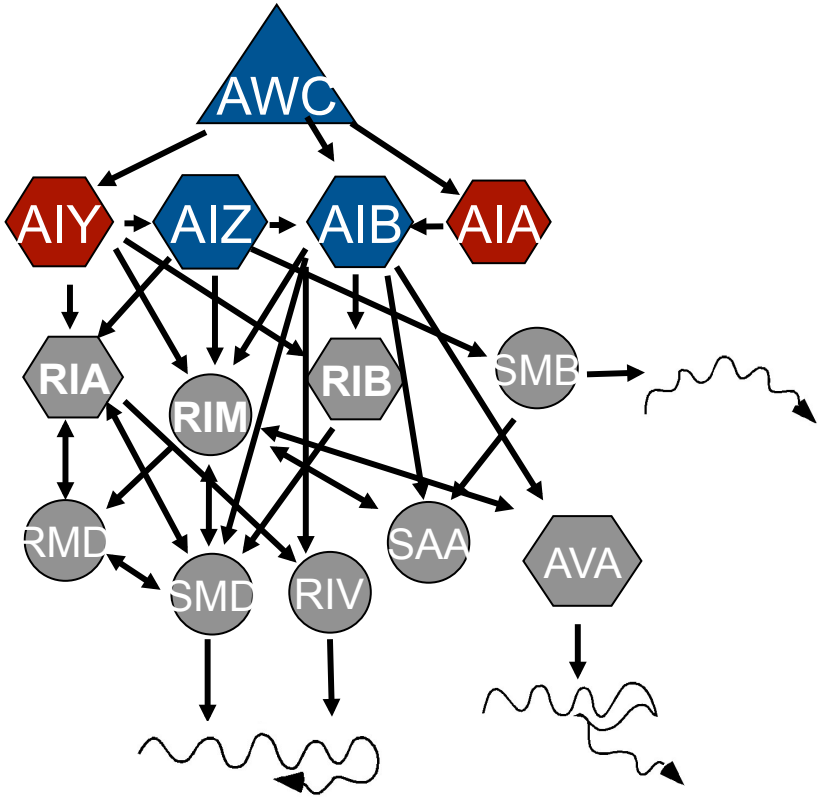
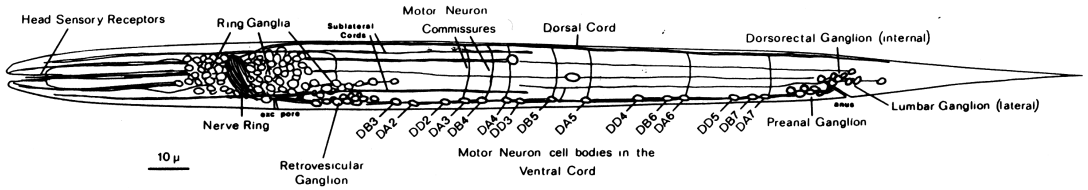
Cracking circuits for olfaction: Odors, neurons, genes and behavior



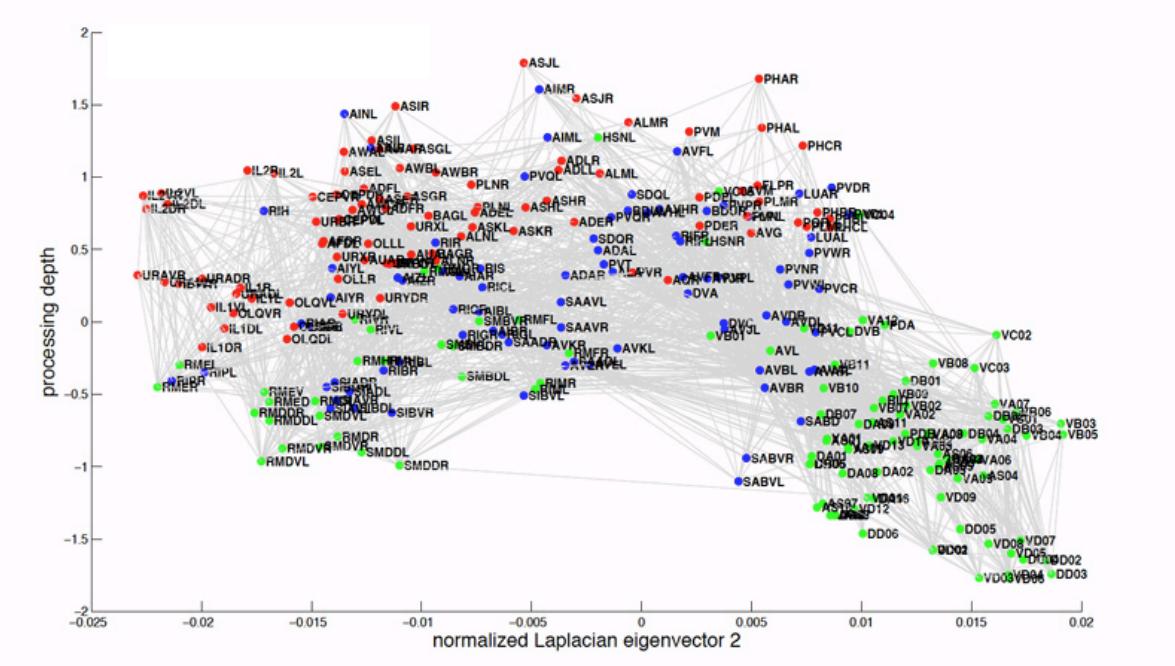
Cori Bargmann
Howard Hughes Medical Institute
The Rockefeller University
New York, NY USA

The human brain:
10 billion neurons, 10 trillion synapses
25,000 genes



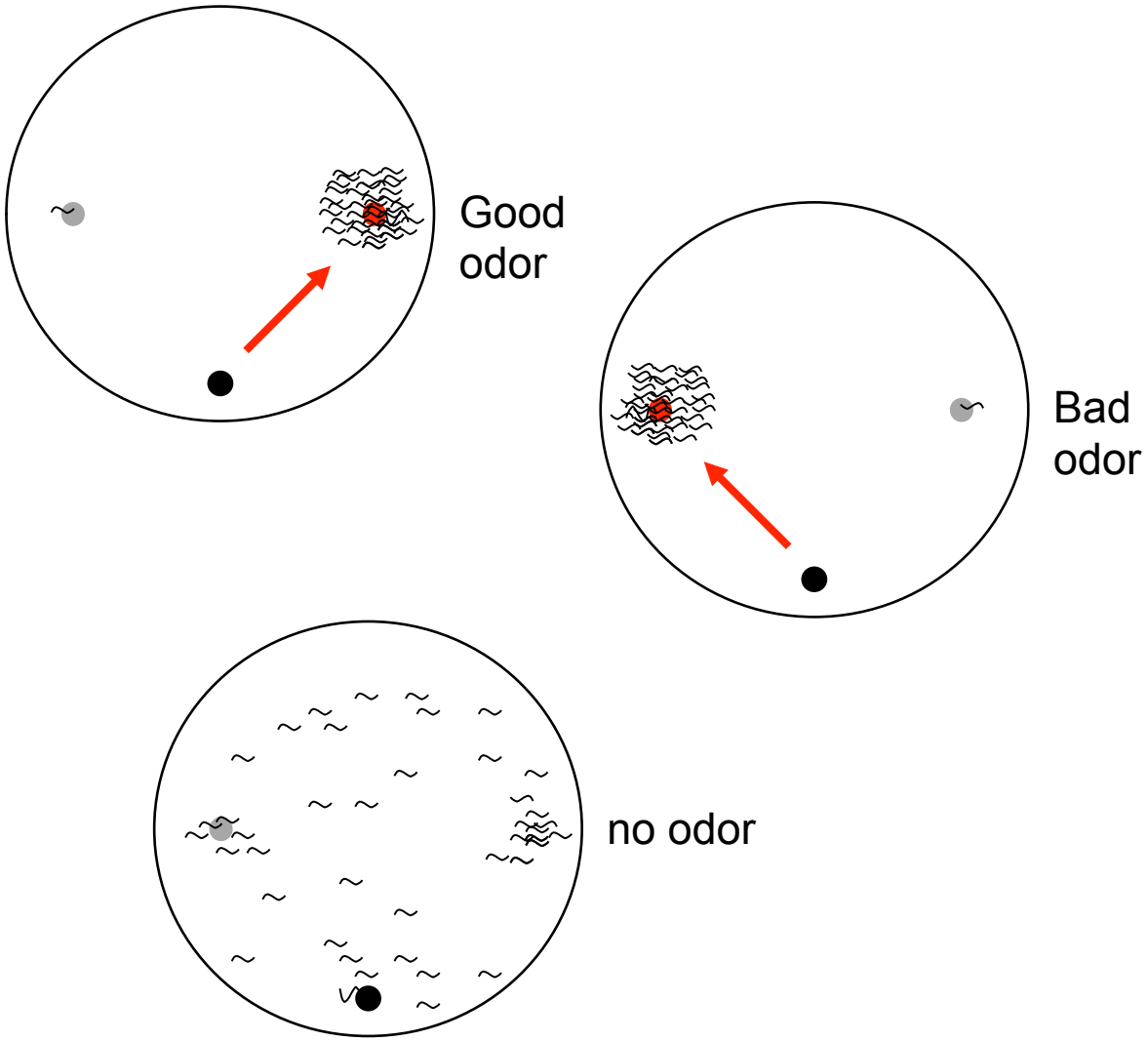
The *C. elegans* nervous system
302 neurons, ~7,000 synapses,
~600 gap junctions
20,000 genes
Known connectivity
Similar neurotransmitters, channels,
developmental genes as humans

The *C. elegans* wiring diagram



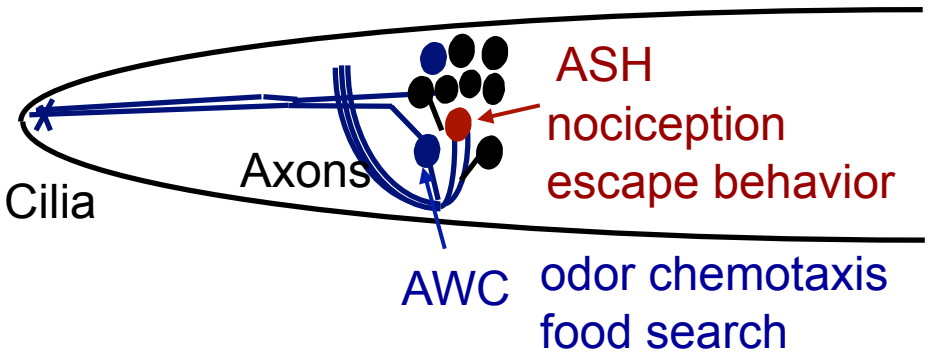
White et al., Proc Royal Soc Lond B 1986
Varshney et al, Neurons and Cognition 2010

C. elegans has robust behavioral responses to odors



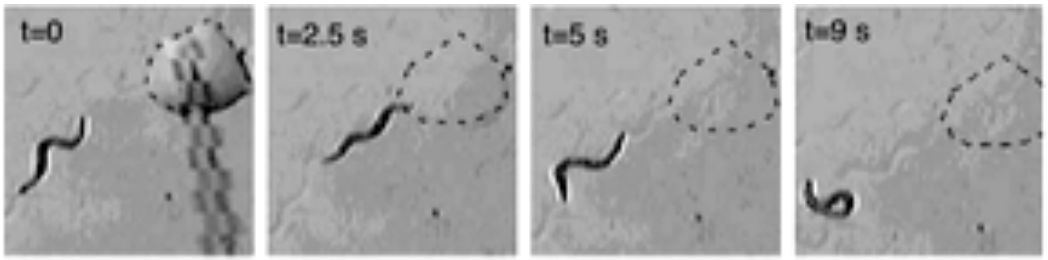
Specific neurons detect odors and initiate behaviors

Loss of function

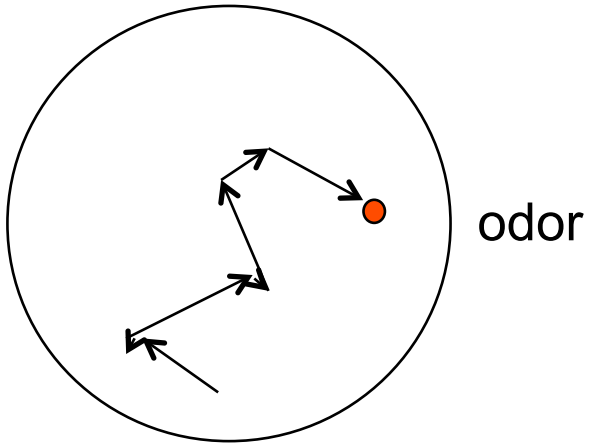


Gain of function

Escape behavior is deterministic.



But chemotaxis is probabilistic.



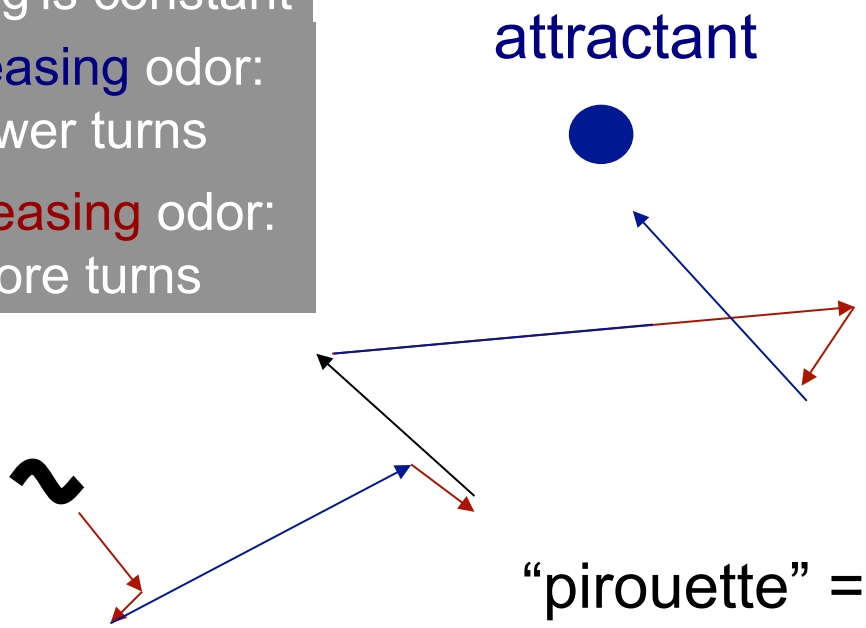
Needed: a model for chemotaxis

The biased random walk for chemotaxis
Odors regulate turning frequency

Constant odor:
Turning is constant

Increasing odor:
Fewer turns

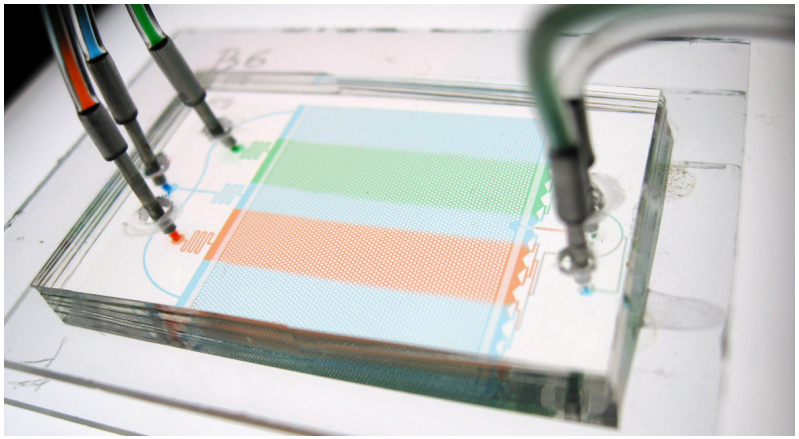
Decreasing odor:
More turns

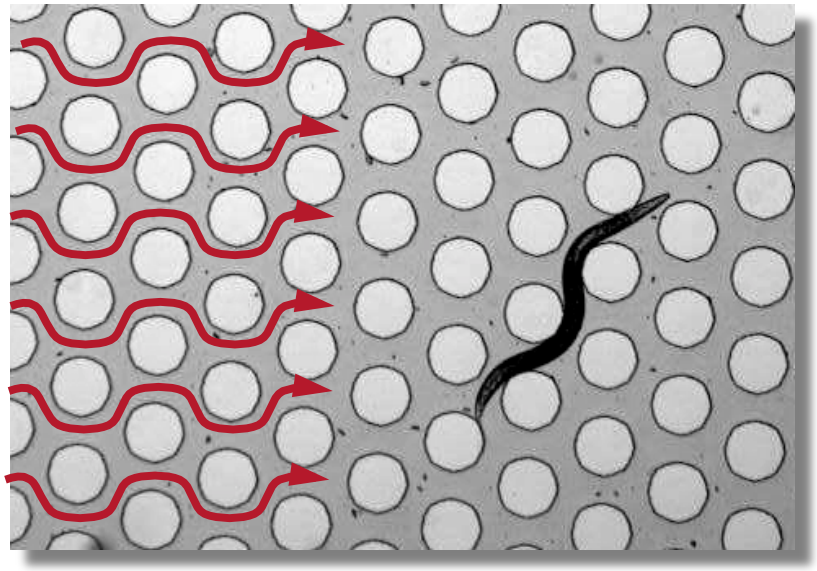


“pirouette” =
reversal or turn

Pierce-Shimomura et al, J. Neurosci. 1999

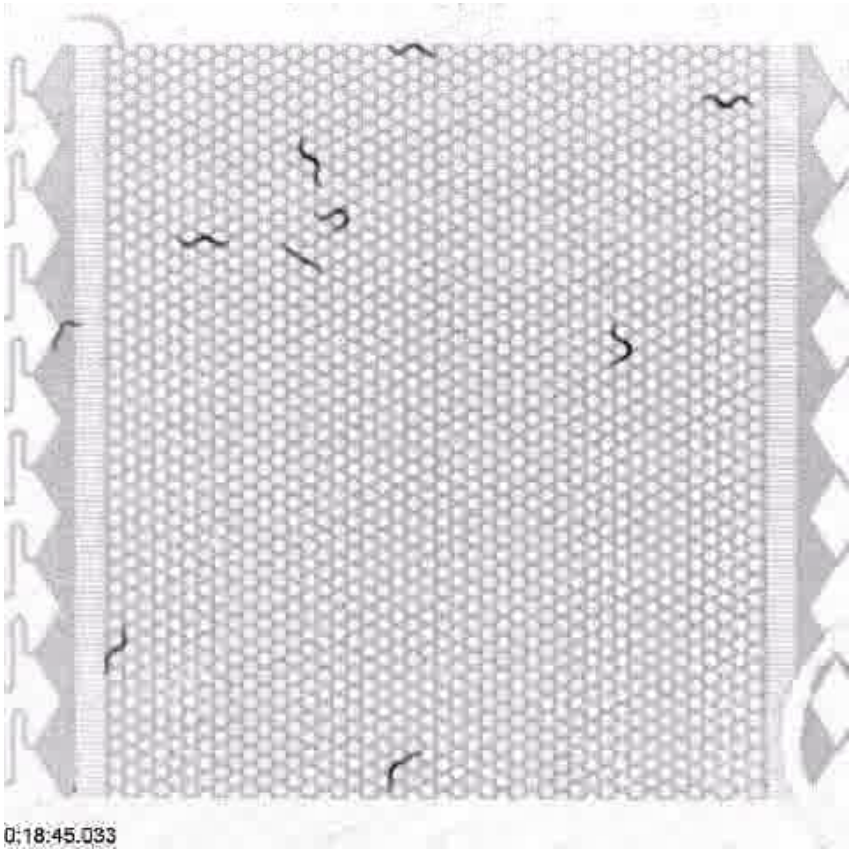
How to test the model? A temporal gradient!





Albrecht and Bargmann, Nature Methods 2011

Turning in temporal odor gradients resembles a biased random walk

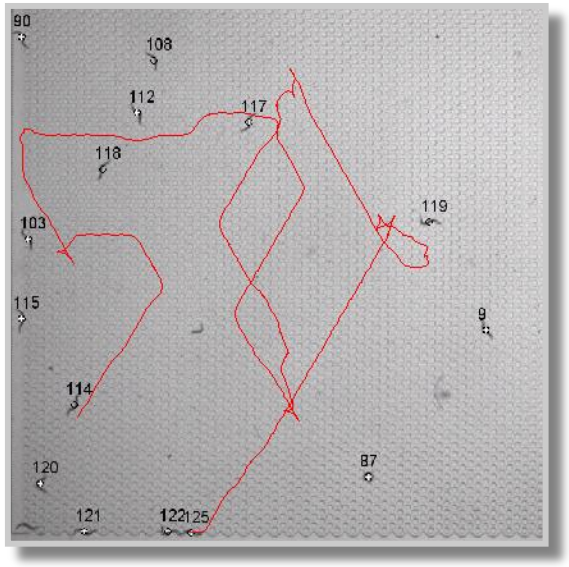


buffer

IAA
1µM

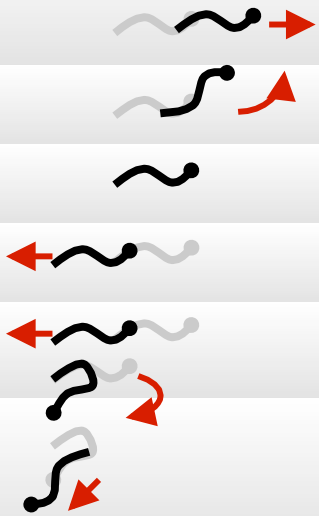
Albrecht and Bargmann, Nature Methods 2011

Automatically analyze turning behaviors

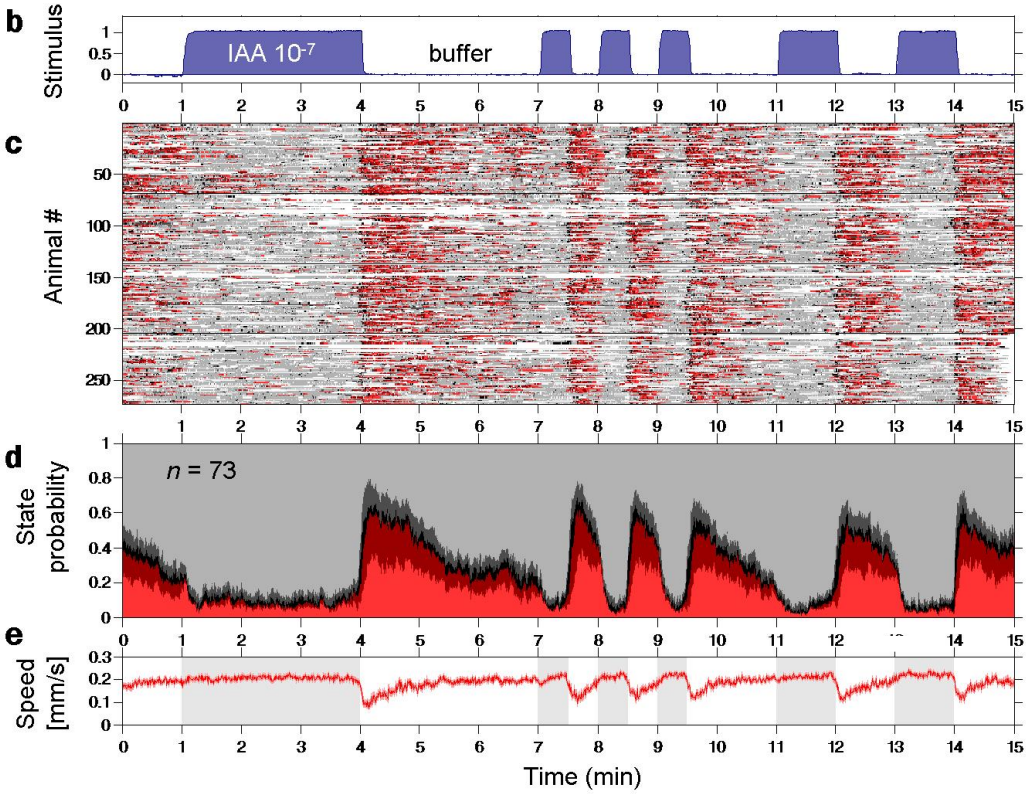


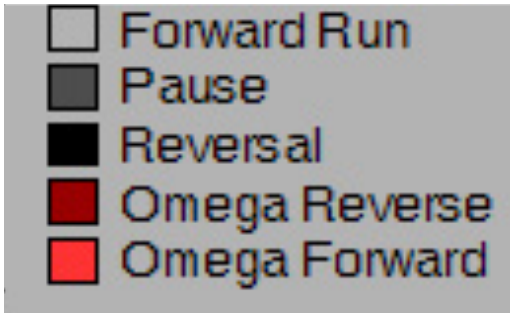
Locomotion States

1. *Forward*
2. *Forward Turn*
3. *Pause*
4. *Reversal*
5. *5a. Pirouette rev.*
6. *5b. Pirouette fwd.*



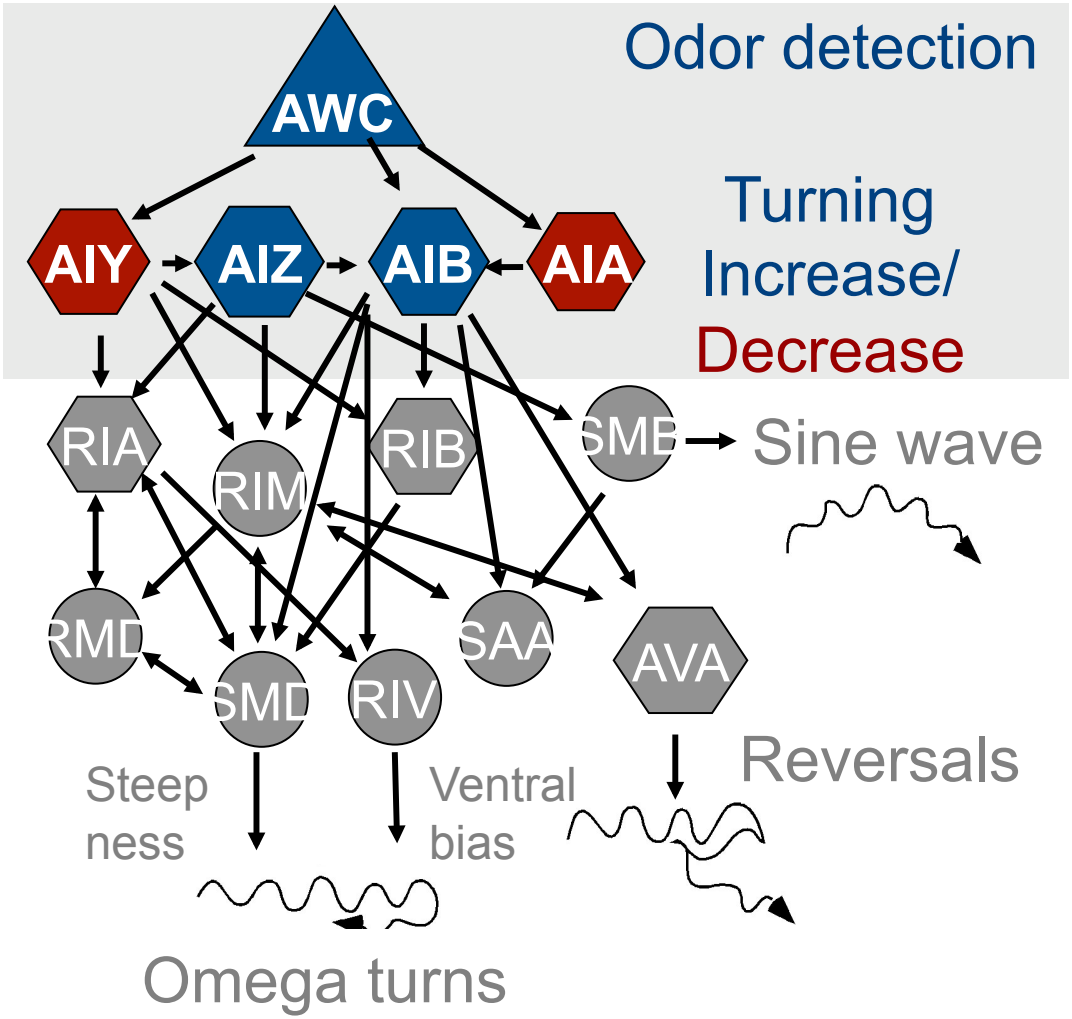
A quantitative view of chemotaxis





Albrecht and Bargmann, Nature Methods 2011

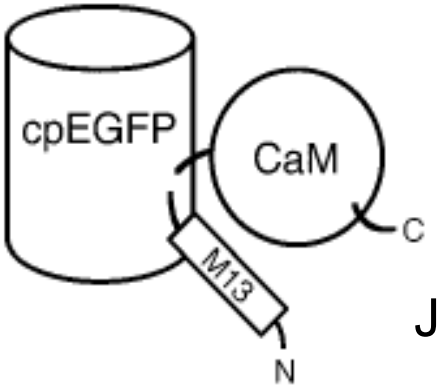
A circuit for odor chemotaxis and food search



Gray et al., PNAS 2005

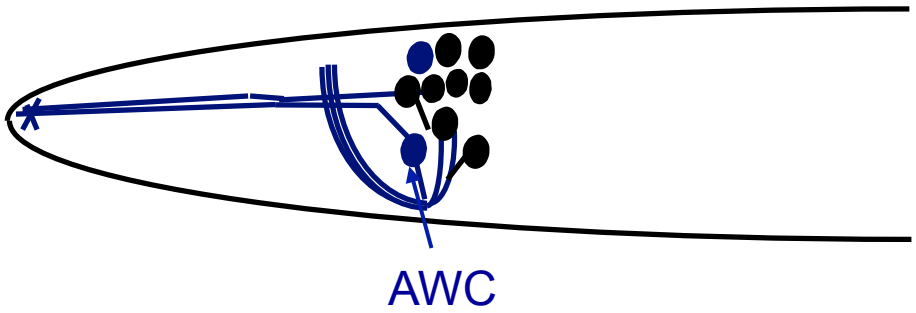
How do neurons respond to odors?

1. Genetically-encoded calcium indicator



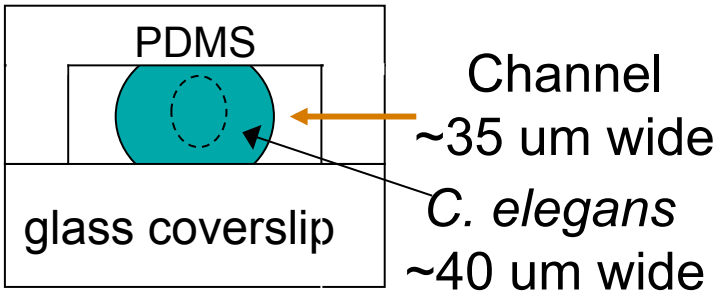
Junichi Nakai

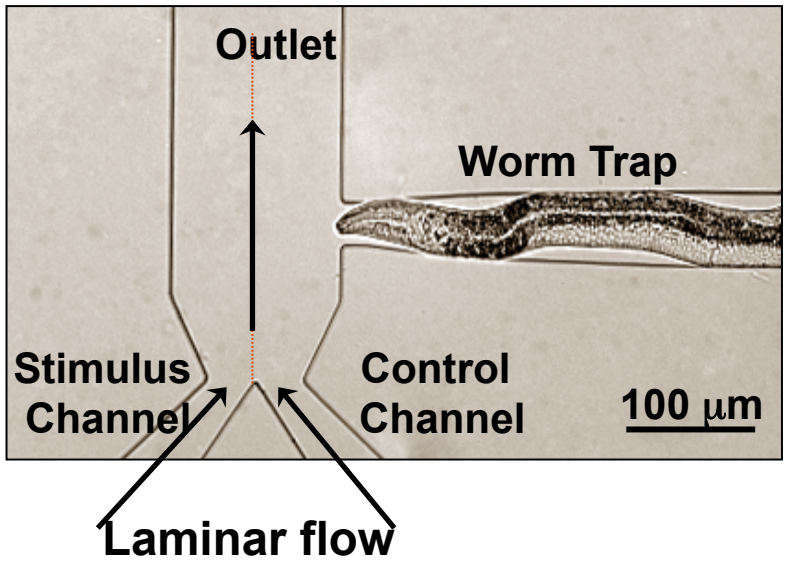
2. Cell type-specific promoters



3. Odor delivery: Microfabricated worm trap

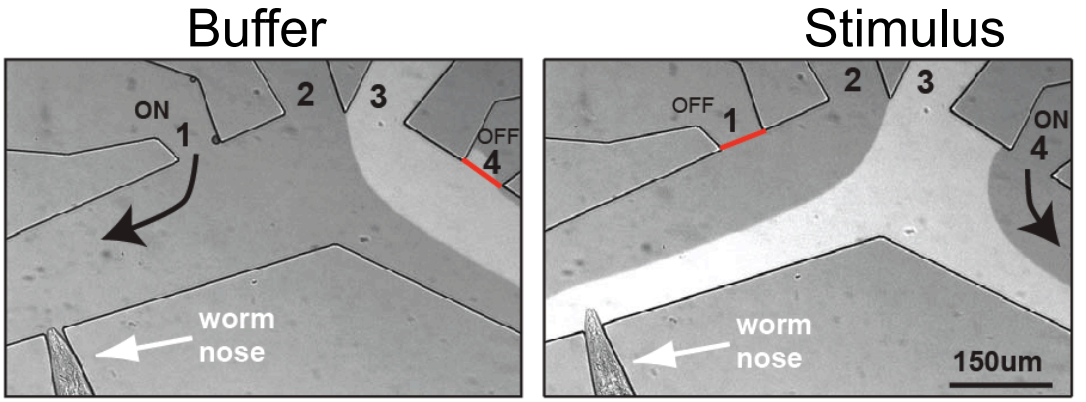
cross sectional view:

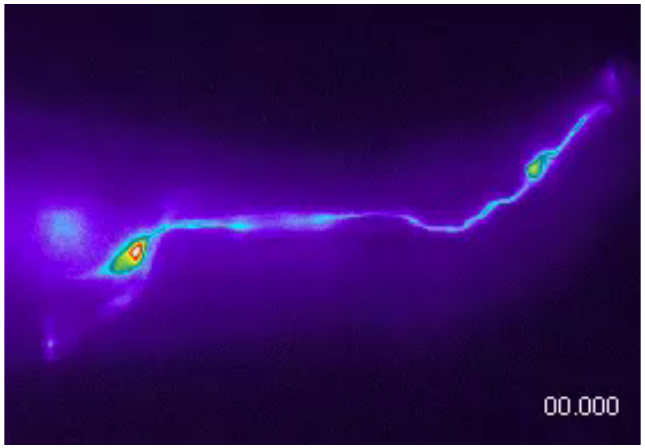




Chronis et al., Nature Methods 2007

Delivering odor and imaging activity in a microfluidic chip

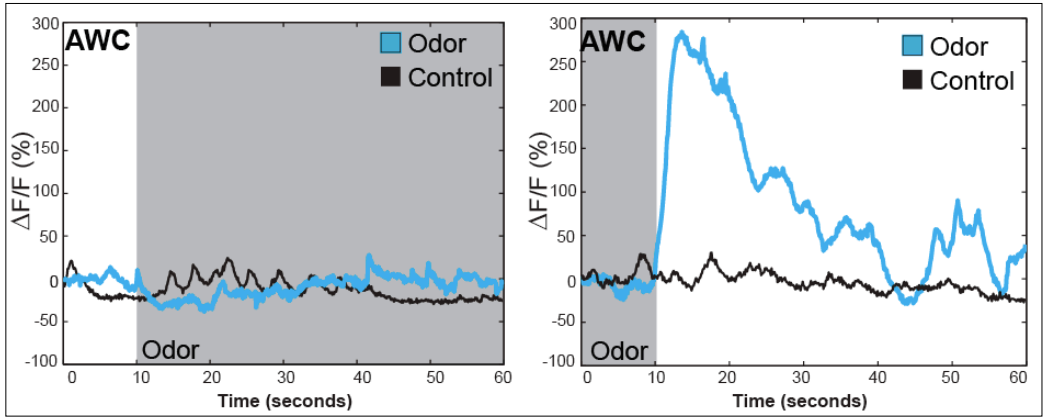


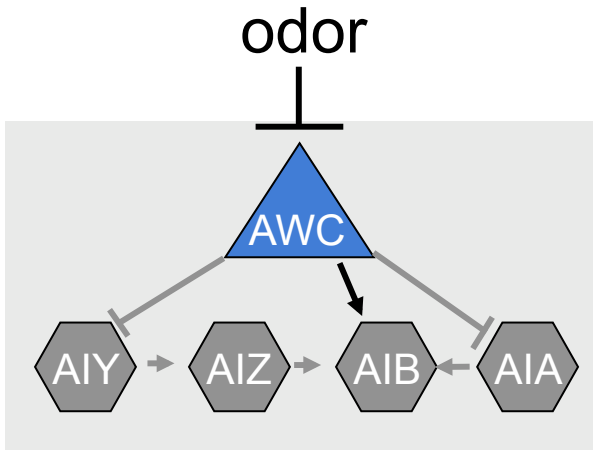


Odor **removal** activates AWC

Odor addition

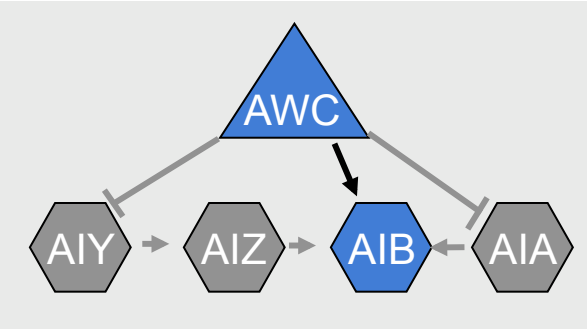
Odor removal

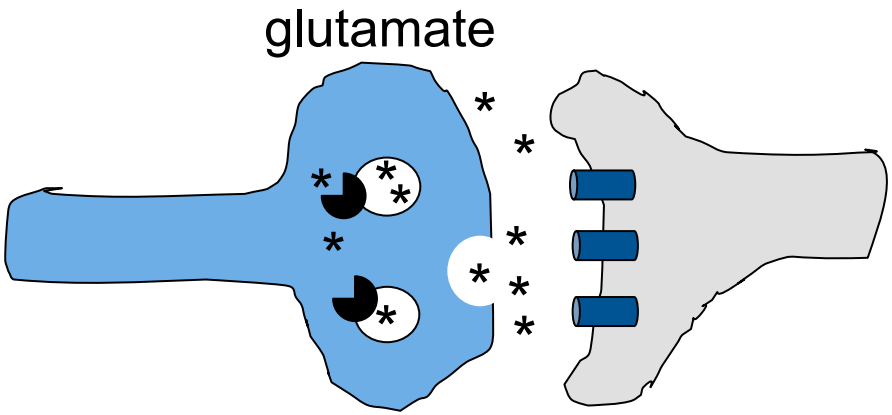




Chalasani et al., Nature 2007

How does AWC communicate with target neurons?

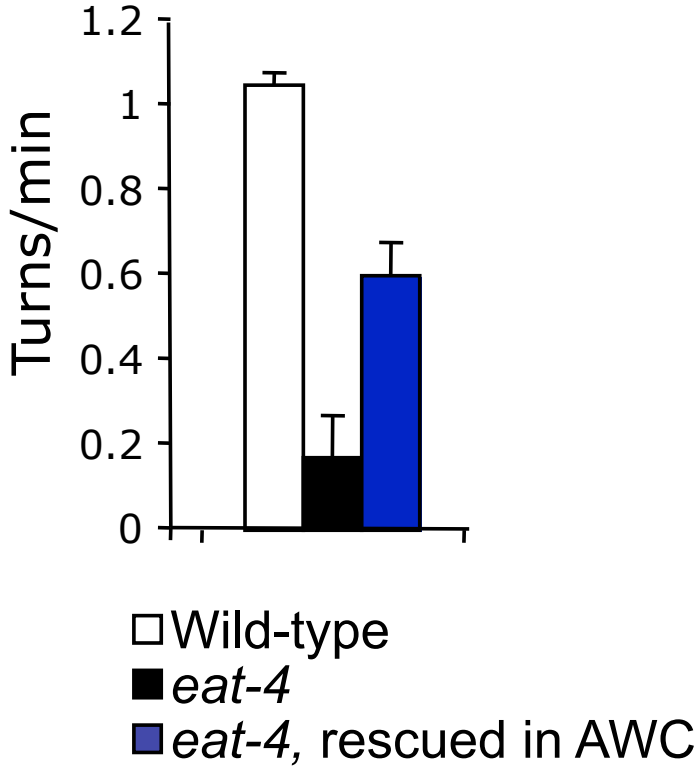




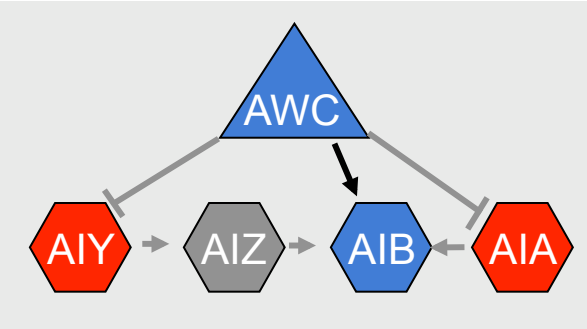
Vesicular Glutamate Transporter
= EAT-4

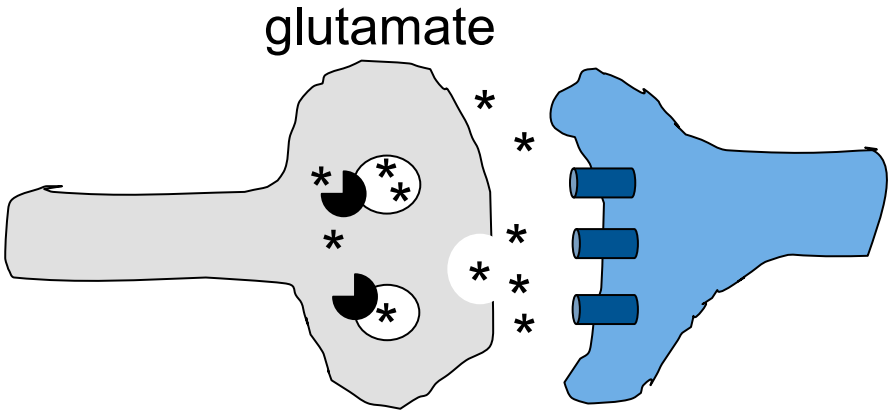
Glutamate is the AWC neurotransmitter
Glutamate from AWC promotes turning

Quantitative response to odor/food removal



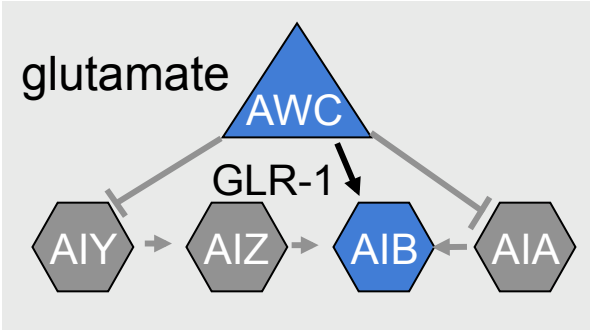
How does AWC communicate with target neurons?





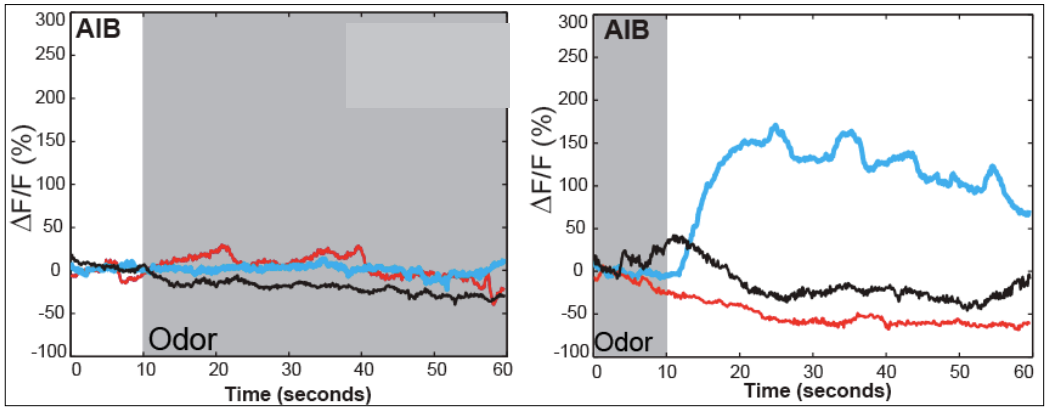
Glutamate receptors:
Cation channel: GLR-1
Anion channel: GLC-3
(and many others)

AWC **activates** AIB through **GLR-1,** an AMPA-type excitatory glutamate receptor



Calcium imaging in AIB

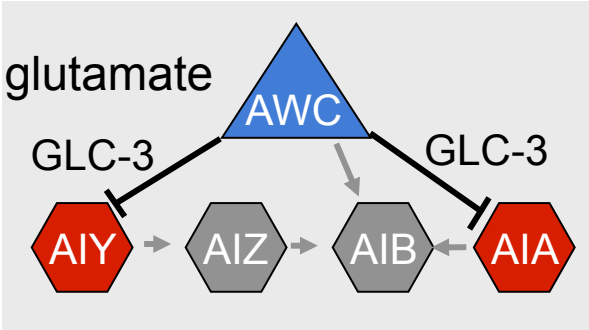
Odor addition Odor removal



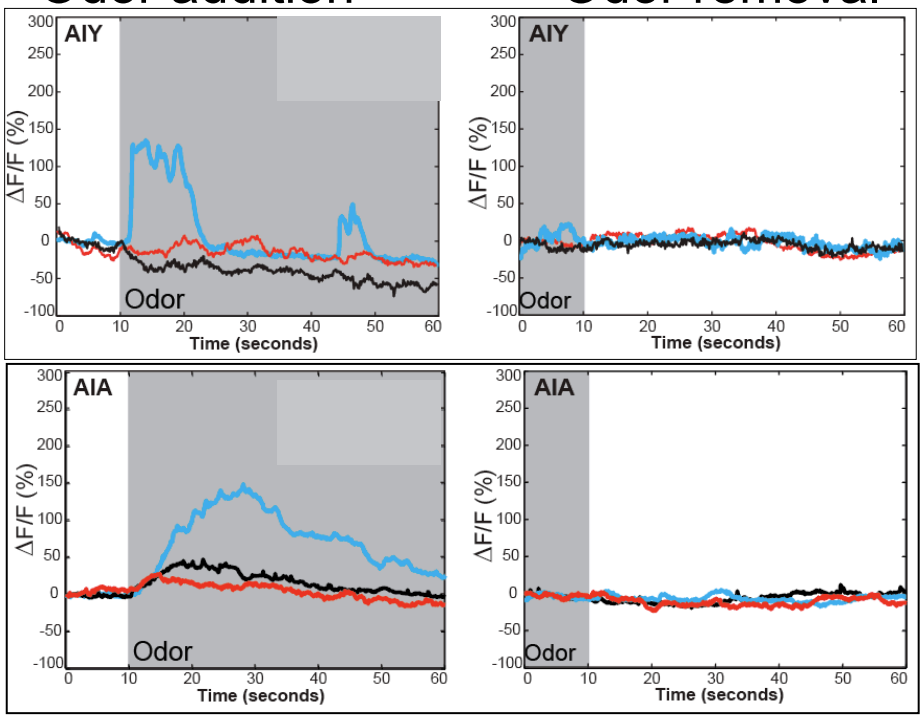
- Wild-type
- *glr-1* mutant
- AWC ablation

Chalasani et al., Nature 2007

AWC inhibits AIA and AIY through GLC-3



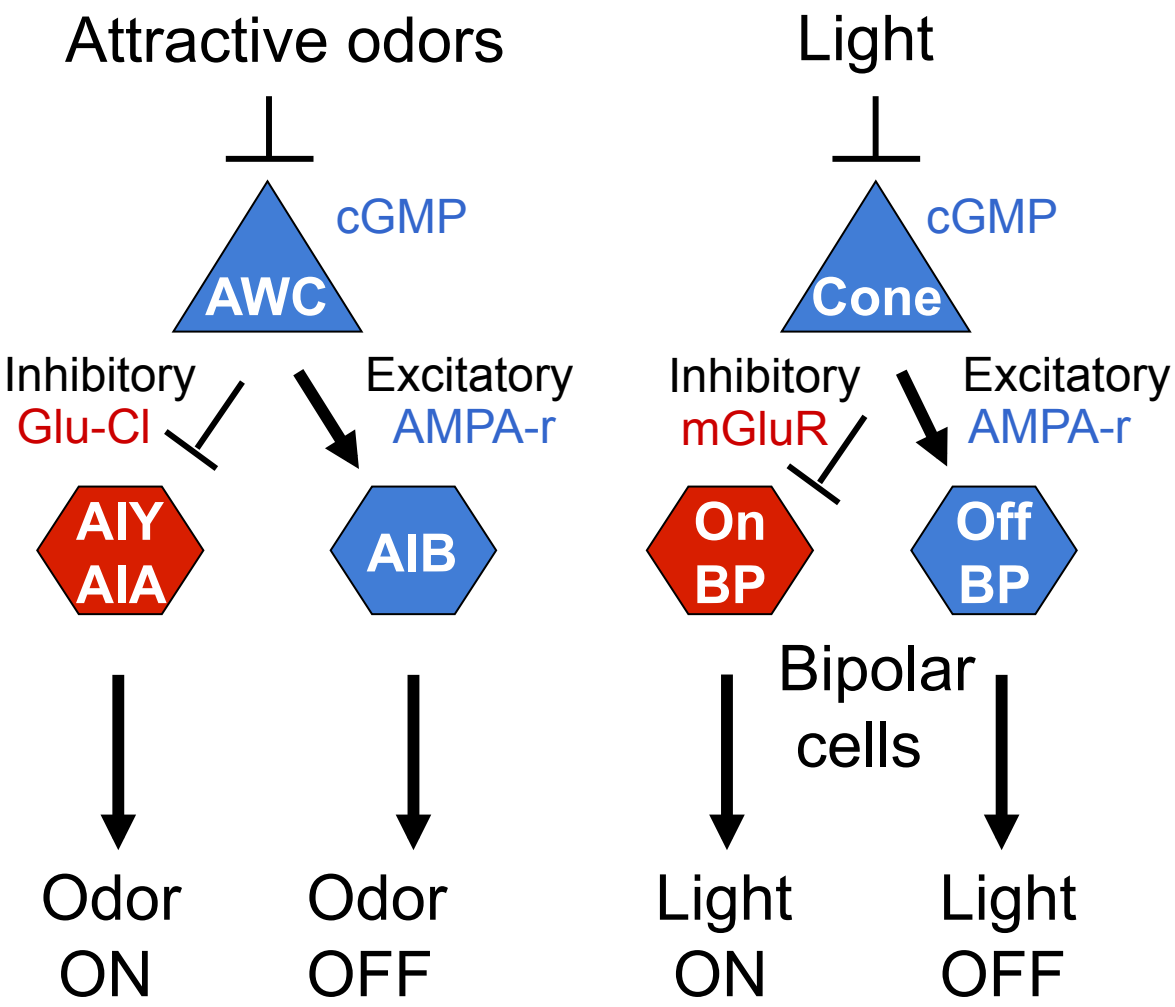
Odor addition Odor removal



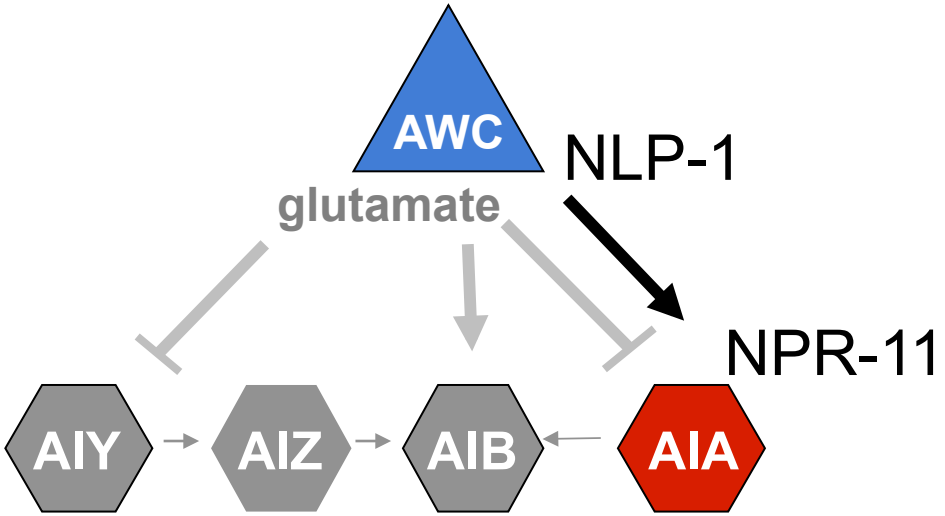
Wild-type
glc-3 mutant
AWC ablation

Chalasani, 2007 & 2010

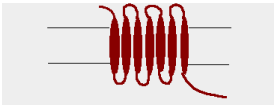
A *C. elegans* odor circuit, the vertebrate retinal circuit



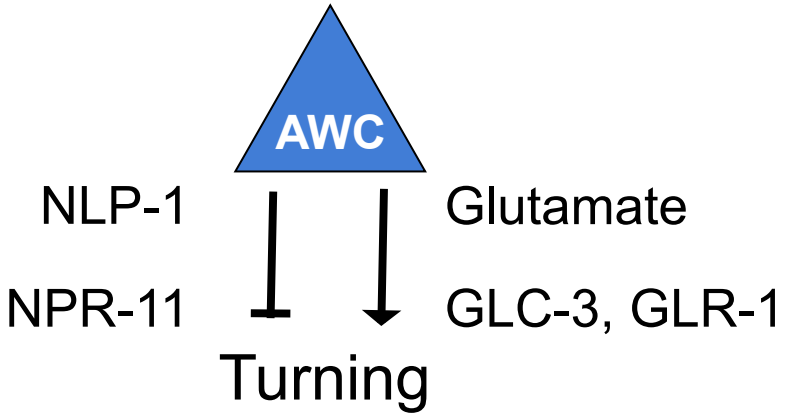
AWC also makes a neuropeptide transmitter

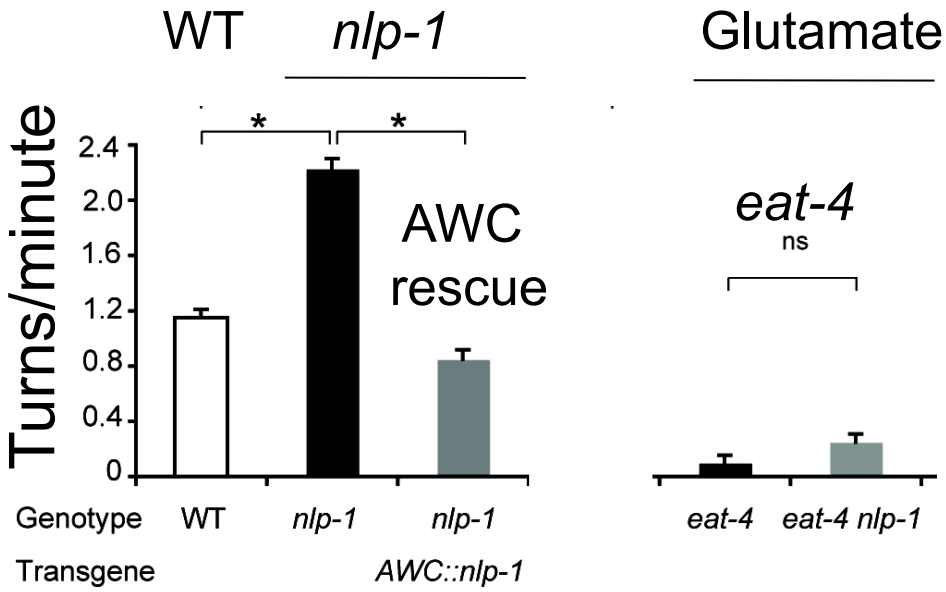


NLP-1 (buccalin-like neuropeptide)

NPR-11 (sNPFR-like GPCR) 

The NLP-1 neuropeptide antagonizes AWC glutamate

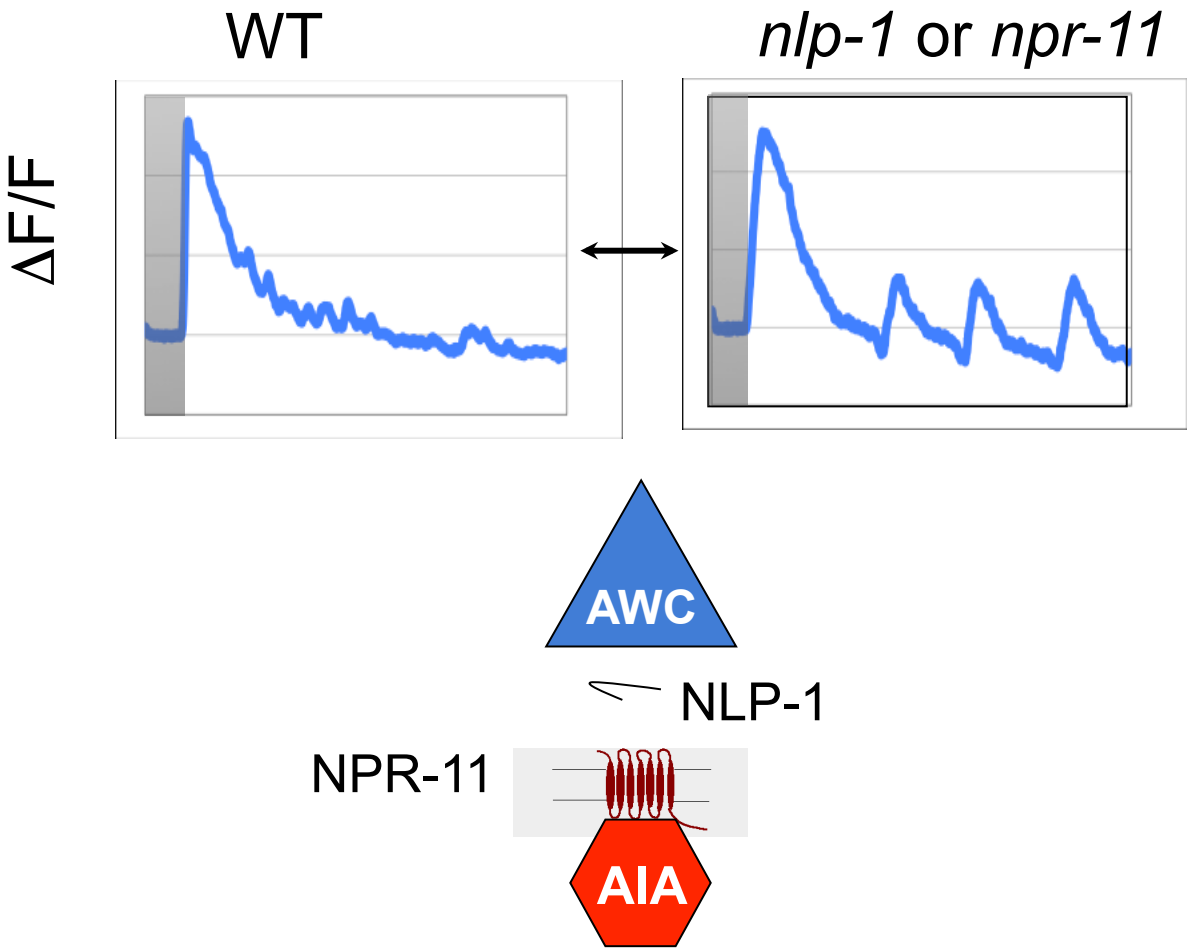




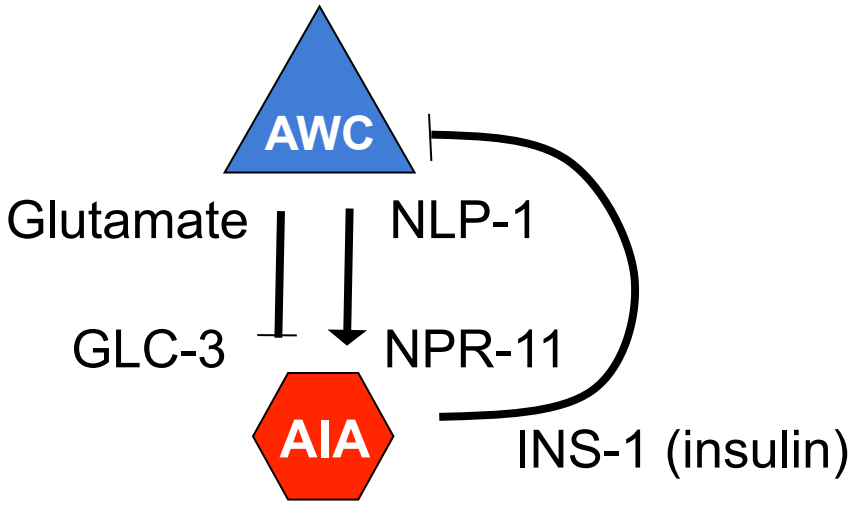
Chalasani et al., Nature Neuroscience 2010

NLP-1 (AWC peptide) and NPR-11 (AIA receptor) affect odor responses in **AWC**

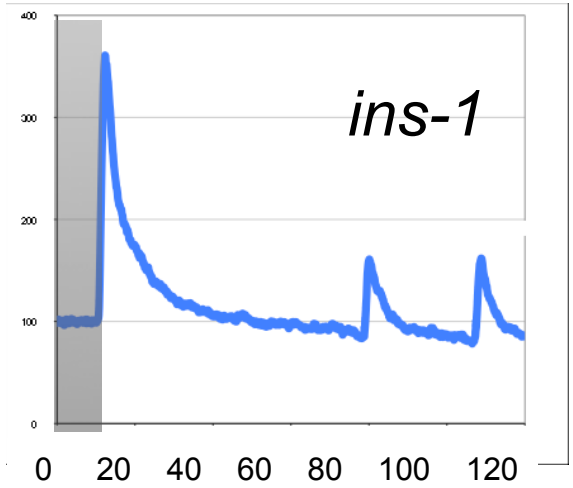
Calcium imaging (odor removal)



An insulin-like peptide made by AIA feeds back onto AWC

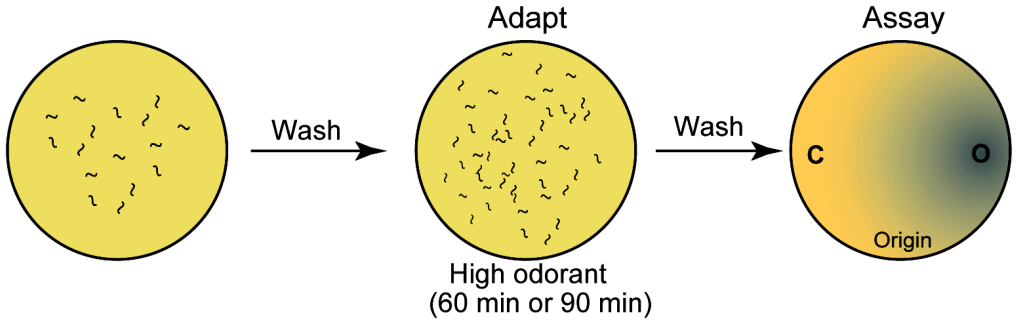


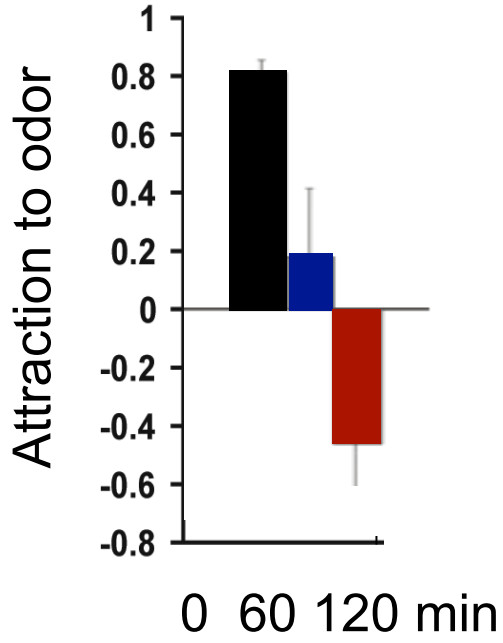
AWC calcium imaging



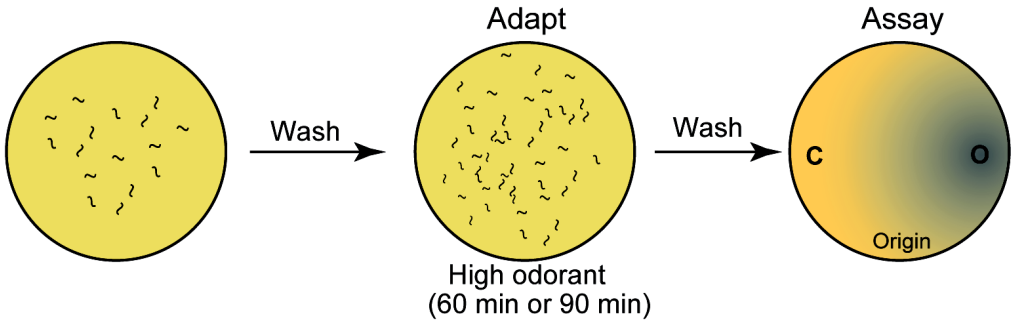
Chalasani et al., Nature Neuroscience 2010

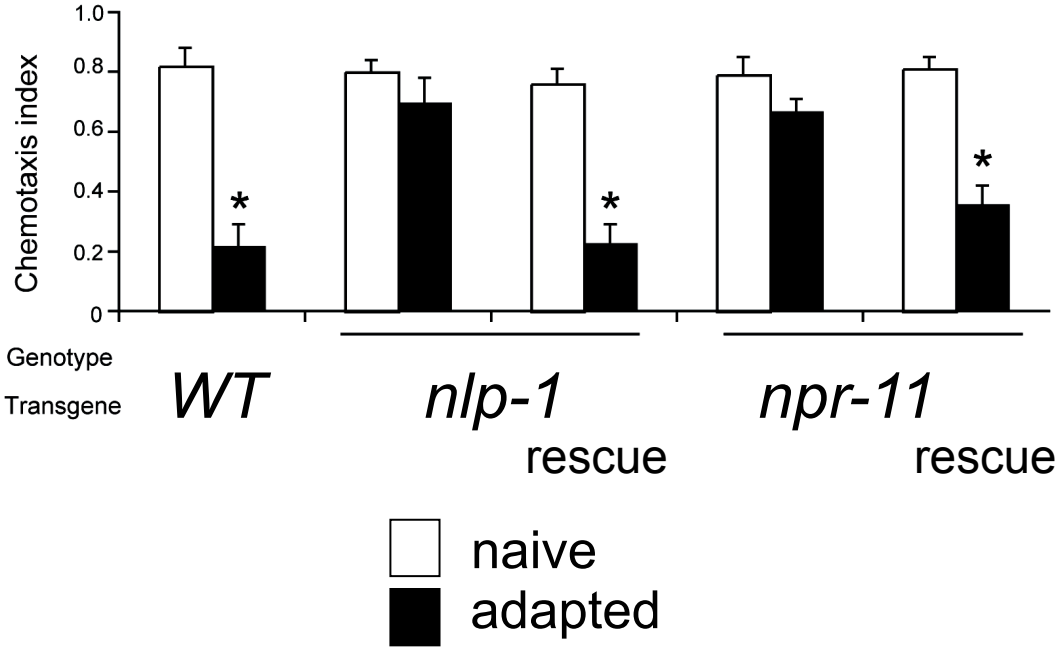
Odor preference is modified by odor experience





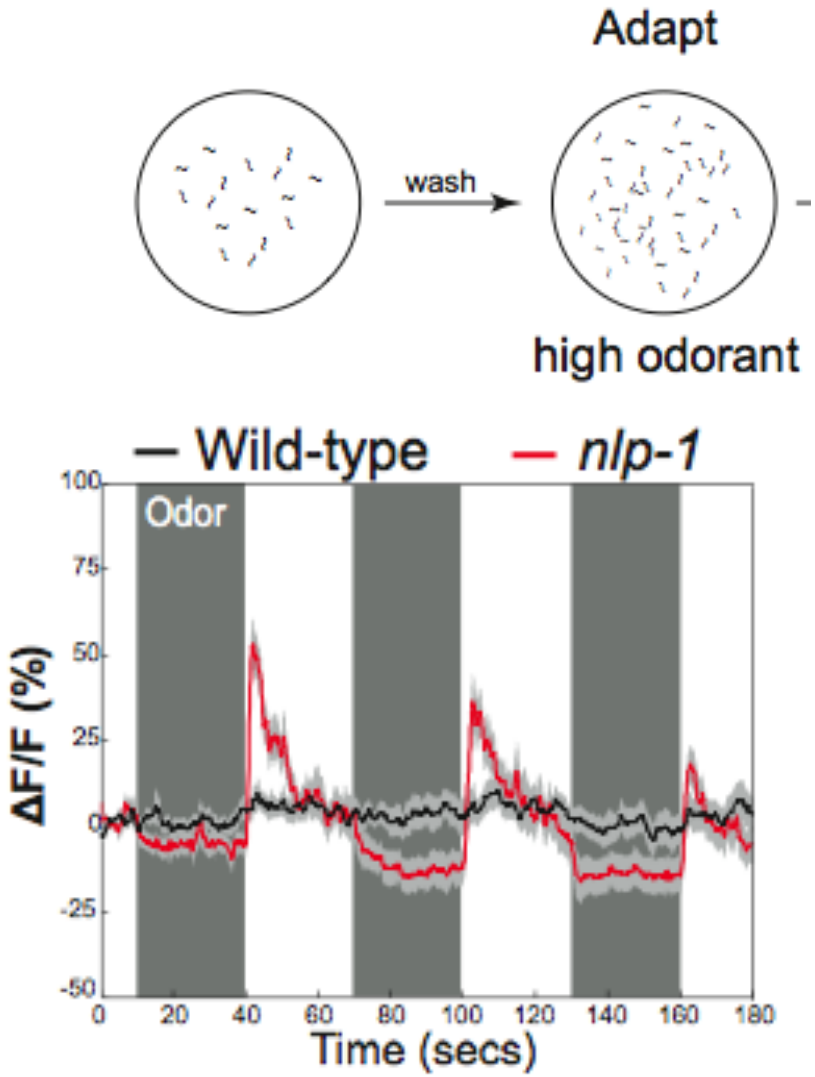
The NLP-1/INS-1 feedback loop drives olfactory adaptation





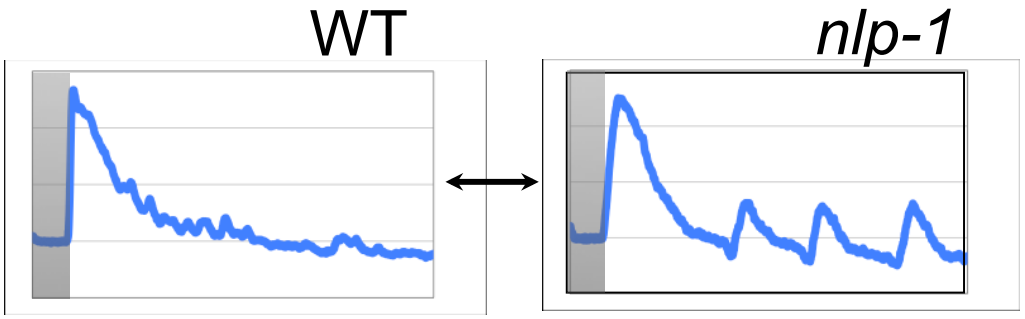
Chalasani et al., Nature Neuroscience 2010

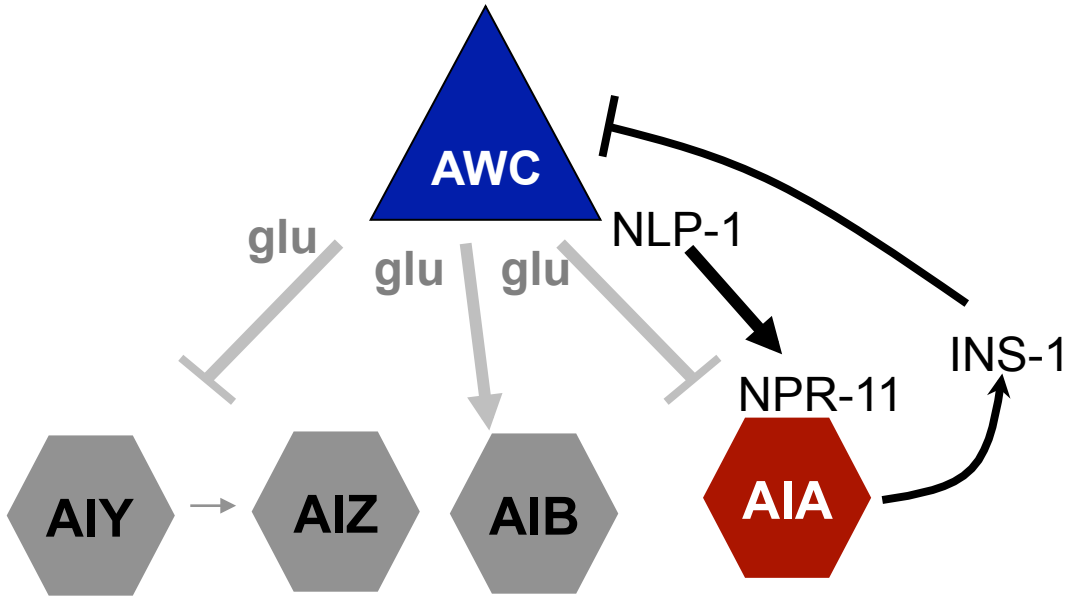
Adaptation reduces AWC odor responses -- This requires *nlp-1, npr-11,* and *ins-1*



Chalasani et al., Nature Neuroscience 2010

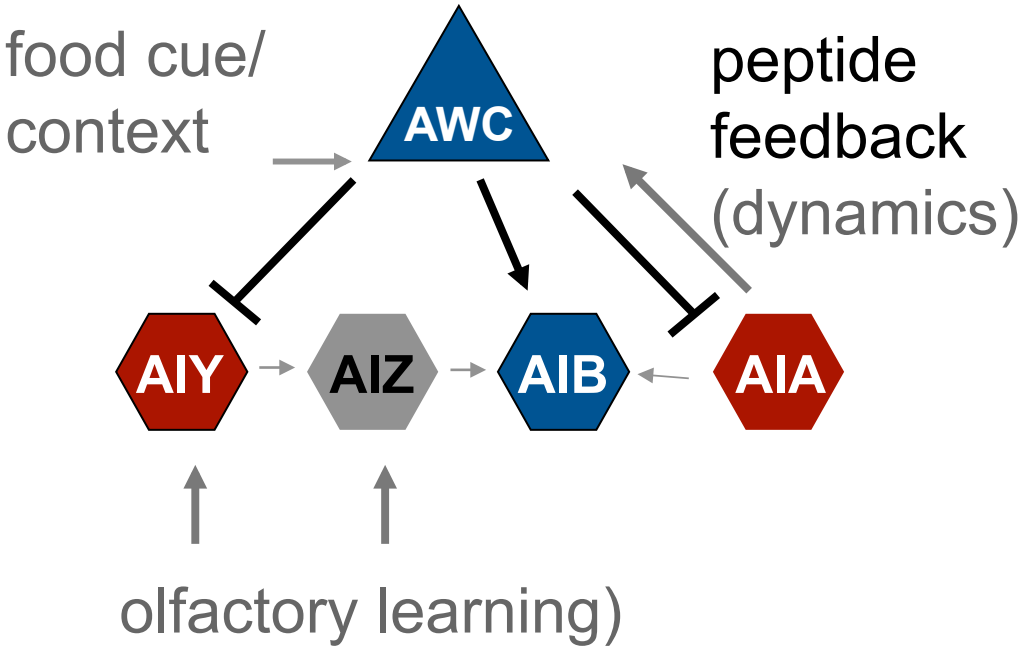
Neuropeptide feedback shapes sensory dynamics





Chalasani et al., Nature Neuroscience 2010

Circuits change over time



Dirk Albrecht

Sreekanth Chalasani (now at Salk)