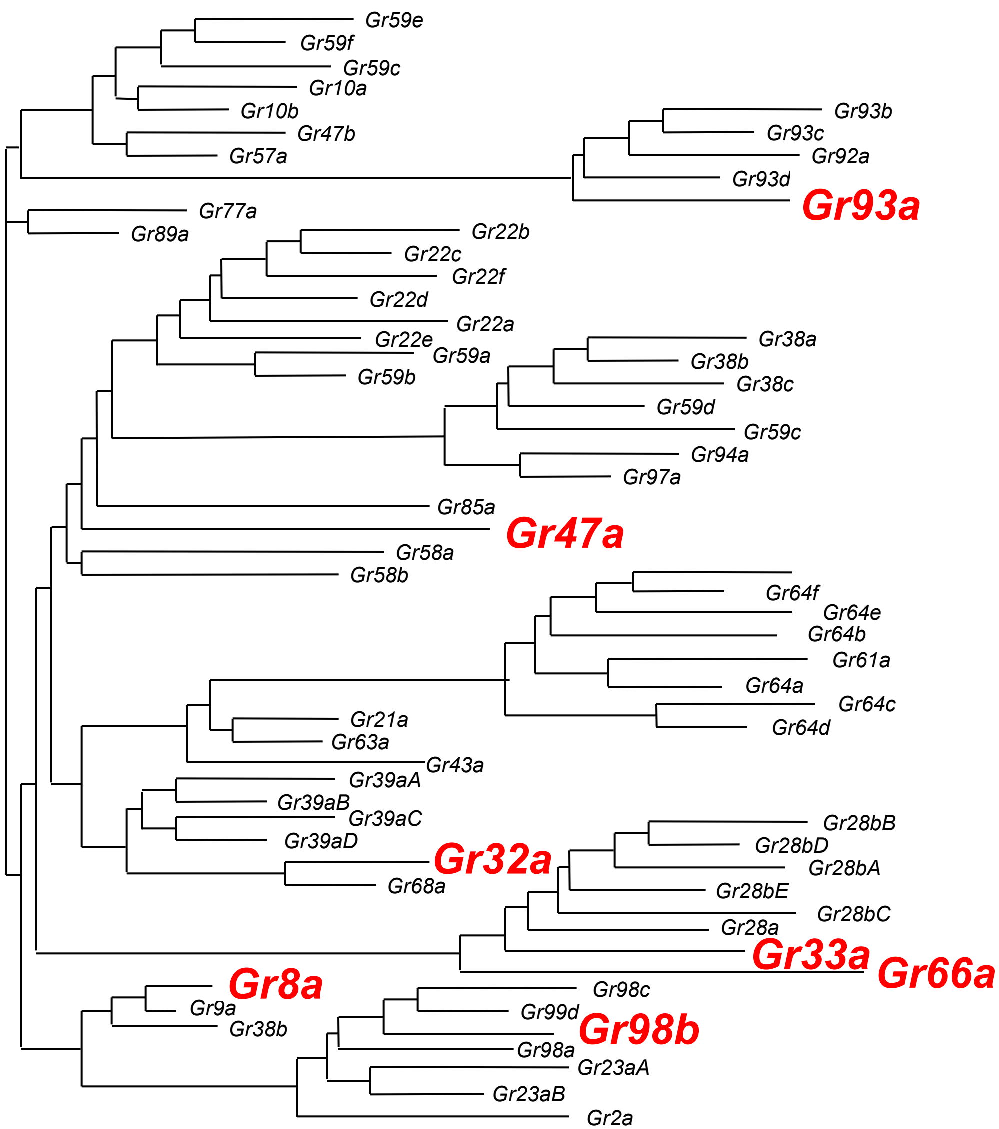
Slone, Daniels and Amrien. Curr. Biol. 2007

Jiao, Moon, Wang, Ren and Montell. Curr. Biol. 2008

Freeman, Wisotsky and Dahanukar. PNAS. 2014

Fuji, Yavuz, Stone, Jagge, Song and Amrien. Curr. Biol. 2015

Fly Gustatory Receptors: Aversive GRs



Core Receptors

Gustatory Receptor	Aversive Tastant
GR32a	most
GR33a	most
GR66a	most

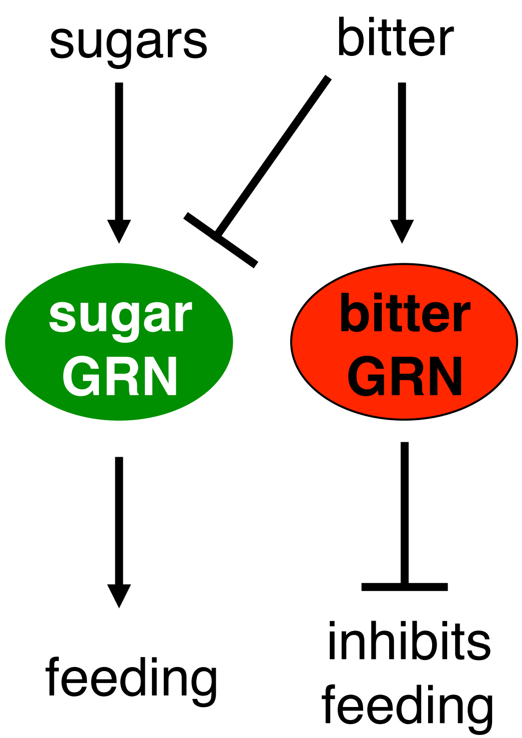
Specificity Receptors

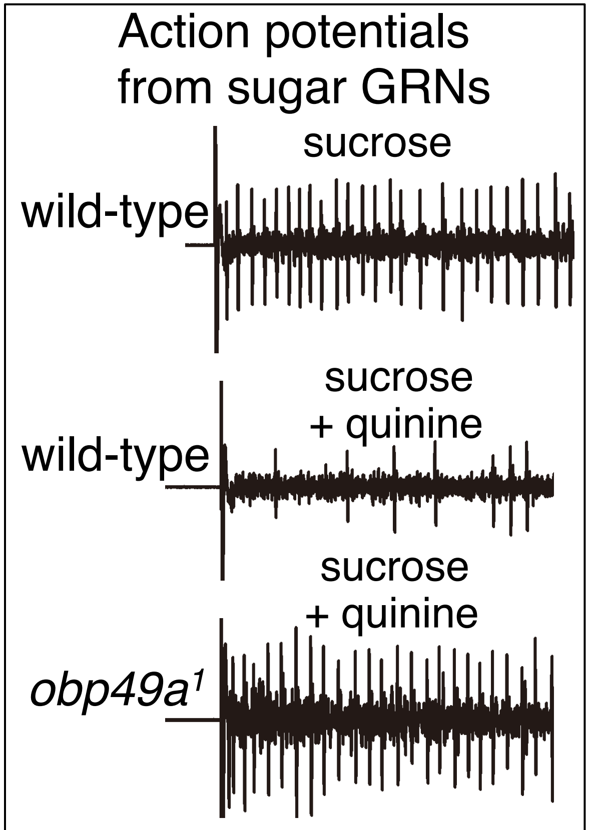
GR93a	caffeine
GR47a	strychnine
GR8a	L-canavanine
GR98b	L-canavanine

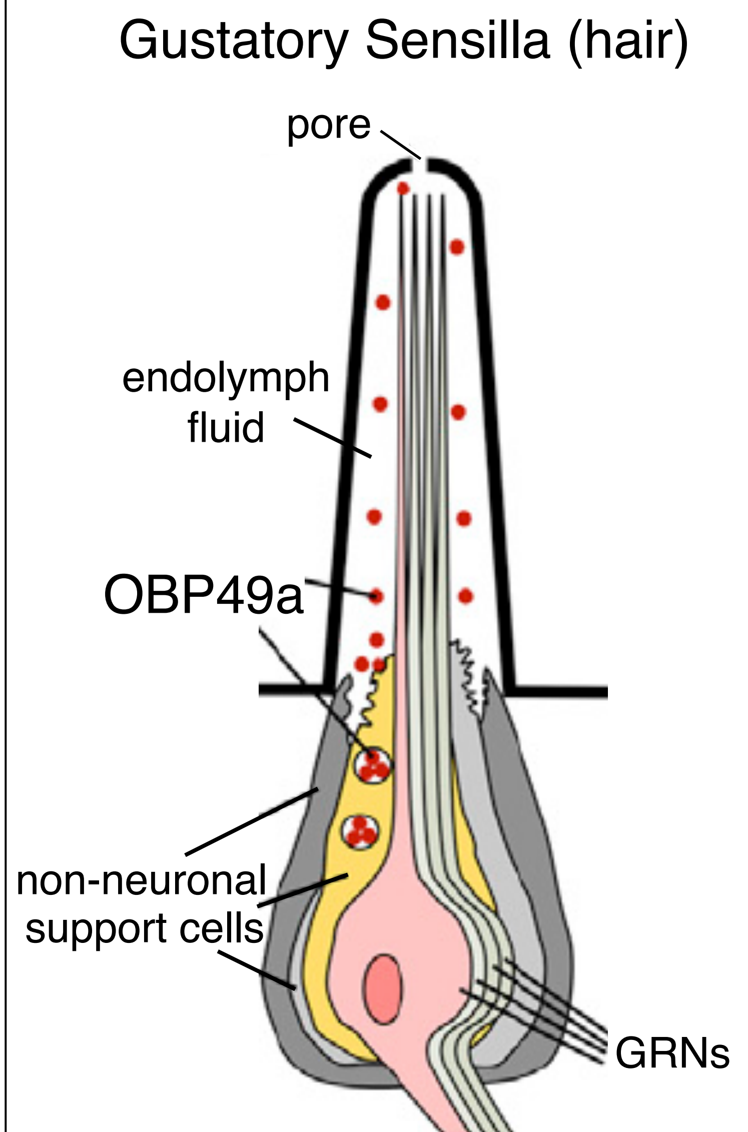
Moon, Köttgen, Jiao, Xu and Montell. Curr. Biol. 2006
Lee, Moon, and Montell. PNAS. 2009
Moon, Lee, Jiao and Montell. Curr. Biol. 2009
Lee, Kim and Montell. Neuron 2010
Lee, Kang, Shim, Cheong, Moon and Montell. J. Neurosci. 2012
Shim et al. Nat. Commun. 2015

How bitter compounds inhibit sugar activated GRNs

OBPs (odorant binding proteins) are extracellular proteins that are molecular carriers

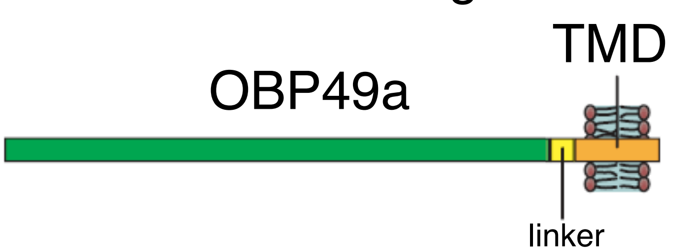






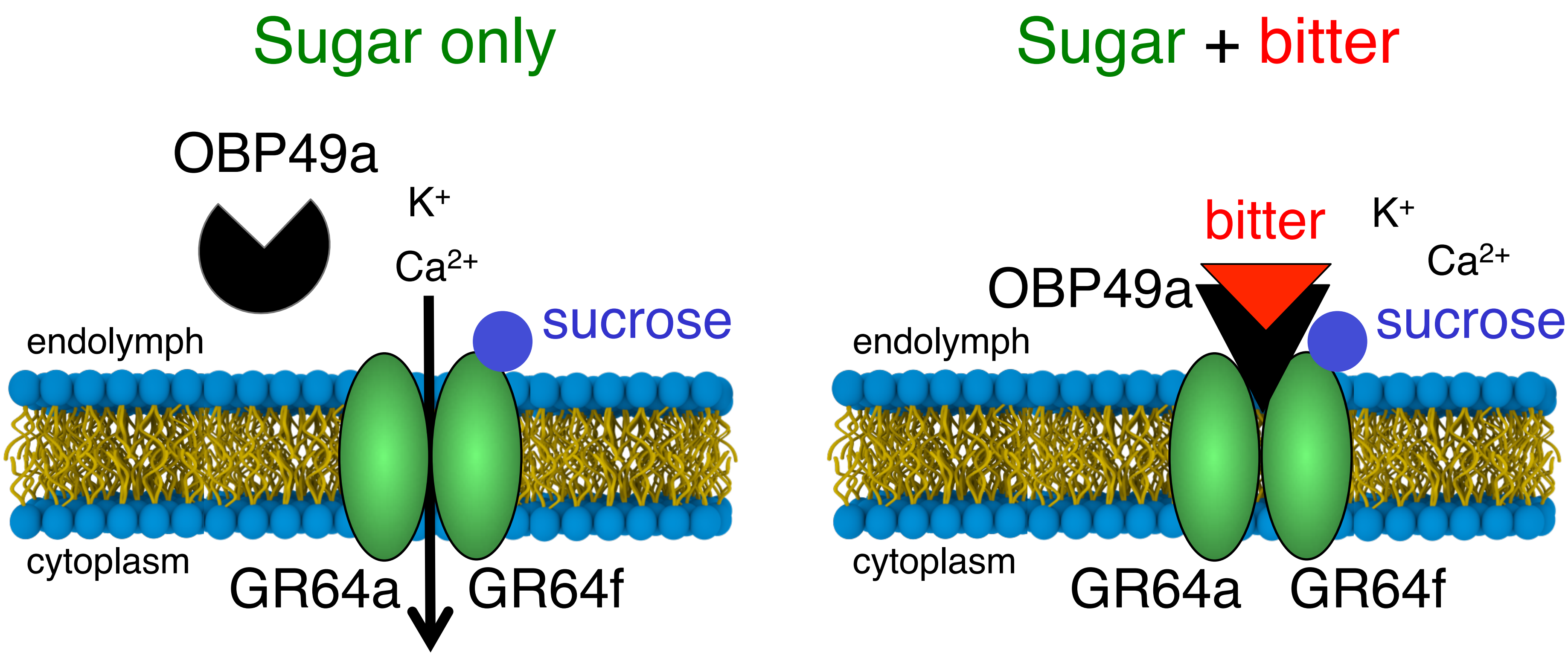
Preview from Lvovskaya and Smith. Neuron, 2013

OBP49a acts on sugar GRNs



Jeong, Shim, Oh, Yoon, Kim, Moon, Montell. Neuron 2013

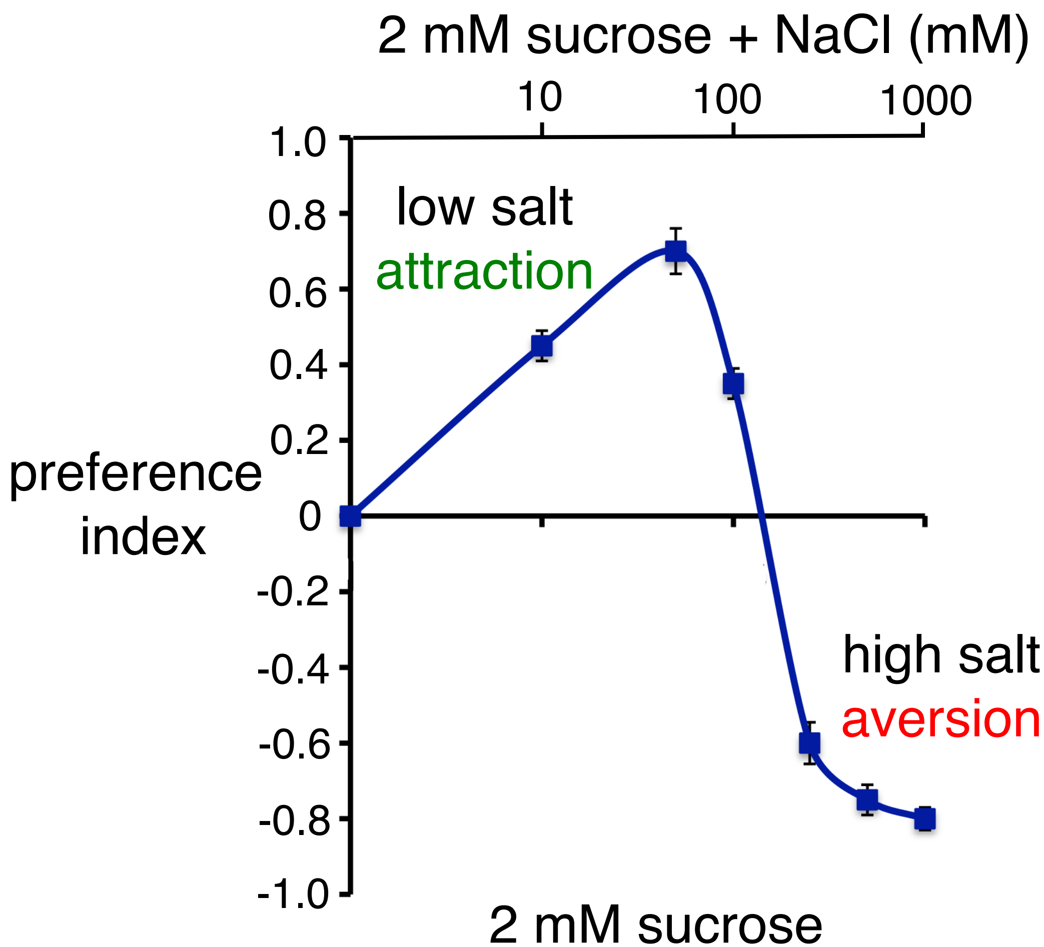
OBP/bitter complex binds to and inhibits sugar receptors



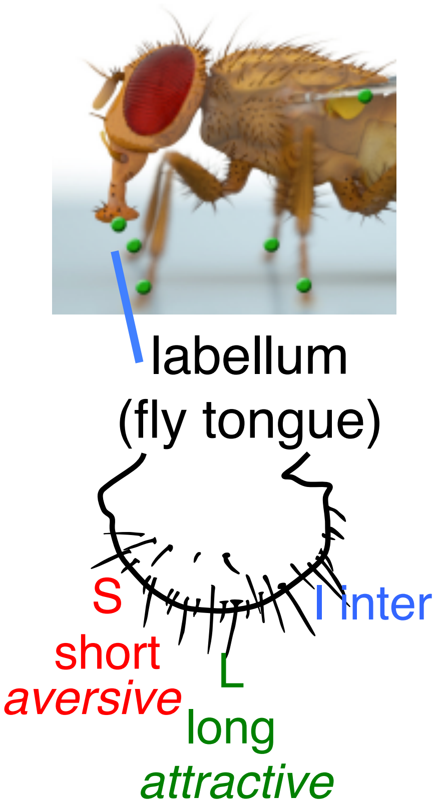
Jeong, Shim, Oh, Yoon, Kim, Moon, Montell. Neuron 2013

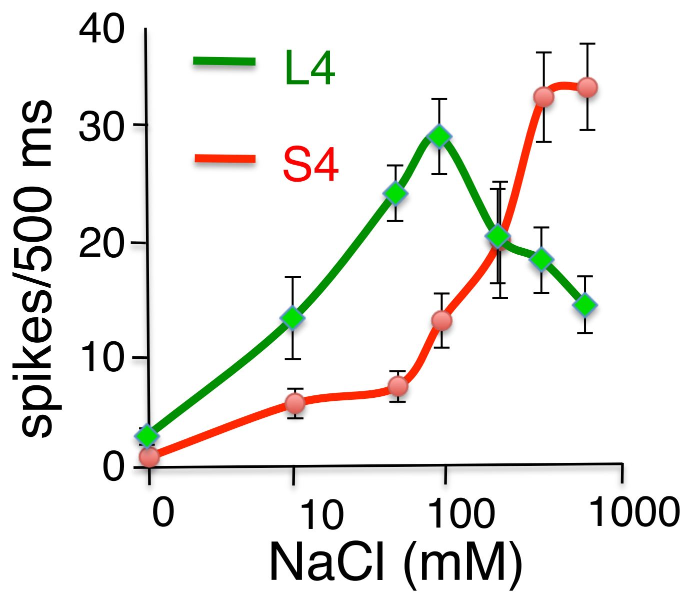
Salt
A double-edged sword

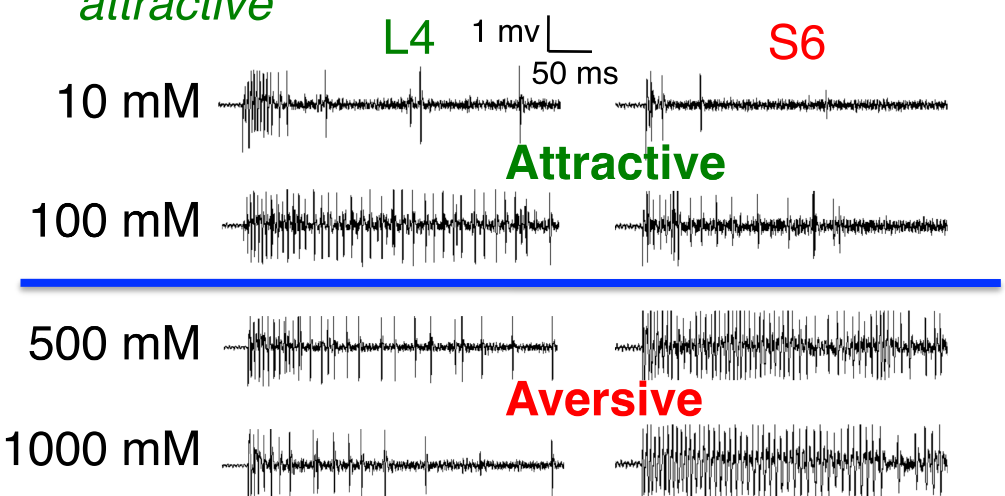
Bivalent salt response distinct from sugar and bitter response

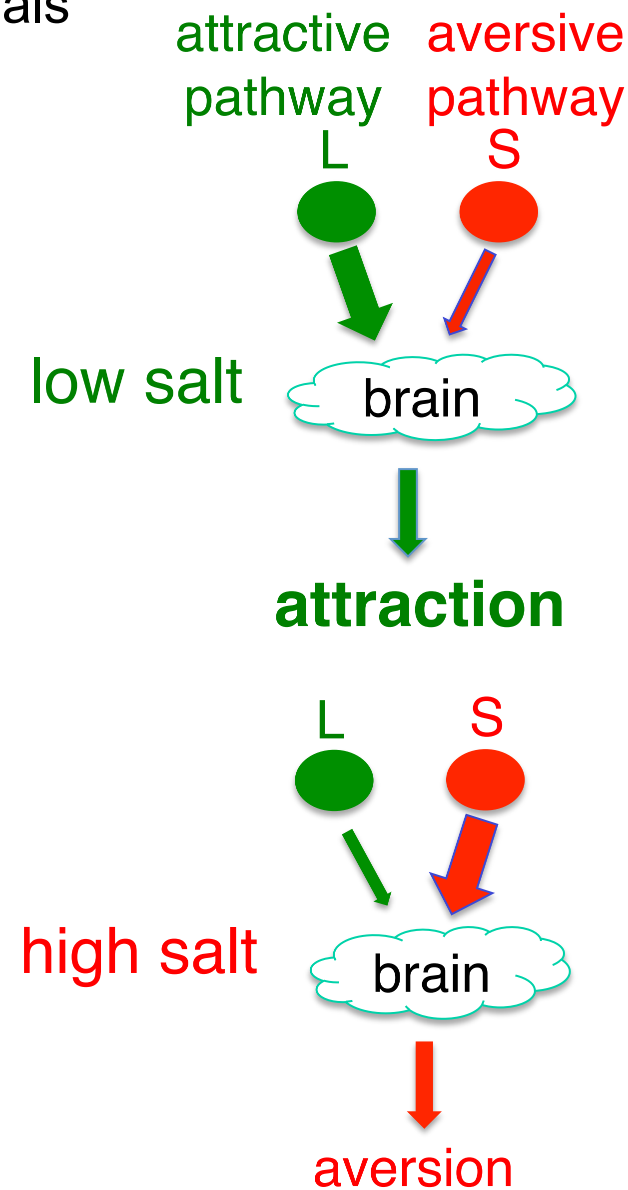


Cellular Competition Defines Behavioral Output





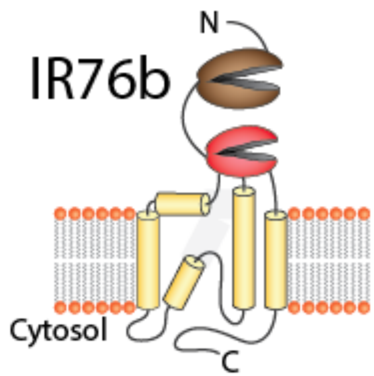


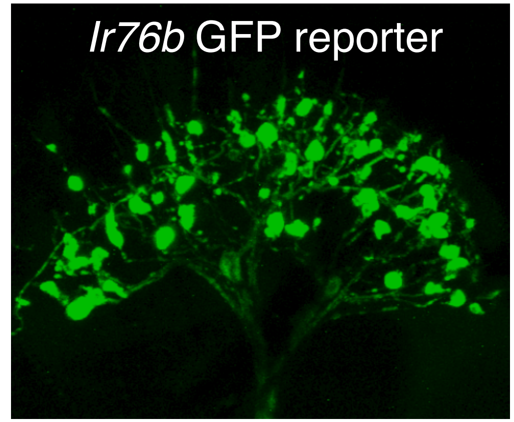


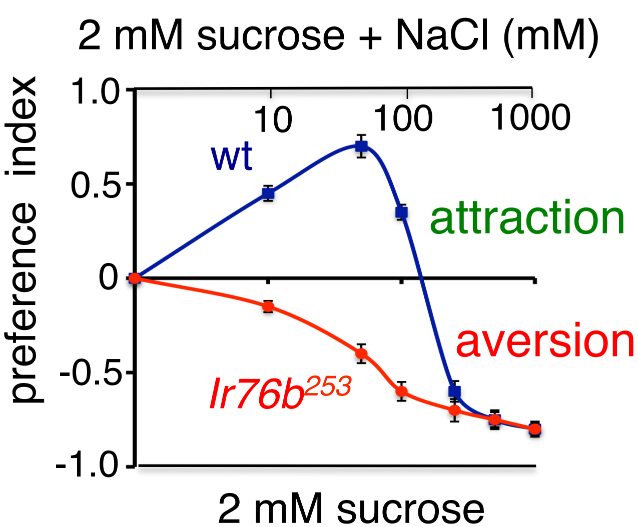
Zhang, Ni and Montell. Science (2013)

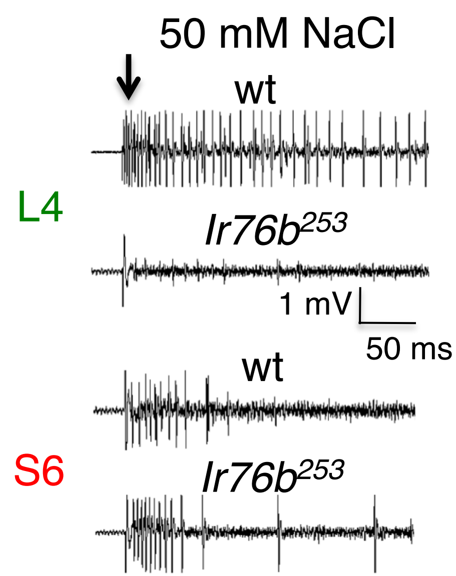
Molecular Basis for Attraction to Low Salt Taste

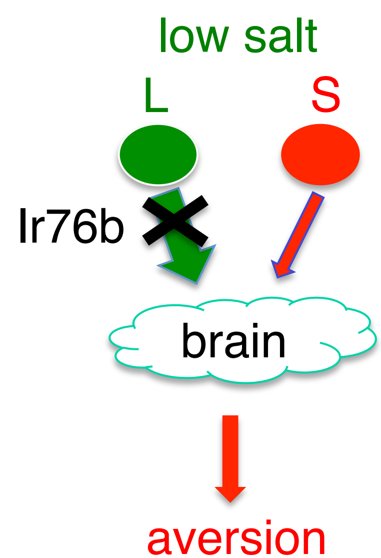
Non-canonical iGluR
(**IR**s) >60 in flies





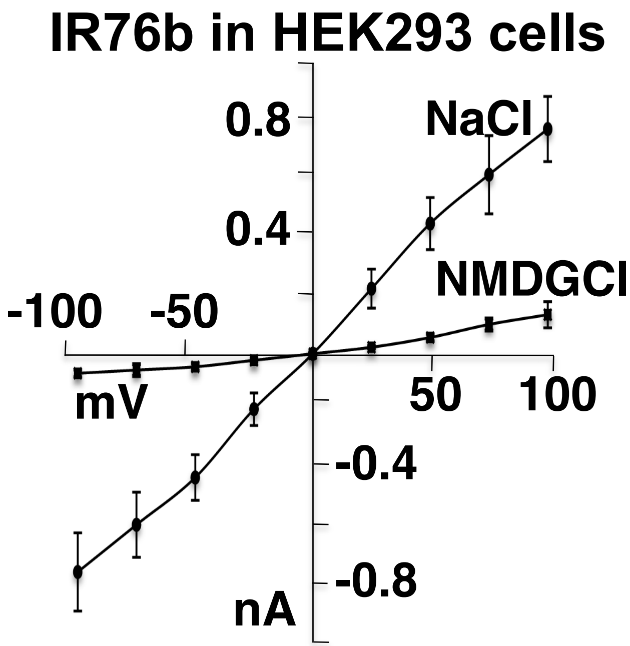


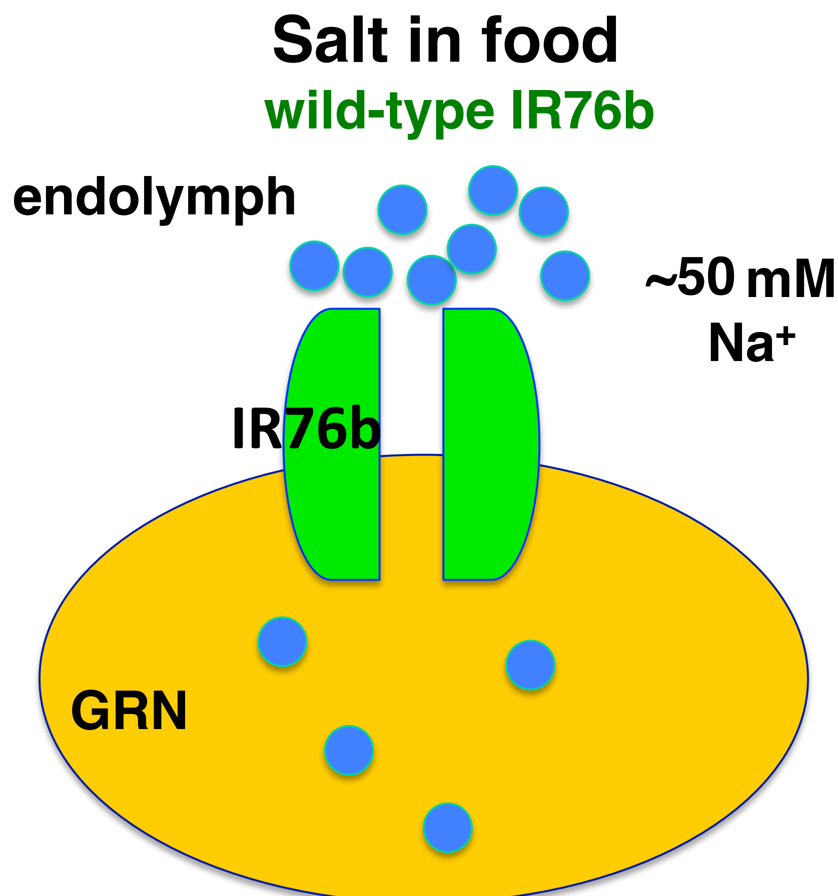


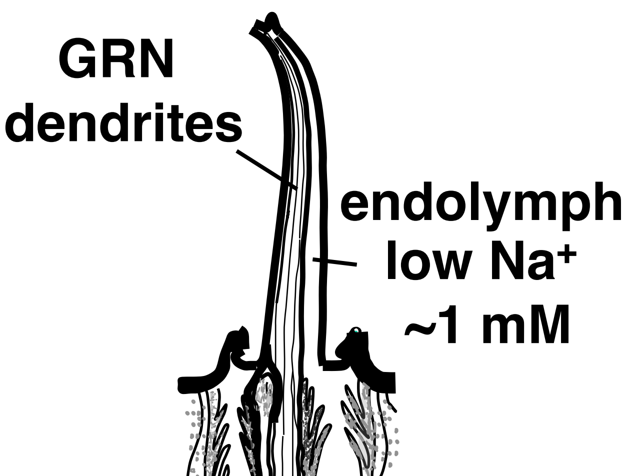


Zhang, Ni and Montell. Science (2013)

A Gate-less Sensory Signaling Channel







Zhang, Ni and Montell. Science (2013)

Sensory integration in the fly gustatory system

Accept or reject?

Sugars

Salts

Bitter compounds

pH

Temperature

Aromas & odors

Color

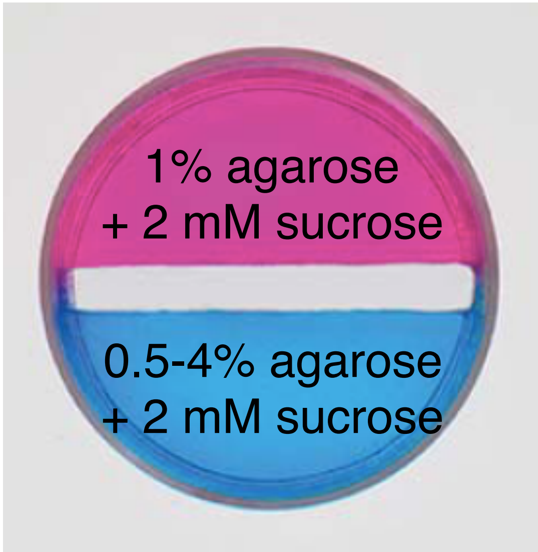
Texture

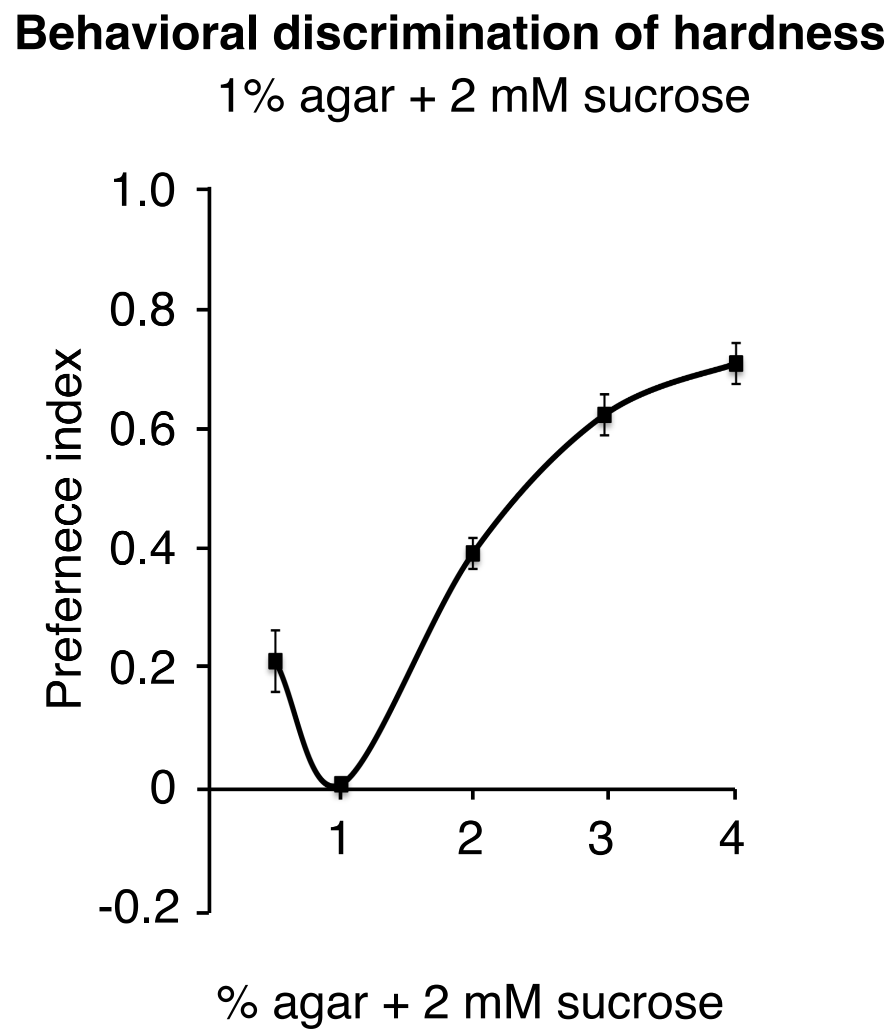
Food texture affects taste preference

Food texture: hardness and viscosity

Crunchy, chewy, crispy, solid, hard, soft, soggy, firm, creamy etc

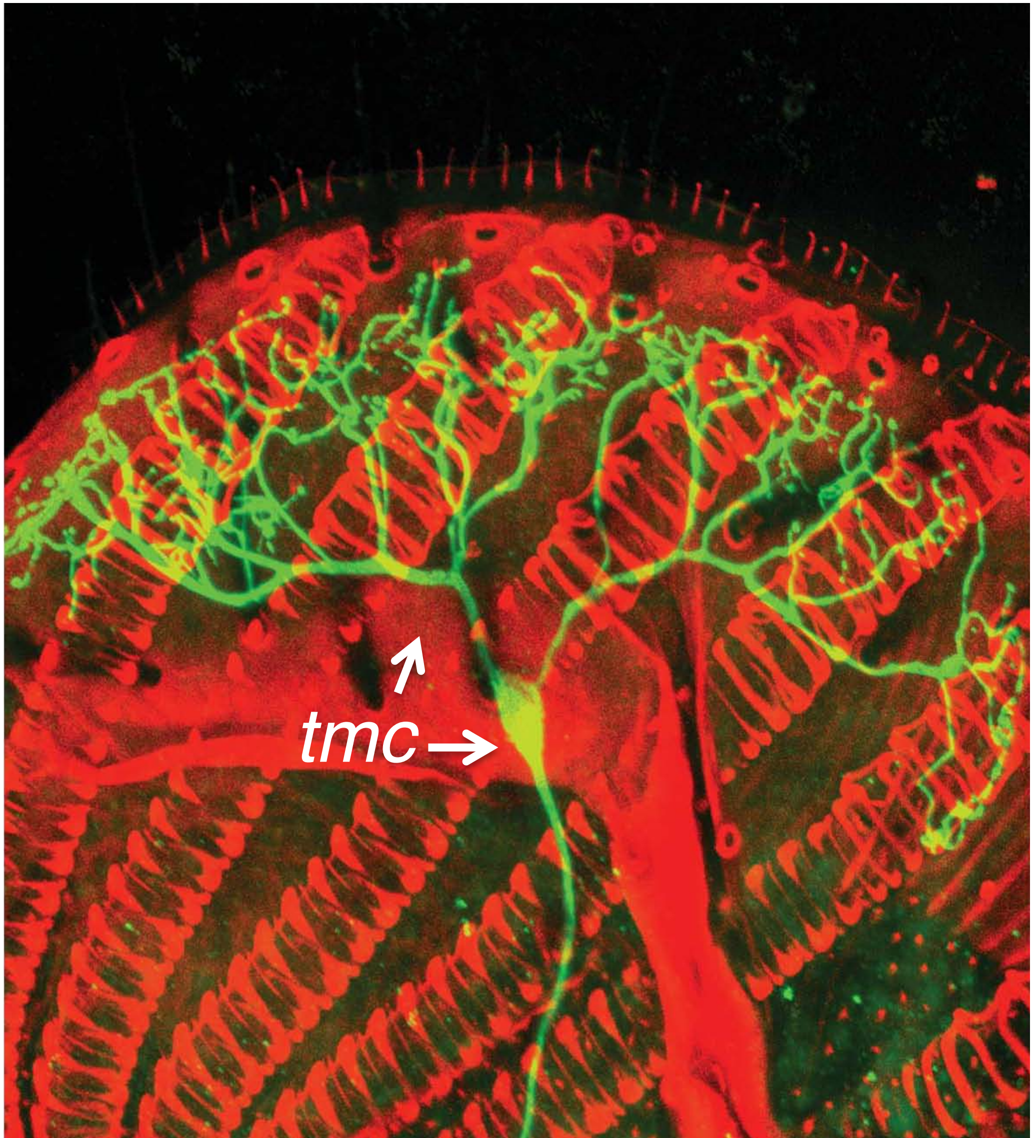
Taste discrimination based on hardness

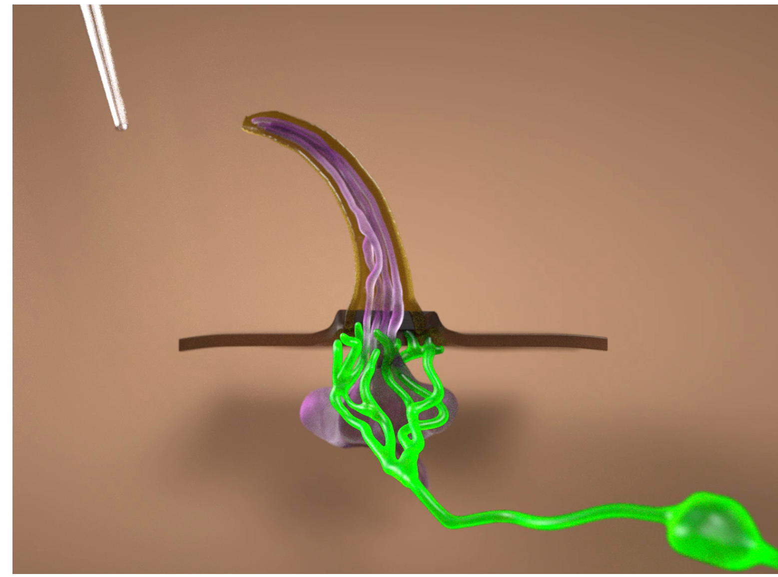




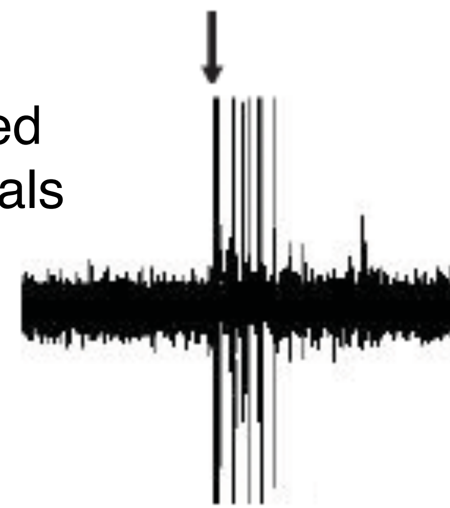
Zhang, Aikin, Li and Montell. 2016. Neuron

Multidendritic neuron (md-L) is force activated



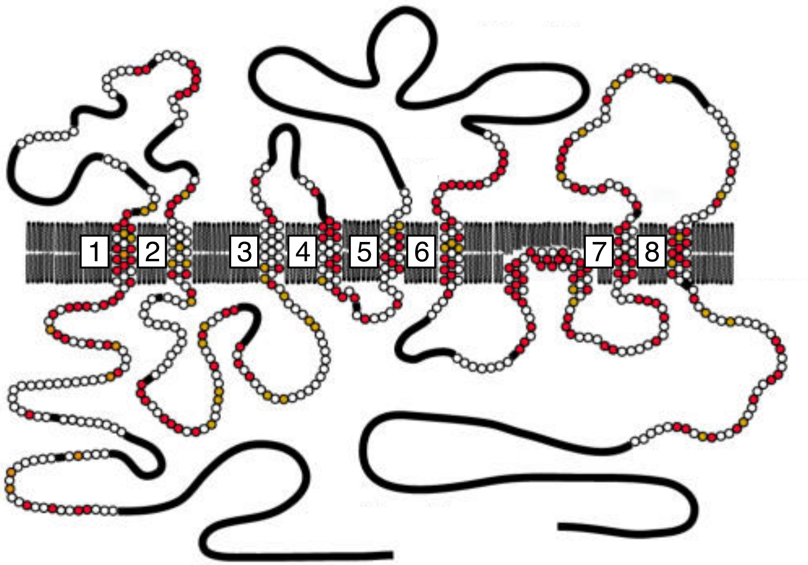


Force-induced action potentials

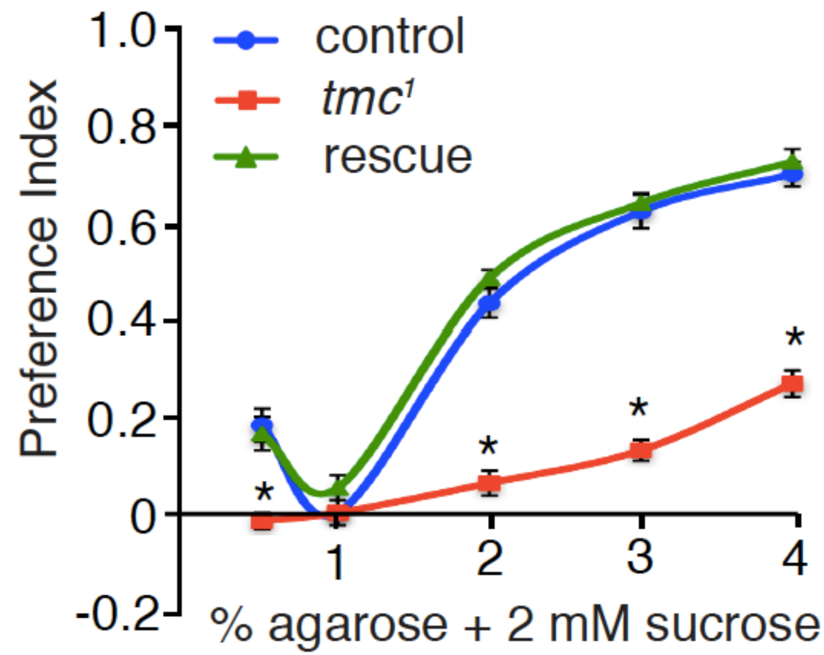


Zhang, Aikin, Li and Montell. Neuron (2016)

TMC required for food texture sensation



Transmembrane channel-like (TMC)



Zhang, Aikin, Li and Montell. Neuron (2016)

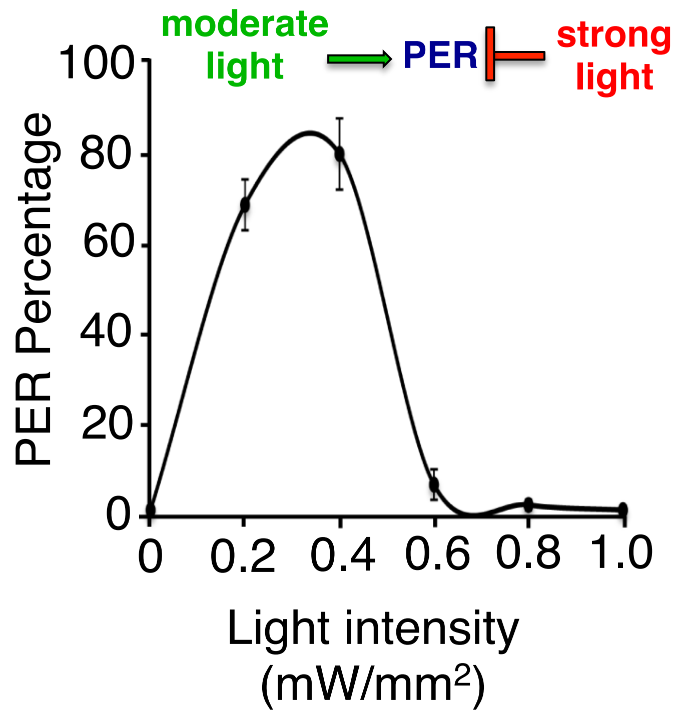
Intensity coding mechanism

Optogenetic stimulation of md-L neurons

(Flies expressing CsChrimson in md-L neurons)

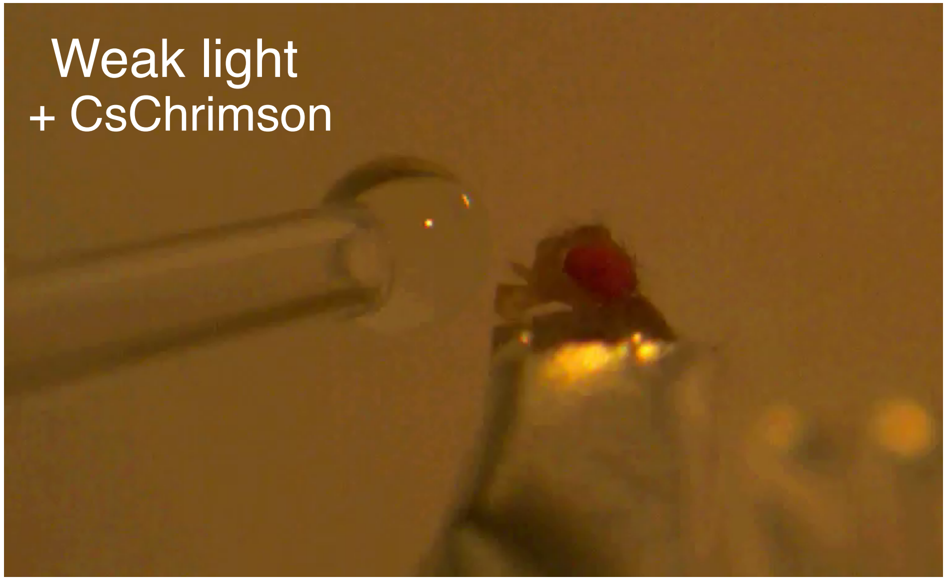
Low light stimulation

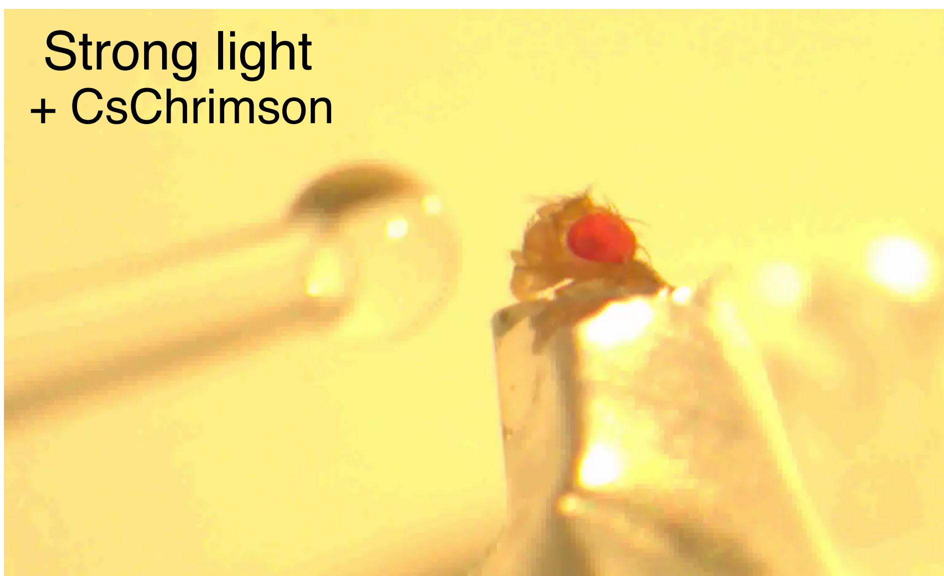
High light stimulation

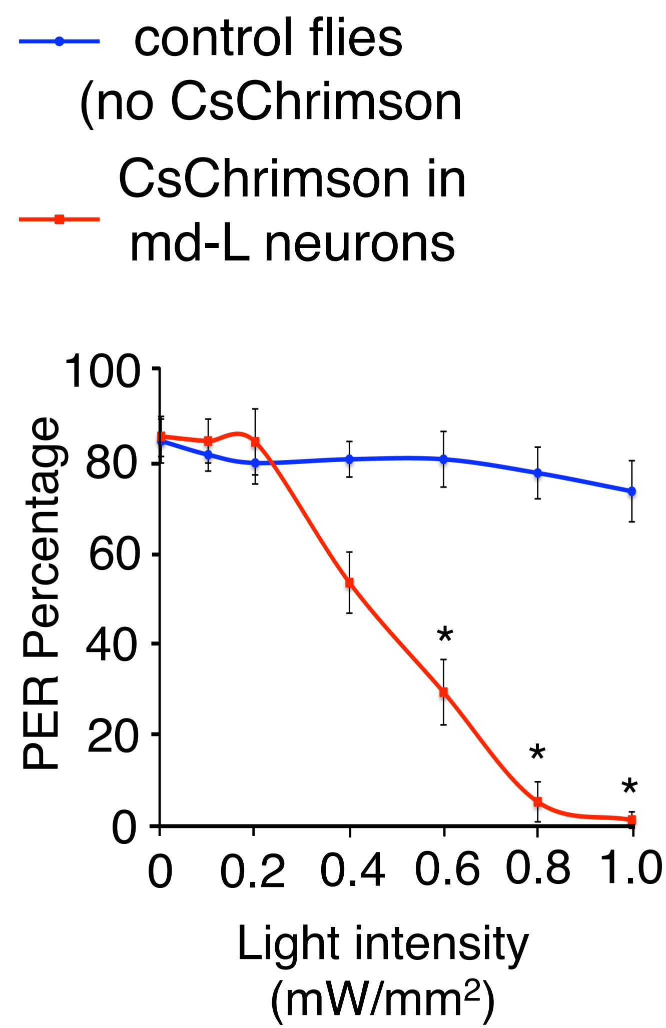


Zhang, Aikin, Li and Montell. Neuron (2016)

Intense optogenetic stimulation of md-L neurons suppresses sugar attraction







Acknowledgments

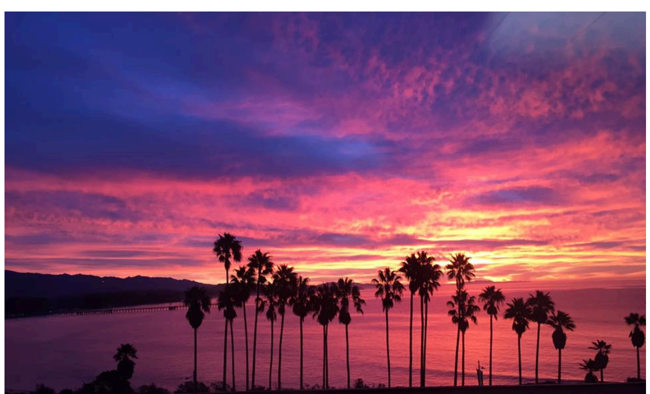
Current lab members

Zijing Chen
Nicole Leung
Nick Debeaubien
Yijing Wang
Adishthi Gurav
Jiangqu Liu
Adi Gurav
Avinash Chandel
Ben Nguyen

Qiaoran Li
Itzel Tekin
Zach Calilung
Jieyan Chen
Angela Morales
Yinpeng Zhan
Anindya Ganguly
Menglin Li

former lab members

Yali Zhang
Jinfei Ni
Wei Shen



Funding

NEI (EY08117-29)
NEI (EY10852-25)
NIDCD (DC007864-12)
NIDCD (DC16278-02)
NIH Pioneer Award
DARPA
ICB/US Army