

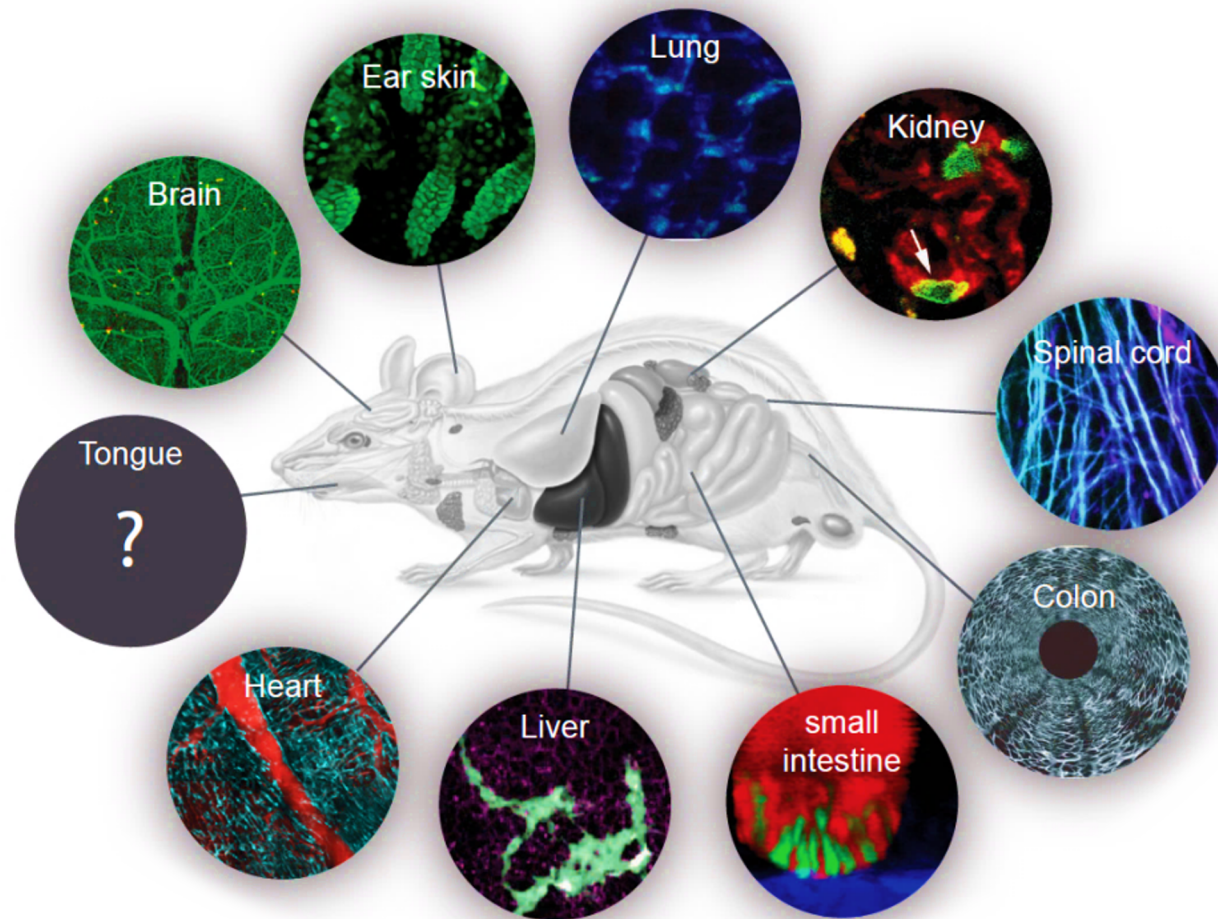
# In vivo imaging of taste cells in action

Myunghwan Choi, Ph.D.

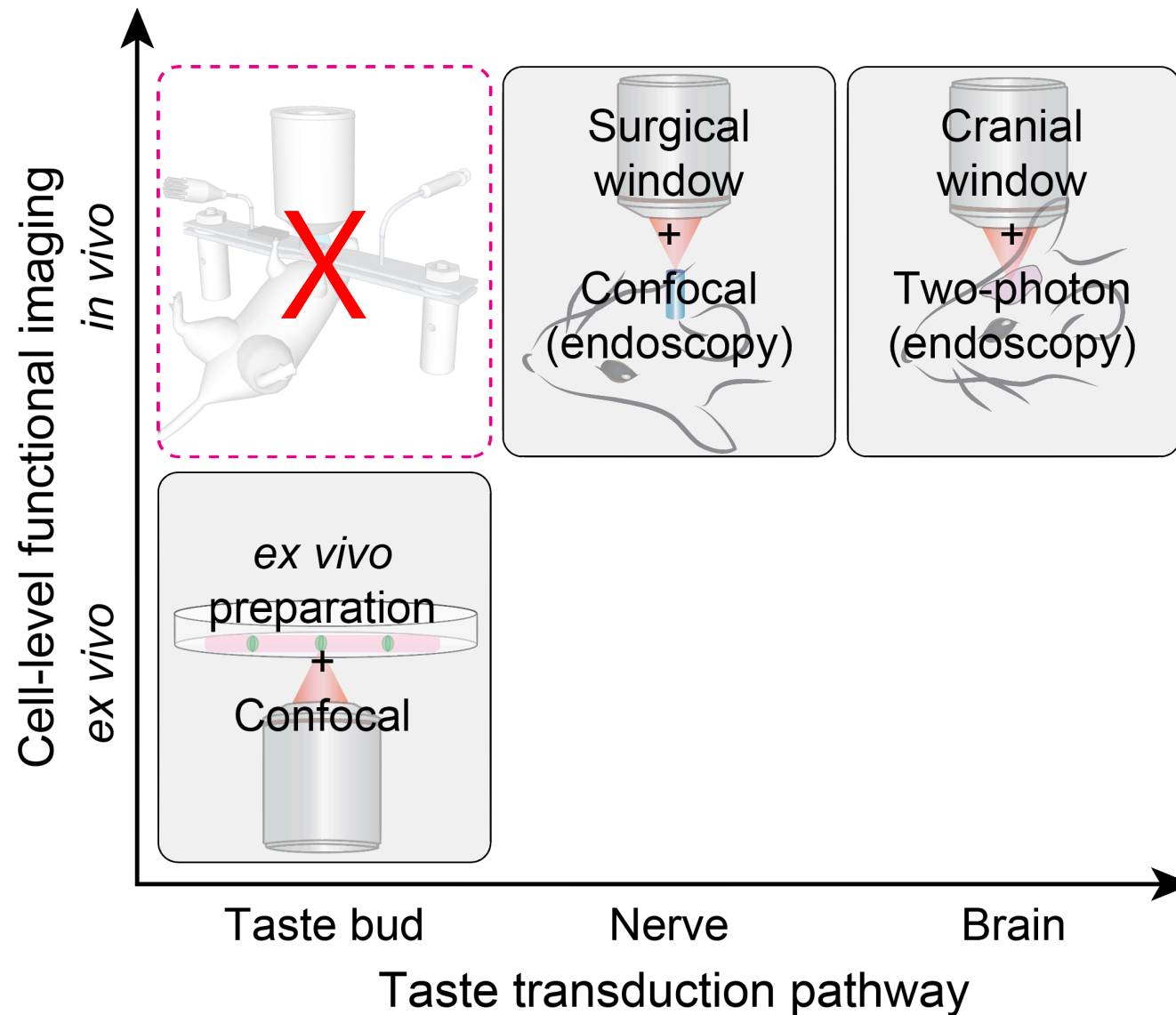
Neurophotronics Lab @ Seoul National University



# *In vivo* microscopy

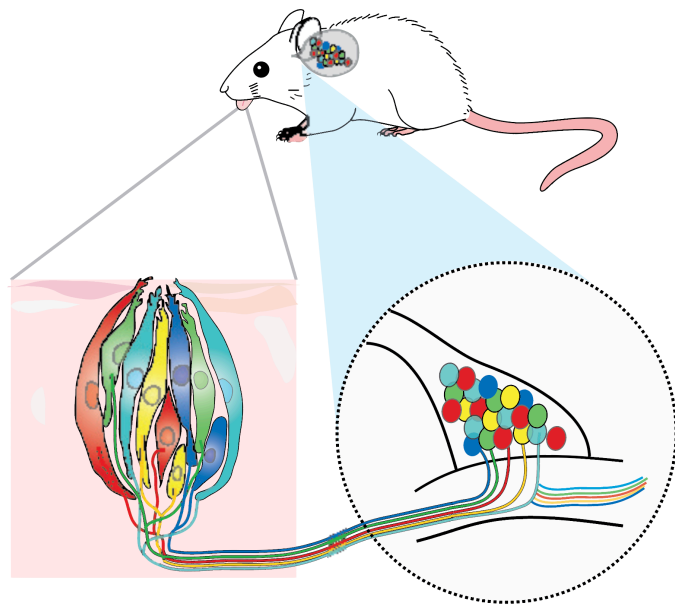


# Imaging in the **taste field**



# Labelled-line model ?

Labelled-line model is the dominating hypothesis in the taste field.  
(found using isolated taste buds / cells)



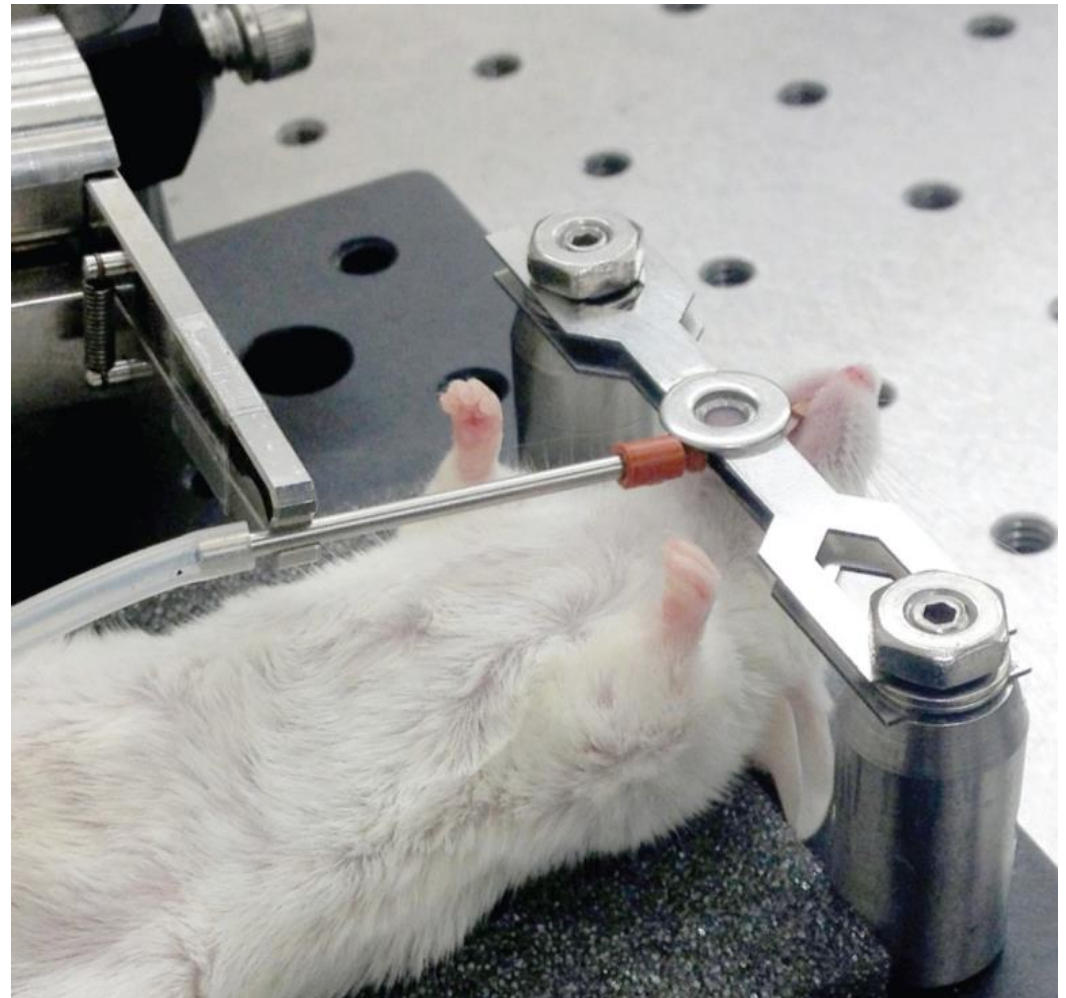
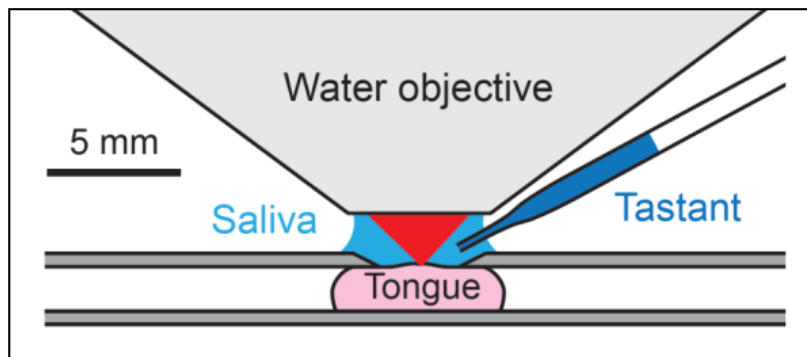
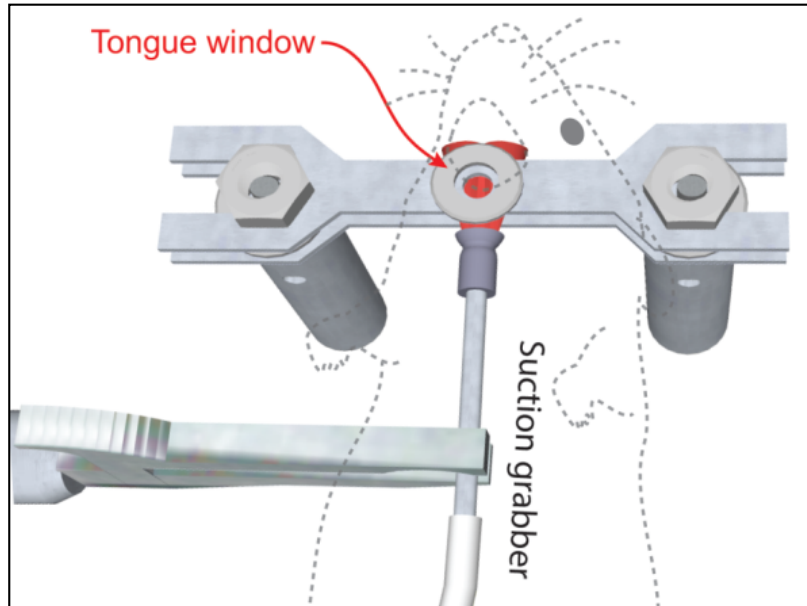
■ Bitter ■ Sweet ■ Salty ■ Sour ■ Umami

*Lee et al., Nature 2017*

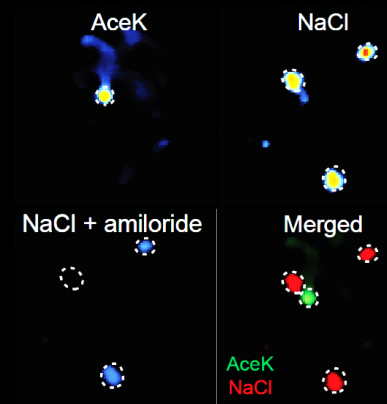
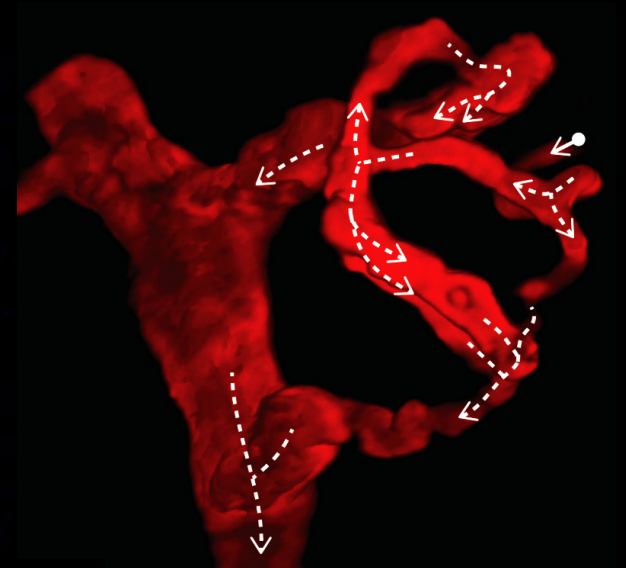
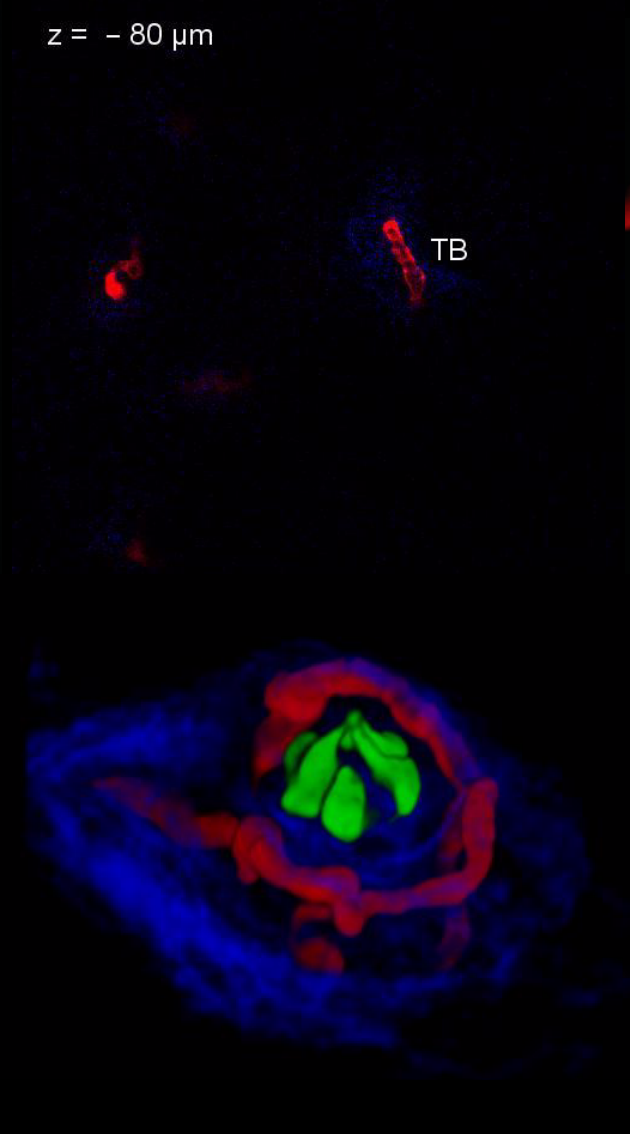
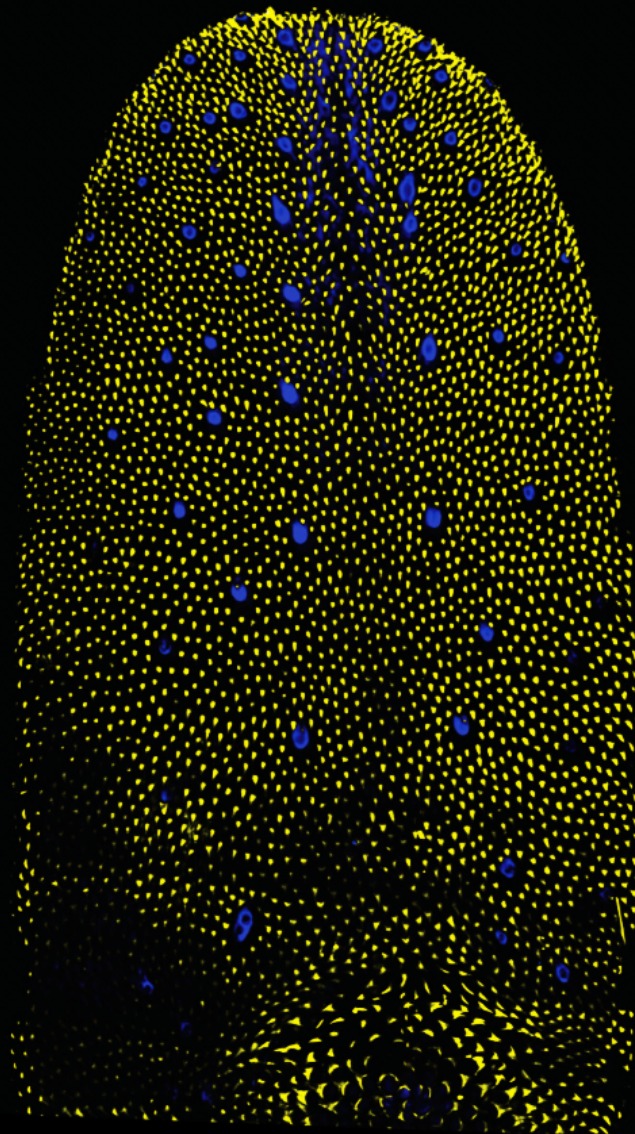


*Vosshall lab*

# 1<sup>st</sup> tongue imaging chamber

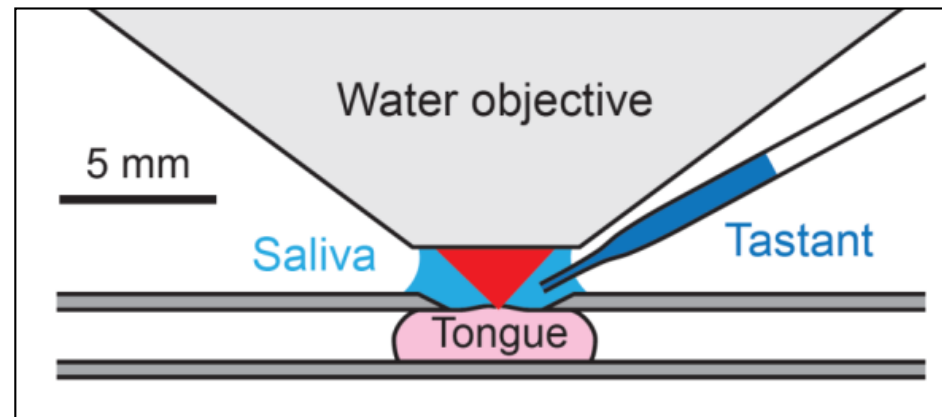


# Live imaging on taste bud



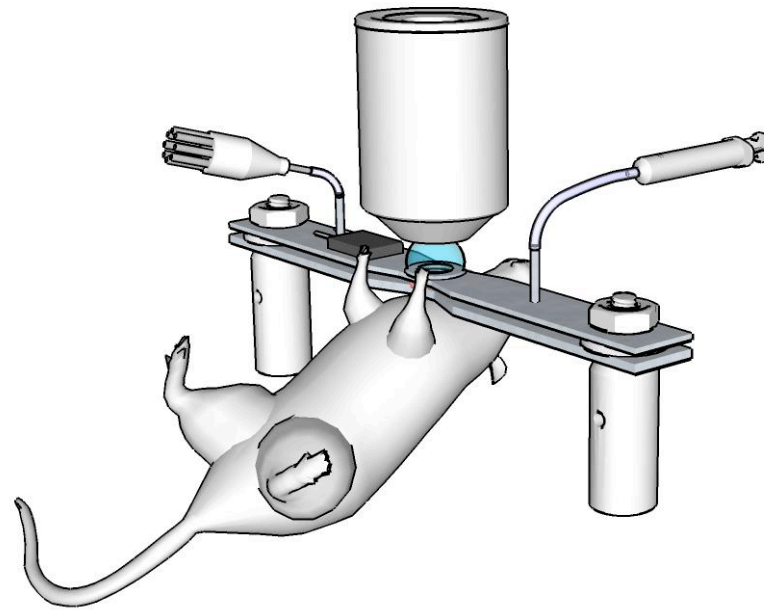
## Limitation of the previous approach

Can we study cellular-level taste coding logic?

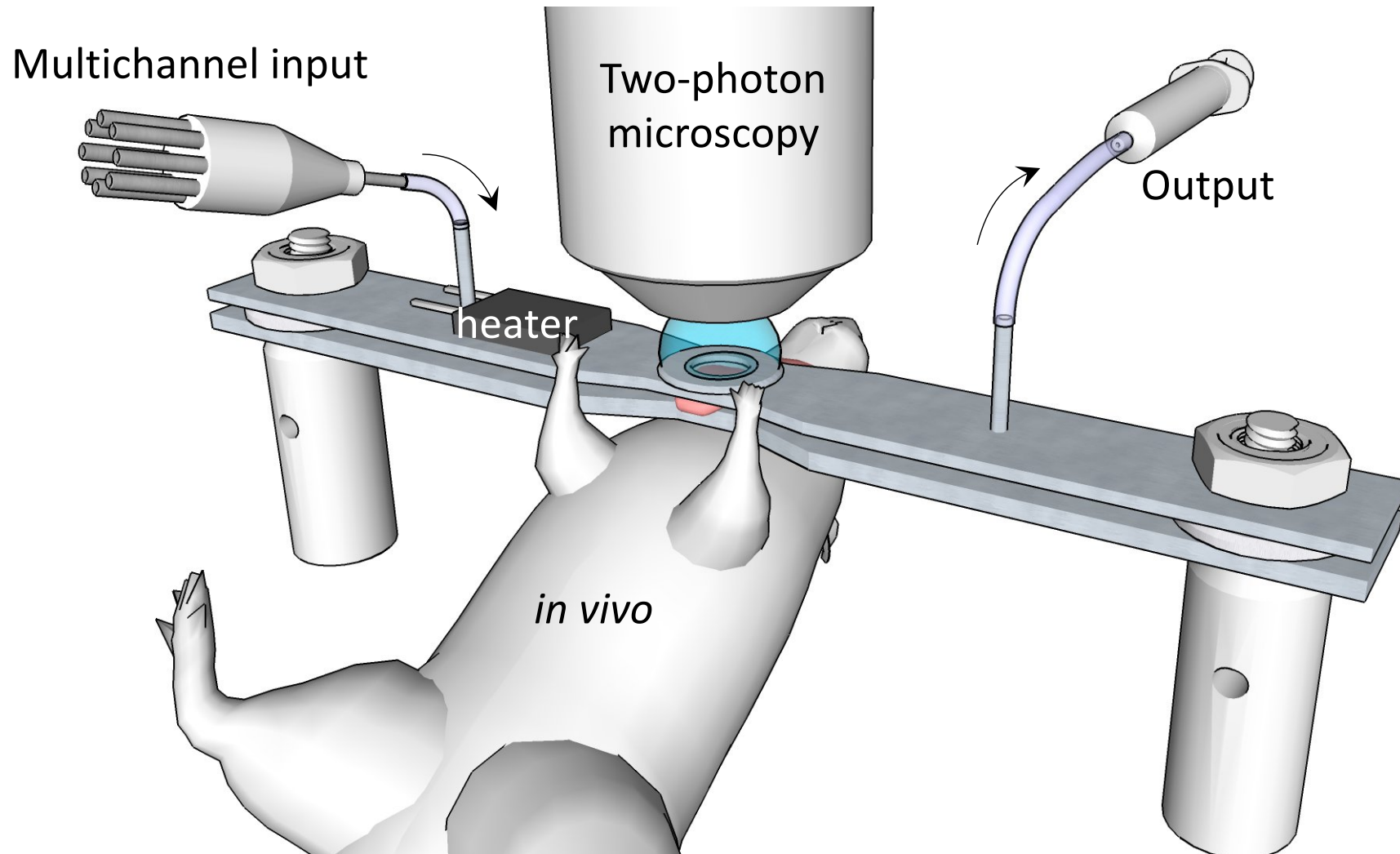


1. Low throughput
2. Motion artifact
3. Imaging artifact

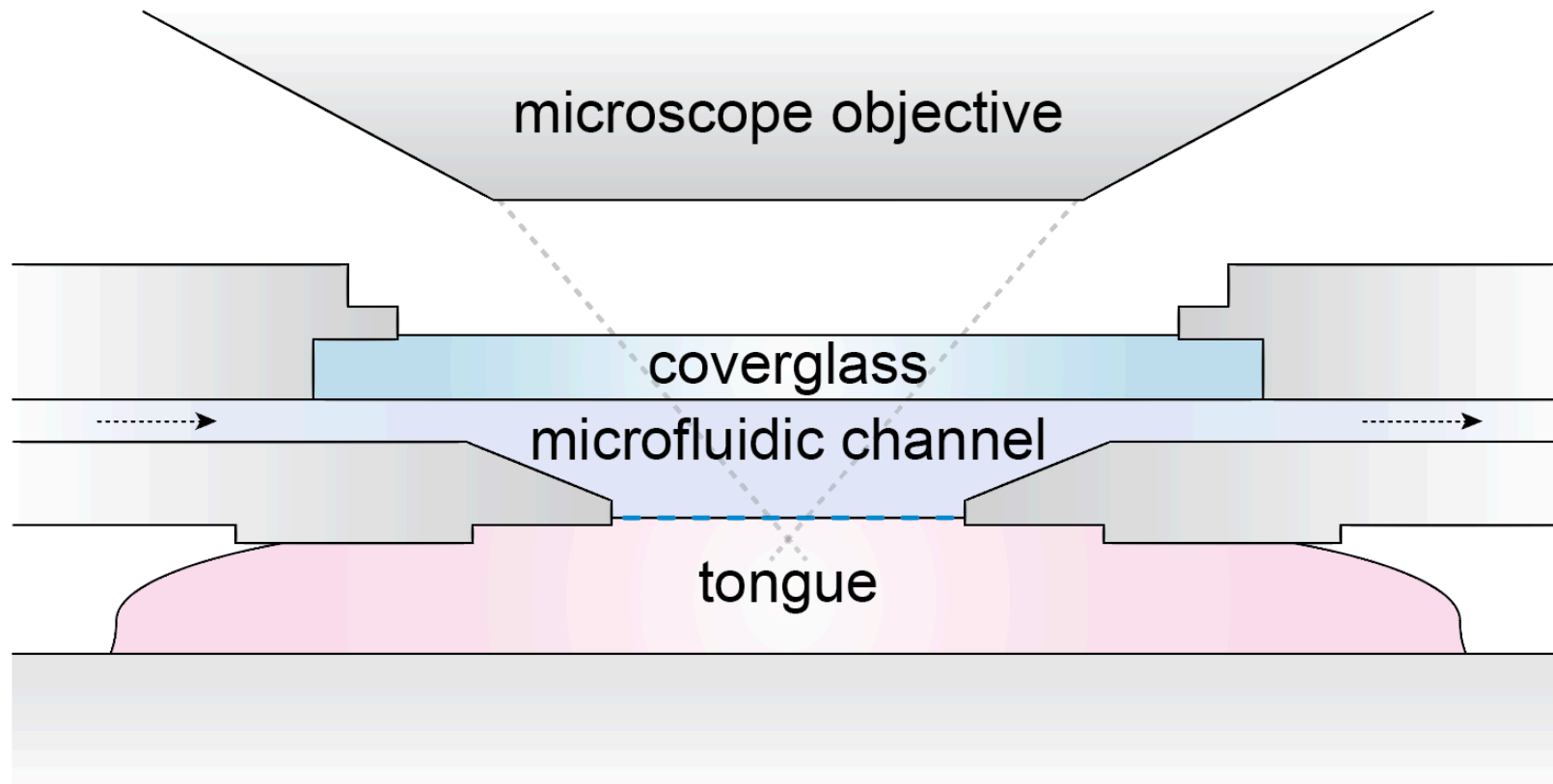
# Microfluidics-on-a-tongue device



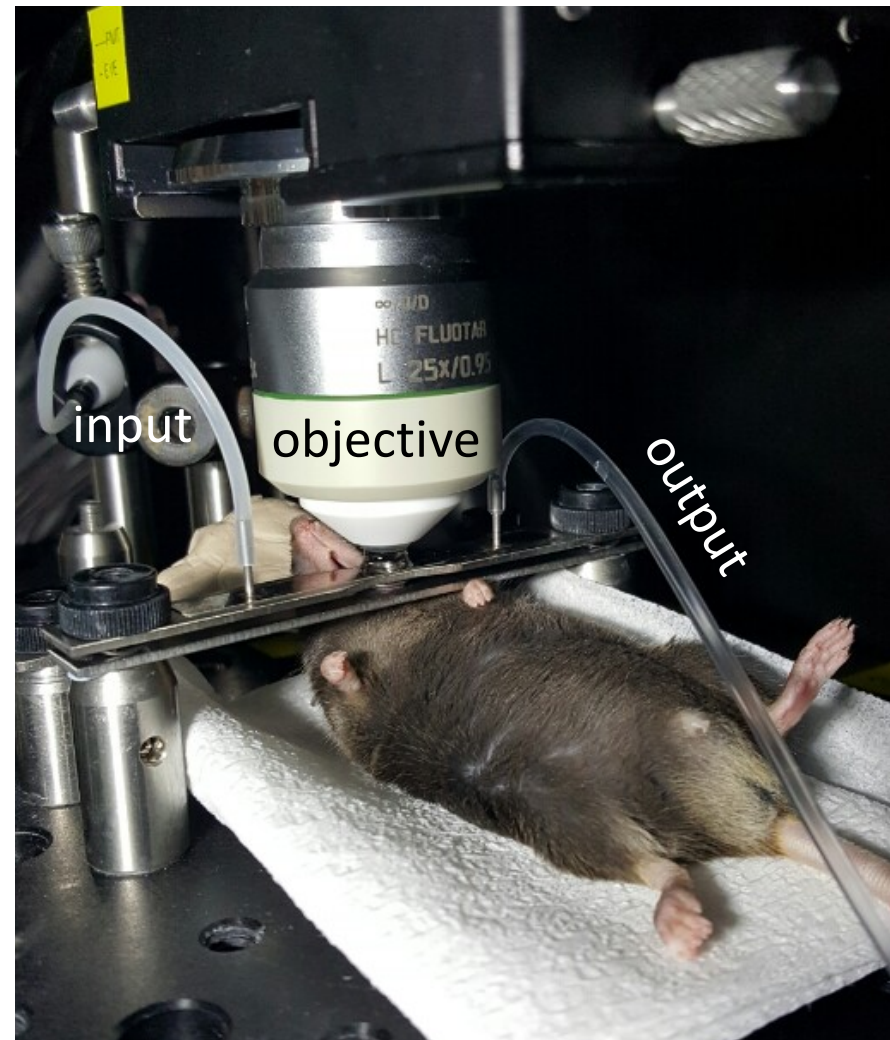
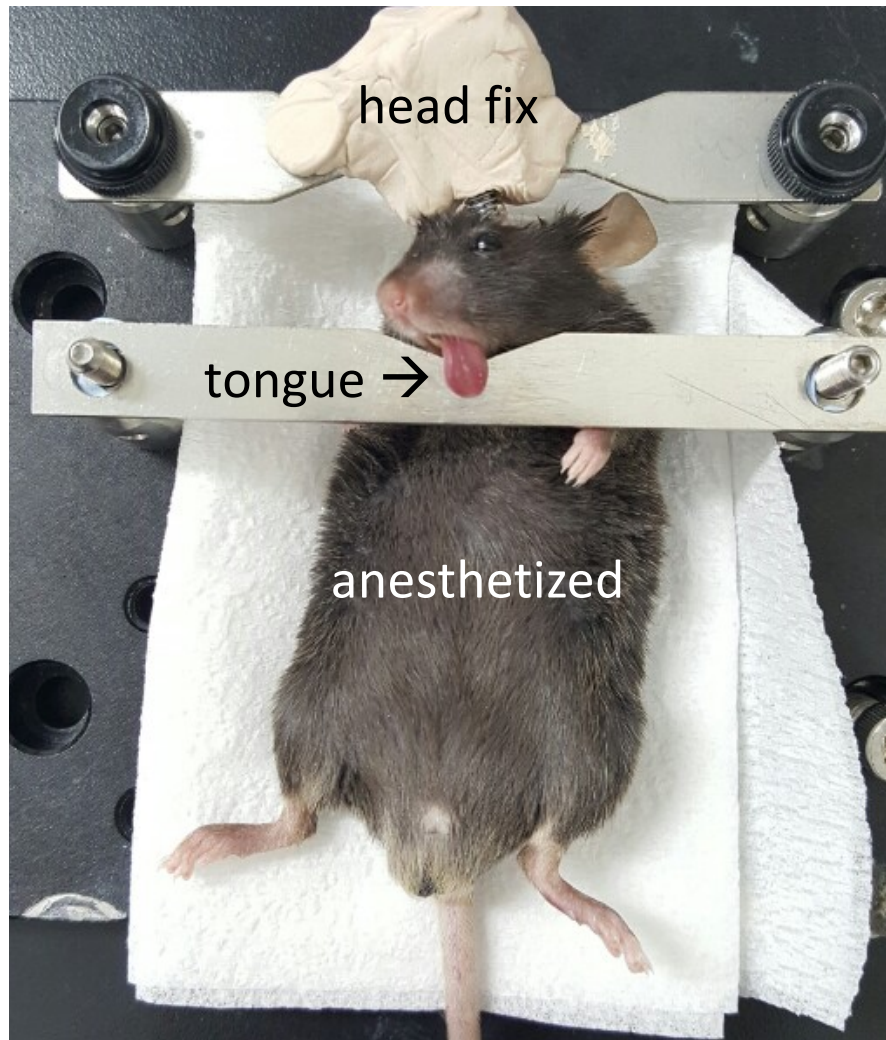
# Microfluidics-on-a-tongue device



# Microfluidics-on-a-tongue device

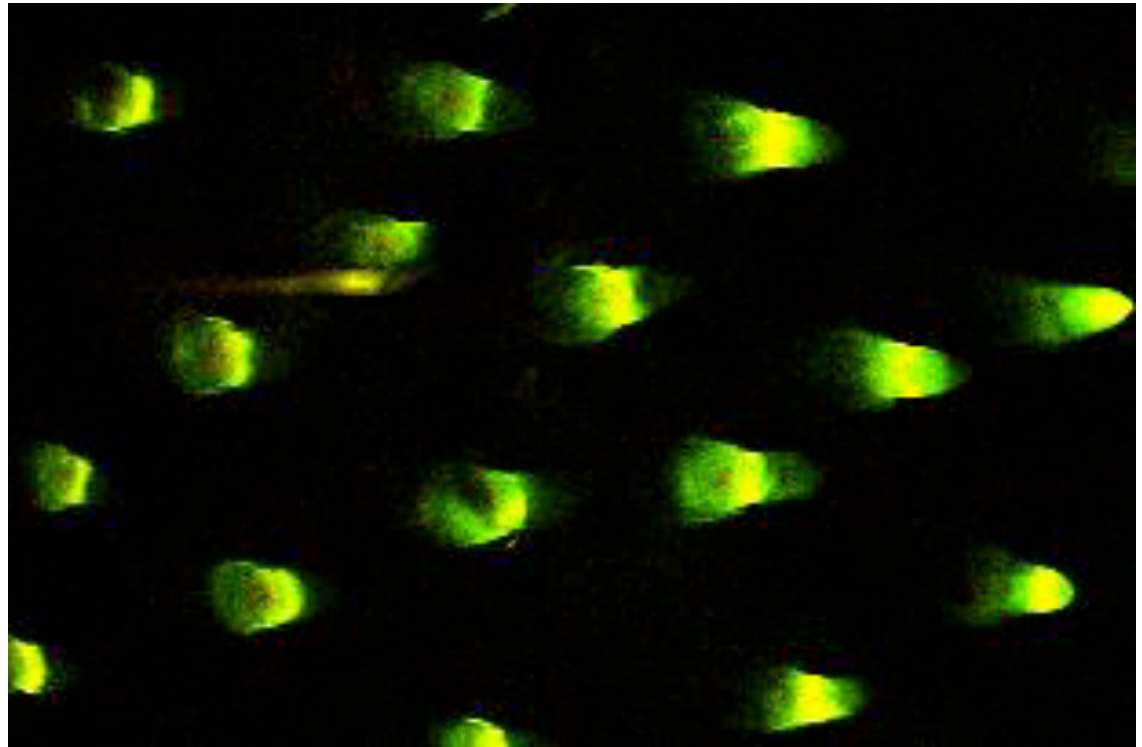
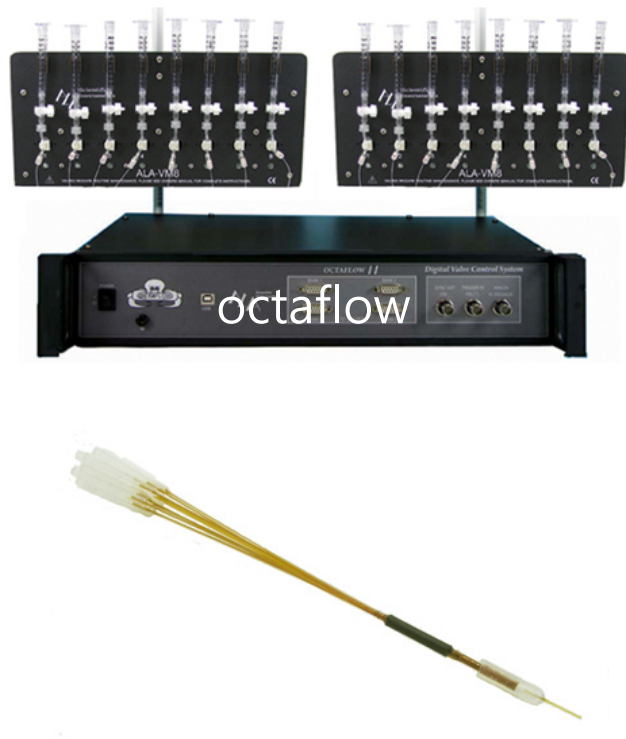


## Microfluidics-on-a-tongue device

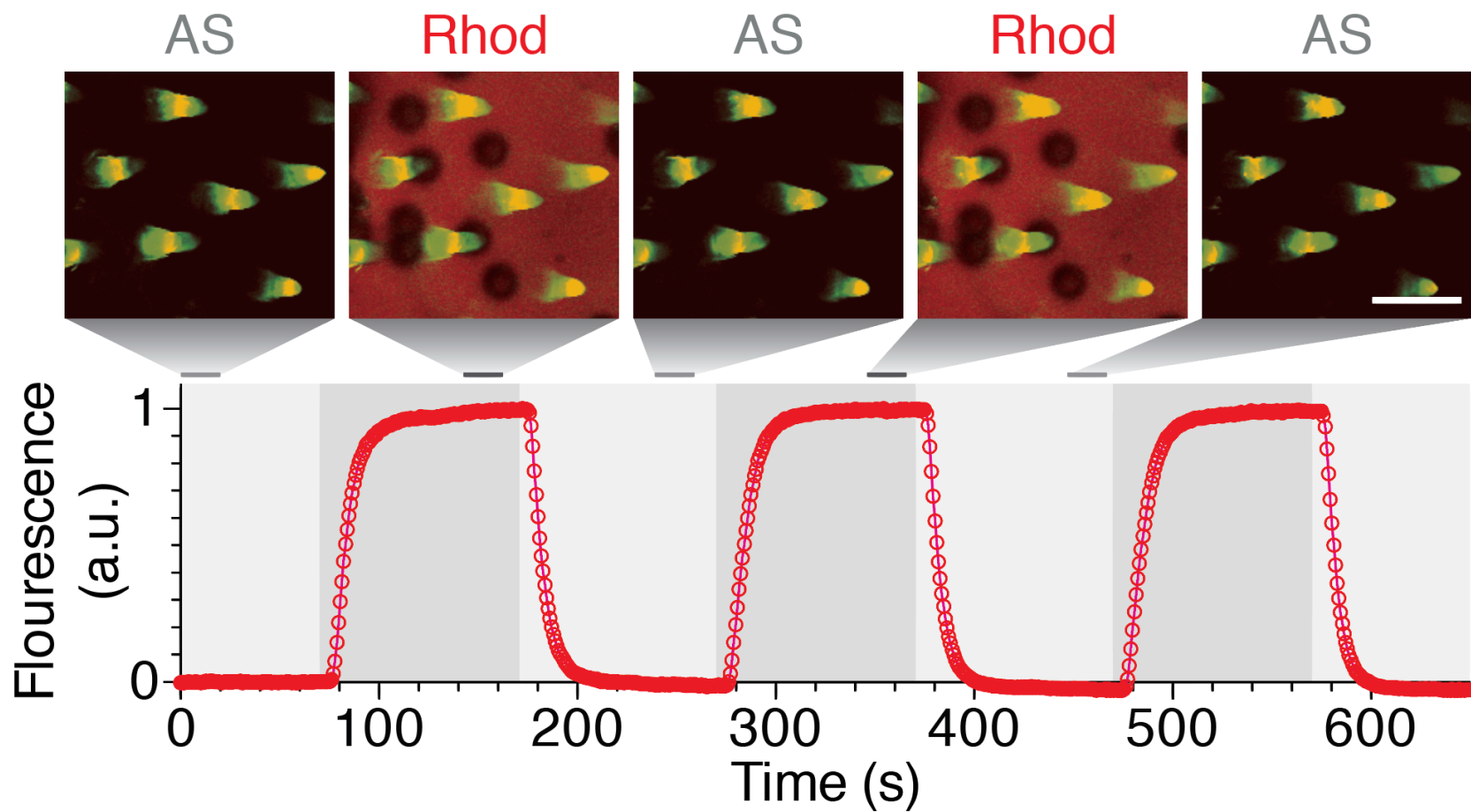


# High-throughput fluidic control

rhodamine



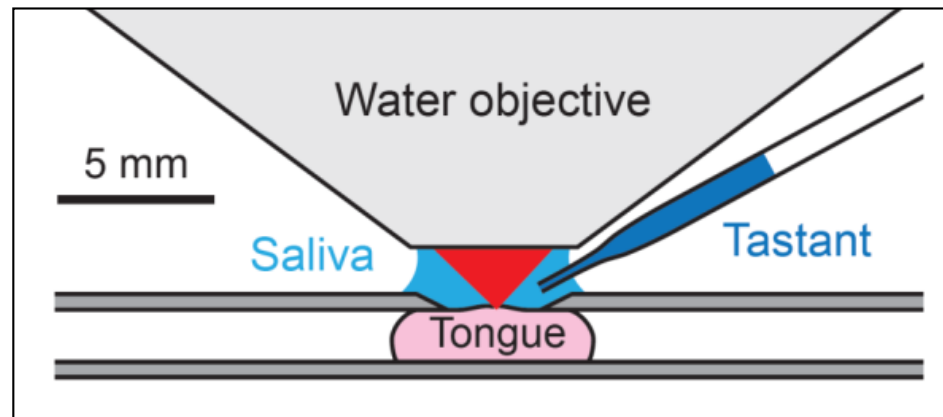
## High-throughput fluidic control



Fluidics was not enough!

# Limitation

Can we study cellular-level taste coding logic?



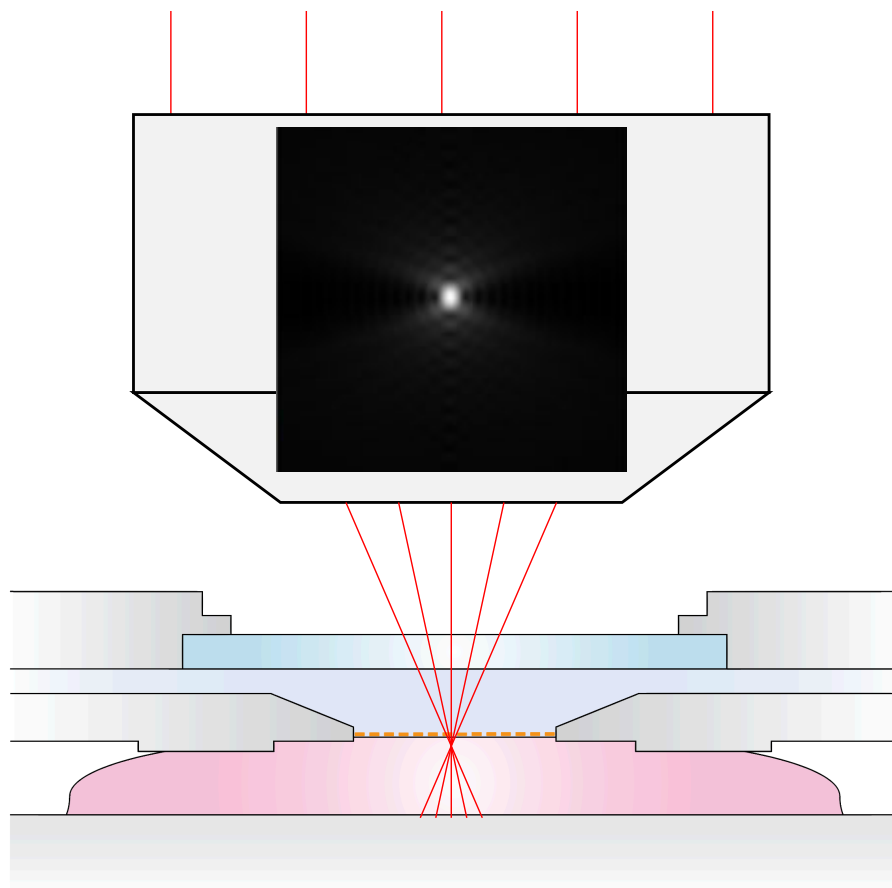
~~1. Low throughput~~

~~2. Motion artifact~~

**3. Imaging artifact**

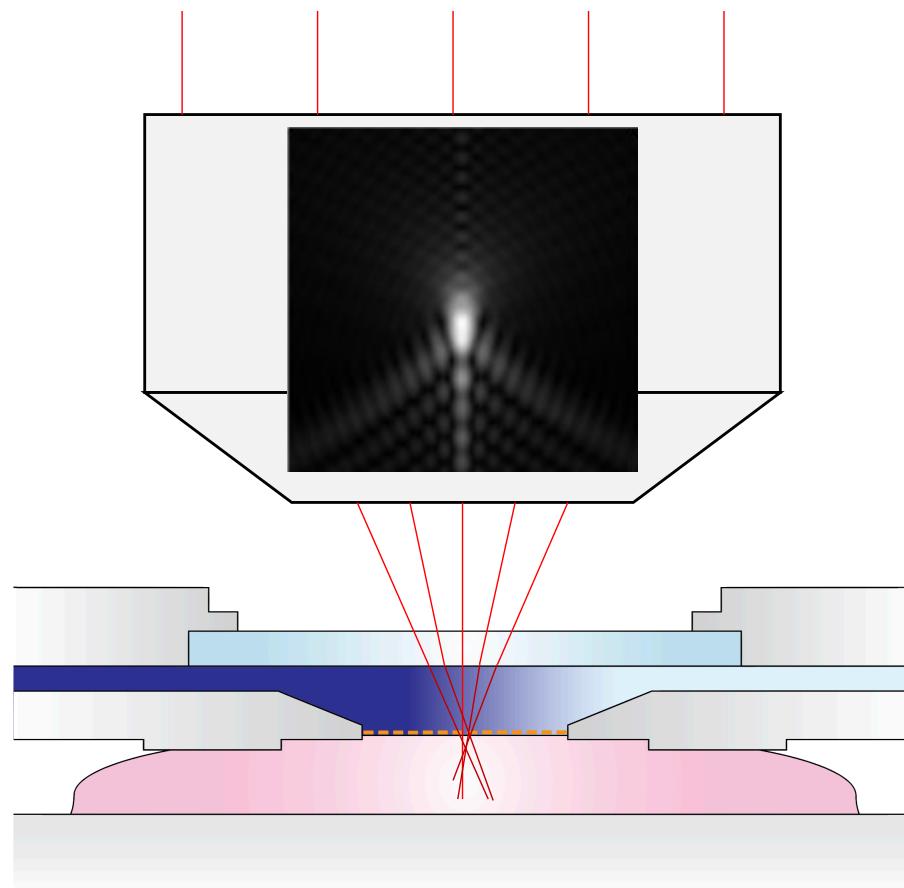
# Imaging artifact

Saliva



Stable focus

Tastant (higher index)

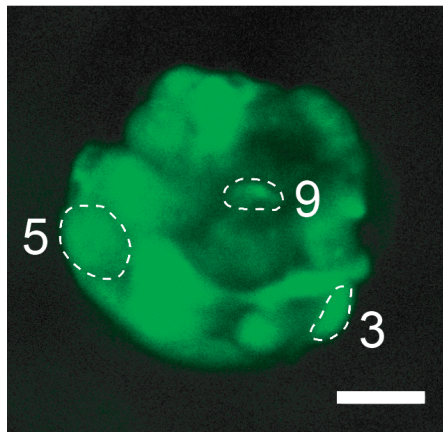


Unstable focus

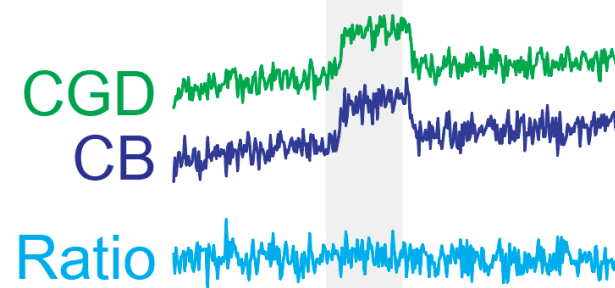
# Ratiometric analysis

CGD: calcium-sensitive  
CB: calcium-insensitive

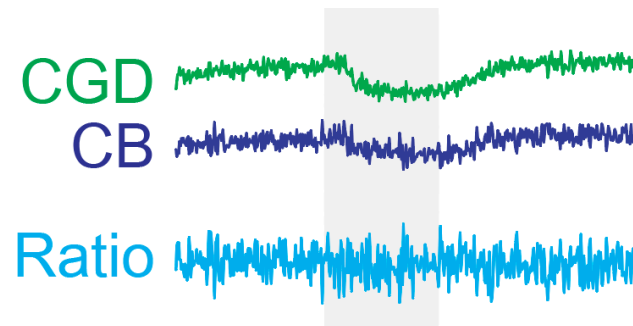
$$\text{Ratio} = \frac{\text{CGD}}{\text{CB}}$$



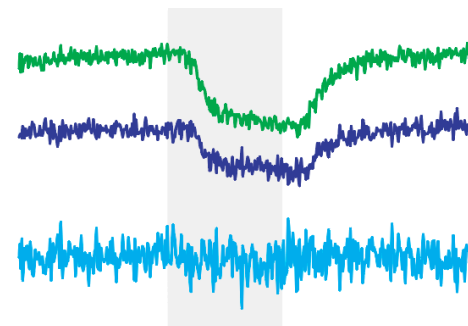
Power 7%



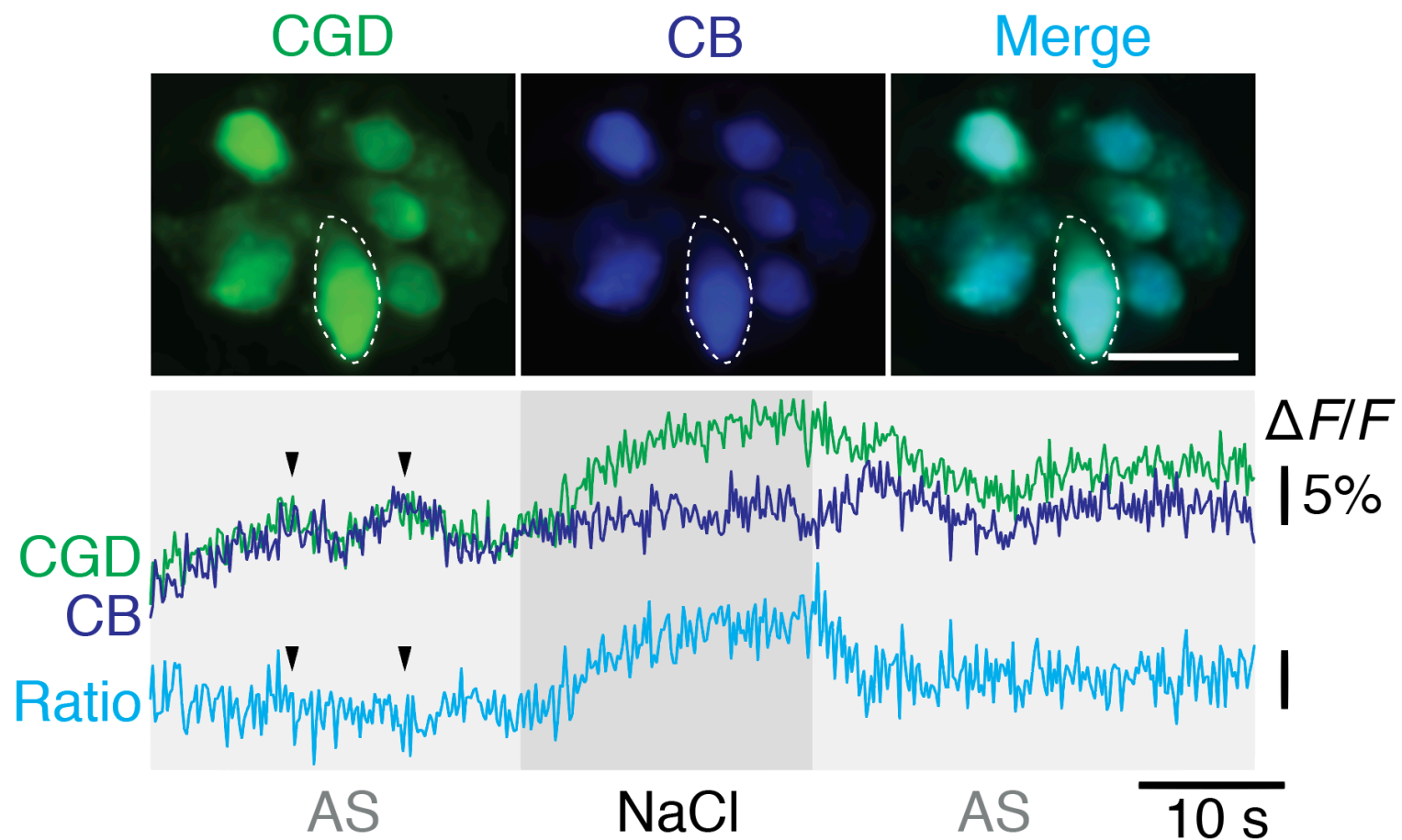
Sucrose 5%



Sucrose 10%

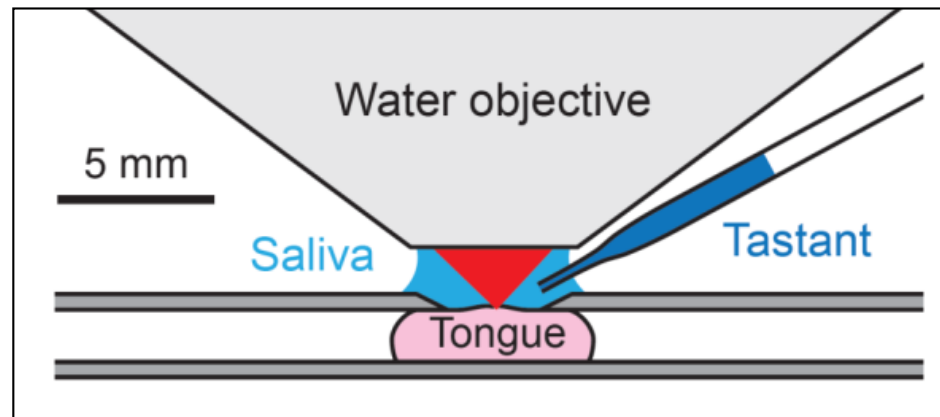


# Ratiometric analysis



# Limitation

Can we study cellular-level taste coding logic? **Yes**



~~1. Low throughput~~

~~2. Motion artifact~~

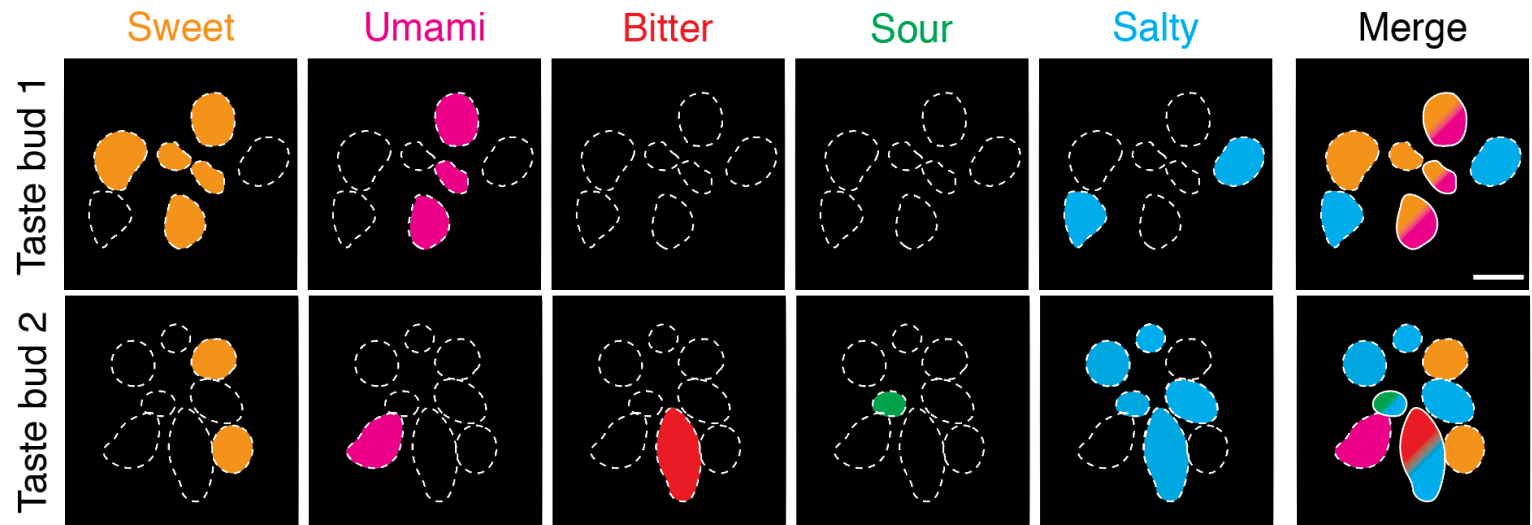
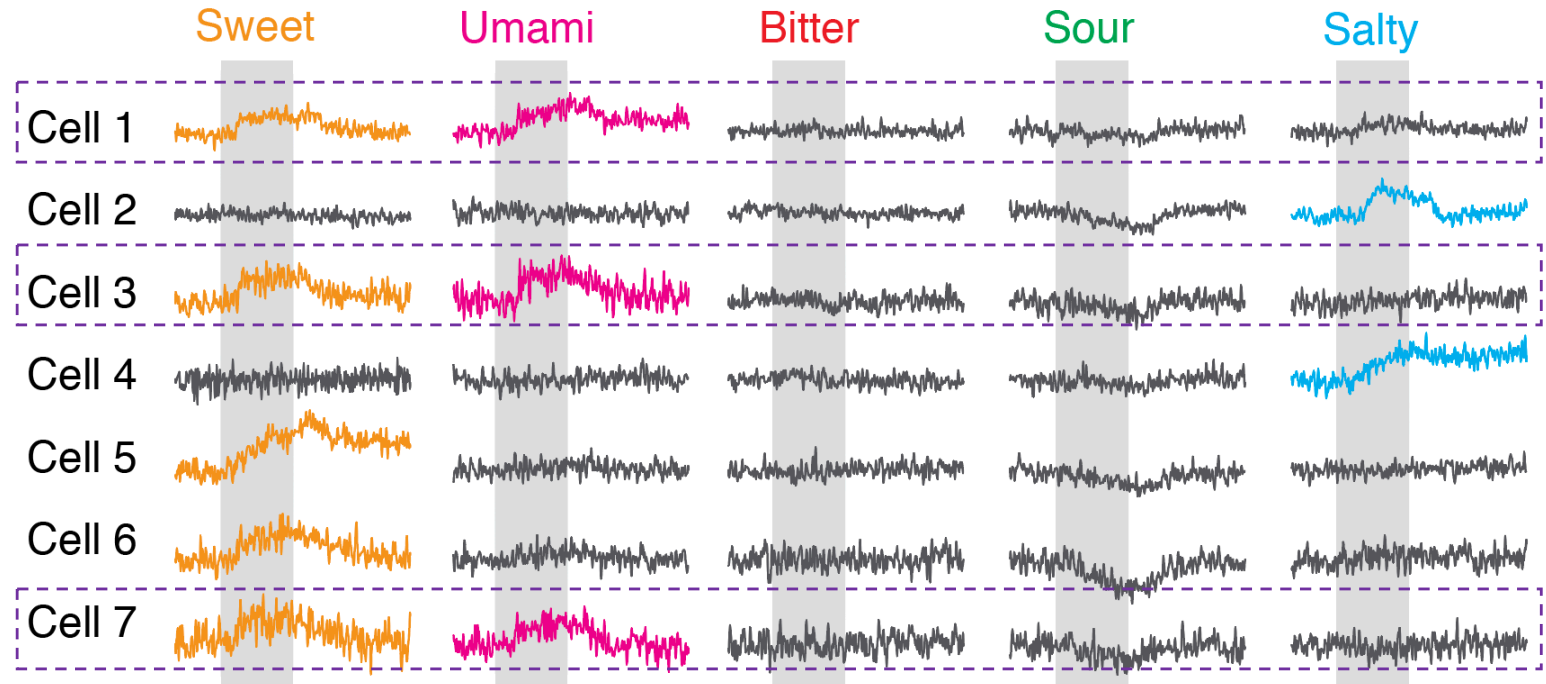
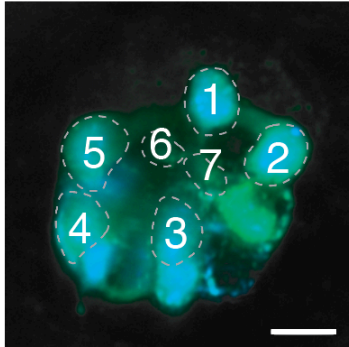
~~3. Imaging artifact~~

Microfluidics / Ratiometric

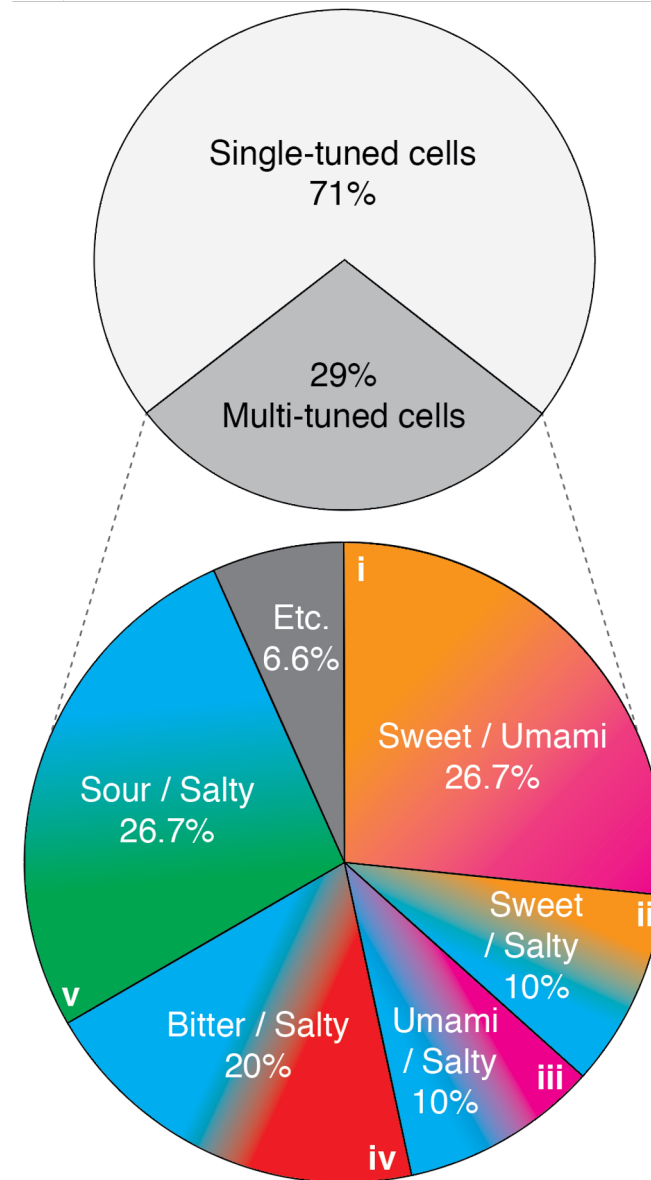
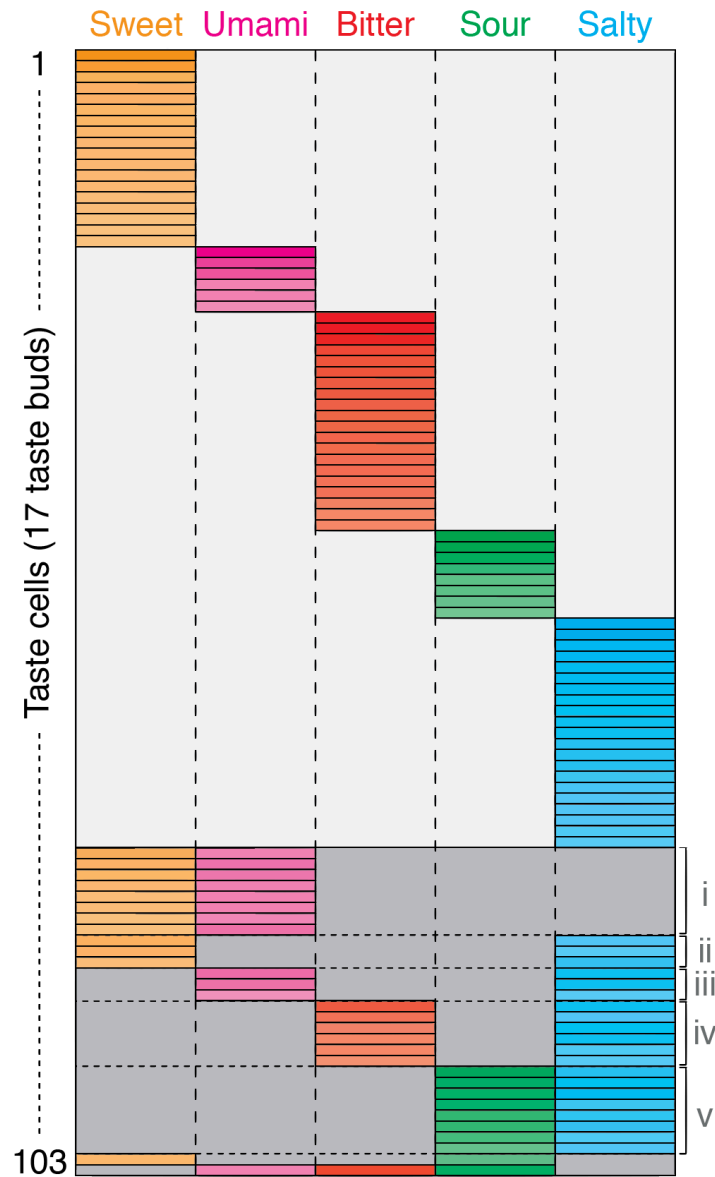
Screening for multiple tastants

# Real-time calcium imaging

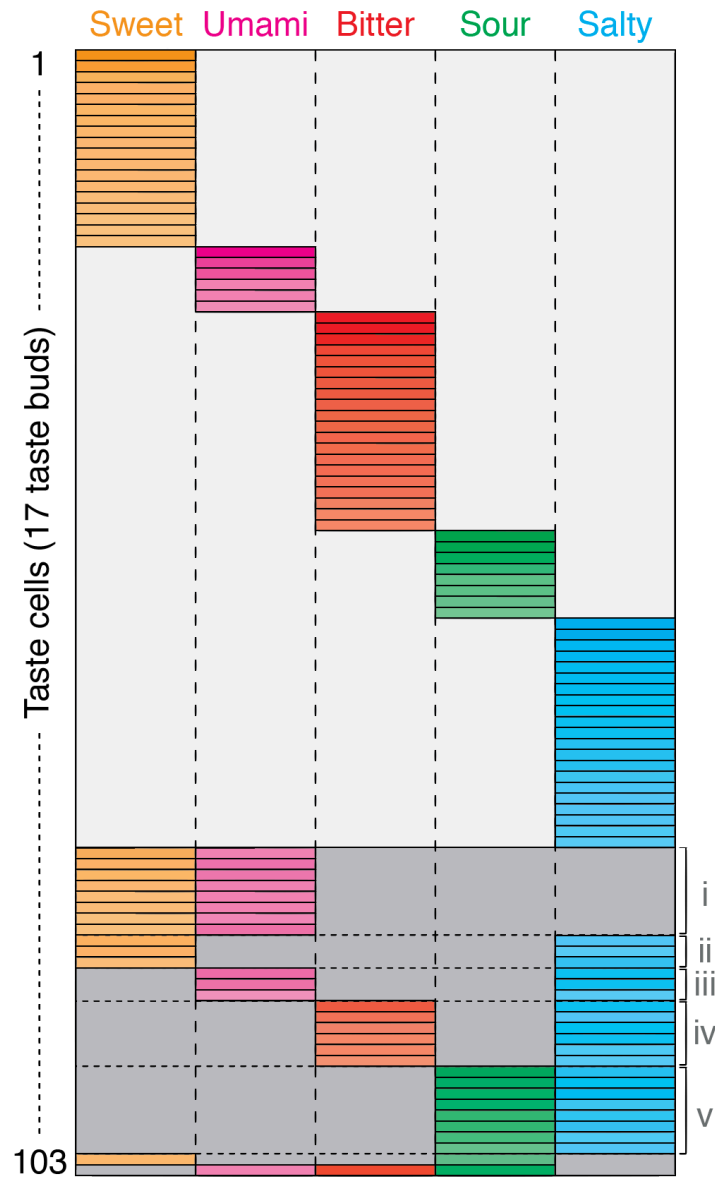
Taste bud 1



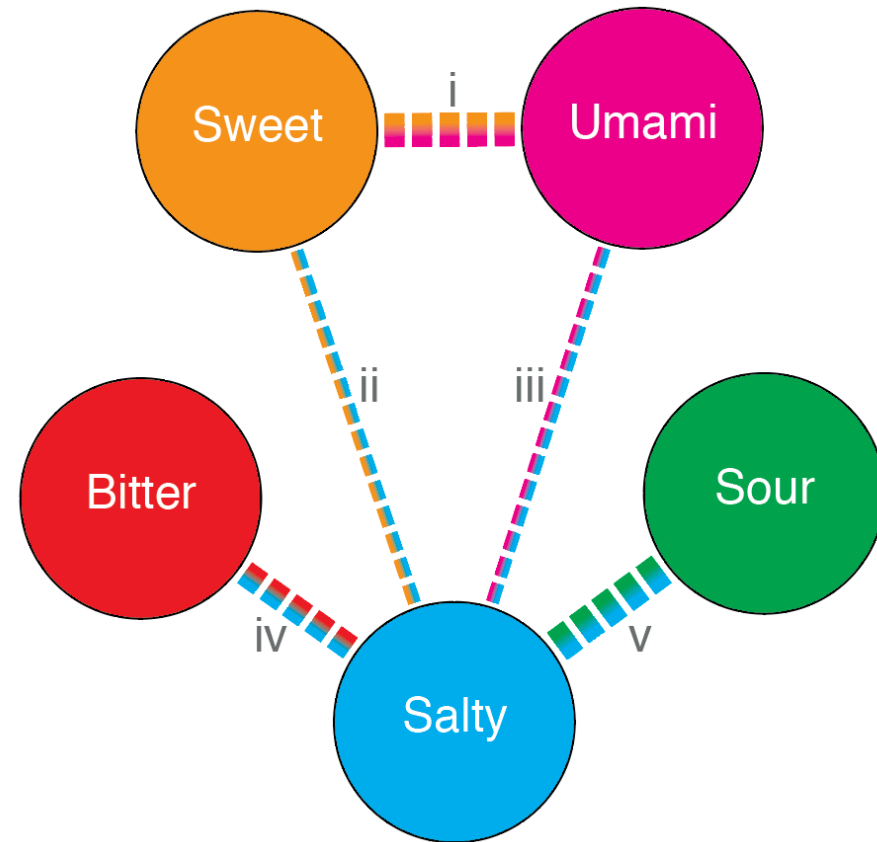
# Comprehensive *in vivo* screening



# Comprehensive *in vivo* screening



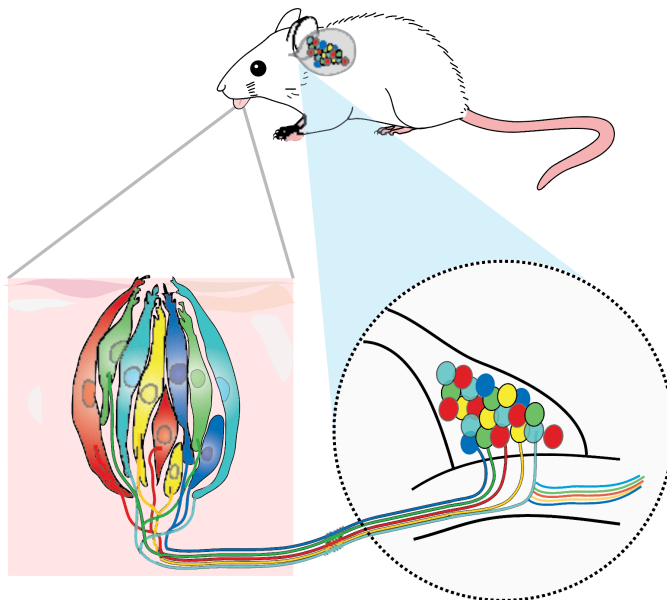
## Dual-tuned cells



# Tuning of taste cells

## Previous works

sweet cell  
umami cell  
sour cell  
bitter cell } high salt  
sodium cell



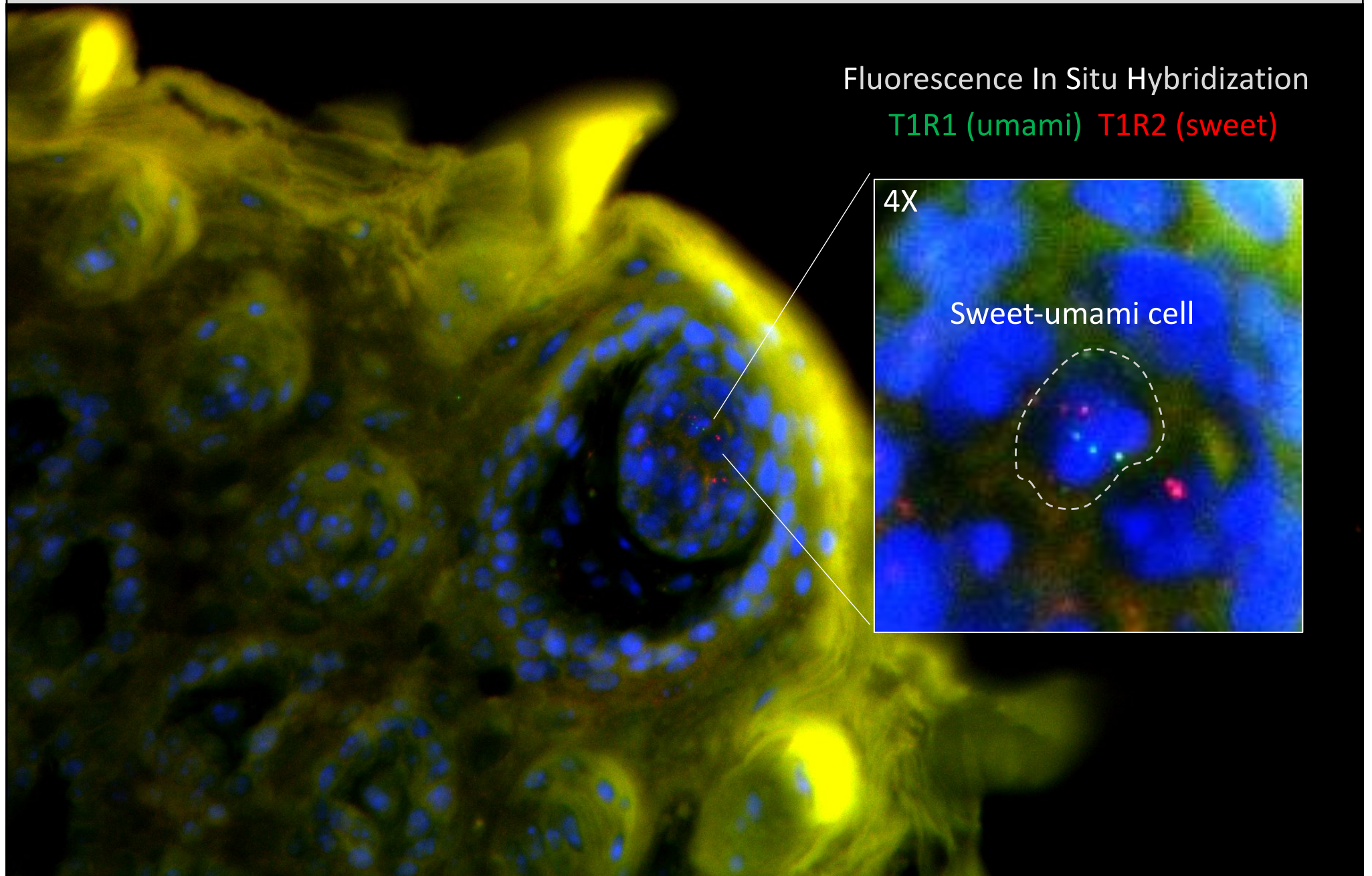
■ Bitter ■ Sweet ■ Salty ■ Sour ■ Umami

*Lee et al., Nature 2017*

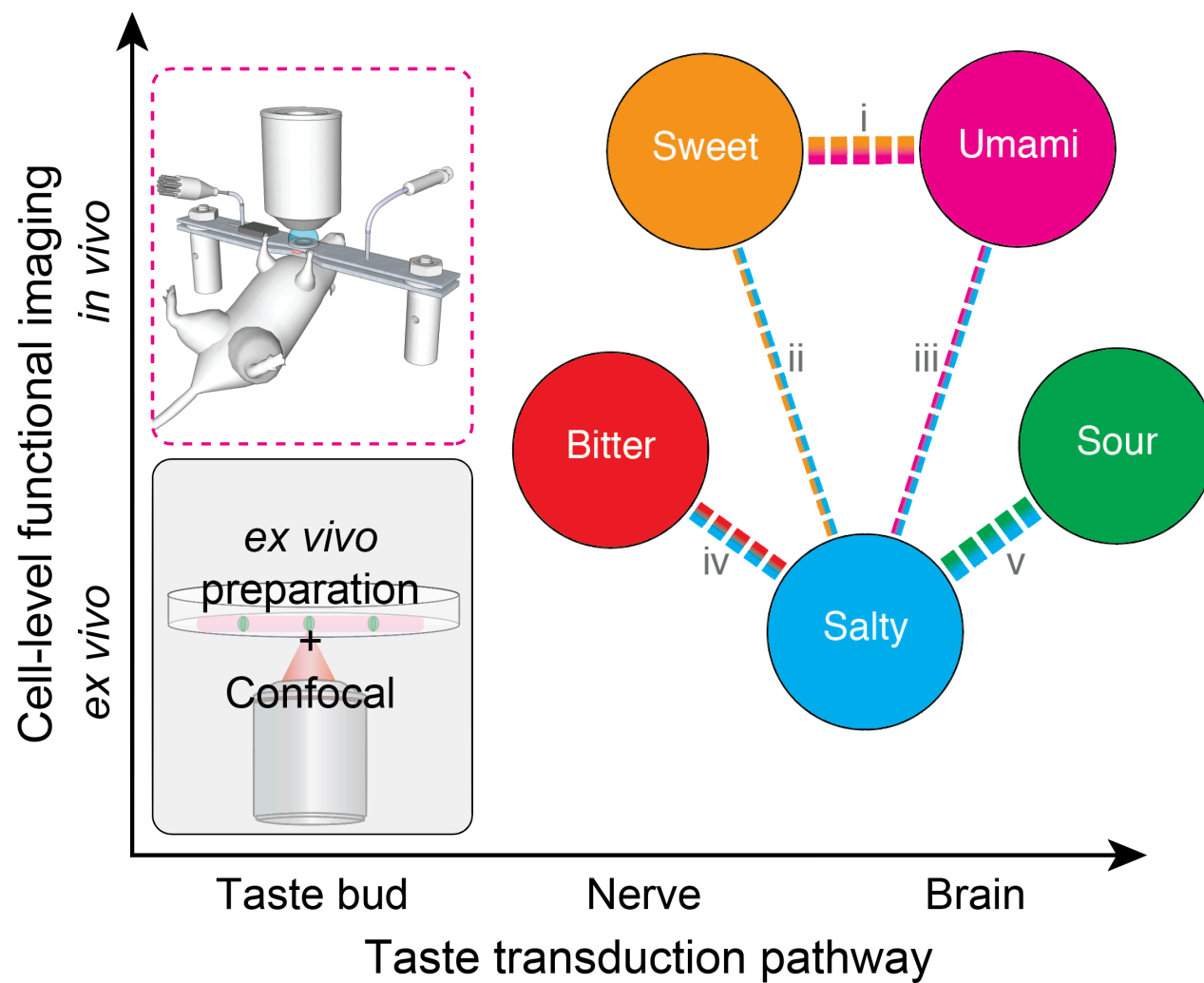
## This work

sweet cell  
umami cell  
sour cell  
bitter cell } high? salt  
sodium cell  
sweet-umami cell  
:

# Molecular identity of dual-tuned cells

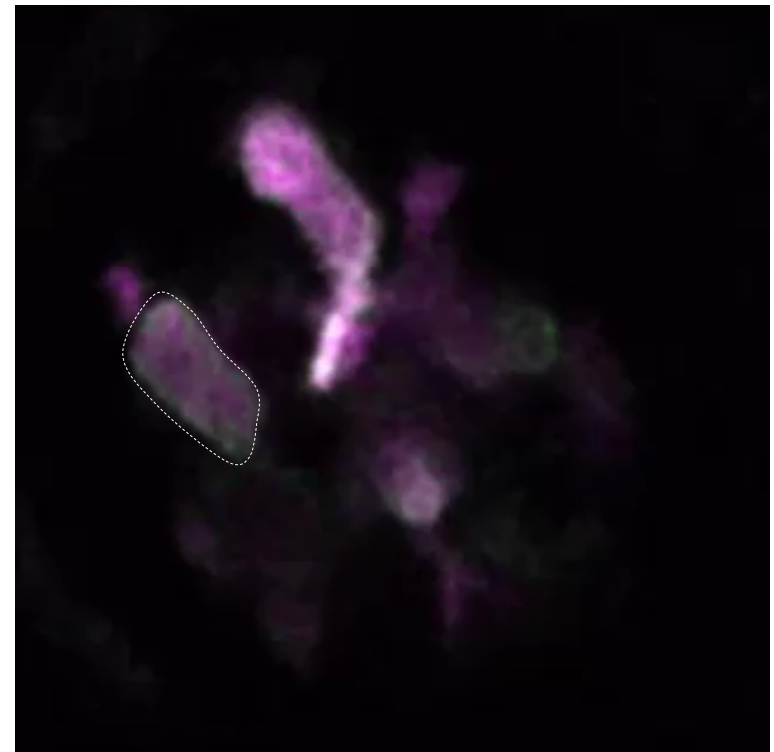
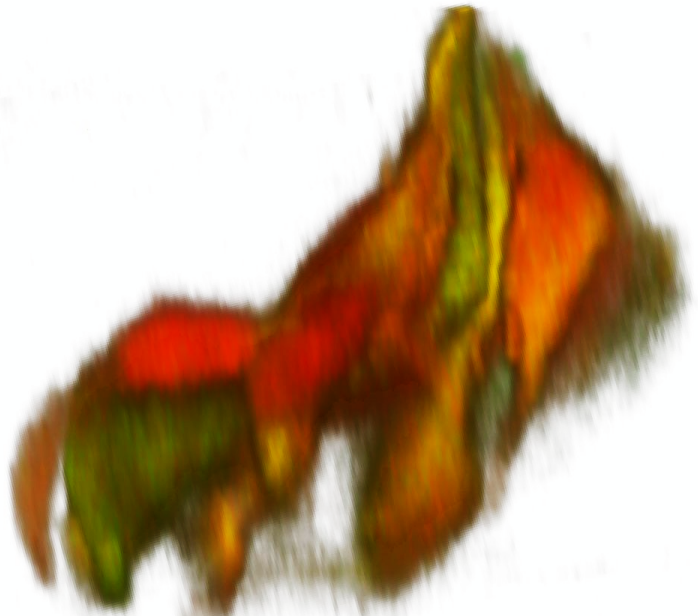


# A new tool for taste research in vivo



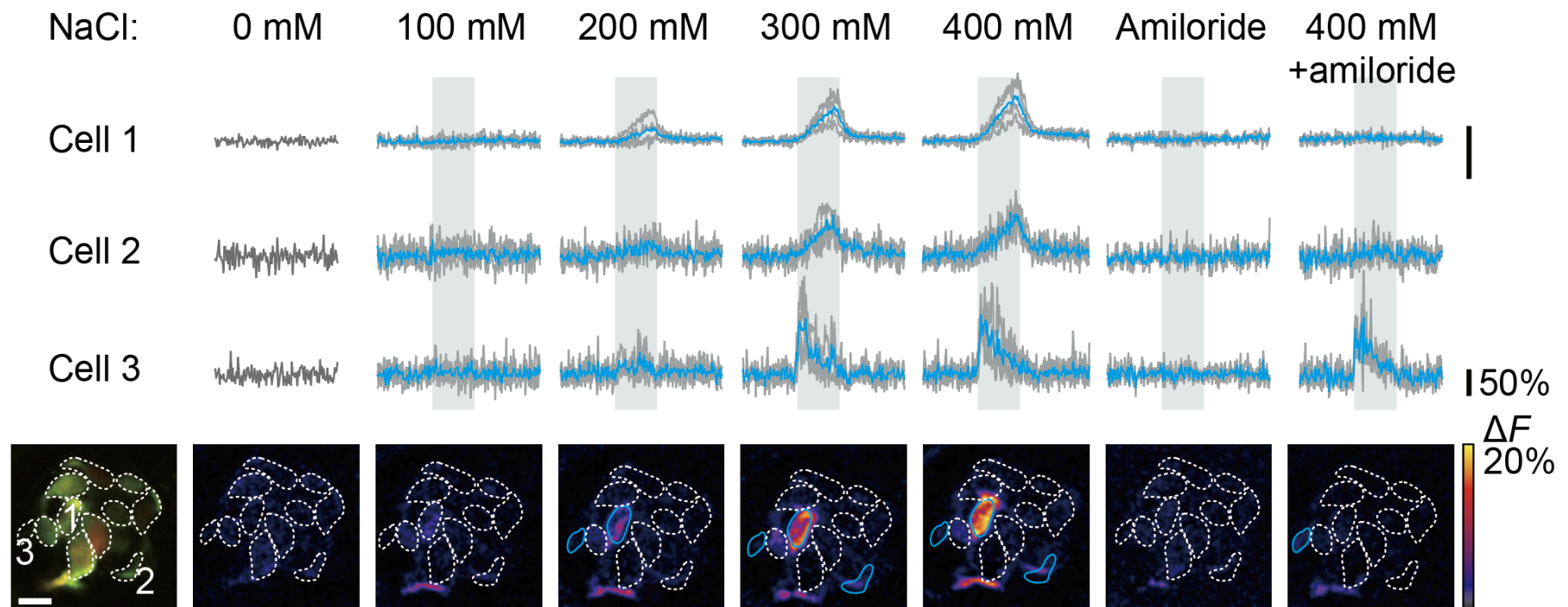
## Cell-type specific labeling

pirt-cre  
gad2-cre x floxed-tdTomato-GCaMP

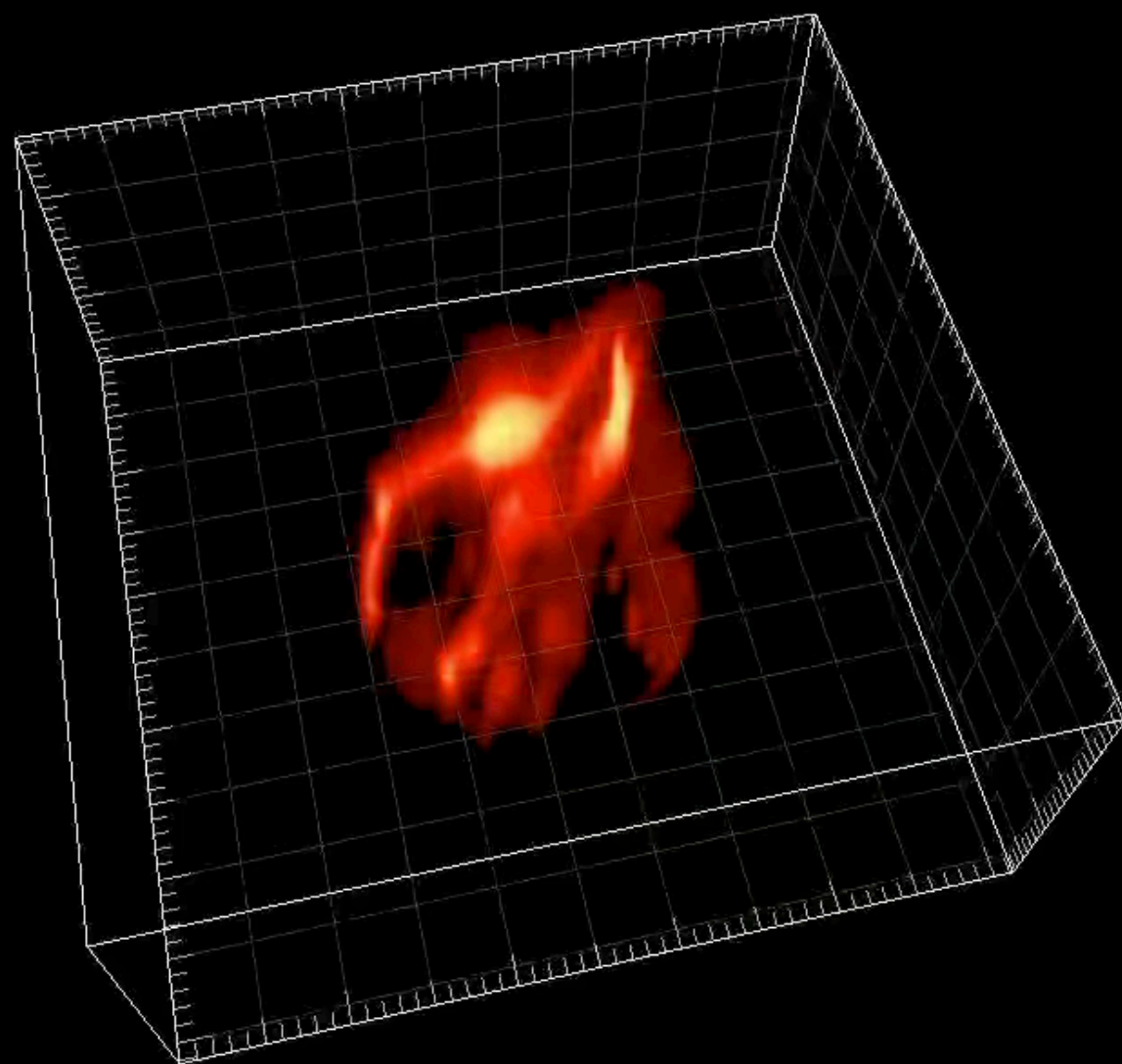


Screening for dose dependency

## Long-term screening

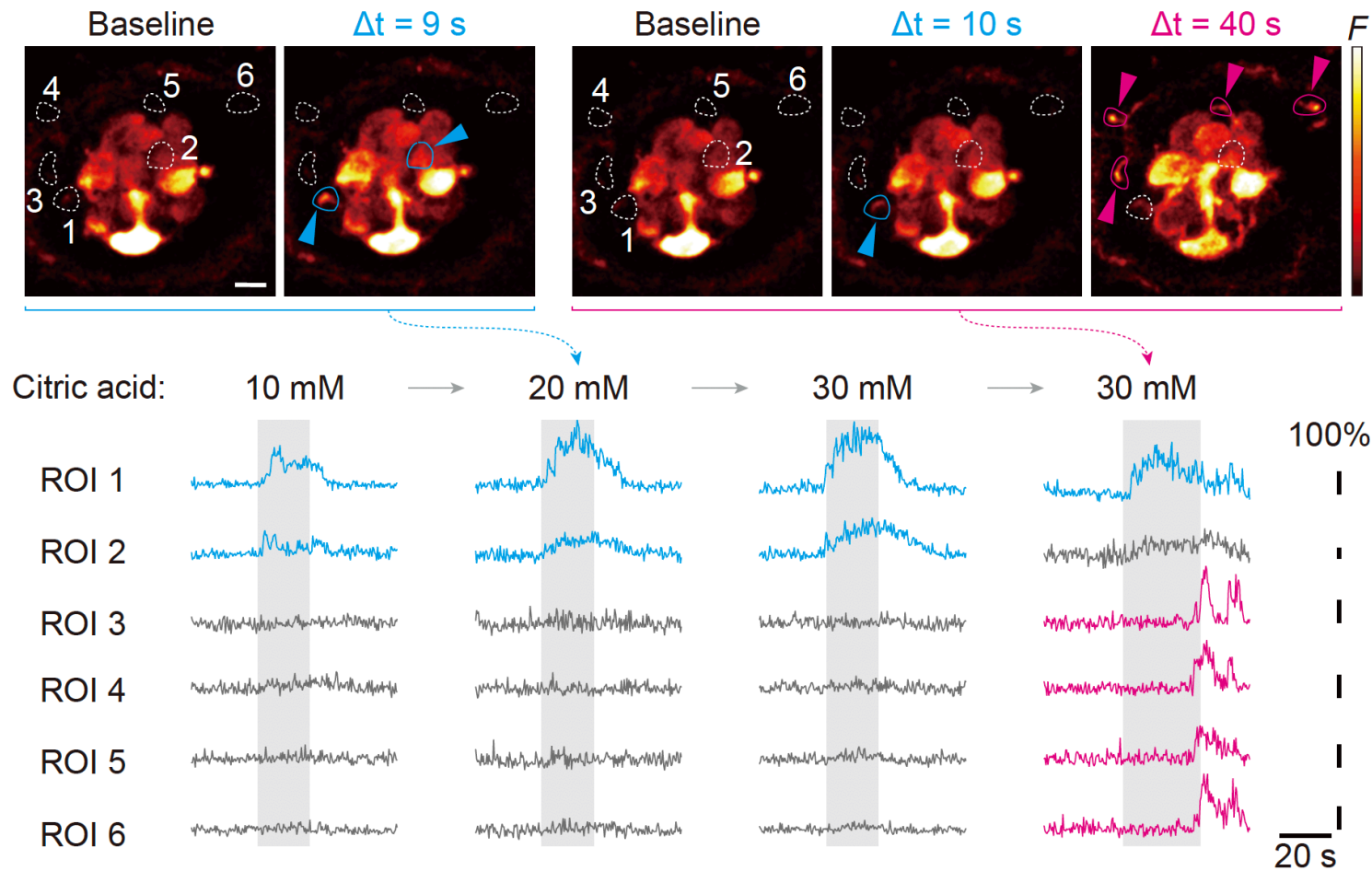


Genetically-encoded indicators allow to study **trial-by-trial variability**.



20  $\mu\text{m}$

# Taste encoding is not really simple...

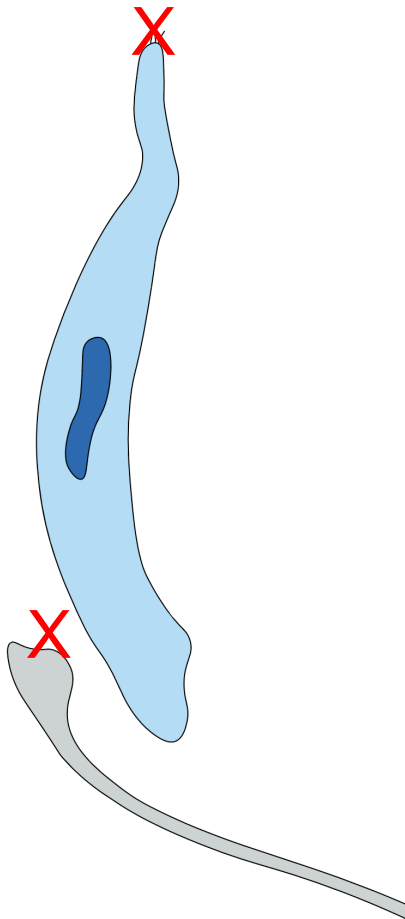


Variation from trial to trial: **state-dependency** (memory-like effect)

# Type-1 taste cells

Type-1 taste cells are glia-like cells in the taste bud.

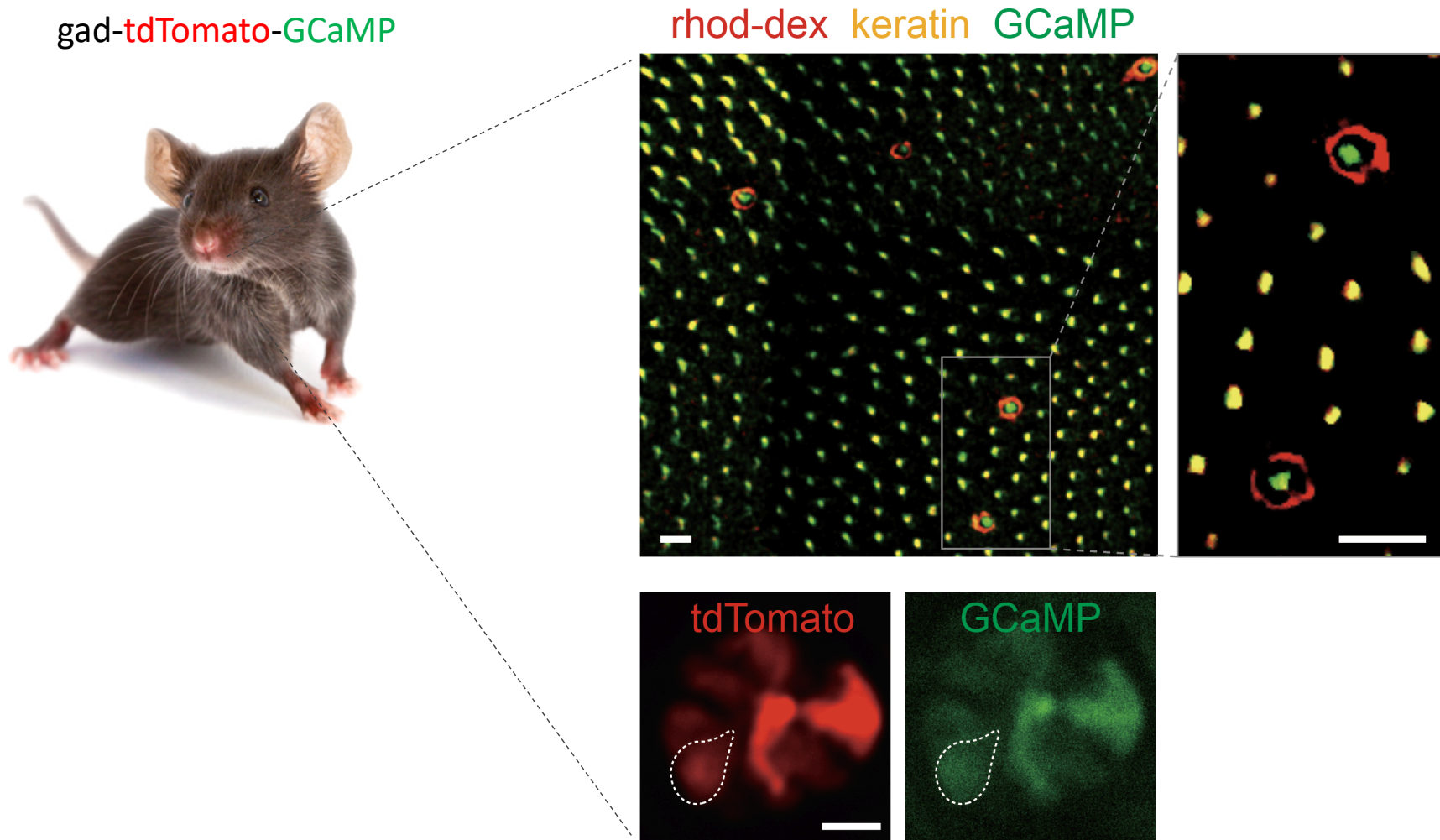
The role of type-1 taste cells is mostly veiled.



- Most abundant cell in the taste bud (~50%)
- No taste receptors (Medler, 2003)
- No synaptic contact (Yuzo Ninomiya, 2016)
- Lamellate processes to wrap around other cells (Farbman, A.I., 1965, Murray, R.G., 1973)
- Expression of GLAST (Lawton, 2000), Ecto-ATPase2 (Bartel, 2006)

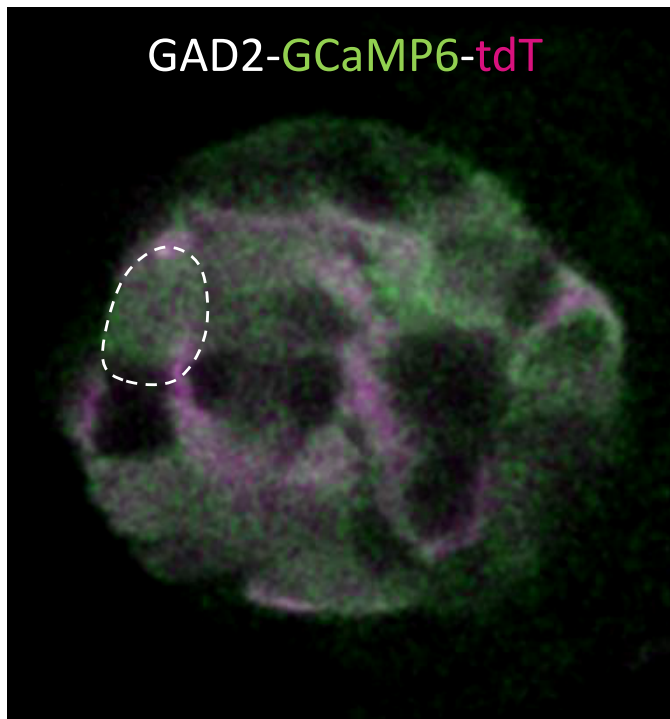
# Naïve question...

Are they really not doing anything during taste sensation?

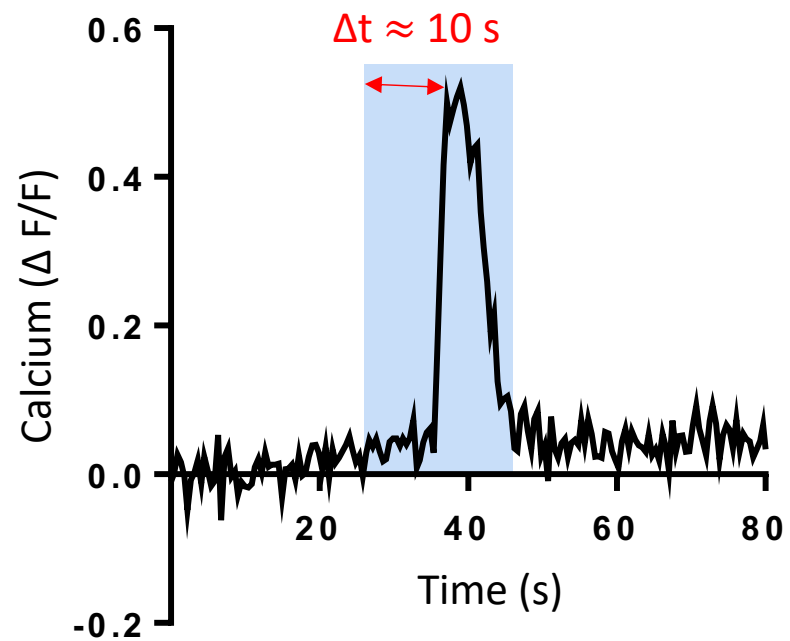


# Type-1 cells are responsive to tastants

+ high salt (400 mM NaCl)

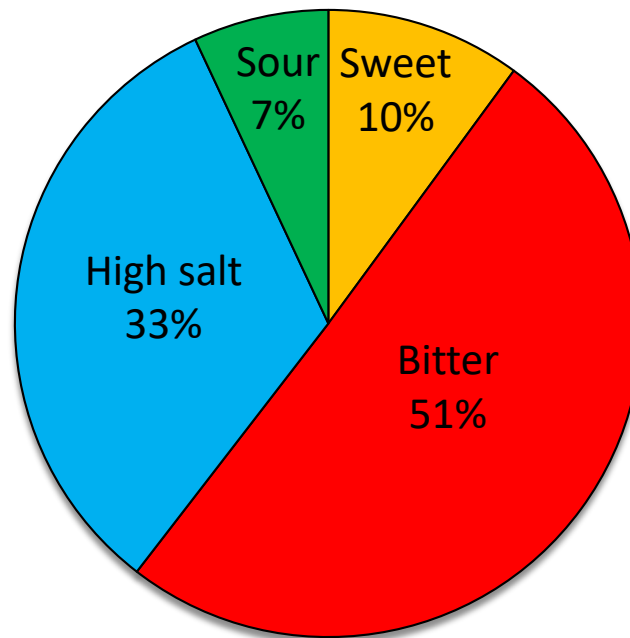


Delayed response



# Tuning of type-1 cells

Type-1 cell responsiveness

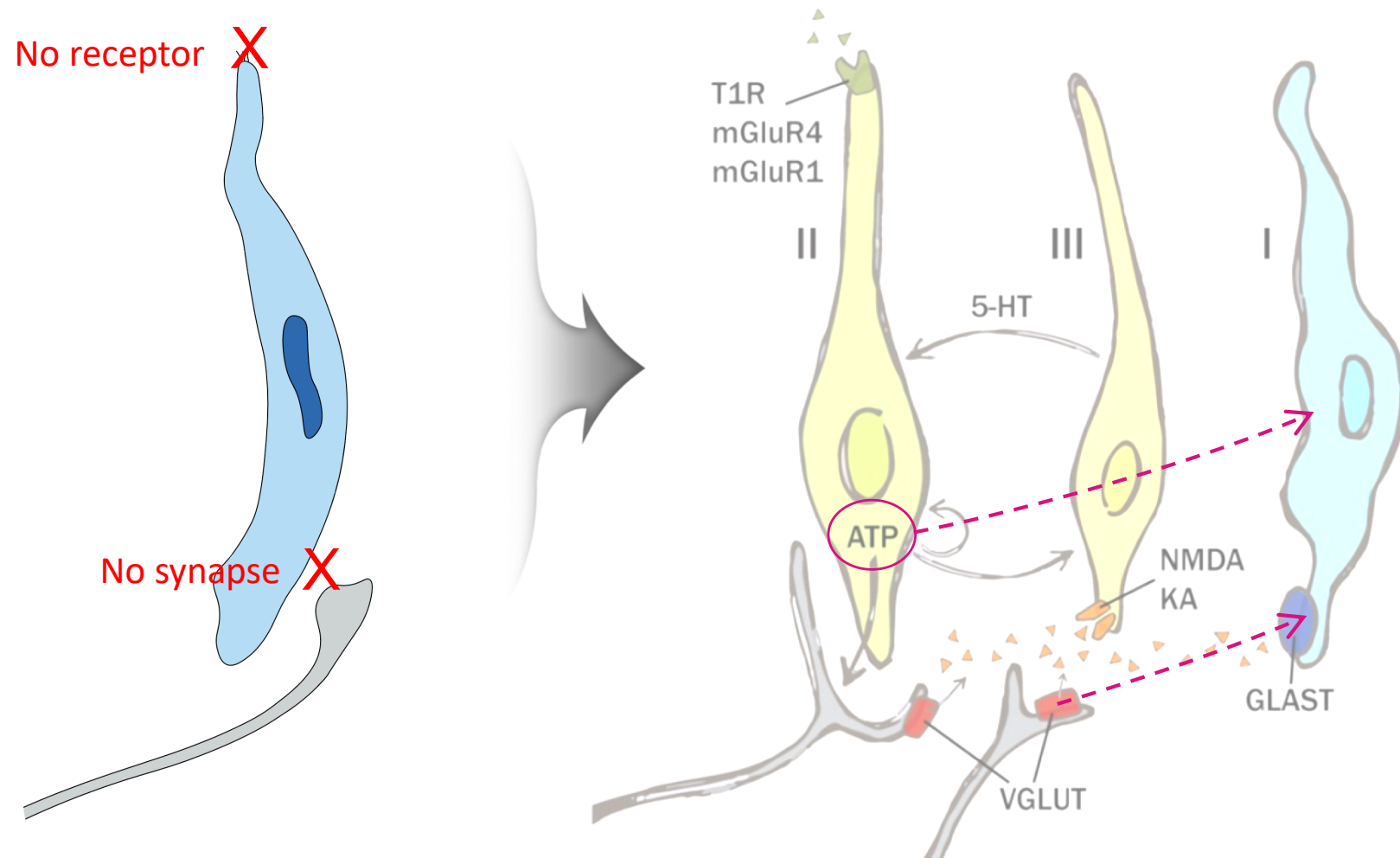


- Delayed response ( $> 5$  sec)
- Heterogeneity in cell-level response
- Temporal coding (adaptation?)

A new view

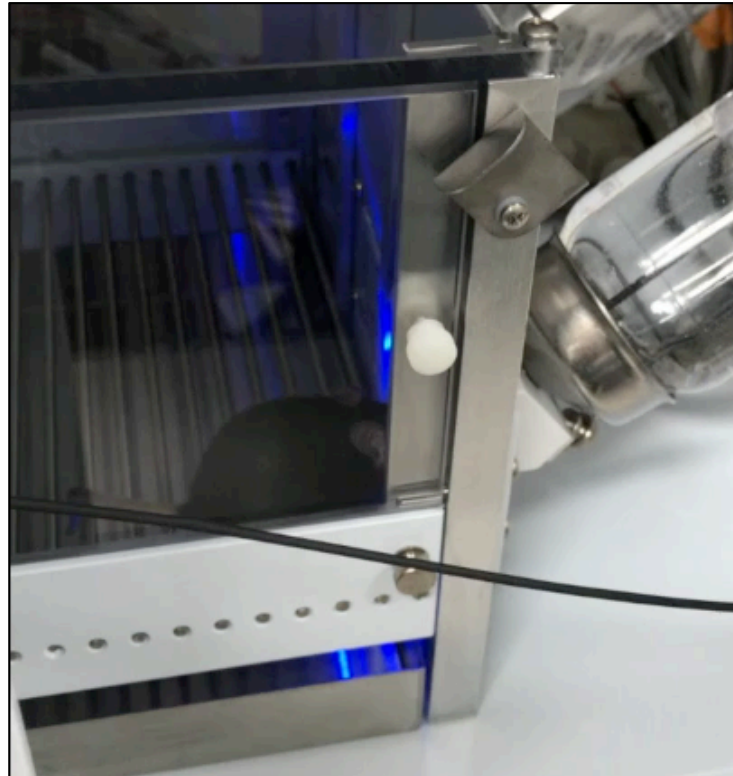
Cell-to-cell communication within the taste bud may modulate sense of taste.

(clustered morphology, neurotransmitters, receptors, ...)



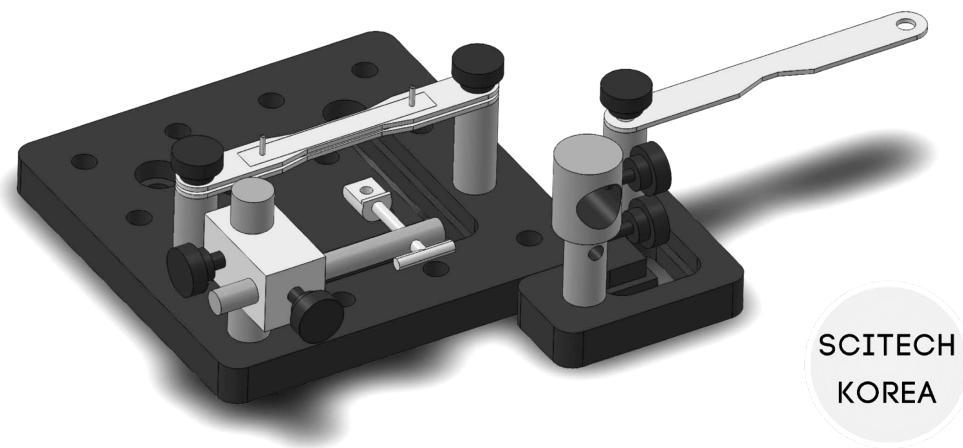
## How about **perception** level?

Water bottle emits **blue light** in response to licking.



1. Thirsty wildtype + **Light** → Drinking
2. GAD2-ChR2 + **Light** → Avoidance (high salt?)
3. GAD2-ChR2 + No Light → Drinking

# Thank you



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Grant supported by Samsung Science & Technology Foundation & Institute of Basic Science