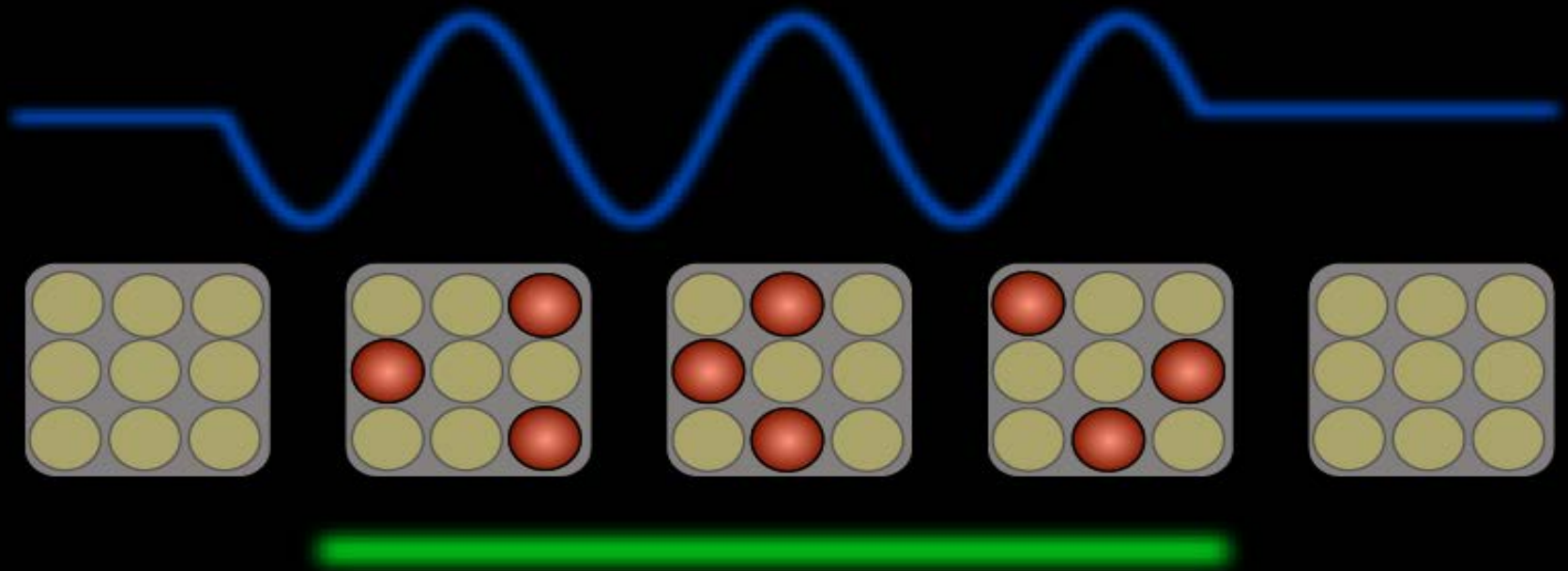


# Neural codes for the sense of taste

Mark Stopfer  
NIH / NICHD



# Section on sensory coding and neural ensembles



# Section on sensory coding and neural ensembles



Basic rules populations of neurons  
use to process information



# Section on sensory coding and neural ensembles



Electrophysiology

Anatomy

Optogenetics

Genetic manipulations

Computational modeling

Behavioral tests



The sense of taste is important!



# What we learned in school

4 basic tastes

Sweet

Sour

Salty

Bitter

# What we learned in school

4 basic tastes

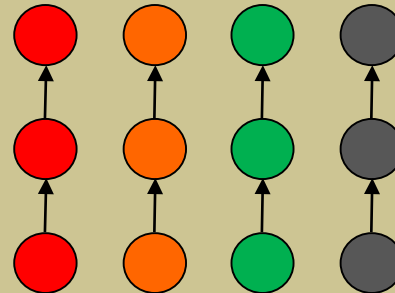
Sweet

Sour

Salty

Bitter

Labeled line coding





# What we learned in school

4 basic tastes

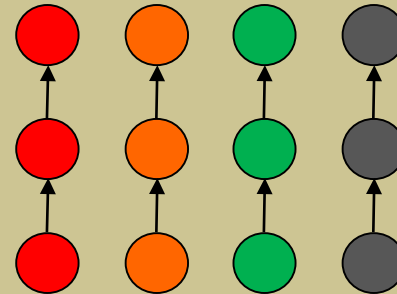
Labeled line coding

Sweet

Sour

Salty

Bitter



**Must be quick**

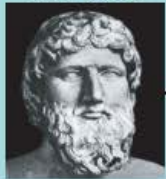
**Must be accurate**



# Ideas about taste are not new...

## Classical-Modern Philosophy

Aristotle  
~300 B.C.E.



Locke  
1690



## Psychophysics

Meuller  
1833



Helmholtz  
1850



Henning  
1916



Young  
1793

## Neuroscience

Pfaffman



Frank



Gustatory Labeled  
Line Code  
1973

Gustatory Across  
Fiber Pattern Code  
1941

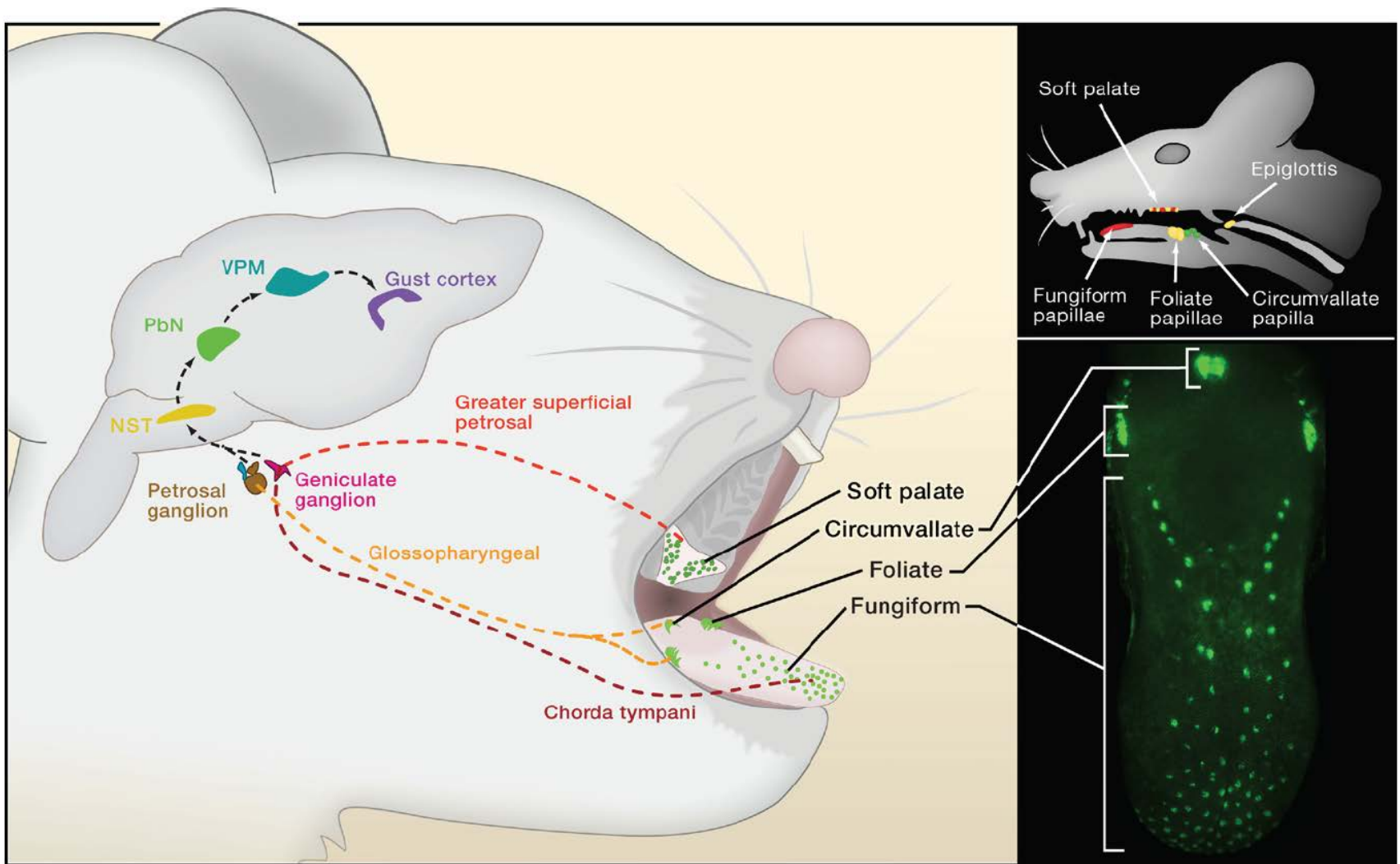


Adrian

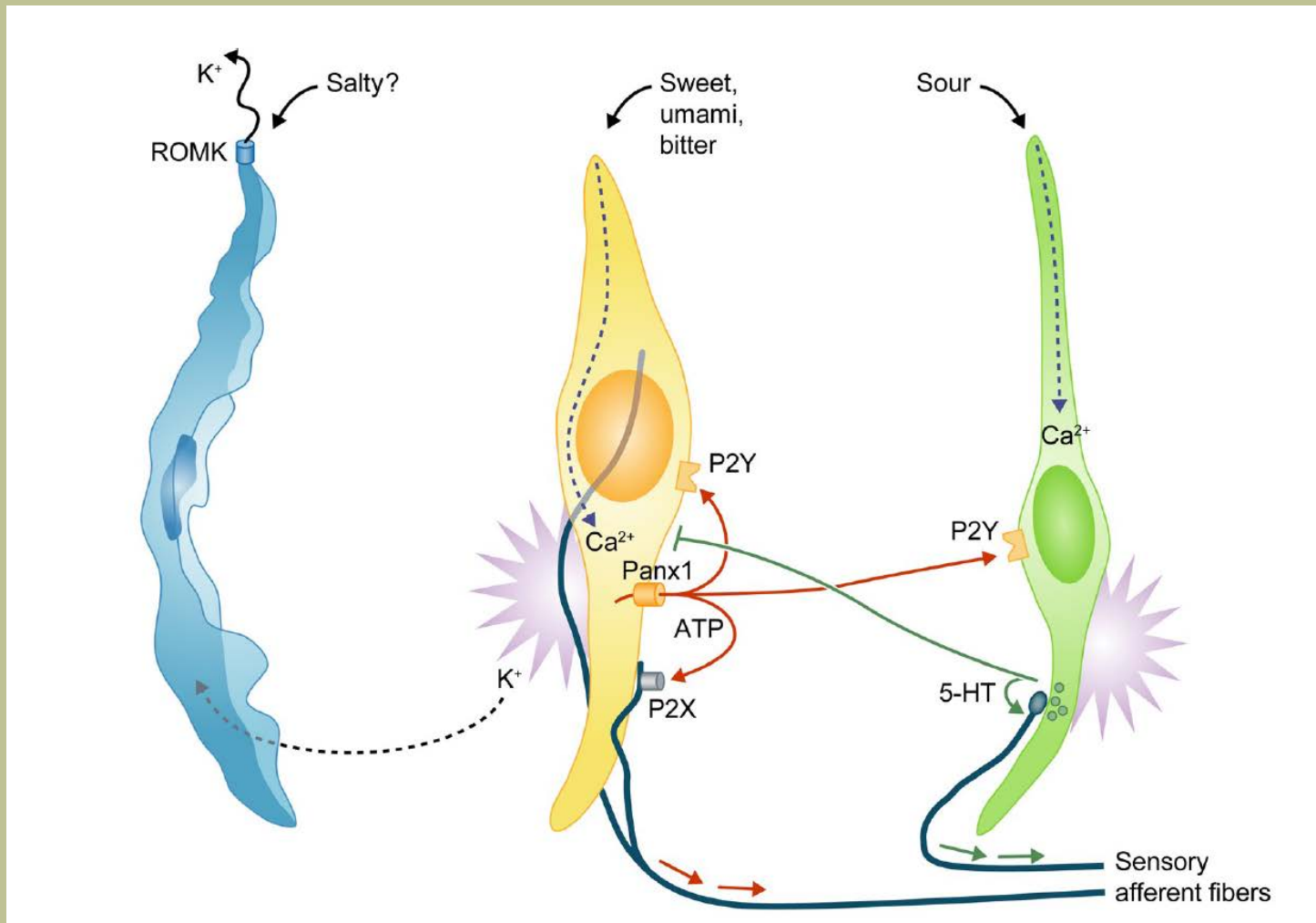
Modern Ideas about  
olfaction  
1950s-

... but they're very hard to test

# Vertebrates are complicated!



# Vertebrates are complicated!



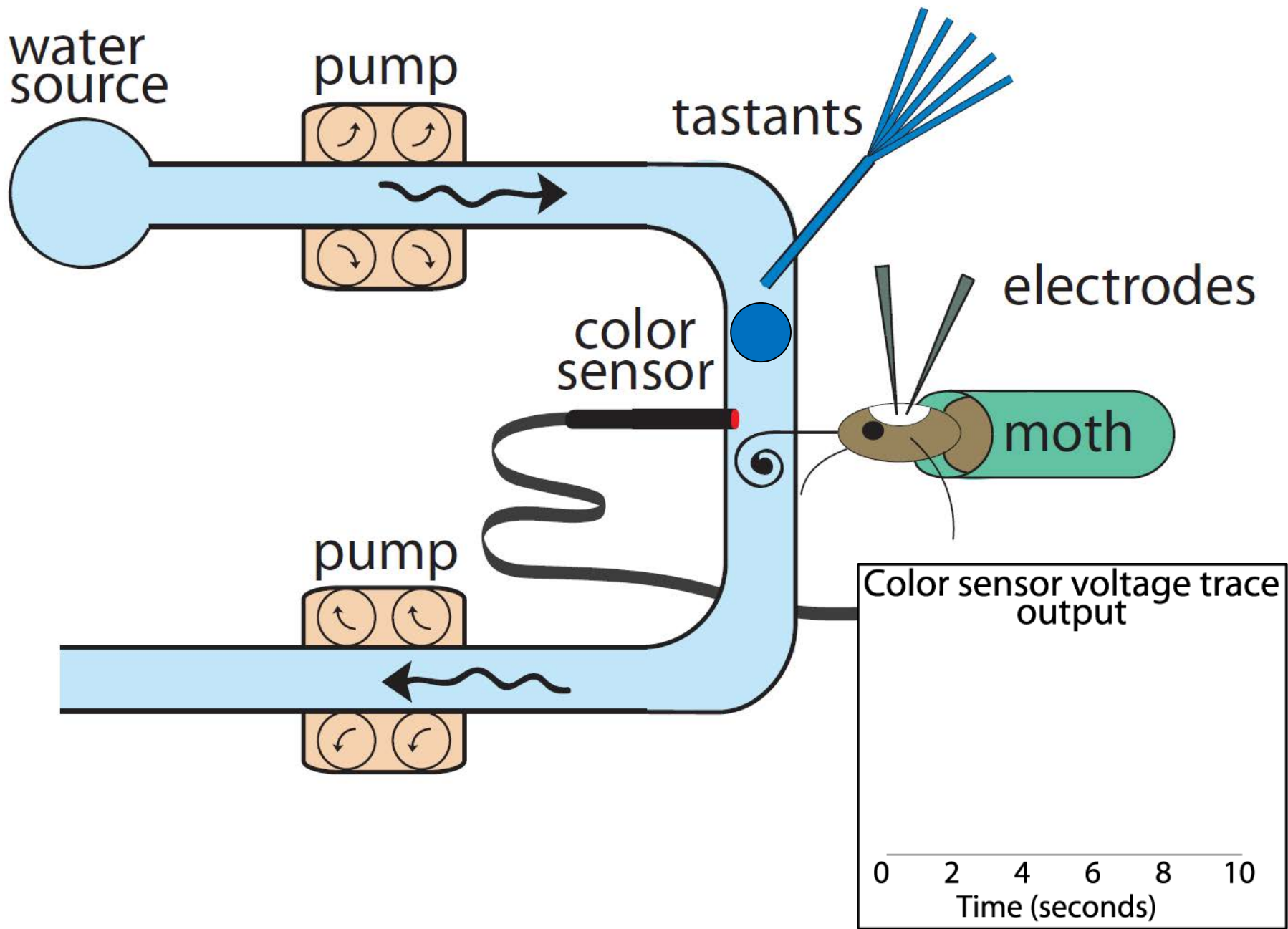


# A simple systems approach



- Fewer neurons than vertebrates
- Work with intact, awake animals
- Point – by – point analysis of function

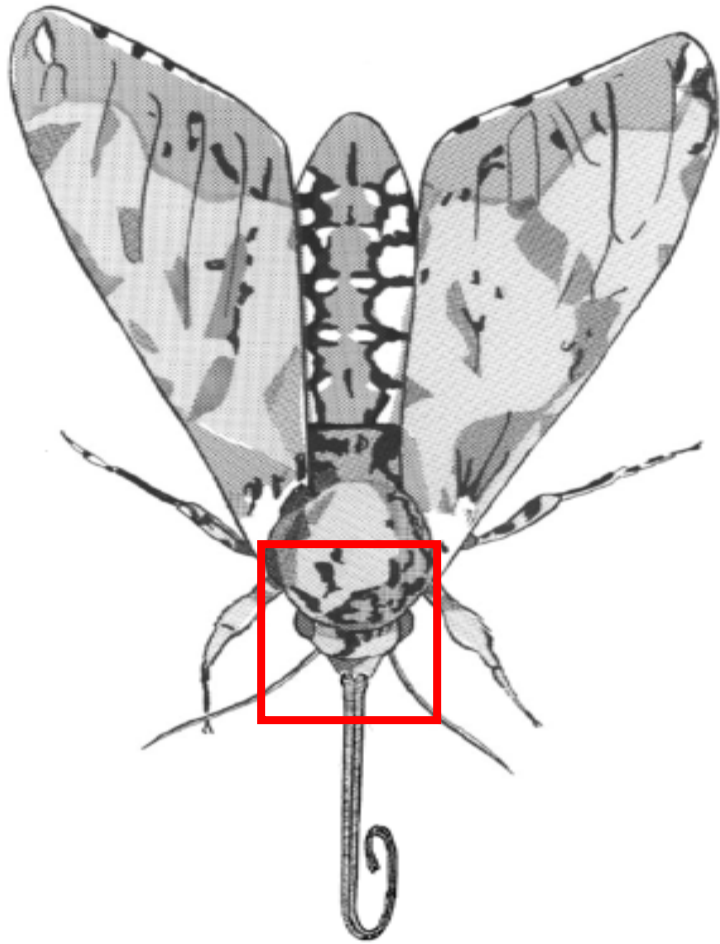


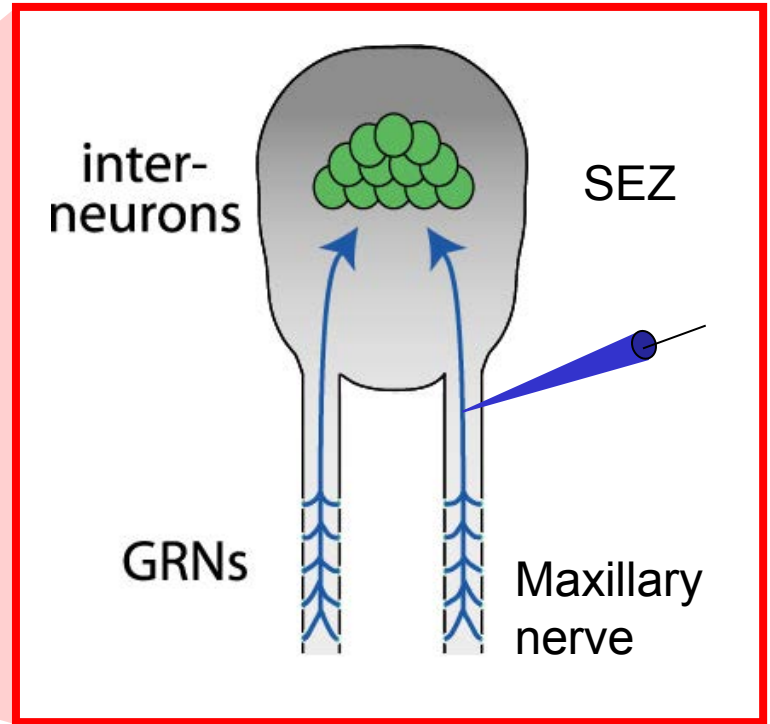
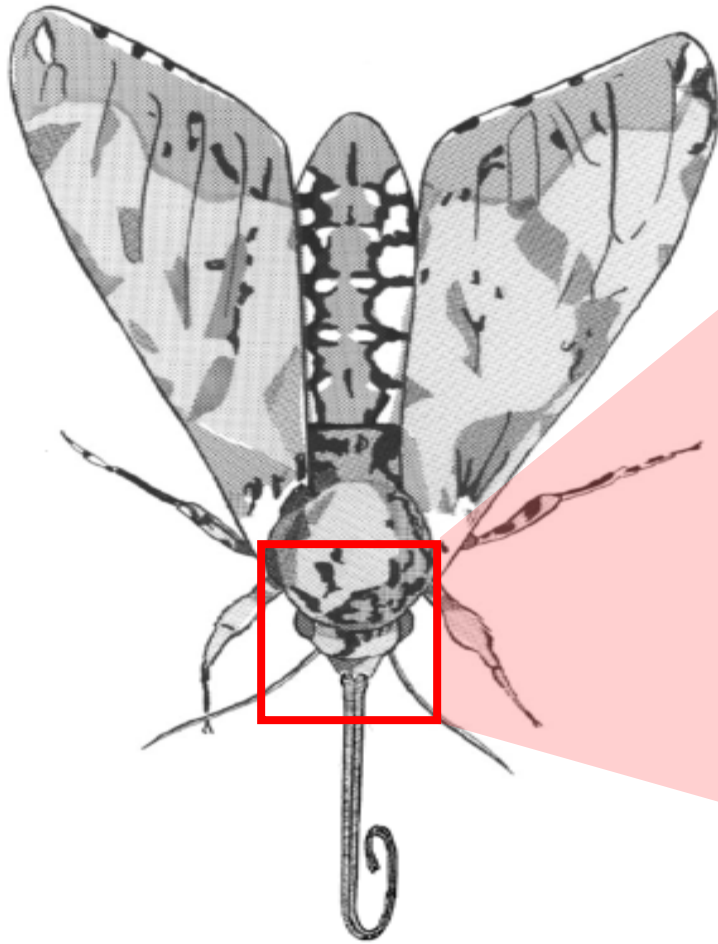




# Questions:

- *Are there only a few basic tastes, or are taste chemicals each encoded uniquely?*
- *What is the nature of the neural code for taste? Is it quick and accurate?*
- *Is taste processed by labeled lines?*



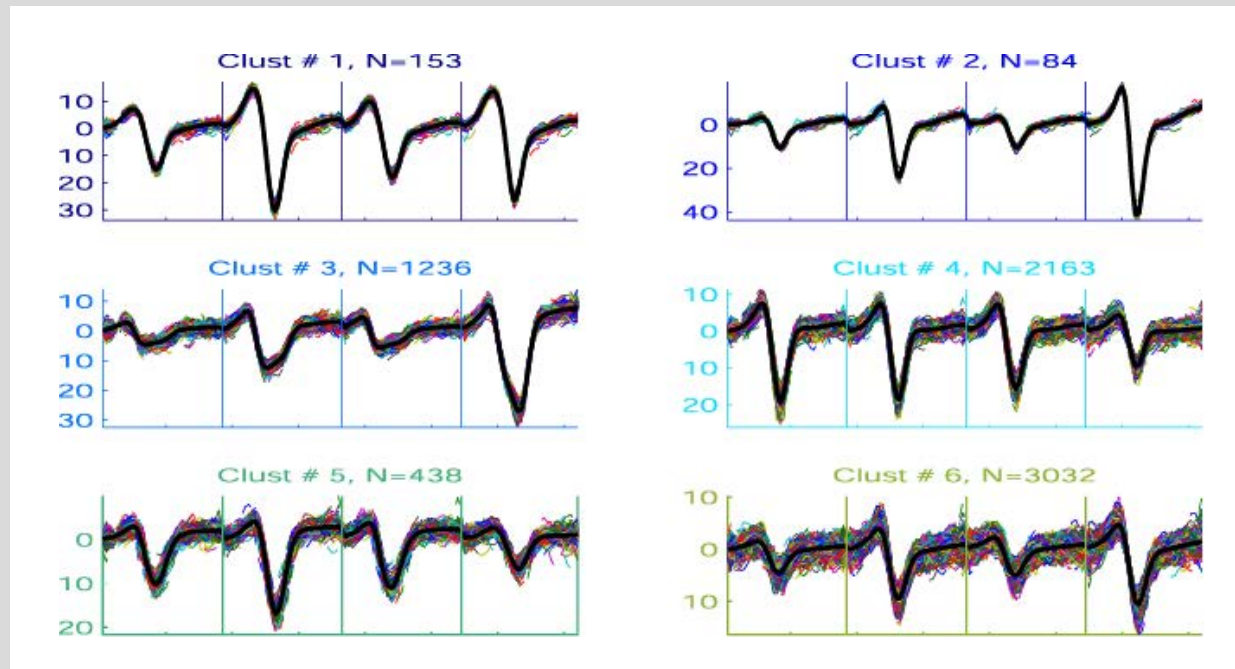




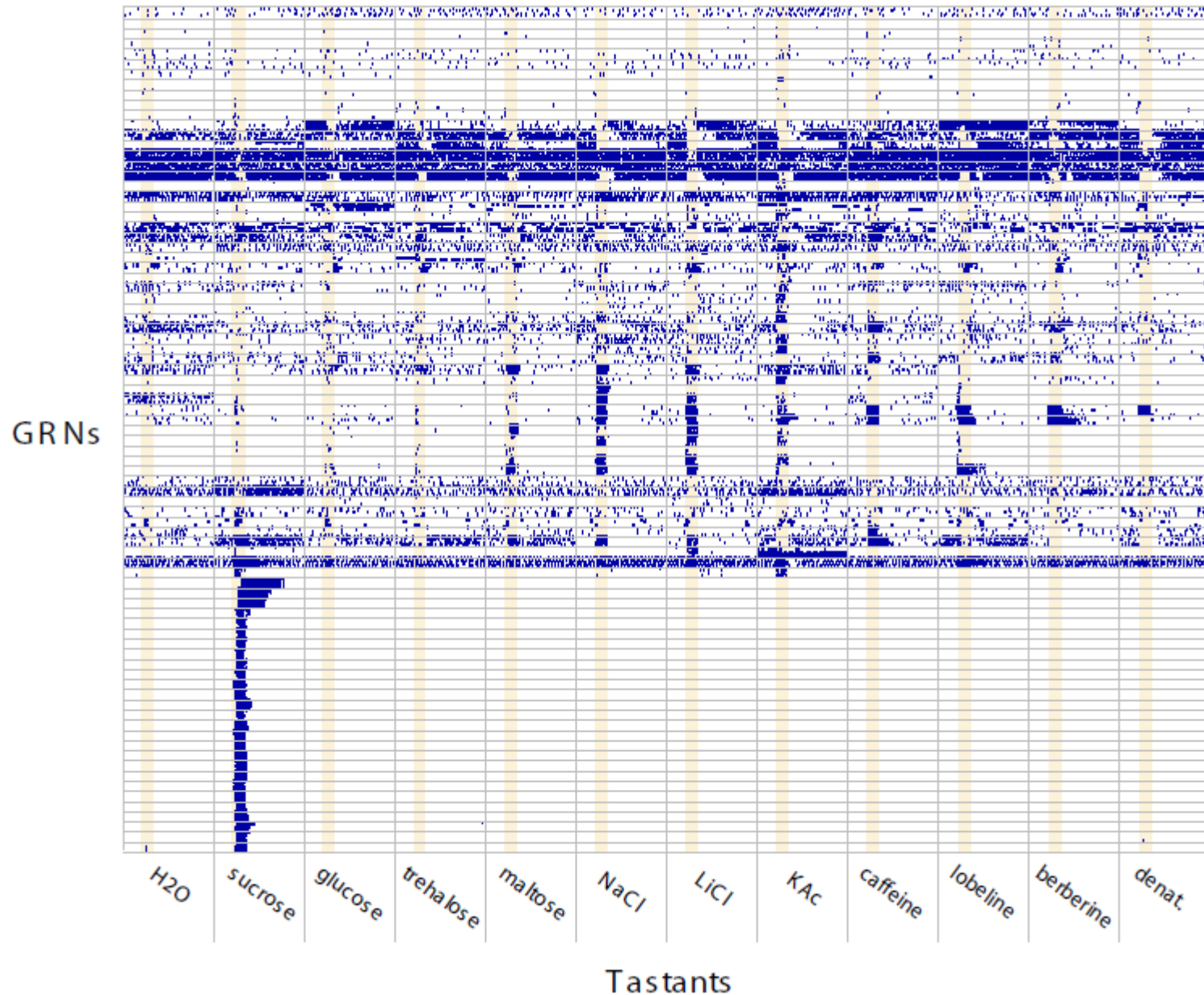
“tetrode” extracellular recordings

# GRNs

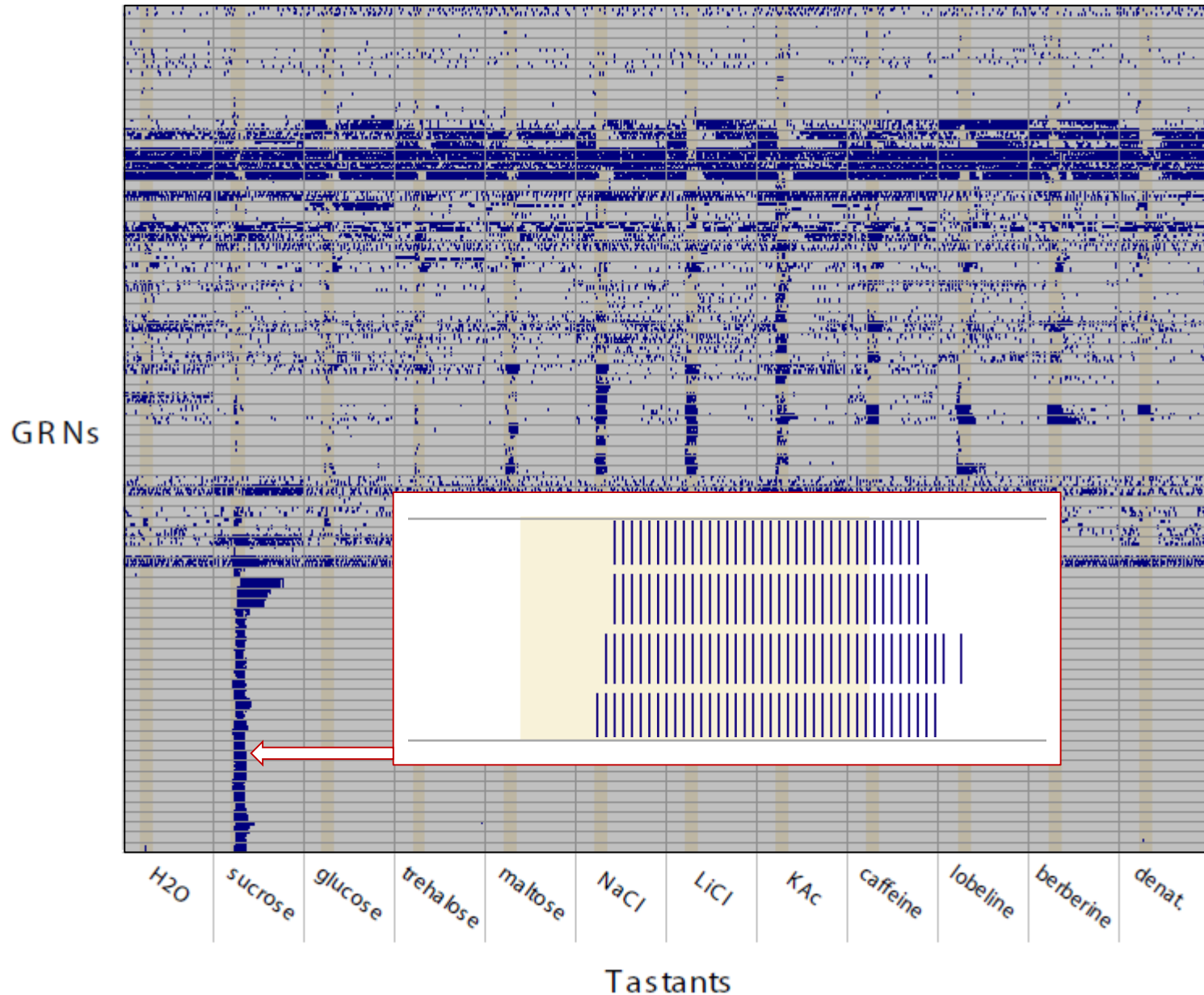
Gustatory  
Receptor  
Neurons



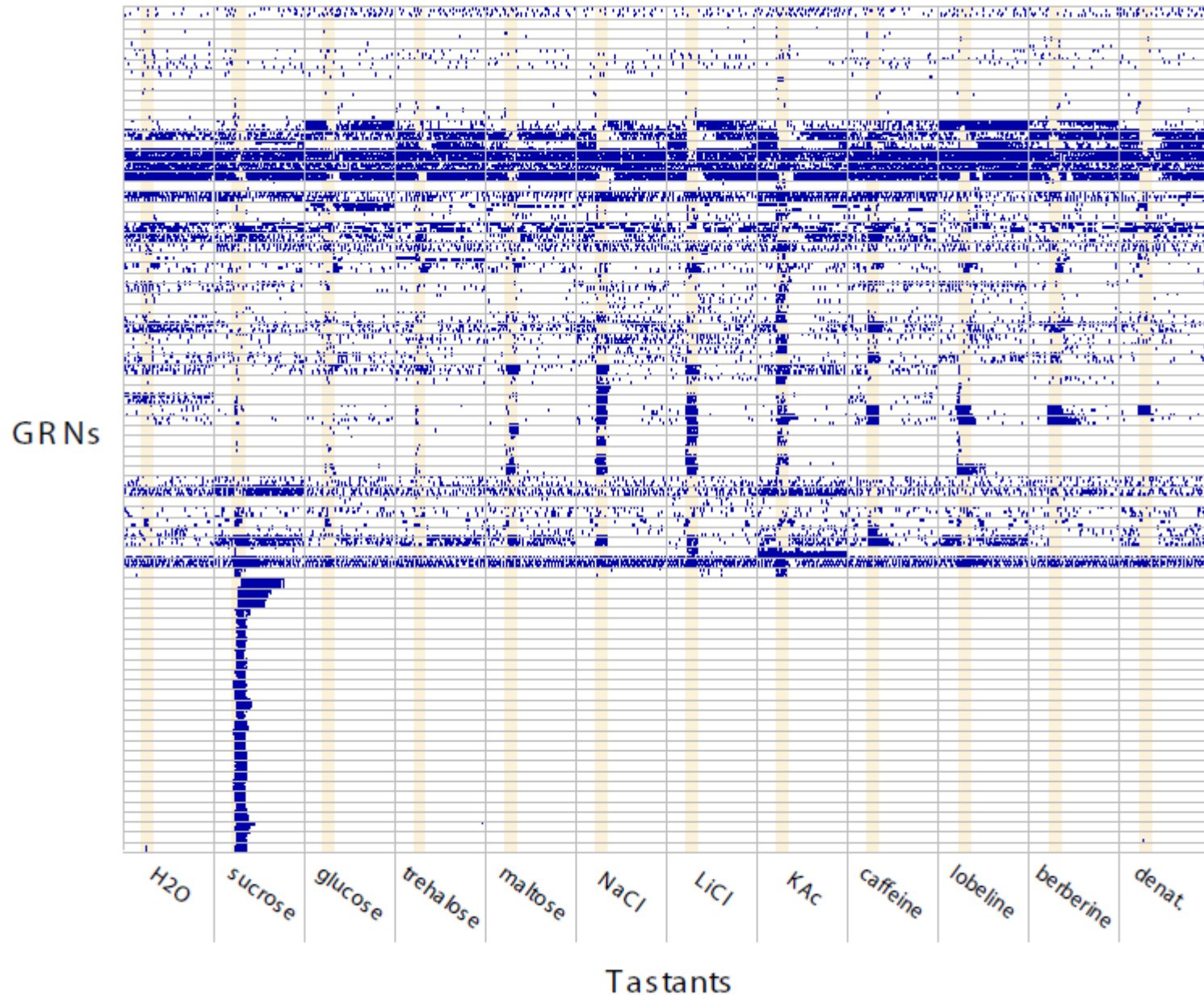
# Encoding Tastant Identity



# Encoding Tastant Identity



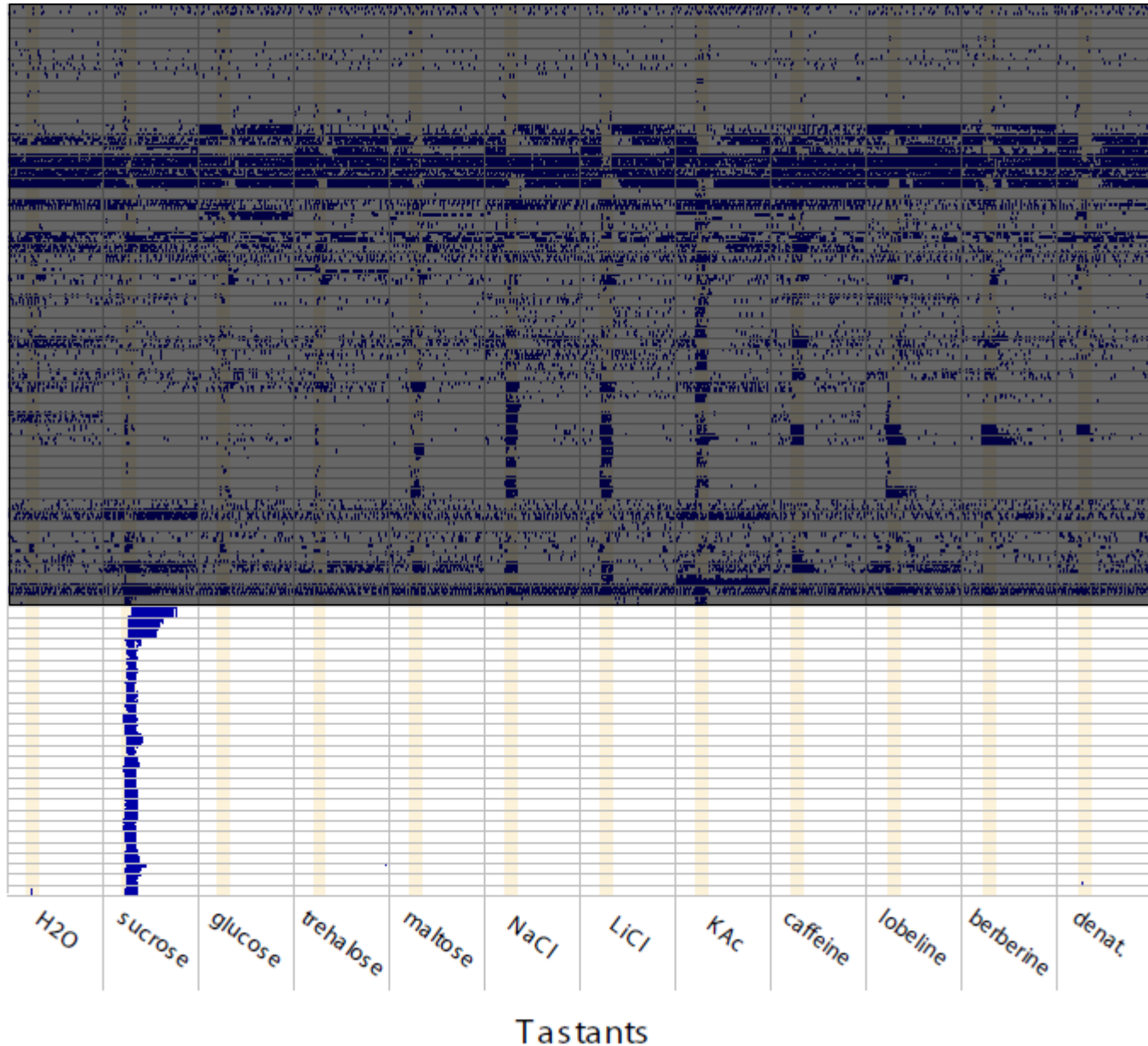
# Encoding Tastant Identity





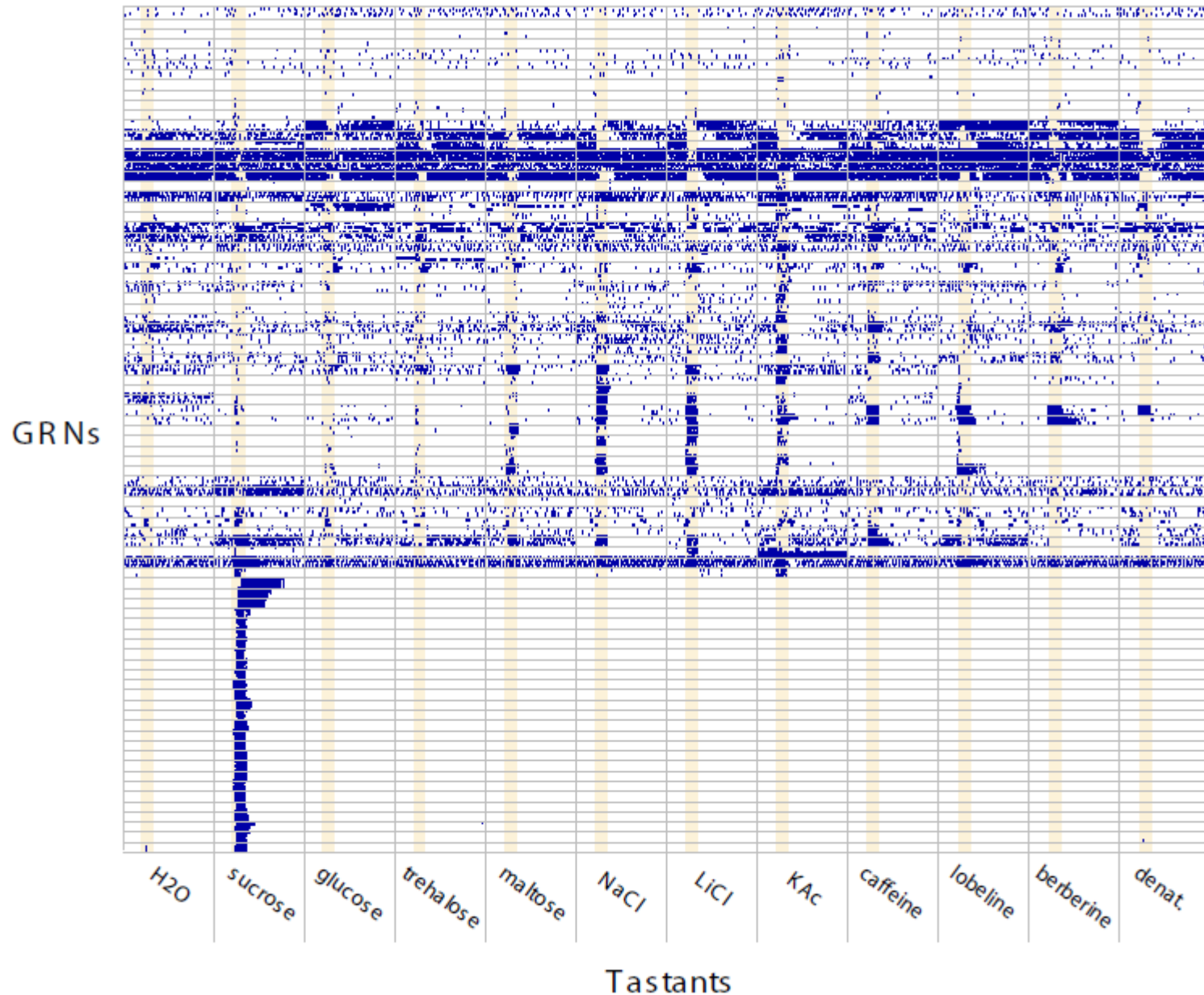
# Encoding Tastant Identity

GRNs



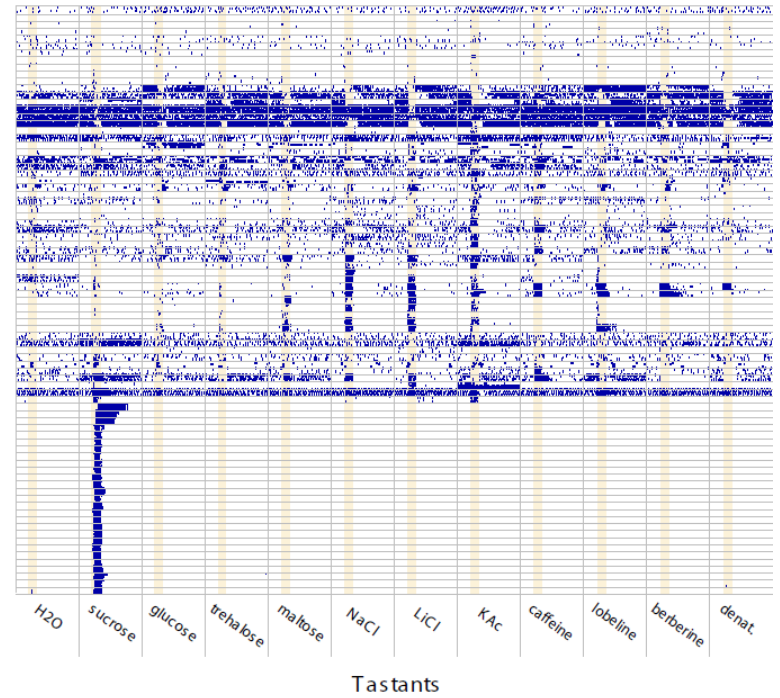


# Encoding Tastant Identity



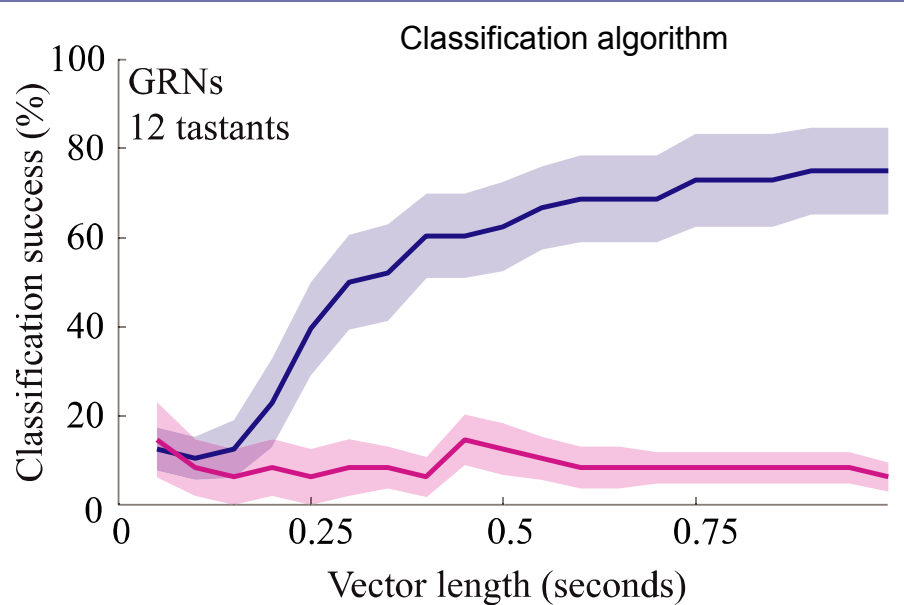
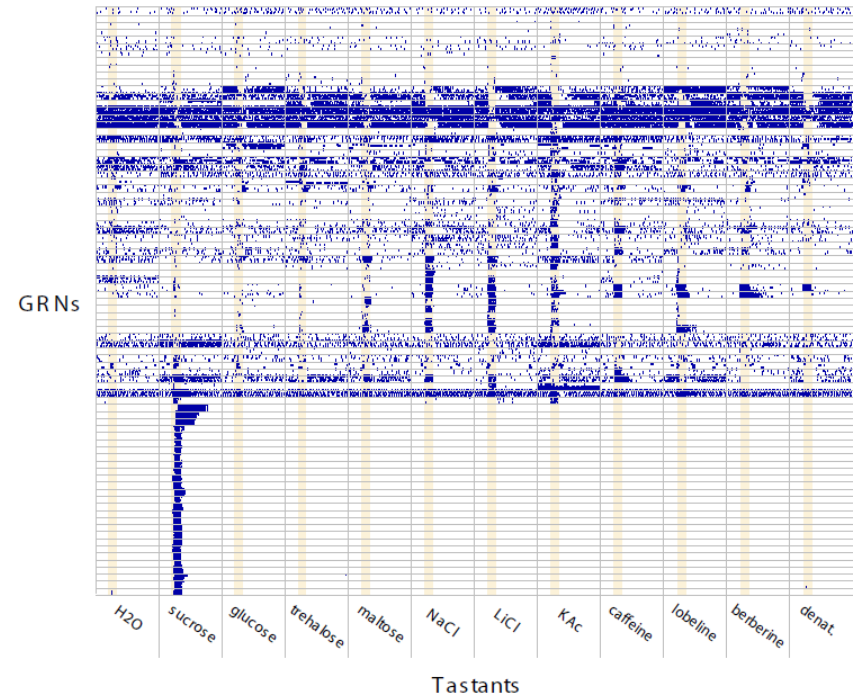
# Information content of GRNs

GRNs

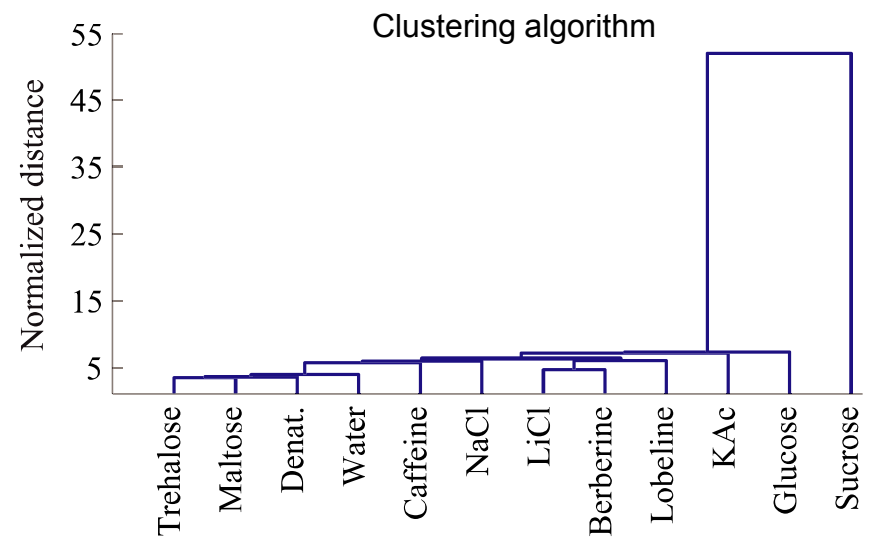
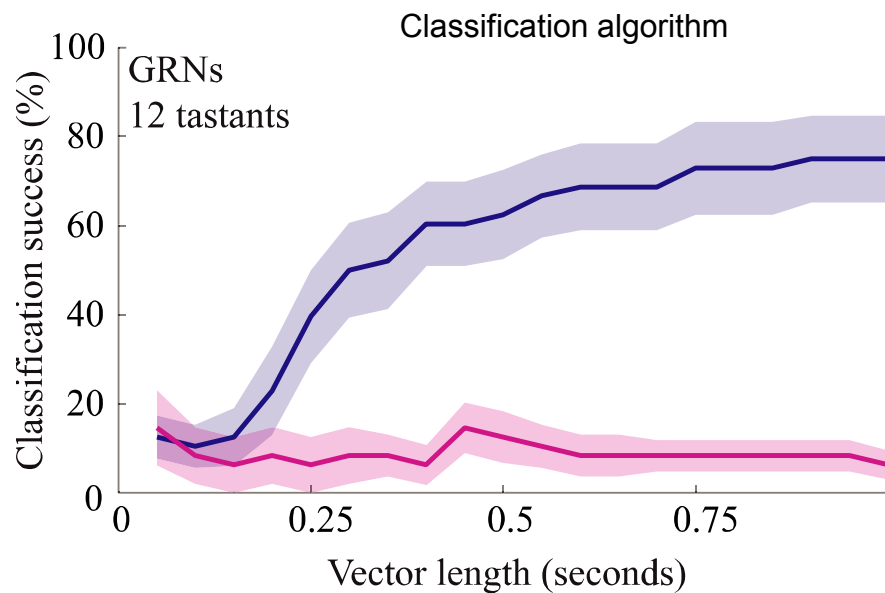
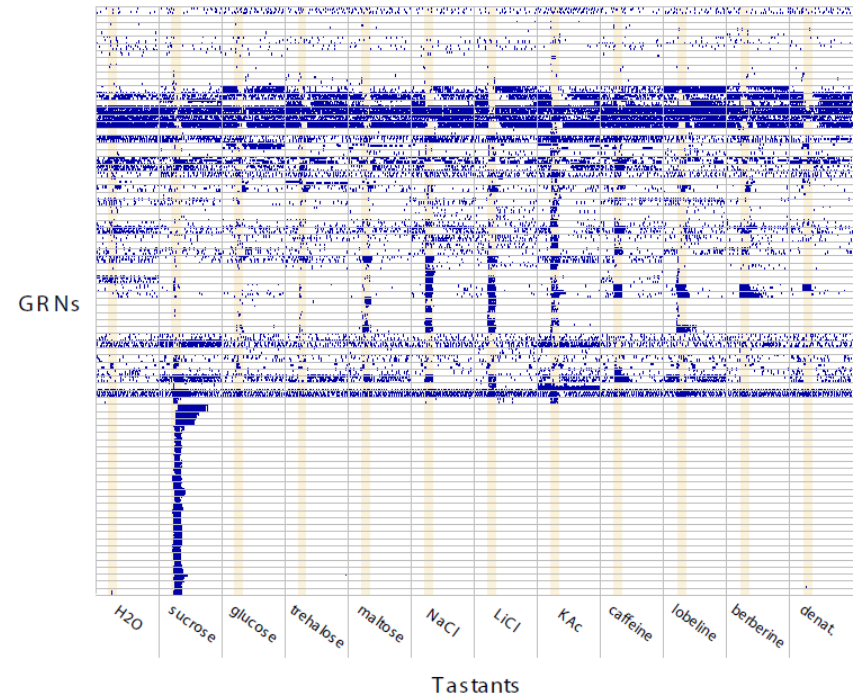




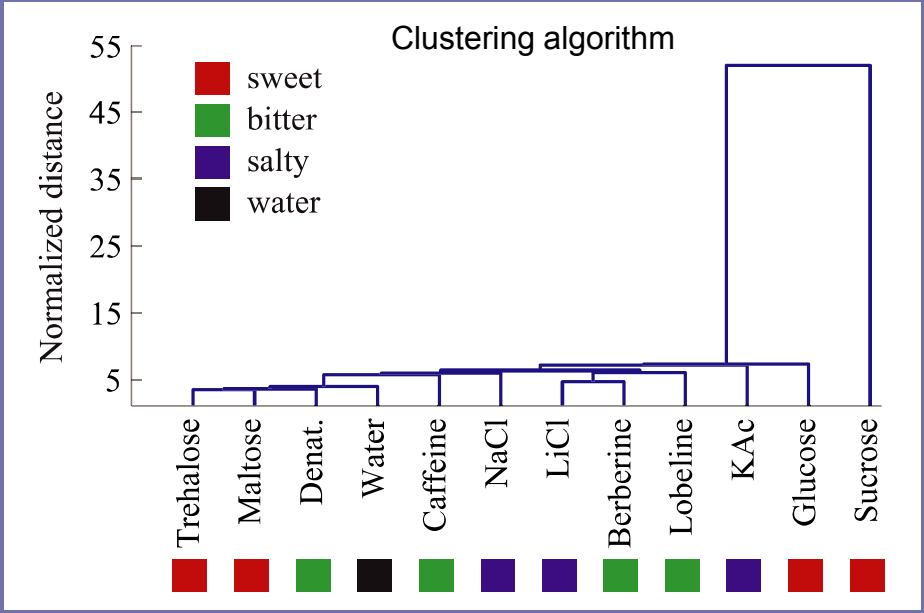
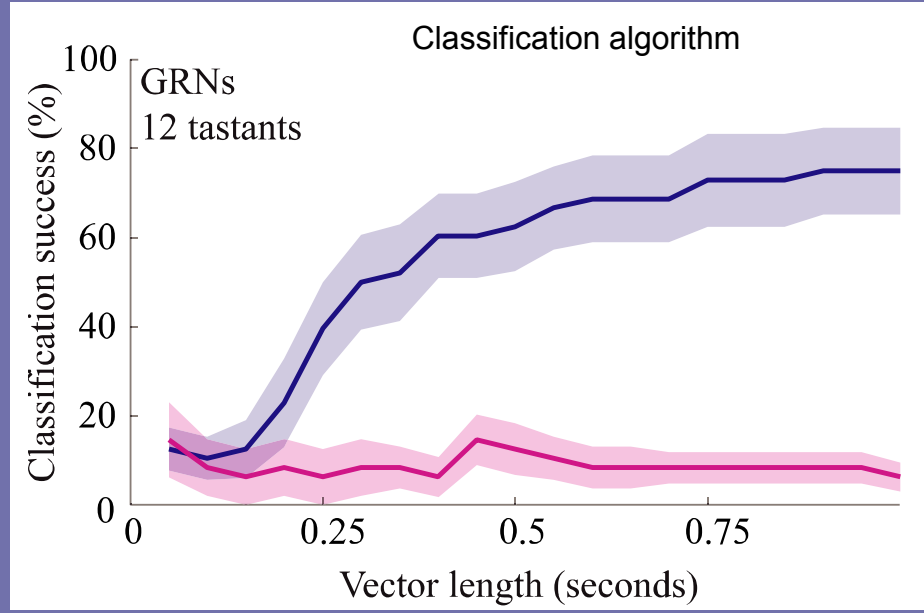
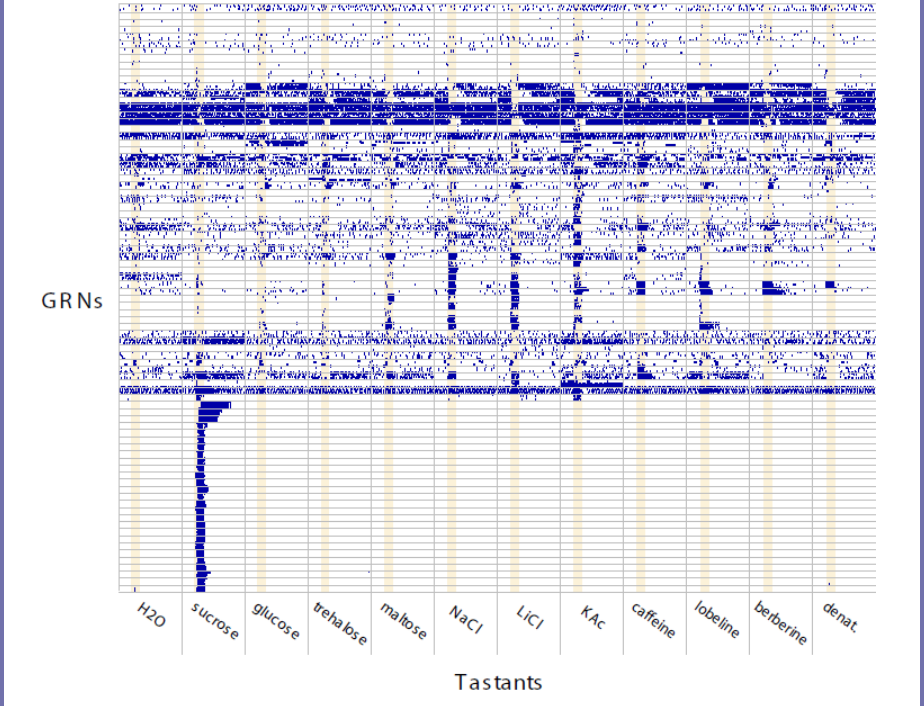
# Information content of GRNs



# Information content of GRNs



# Information content of GRNs



-GRNs respond to different numbers of tastants



-GRNs respond to different numbers of tastants

-GRNs can respond to some tastants in a basic taste category but not others

-GRNs respond to different numbers of tastants

-GRNs can respond to some tastants in a basic taste category but not others

-GRNs can respond to tastants from more than one basic taste category

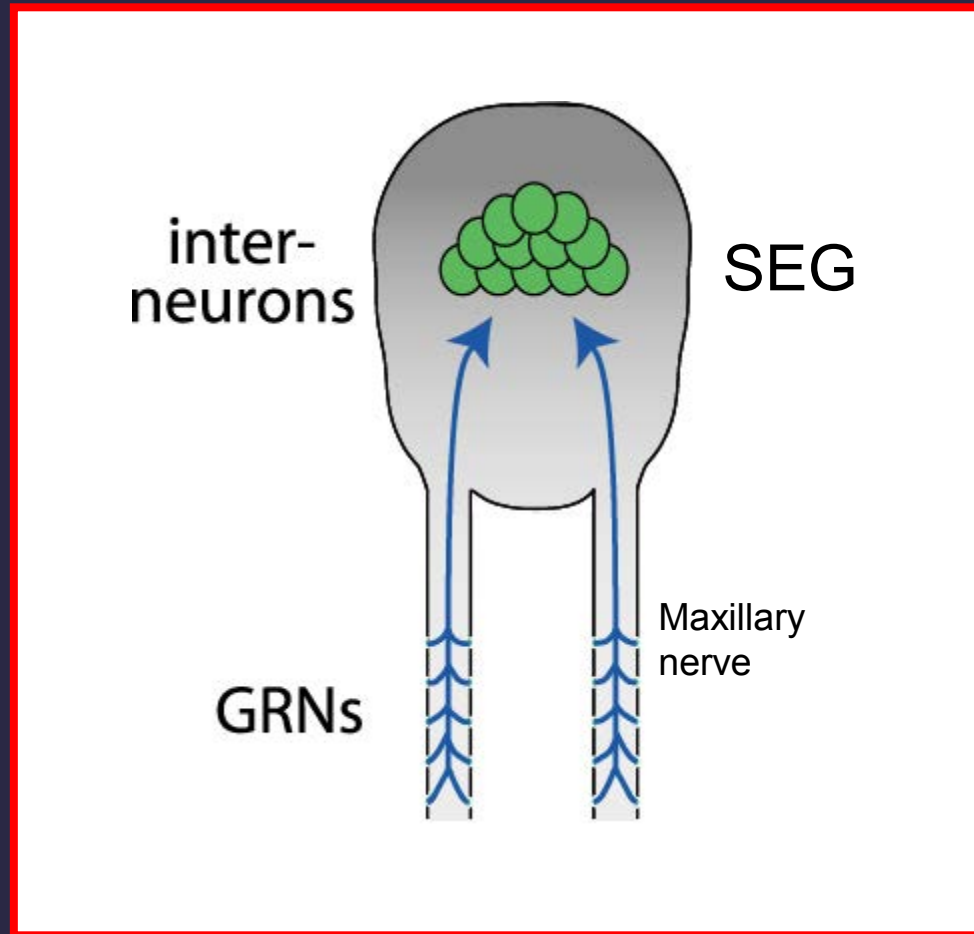
- GRNs respond to different numbers of tastants
- GRNs can respond to some tastants in a basic taste category but not others
- GRNs can respond to tastants from more than one basic taste category
- GRNs show a diversity of temporal responses

- GRNs respond to different numbers of tastants
- GRNs can respond to some tastants in a basic taste category but not others
- GRNs can respond to tastants from more than one basic taste category
- GRNs show a diversity of temporal responses

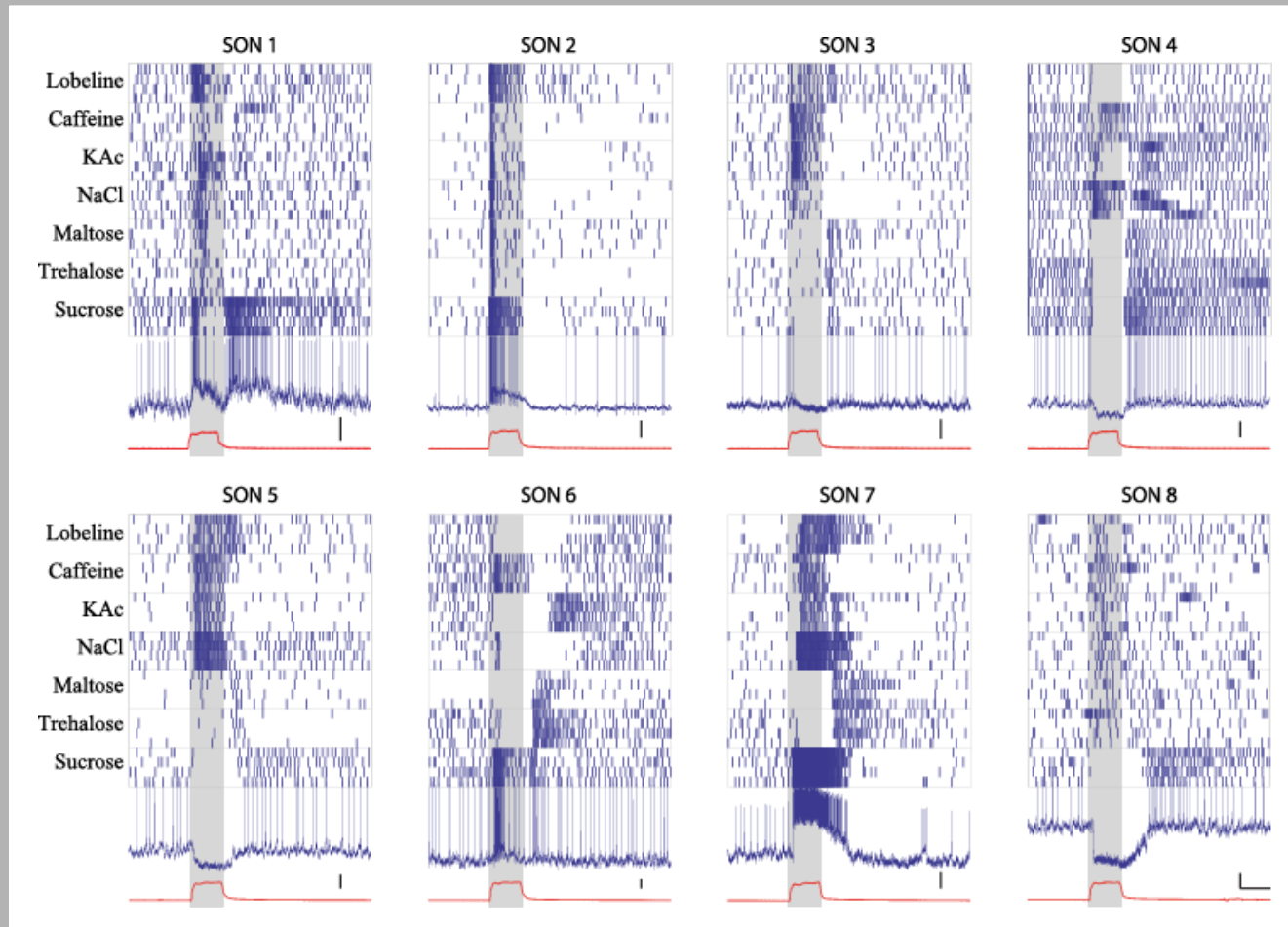
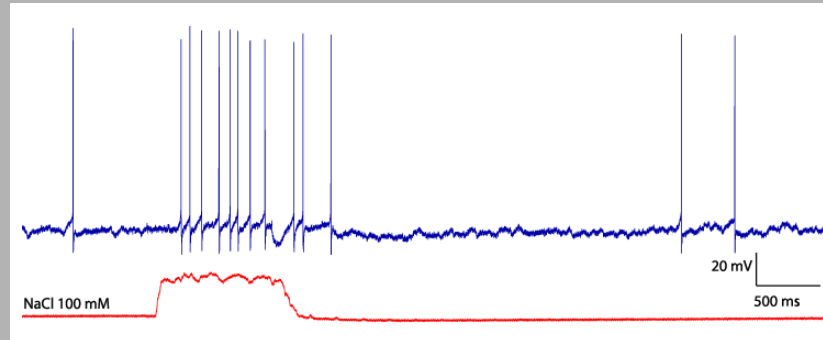
*Where does information from GRNs go next?*



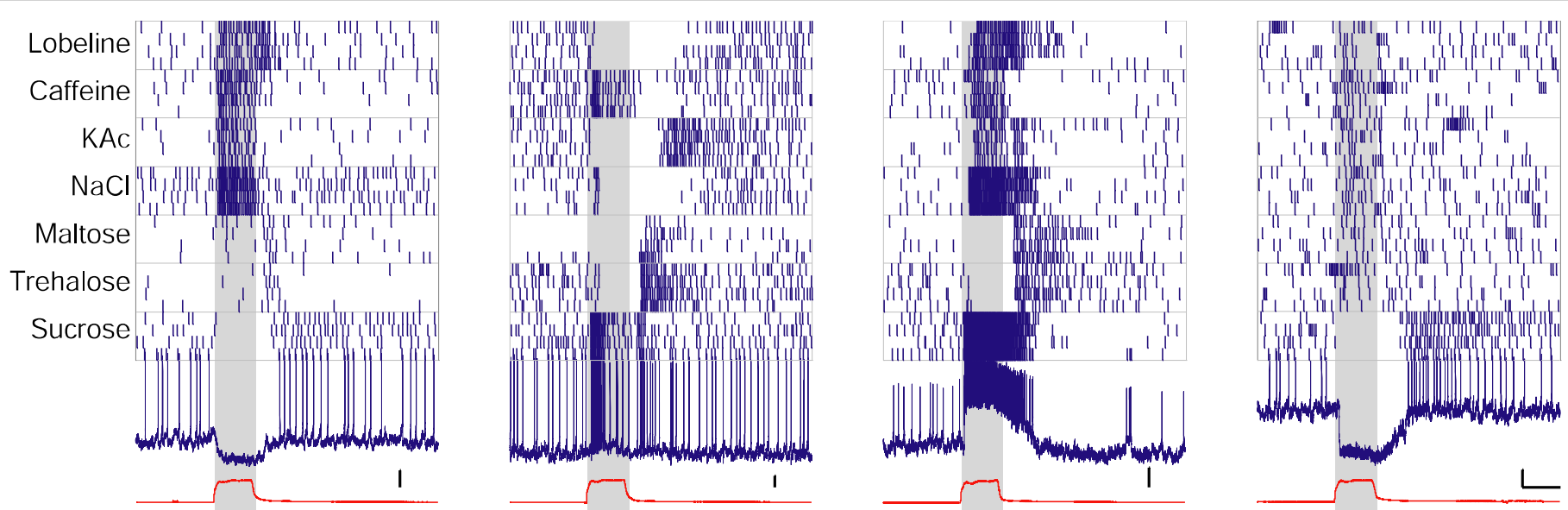
# GRNs project to the SEG



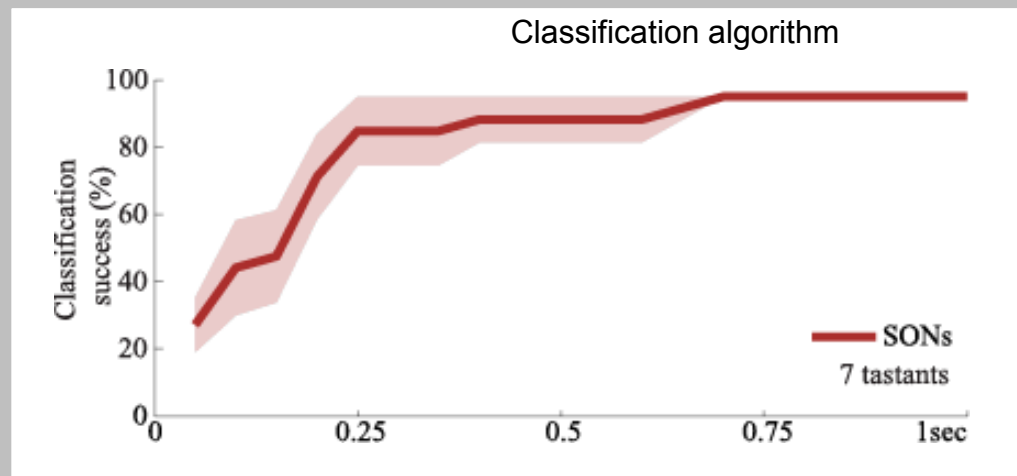
# Sharp-electrode intracellular: second order neurons



# Sharp-electrode intracellular: second order neurons

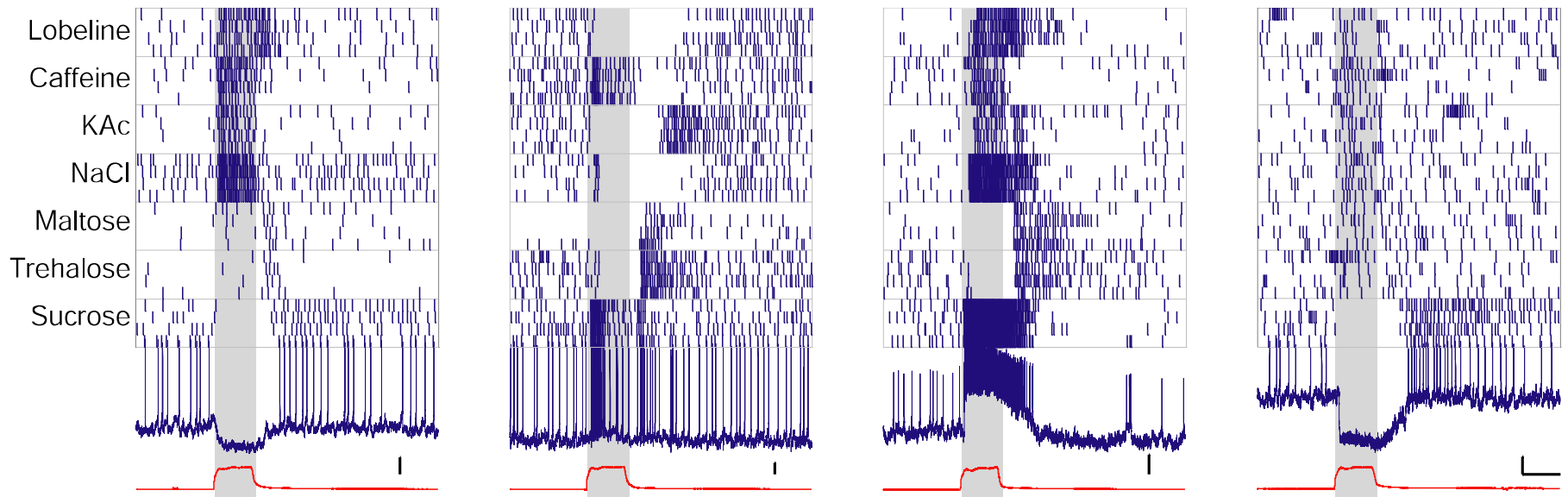


Information content  
of SONs

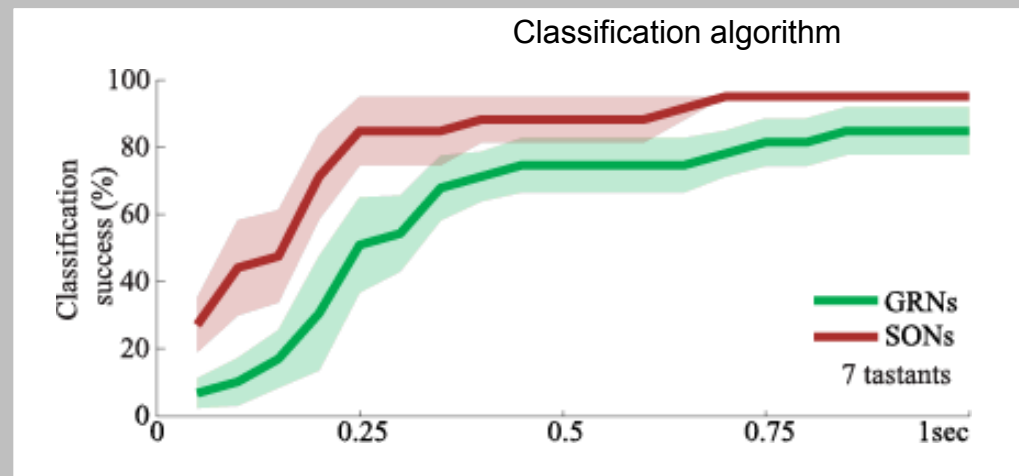


Classification accuracy and speed

# Sharp-electrode intracellular: second order neurons



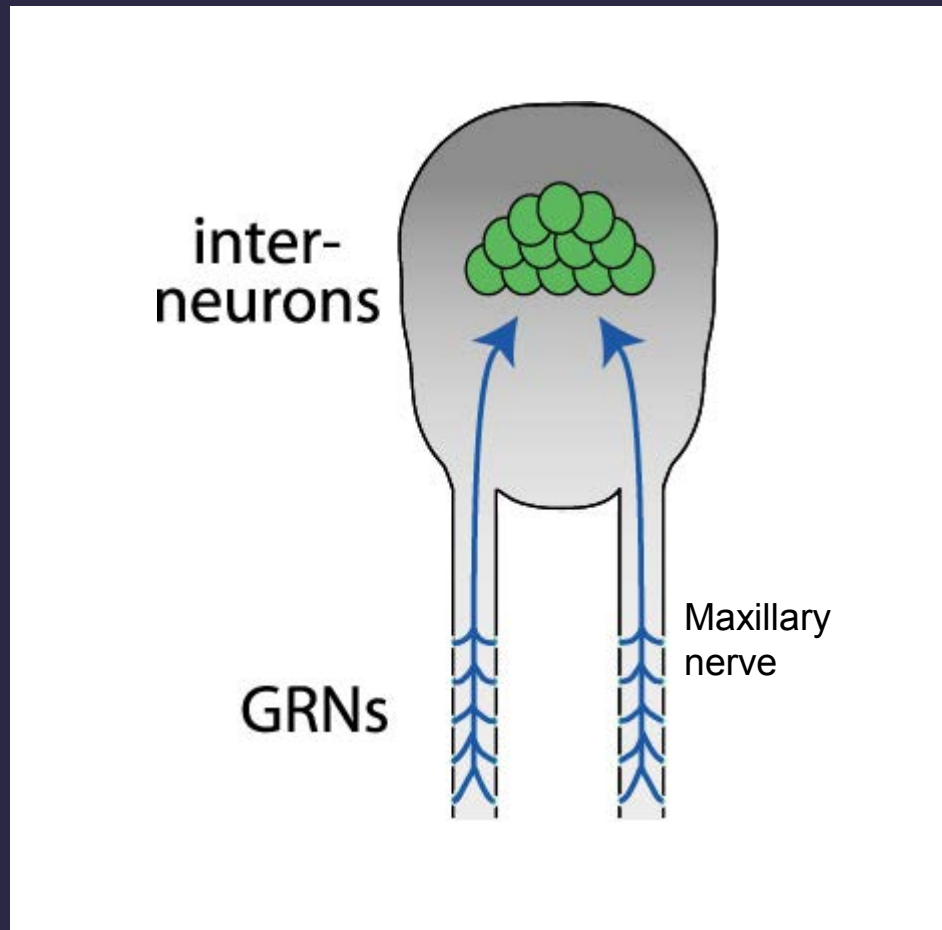
Information content  
of SONs



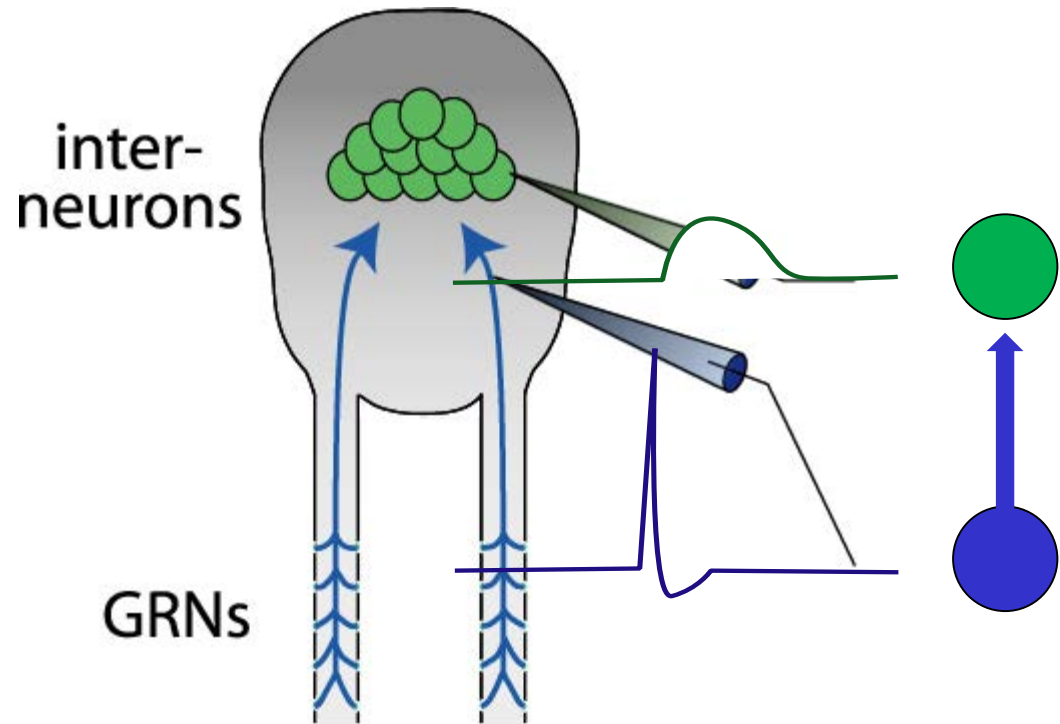
Classification accuracy and speed



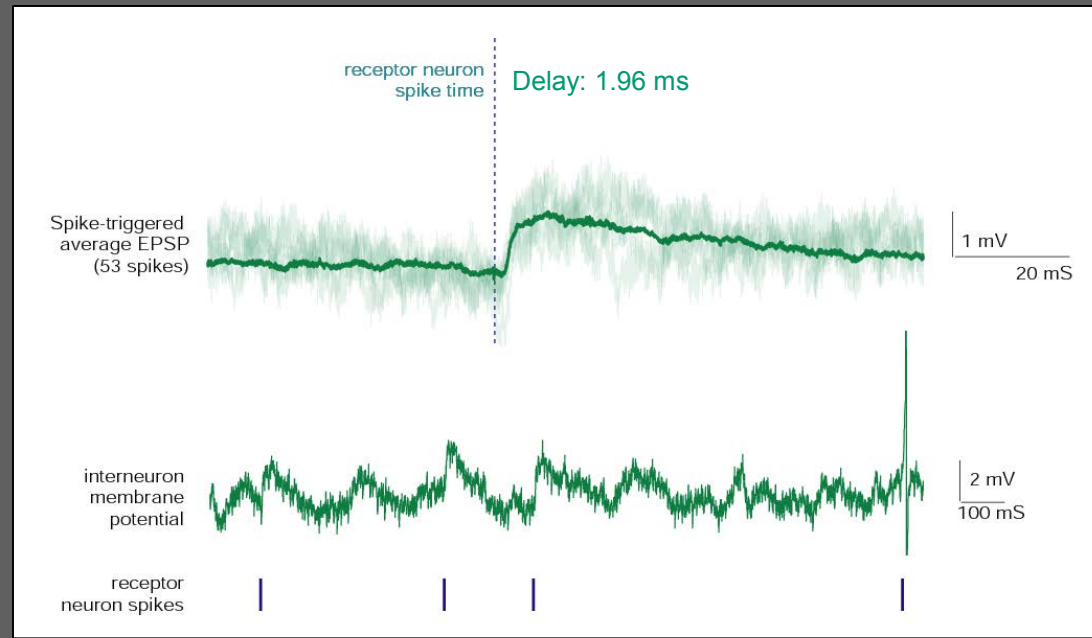
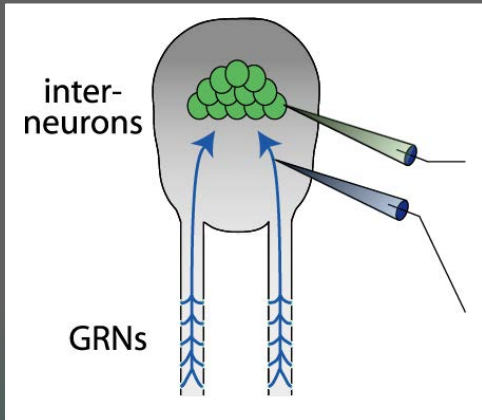
How are these cells wired?  
As labeled lines?



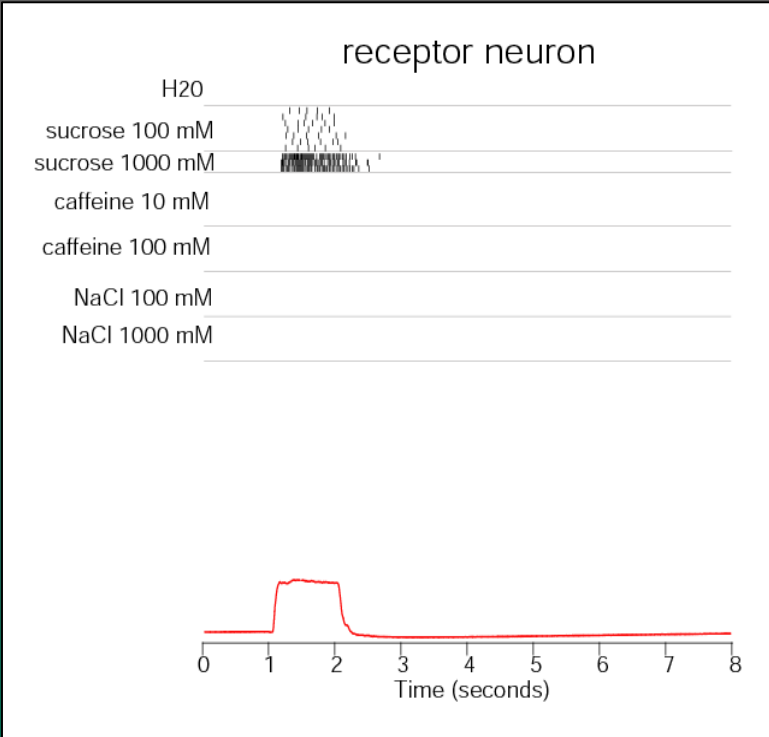
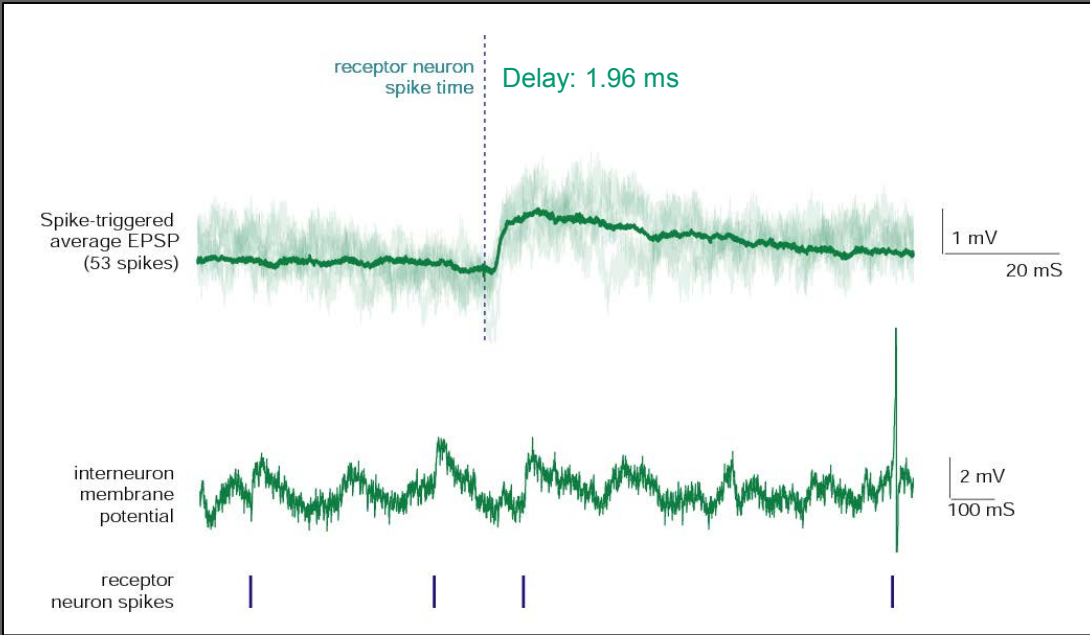
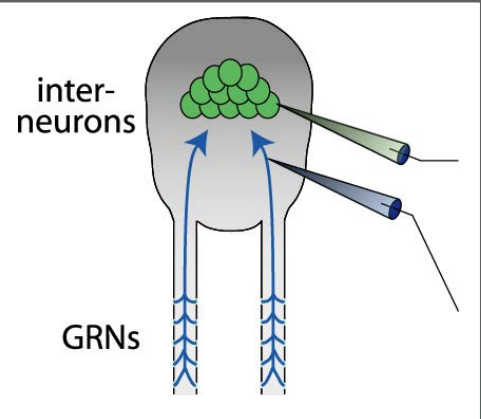
# Finding direct, monosynaptic connections



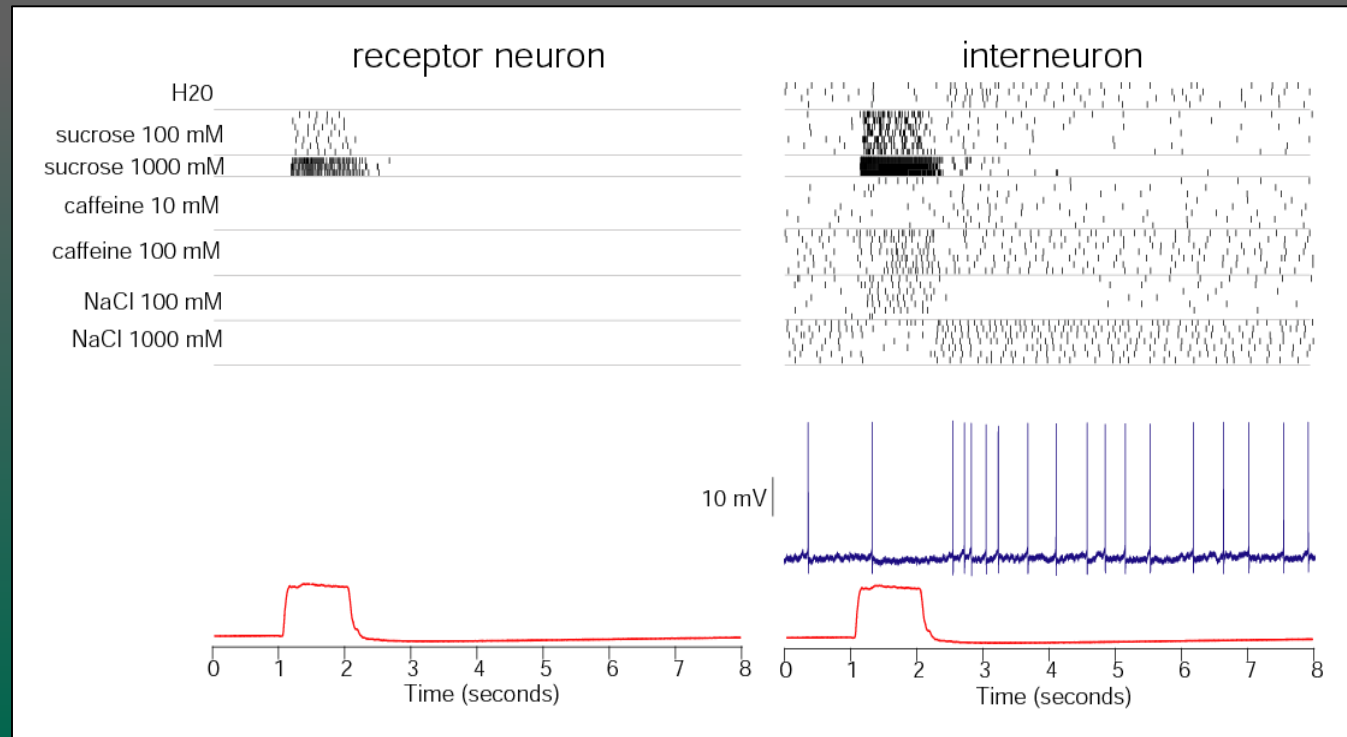
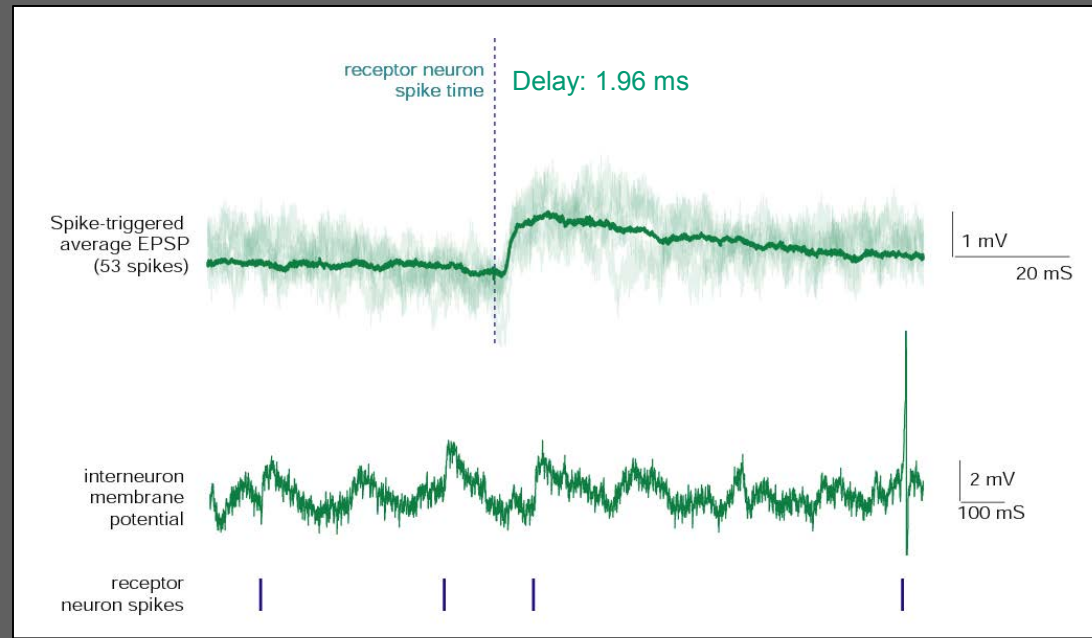
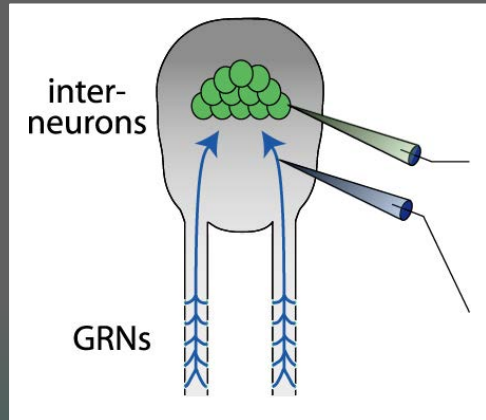
# GRN → follower connectivity and integration



# GRN → follower connectivity and integration

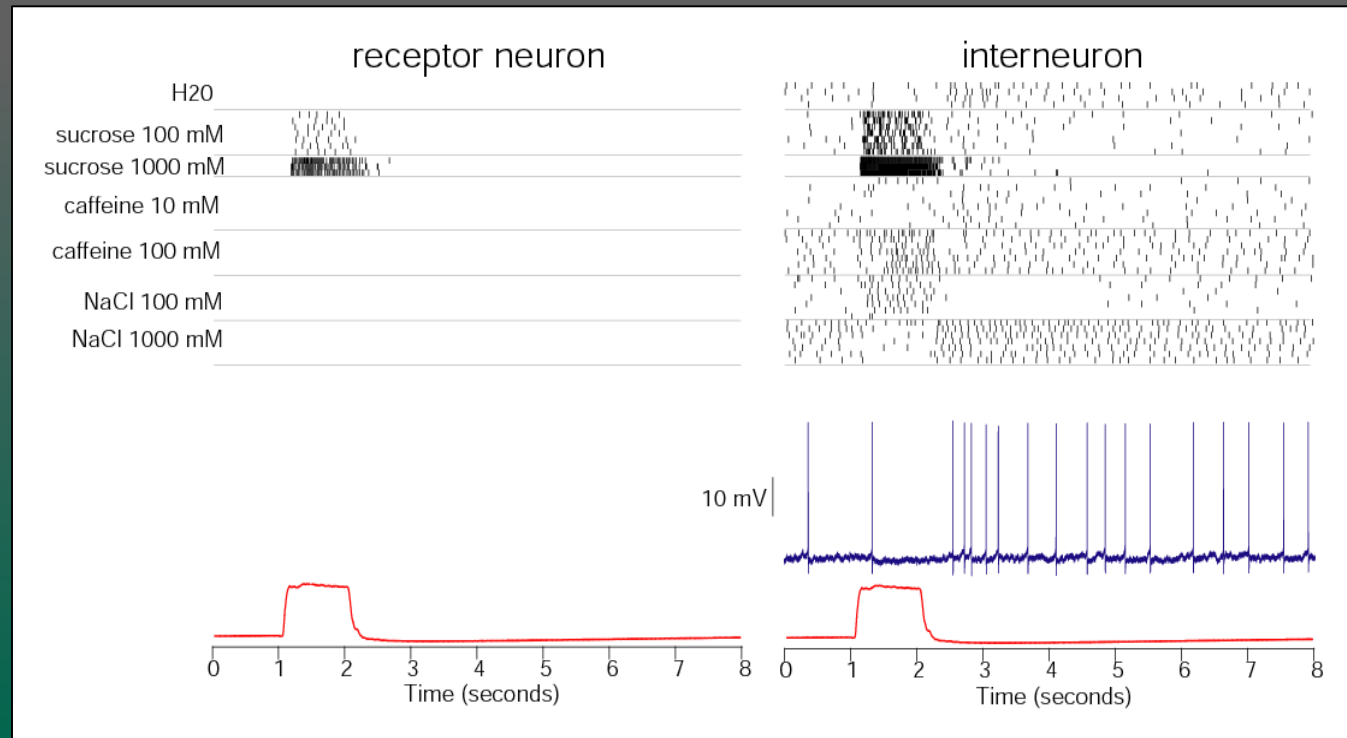
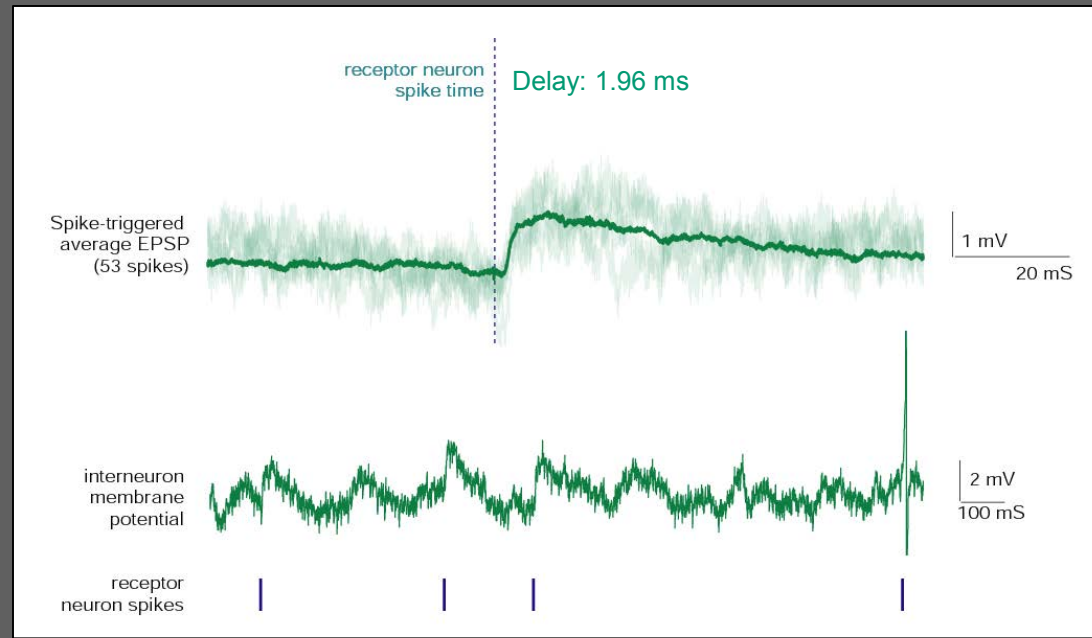
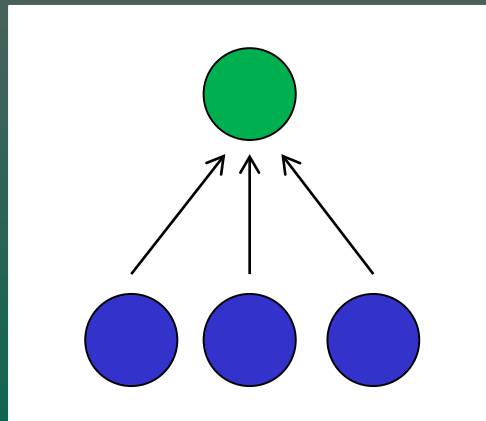
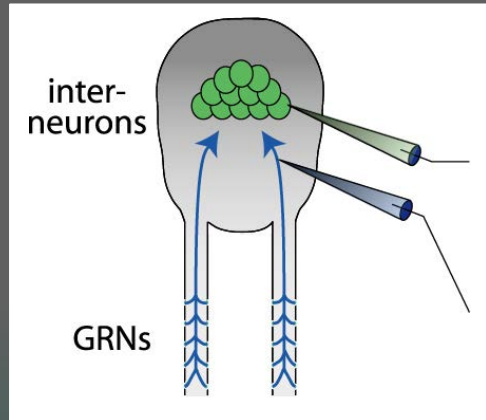


# GRN → follower connectivity and integration





# GRN → follower connectivity and integration



- **Follower neurons fire patterns of spikes, including inhibition, that vary with the odorant**

- **Follower neurons fire patterns of spikes, including inhibition, that vary with the odorant**
- **Follower neurons are more broadly tuned than receptor neurons**

- **• Follower neurons fire patterns of spikes, including inhibition, that vary with the odorant**
- **• Follower neurons are more broadly tuned than receptor neurons**
- **• Multiple types of GRNs converge upon follower neurons**

- **• Follower neurons fire patterns of spikes, including inhibition, that vary with the odorant**
- **• Follower neurons are more broadly tuned than receptor neurons**
- **• Multiple types of GRNs converge upon follower neurons**

*Where does that leave us?*



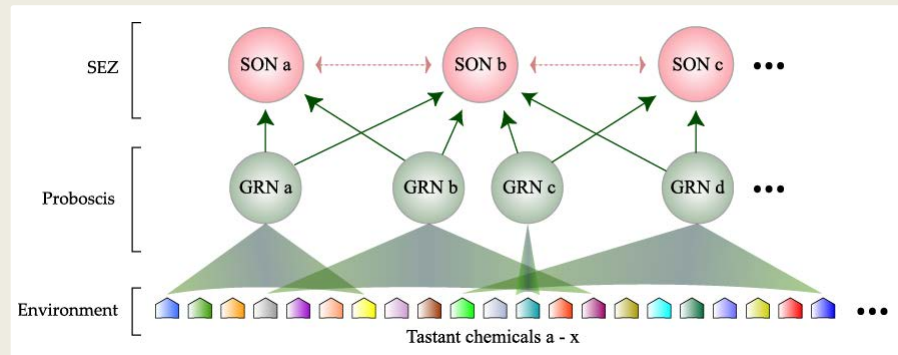
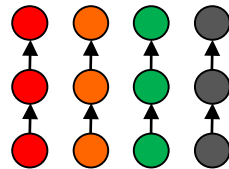
# Questions:

- *Are there only a few basic tastes, or are taste chemicals each encoded uniquely?*
- *What is the nature of the neural code for taste? Is it quick and accurate?*
- *Is taste processed by labeled lines?*

4 basic tastes?

Sweet  
Sour  
Salty  
Bitter

Labeled line coding?



Quick

Accurate

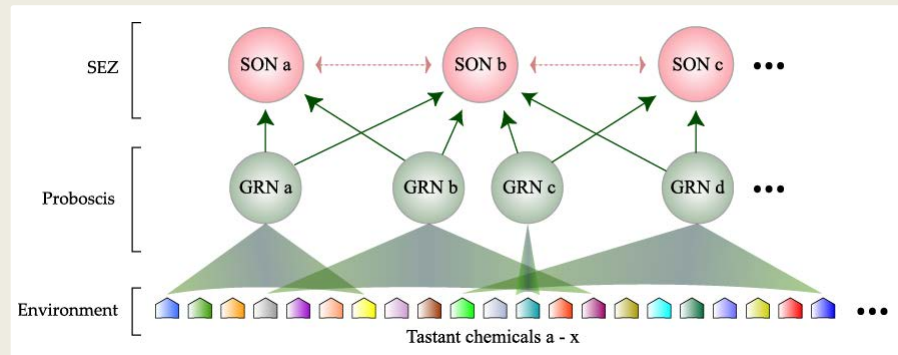
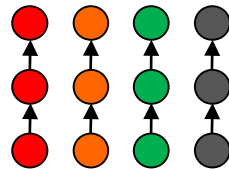
# Questions:

- *Are there only a few basic tastes, or are taste chemicals each encoded uniquely?*  
**Each tastant is encoded uniquely**
- *What is the nature of the neural code for taste? Is it quick and accurate?*
- *Is taste processed by labeled lines?*

4 basic tastes?

Sweet  
Sour  
Salty  
Bitter

Labeled line coding?

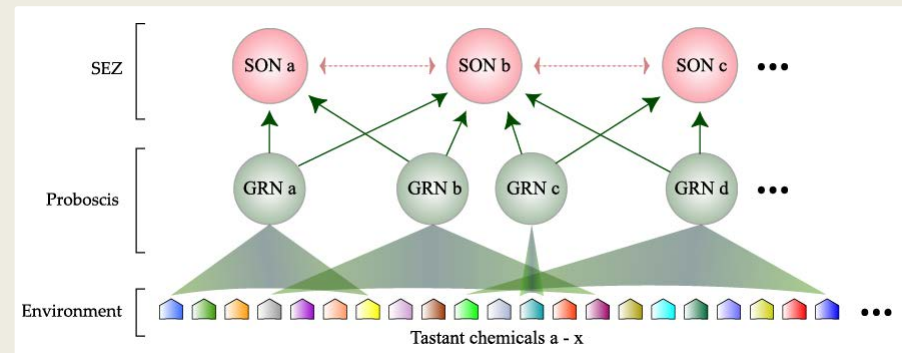
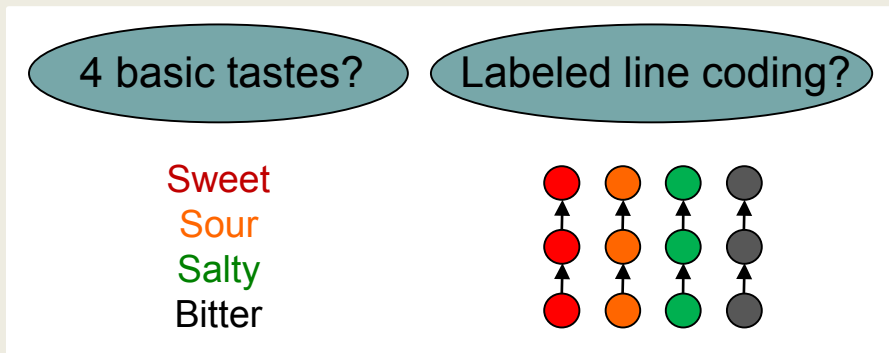


Quick

Accurate

# Questions:

- *Are there only a few basic tastes, or are taste chemicals each encoded uniquely?*  
**Each tastant is encoded uniquely**
- *What is the nature of the neural code for taste? Is it quick and accurate?*  
**Spatio-temporal, combinatorial code**
- *Is taste processed by labeled lines?*



**Quick**

**Accurate**

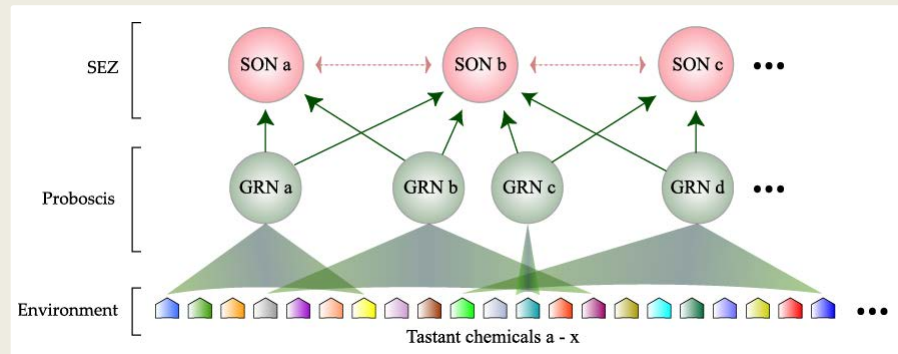
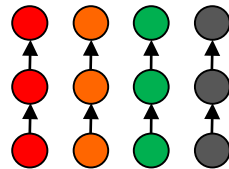
# Questions:

- *Are there only a few basic tastes, or are taste chemicals each encoded uniquely?*  
**Each tastant is encoded uniquely**
- *What is the nature of the neural code for taste? Is it quick and accurate?*  
**Spatio-temporal, combinatorial code**
- *Is taste processed by labeled lines?* **No**

4 basic tastes?

Sweet  
Sour  
Salty  
Bitter

Labeled line coding?



Quick

Accurate

Is this just a moth thing?



# Is this just a moth thing?

## Broad GRN tuning in *Drosophila* and vertebrates...

- GRNs have been shown to respond to only some, but not all, tastants from a basic taste category (Dahanukar et al., 2007; Weiss et al., 2011; Miyamoto et al., 2012; Caicedo and Roper, 2001; Caicedo et al., 2002).
- GRNs have been shown to respond to some, but not all, tastants from multiple categories (Wisotsky et al., 2011; Charlu et al., 2013; Jeong et al., 2013; Masek and Keene, 2013, Caicedo et al., 2002; Nelson et al., 2002; Oka et al., 2013).

# Is this just a moth thing?

## Broad GRN tuning in *Drosophila* and vertebrates...

- GRNs have been shown to respond to only some, but not all, tastants from a basic taste category (Dahanukar et al., 2007; Weiss et al., 2011; Miyamoto et al., 2012; Caicedo and Roper, 2001; Caicedo et al., 2002).
- GRNs have been shown to respond to some, but not all, tastants from multiple categories (Wisotsky et al., 2011; Charlu et al., 2013; Jeong et al., 2013; Masek and Keene, 2013, Caicedo et al., 2002; Nelson et al., 2002; Oka et al., 2013).

## Informative spike timing in gustatory neurons...

- The timing of spikes has been shown to contain information about tastants in neurons at several stages along the gustatory pathway (Katz et al., 2001; Hallock and DiLorenzo, 2006; Lemon and Katz, 2007; Fontanini et al., 2009; Rosen et al., 2011; Wilson et al., 2012).

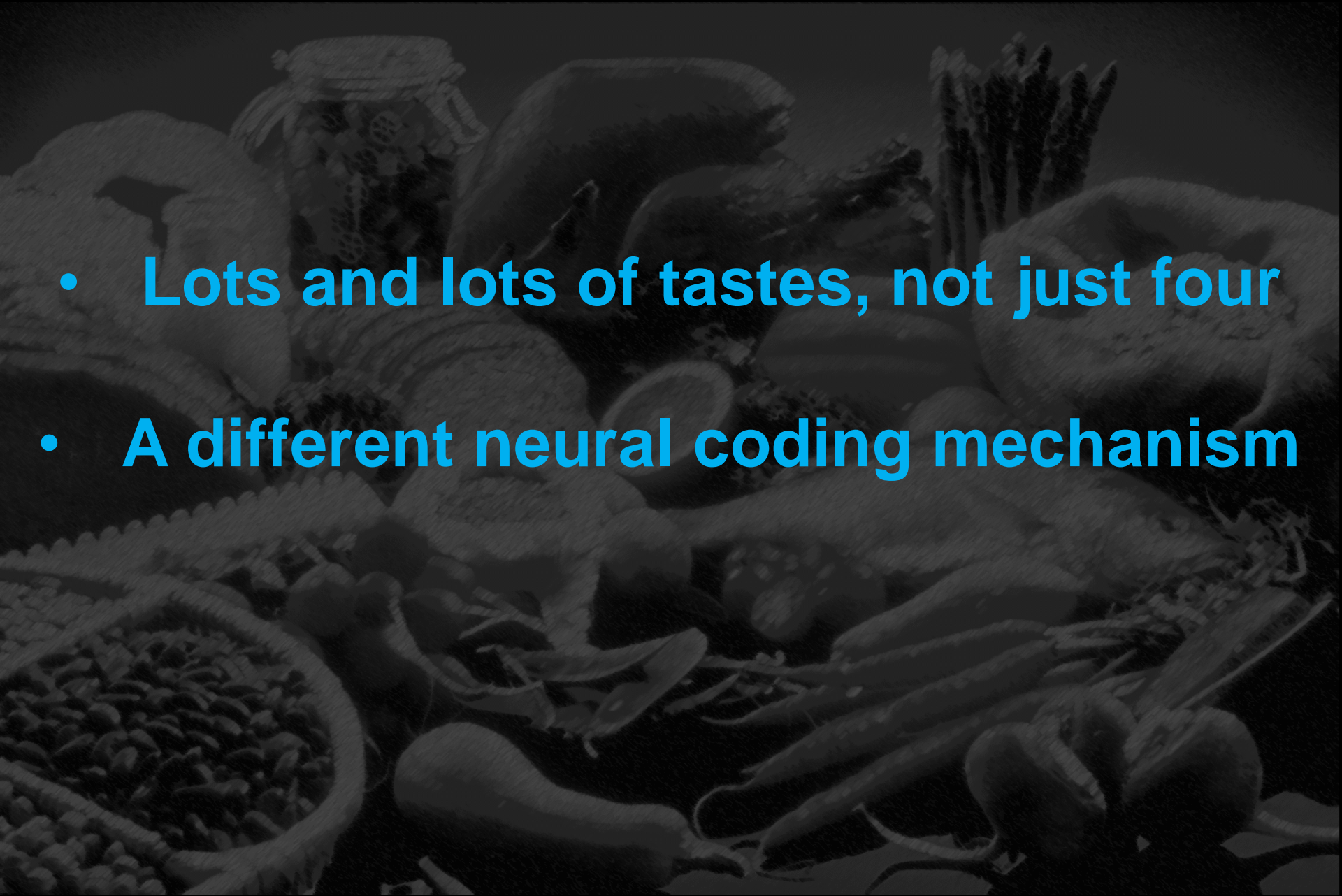
Let's change the way we think about taste:





# Let's change the way we think about taste:

- **Lots and lots of tastes, not just four**
- **A different neural coding mechanism**



**Sam  
Reiter**

NIH-Brown-GPP  
PhD 2014



**Chelsey  
Campillo  
Rodriguez**  
High school intern

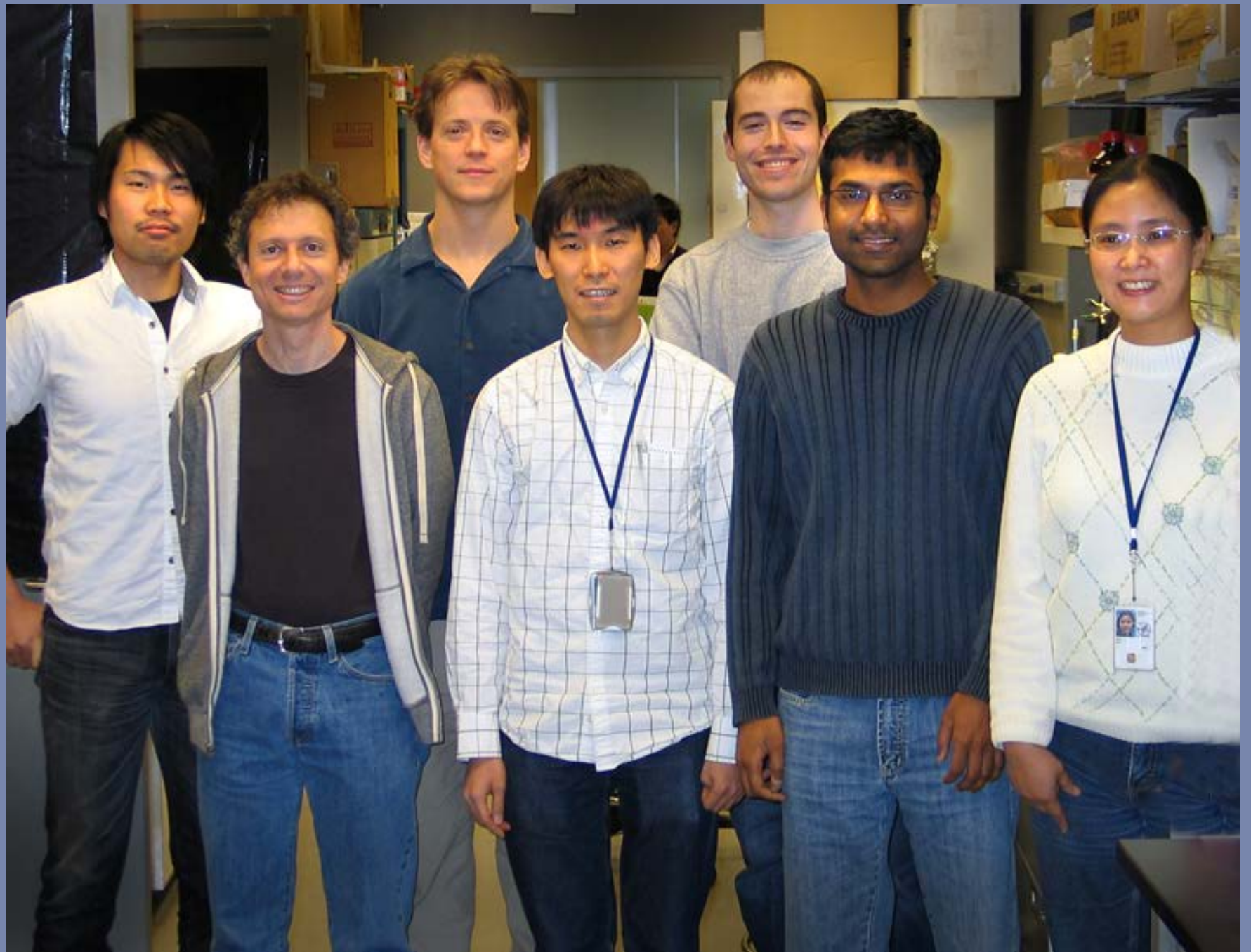


**Kui  
Sun**  
technician



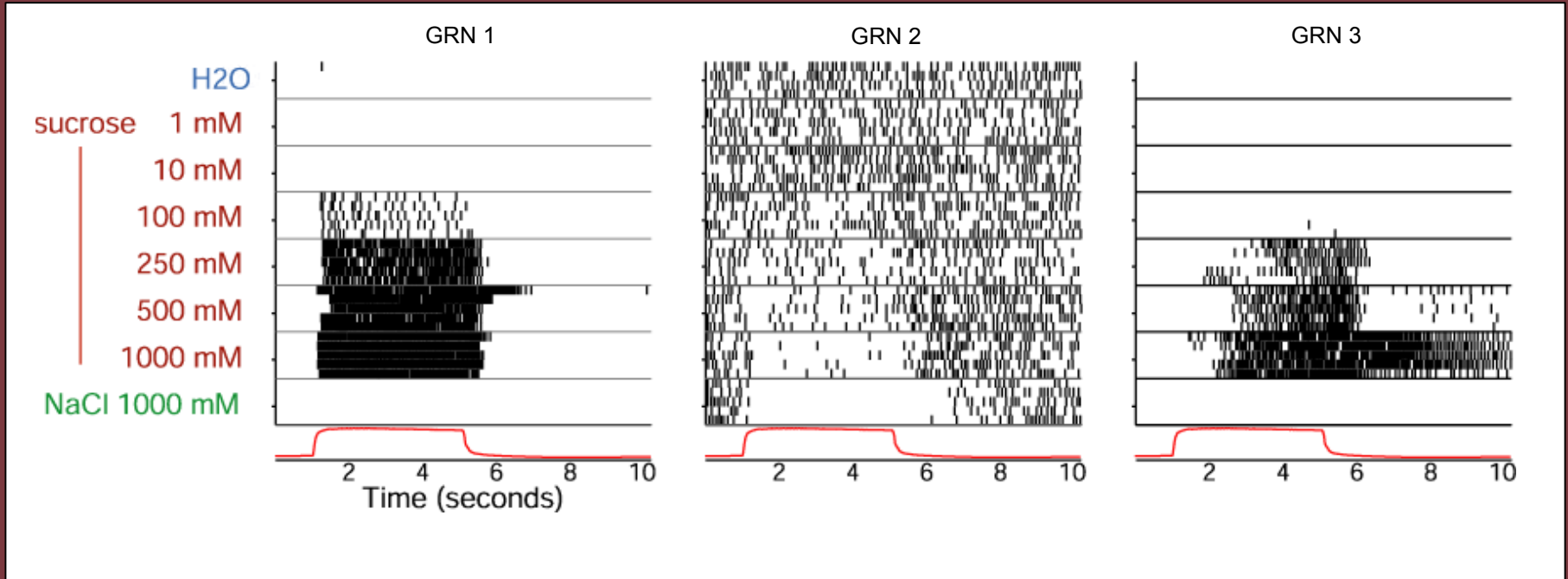
<b>Sam's thesis committee:</b>	Gilad Barnea Leonardo Belluscio David Berson Chi-Hon Lee Chris McBain Dmitry Rinberg
<b>Tastant delivery system:</b>	George Dold Tom Talbot
<b>Light microscopy:</b>	Vincent Shram
<b>Scanning electron microscopy:</b>	Pat Zerfas Chris Brantner



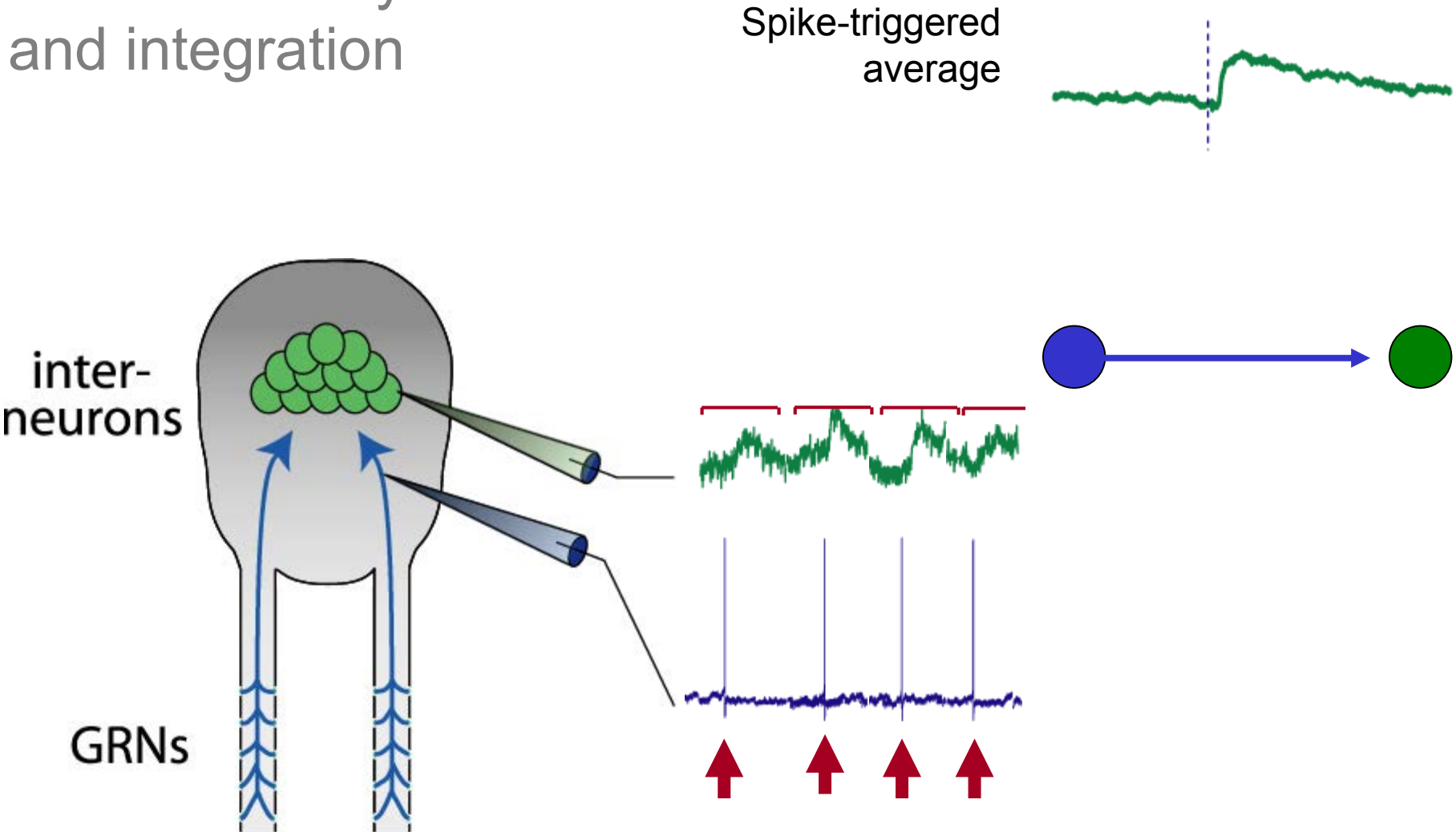




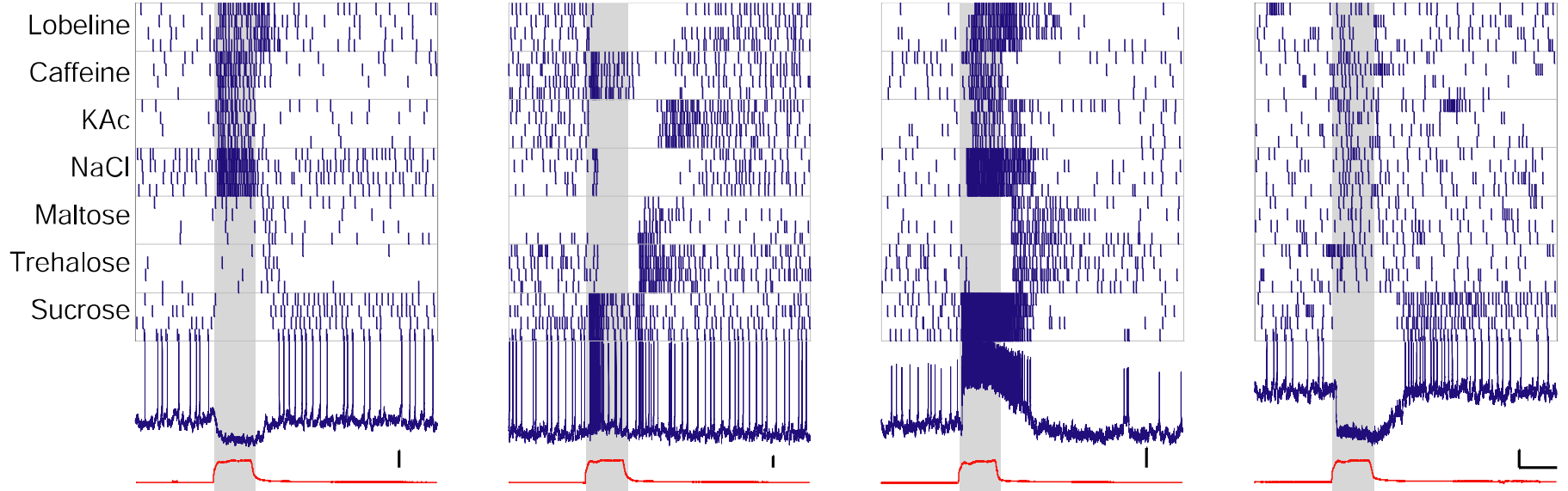
As tastant concentration increases,  
more types of GRNs respond, and more strongly



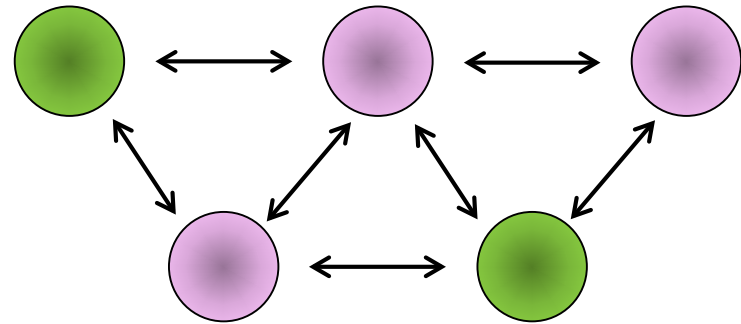
# GRN → follower connectivity and integration



# Sharp-electrode intracellular: second order neurons



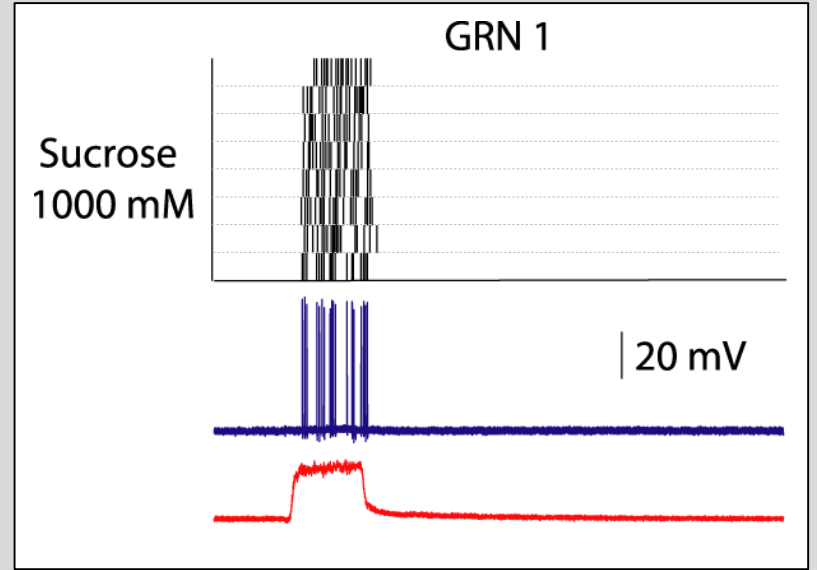
Temporal patterning  
In SONs



# GRNs

Gustatory  
Receptor  
Neurons

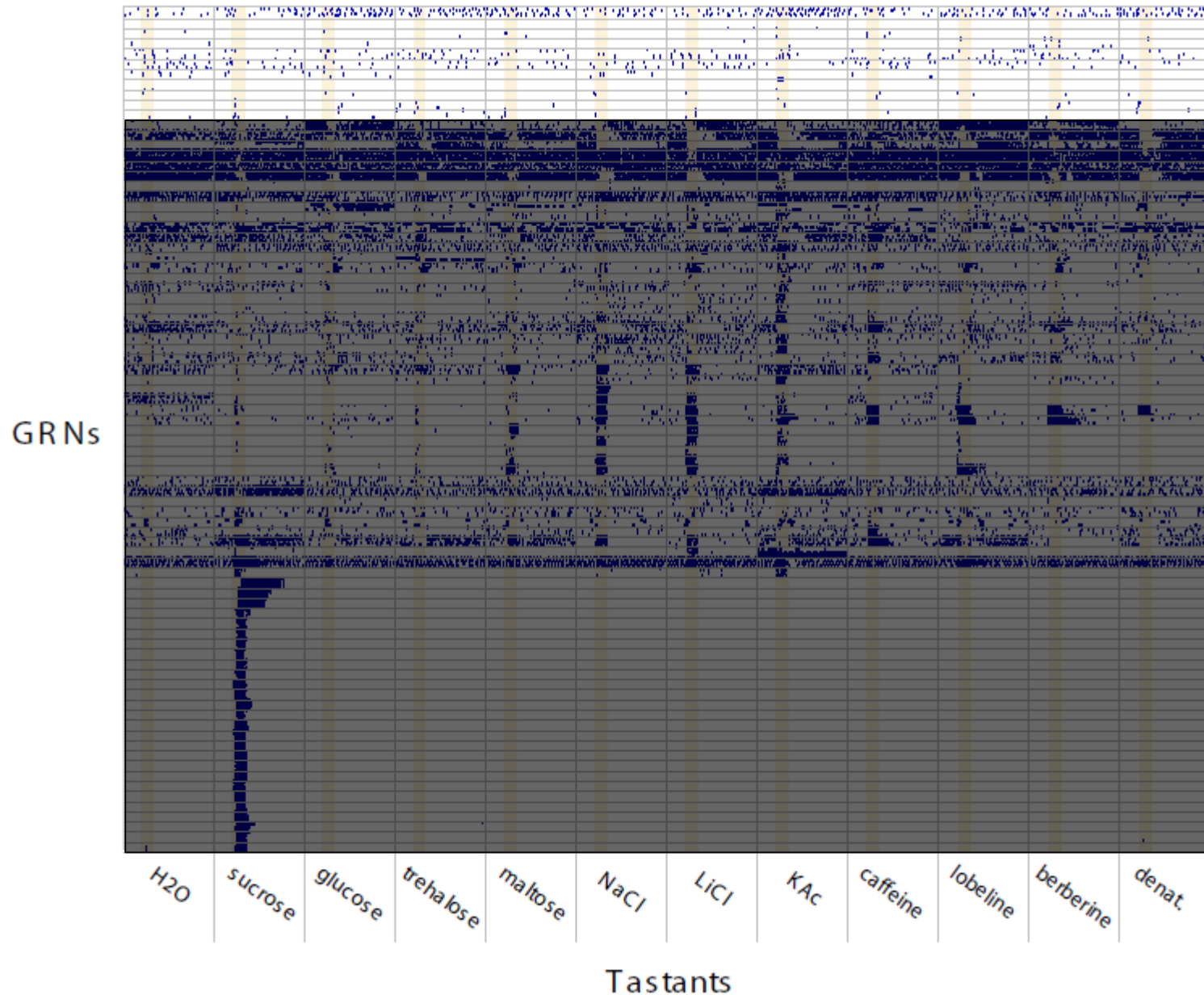
## Sharp-electrode intracellular recordings







# Encoding Tastant Identity



# What's wrong with the basic taste framework?

- There is no single clear, useful definition of a basic taste.
- Many GRNs respond to chemicals not readily associated with any of the basic tastes
  - water (Cameron et al., 2010)
  - fatty acids (Cartoni et al., 2010; Masek and Keene, 2013)
  - carbon dioxide (Fischler et al., 2007)
  - contact pheromones (Lacaille et al., 2007).
- It does not provide the best description of the data.
- Sometimes sets limitations for experiments

# What's wrong with the basic taste framework?

- There is no single clear, useful definition of a basic taste.
- Many GRNs respond to chemicals not readily associated with any of the basic tastes
  - water (Cameron et al., 2010)
  - fatty acids (Cartoni et al., 2010; Masek and Keene, 2013)
  - carbon dioxide (Fischler et al., 2007)
  - contact pheromones (Lacaille et al., 2007).
- It does not provide the best description of the data.
- Sometimes sets limitations for experiments

An “individual taste framework”

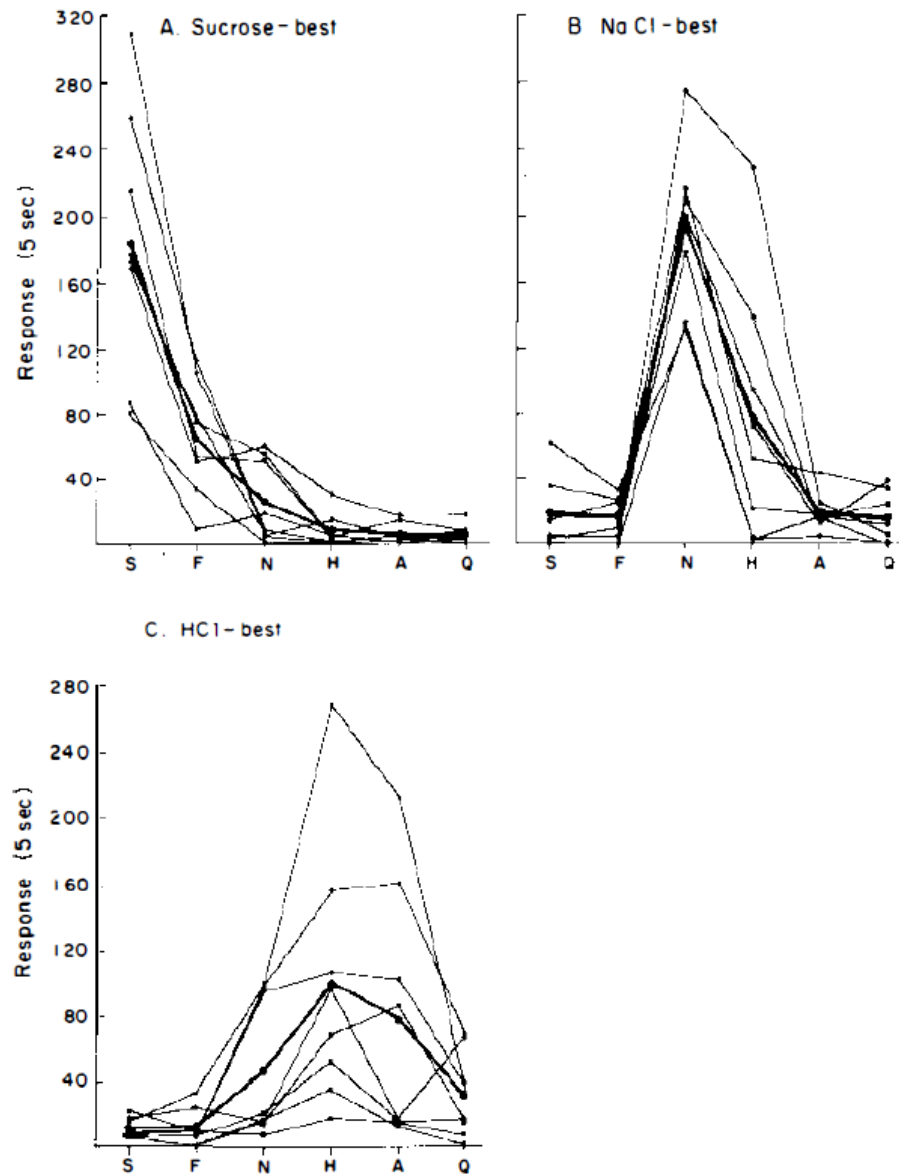
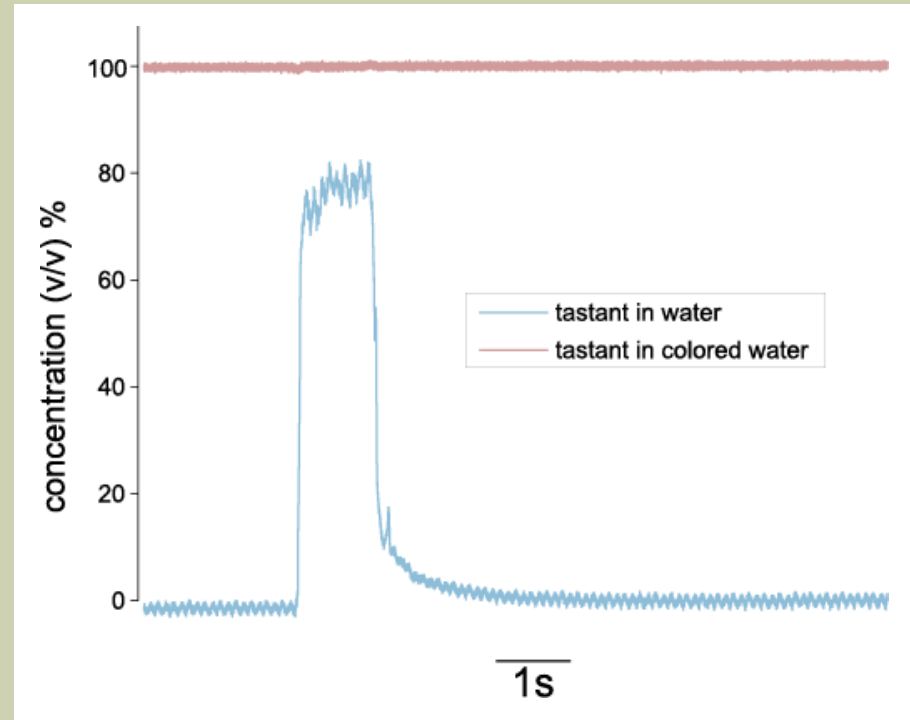
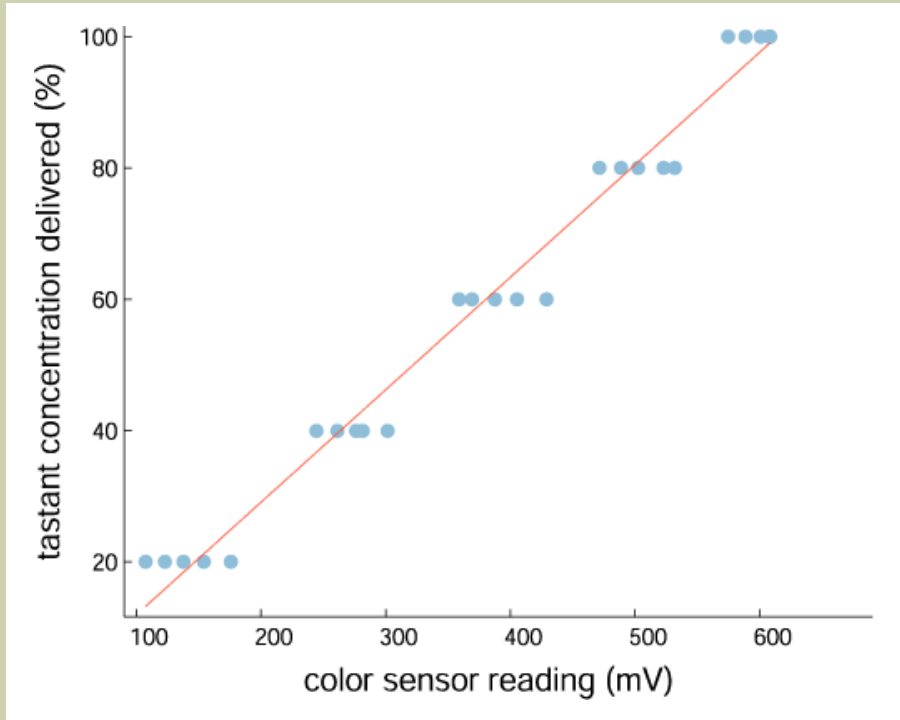
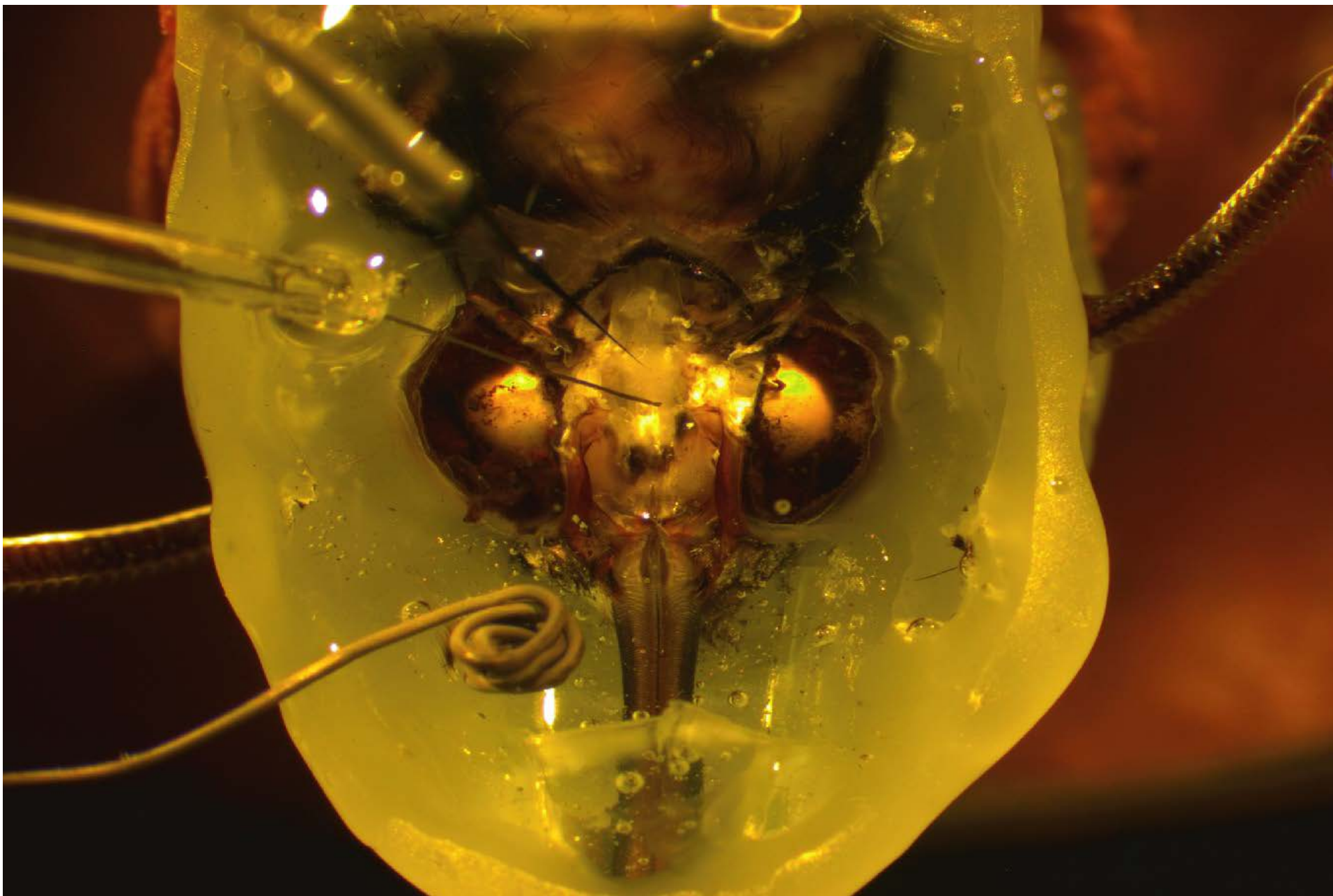


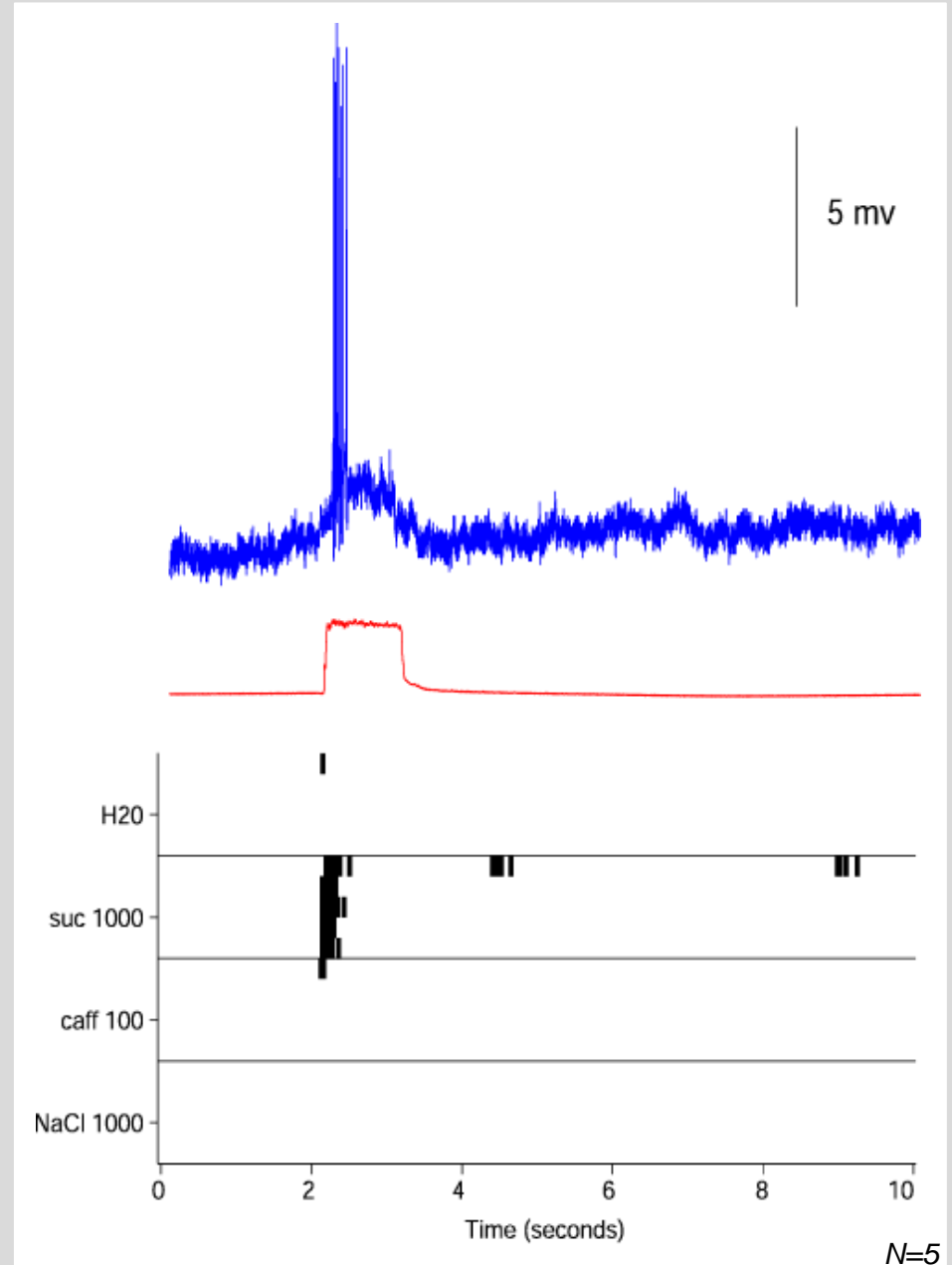
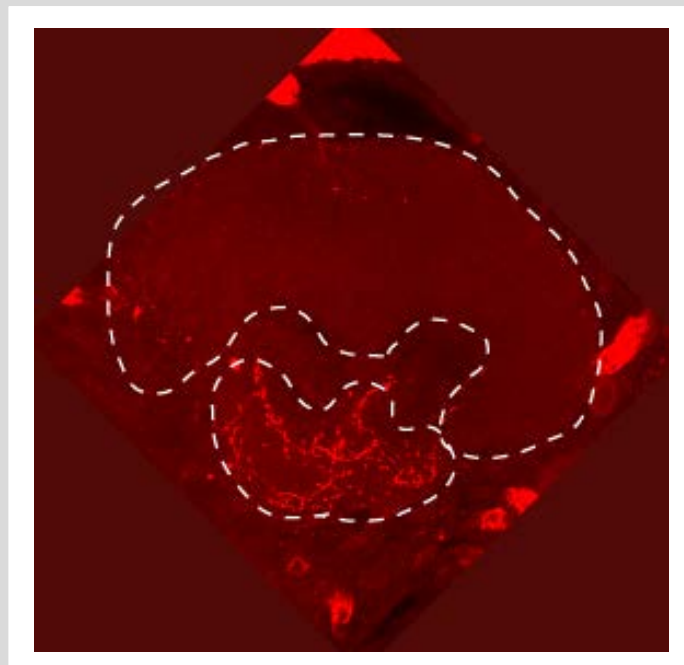
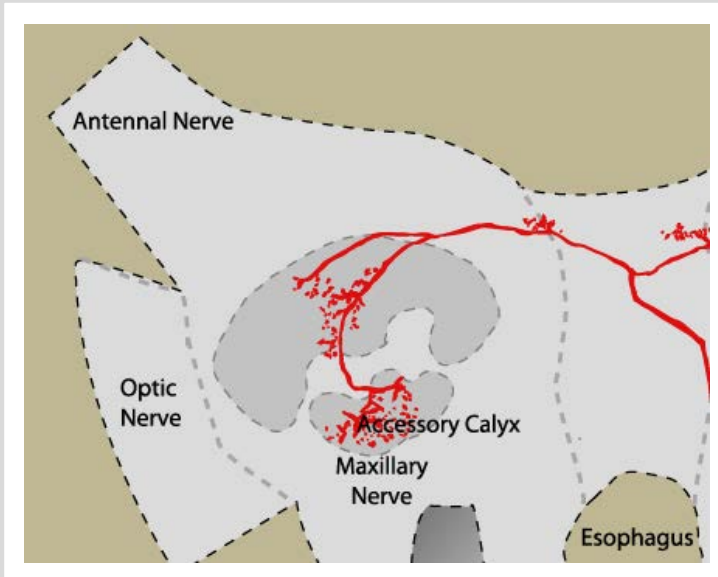
Figure 3 Hamster chorda tympani response profiles. *S* is 0.1 M sucrose; *N*, 0.03 M NaCl; *H*, 0.003 M HCl; *Q*, 0.001 M quinine hydrochloride; *F*, 0.3 M fructose; and *A*, 0.03 M NH<sub>4</sub>Cl. Modified from Frank (62)

Pfaffmann, Frank, and Norgren, 1979



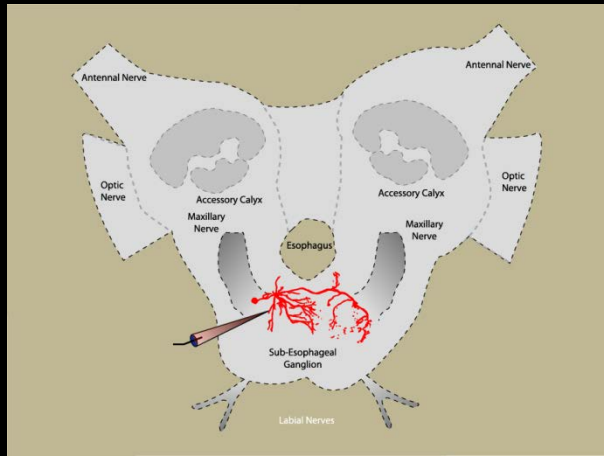


# Gustatory Projection Neurons: Ascending

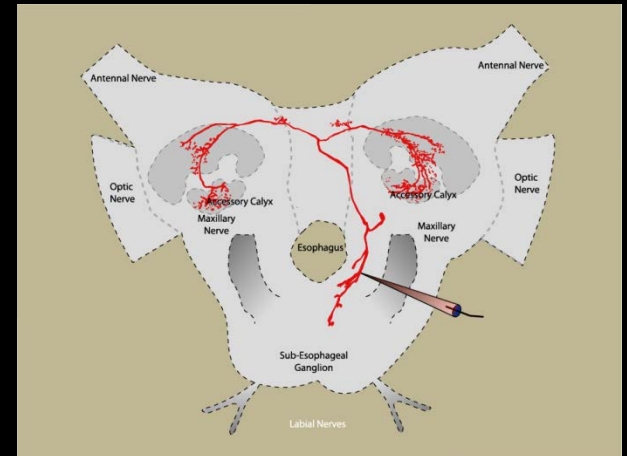
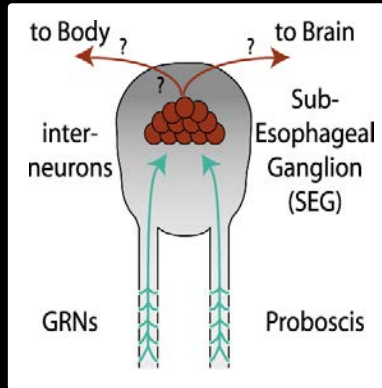




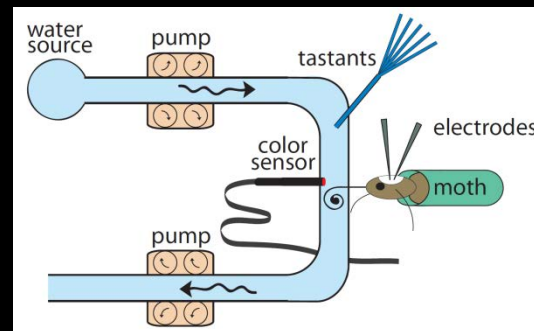
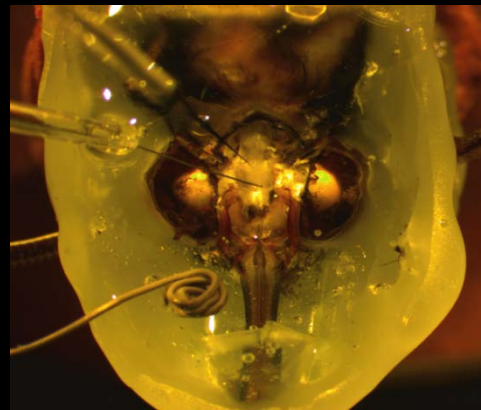
# Projection Neurons



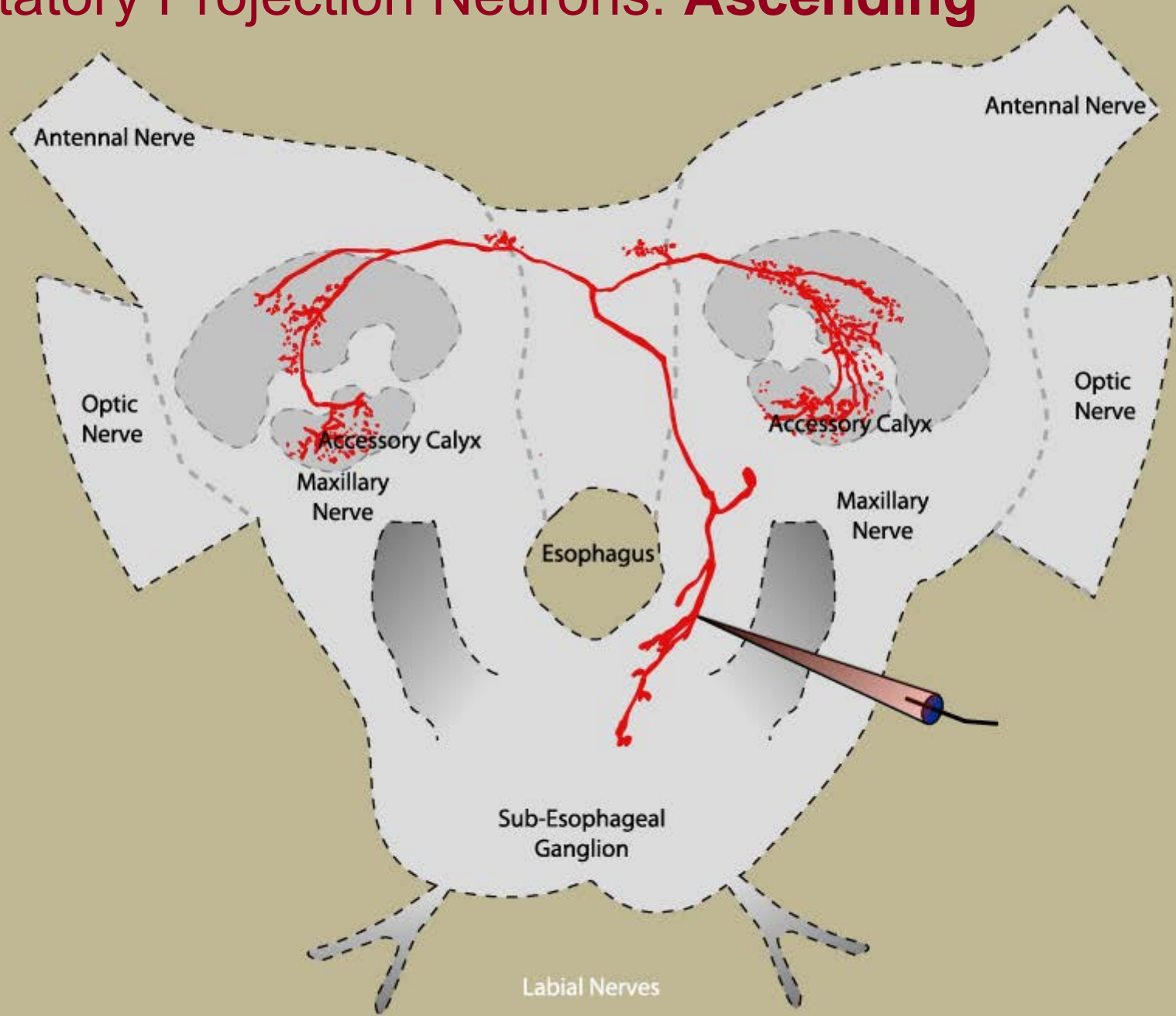
descending



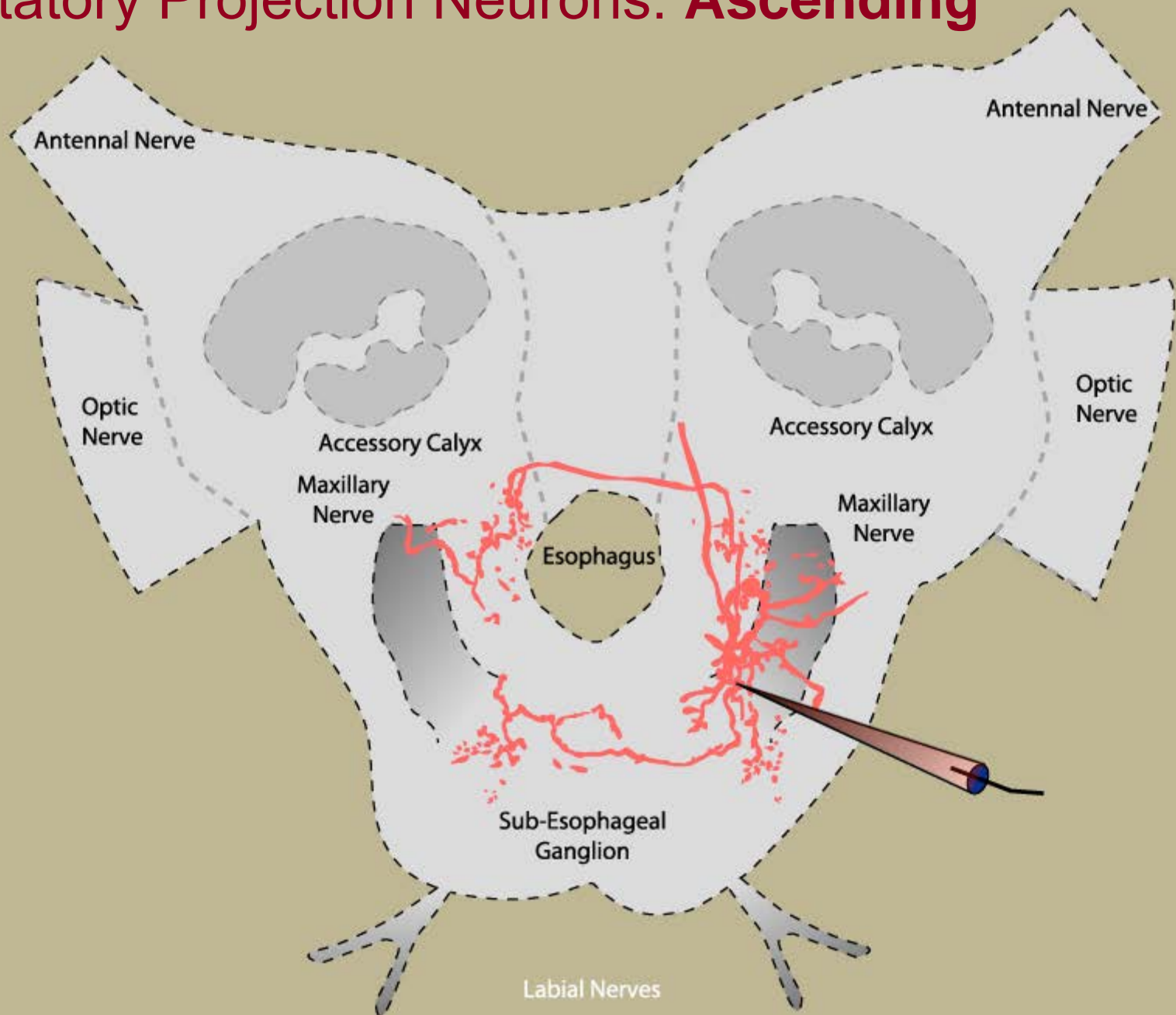
ascending



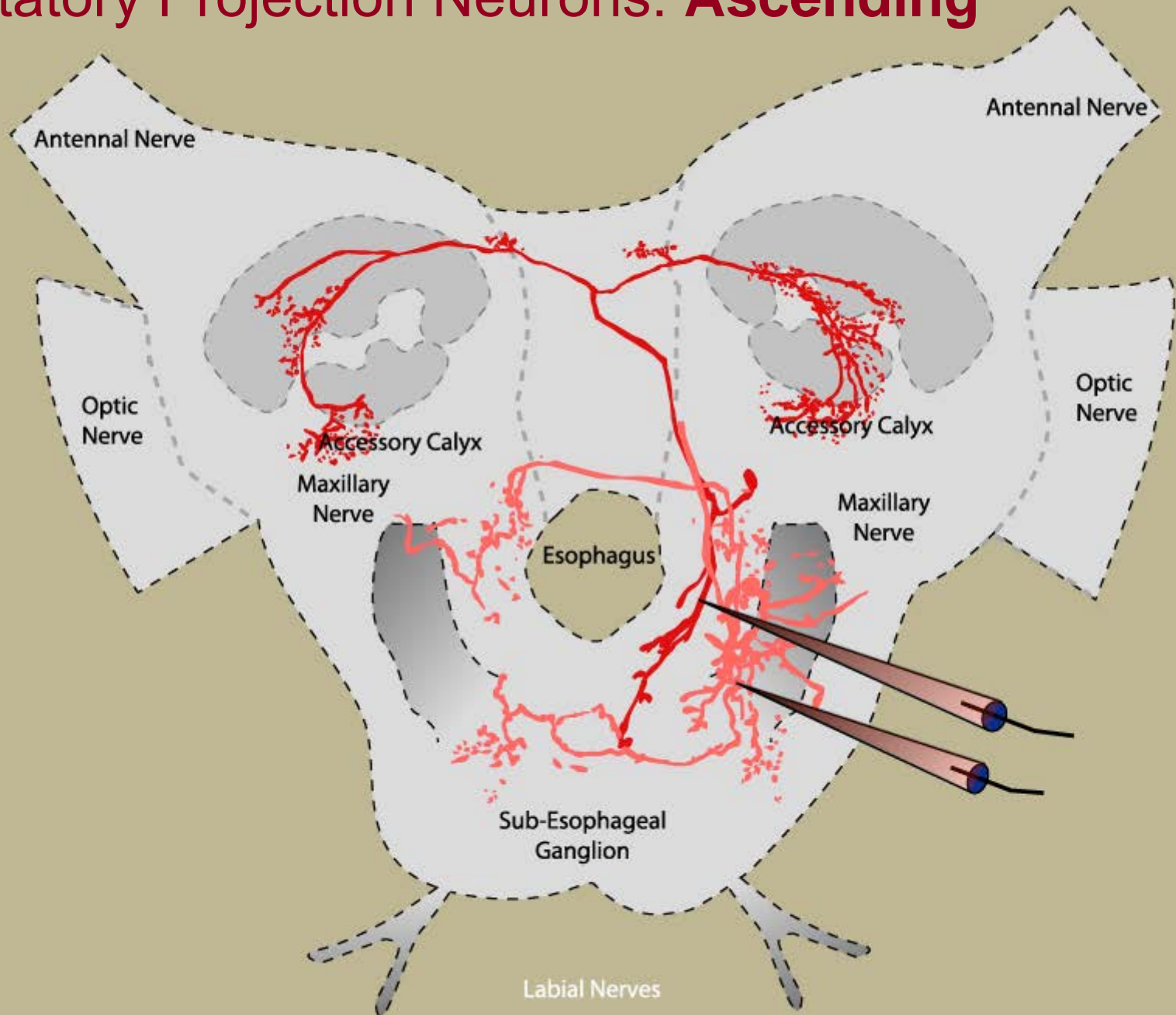
# Gustatory Projection Neurons: Ascending



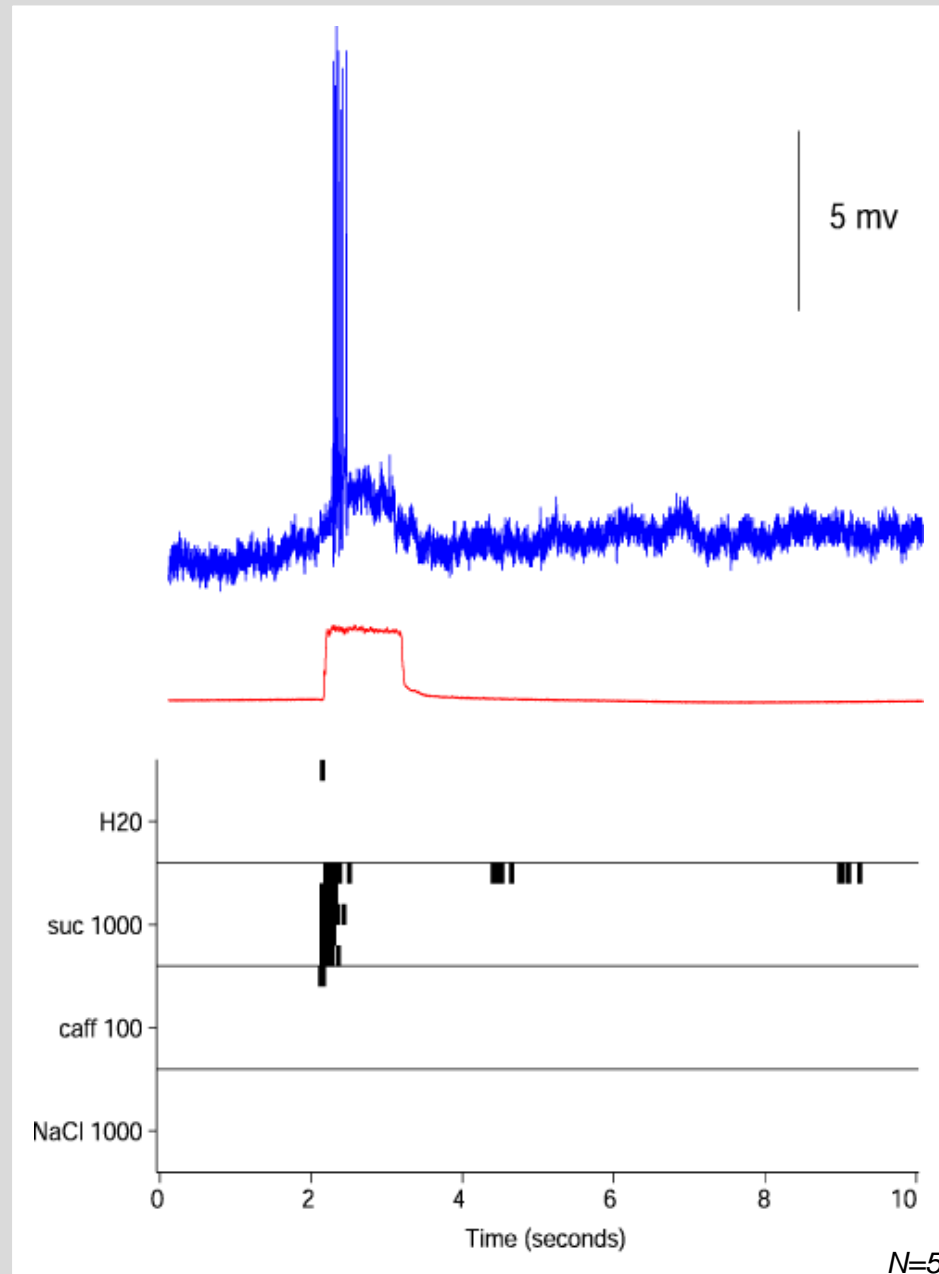
# Gustatory Projection Neurons: Ascending



# Gustatory Projection Neurons: Ascending

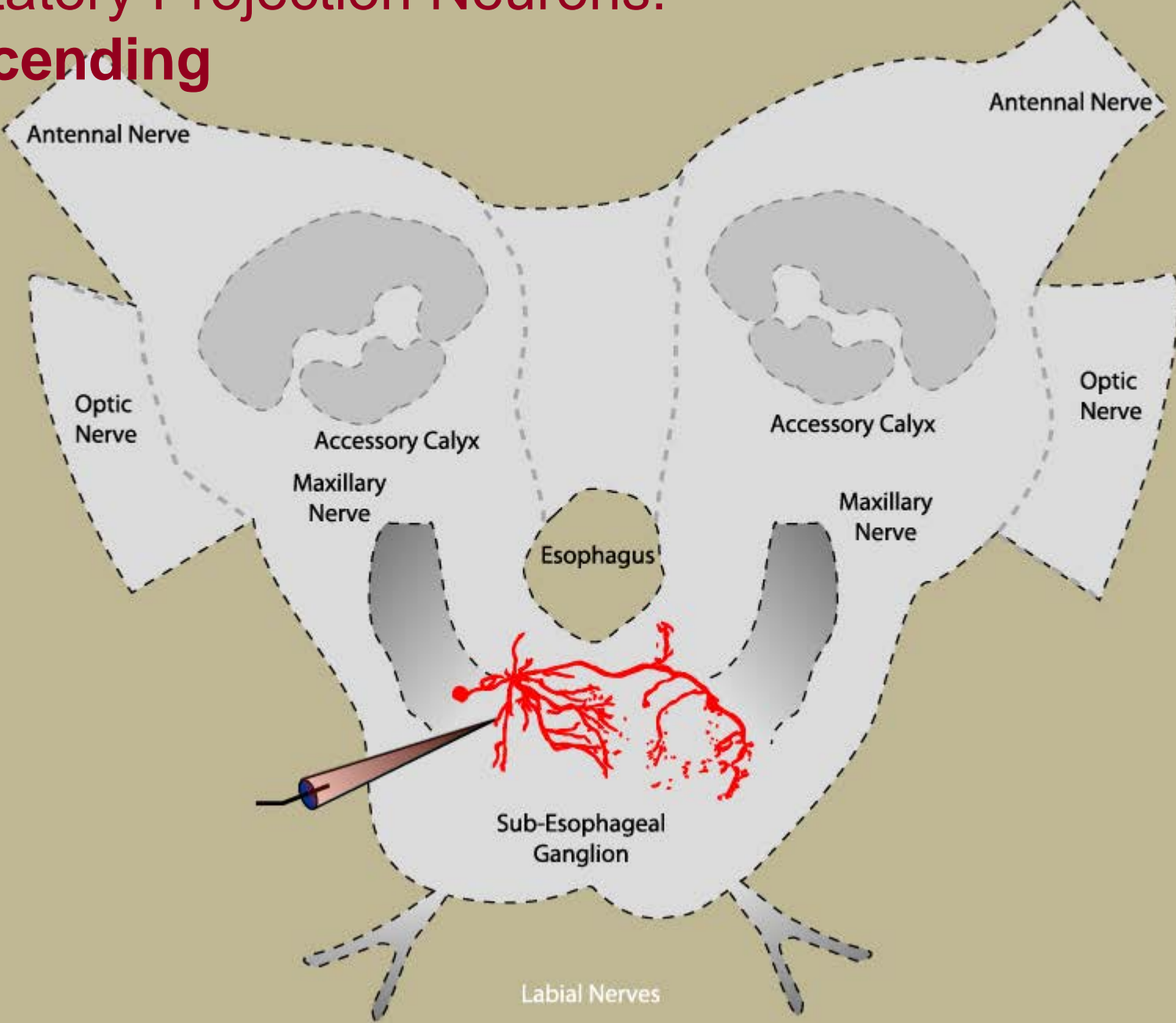


# Gustatory Projection Neurons: Ascending

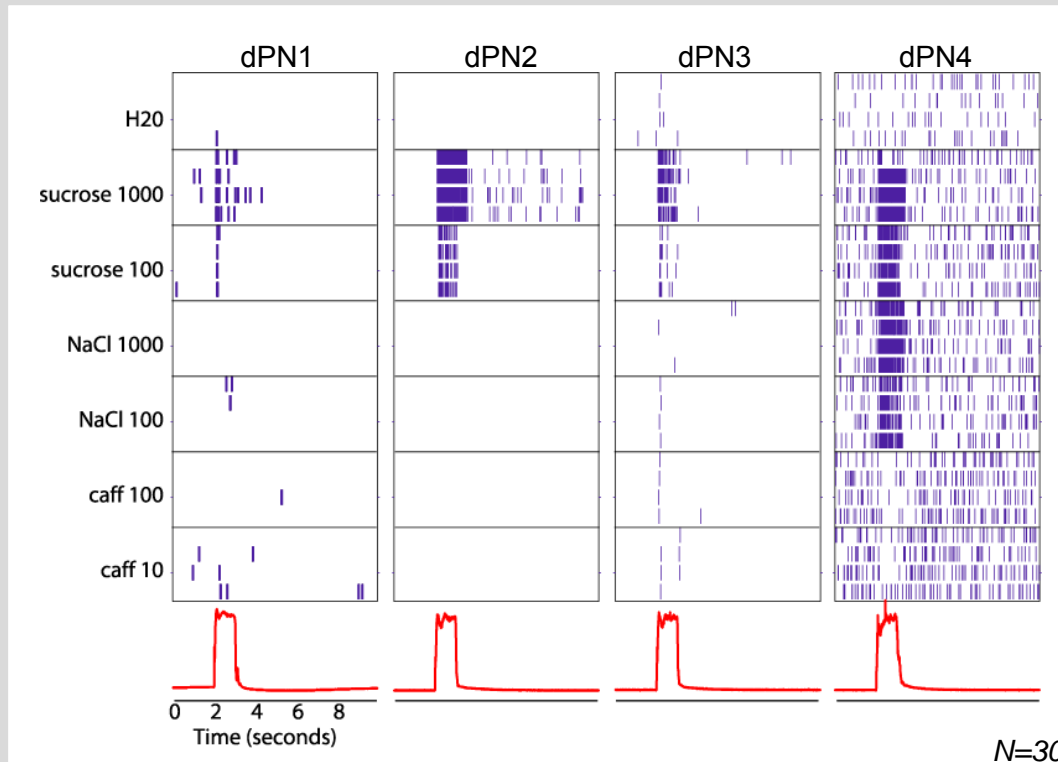
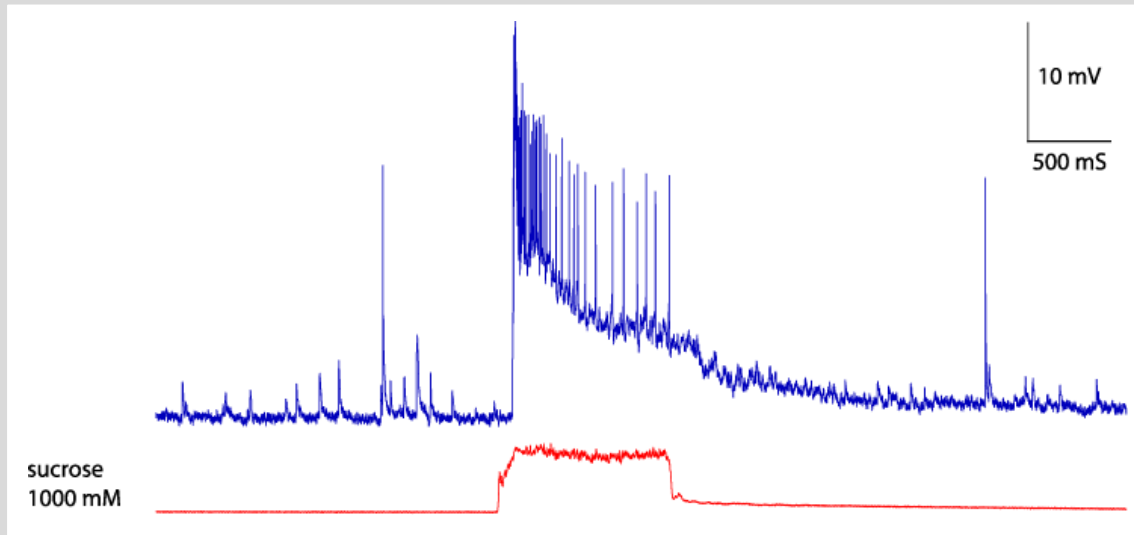




# Gustatory Projection Neurons: Descending



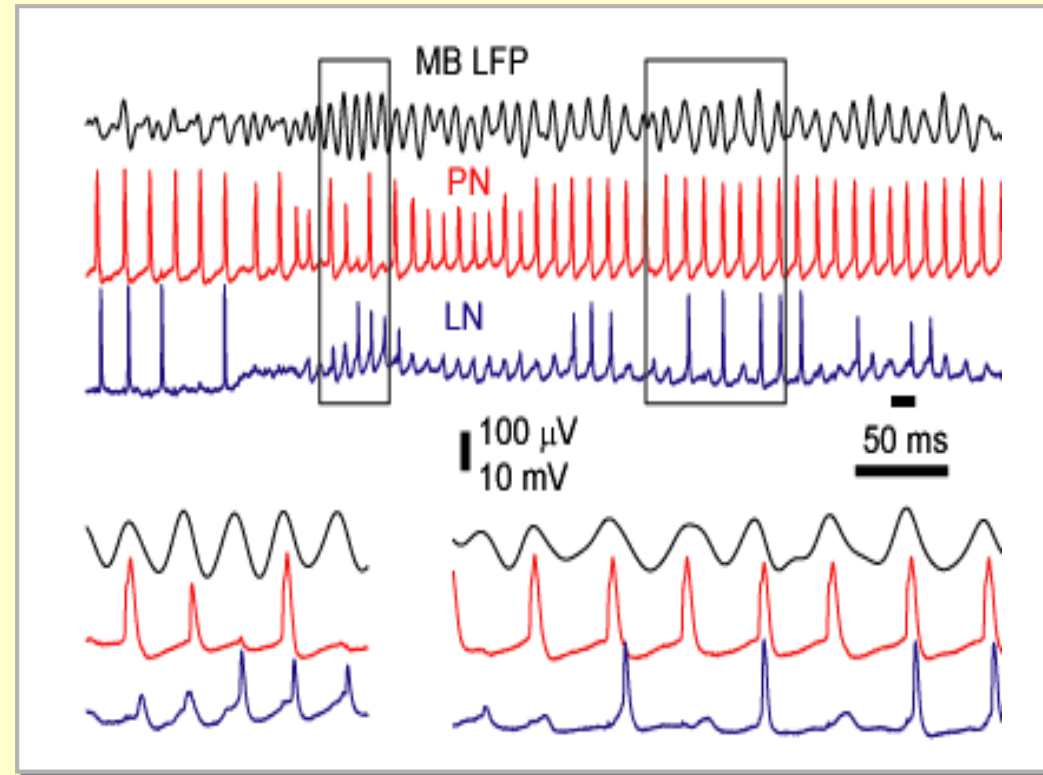
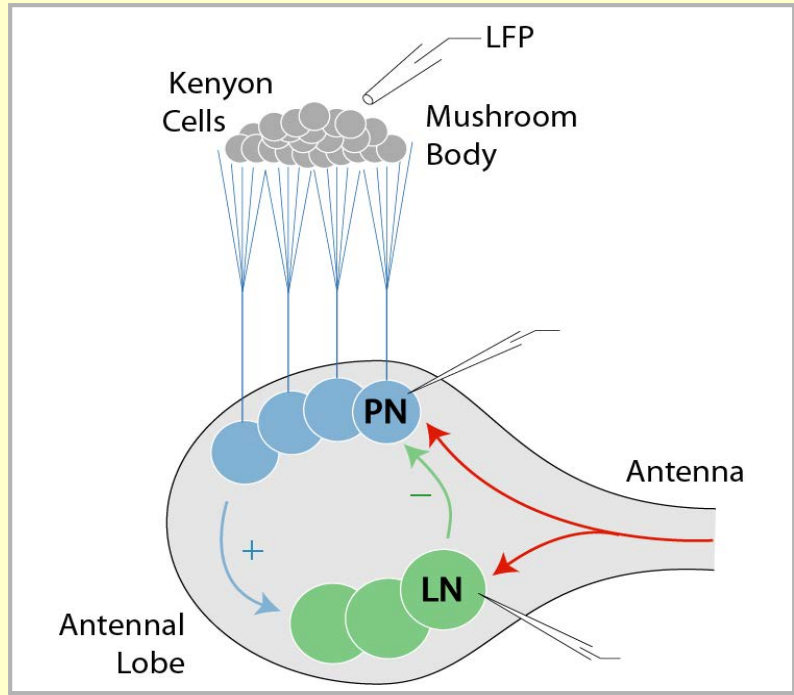
# Gustatory Projection Neurons: Descending



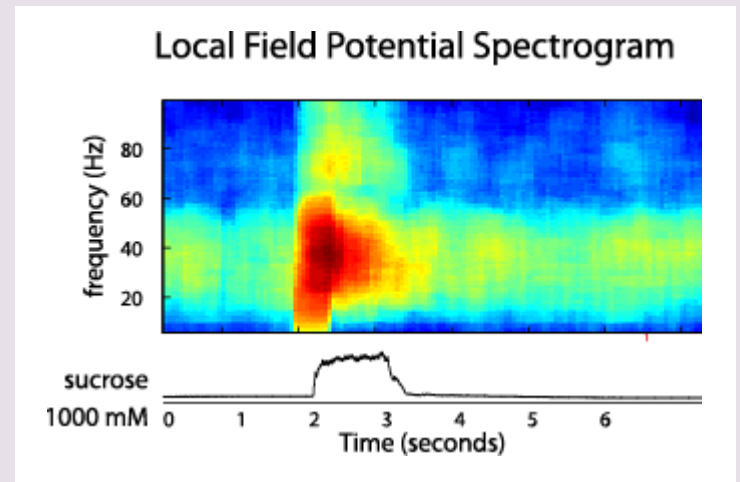
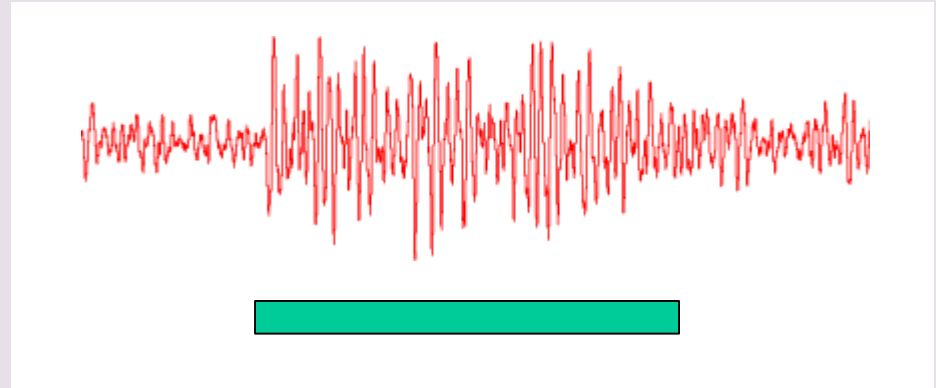
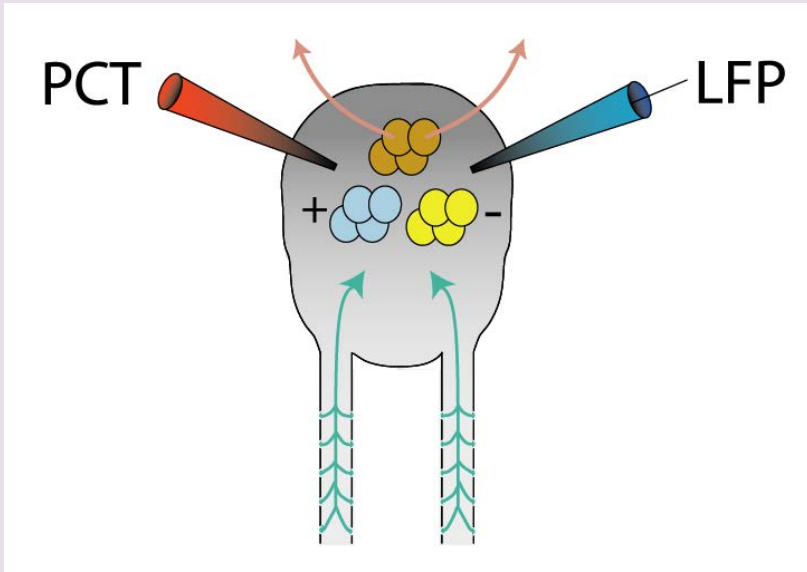


# Olfactory System

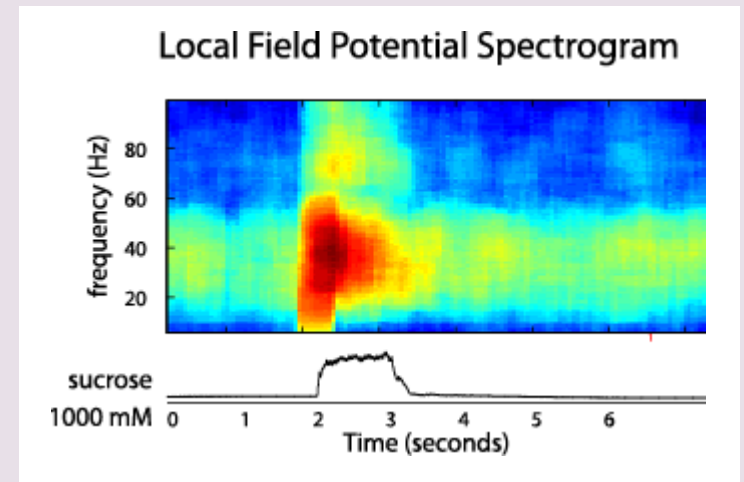
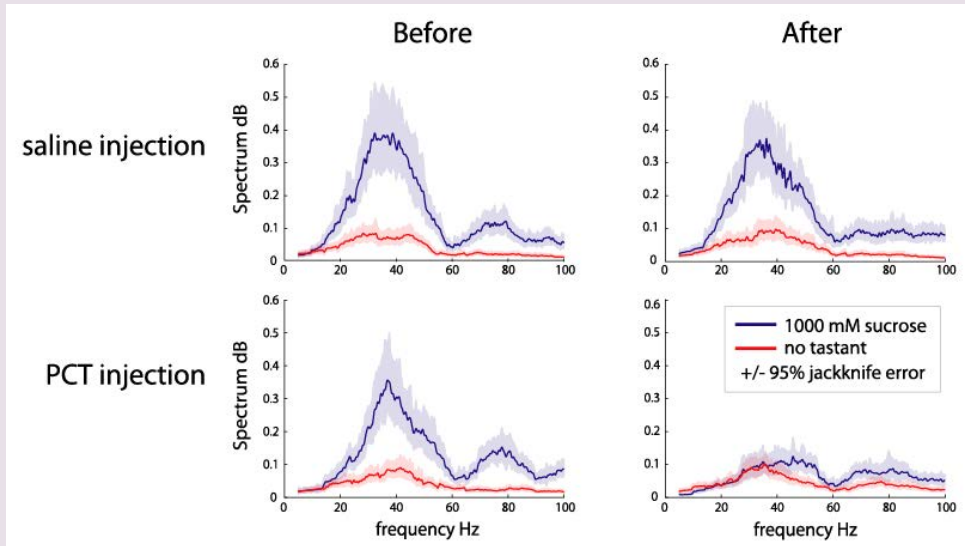
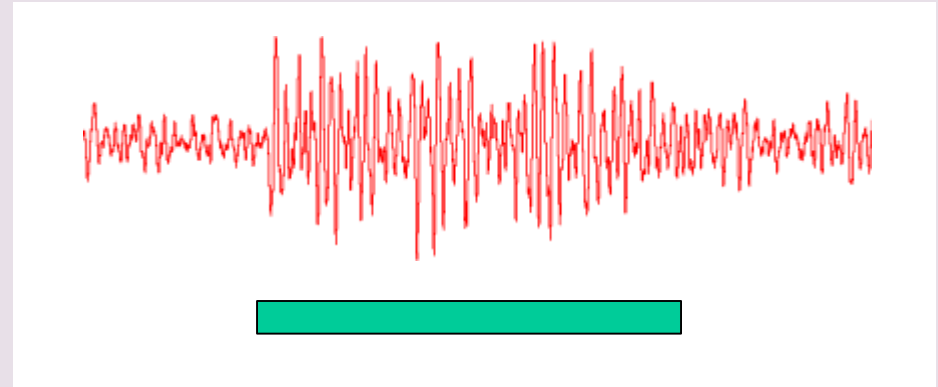
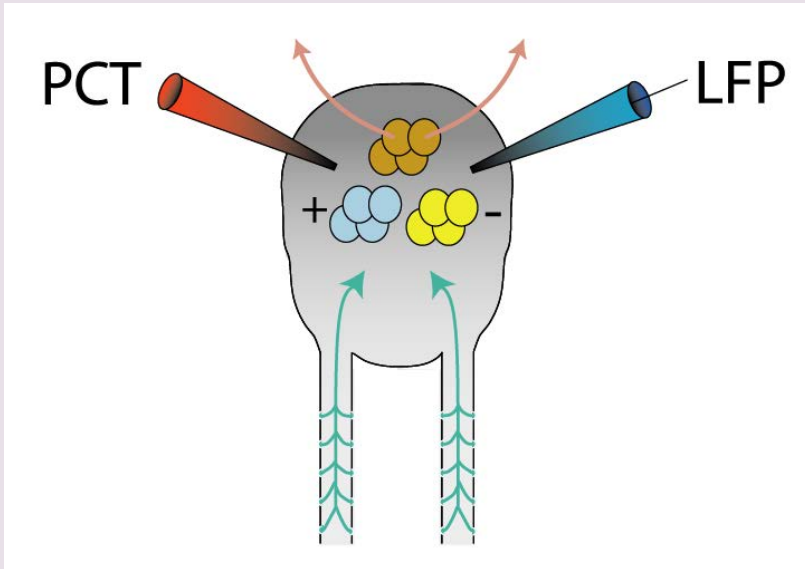
Antennal lobe  
neurons tend to  
synchronize



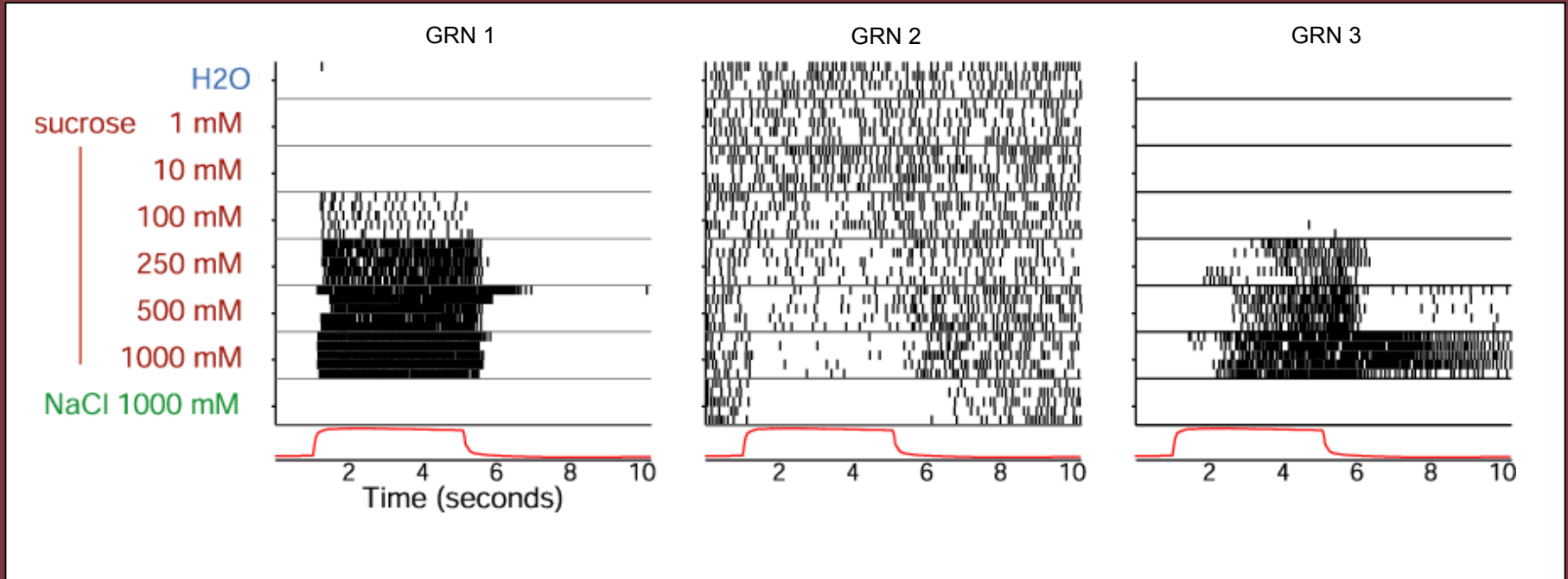
# Tastant-elicited oscillations



# Tastant-elicited oscillations



As tastant concentration increases,  
more types of GRNs respond, and more strongly



# The predominant view

*“... tastant quality is mediated by labeled lines, whereby distinct and strictly segregated populations of taste receptor cells encode each of the taste qualities.”*

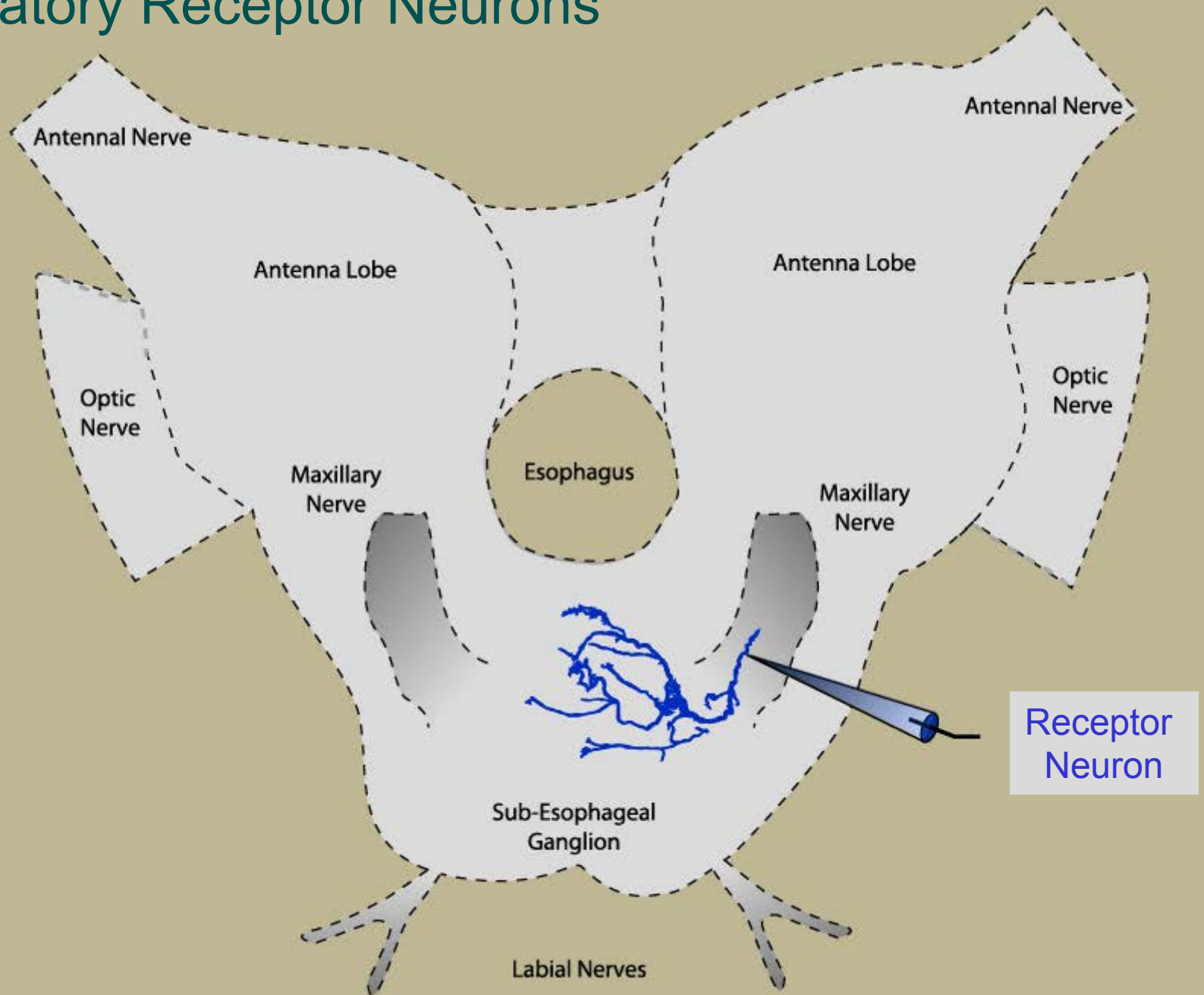
Common sense about taste: from mammals to insects.

Yarmolinsky, Zuker, & Ryba,  
Cell 139(2):234-44. (2009)

**Must be quick**

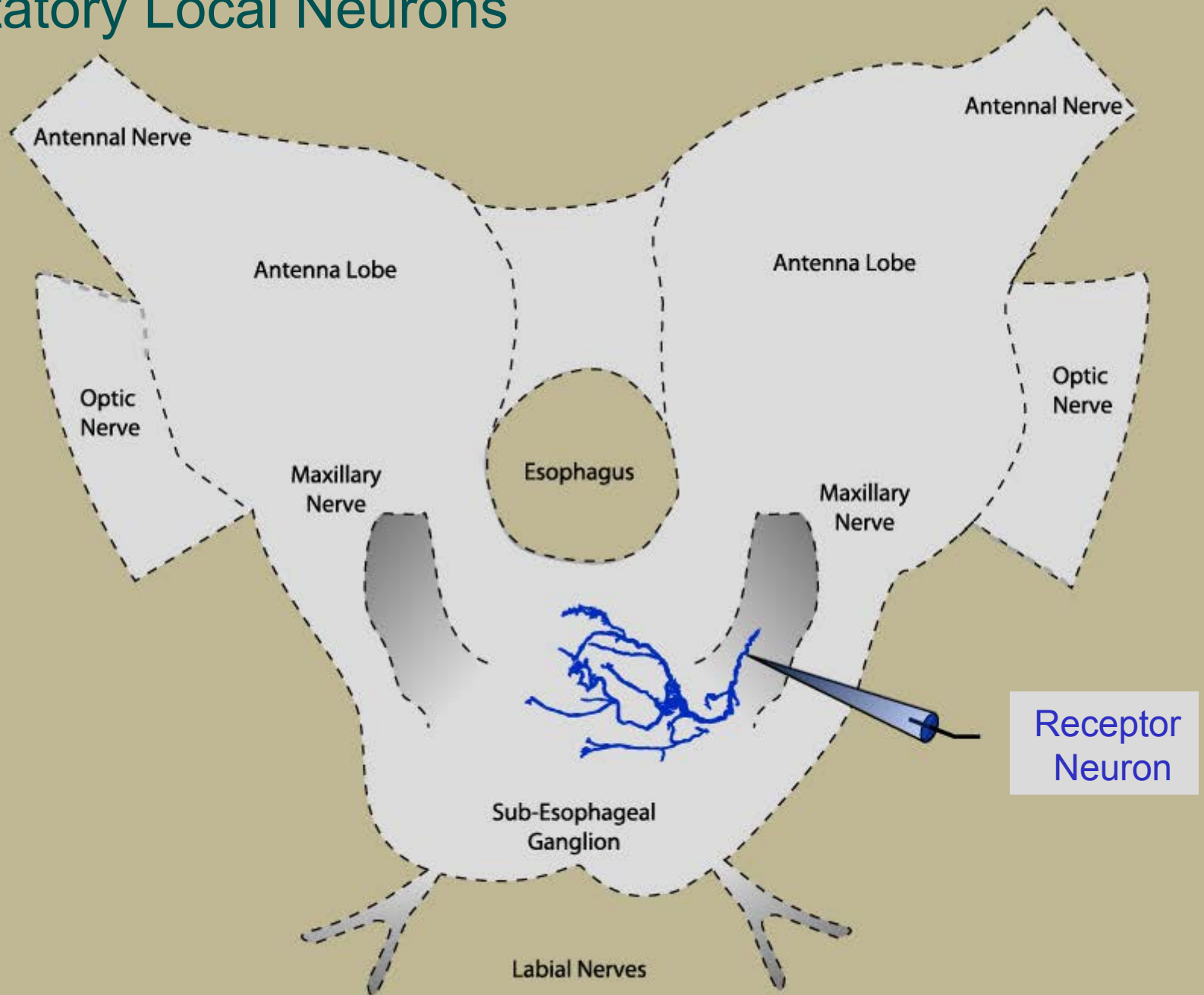
**Must be accurate**

# Gustatory Receptor Neurons





# Gustatory Local Neurons



# Gustatory Local Neurons

