Sniffing: A master clock for orofacial rhythms?

David Kleinfeld
16 June 2015
KITP - Deconstructing the sense of smell

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(http://neurophysics.ucsd.edu/)

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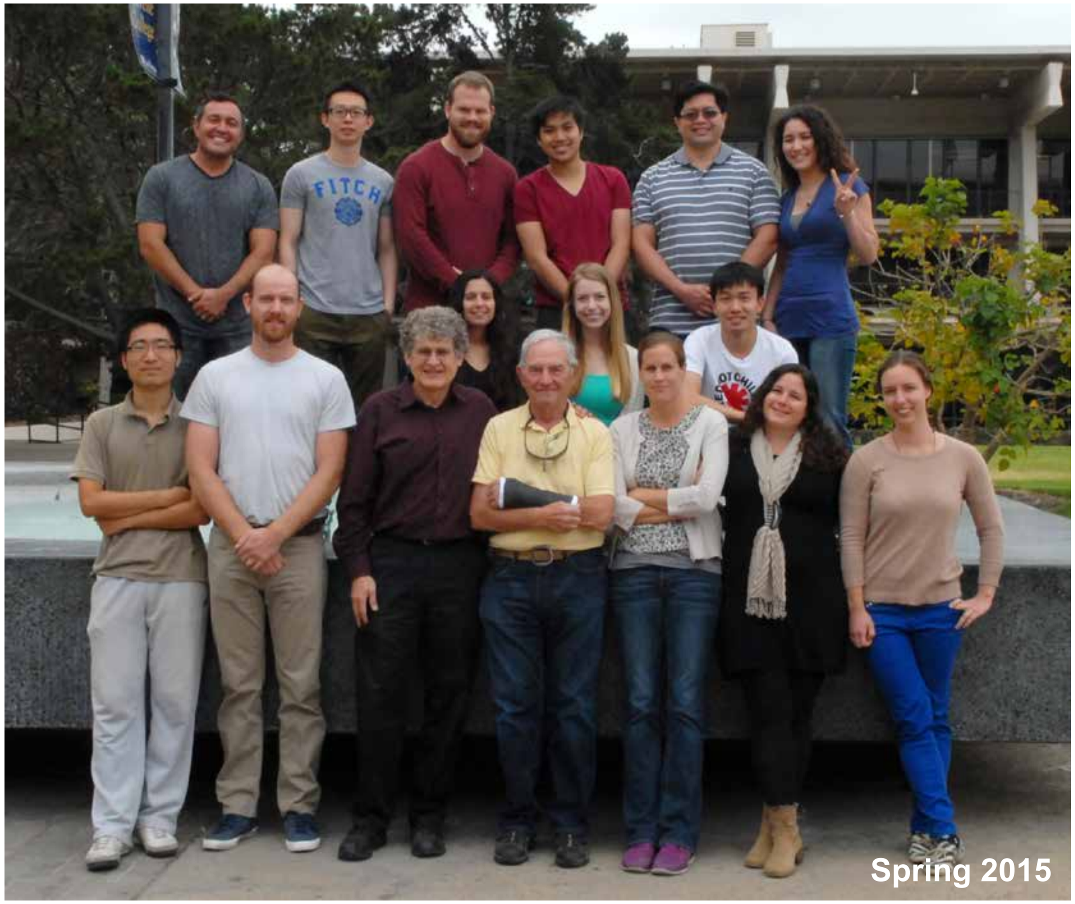

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With thanks for past and ongoing financial support

BEBRF, HFSP, NIH (Director's Pioneer Award, NCRR,
NIA / CNCRS, NIBIB / BRP, NIDA, NIDA / CEBRA, NIDCD,
NIMH, NIMH / EUREKA, NINDS & NINDS / BRAIN STEM),
NSF (DBI, PoLS / BRAIN EAGER, IBN, IGERT & Physics),
Packard, Roche, Whitehall, UCSD CBAM & US/Israel BSF.

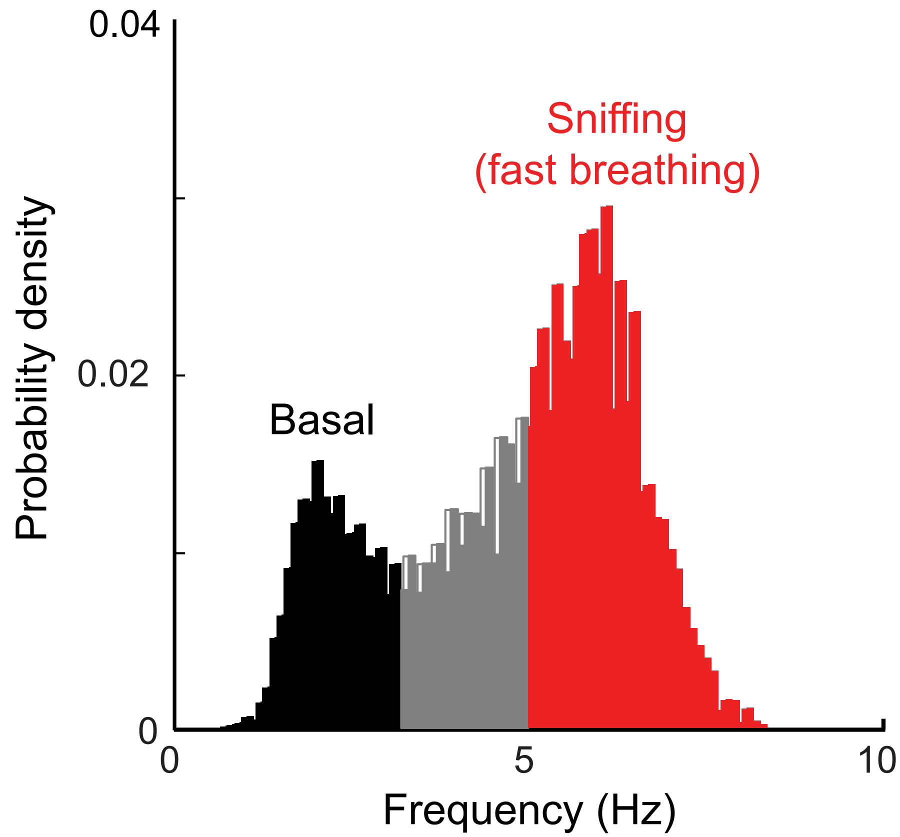
Sniffing: A master clock for orofacial rhythms?

- **Coordination of orofacial actions during exploration**

- **Brainstem circuits for control of rapid vibrissa motion**

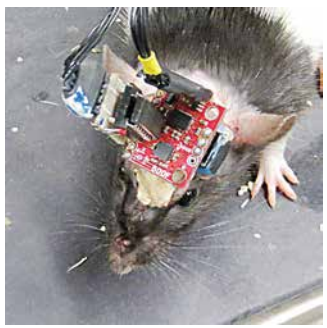
- **Circuitry for coordination of *all* orofacial motor actions**

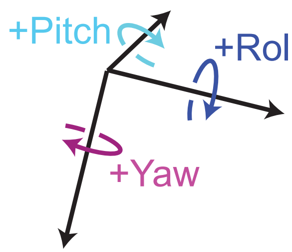
Following Welker's behavioral study (1964), what orofacial actions are linked to sniffing?

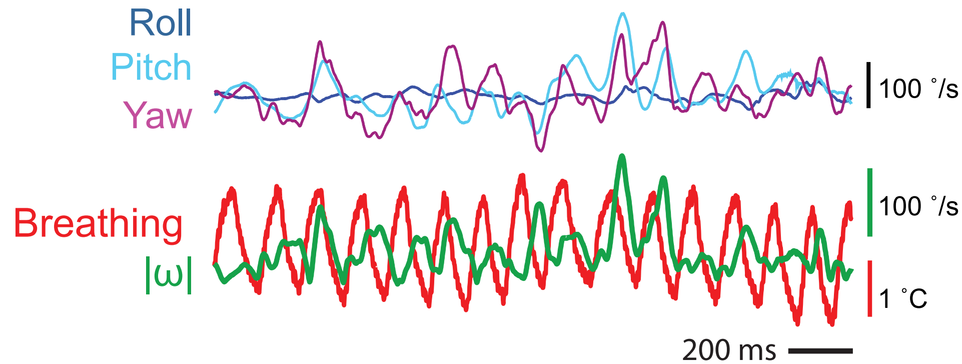


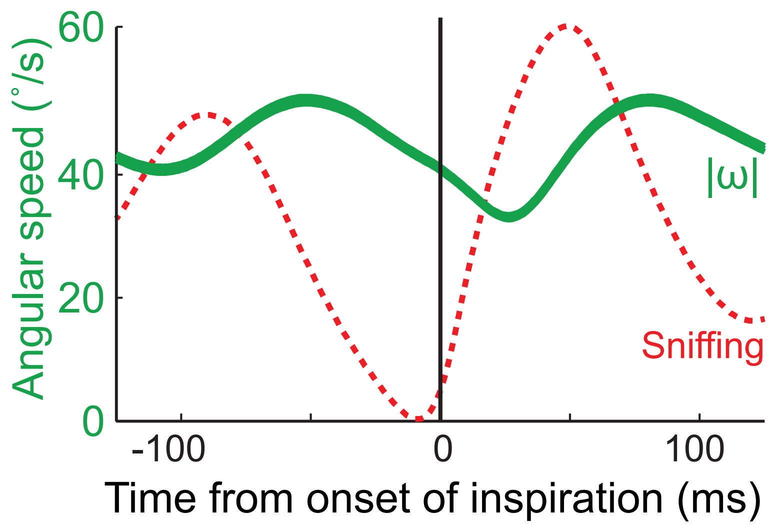
Moore*, Deschenes*, Huber, Smear, Demers & Kleinfeld (Nature 2012)
See also Kepecs, Uchida & Mainen (J Neurophysiology 2007)

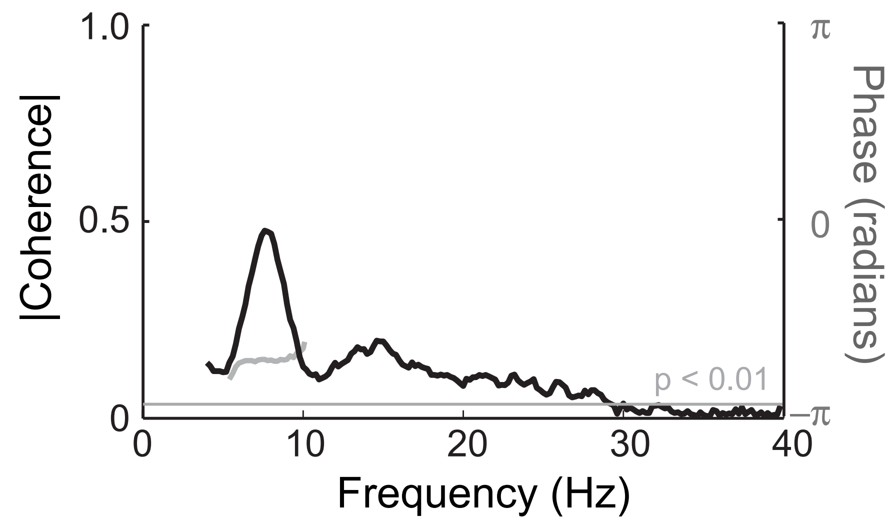
Coordination of head bobbing with sniffing





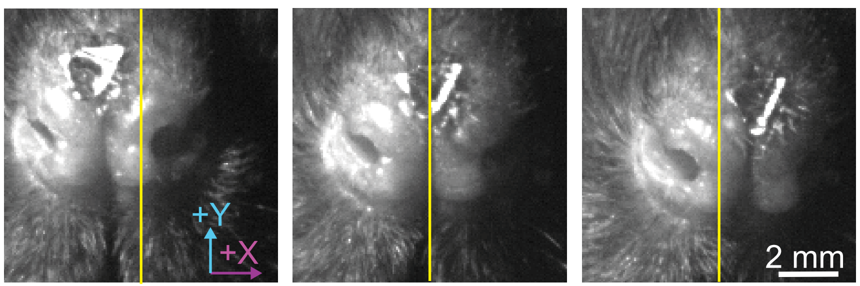


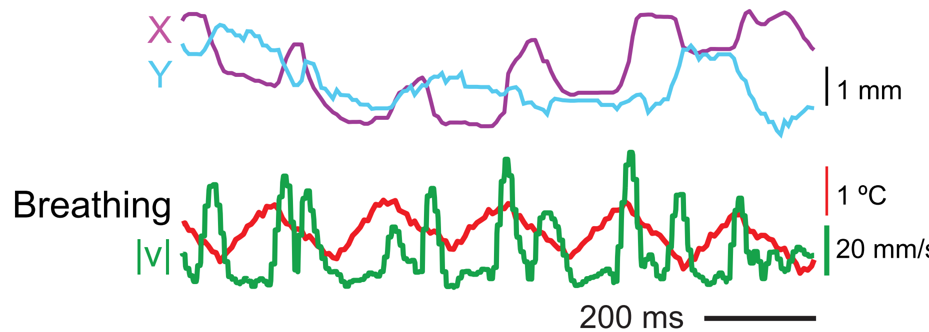


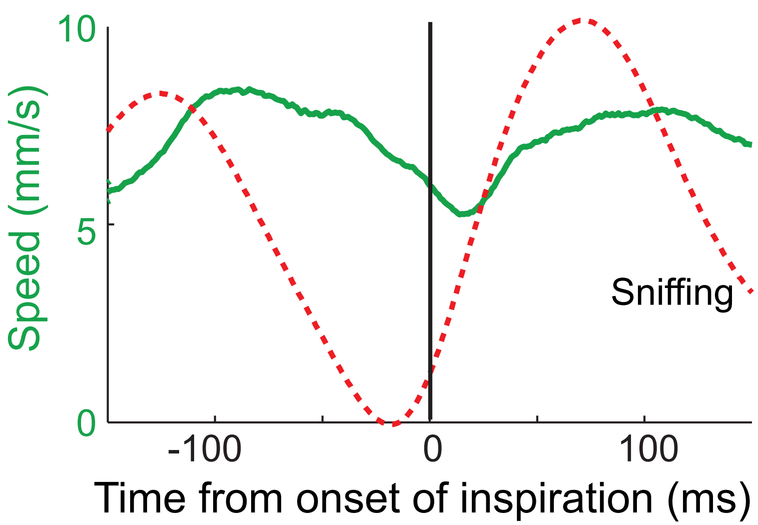


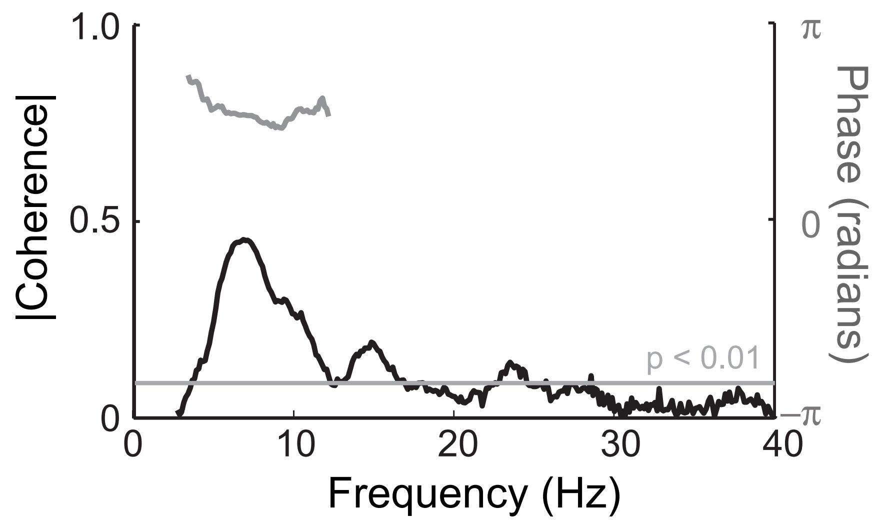
Moore, Deschenes & Kleinfeld (unpublished)

Coordination of nose wiggling with sniffing



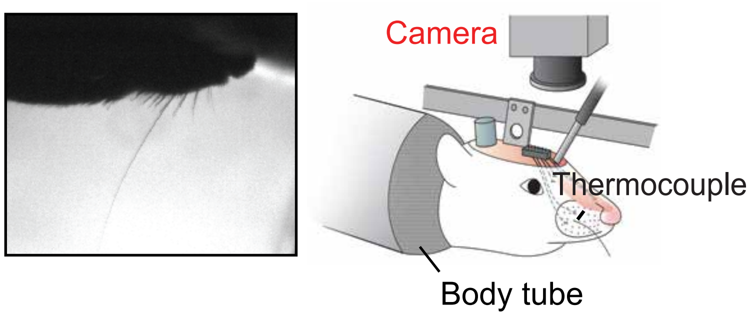


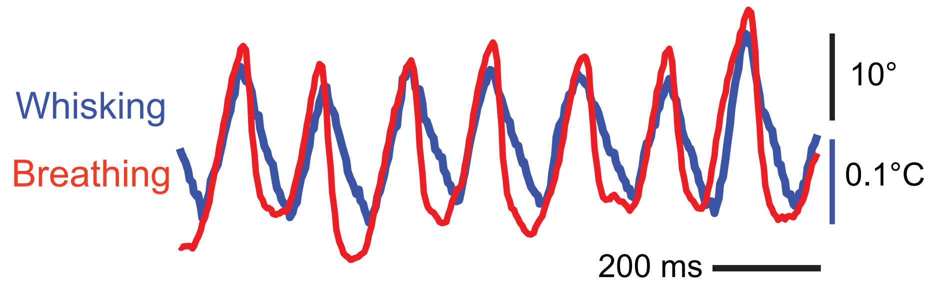


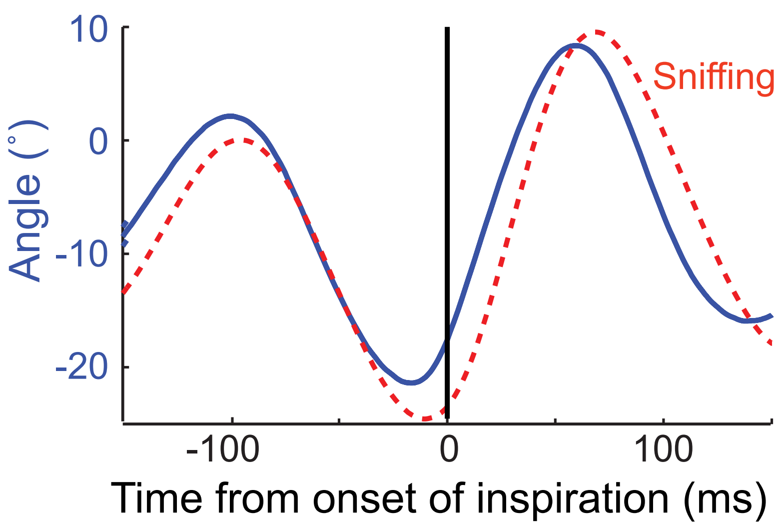


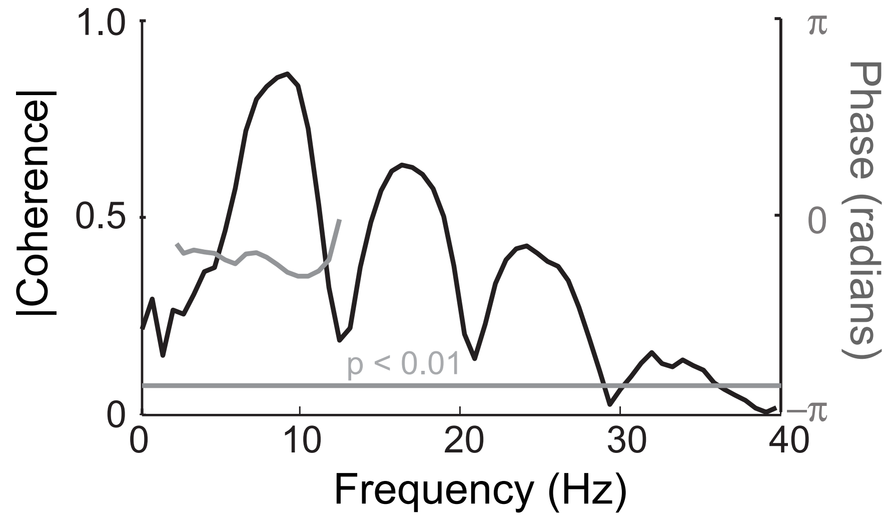
Moore, Deschenes & Kleinfeld (unpublished)

Coordination of whisking with sniffing



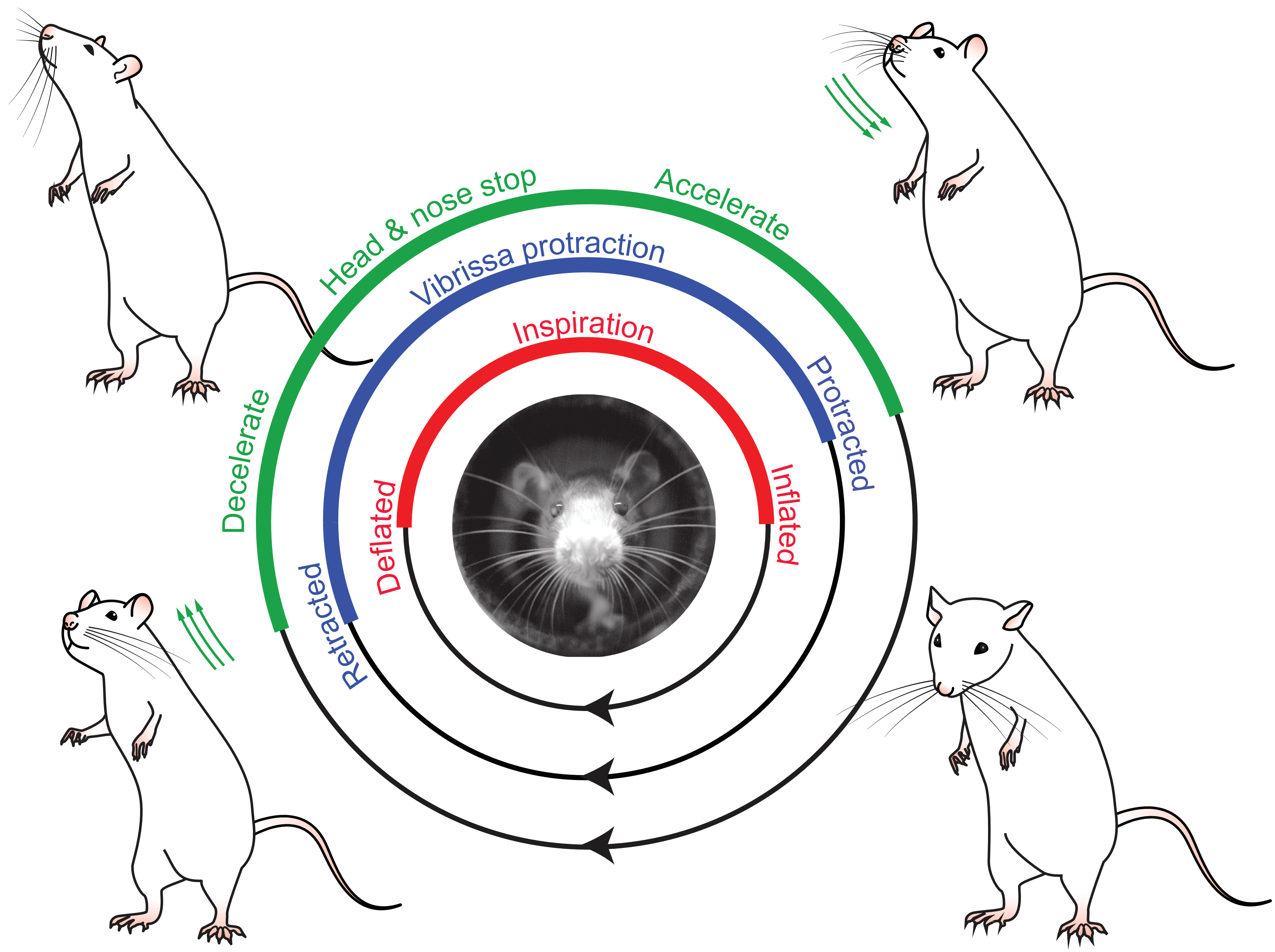






Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
see also Ranade, Hangya & Kepecs (J Neuroscience 2013)

The cycle of exploratory orofacial actions linked to sniffing



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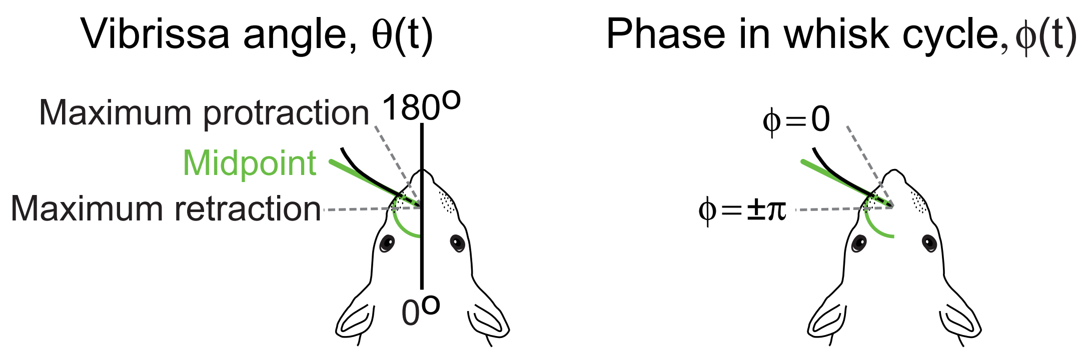
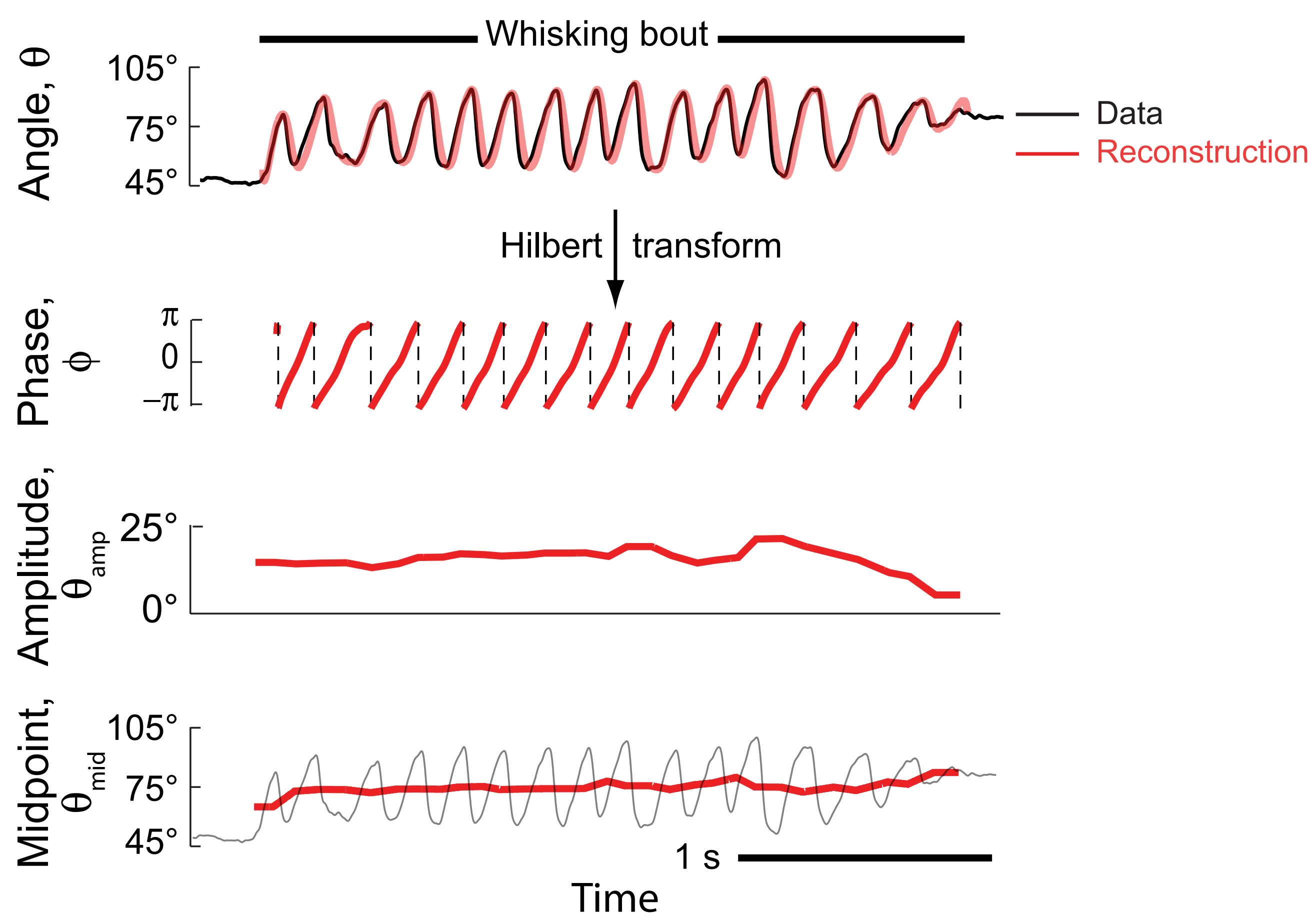
Angular versus phase coordinates for whisking



Decomposition of the whisking signal into phase, amplitude and midpoint



Hill, Curtis, Moore & Kleinfeld (Neuron 2011)

Lesson

Whisking is generated by a control signal of the form

$$\theta(t) \;=\; \theta_{amplitude}(t) \cdot \mathit{cos}\,\phi(t) \;+\; \theta_{midpoint}(t)$$

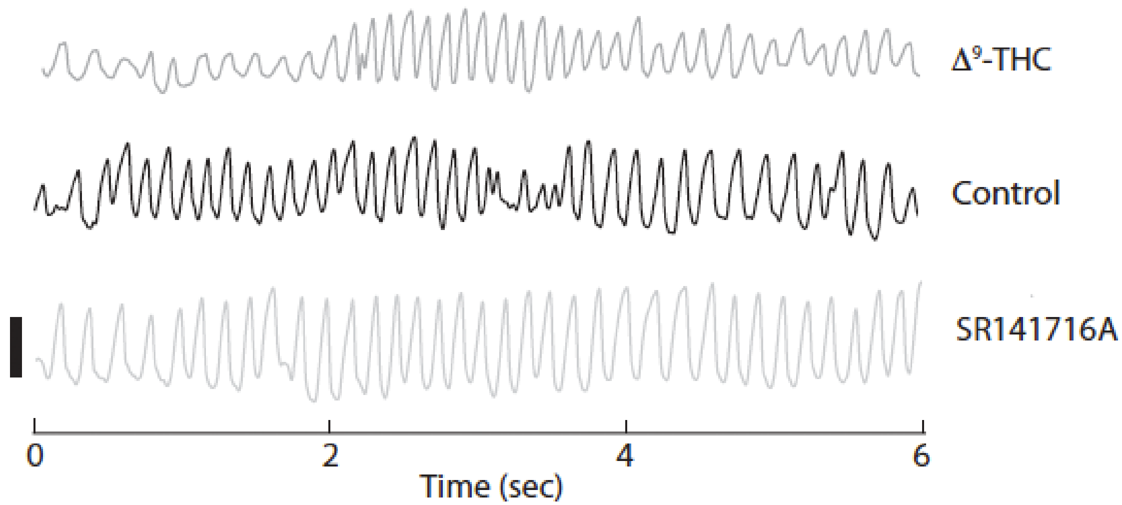
slow   fast   slow

with $d\phi(t)/dt = 2\pi f_{whisk}$ for rhythmic whisking

Question

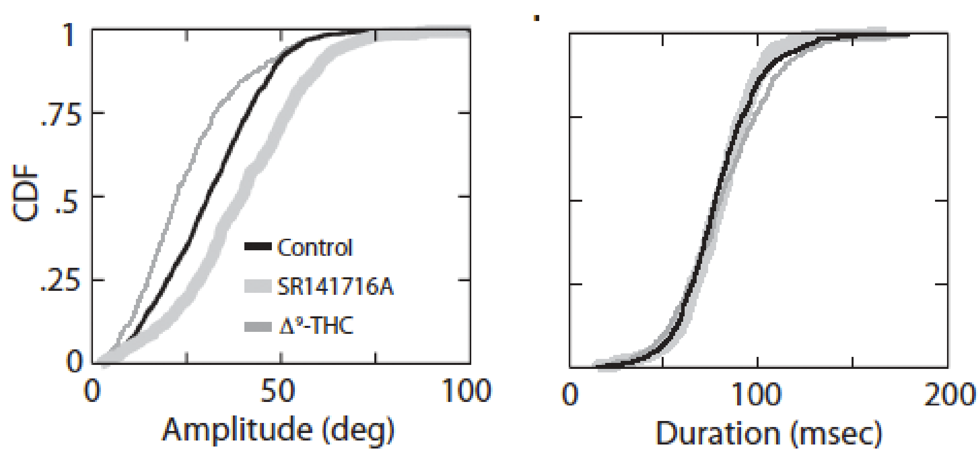
Where, if anywhere, is the locus for generation of the fast signal?

Pharmacological decoupling of the control for whisking amplitude and frequency (Pietr, Knutsen, Shore, Ahissar & Vogel 2010)



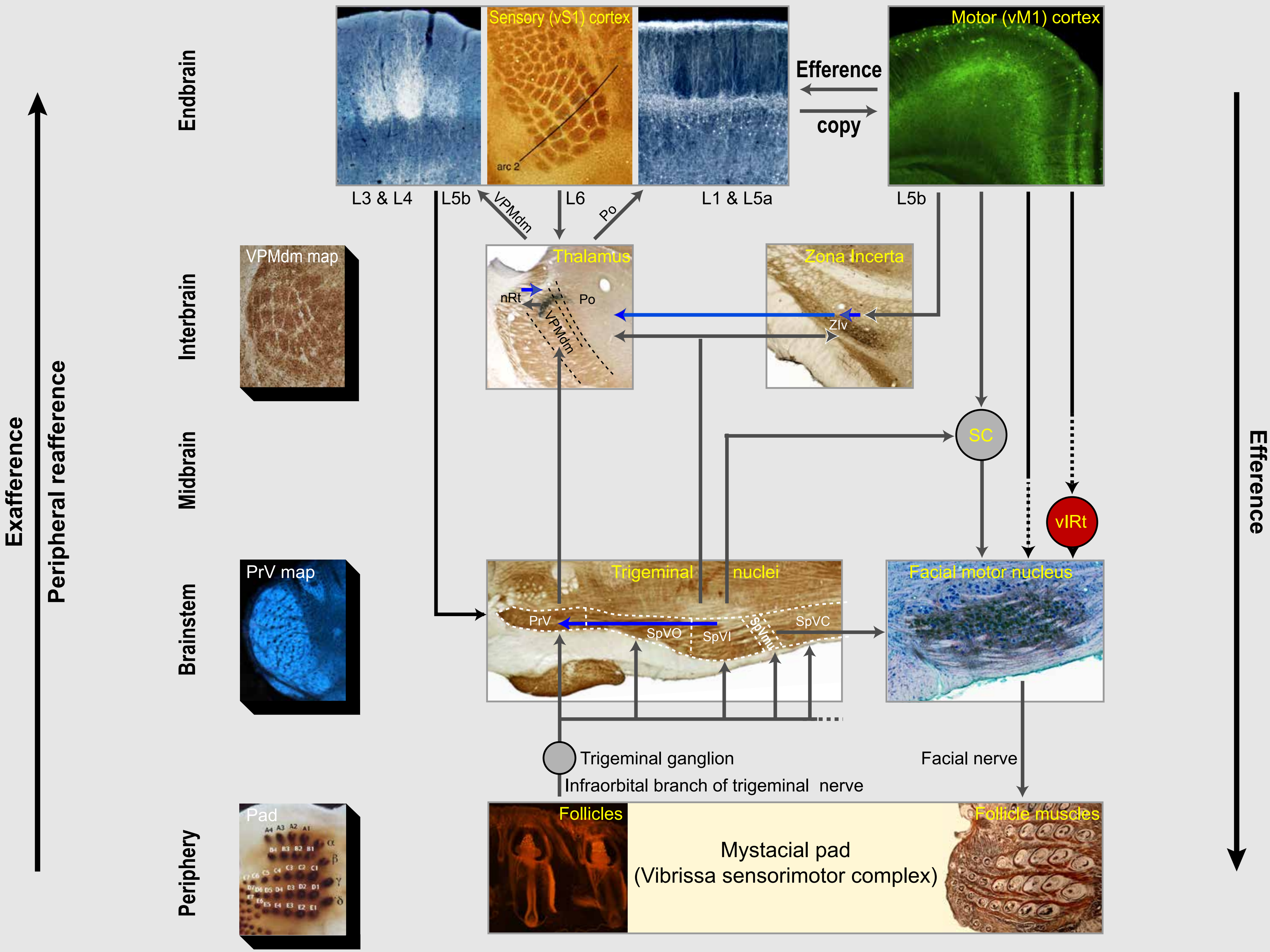
Endocannabinoid agonist

Endocannabinoid antagonist



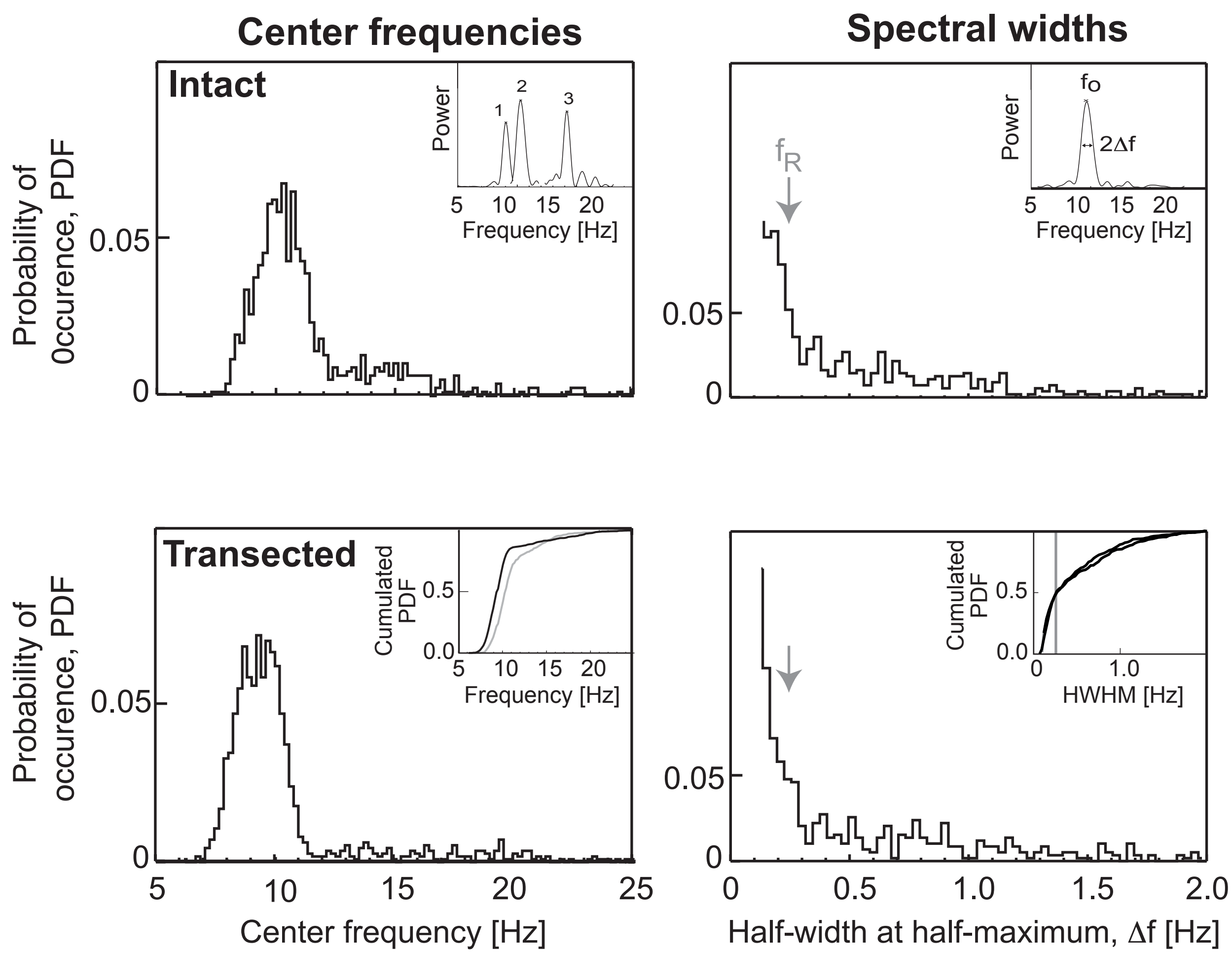
Suggests selected control of fast versus slow whisking parameters

Signal flow and computing in sensorimotor loops of the vibrissa system



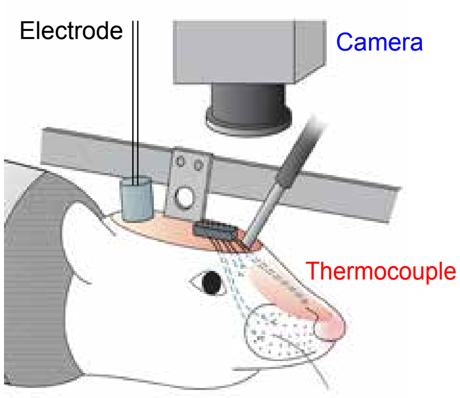
Modified from Kleinfeld & Deschenes (Neuron 2011)

Whisking occurs without sensory feedback

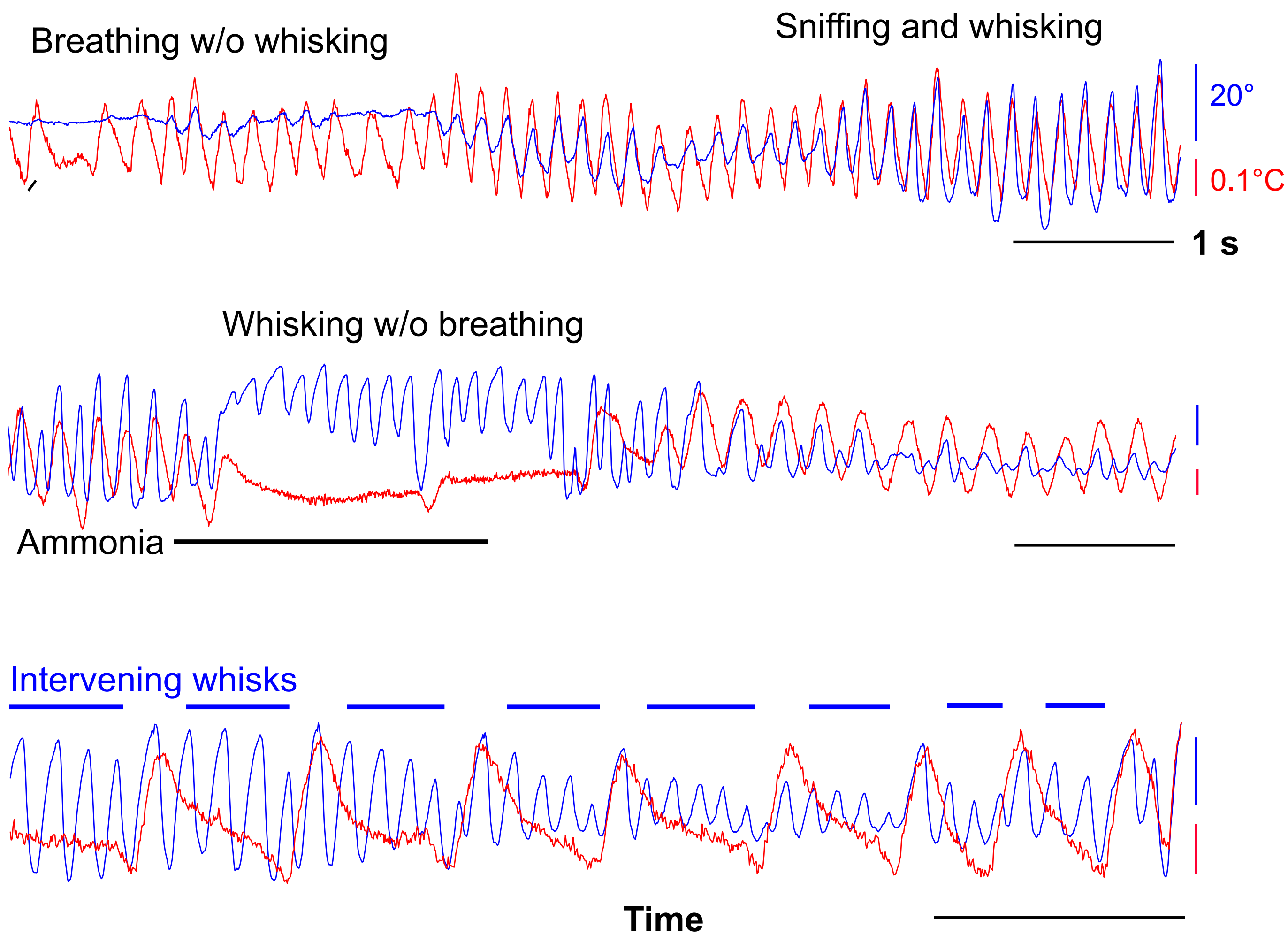


Implies presence of a CPG

Berg & Kleinfeld (2004 J Neurophysiol)

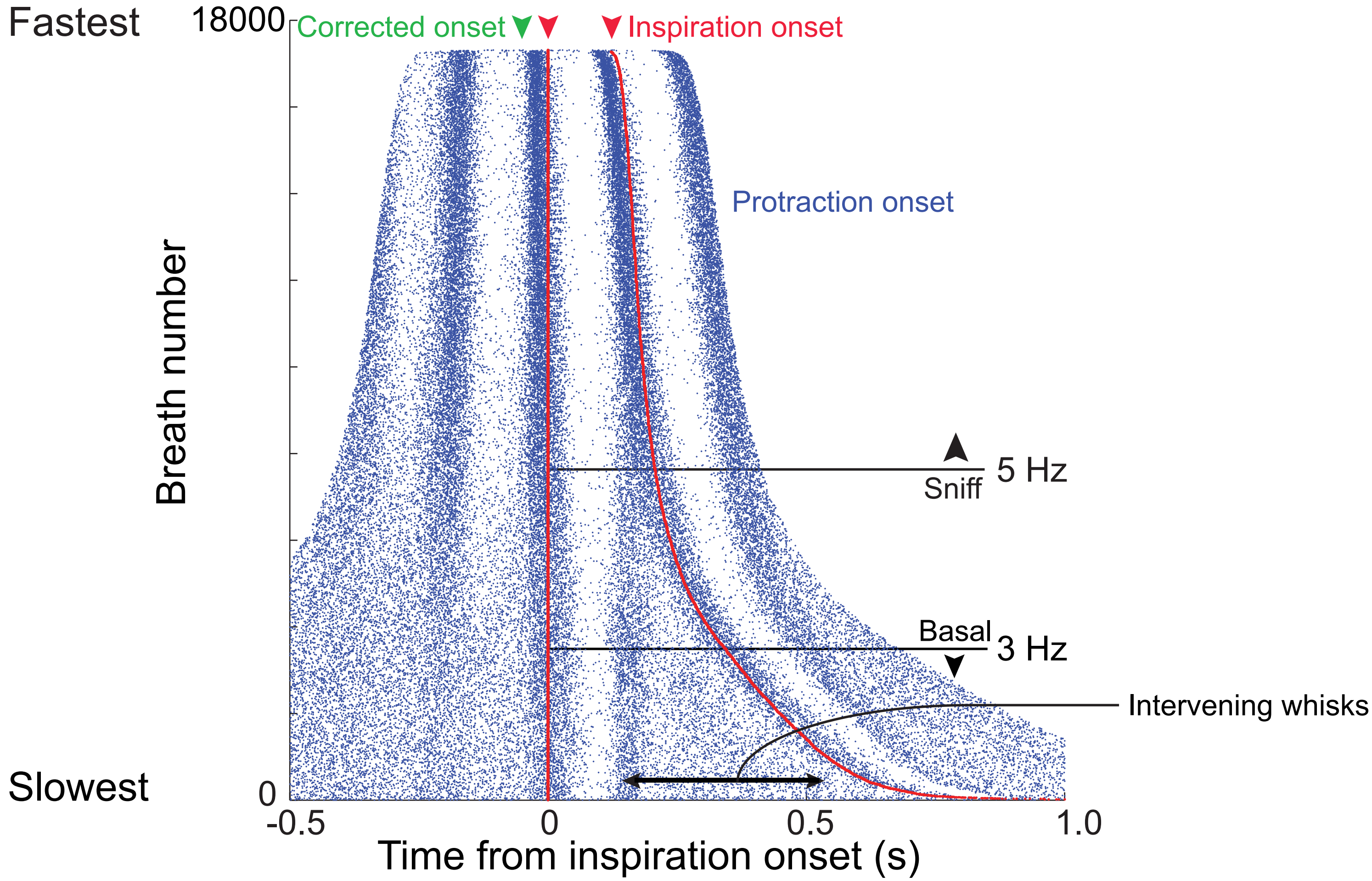


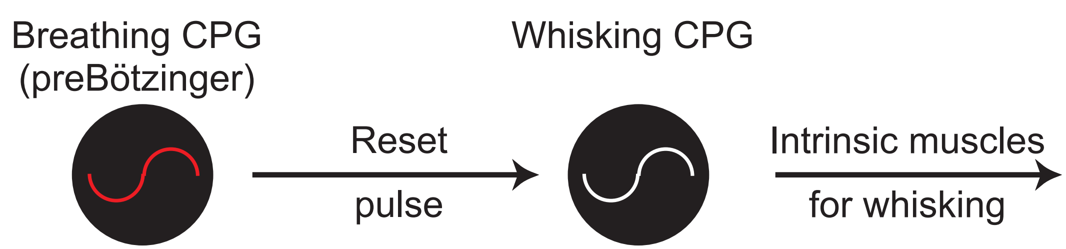
Phase resetting of rhythmic whisking by breathing (sniffing & basal respiration)



Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

Respiration resets whisking oscillations



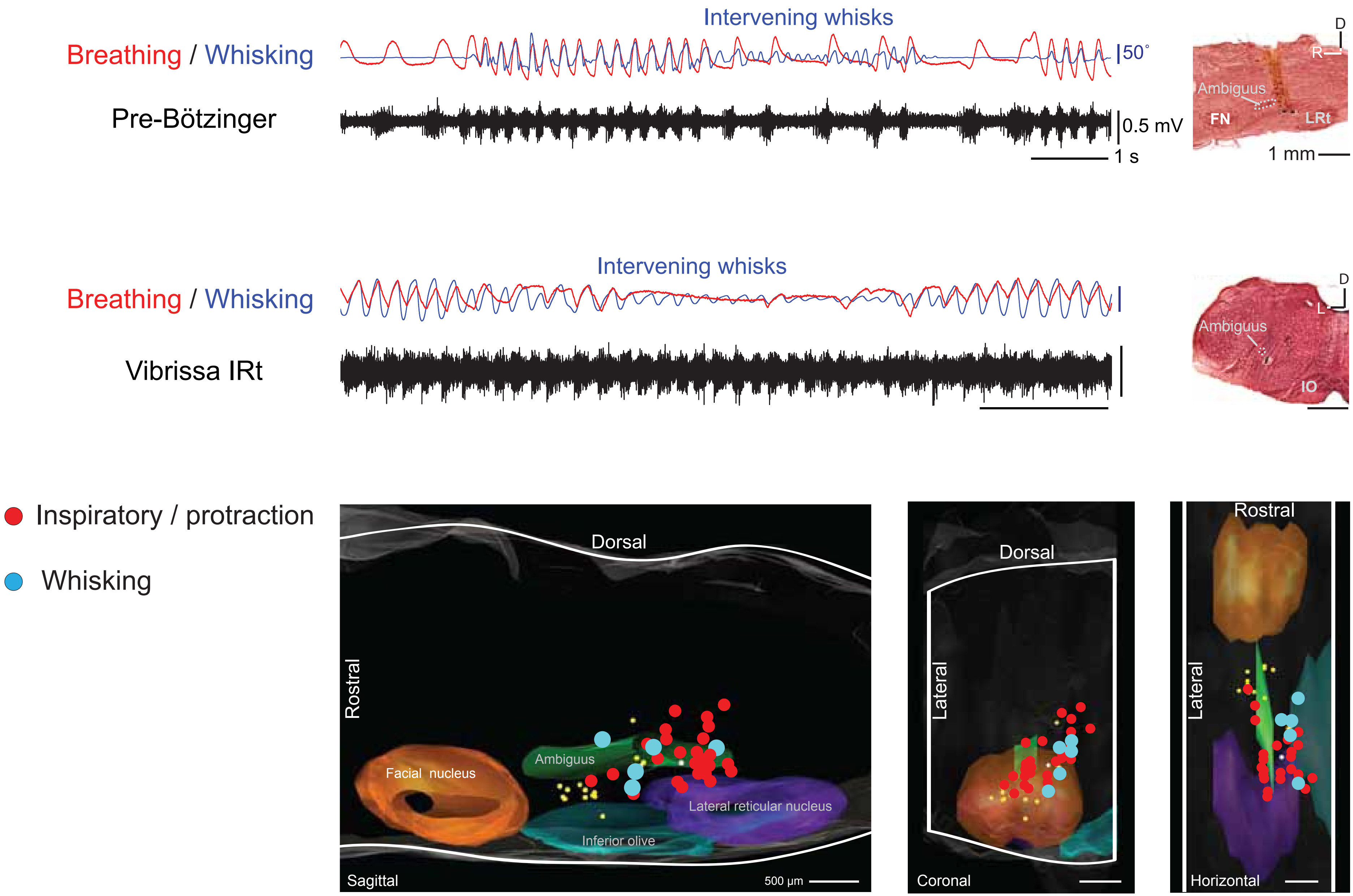


Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

Lesson

PreBötzinger respiratory complex is involved in protraction phase of whisking pattern generation

Units in the intermediate reticular formation (IRt) that report inspiration versus protraction



Moore*, Deschenes*, Huber, Smear, Demers & Kleinfeld (under revision)

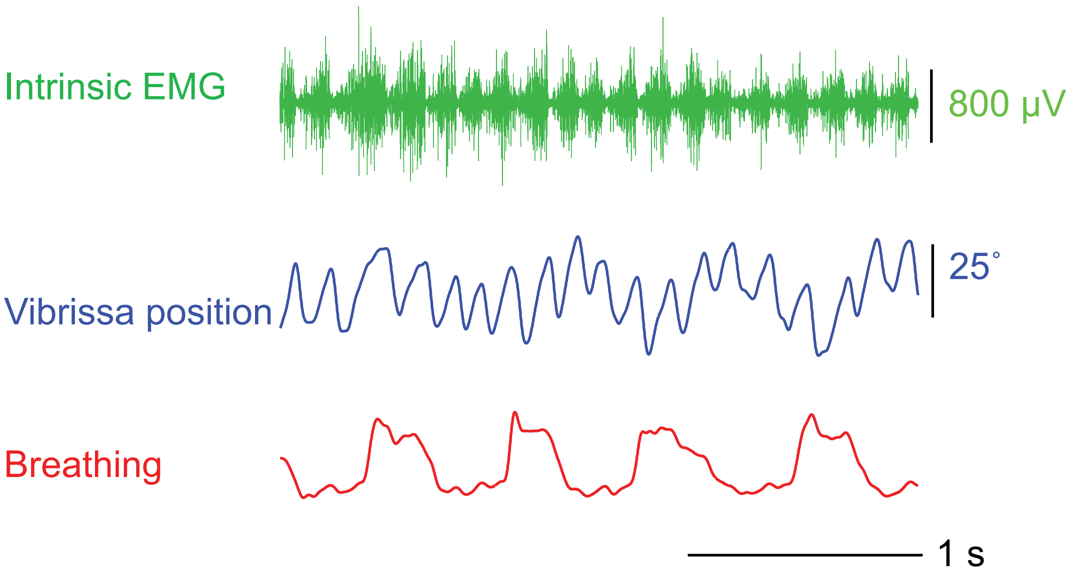
Lesson

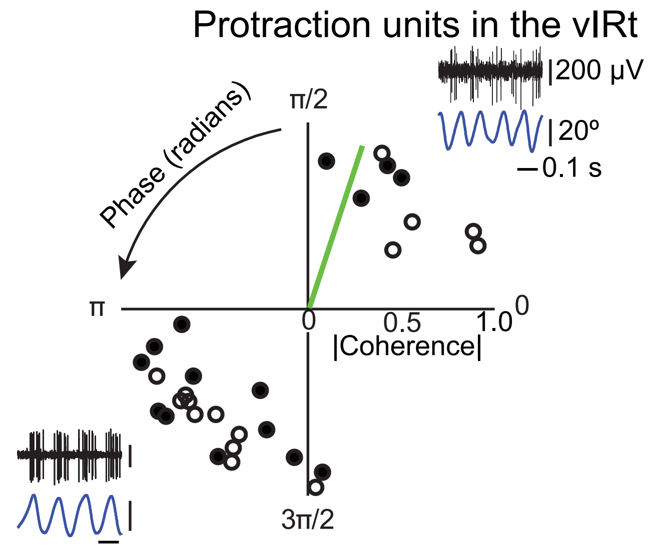
A newly recognized zone of neurons in the IRt formation code rhythmic motion of the vibrissa

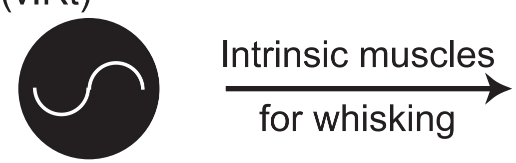
Question

Are these units sufficient to drive rhythmic motion?

Kainic acid activates the vIRt, which drives facial motoneurons







Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Moore, Deschenes, Kurnikova & Kleinfeld (Nature Protocols 2014)

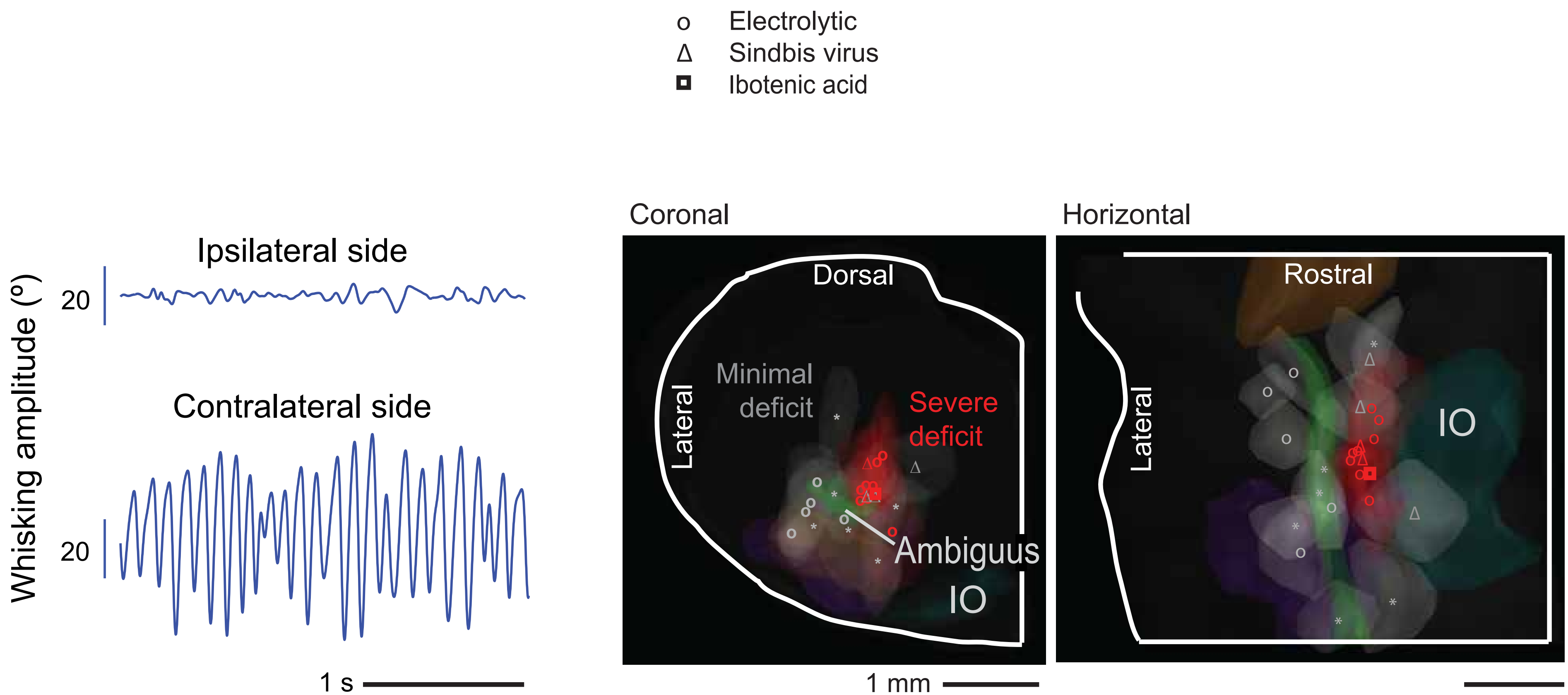
Lesson

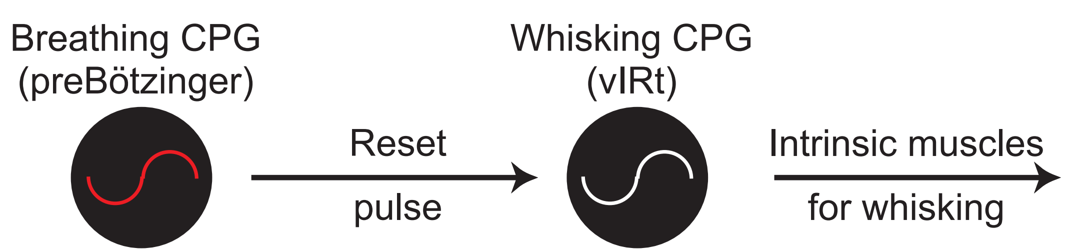
A newly recognized zone of neurons in the IRt formation can drive rhythmic motion of the vibrissa

Question

Are these units necessary to drive rhythmic motion?

Lesion of the vIRt blocks exploratory whisking





Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

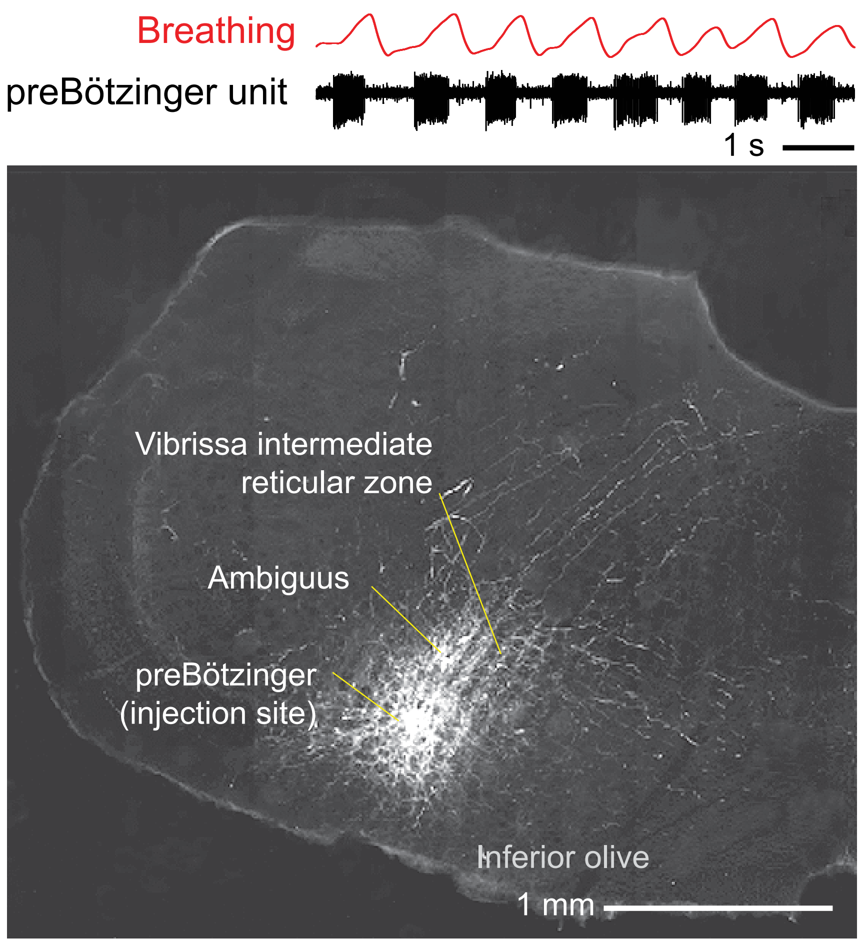
Lesson

Units in the vIRt are necessary for rhythmic motion of the vibrissae

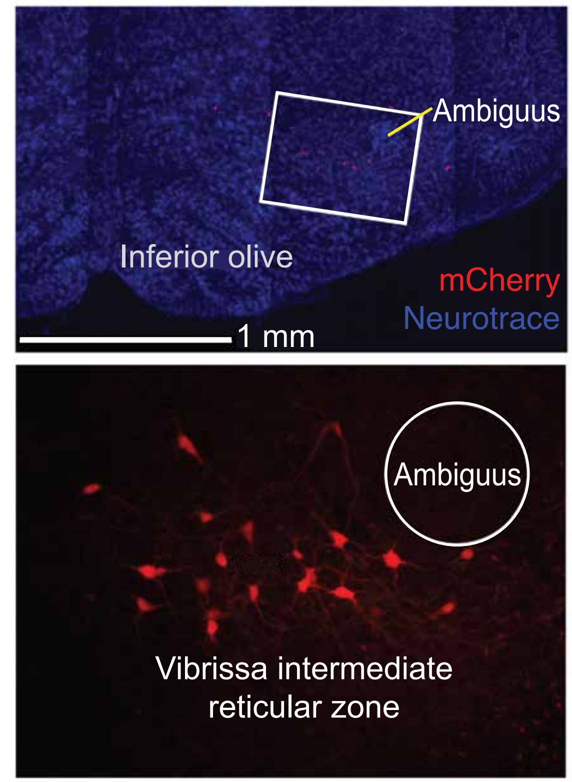
Question

Can we identify the monosynaptic connections of a minimal breathing and whisking circuit?

PreBötzinger units project to the vibrissa zone of the IRt while facial motoneurons receive premotor input from the vIRT

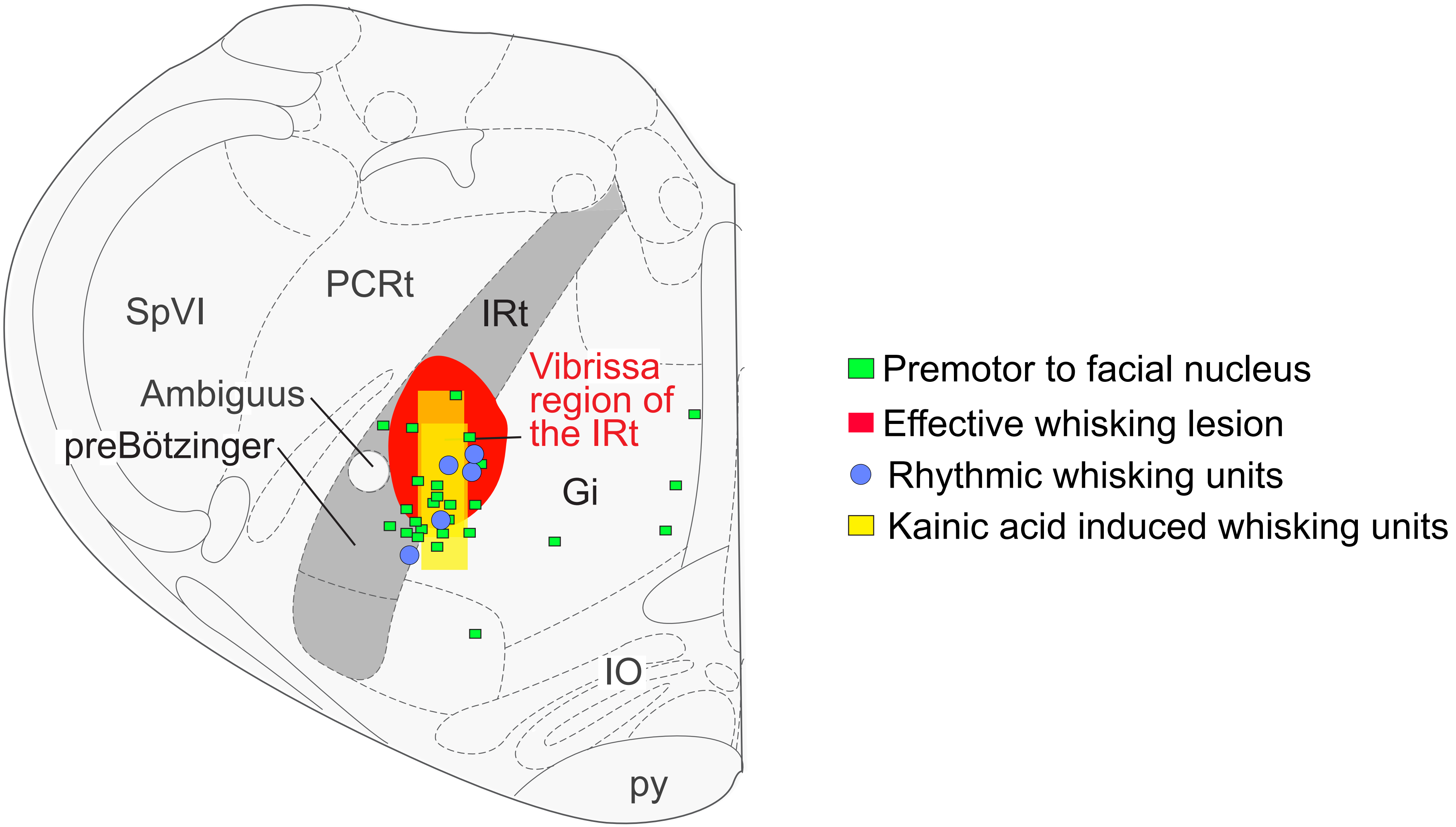


Disynaptic retrograde labeling:
ΔG-rabies injected into vibrissa muscles of ChAT-RG mice



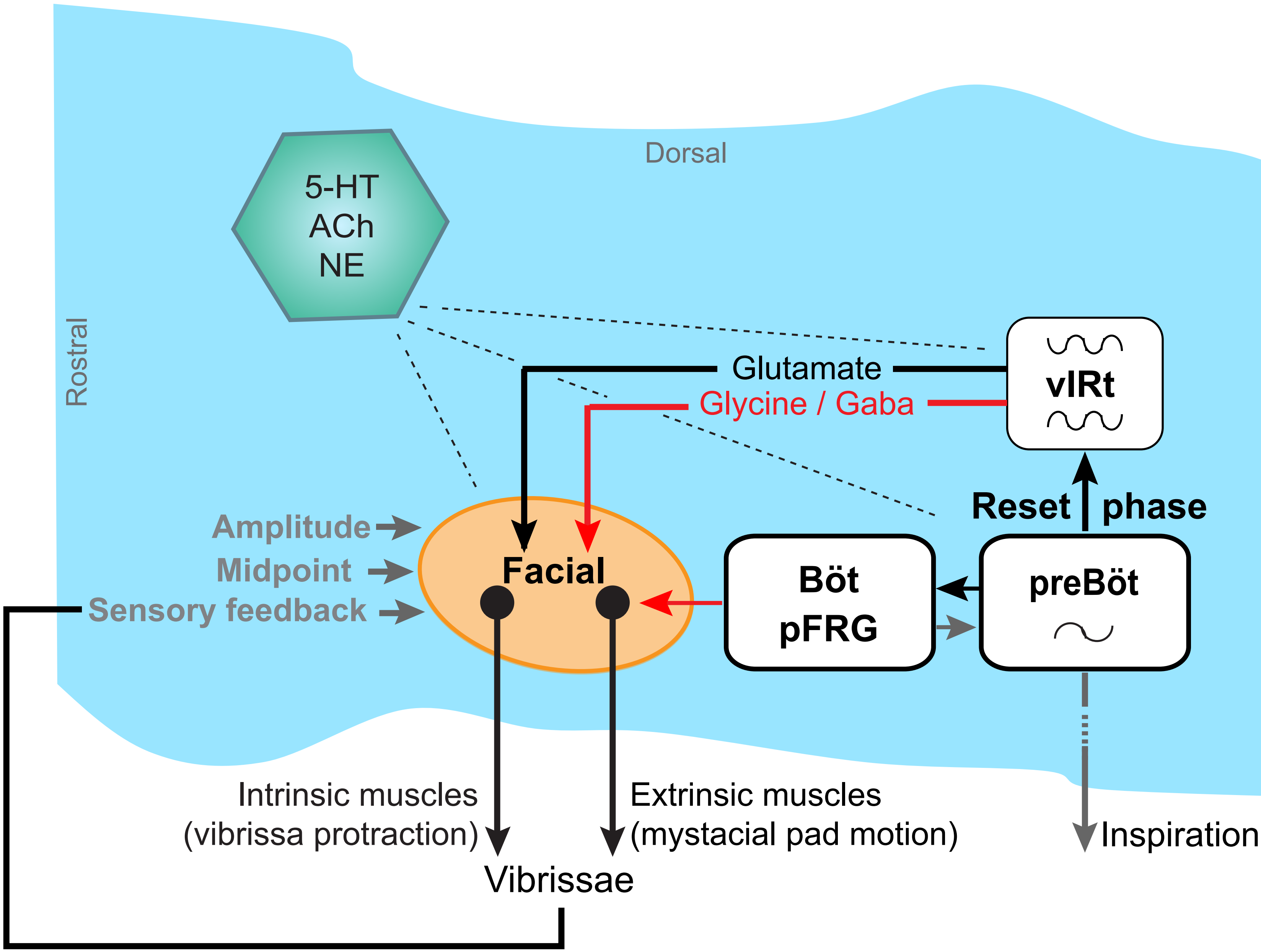
Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Takatoh, Nelson, Zhou, Bolton, Ehlers, Arenkiel, Mooney & Wang (Neuron 2012)

Compendium of evidence for a vibrissa pattern generator region within the intermediate reticular formation (vIRt)



Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

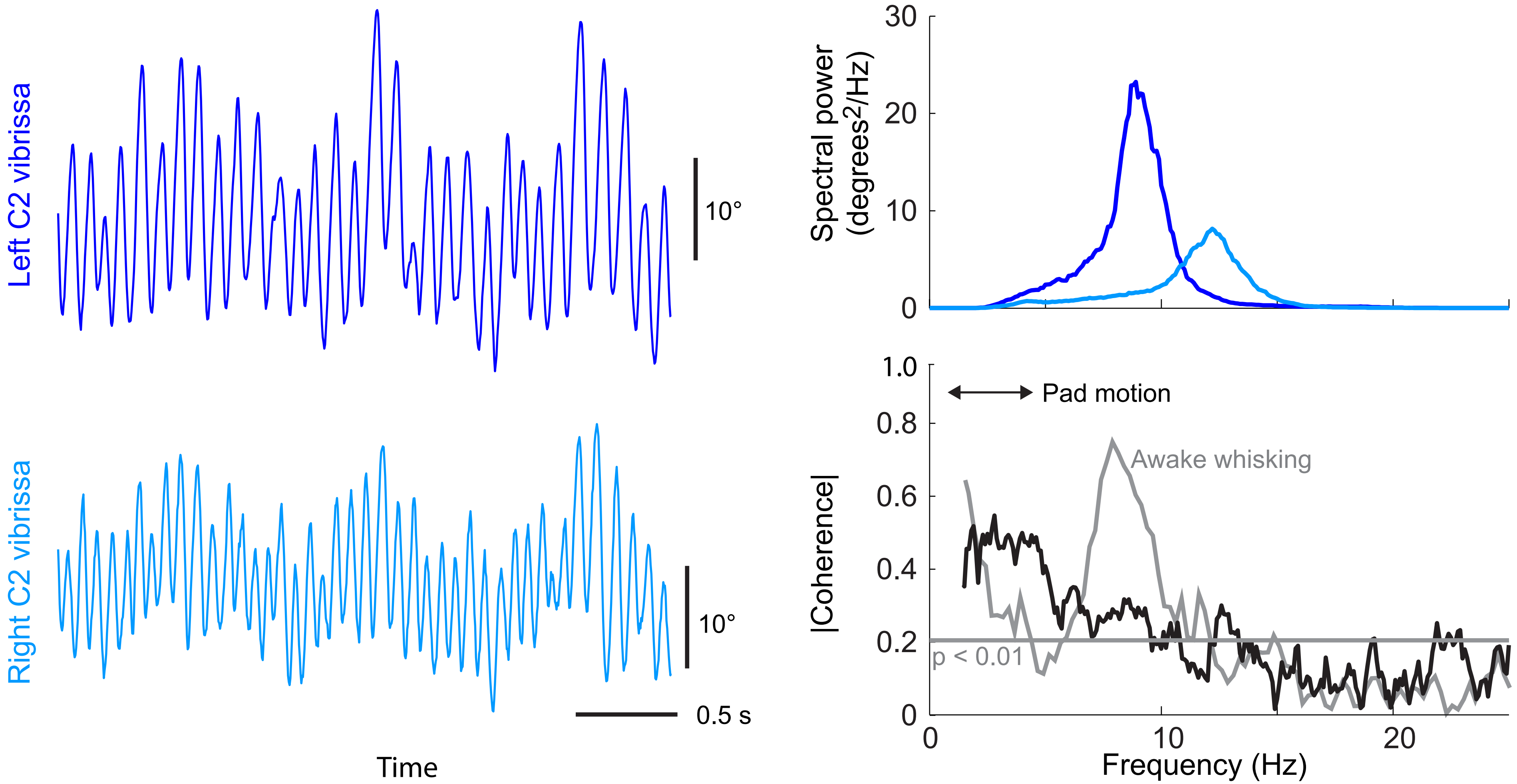
Model of the brainstem rhythmic generator for whisking



Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

Matthews, Deschênes, Furuta, Moore, Wang, Karten* & Kleinfeld* (Journal of Comparative Neurology 2015)

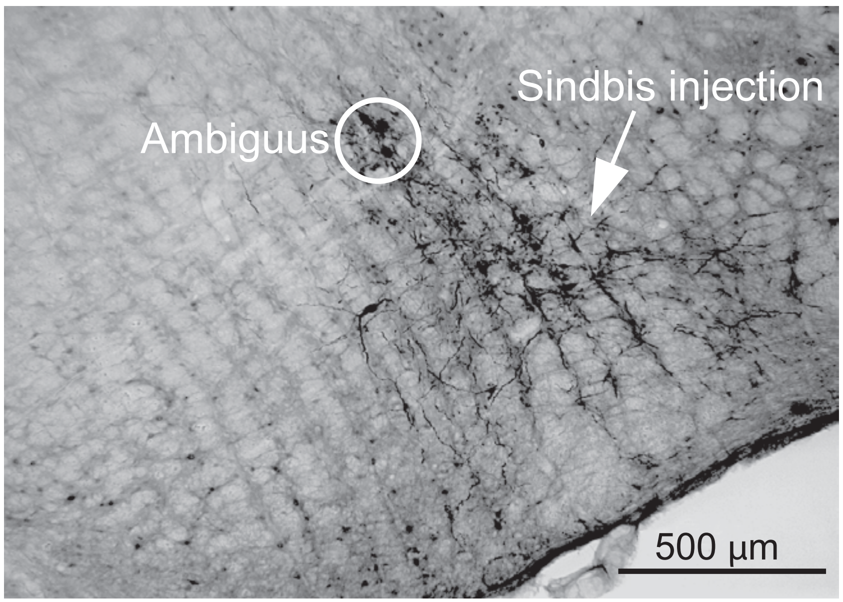
Kainic acid induced whisking is asynchronous



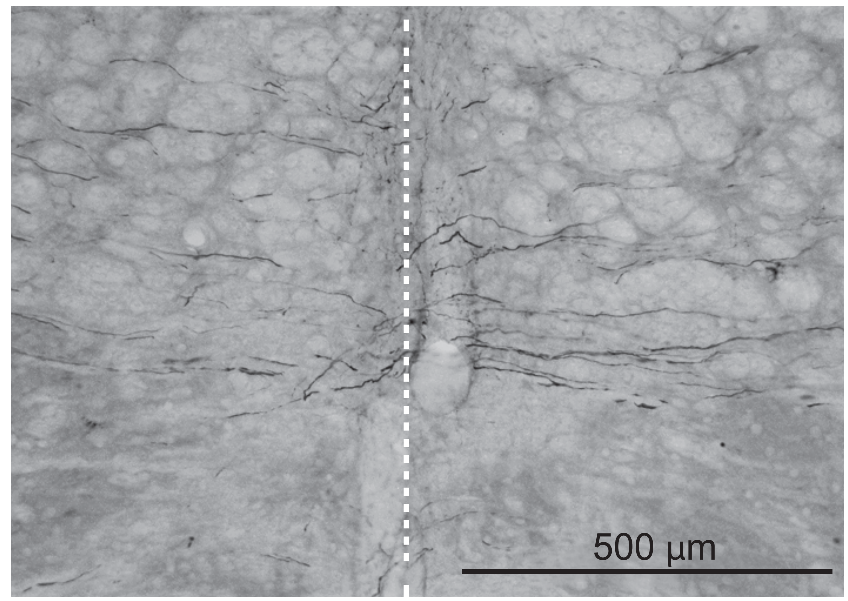
Moore, Deschênes, Kurnikova & Kleinfeld (Nature Protocols 2014)

Respiratory premotor neurons (preBötzinger) in opposite hemispheres are connected by commissural projections

(Koizumi, Koshiya, Chia, Cao, Nugent, Zhang & Smith, J Neurosci 2013)

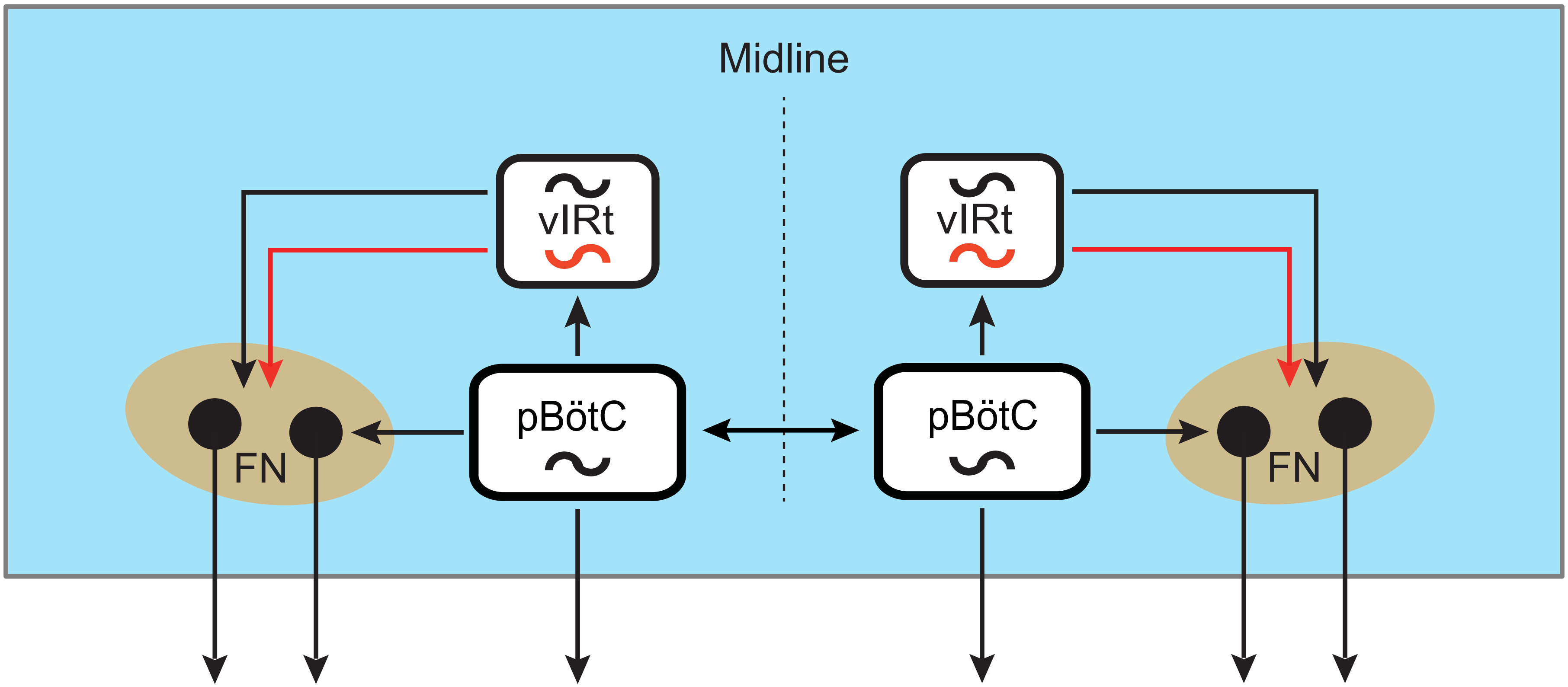


Midline



Deschênes, Moore, Demers, Takatoh, Furuta, Kurnikova, Wang & Kleinfeld (manuscript in preparation)

Synchronization of bilateral rhythmic whisking is mediated by the preBötzinger interhemispheric connections



Deschênes, Moore, Demers, Takatoh, Furuta, Kurnikova, Wang & Kleinfeld (manuscript in preparation)

Summary lesson

Breathing coordinates rhythmic whisking

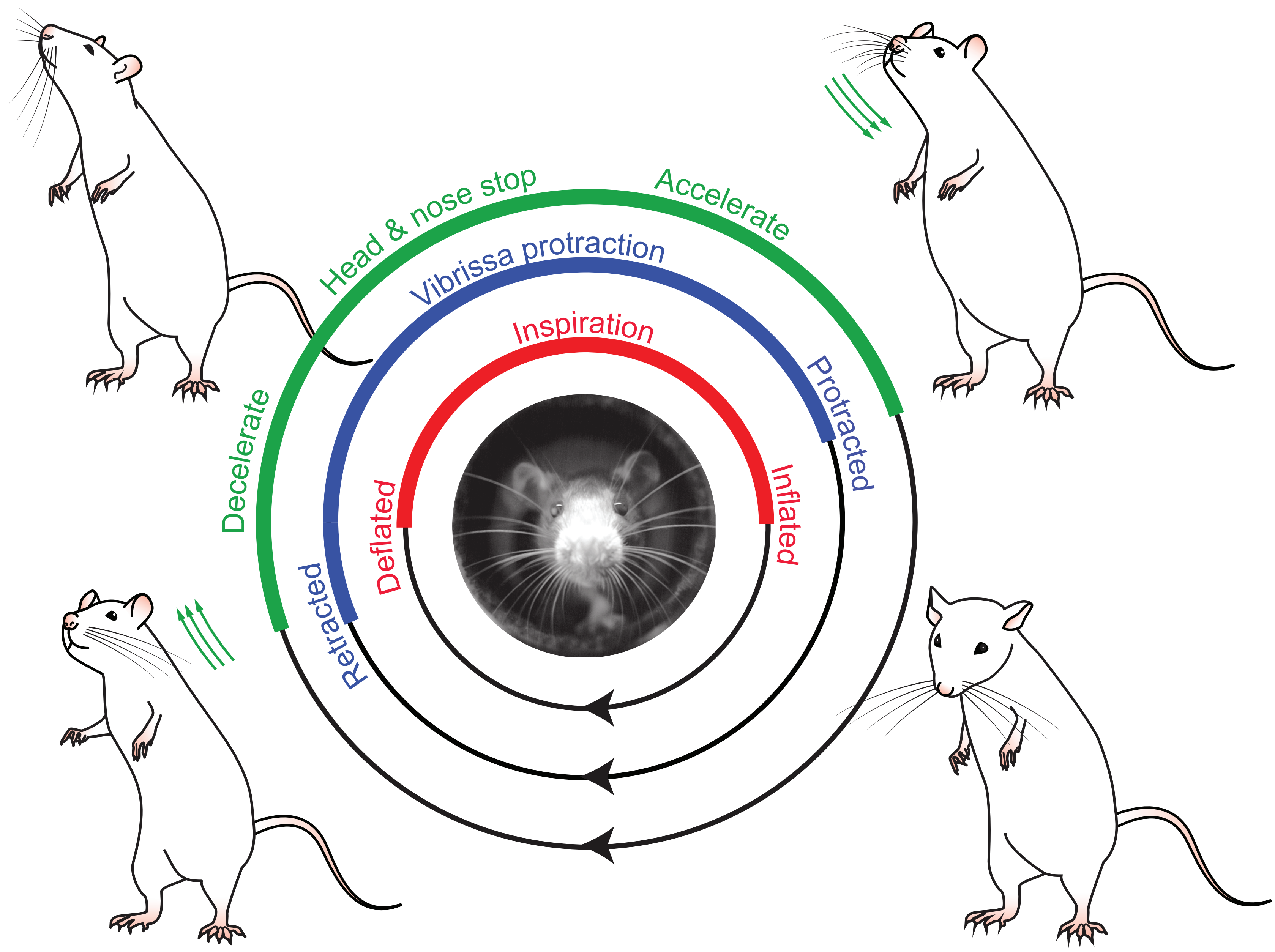
Sniffing: A master clock for orofacial rhythms?

- Coordination of orofacial actions during exploration

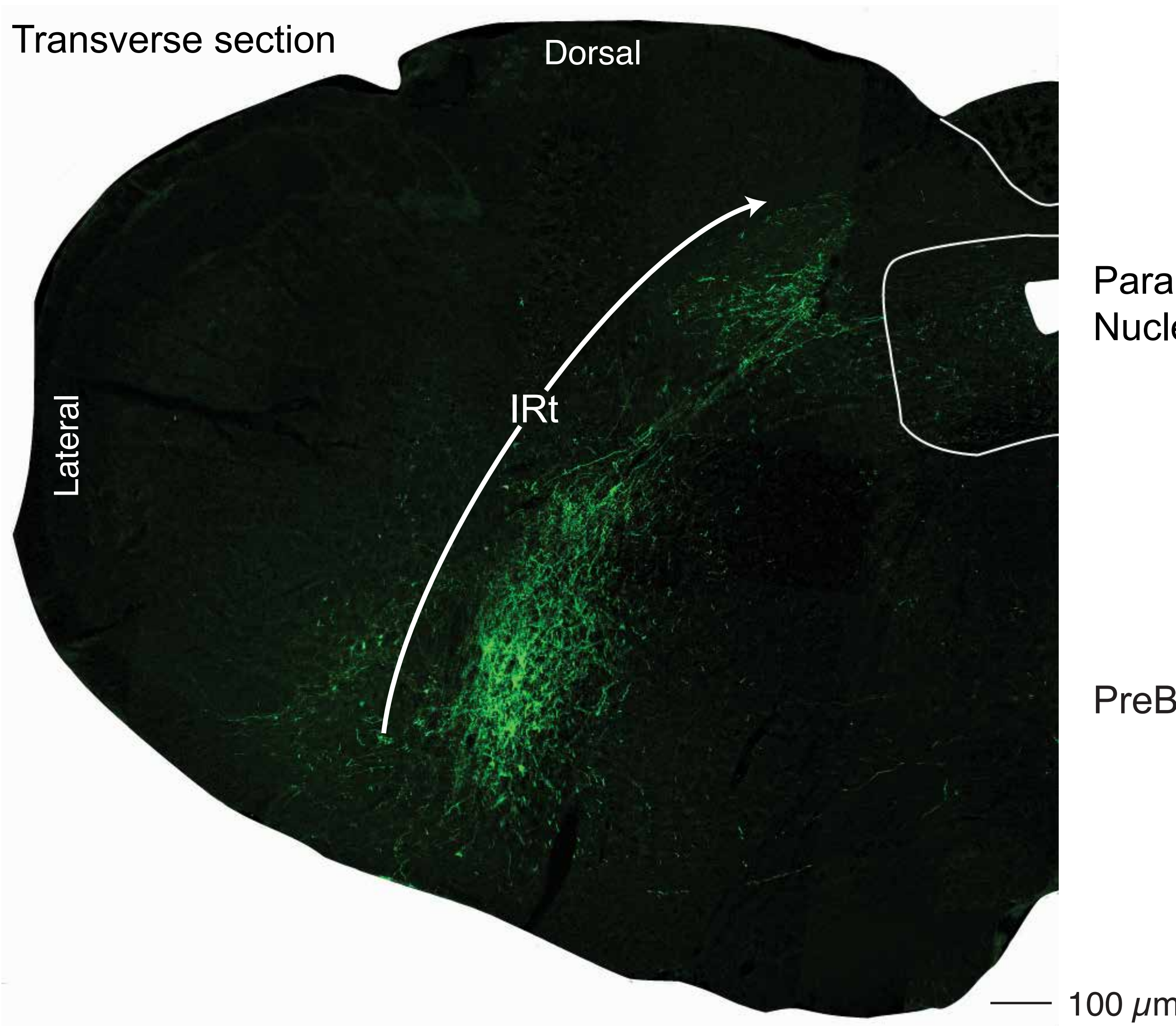
- Brainstem circuits for control of rapid vibrissa motion

- Circuitry for coordination of *all* orofacial motor actions

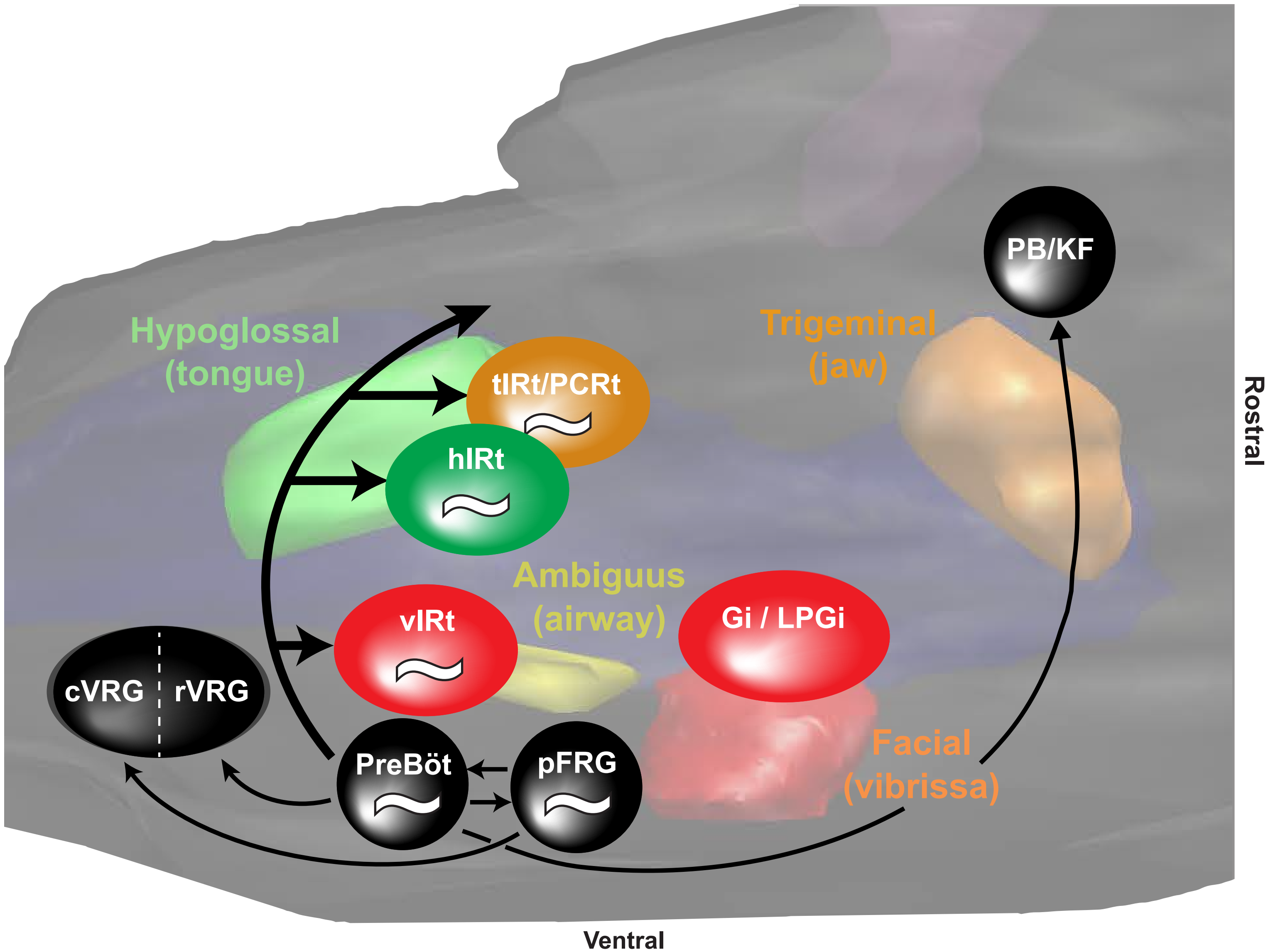
The cycle of exploratory orofacial actions linked to sniffing



Axon collaterals from the preBötzinger, the inhalation oscillator, span the full extent of the intermediate reticular zone (IRt)
(Tan, Pagliardini, Yang, Janczewski & Feldman, J Comp Neurol 2010)



Connections from preBötzinger, the inhalation CPG, to brainstem premotor nuclei involved in orofacial actions



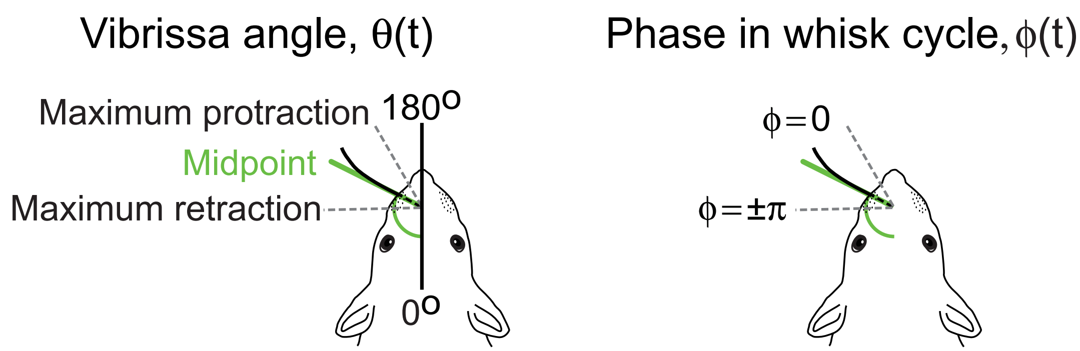
Kleinfeld, Deschenes, Wang & Moore (Nature Neuroscience 2014)
Moore, Kleinfeld & Wang (Trends in Neuroscience 2014)

These data open up questions in both motor control and sensory coding

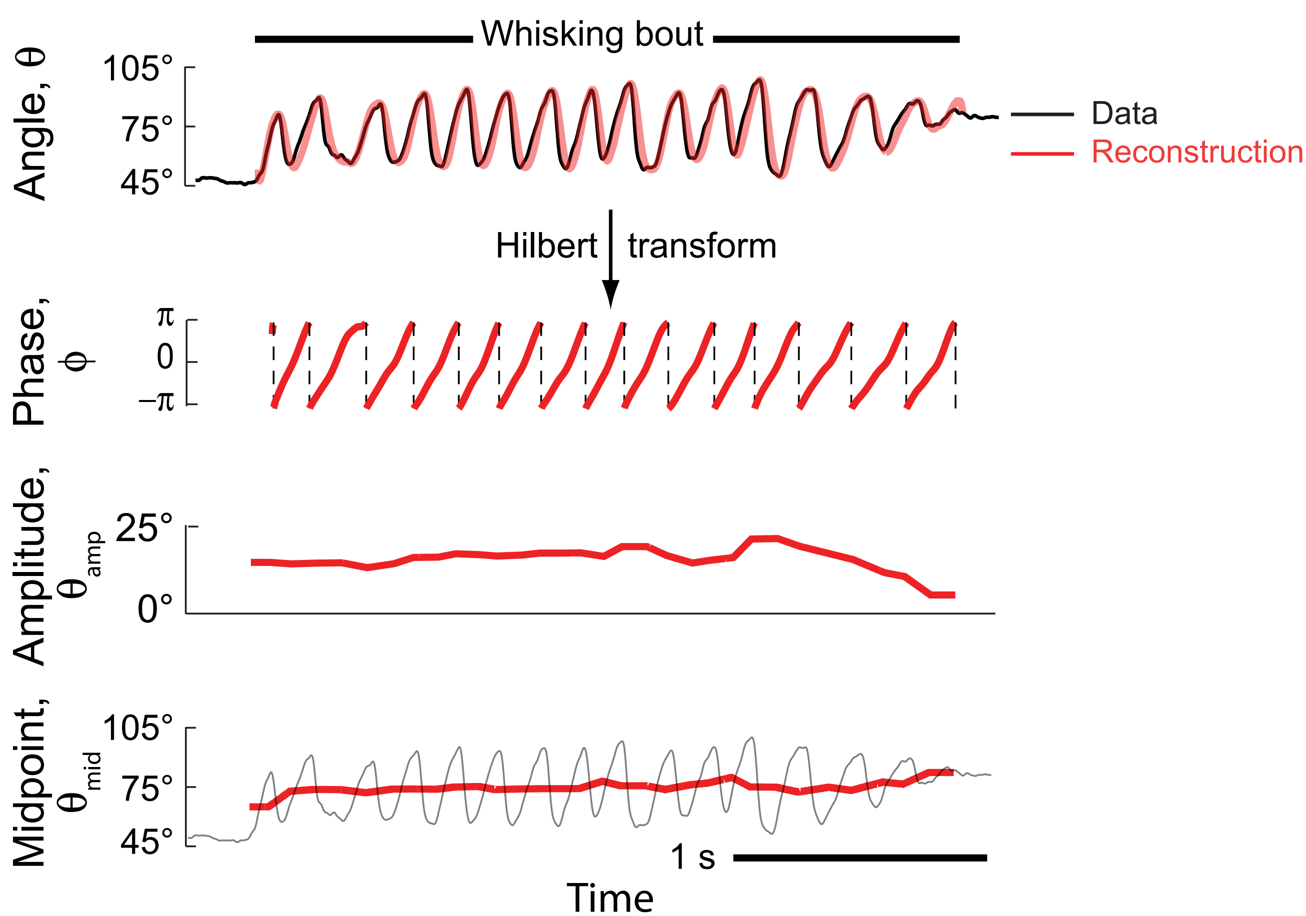
What regulates the slowly varying midpoint of whisking, where midpoint plays the role of posture in locomotion?

Does the breathing clock act as a temporal signature to bind separate sensory inputs?

Angular versus phase coordinates for whisking

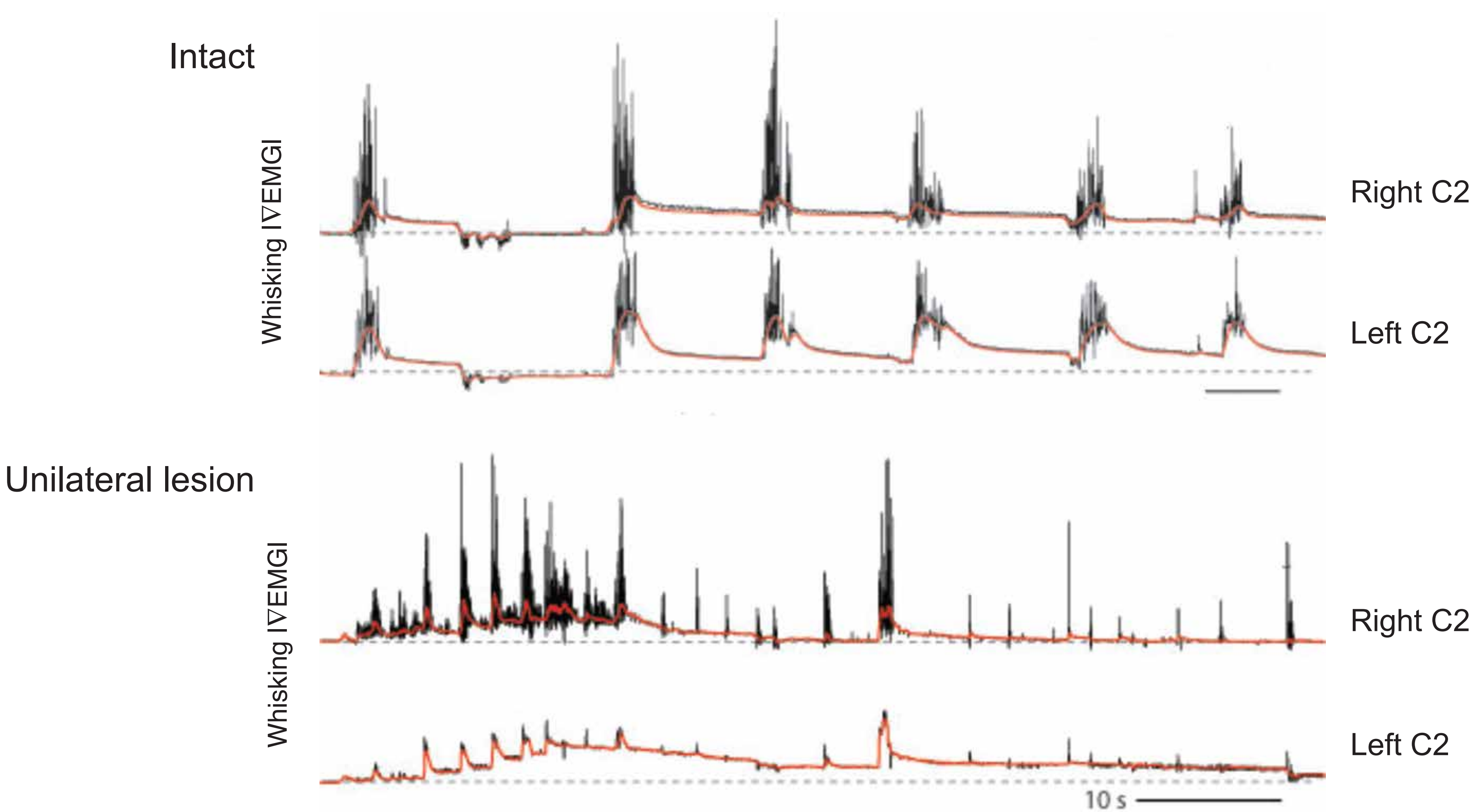


Decomposition of the whisking signal into phase, amplitude and midpoint



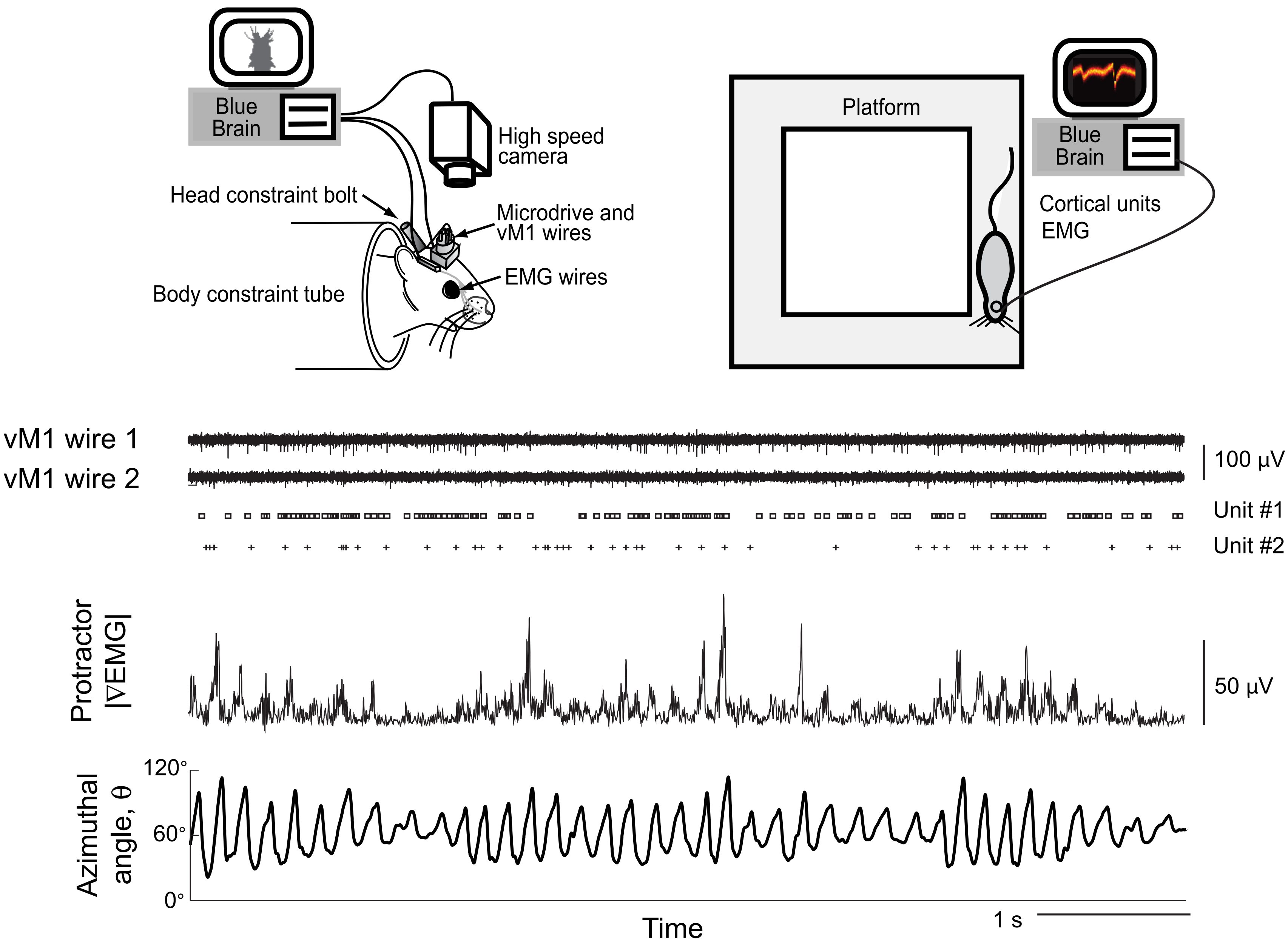
Hill, Curtis, Moore & Kleinfeld (Neuron 2011)

Lesion of the whisking oscillator (vIRt) does *not* effect the midpoint: Preliminary evidence for decoupled fast versus slow brainstem control



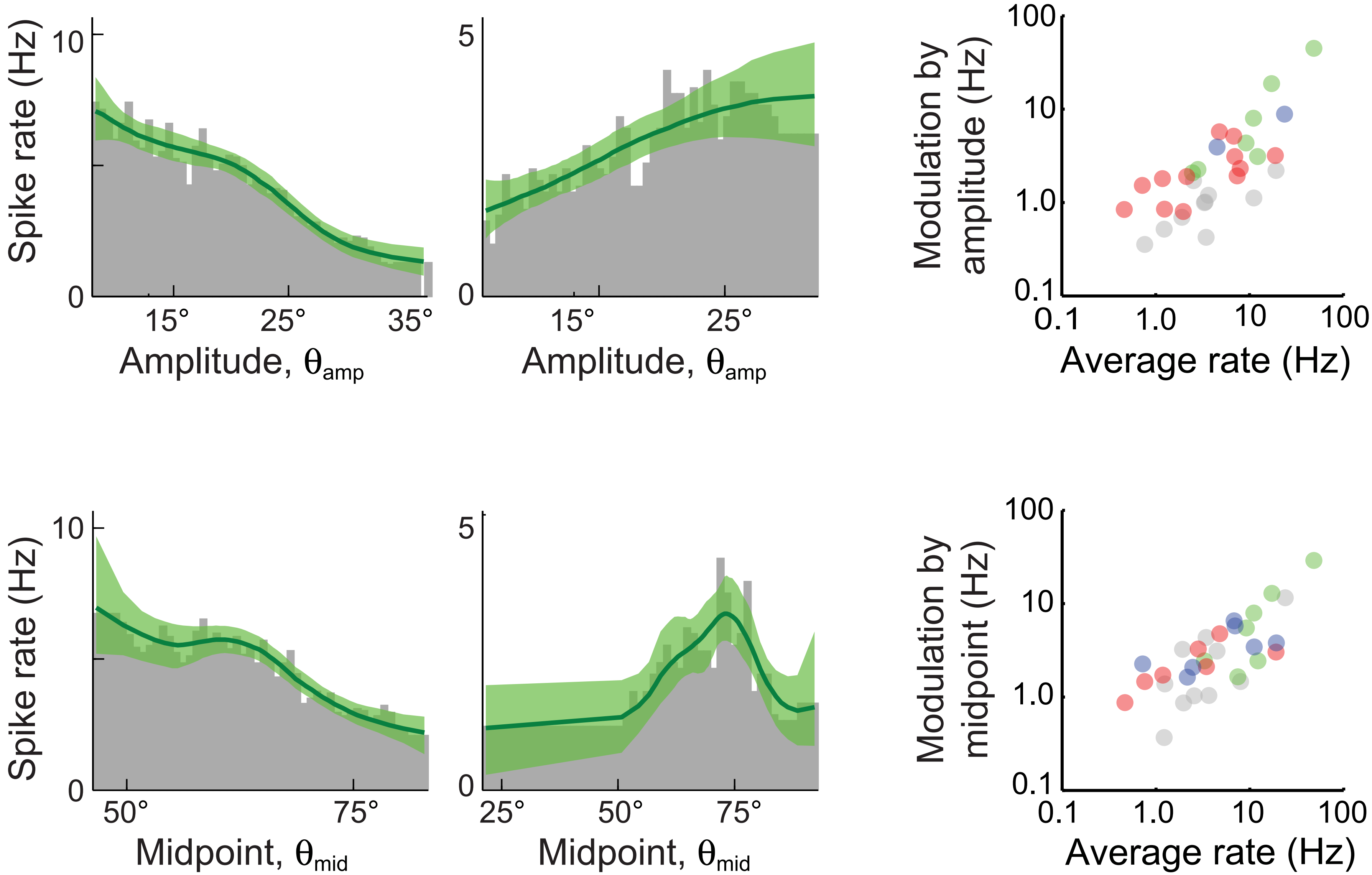
Deschenes, Moore & Kleinfeld (unpublished)

Whisking and unit activity in vibrissa primary motor (vM1) cortex



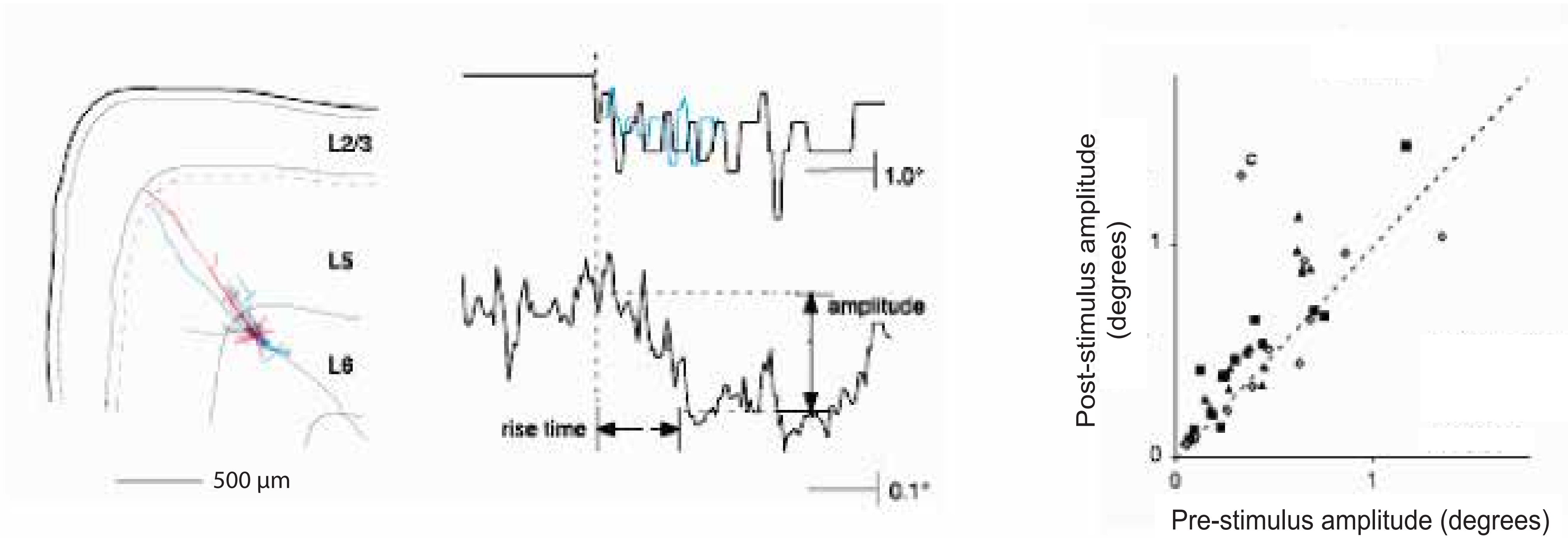
Hill, Curtis, Moore & Kleinfeld (Neuron 2011)

Rodent vM1 cortex reports the slowly varying amplitude and midpoint of whisking



Hill, Curtis, Moore & Kleinfeld (Neuron 2011)

Much previous work showed that stimulation of motor *and* sensory cortices change vibrissa position and/or activate whisking

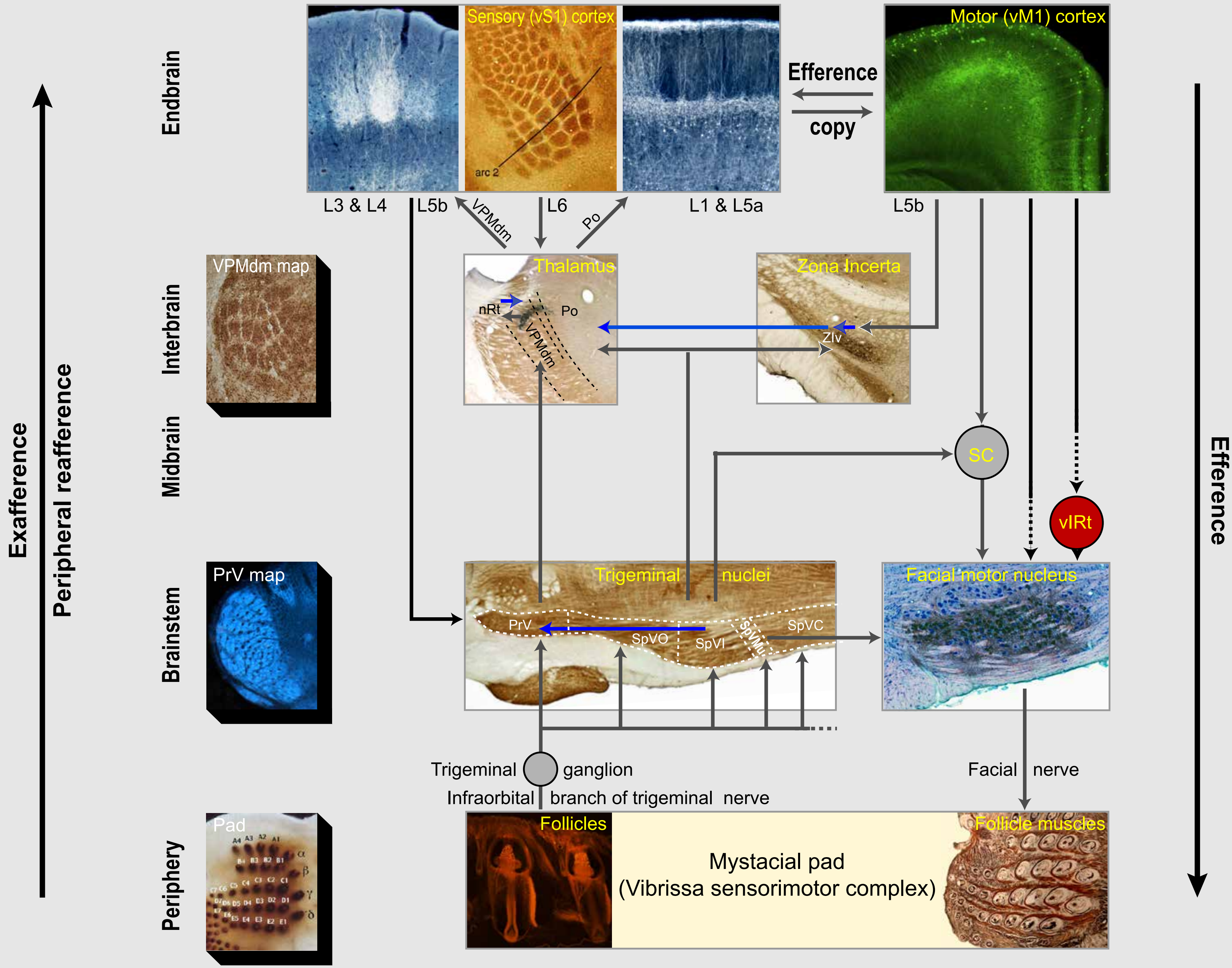


Single neuron stimulation data of Brecht, Schneider, Sakmann & Margrie (Nature 2004)

The pathways for this control are incompletely understood

Here we consider the spinal trigeminal nuclei as premotor nuclei

Signal flow and computing in sensorimotor loops of the vibrissa system



Modified from Kleinfeld & Deschenes (Neuron 2011)

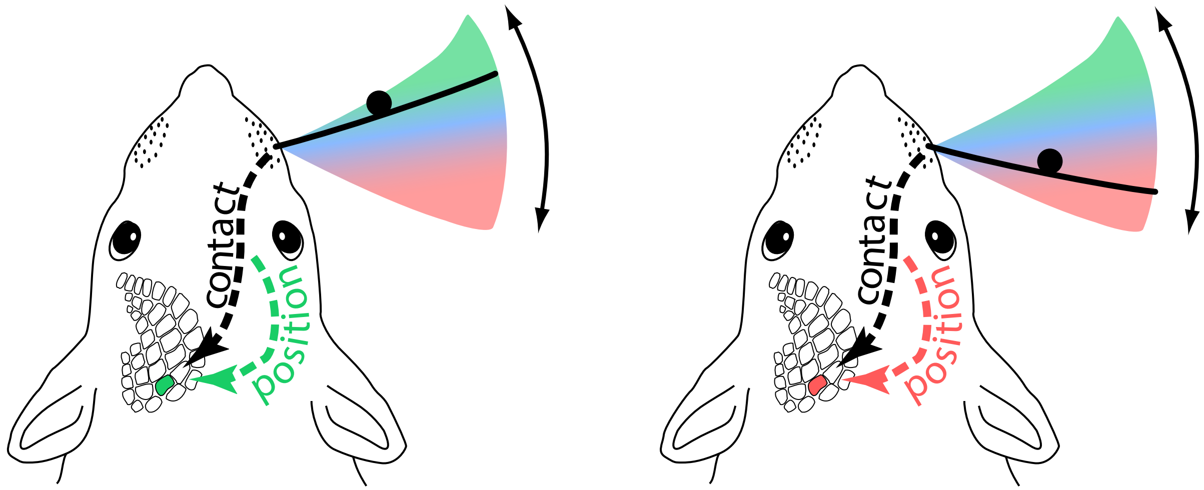
Five Slides of Unpublished Material Were Removed

These data open up questions in both motor control and sensory coding

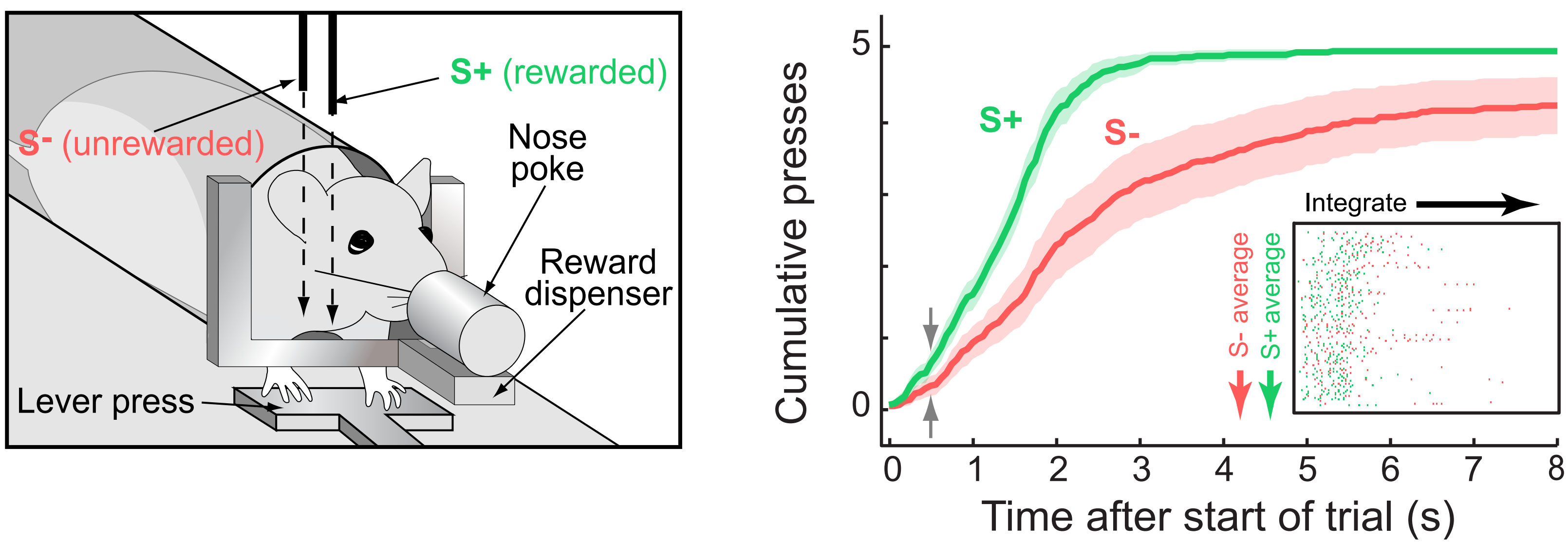
What regulates the slowly varying midpoint of whisking, where midpoint plays the role of posture in locomotion?

Does the breathing clock act as a temporal signature to bind separate sensory inputs?

Paradigm to test if rodents code the azimuthal position of their vibrissae

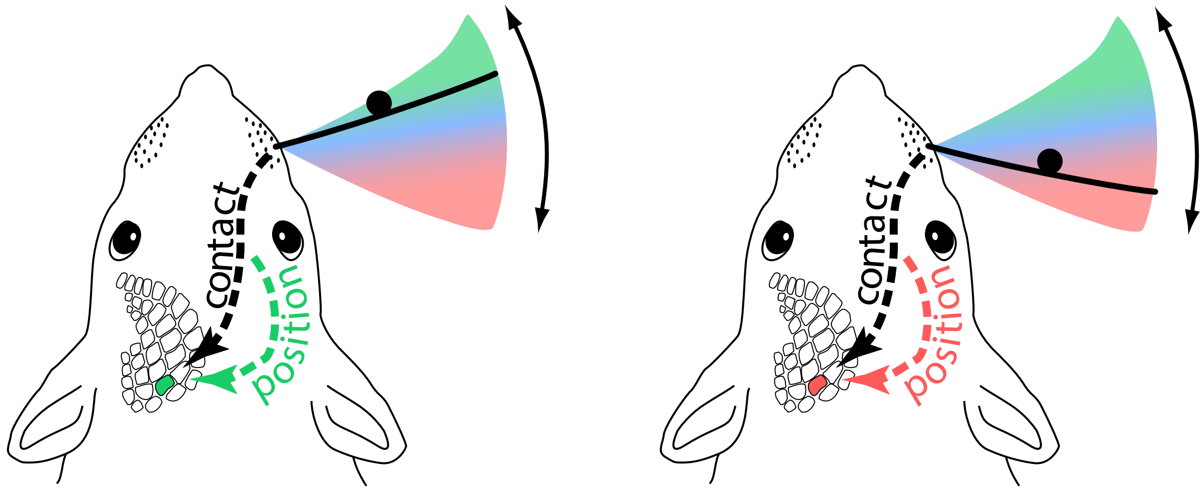


Behavioral evidence that rodents know the position of their vibrissae



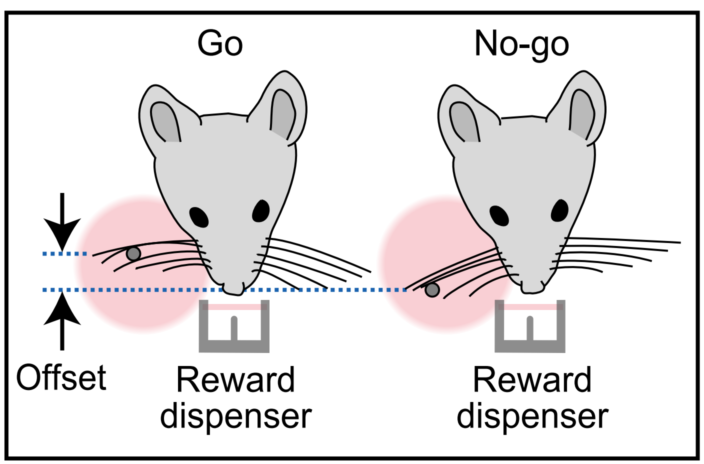
Mehta, Whitmer, Figueroa, Williams & Kleinfeld (PLoS Biology 2007)

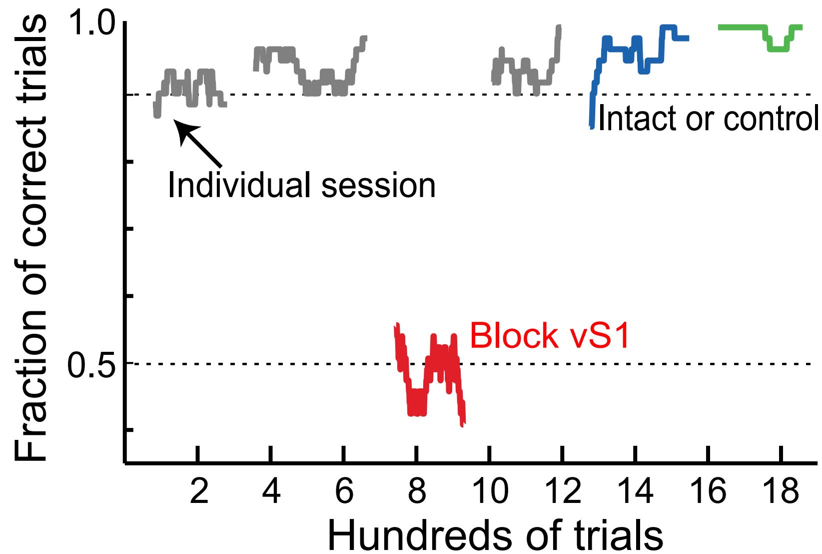
Paradigm to test if rodents code the azimuthal position of their vibrissae



Evidence that vS1 cortex is necessary to report vibrissa position

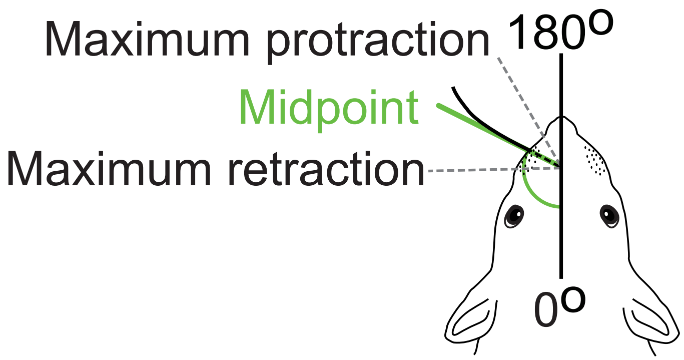
(O'Connor, Clack, Huber, Komiyama, Myers & Svoboda, Journal of Neuroscience 2010)





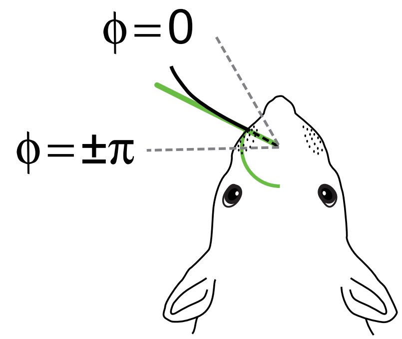
Is the vibrissa touch response conditioned solely by phase?

Touch referenced to vibrissa angle, $\theta(t)$



versus

Touch referenced to phase in whisk cycle, ϕ (t)

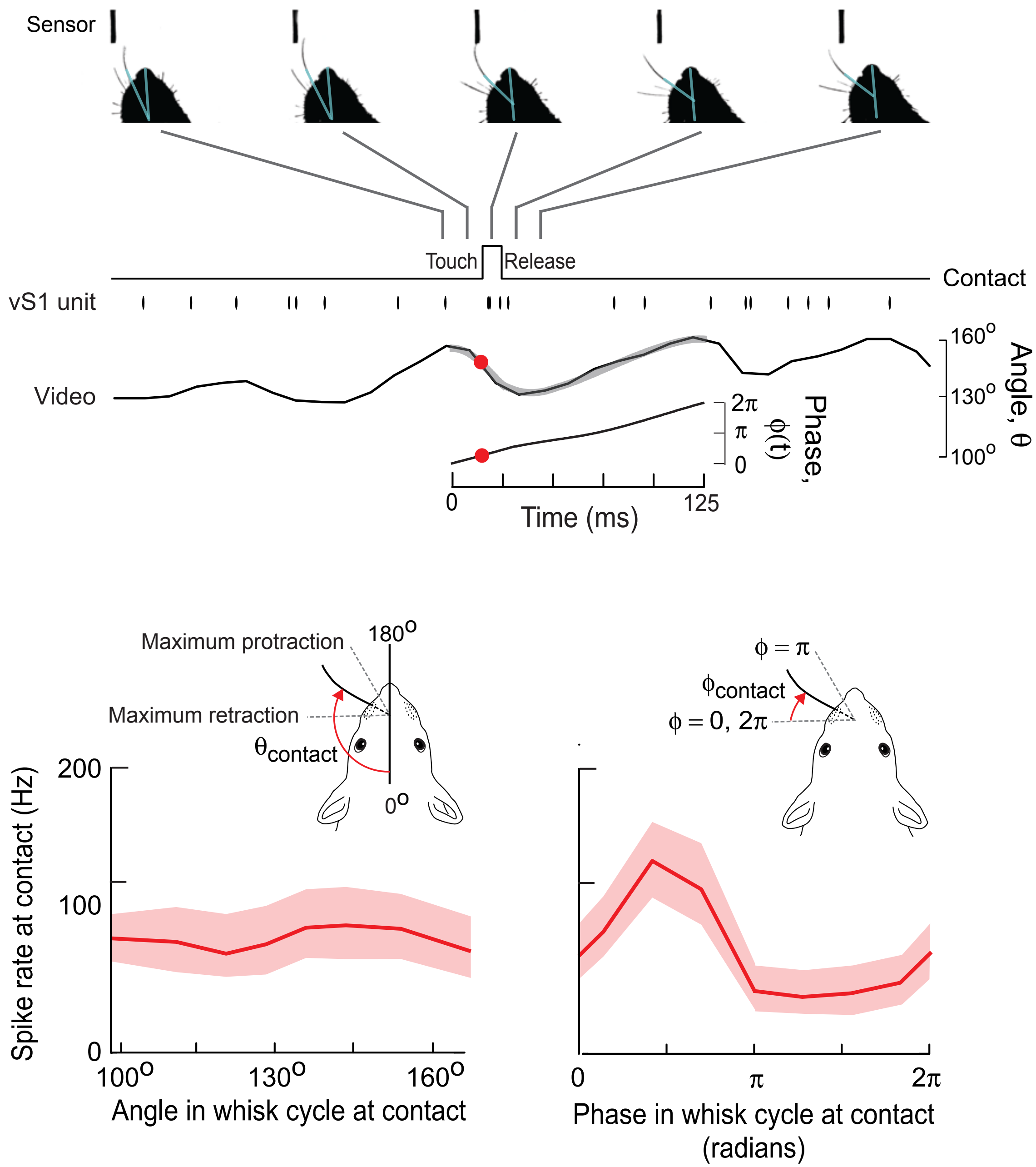


$$\theta(t) = \theta_{amplitude}(t) \cdot \cos\phi(t) + \theta_{midpoint}(t)$$

slow   fast   slow

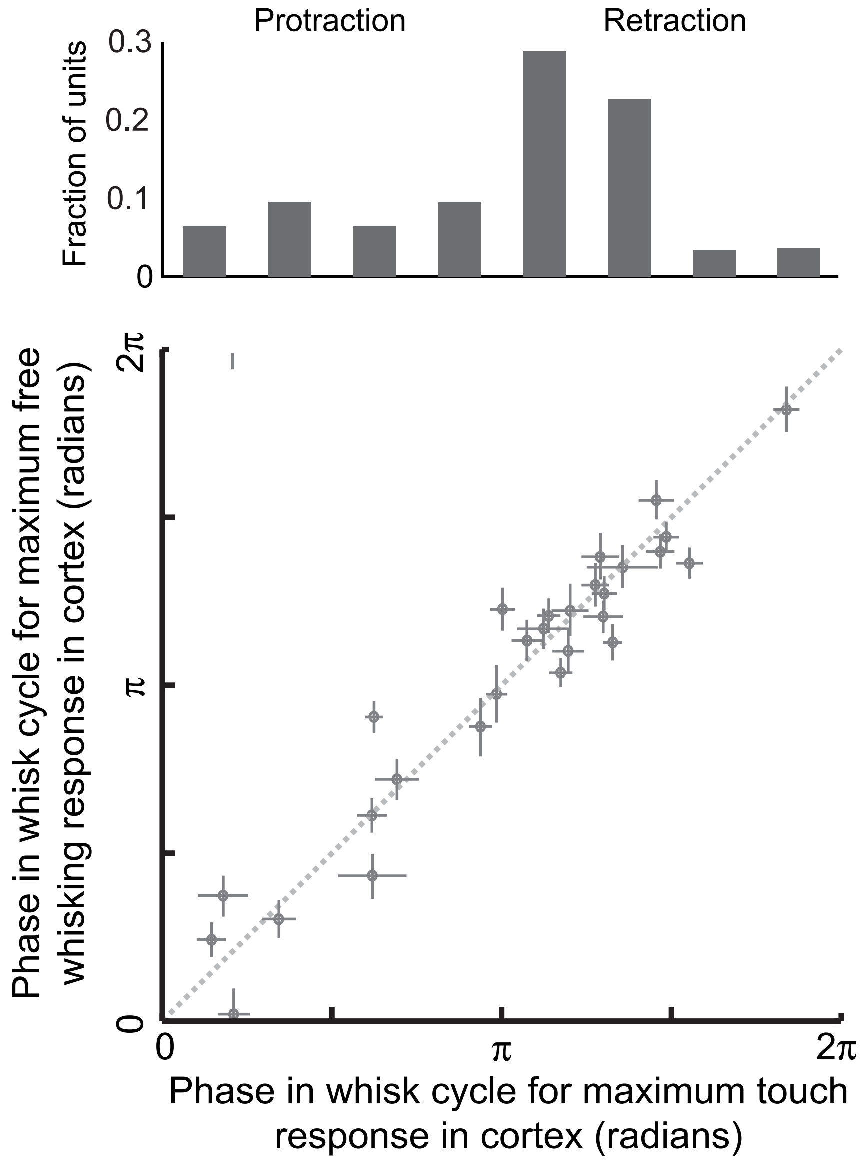
with $d\phi(t)/dt = 2\pi f_{whisk}$ for rhythmic whisking

Vibrissa S1 cortex codes azimuth of vibrissa touch by phase in the whisk (= respiratory) cycle



Curtis & Kleinfeld (Nat Neurosci 2009)

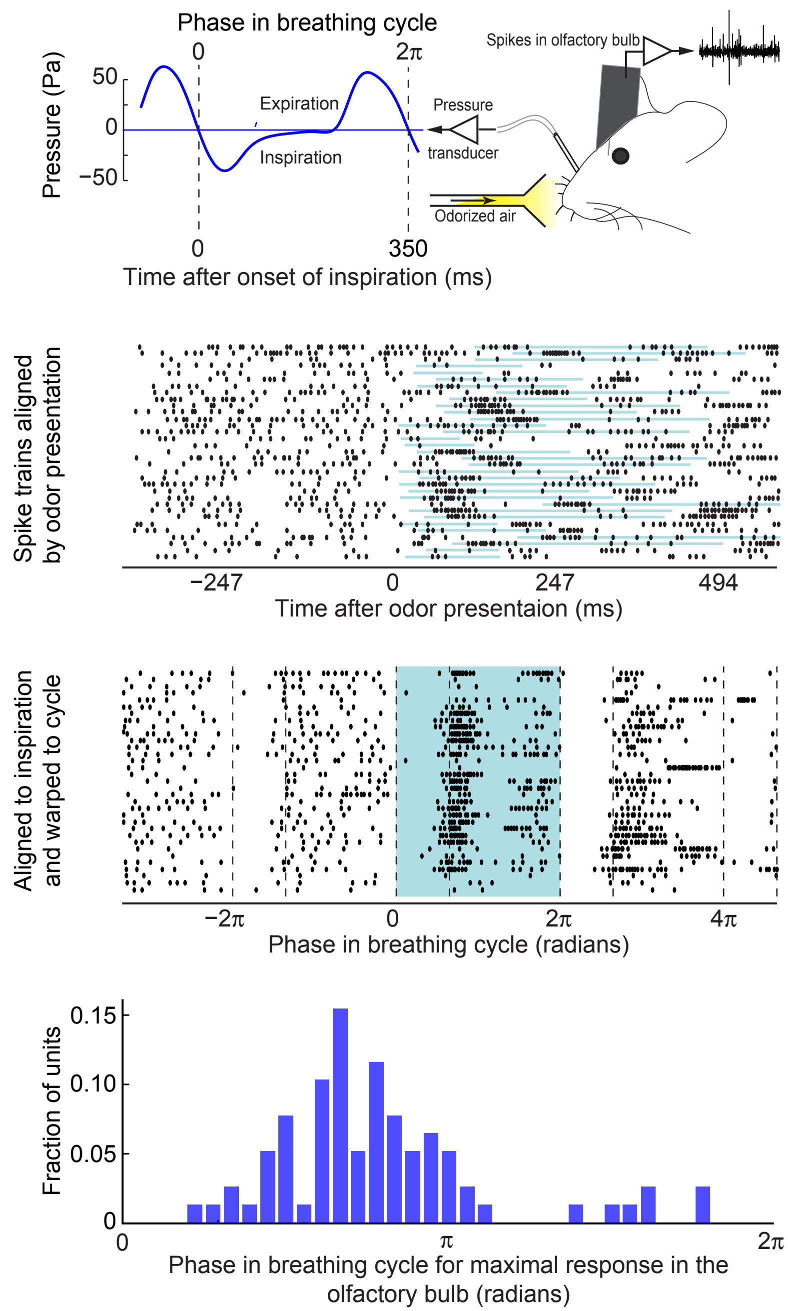
Vibrissa S1 cortex codes azimuth of vibrissa touch, as well as free whisking, by phase in the whisk (= respiratory) cycle



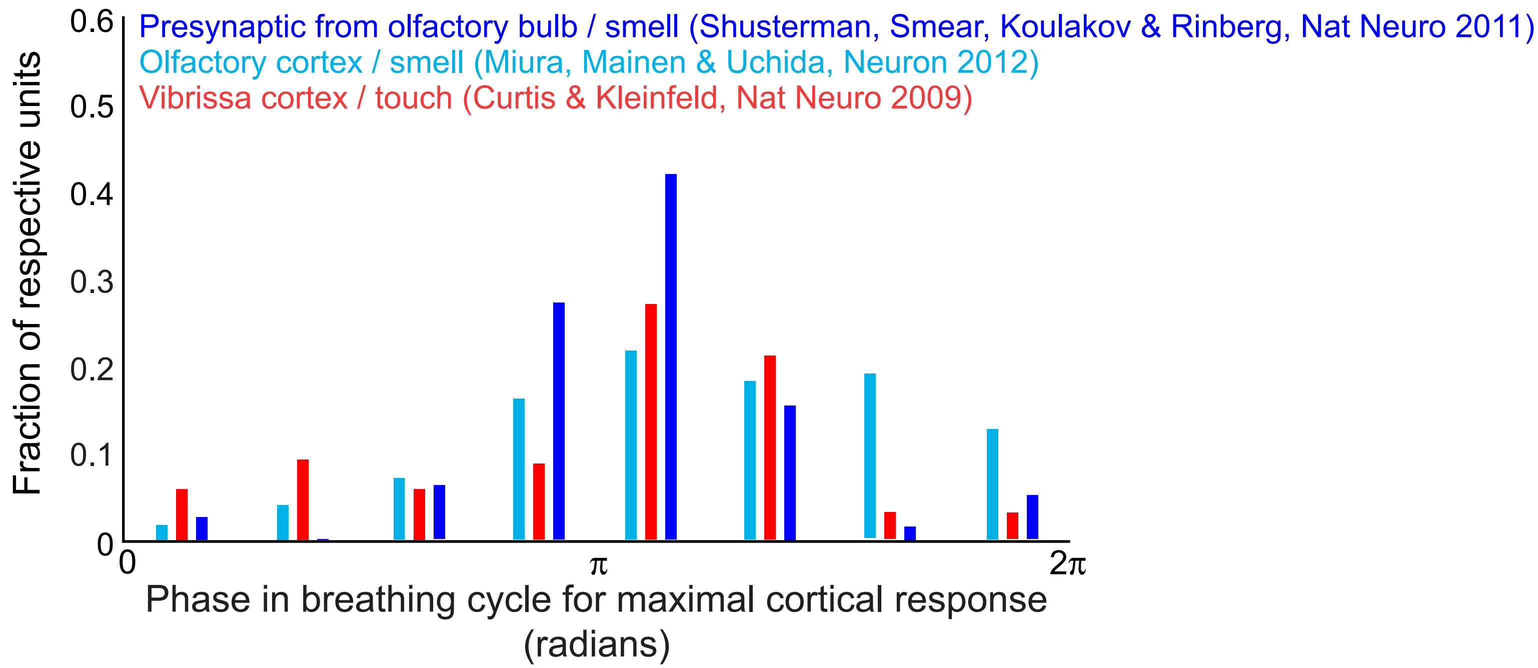
Curtis & Kleinfeld (Nat Neurosci 2009)

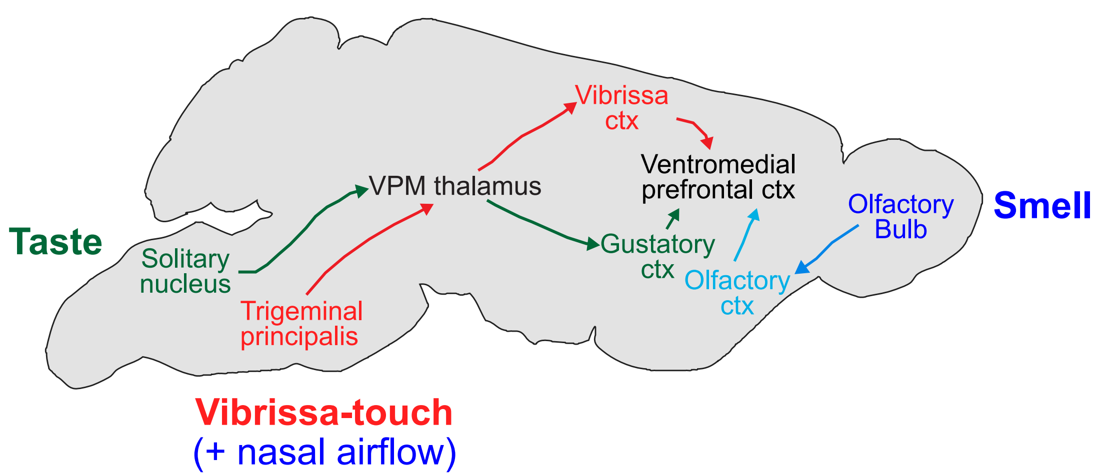
Olfactory bulb codes odor by phase in respiratory (= whisk) cycle

(Shusterman, Smear, Koulakov & Rinberg Nature Neuroscience 2011)



Coordination of sniffing and whisking and their spiking representation in sensory cortices





Kleinfeld, Deschenes, Wang & Moore (Nature Neuroscience 2014)

Lesson

A common clock for the phase sensitivity of sniffing and whisking

Conjecture

Inhalation as the *master clock* to bind percepts based on orofacial (smell, touch, and taste) inputs

Sniffing: A master clock for orofacial rhythms?

Thank you for your attention!