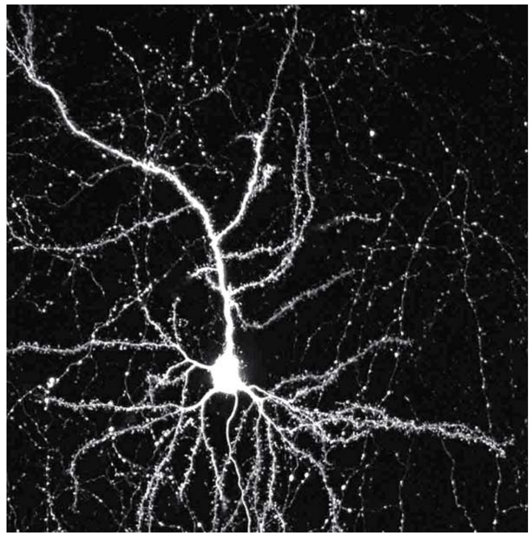
Welcome to BRAIN 18

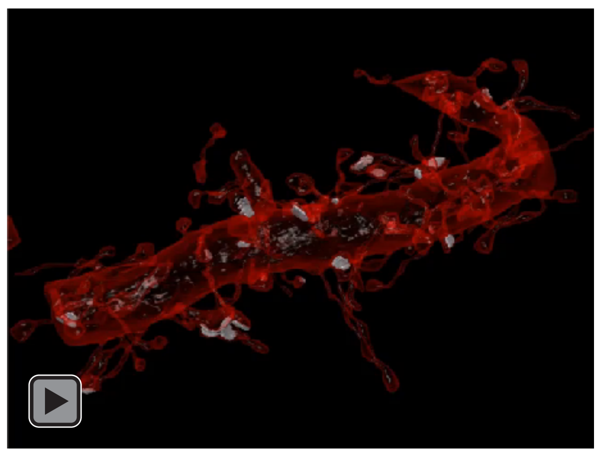
Recording, analyzing, manipulating, and modeling whole brain activity

"***A great deal remains to be learned about the brain and spinal cord, a task that will take centuries not years to complete.***"

Santiago Ramón Y Cajal (1852-1934)

Brains and cords follow the neuron doctrine - that individual cells comprise the nervous system - yet come in many flavors



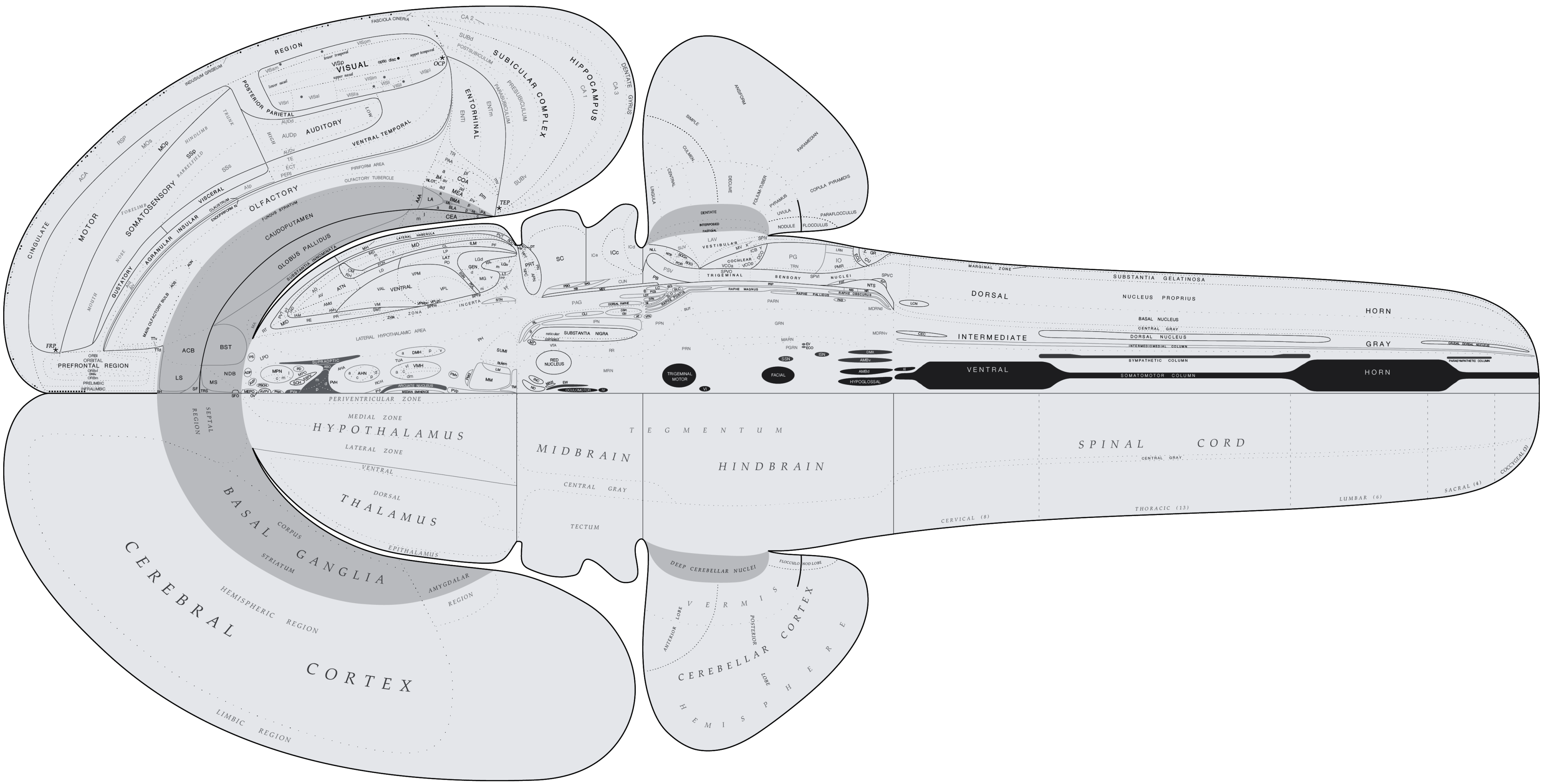


Kasthuri, Hayworth, Berger , Schalek, Conchello, Knowles-Barley, Lee, Vázquez-Reina, Kaynig, Jones, Roberts, Morgan, Tapia, Seung, Roncal, Vogelstein, Burns Sussman, Priebe, Pfister Lichtman (Cell 2015)

Neural net (jells)

Distributed ganglia (cephalopoda - with excessive RNA editing)

Vertebrate nervous plan



Vertebrate nervous plan from different perspectives

"All parts of the visual system are co-excited within 40 milliseconds ..."

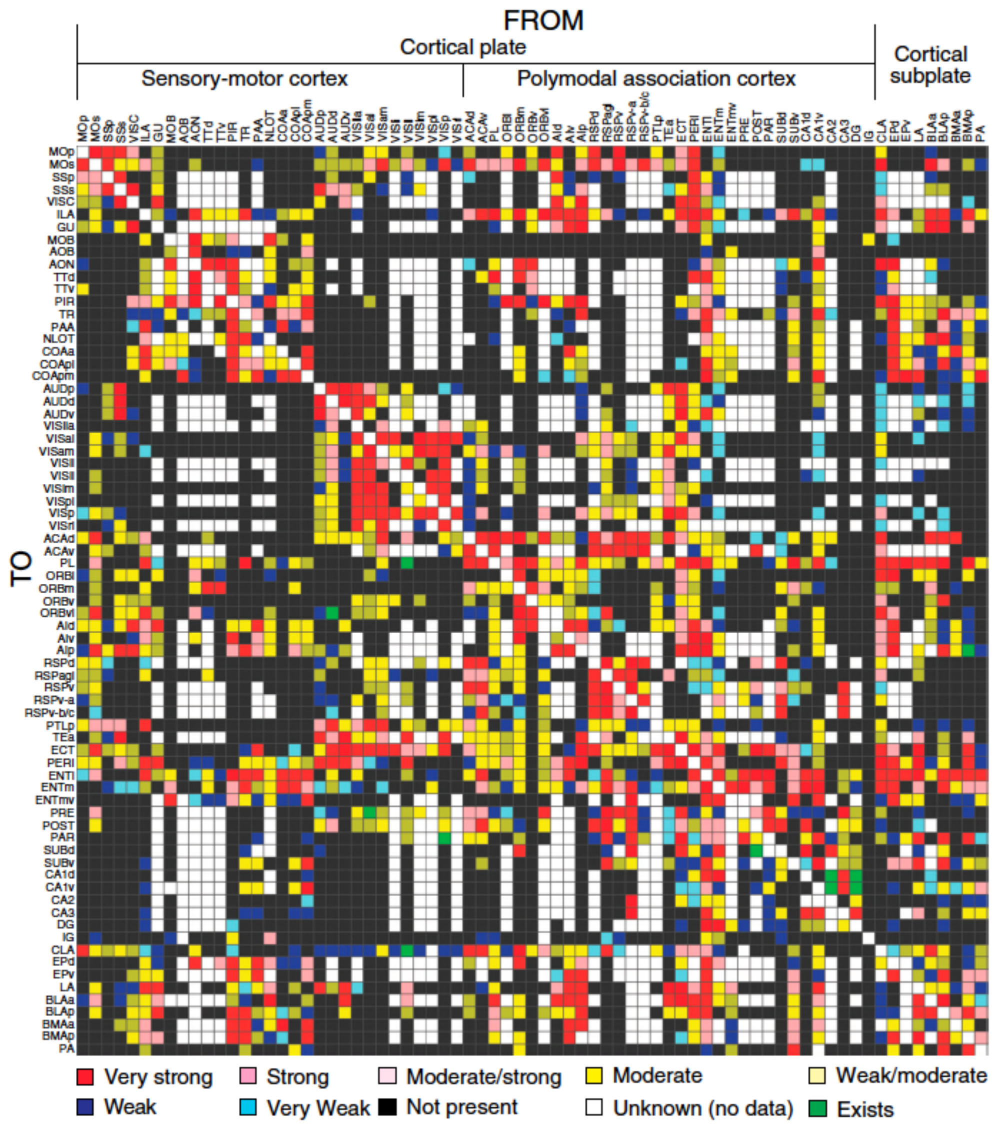
Kevan A C Martin (ca 1990)

Clustering of the connectome and hubs of interacting neuronal regions

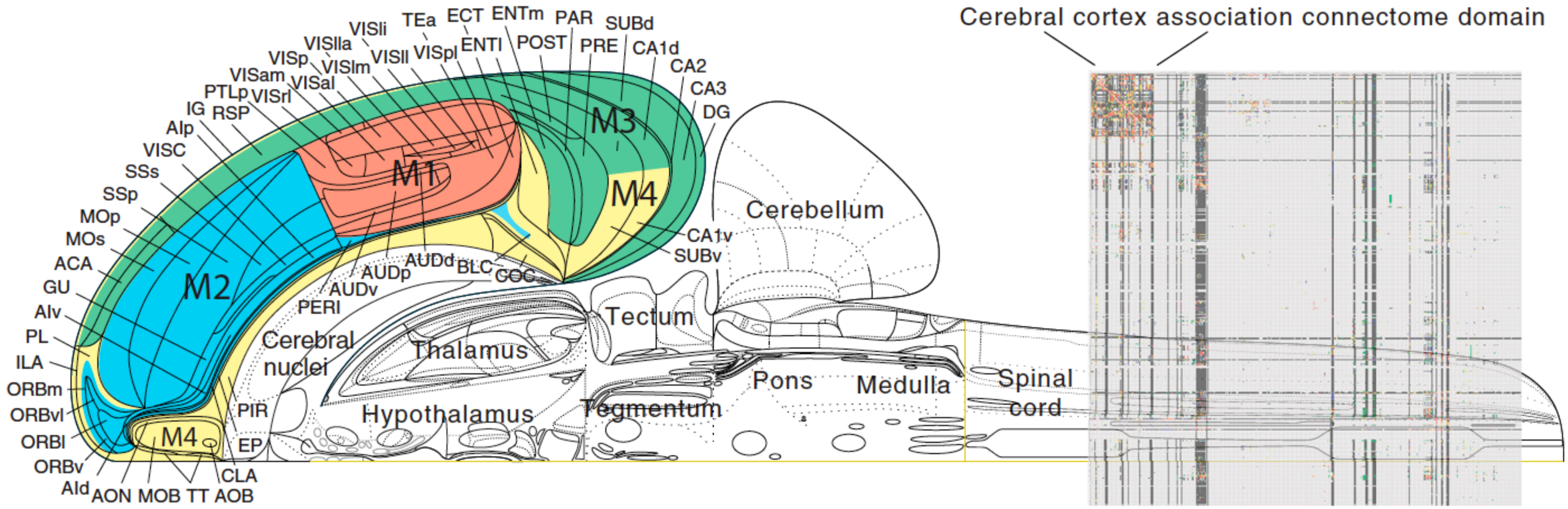
Hierarchy of projections into nested loops

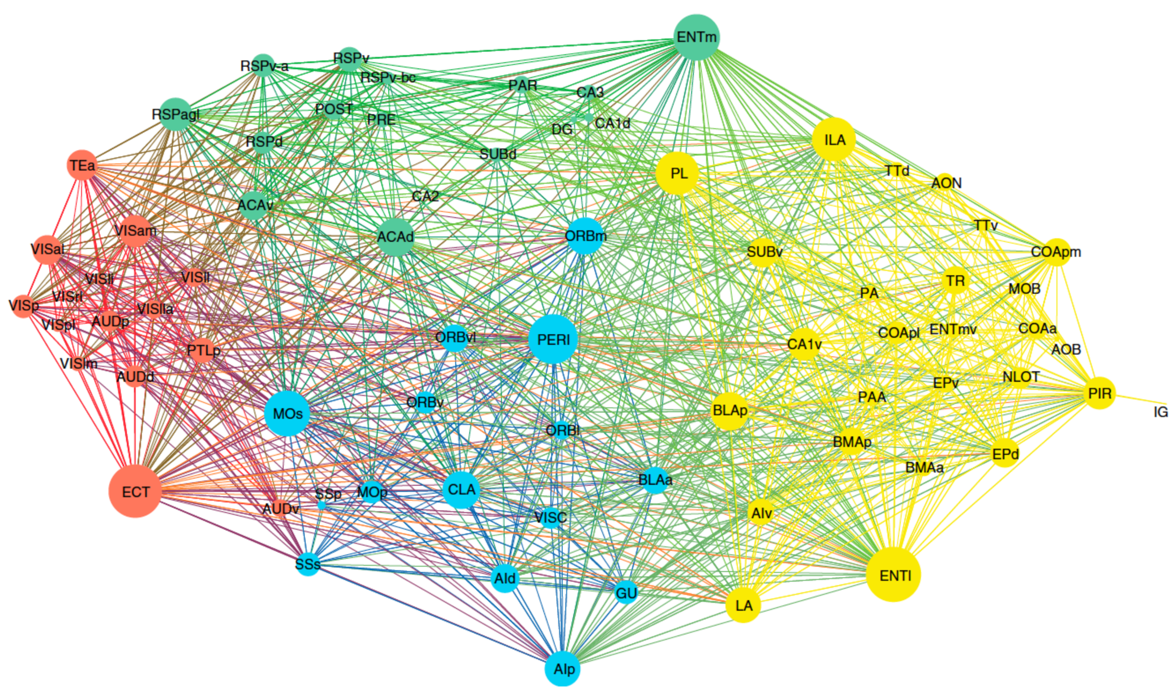
A solely feedforward perspective

Meta-analysis of rat cortical connectivity reveals functionally distinct clusters, e.g., near vs. far sensation



Bota, Sporns & Swanson (PNAS 2015)





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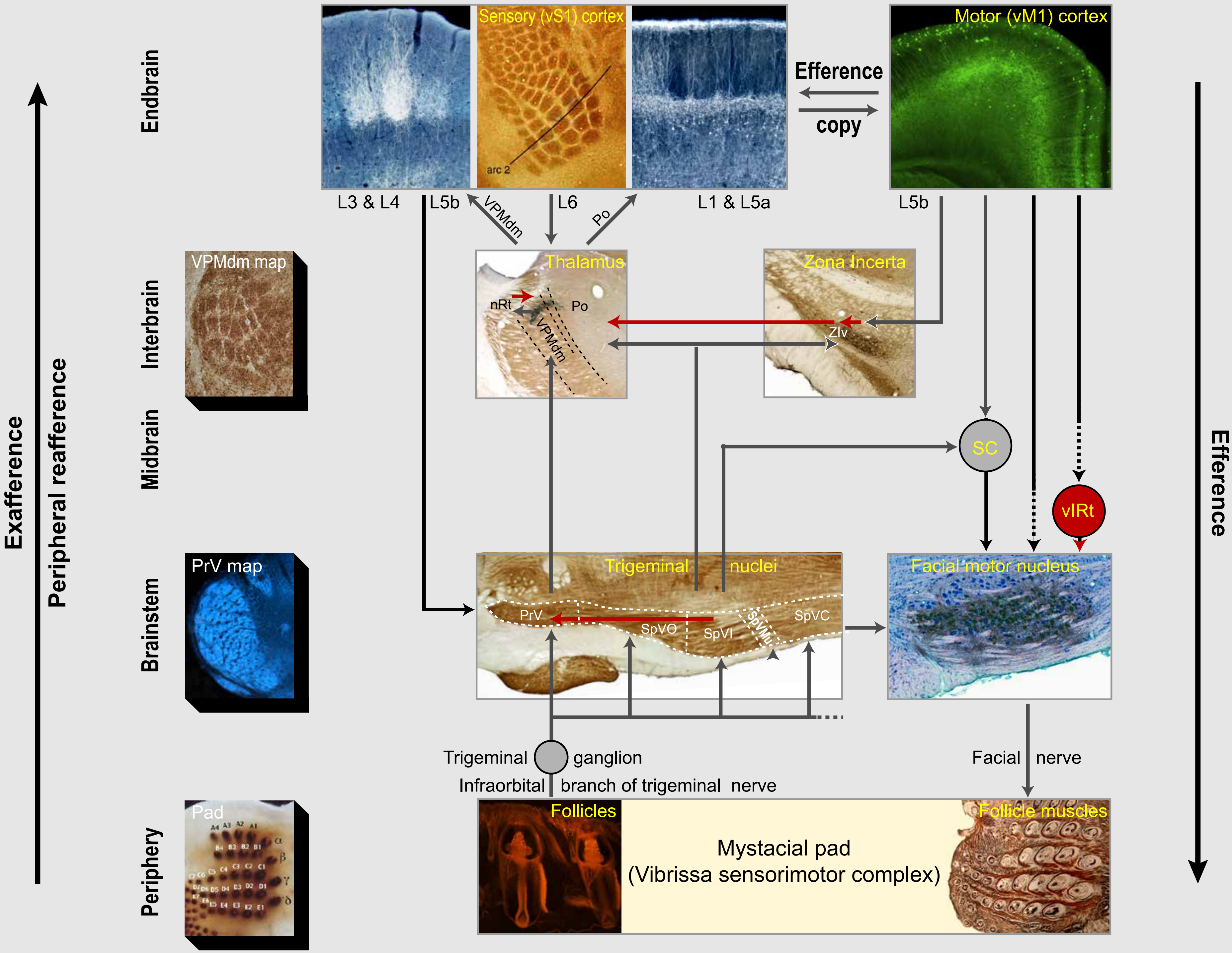
A solely feedforward perspective

Signal flow and computation in nested loops of the vibrissa system



Modified from Kleinfeld & Deschenes (Neuron 2011)

Vertebrate nervous plan from different perspectives

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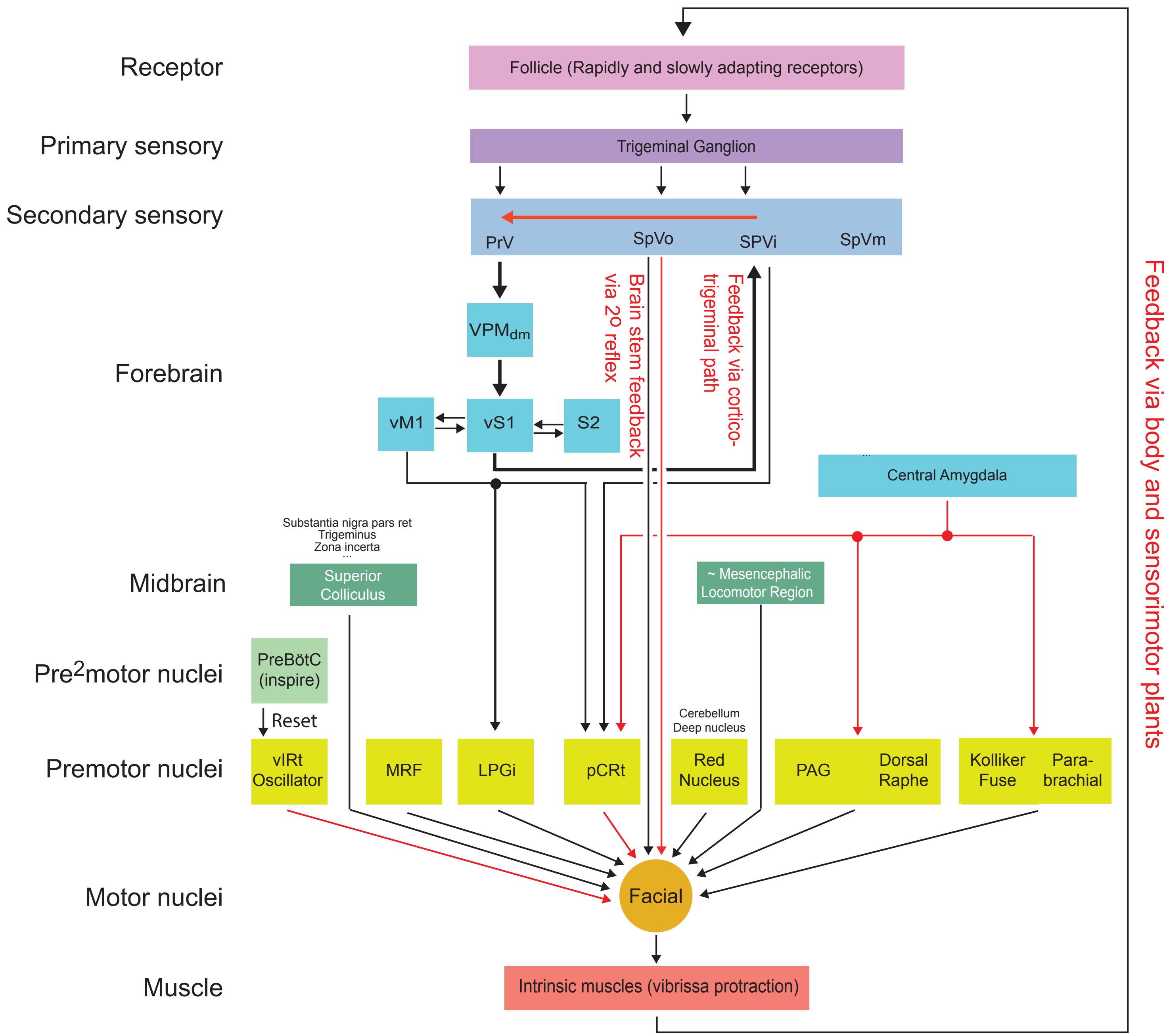
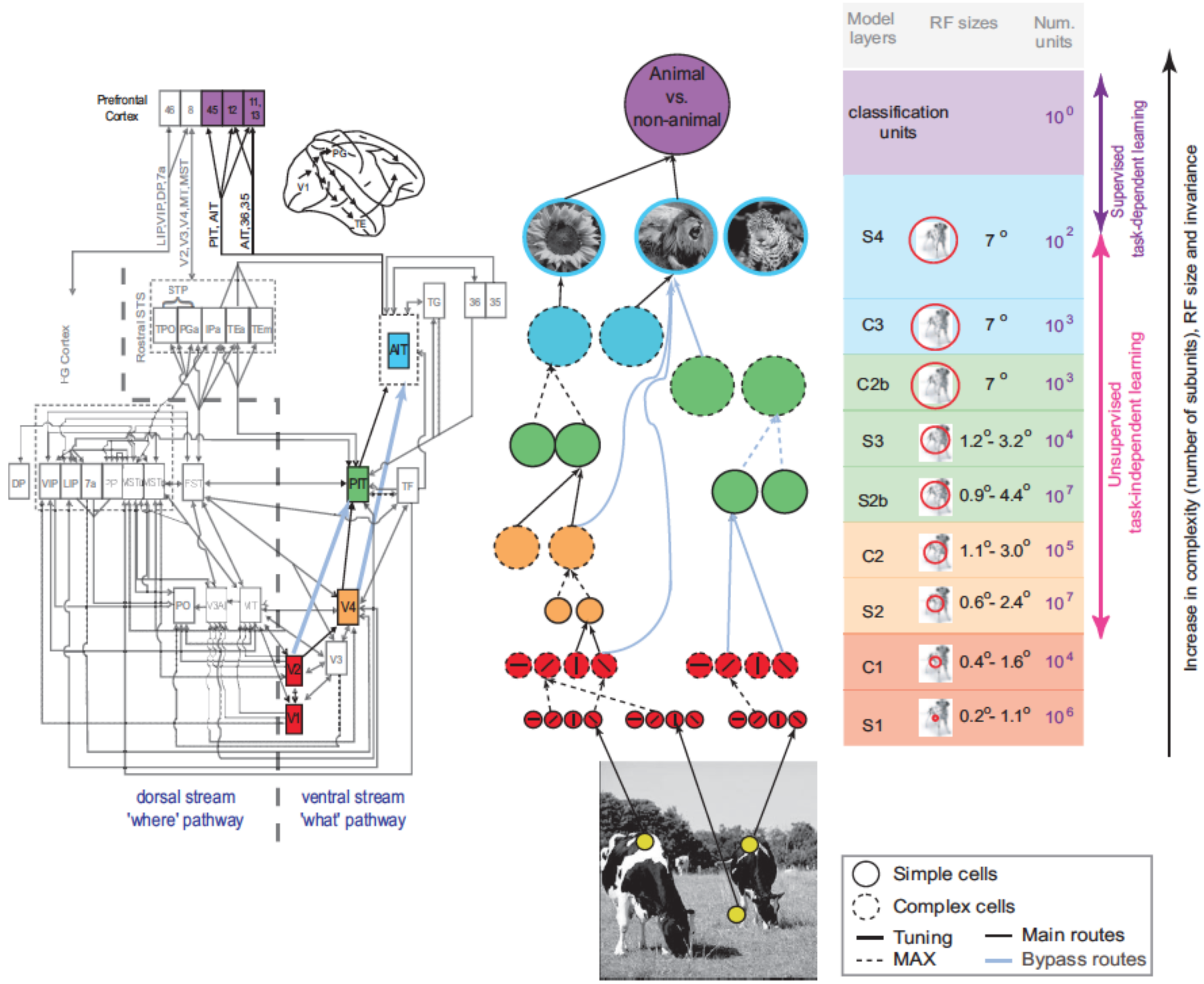
Toward *Nature's* algorithm to form orofacial behaviors from circuits for motor actions (highlighted for vibrissae)

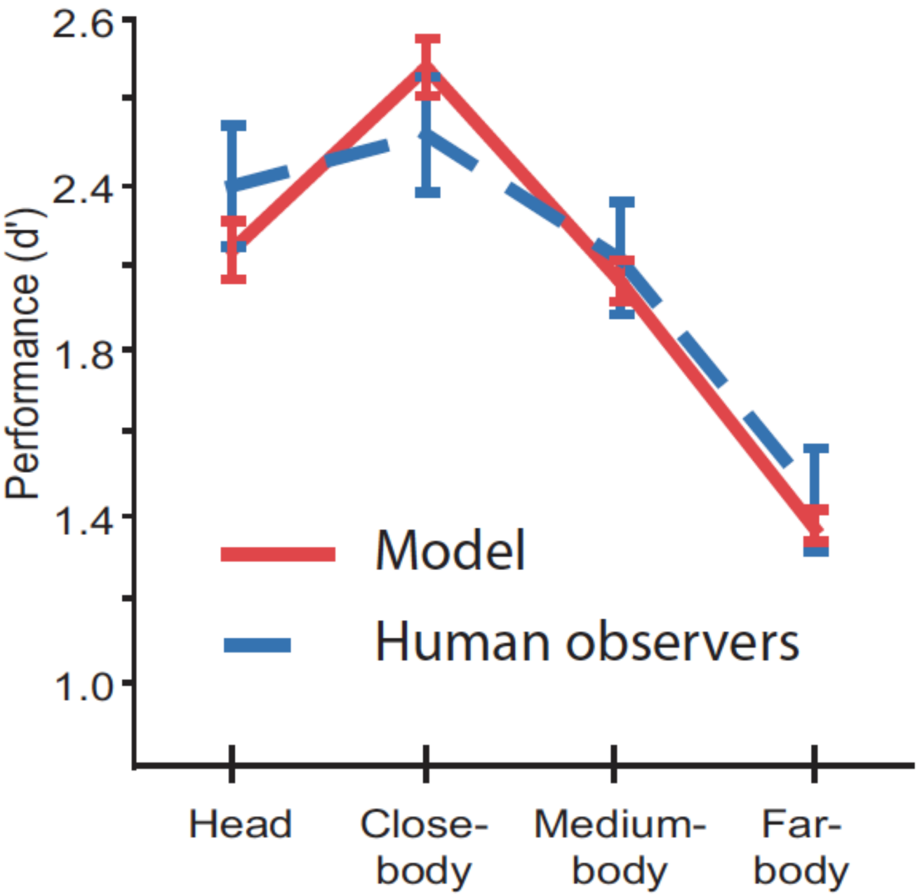


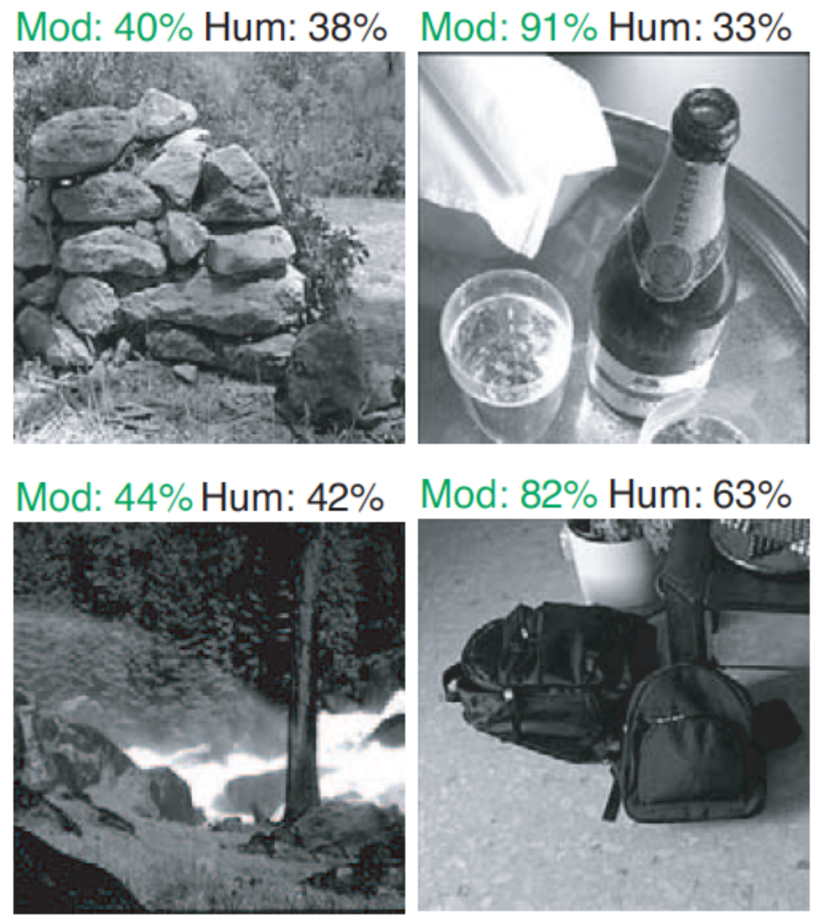
Vision inspired feed forward network for rapid classification



Serre, Oliva & Poggio (PNAS 2007)

The rise of the machines - comparable performance!





Serre, Oliva & Poggio (PNAS 2007)

Guide to contemporary experimental approaches

Classic wisdom: Choose the most ethologically relevant animal for your question

Modern wisdom: Make no pretense about statistics and measure everything

Behavior

- **Reference signals and constraints on components (physiology) and wiring (anatomy)**

Physiological recording

- **Medium: Optical- versus electrical-based**
- **Number: Multisite versus single cell**
- **Selection: Expression- versus projection- versus location-based**

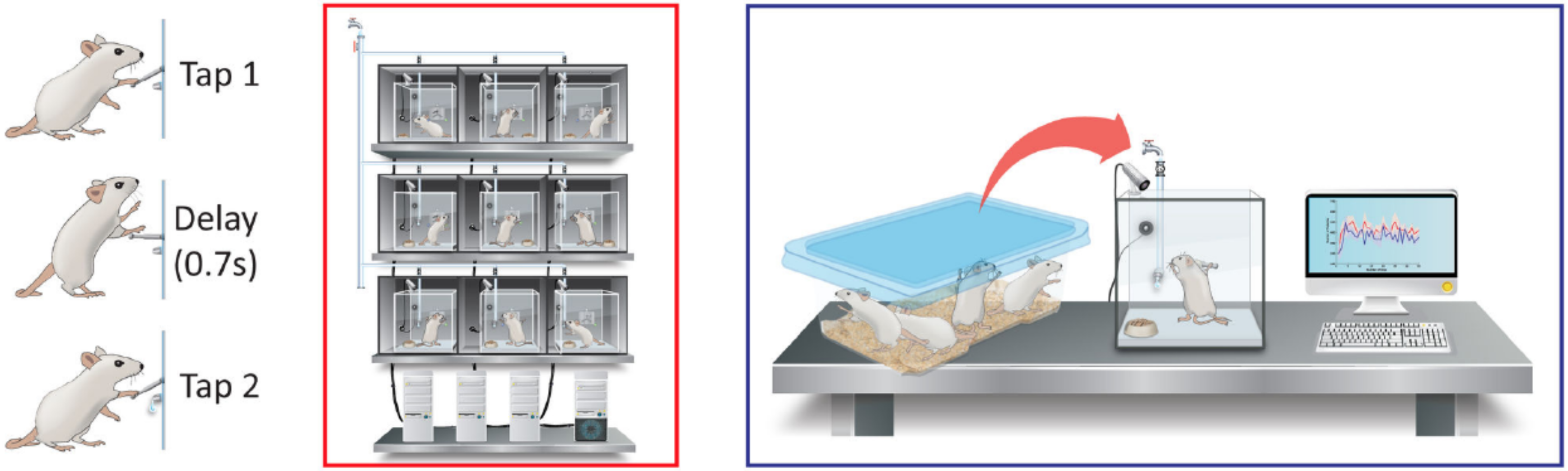
Physiological manipulation

- **Medium chemical versus optical**

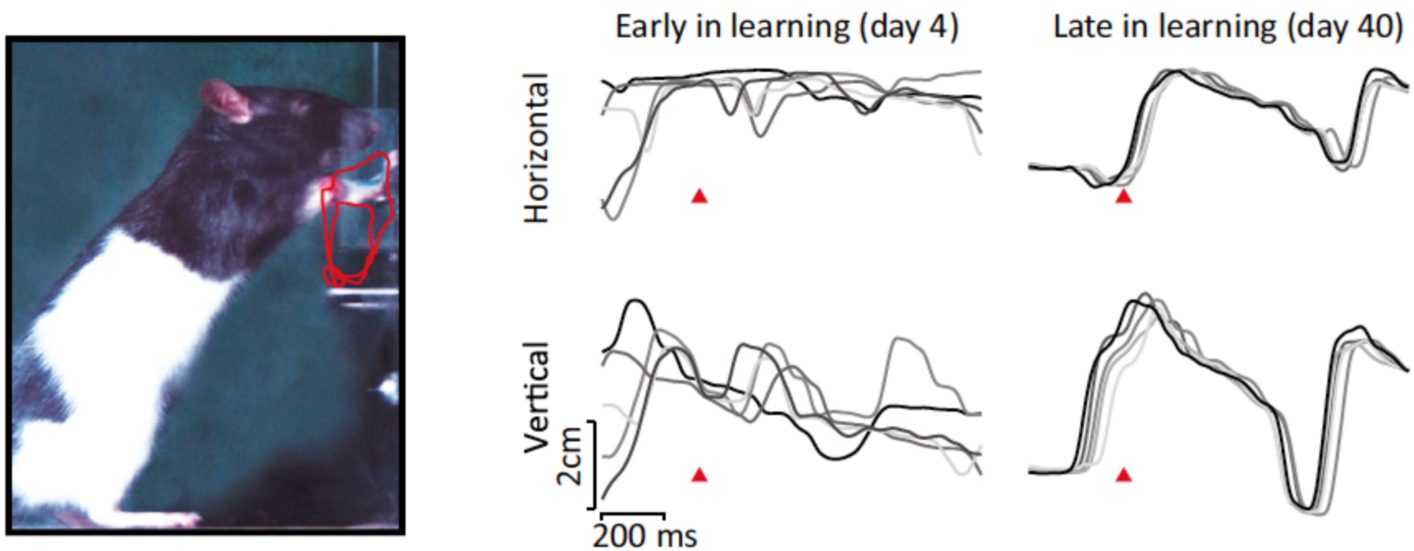
Anatomy

- **Cell markers**
- **Cell projections**
- **Polysynaptic pathways**

High-throughput behavior to train a stereotypic task

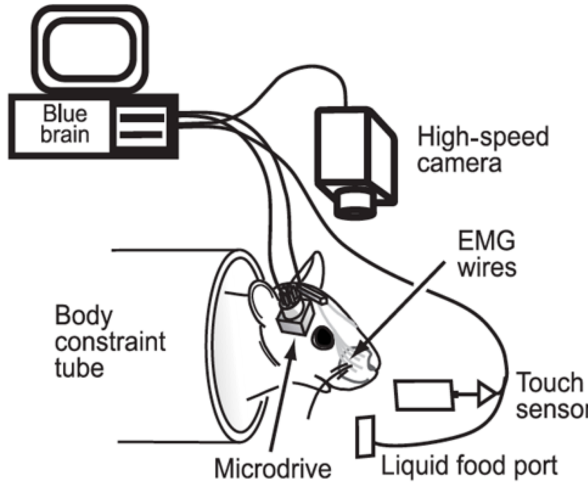


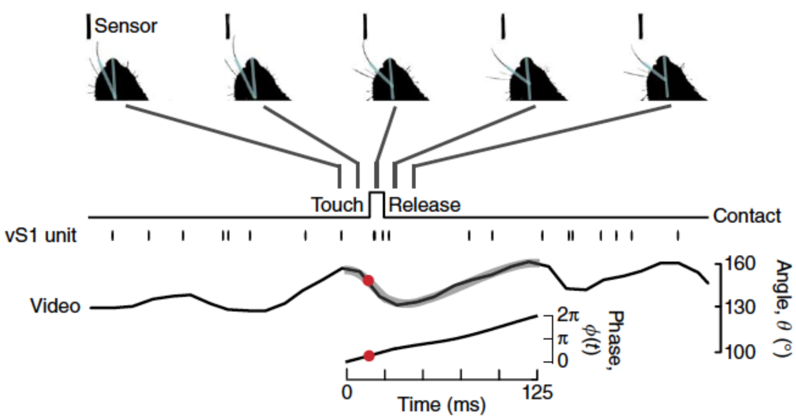
Poddar, Kawai & Ölveczky (PLoS ONE 2013)

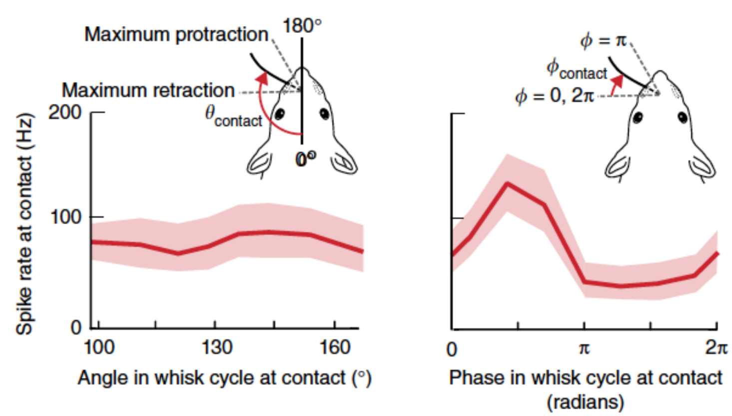


Markman, Poddar, Ko, Fantana, Dhawale, Kampff & Ölveczky (Neuron 2015)

Automated monitoring of an innate behavior as a reference for physiological correlates







Cutis & Kleinfeld (Nat Neuro 2013)

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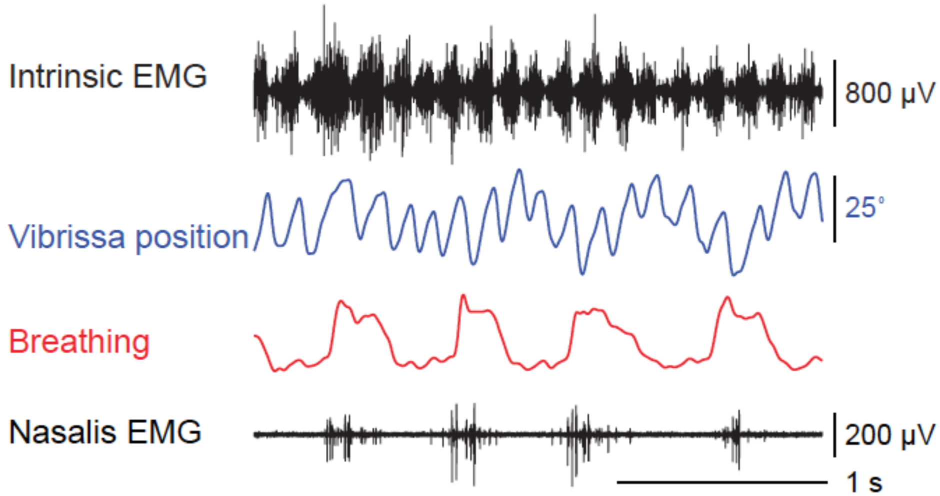
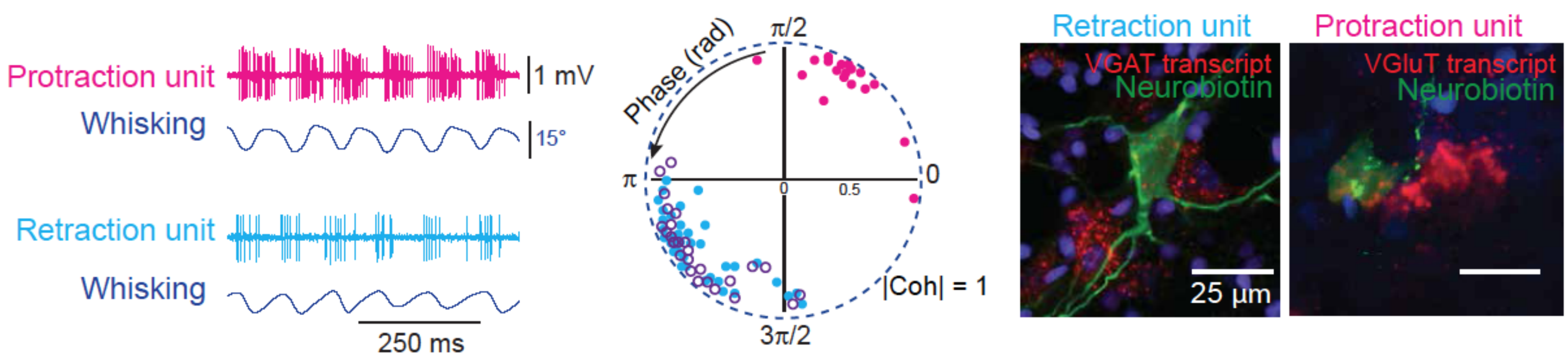
Intracellular recordings are information rich and allow you to manipulate as well as record

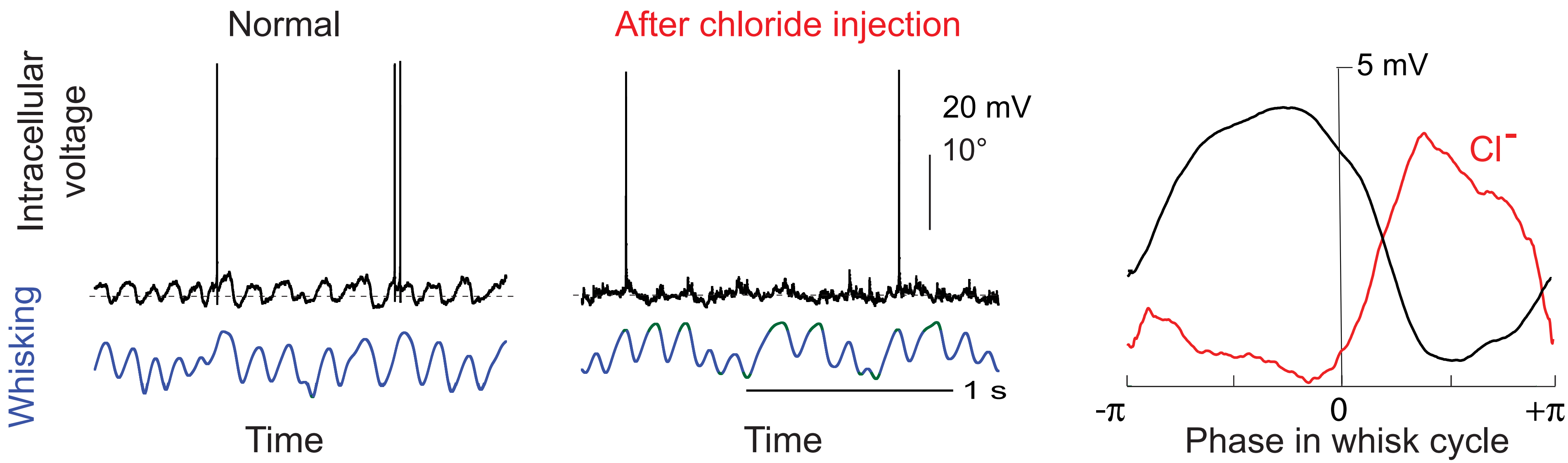




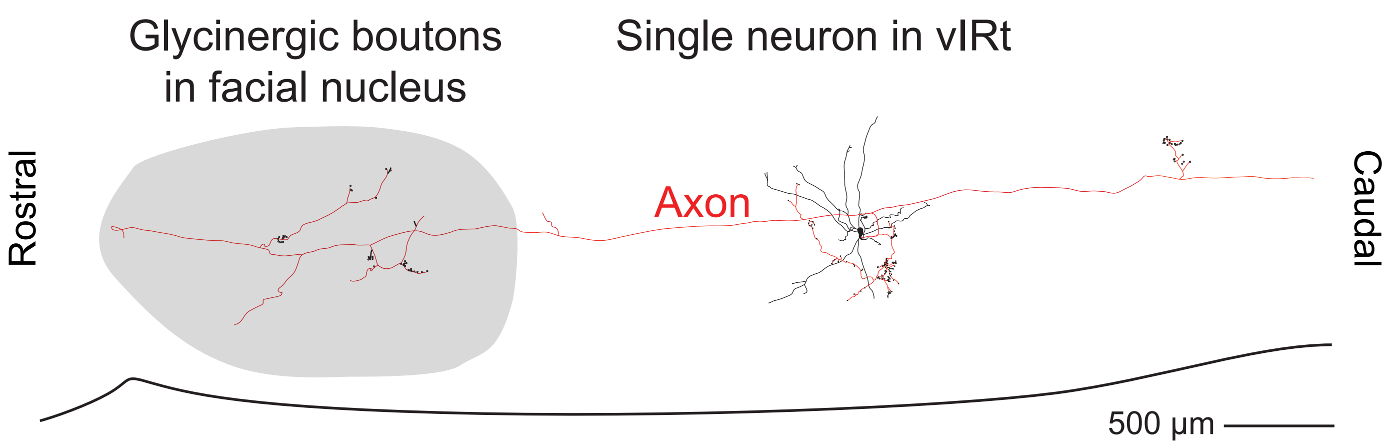
Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

Deschenes, Takatoh, Kurnikova, Moore, Demers, Elbaz, Furuta, Wang & Kleinfeld (Neuron 2016)

Intracellular recording from facial motoneurons reveals that the rhythmic input is predominantly inhibitory

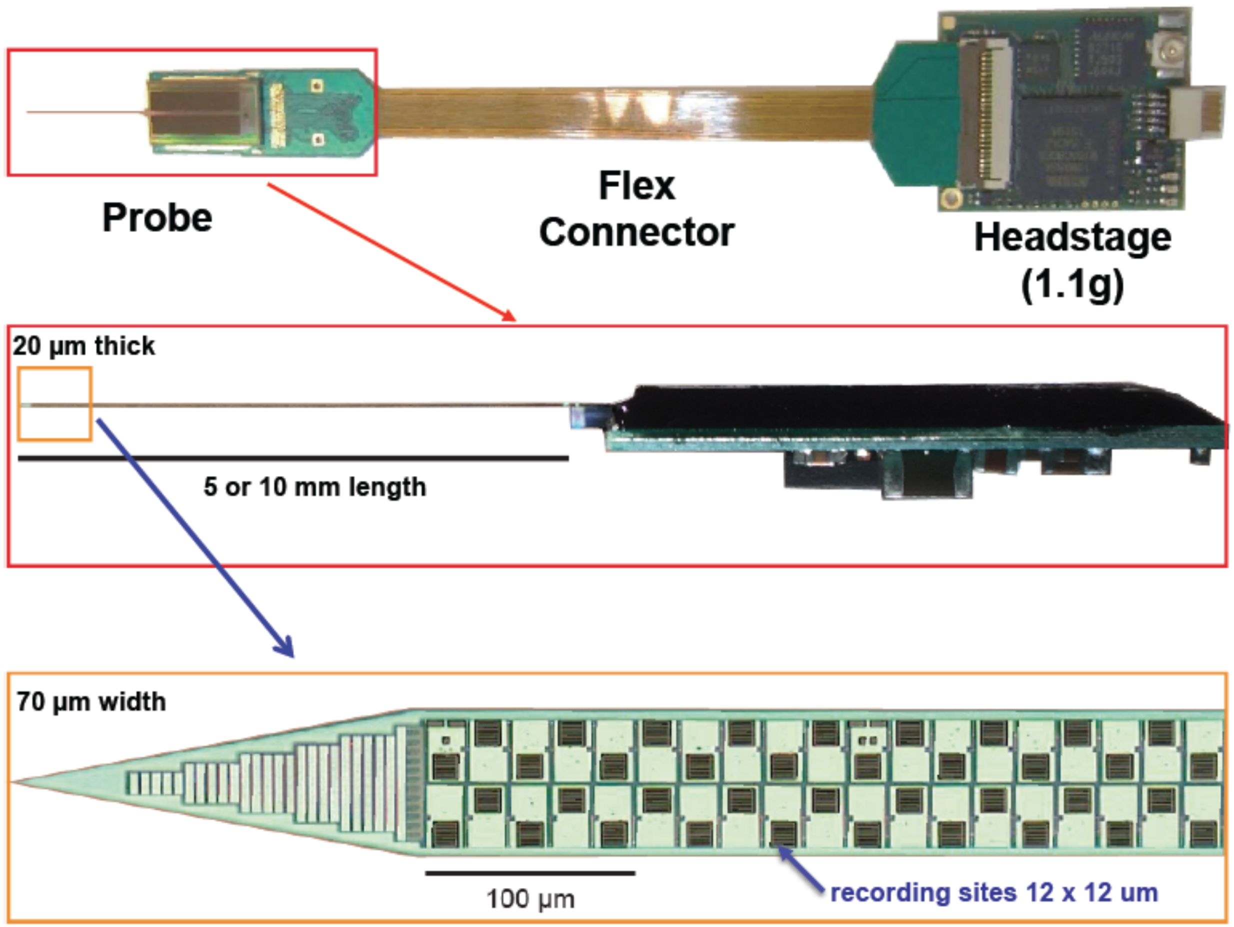


This is consistent with intracellular fills from vIRt neurons



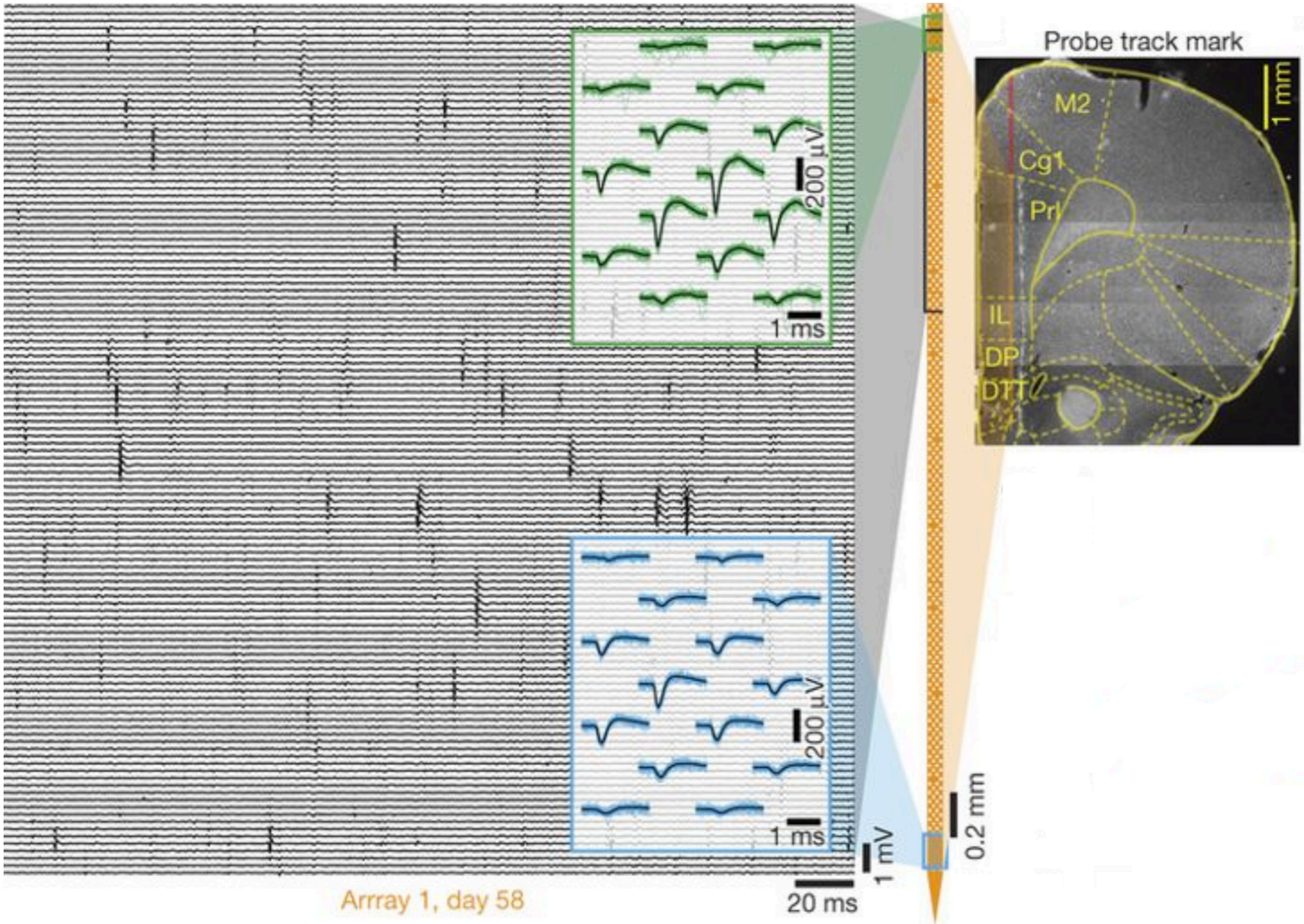
Deschenes, Takatoh, Kurnikova, Moore, Demers, Elbaz, Furuta, Wang & Kleinfeld (Neuron 2016)

Extracellular recording used microfabrication to approach 10^3-sites per electrode (IMEC neuropixels)



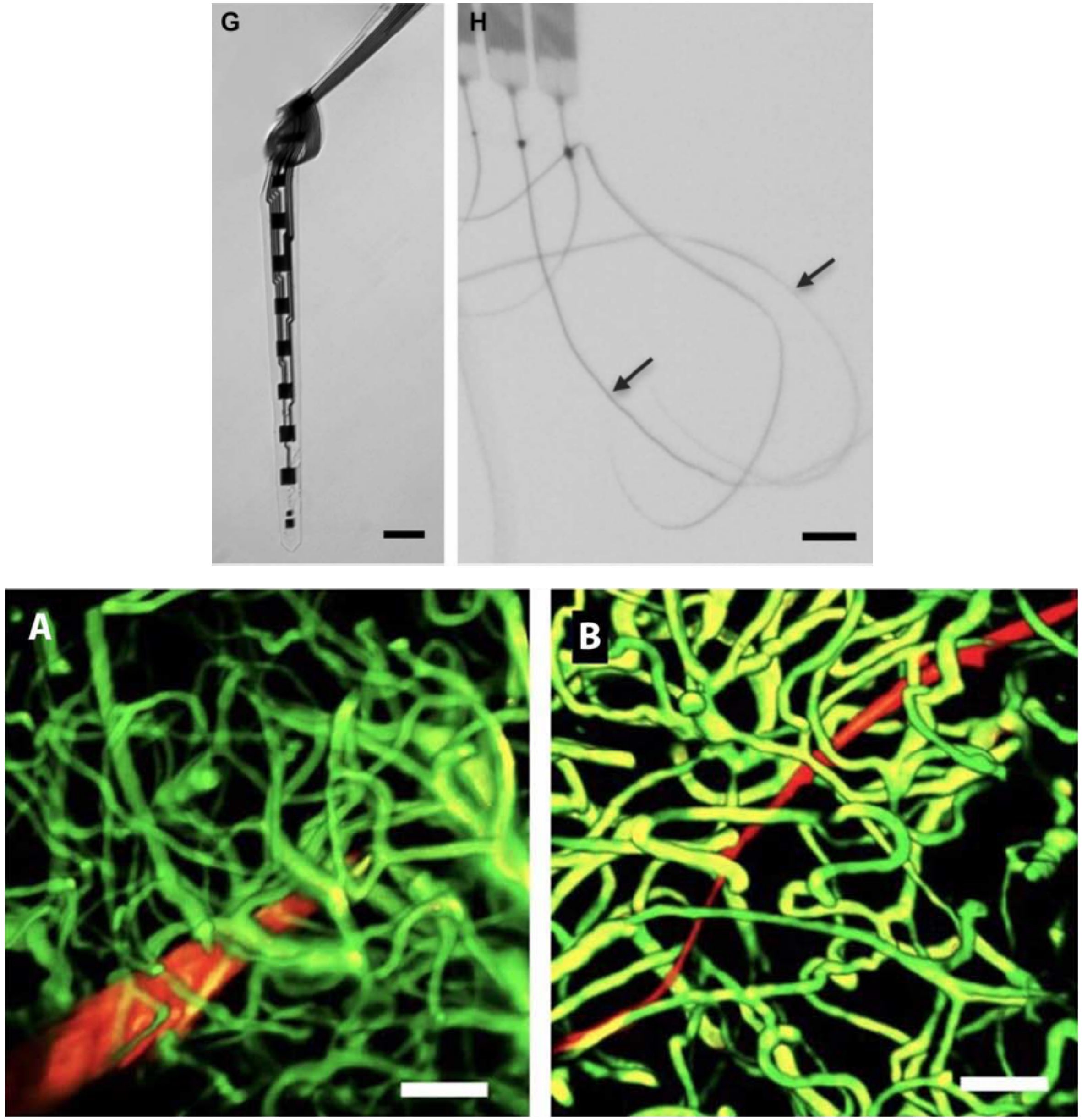
Calculations suggest that material strength and electrical properties can spikes to be concurrently recorded from all neurons in the cortical mantle.

Multiregional measurements enables by Neuropixels



Jun*, Steinmetz*, Siegle*, Denman*, Bauza*, Barbarits*, Lee*, Anastassiou, Andrei, Aydın, Barbic, Blanch, Bonin, Couto, Dutta, Gratiy, Gutnisky, Hausser, Karsh, Ledochowitsch, Lopez, Mitelut, Musa, Okun, Pachitariu, Putzeys, Rich, Rossant, Sun, Svoboda, Carandini, Harris, Koch, O'Keefe & Harris (Nature 2017)

Toward free floating thin-film flexible electrodes



Luan, Wei, Zhao, Siegel, Potnis, Tuppen, Lin, Kazmi, Fowler, Holloway, Dunn, Chitwood & Xie (Sci Advanc 2017)

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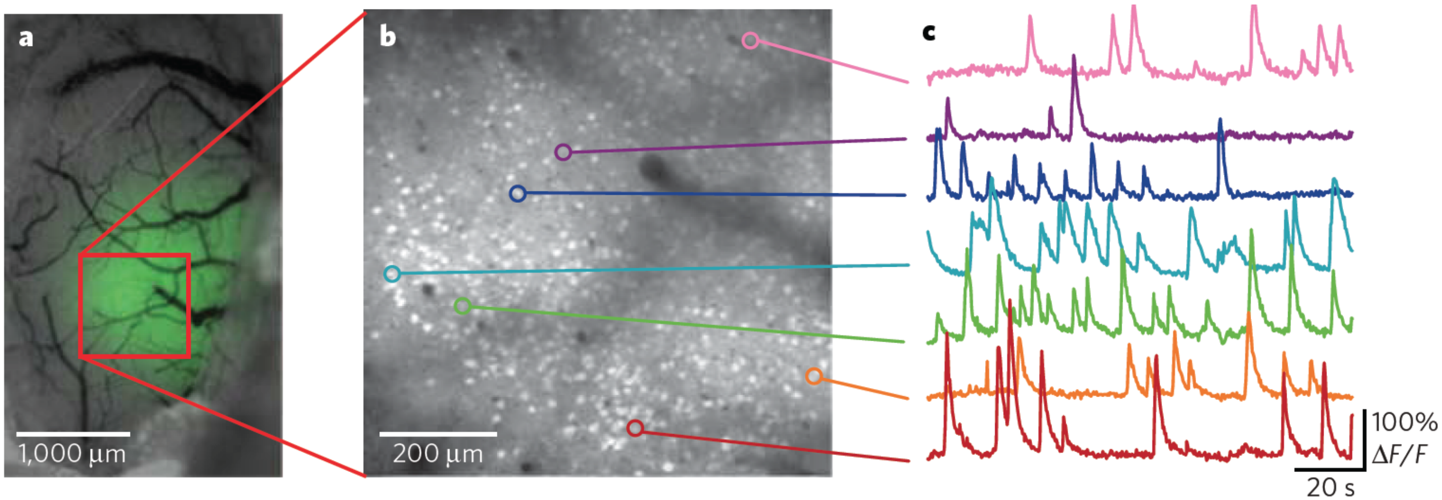
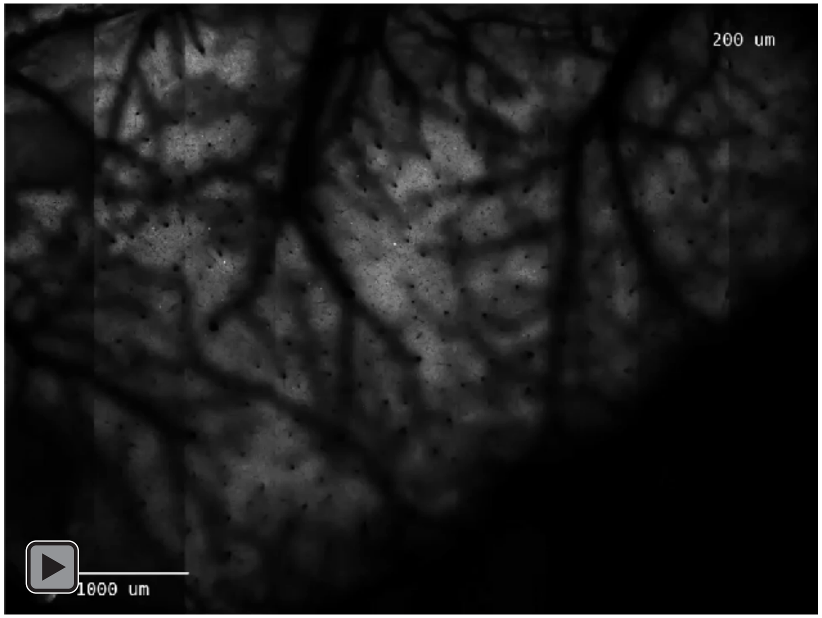
Intracellular Ca^{2+} is surrogate of spiking: Example of broad and superficial imaging with 2-P microscopy

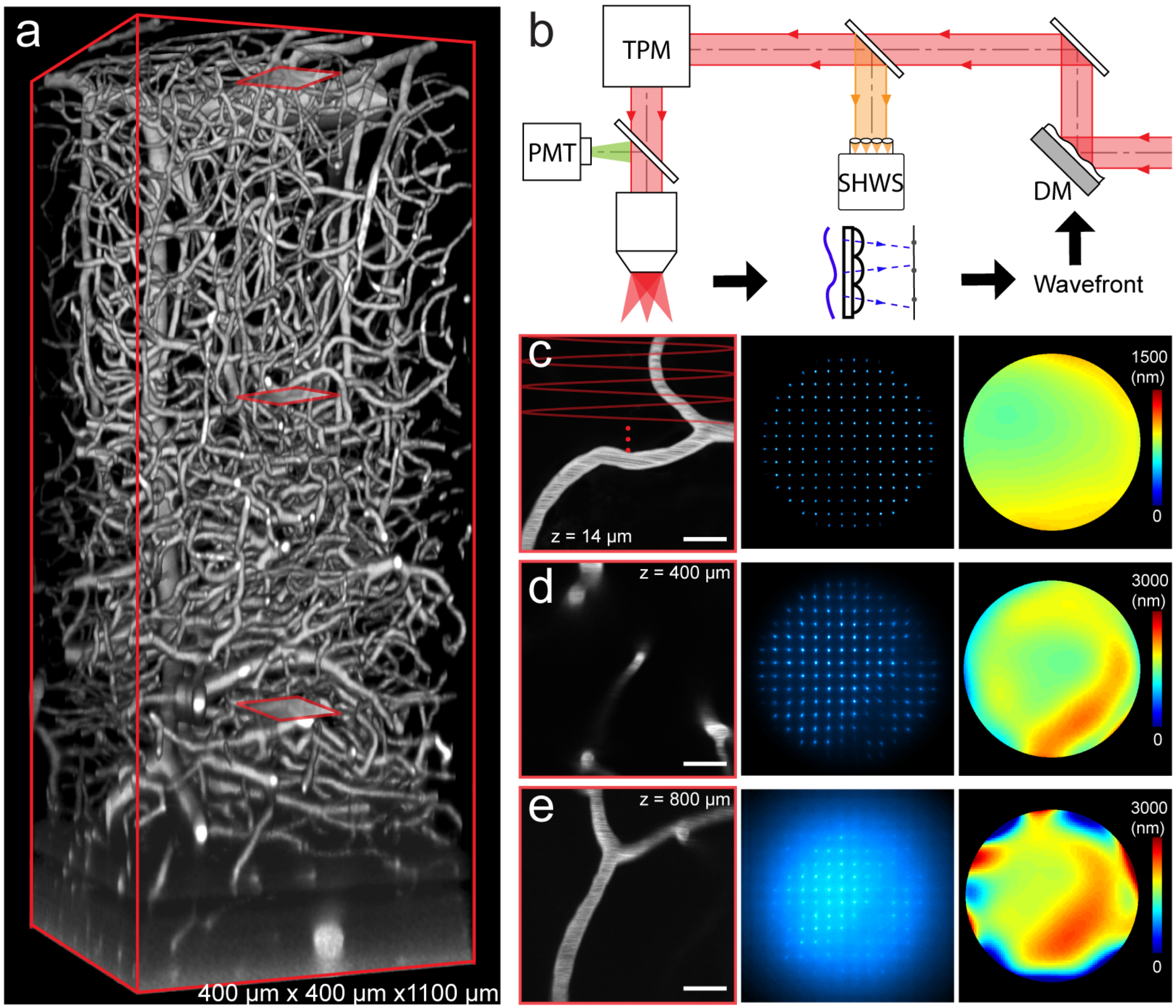


O'Connor, Huber & Svoboda (Nature Insight 2009)



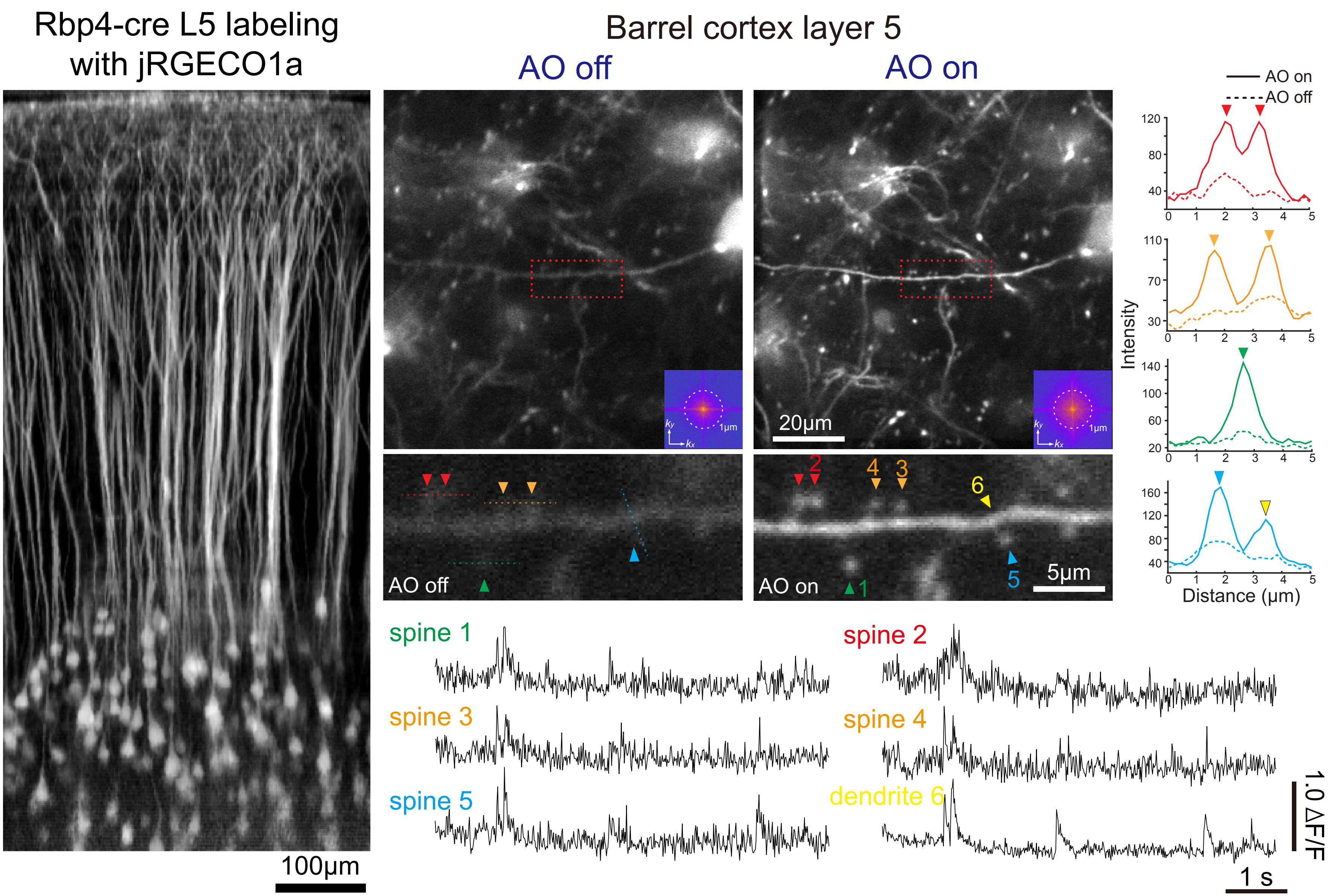
Sofroniew, Flickinger, King. & Svoboda (Elife 2016)

Intracellular Ca^{2+} is surrogate of spiking: Example of deep imaging with AO corrected 2-P microscopy



Liu, Li & Kleinfeld (Submitted 2018)

Imaging spine dynamics in L5b with AO 2P microscopy



Liu, Li & Kleinfeld (submitted 2018)

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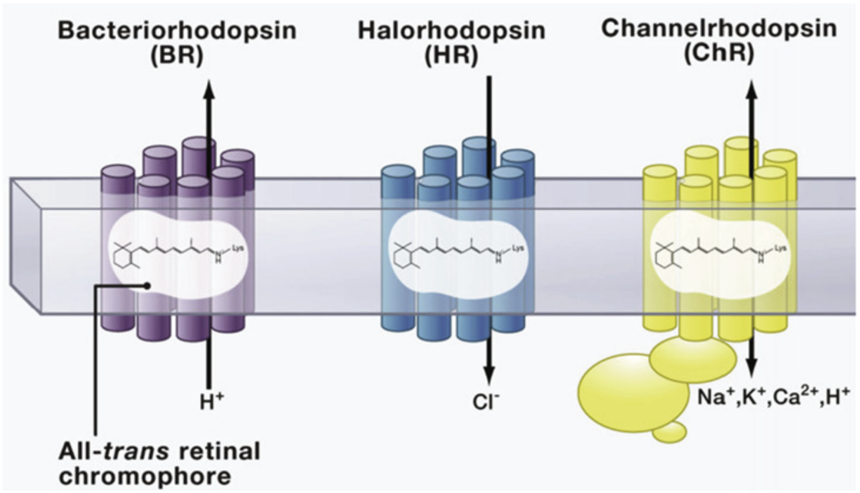
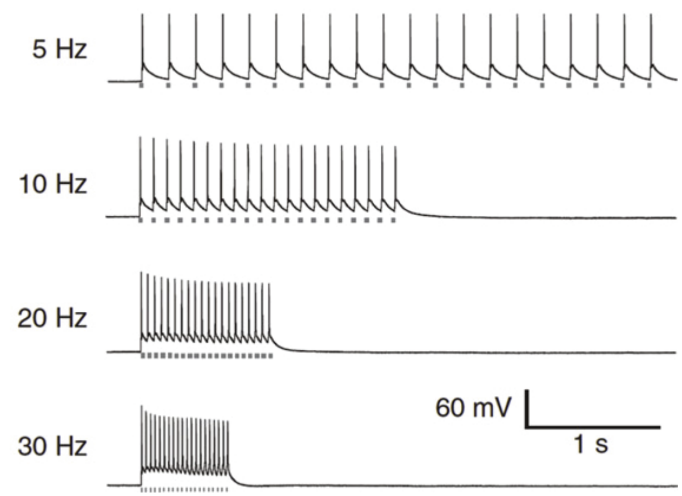
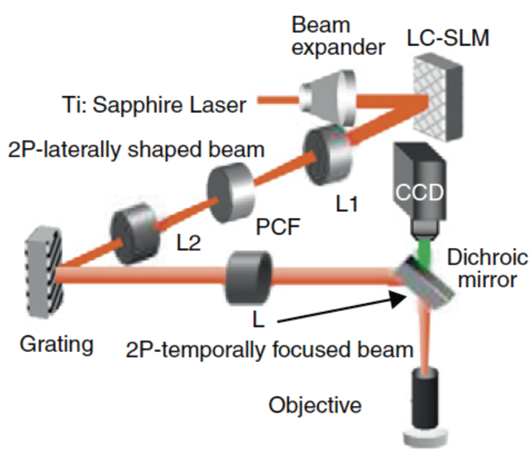
Instructional slide on neuronal activation by microbial rhodopsin (with optimized optical excitation for in vivo studies)

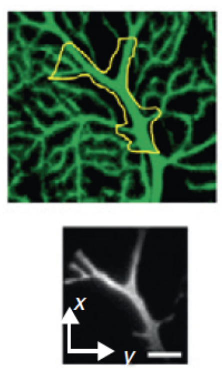


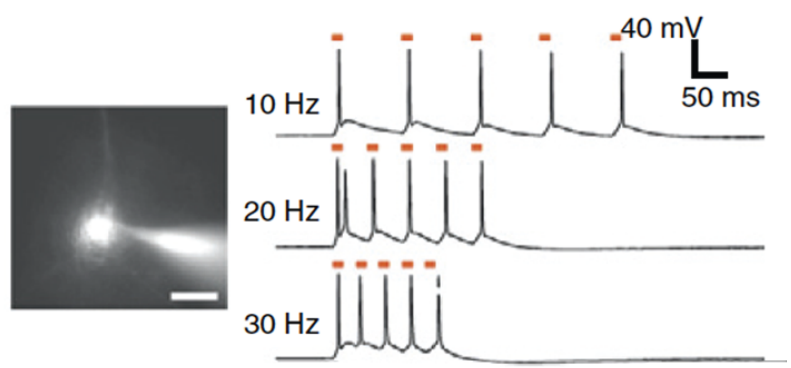


Nagel, Szellas, Huhn, Kateriya, Adeishvili, Berthold Ollig, Hegemann & Bamberg (PNAS 2003)

Boyden, Zhang, Bamberg, Nagel & Deisseroth (Nat Neurosci 2005)



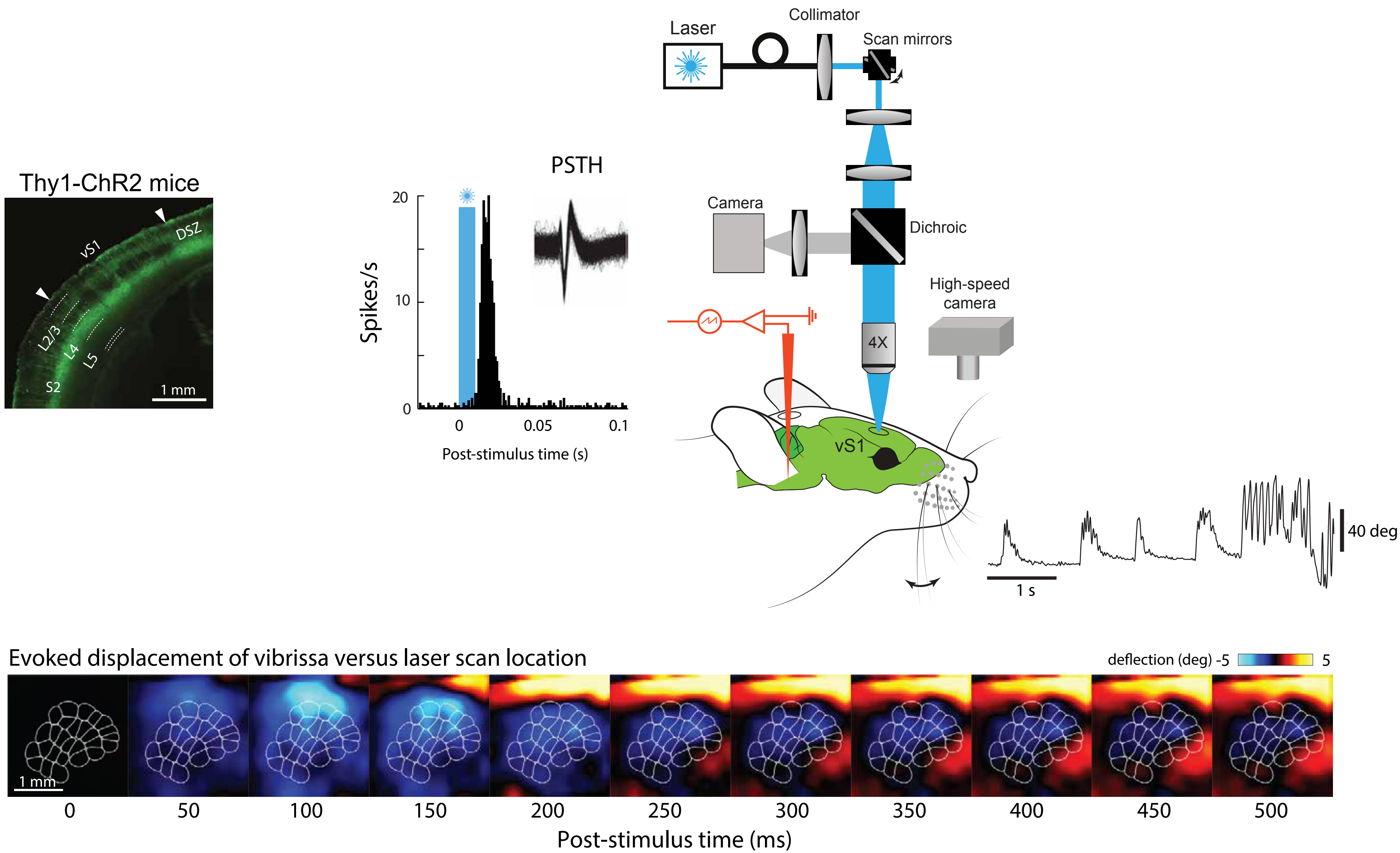




Papagiakoumou, de Sars, Oron & Emiliani (Opt Express 2008)

Andrasfalvy, Zemelman, Tang & Vaziri (PNAS 2010)

Does the output (L5b) of vibrissa cortex modulate neuronal spiking in the input (trigeminal) pathway?



Knutsen, Mercer Lindsay & Kleinfeld (SfN abstract 2015)

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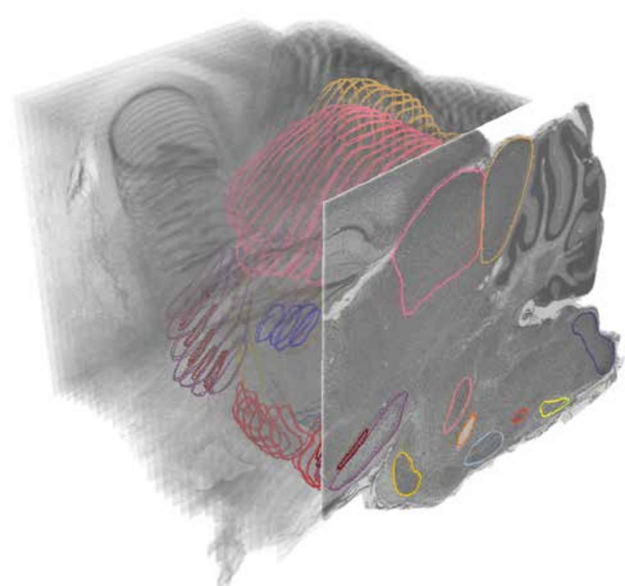
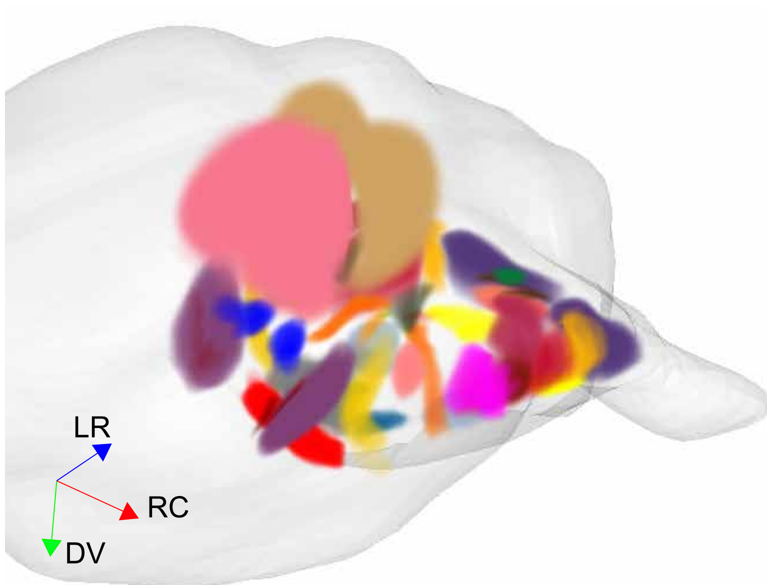
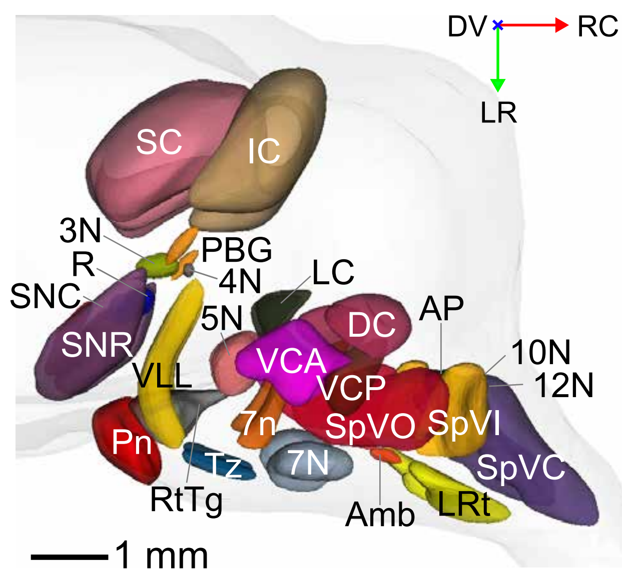
The active digital atlas - raw Nissl stained material

Training of the texture-based digital atlas: Expert annotation to form a reference atlas





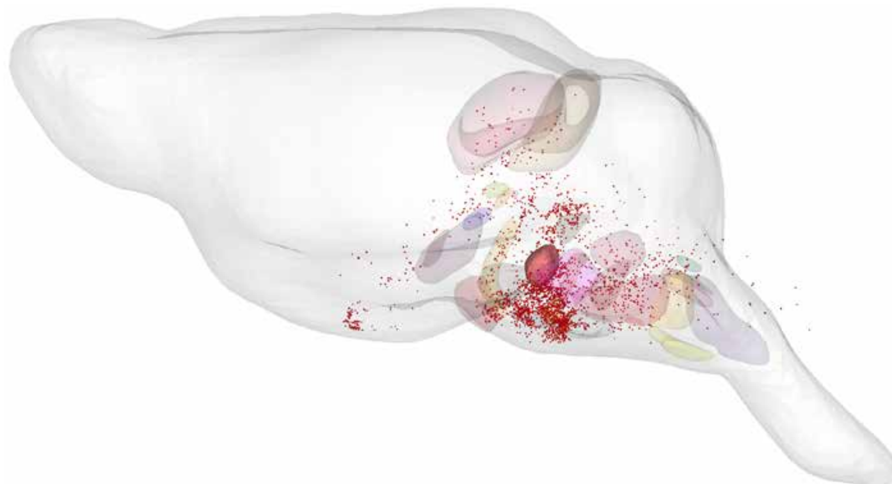


10N dorsal motor nucleus of vagus
12N hypoglossal nucleus
3N oculomotor nucleus
4N trochlear nucleus
5N motor trigeminal nucleus
6N abducens nucleus
7N facial nucleus
7n facial nerve
AP area postrema
Amb ambiguus nucleus
DC dorsal cochlear nucleus
LC locus coeruleus
LPB lateral parabrachial nucleus
LRt lateral reticular nucleus
PBG parabigeminal nucleus
Pn pontine nuclei
RMC red nucleus, magnocellular part
RtTg reticulotegmental nucleus of the pons
SC superior colliculus
SNC substantia nigra, compact part
SNR substantia nigra, reticular part
Sp5C spinal trigeminal nucleus, caudal part
Sp5I spinal trigeminal nucleus, interpolar part
Sp5O spinal trigeminal nucleus, oral part
Tz nucleus of the trapezoid body
VCA ventral cochlear nucleus, anterior part
VCP ventral cochlear nucleus, posterior part
VLL ventral nucleus of the lateral lemniscus

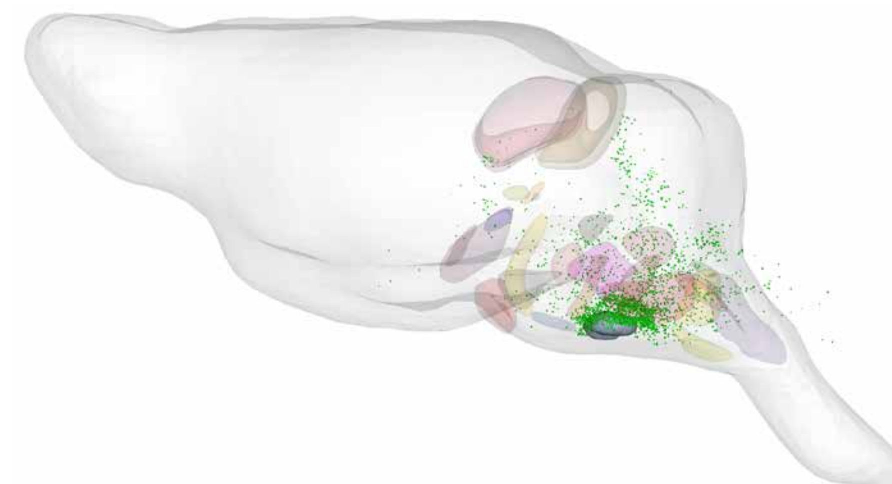
Chen, McElvain, Tolpygo, Ferrante, Friedman, Mitra, Karten, Freund* & Kleinfeld* (submitted)

Automated alignment of transported ∆G rabies across two brains

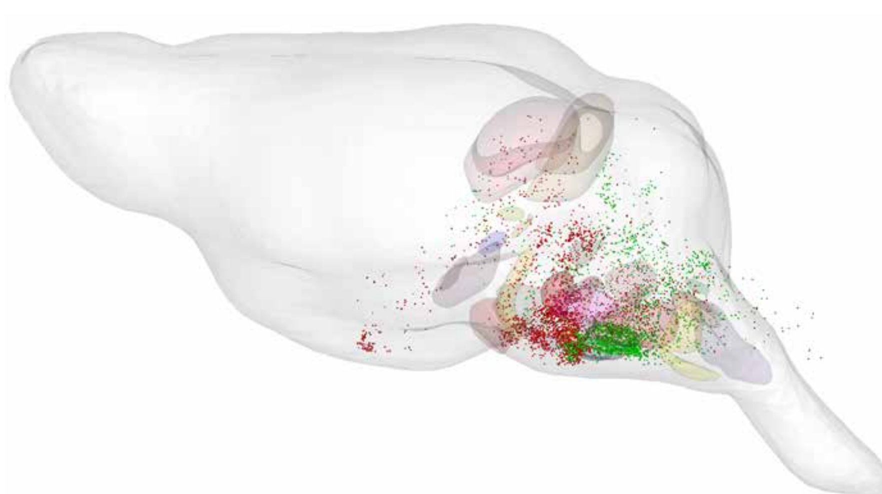
● Premotor 5N (jaw)

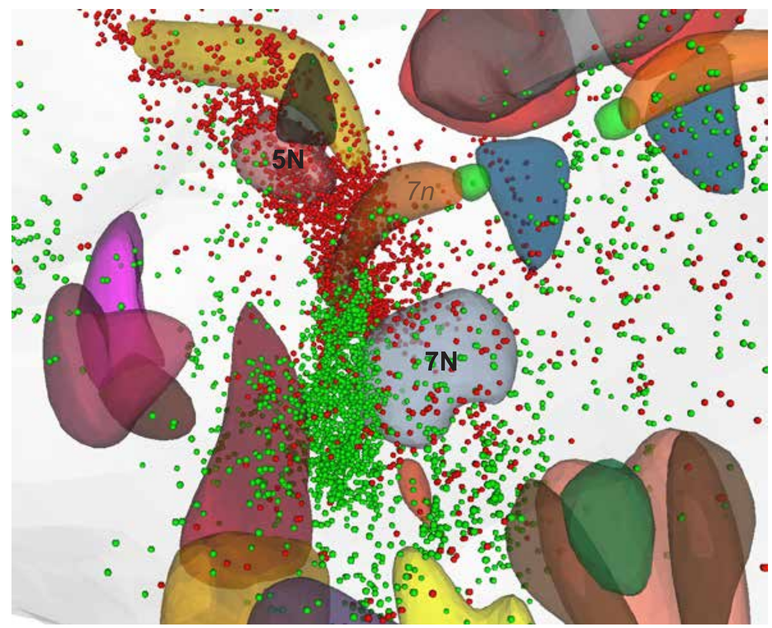


● Premotor lateral 7N (vibrissa)



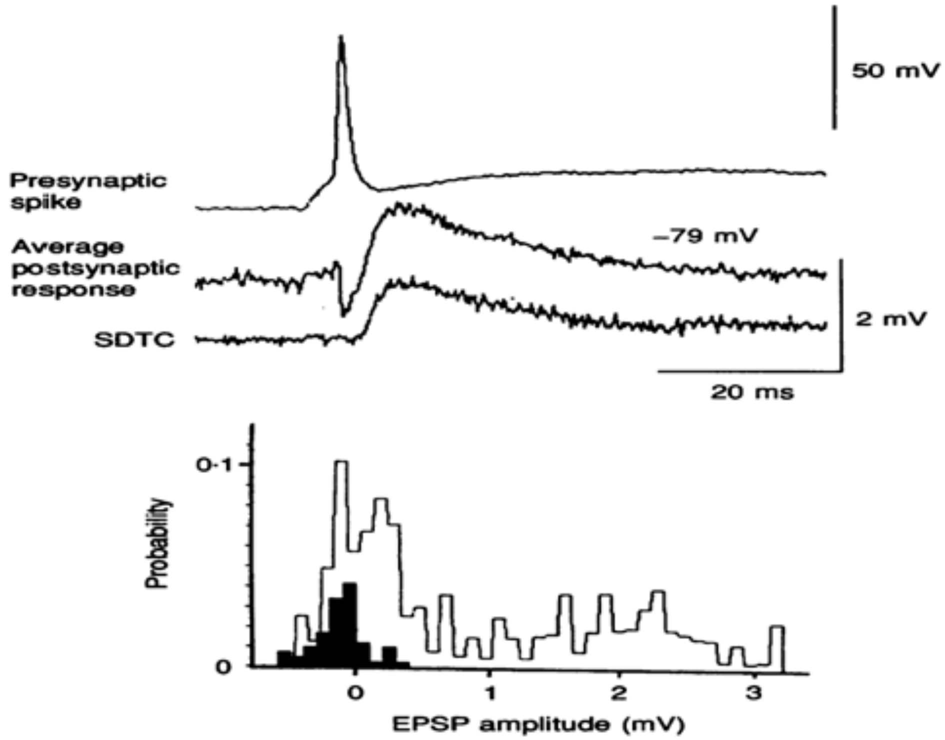
Overlap of premotor neurons in PCRt/IRt





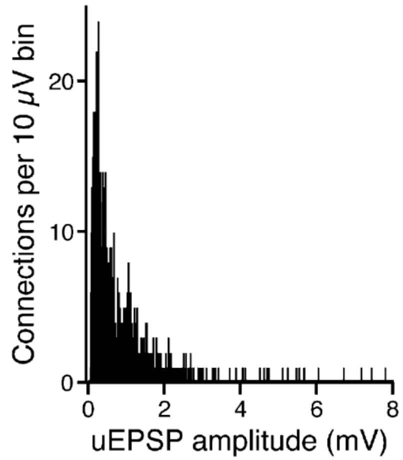
Chen, McElvain, Tolpygo, Ferrant, Friedman, Karten, Mitra, Freund & Kleinfeld (submitted)

Cortical connectivity has few strong and many weak synapses



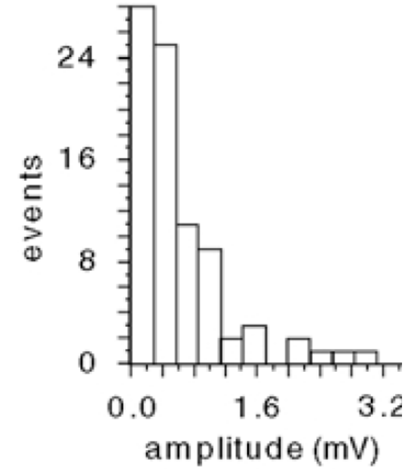
L5/6 pyramidal cells, Deuchars, West, Thomson (1994)

Vibrissa cortex, all excitatory connections



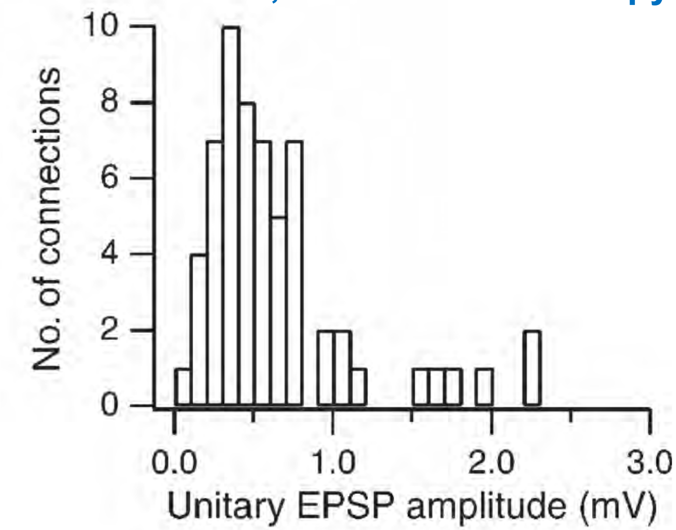
Lefort et al 2009

Visual cortex, L2/3 → L2/3 pyramid



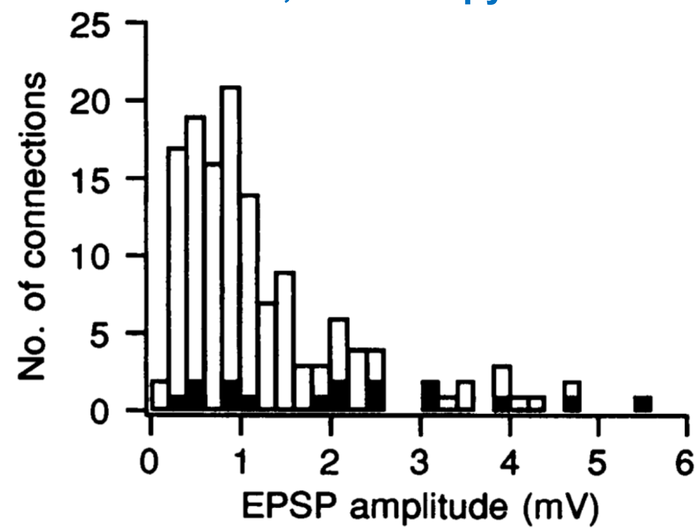
Holmgren et al 2003

Vibrissa cortex, L4 stellate → L2/3 pyramid



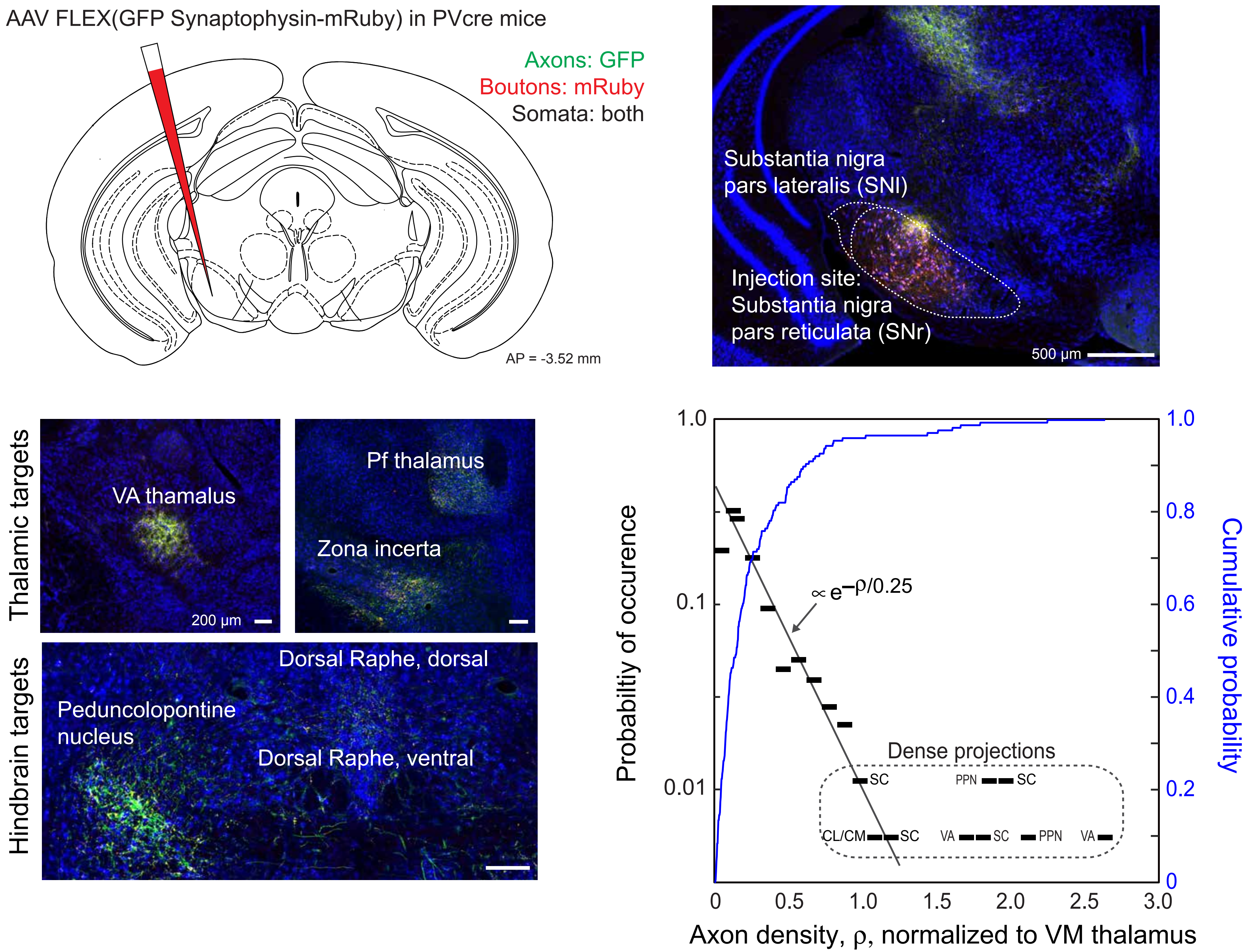
Feldmeyer et al 2002

Vibrissa cortex, L5 → L5 pyramid



Markram et al 1997

Connectivity distribution for anterograde tracing from SNr



McElvain, Chen, Lim,* Costa* & Kleinfeld* (in preparation)

Synopsis

- Neuronal computations occur in nested loops with reflexive through brain-wide feedback

- Far-field and near-field sensory processes are represented by different sets of hubs and cortical connectivity

- Synaptic connections are broad, with the integrated strength of the many weak greater than the few strong

- Physical measurements are (slowly) approaching the level of recording from all cells in the mouse brain, as achieved in the juvenile zebra-fish brain

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Santiago Ramón Y Cajal (1852-1934)

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