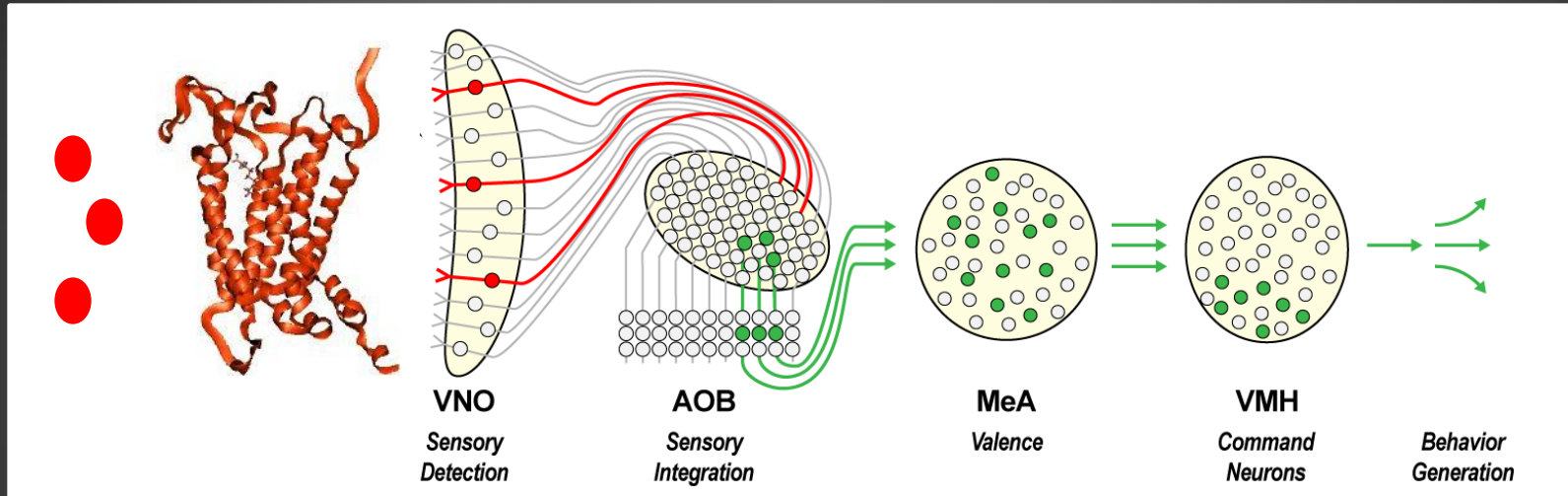


A sensory rationale for the unpredictable nature  
of female behavior



# The brain decodes odor identity and valence to generate appropriate behavior



Identity

Identity

Identity

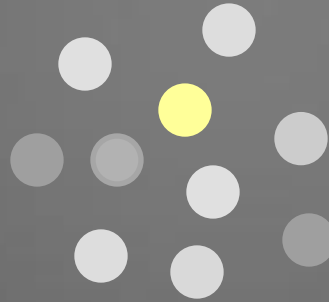
Identity?

Valence?

Decision?



# How does the brain determine how to respond to the odor environment?



# Major Urinary Protein (MUP) ligands instruct male-male aggression



Castrated intruder



Castrated intruder + MUPs

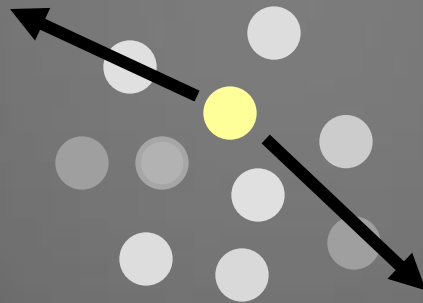
Why would males emit a pheromone that provokes aggression from others?

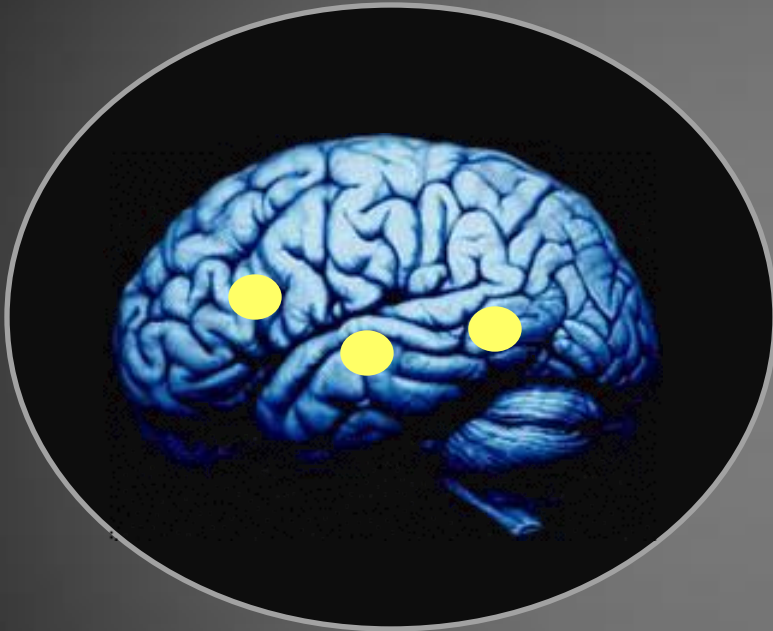
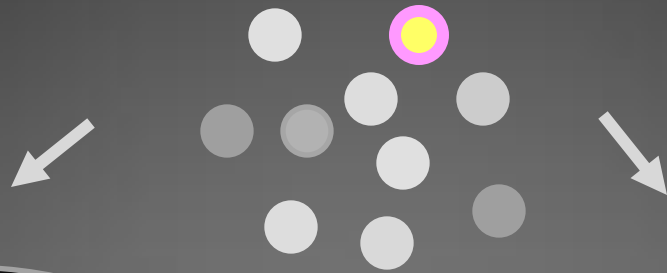


# Male rage cues attracts females



# How does the brain determine how to respond to the odor environment?

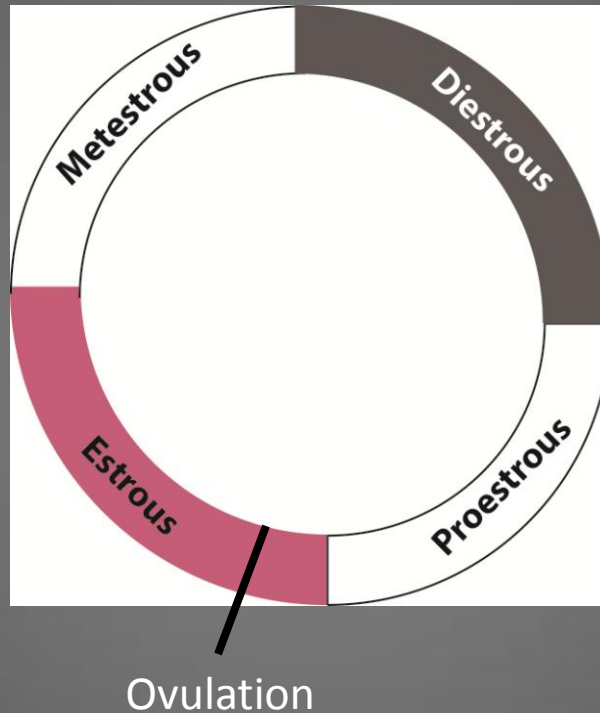
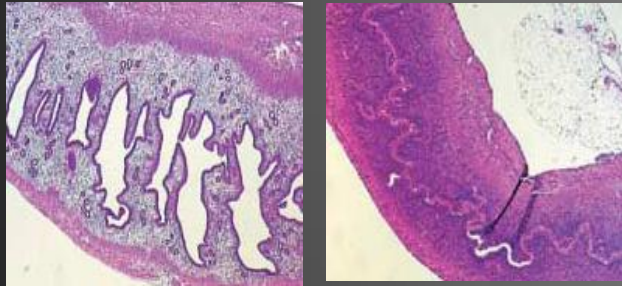






# Dimorphism within gender: Ovulation cycle

Physiological changes

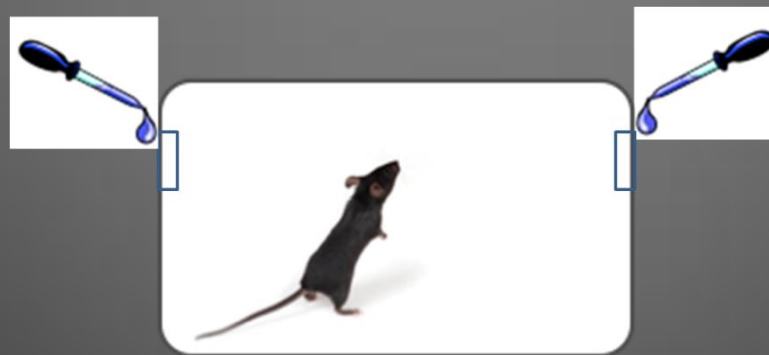
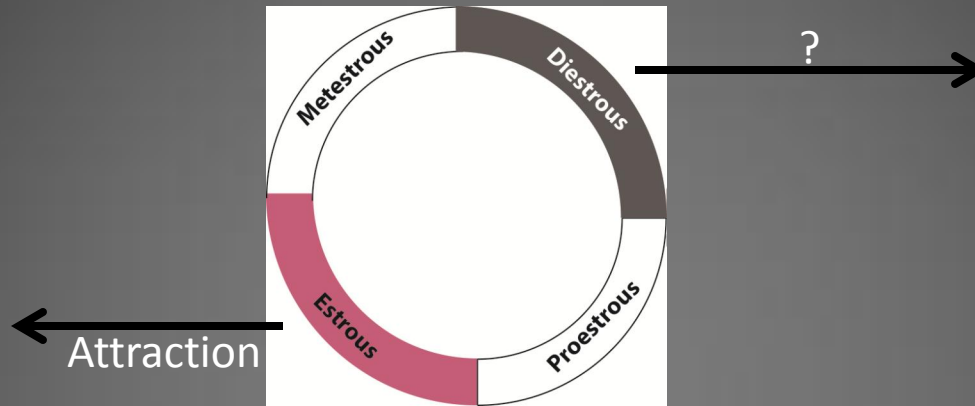


Behavioral changes



Is there an olfactory cue that generates different female behaviors across the estrous cycle ?

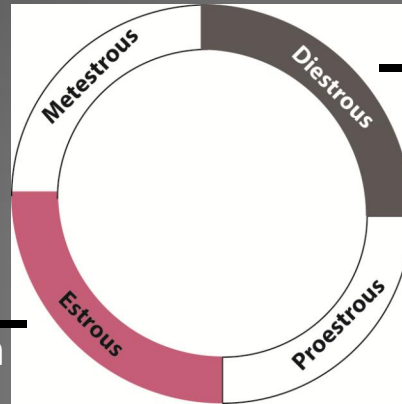
# Olfactory behavior to male odors changes according to estrous cycle



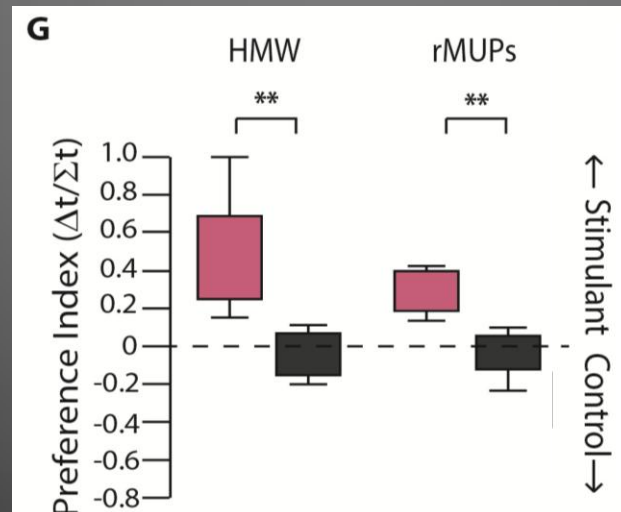
# Olfactory behavior to male odors changes according to estrous cycle

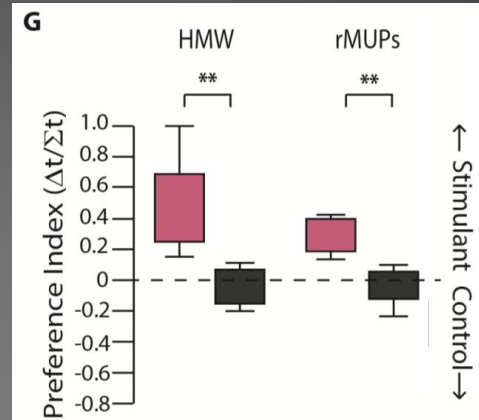
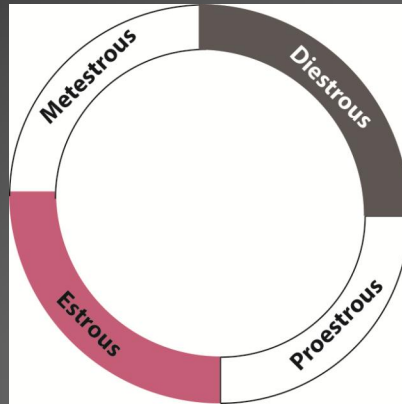


Attraction

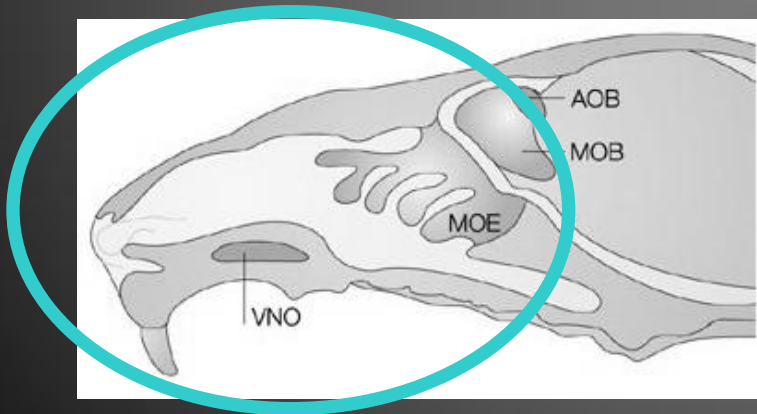


Indifference

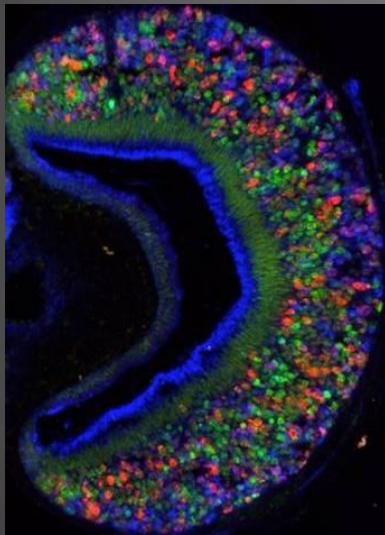




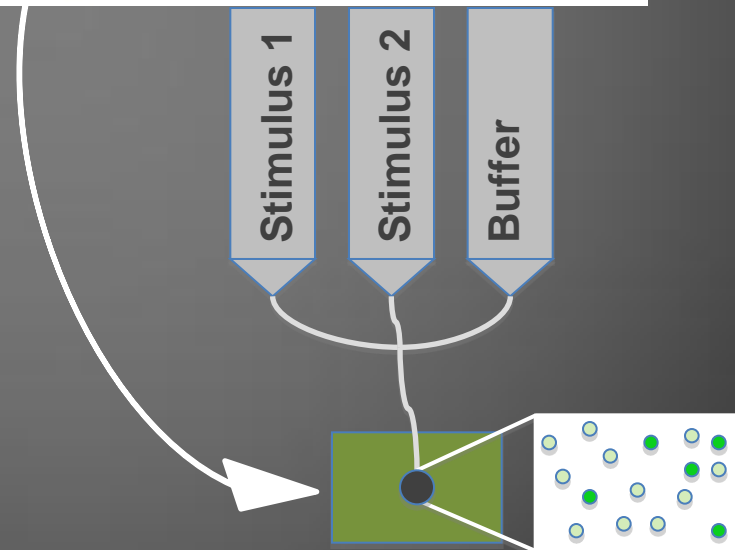
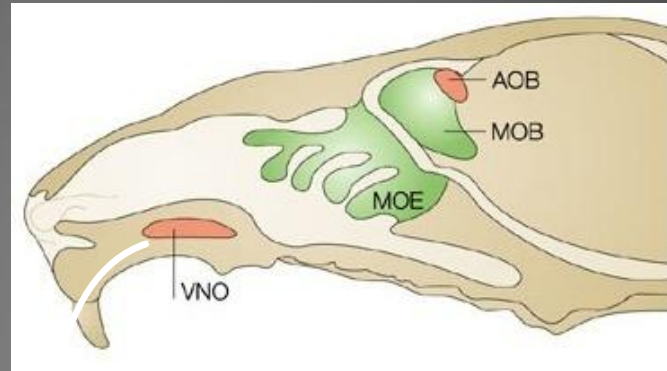
Does the regulation happen in the brain or in the nose ?



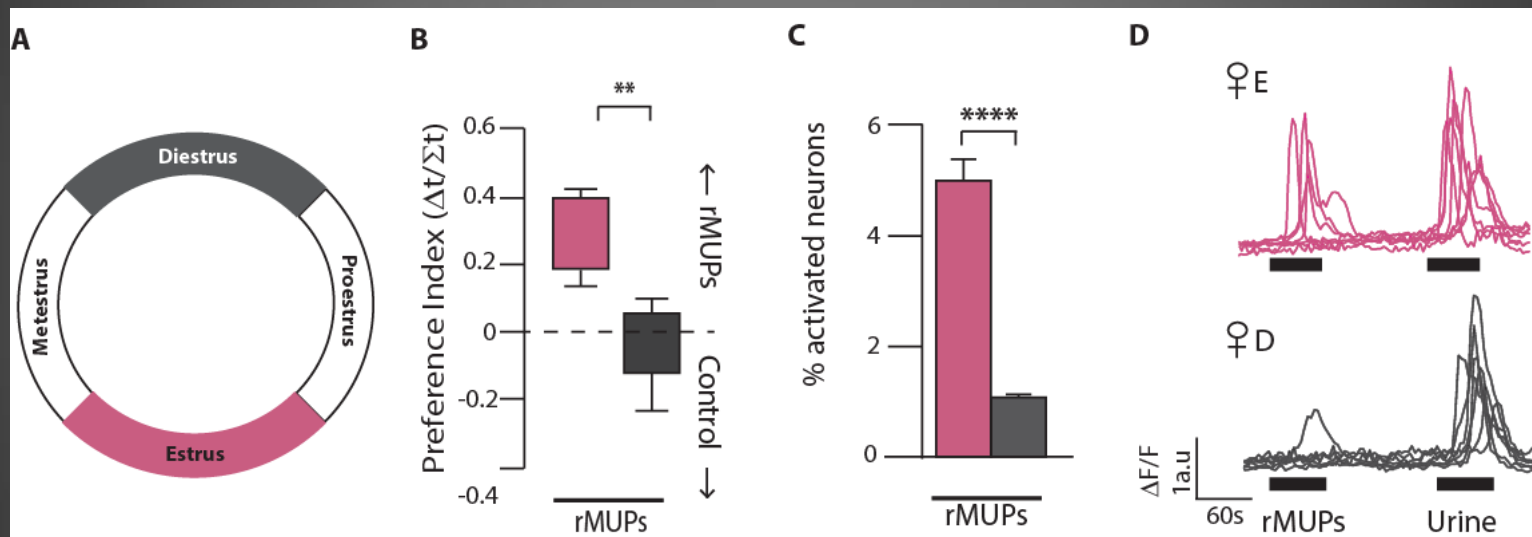
# MUPs are detected by approximately 5% of VSNs



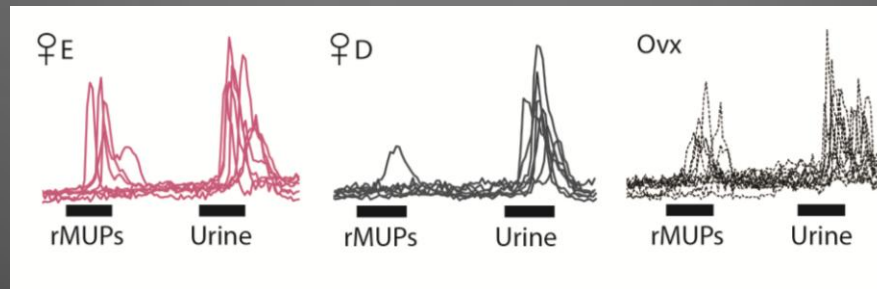
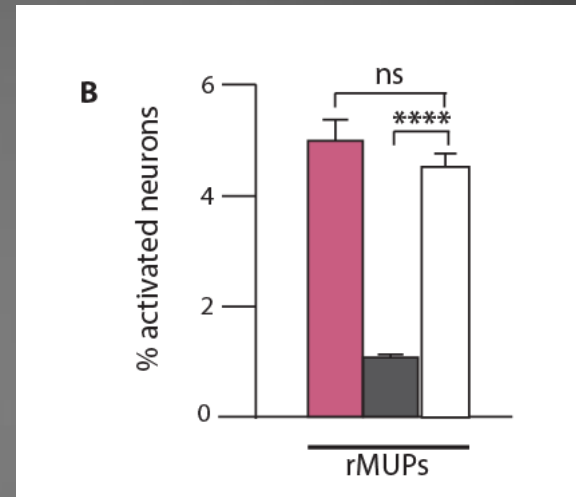
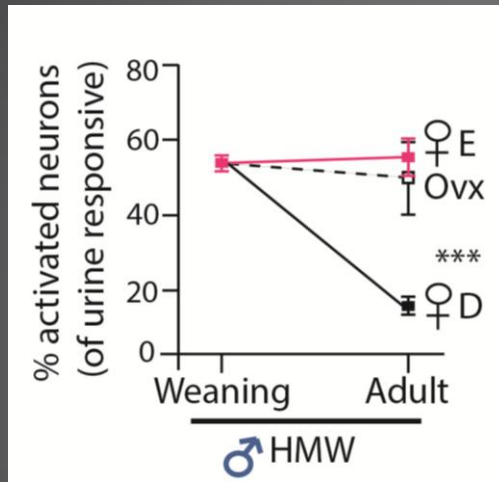
Isogai and Dulac



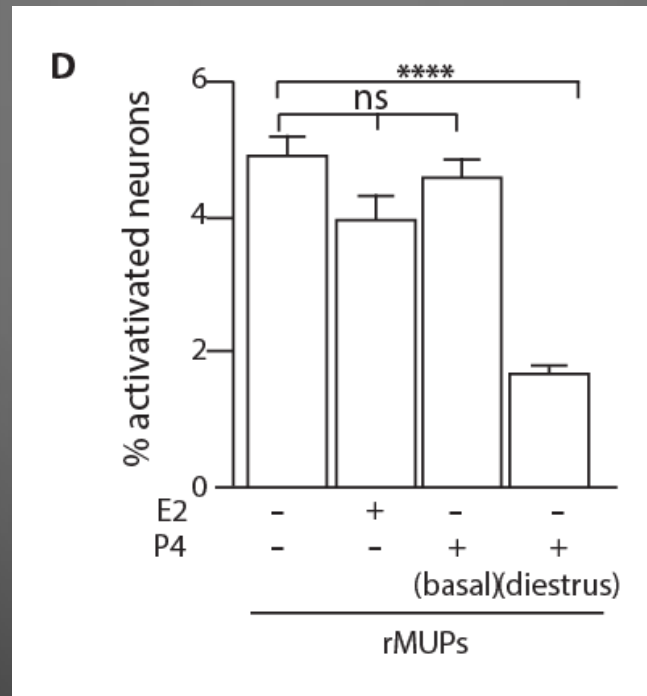
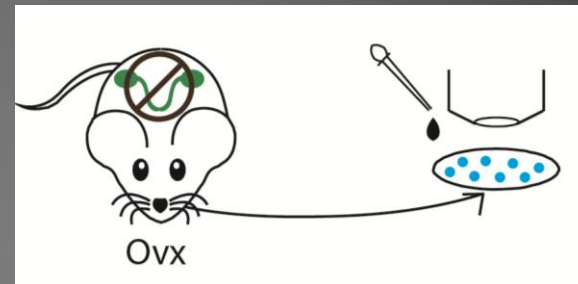
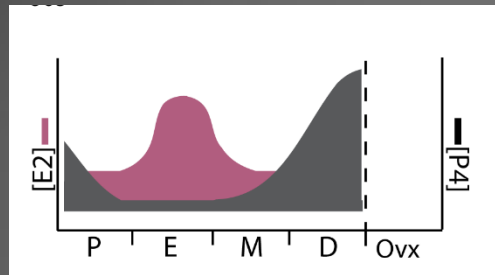
# Changes in female's behavior correlates with silencing sensory activity.



# The ovaries are required for sensory silencing

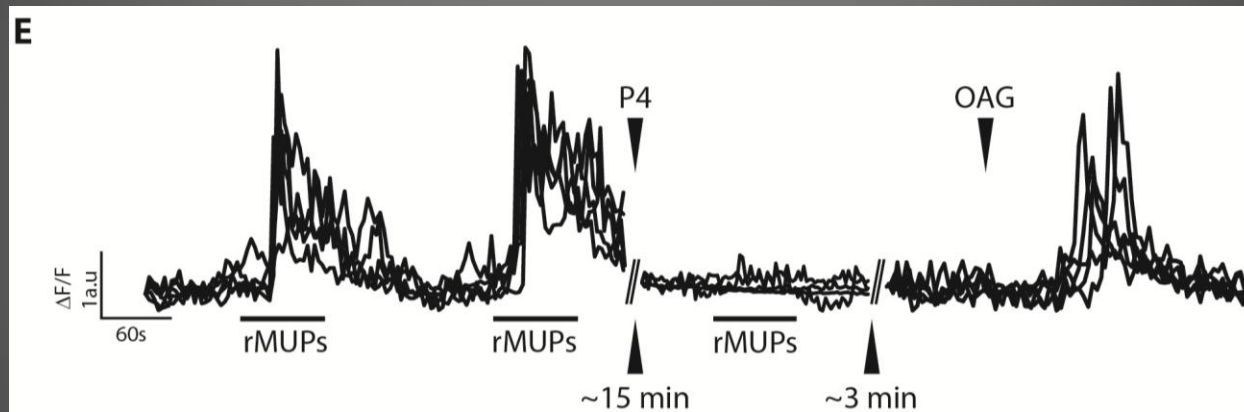


# Progesterone 'tells' VNO the female estrus state



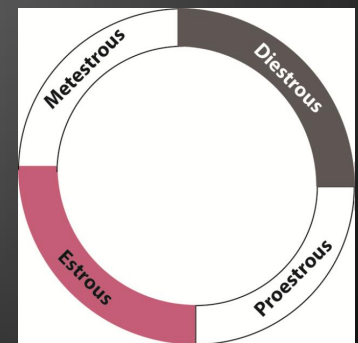


# Progesterone silences sensory neurons without 'killing' them



# How do the sensory neurons detect progesterone?

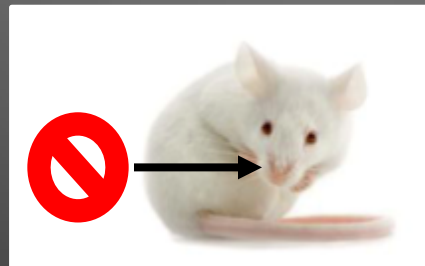
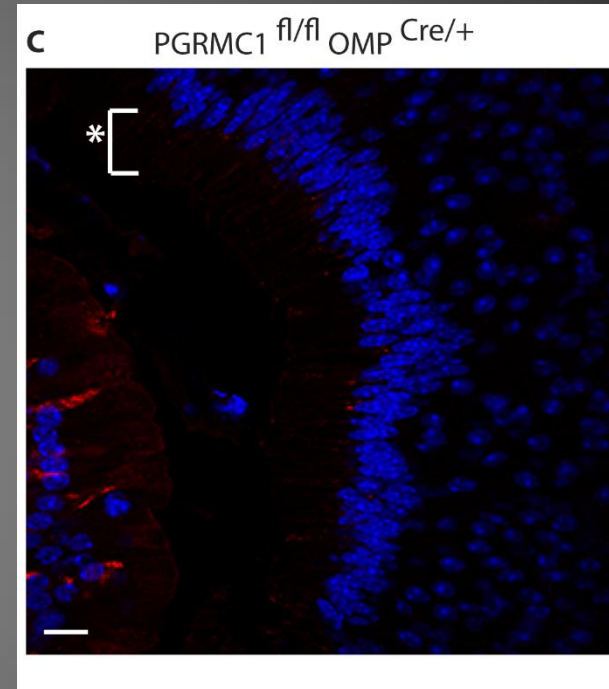
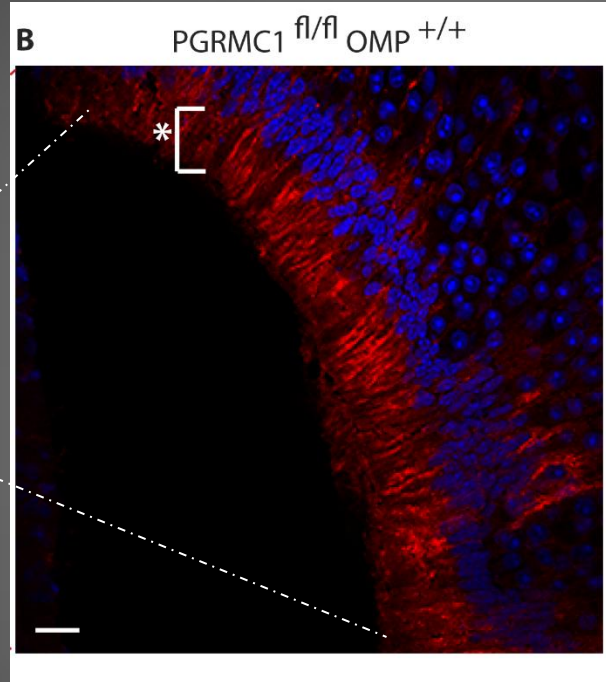
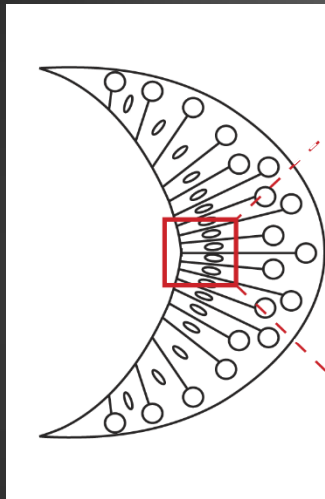
- No progesterone receptors have been described in the VNO.
- Our RNAseq did not reveal expression of classical nPR.
- RNAseq did find expression of non-classical progesterone responsive genes including PGRMC1.



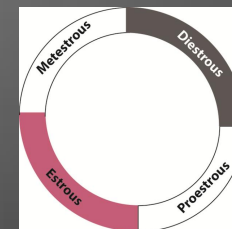
# PGRMC1 localizes to sensory dendrites

Wild type

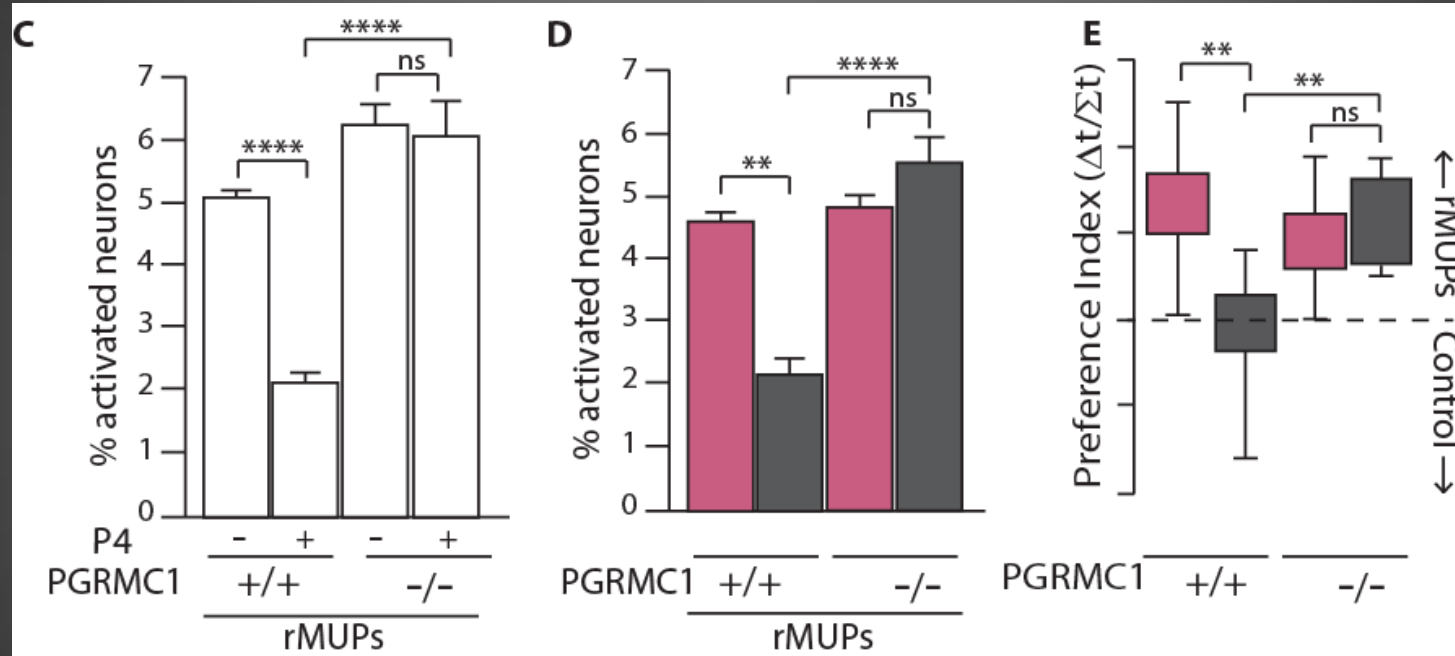
PGRMC1<sup>-/-</sup>



=



# PGRMC1 is necessary for P4 to silence sensory neurons.

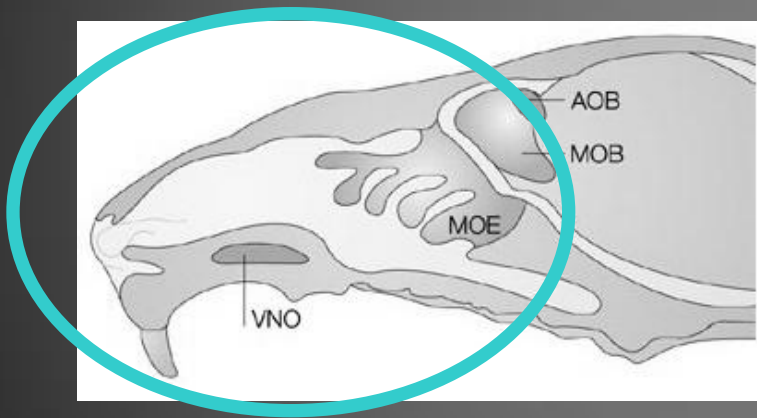


Ex Vivo:  
Pharmacology

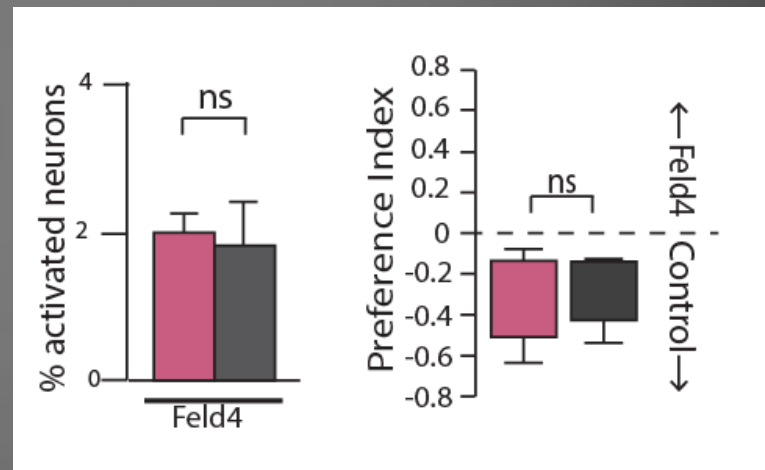
Ex Vivo:  
Natural Estrus Cycle

Female Behavior  
Natural Estrus Cycle

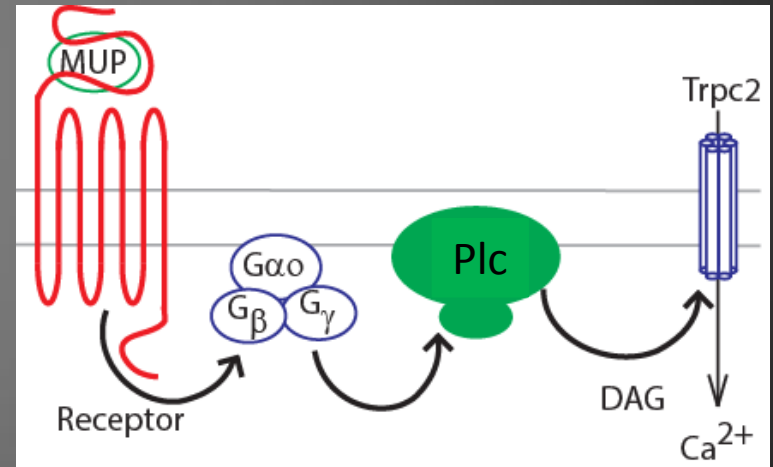
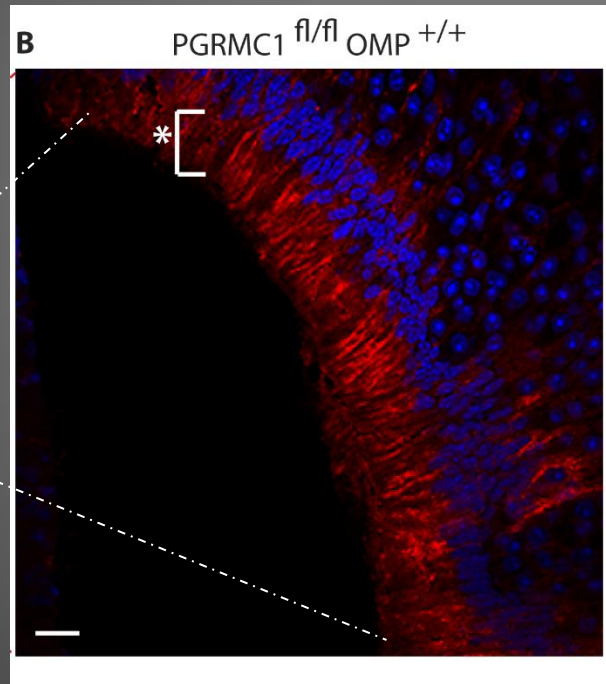
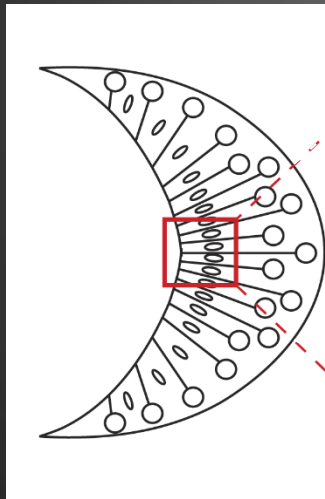
Sensory silencing occurs directly in the VSNs who monitor internal concentration of P4



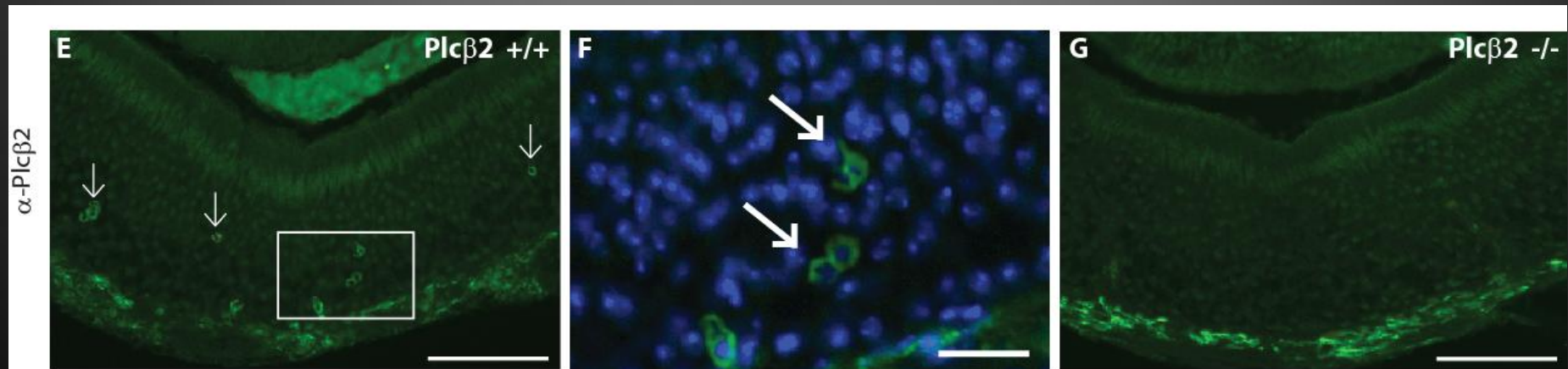
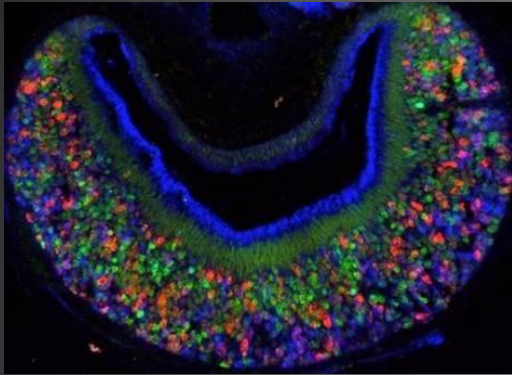
# Is all sensory detection silenced in diestrus?



# Why are male pheromone detecting VSNs silenced while cat detecting VSNs remain active?

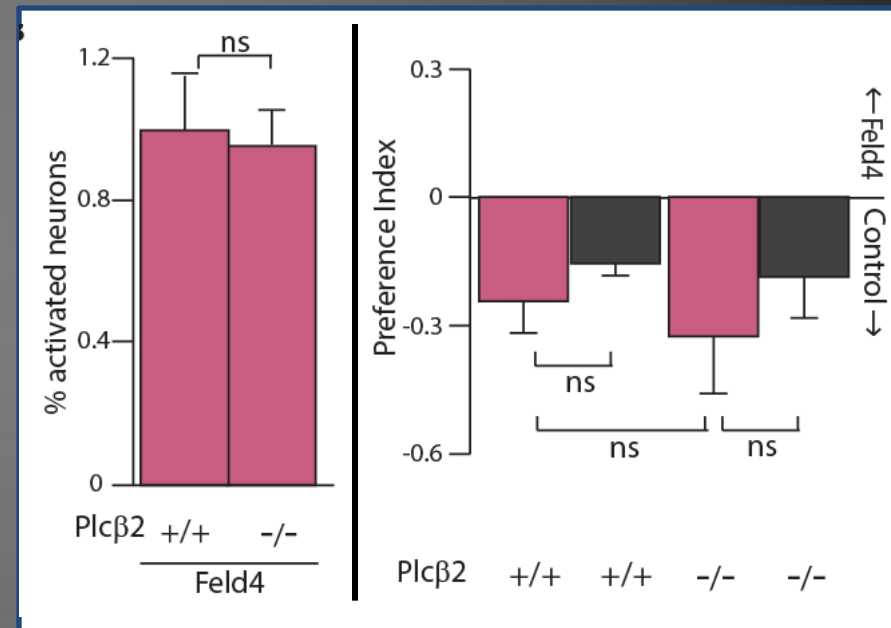
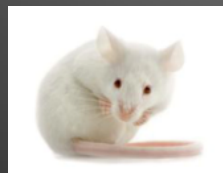
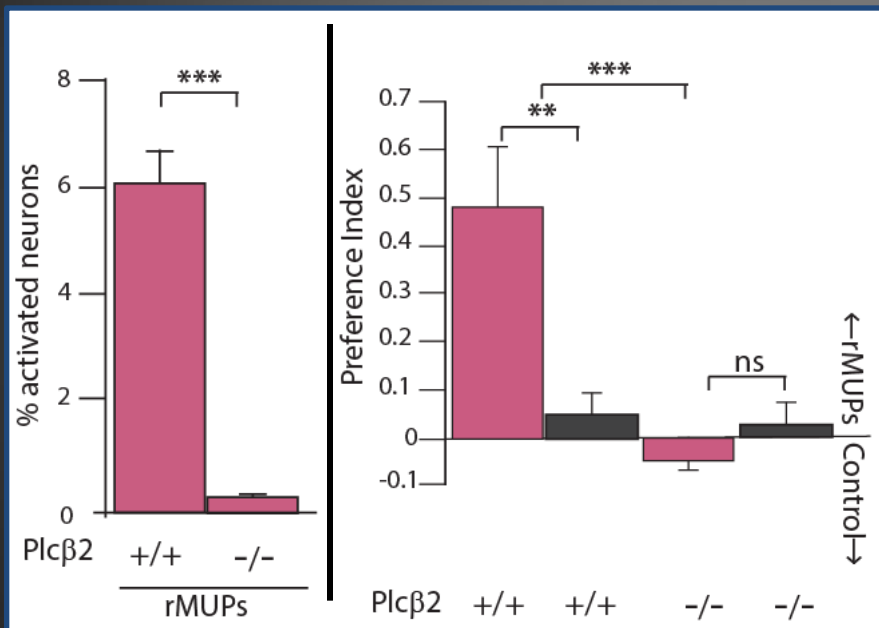


# MUP detecting VSNs are enriched in a specific PLC variant

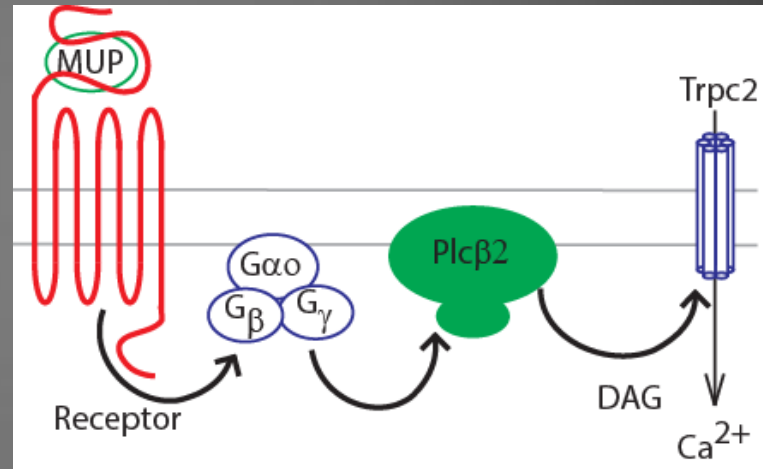
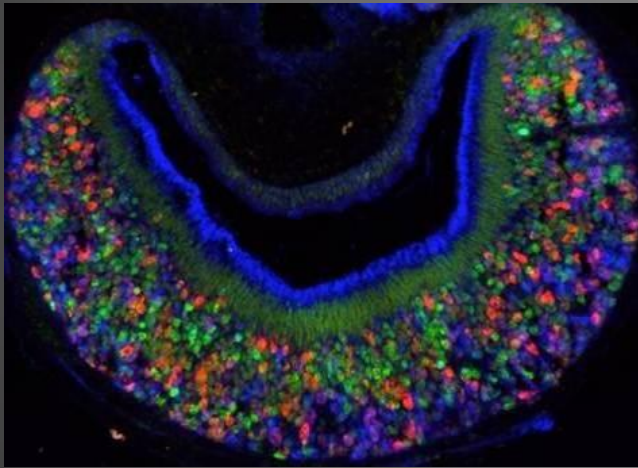




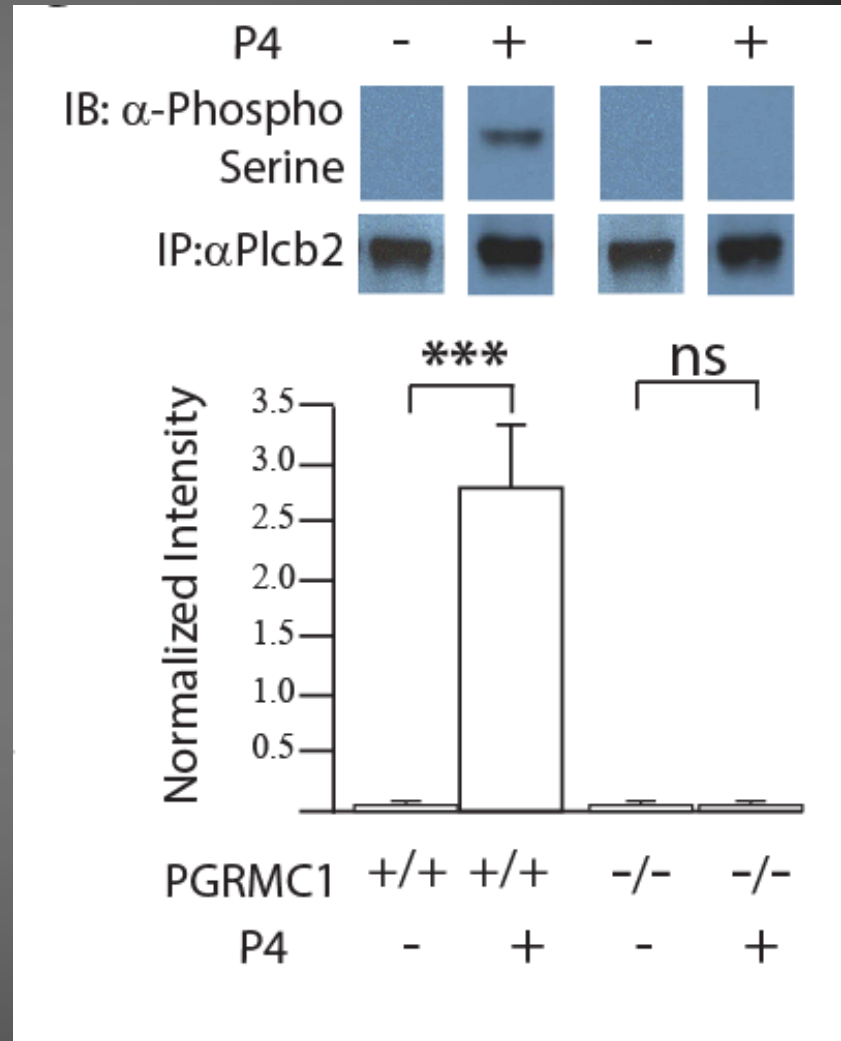
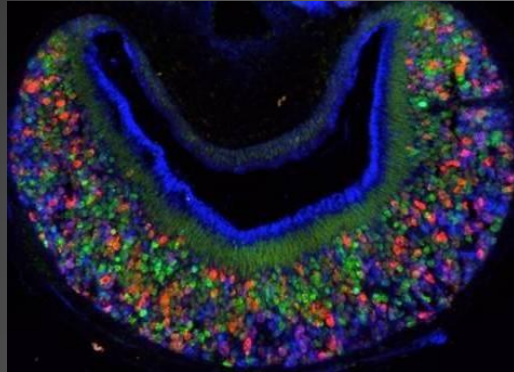
# Different PLC variants are essential for function



# Beyond receptors: sensory neurons are customized to respond to particular odors.

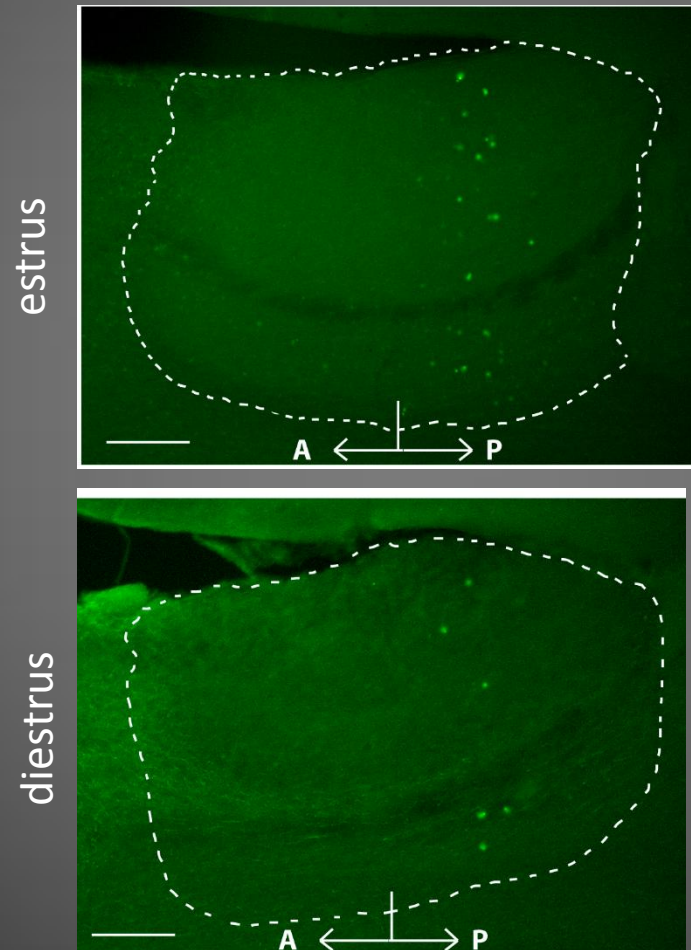


# PGRMC1 initiates a kinase cascade

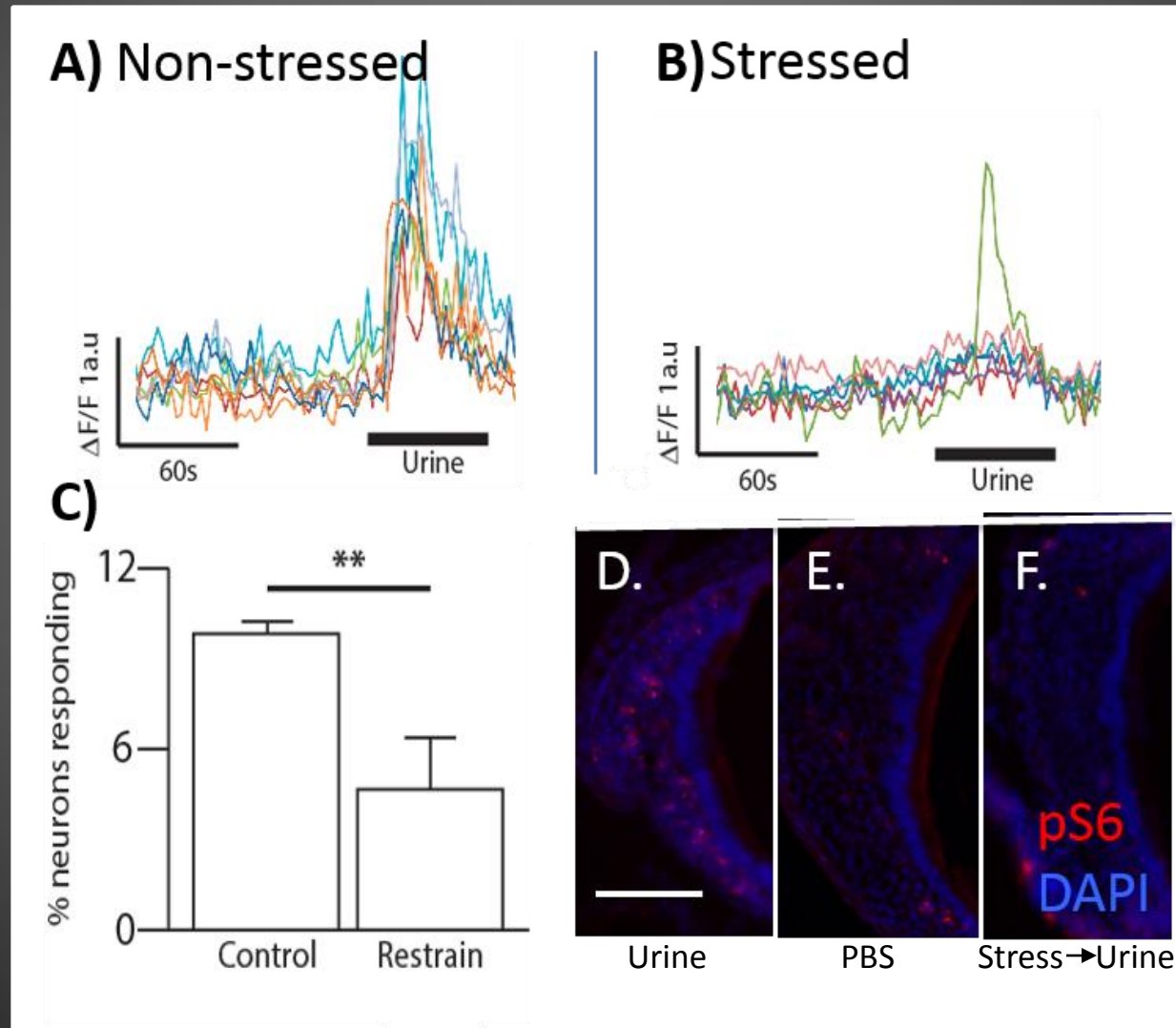


PLCB2 is inactivated by serine phosphorylation

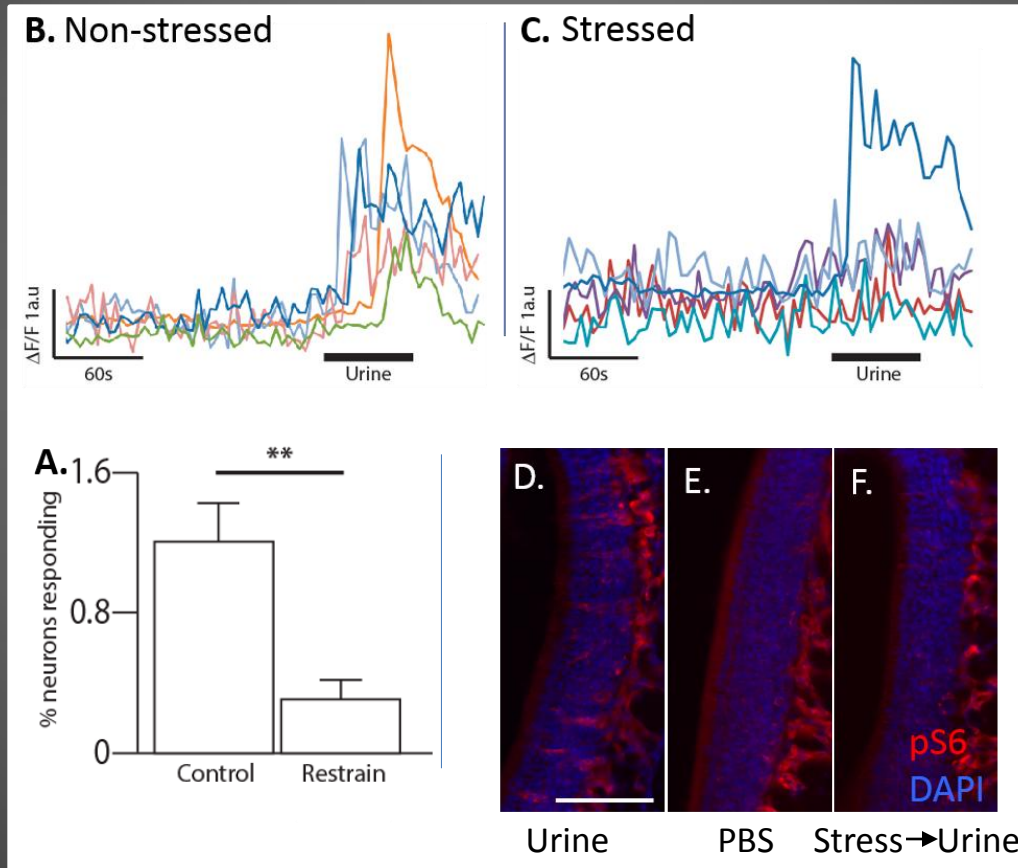
# PGRMC1 + progesterone turns off MUP detecting VSNs.



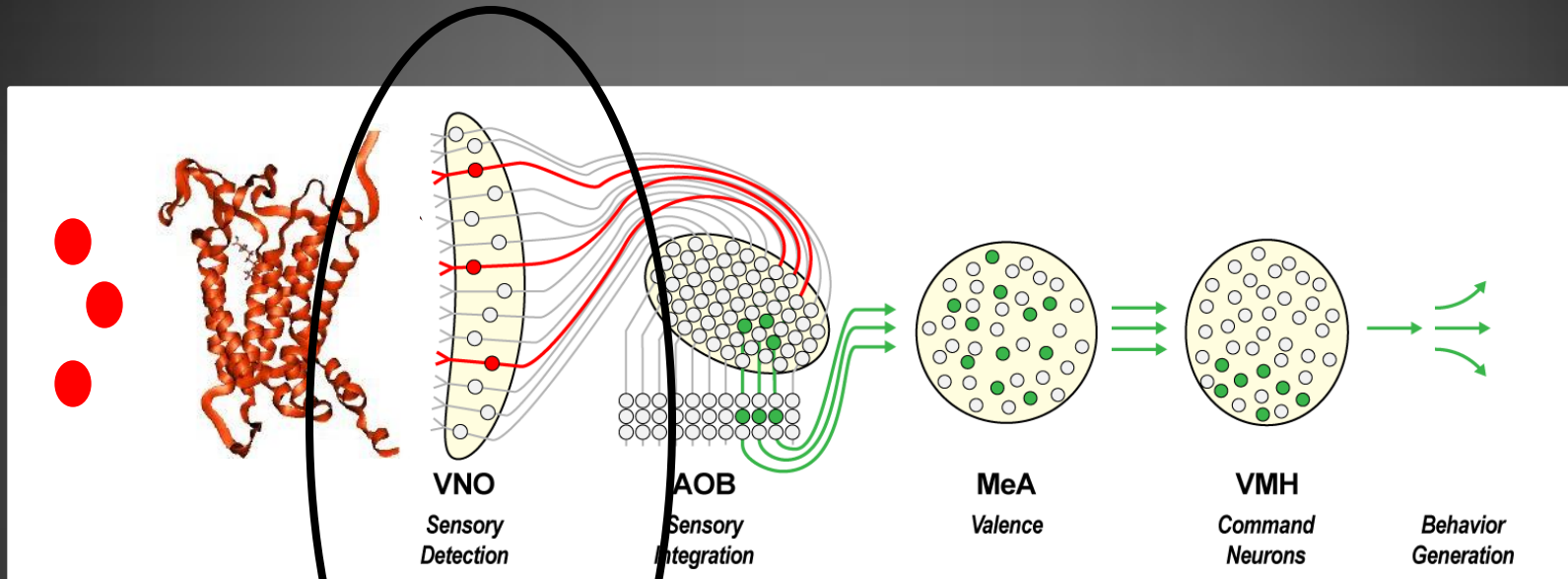
# Males also undergo VNO sensory silencing: stress



# ...and sensory silencing occurs in the mammalian MOE



# The brain decodes odor identity and valence to generate appropriate behavior



Identity

Identity

Identity  
&  
Decision

Identity?

Valence?

Decision?



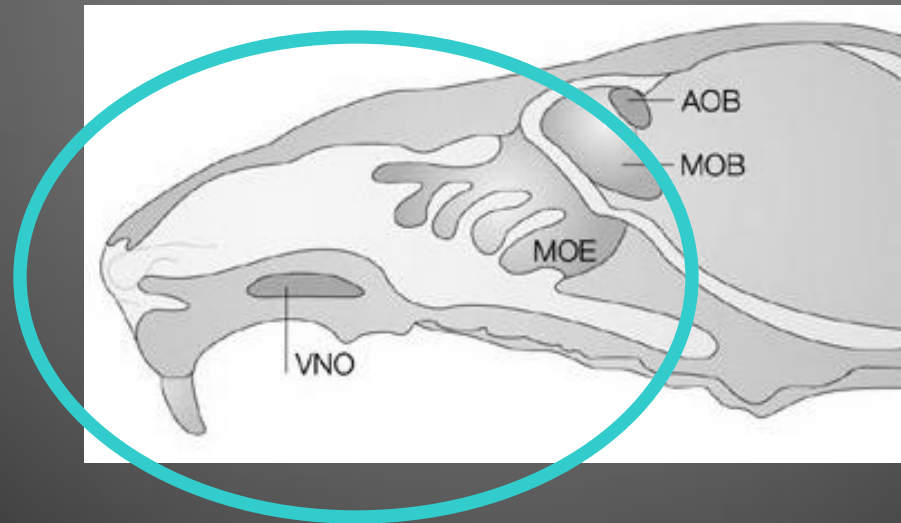
Attraction



Indifference



Females are 'blind' to MUPs every four days.....







- *NIH: NIDCD*
- *Skaggs Foundation*
- *Dorris Neuroscience Center*
- *Ellison Medical Foundation*

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