Nonhuman primate fMRI and everything it has to offer

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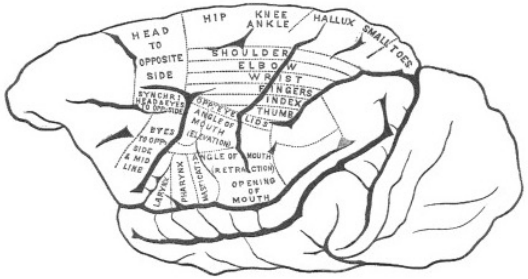
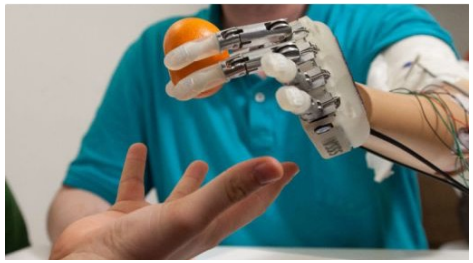
National Institutes of Health

Research in nonhuman primates has always played a paramount role in understanding the human brain:

- electrical microstimulation to study functional organization



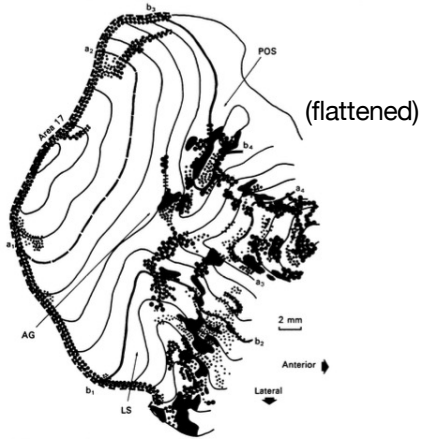
Beevor and Horsley (1890)



Neuroprosthetic control (2016)

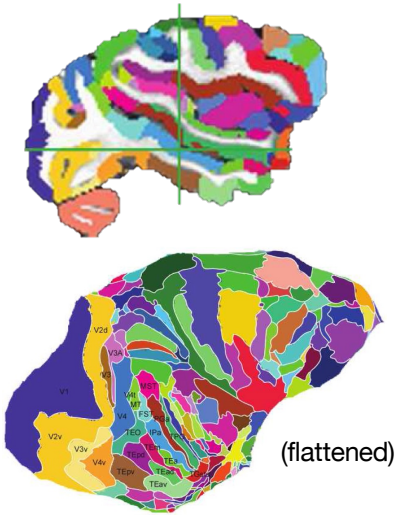
- neuroanatomical connections

Waller method (1850)
Nauta method (1951)



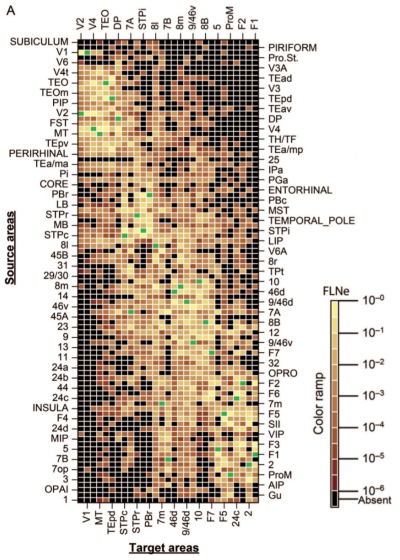
(flattened)

Van Essen and Zeki (1978)



(flattened)

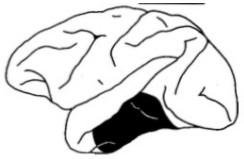
Saleem and Logothetis



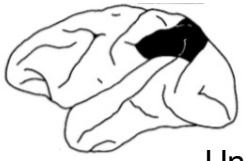
Markov,…, Van Essen, Kennedy (2014)

Research in nonhuman primates has always played a paramount role in understanding the human brain:

- neuropsychological studies



object recognition deficits

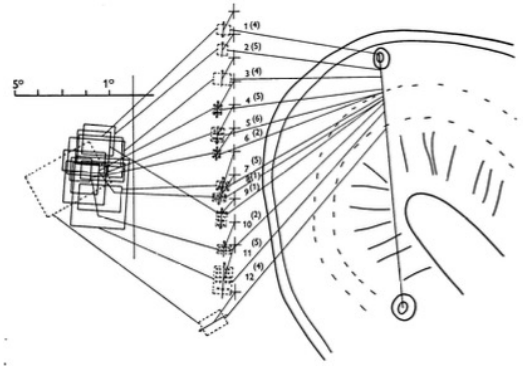


spatial perception deficits

Ungerleider and Mishkin (1982)

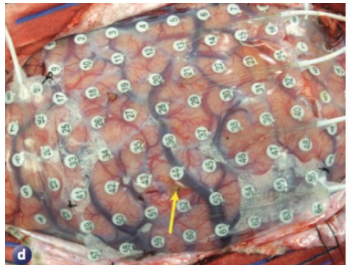
understanding consequences of brain damage

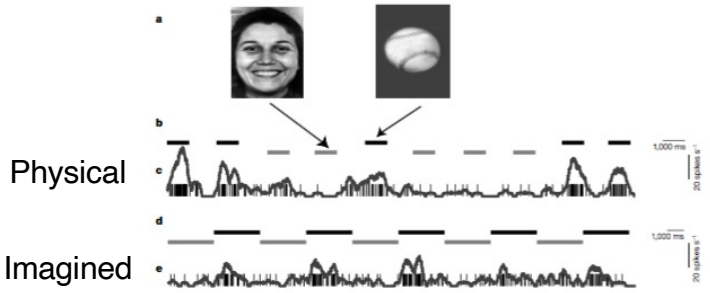
- electrophysiological studies



Hubel and Wiesel (1962)

Bruce, Desimone, Gross (1982)

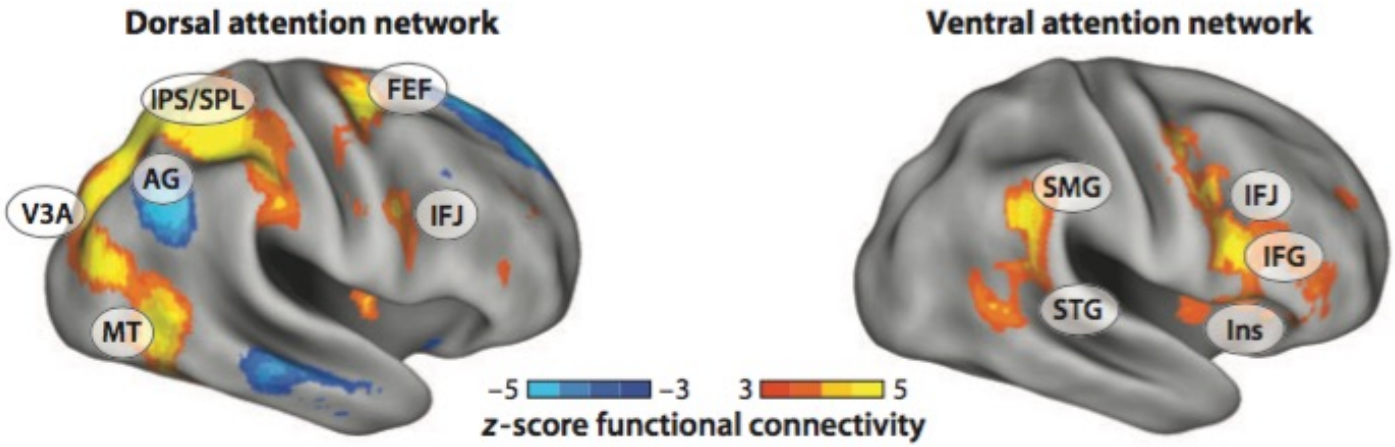




Kreiman, Koch, Fried (2000)

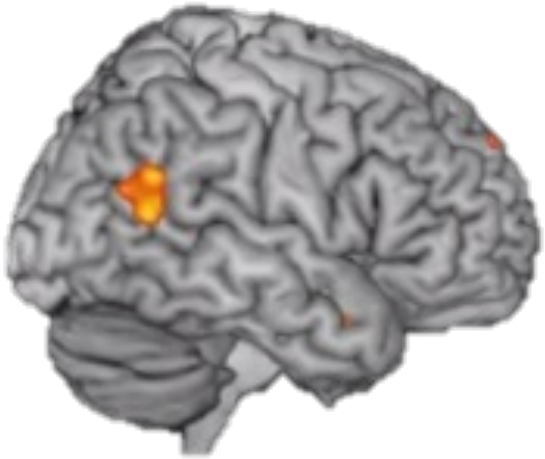
fMRI has revolutionized our understanding of human brain networks

Attention



Maurizio Corbetta

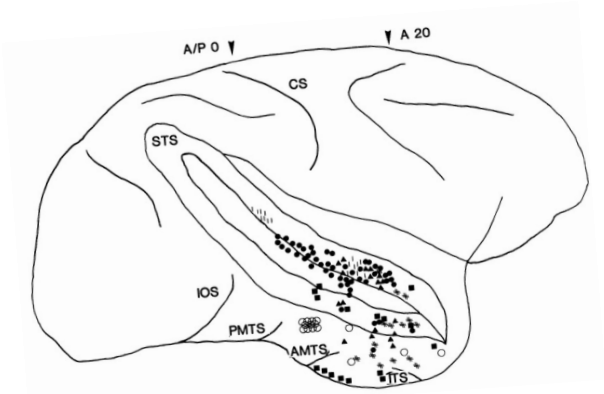
Thinking about what others are thinking



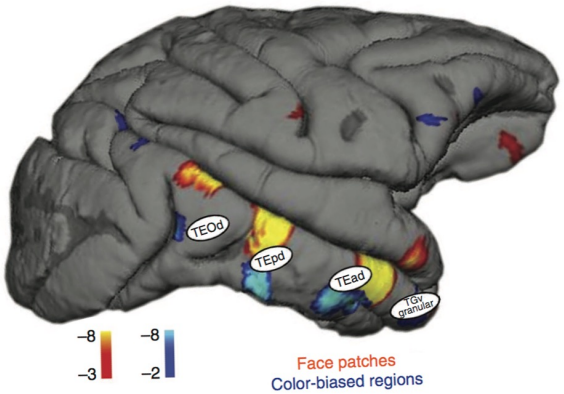
Rebecca Saxe

Monkey fMRI has provided fresh insights into brain systems

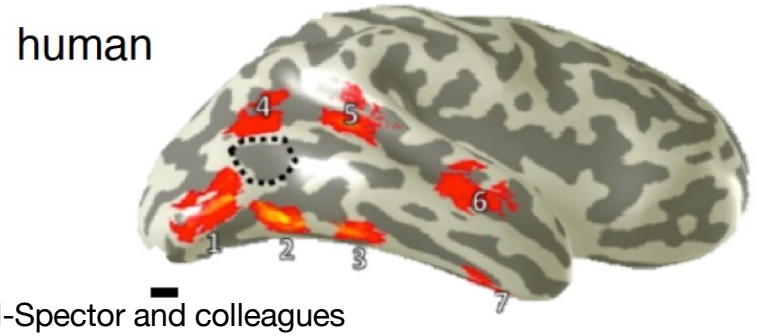
Example: face patches



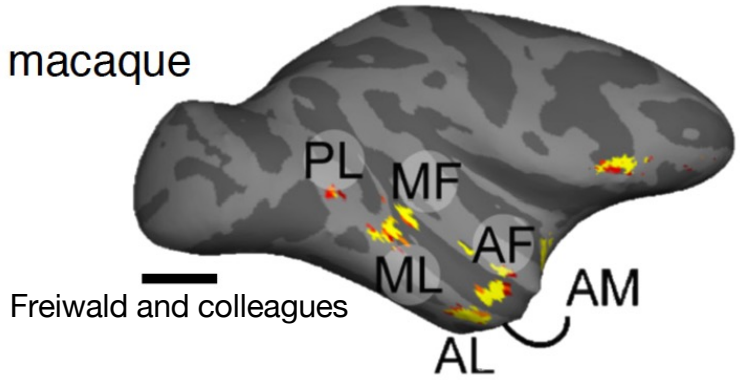
Perrett, Hietanen, Oram, Benson (1992)



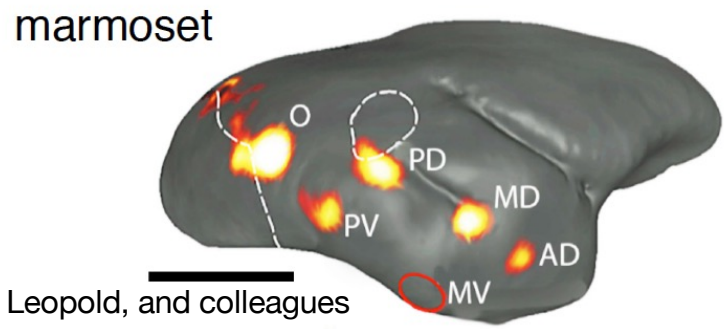
Lafer-Sousa and Conway (2013)



Grill-Spector and colleagues



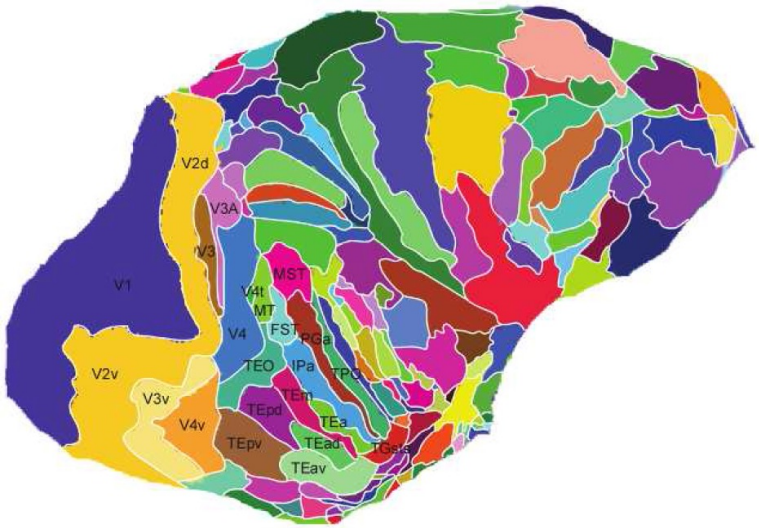
Tsao, Freiwald and colleagues

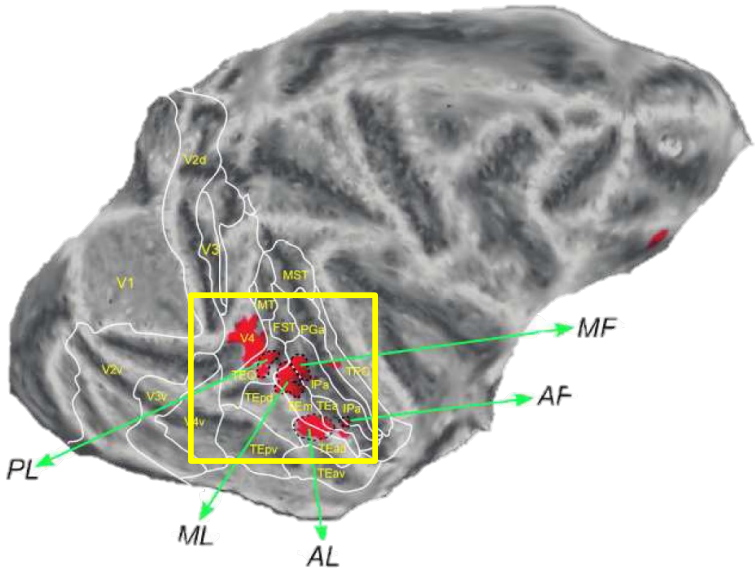


Silva, Leopold, and colleagues

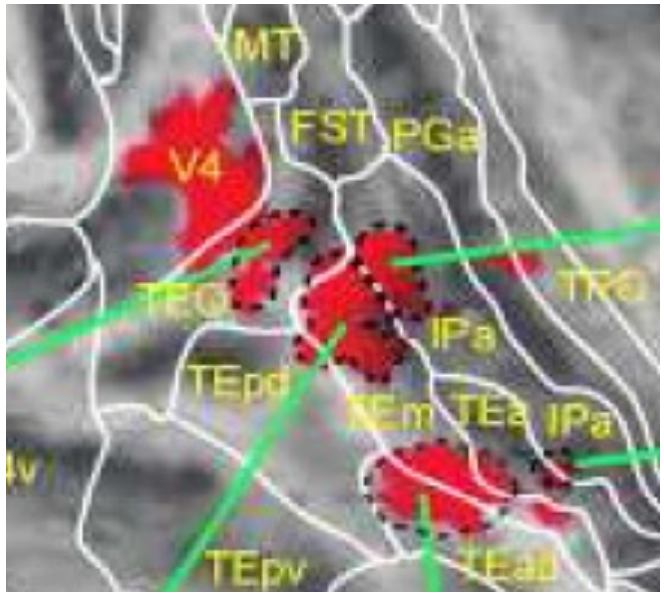
Monkey fMRI has provided new insight into brain systems

Example: face patches





functionally-defined areas
vs.
histologically-defined areas



Reveley, Gruslys, Ye, Samaha, Glen, Russ, Saad, Seth, Leopold and Saleem (in press)

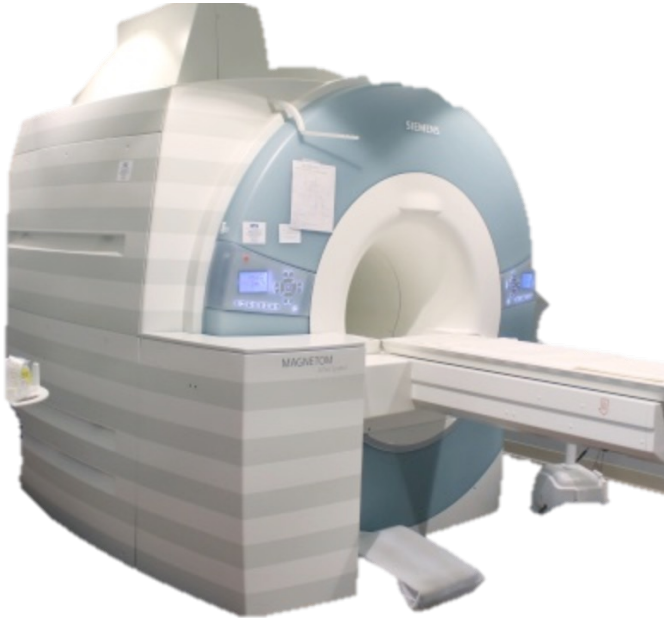
Monkey fMRI: challenges and special considerations

- Custom chairs, holders, all fMRI compatible
- Specialized coils, and sometimes specialized scanners
- Susceptibility artifacts from implants, subject movement
- Use of intravenous contrast agents
- Need for custom analysis
- Small number of subjects

Macaque fMRI in a specialized or commercial scanner

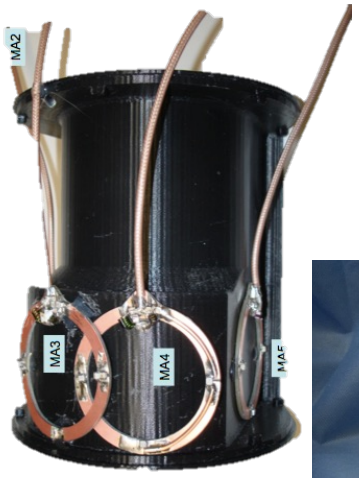
4.7T vertical scanner (Bruker)

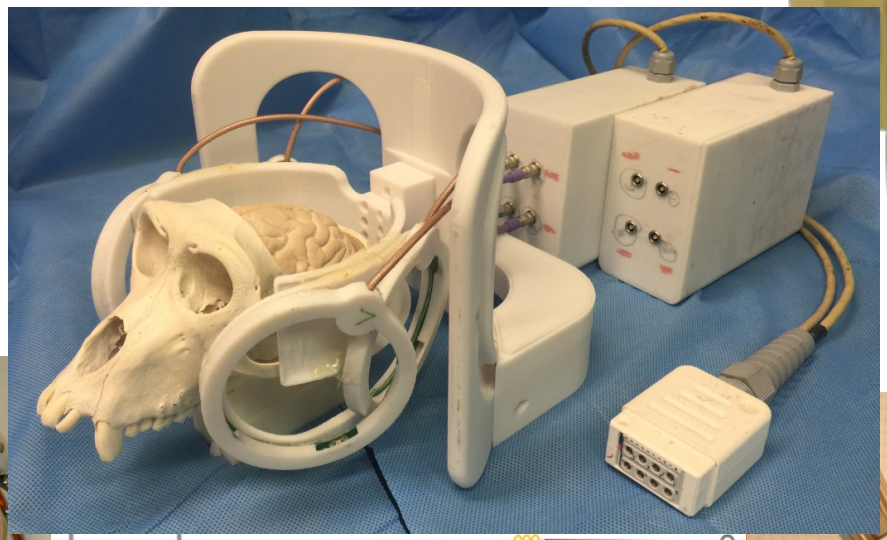
3T horizontal scanner (Siemens)

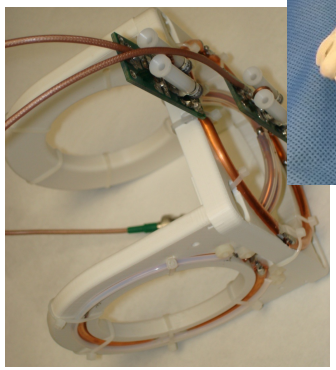


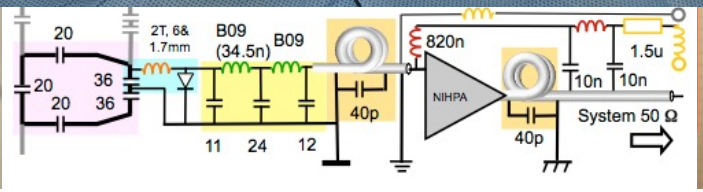
Siemens AC88 Gradient Insert

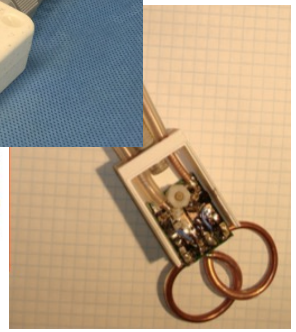
Monkey fMRI depends on custom coil design and manufacture







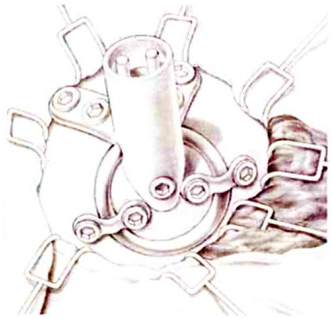


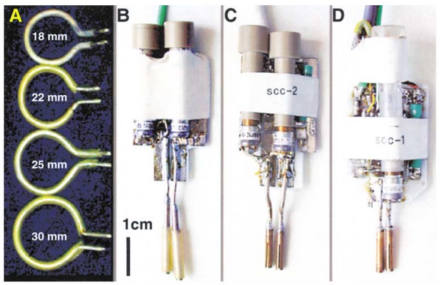


Charles Zhu, NIF

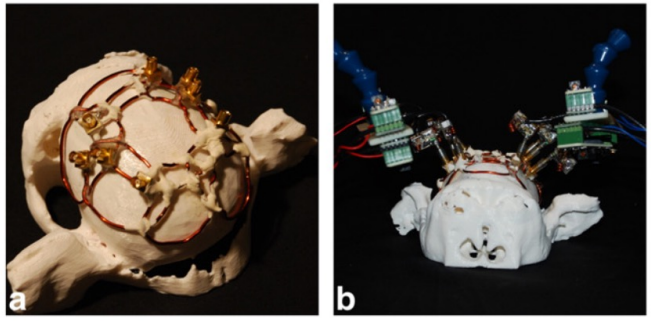
Hellmut Merkle, NINDS

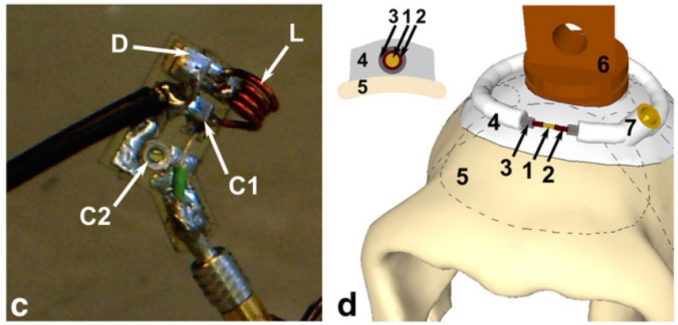
Implanted coils: optimizing signal-to-noise / spatial resolution



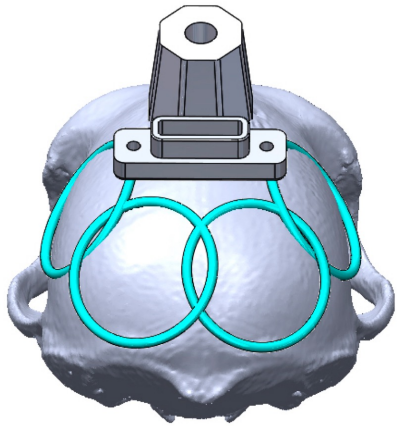


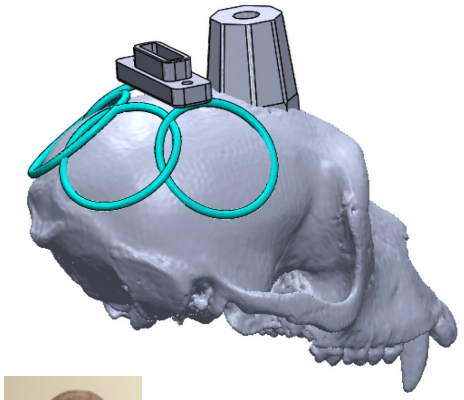
Logothetis, Merkle, Augath, Trinath and Ugurbil (2002)





Janssens, Keil, Farivar, McNab, Polimeni, Gerits, Arsenault, Wald and Vanduffel (2012)



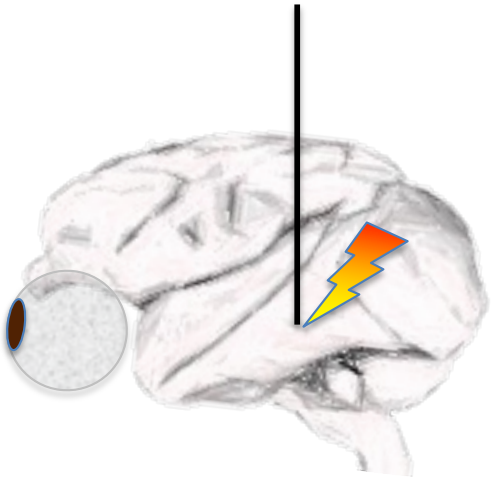


Zhu, Ye, Yu and Leopold (under testing)

What are the merits of fMRI in nonhuman primates?

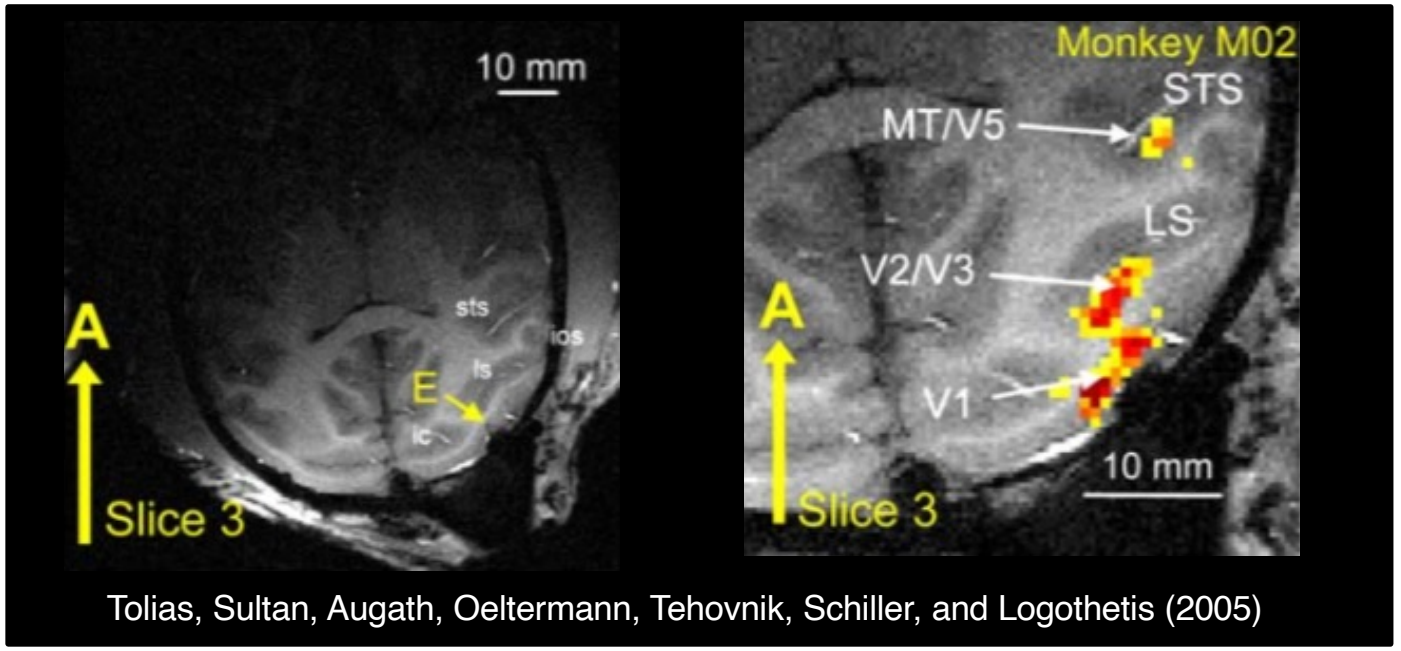
- **Bridging:** monkey fMRI helps link human fMRI results to detailed knowledge of the macaque brain.
- **Functional localization:** determining functional targets for electrophysiological recordings or activity manipulation
- **Combining methods:** reading out whole-brain fMRI activity while applying methods impossible in humans
- **Technical development:** prototyping of coils, sequences, and preparations before use in humans.
- **Comparative research:** targeted investigation of functional homologies across different species.

Combining Electrical Microstimulation with fMRI Responses throughout the Brain



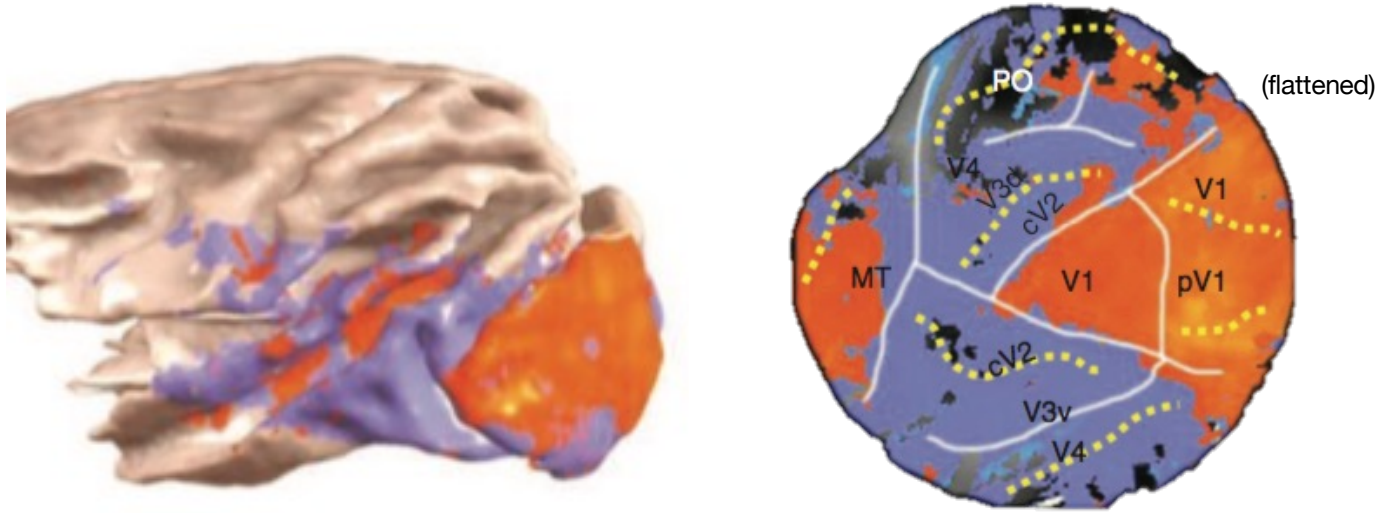
Microstimulation mapping of the **early visual system**

Area V1



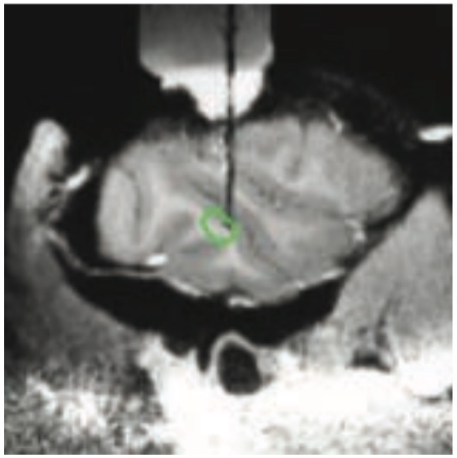
Tolias, Sultan, Augath, Oeltermann, Tehovnik, Schiller, and Logothetis (2005)

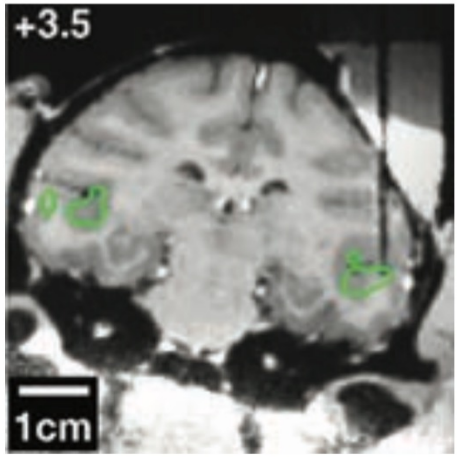
Lateral Geniculate Nucleus (LGN)

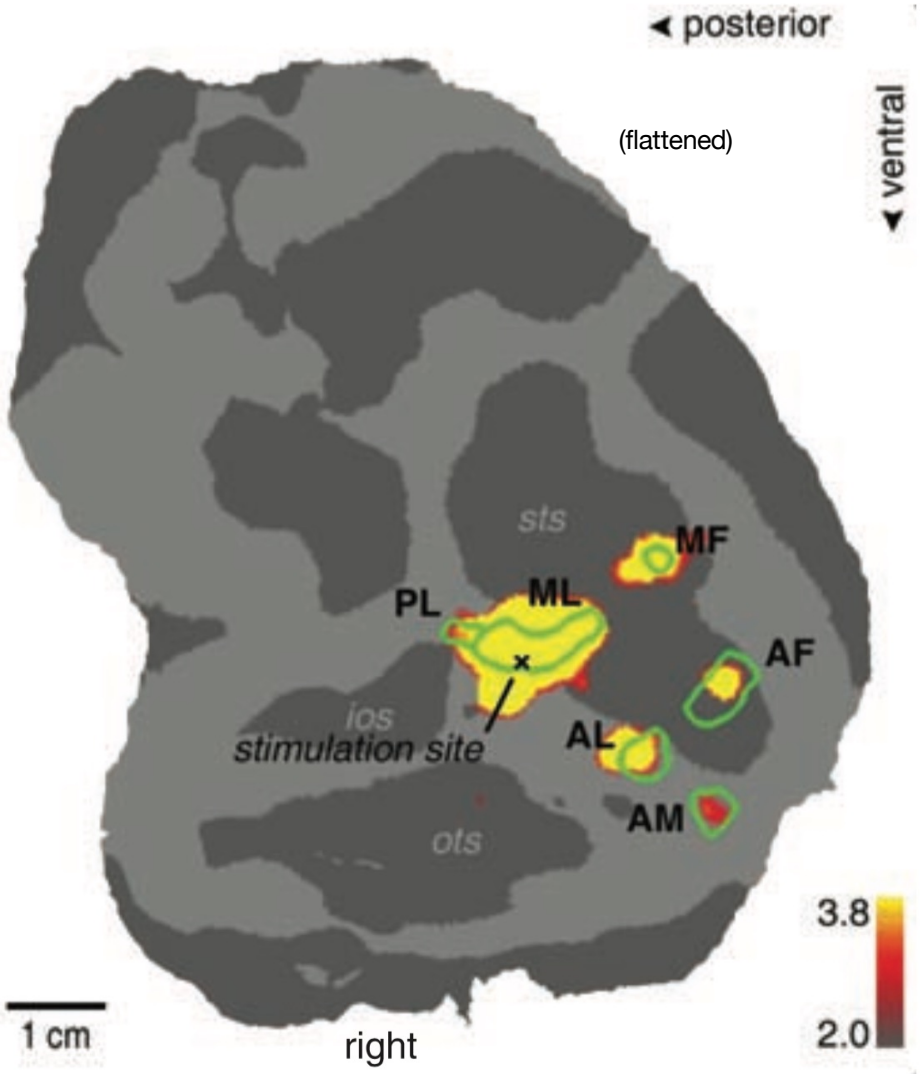


Logothetis, Augath, Murayama, Rauch, Sultan, Goense, Oeltermann, and Merkle (2010)

Microstimulation mapping of **face patches**



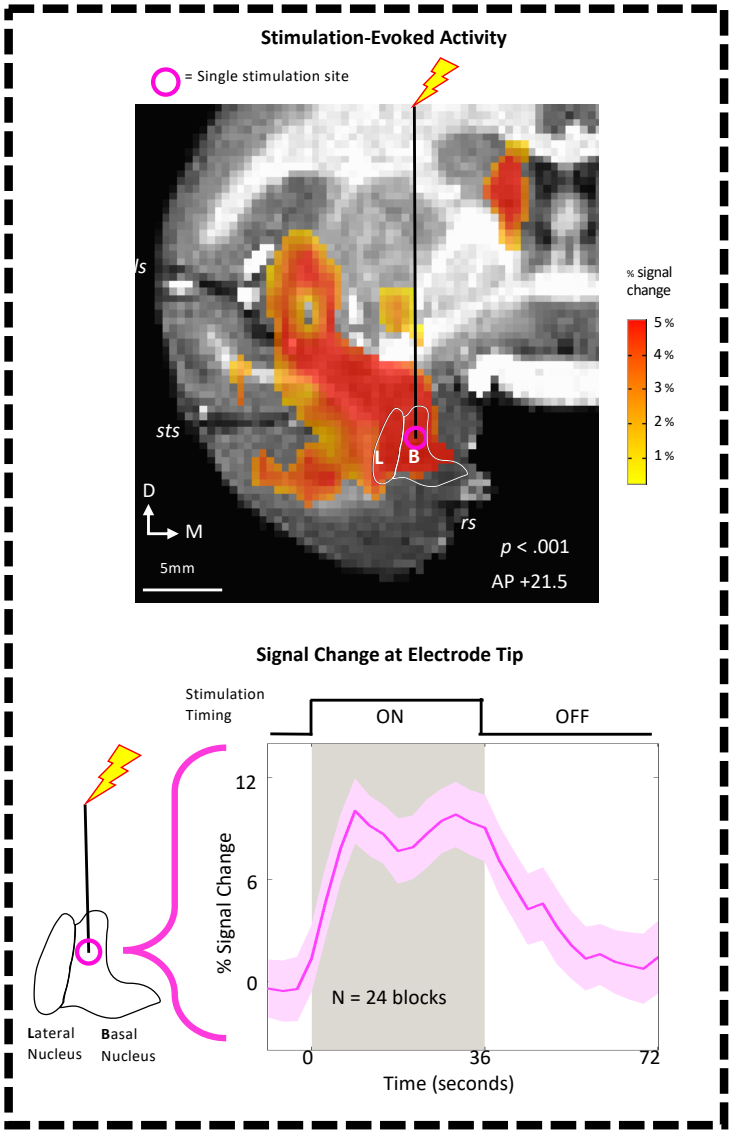




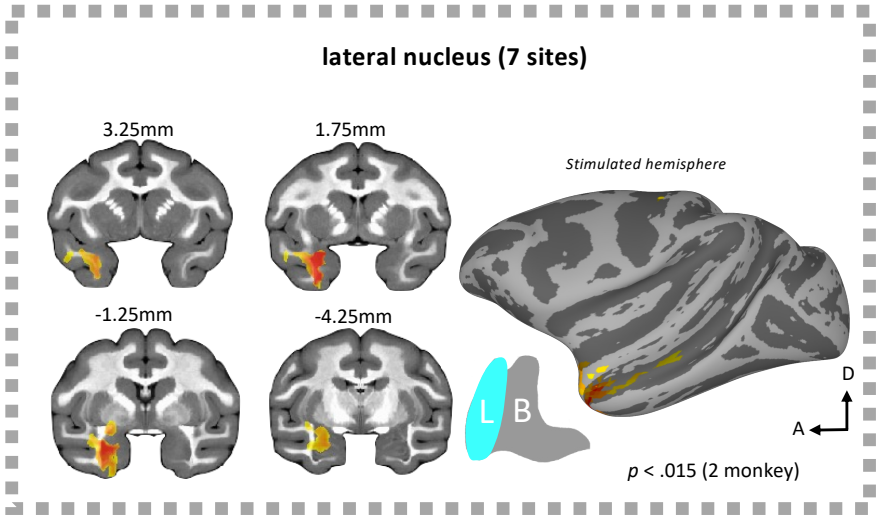
Moeller, Freiwald, Tsao (2008)

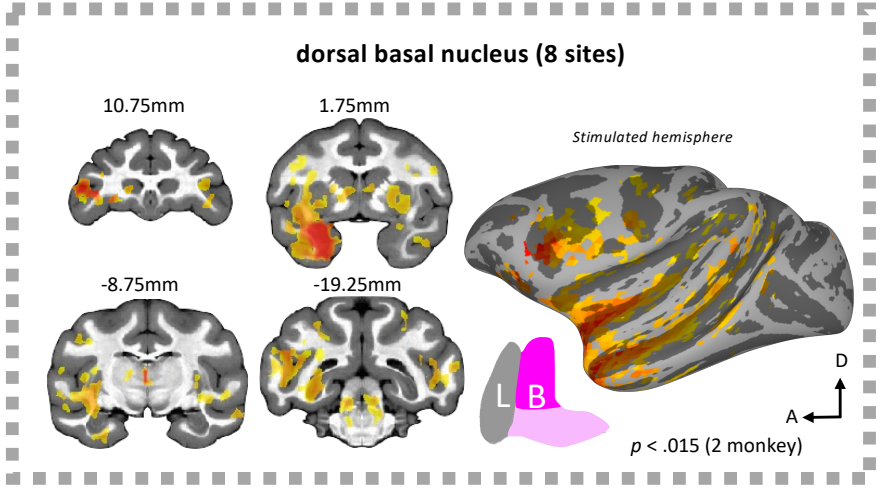
Microstimulation mapping of the **amygdala**

Single-site Amygdala Stimulation



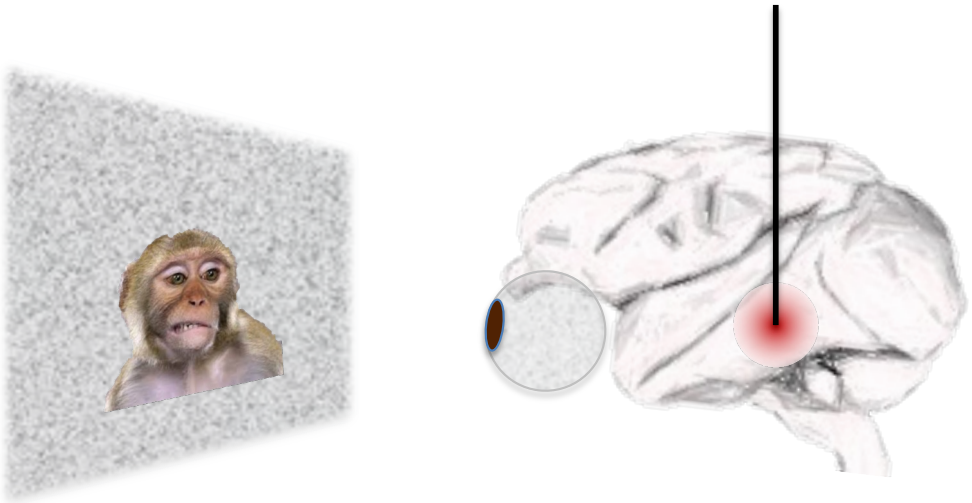
Projections of Lateral vs Basal Nuclei





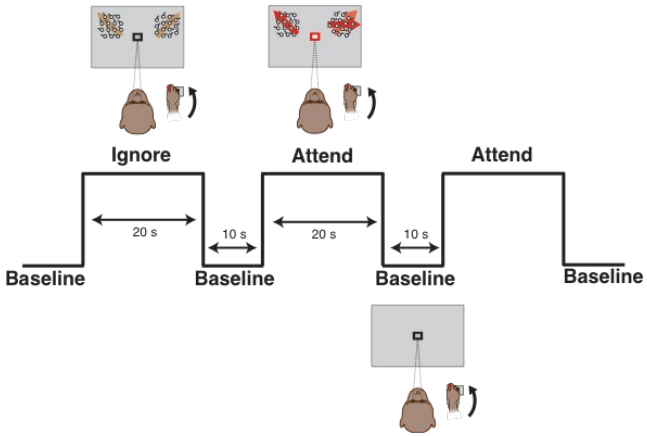
Messinger, Seidlitz, Sponheim, Mei, Tootell, and Ungerleider

Combining Reversible Inactivation with fMRI Responses throughout the Brain



Inactivation of the **superior colliculus**:
effects on the expression of attention

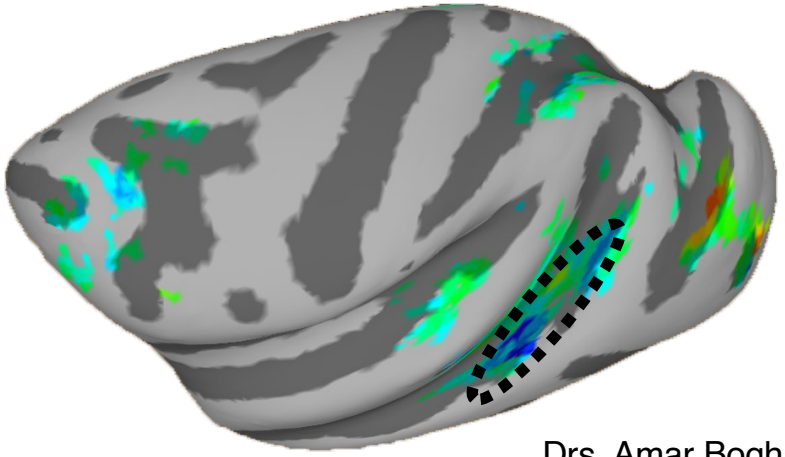
Attention task in fMRI paradigm



Inactivation of superior colliculus causes deficits in spatial attention

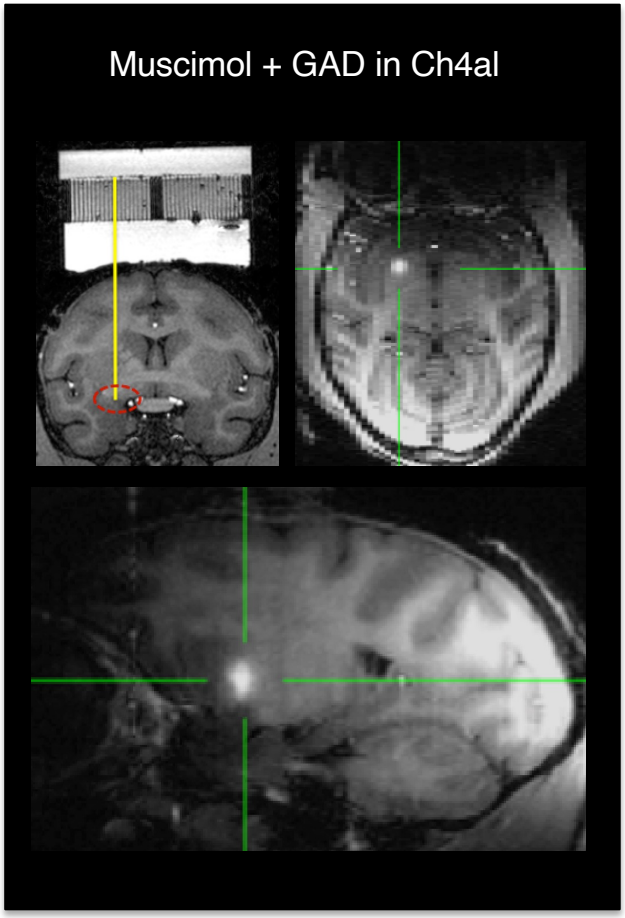
GABA$_A$ Agonist
Muscimol (0.5 µl)

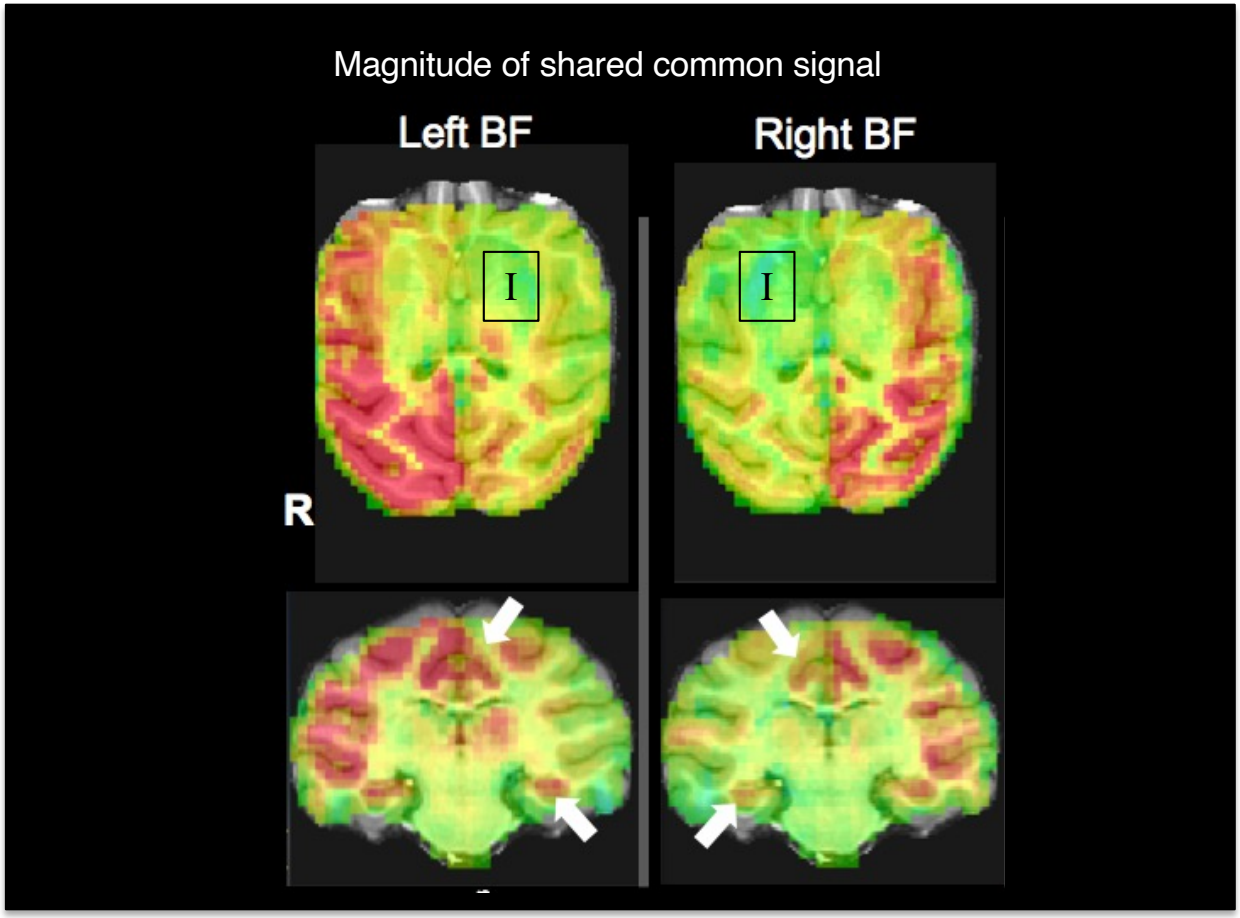
Inactivation affected regions in STS



Drs. Amar Boghadi, Anil Bollimunta, and Rich Krauzlis (NEI)

Inactivation of the **nucleus basalis**:
effects on spontaneous fMRI fluctuations

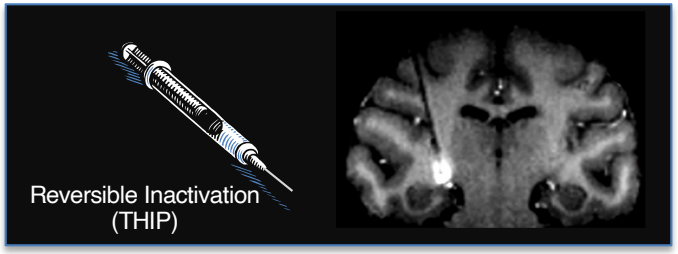




Drs. Janita Turchi (NIMH) and Catie Chang (NINDS)

Lesion of **area V1** + inactivation of the **LGN**:
effects on responses in extrastriate visual areas

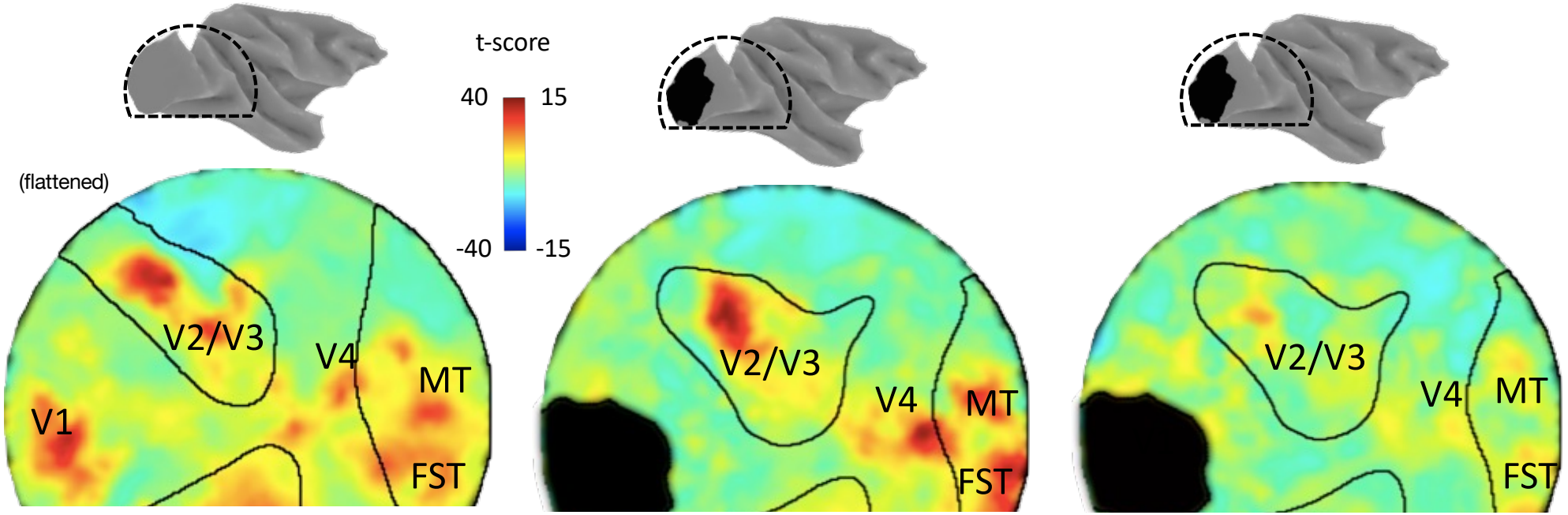
(small visual stimulus)



Intact

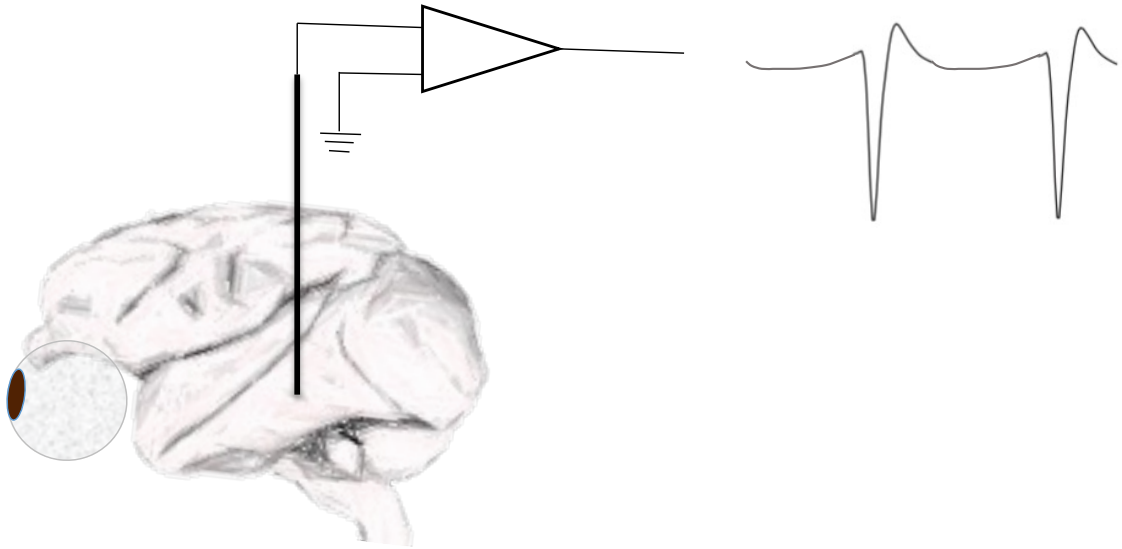
V1-Lesion

V1-Lesion + LGN inactivation

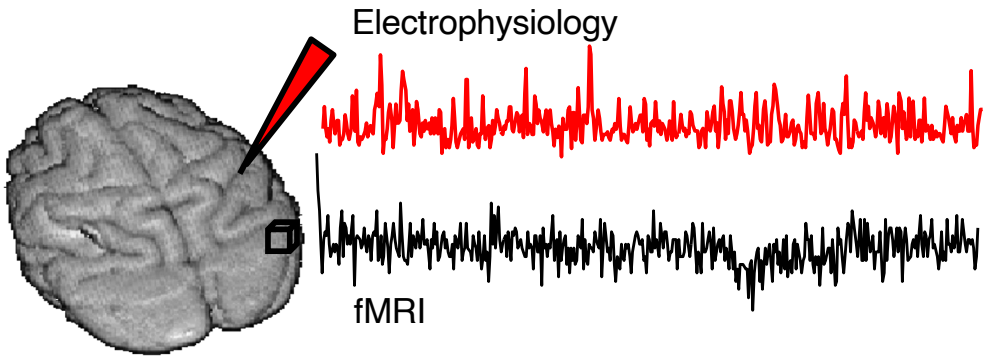


Schmid, Mrowka, Turchi, Saunders, Wilke, Peters, Ye and Leopold (2010)

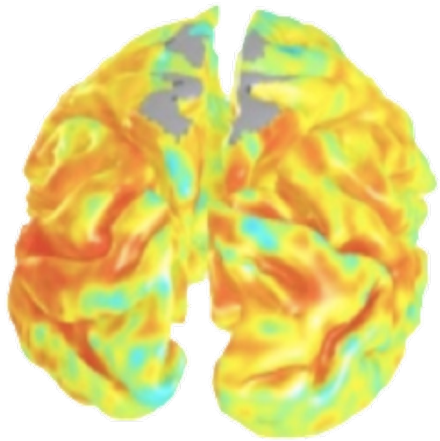
Combining Neural Recordings with fMRI Responses throughout the Brain

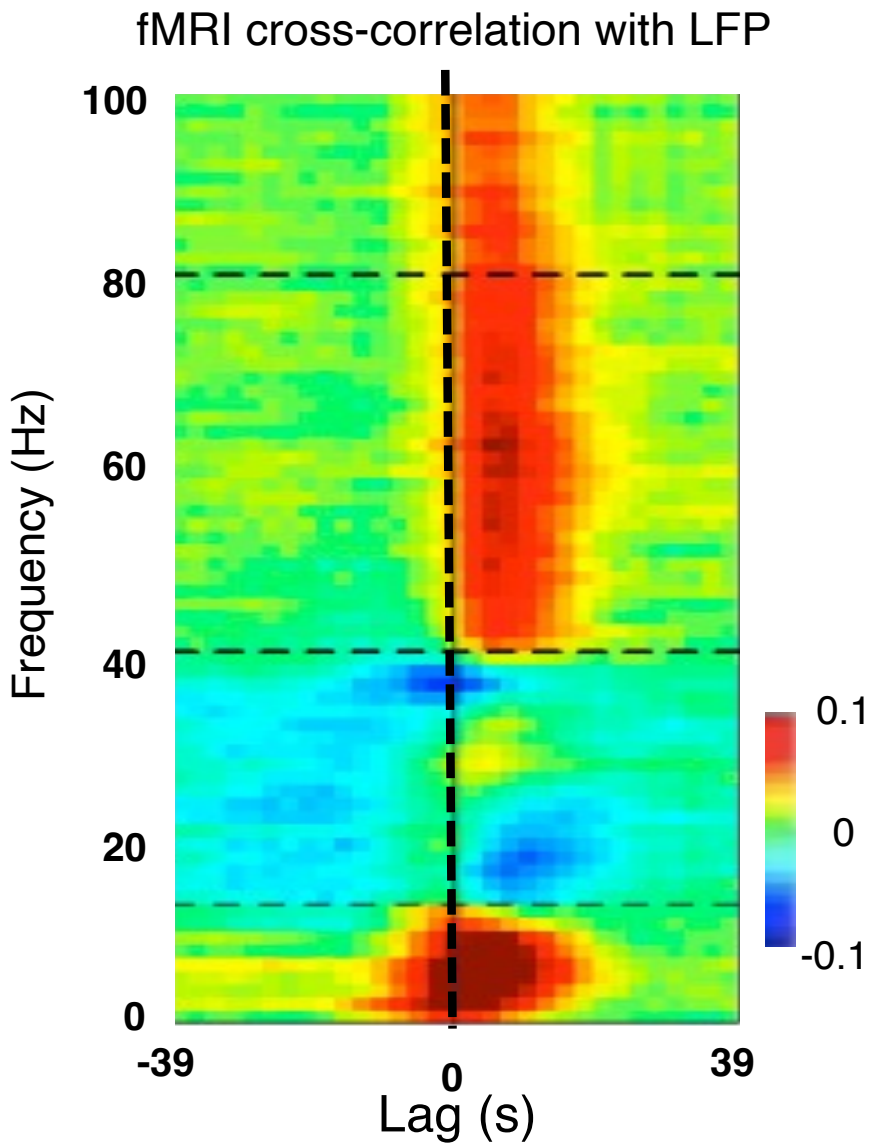


Resting state: comparing **local field activity** to fMRI responses throughout the brain



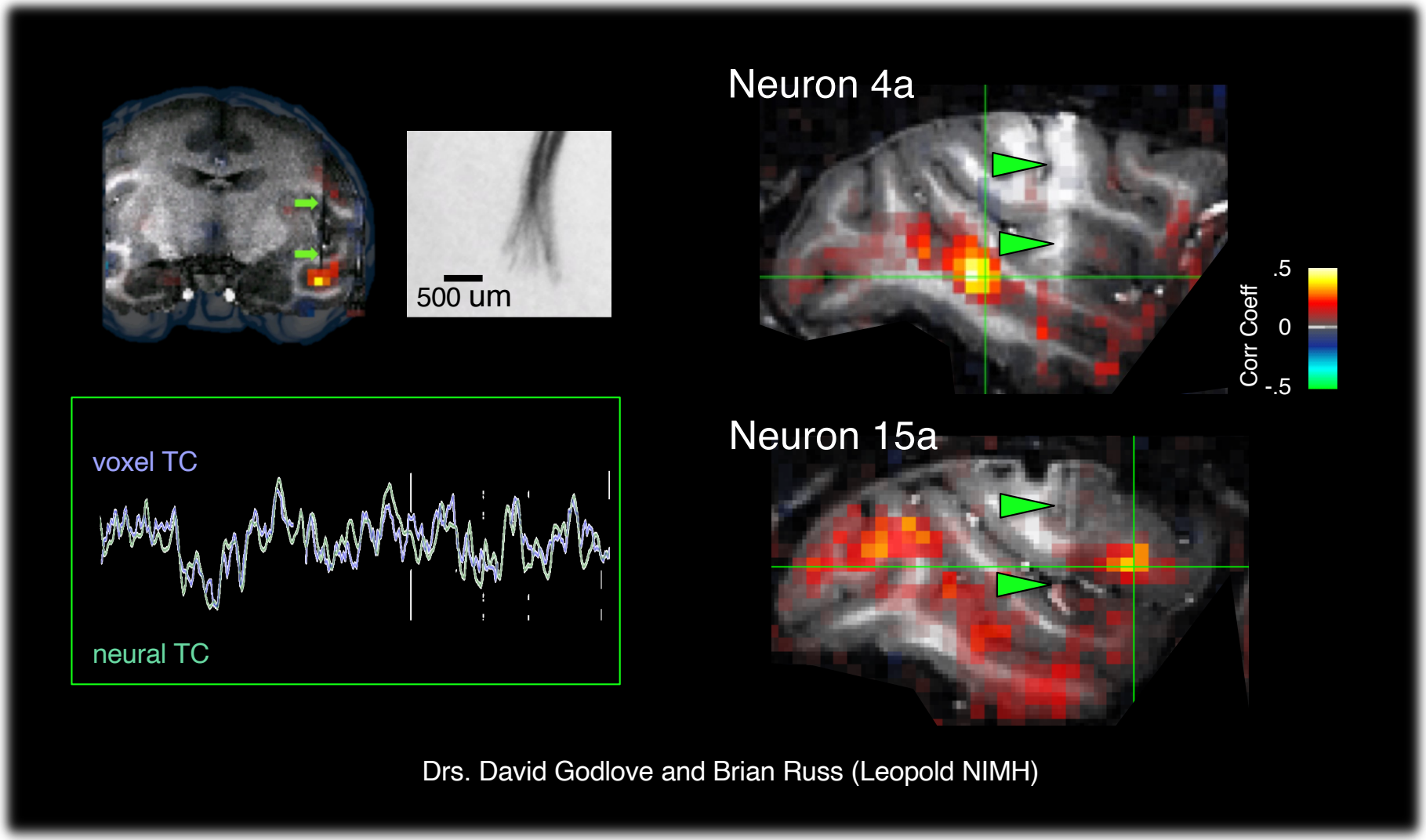
neural basis of global fMRI signal





Schölvinck, Maier, Ye, Duyn and Leopold (2010)

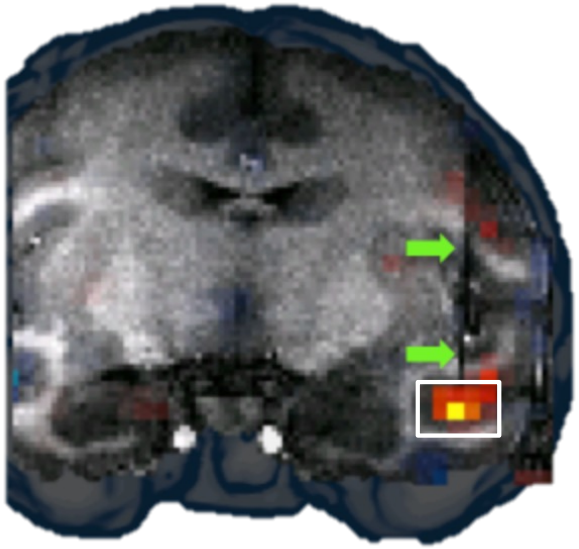
Resting state: comparing **single unit activity** to fMRI responses throughout the brain



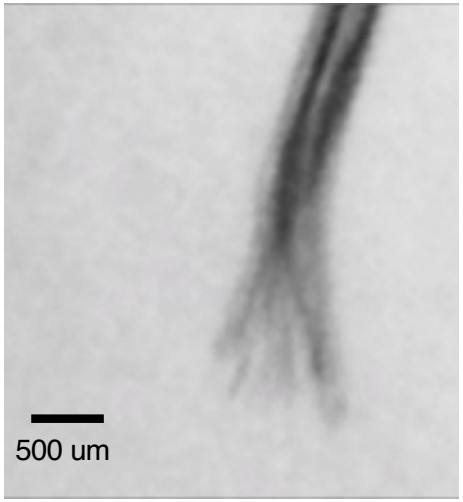
"single-unit fMRI mapping"

Visual responses: understanding local circuits through global mapping

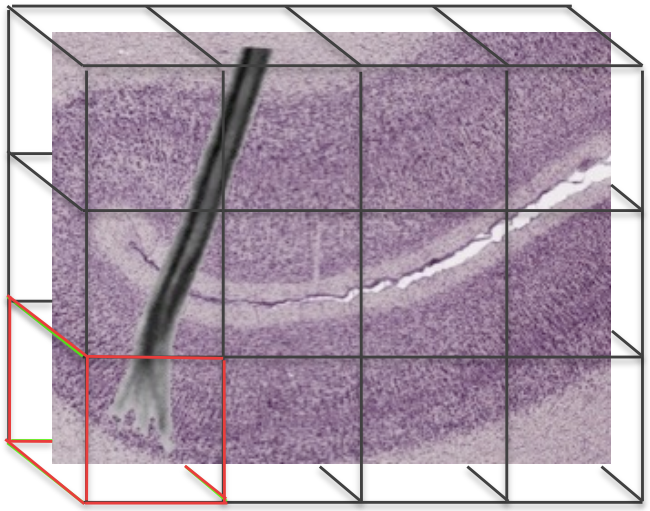
microwire bundle in face patch AF



microCT of bundle *in situ* (post-mortem)



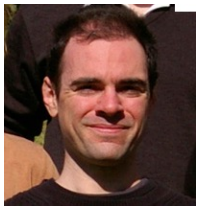
depiction of bundle within a $(1.5\ mm)^3$ voxel



Brian Russ

Soo Hyun Park

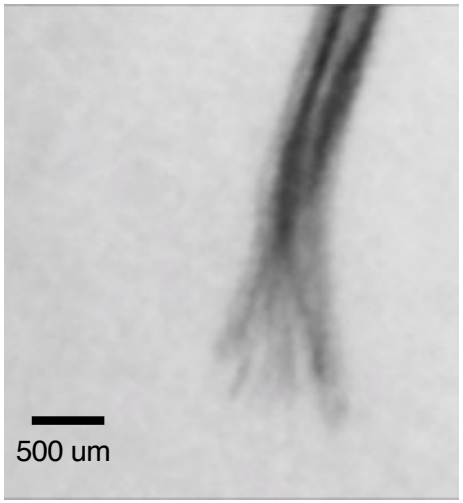
Igor Bondar

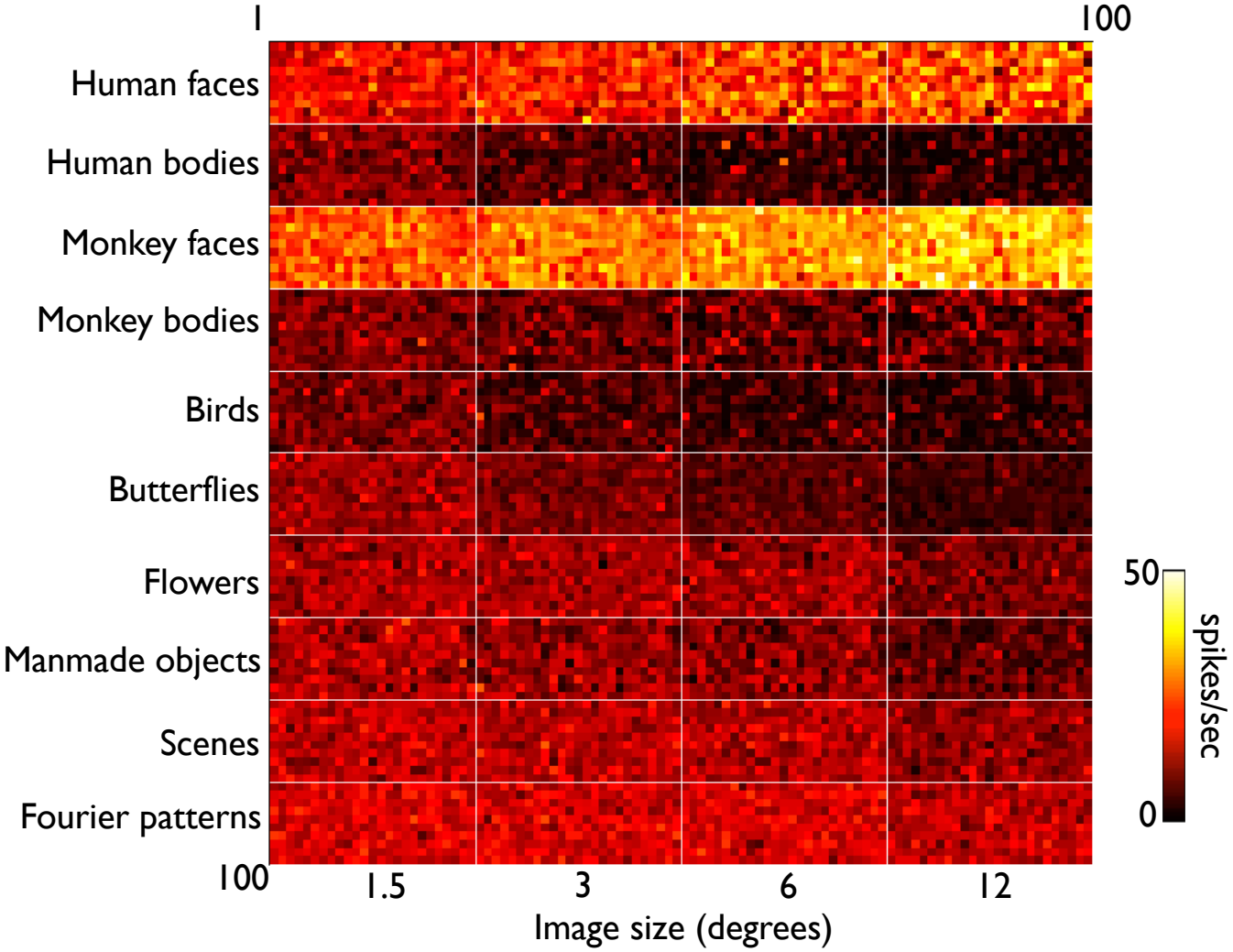


David McMahon

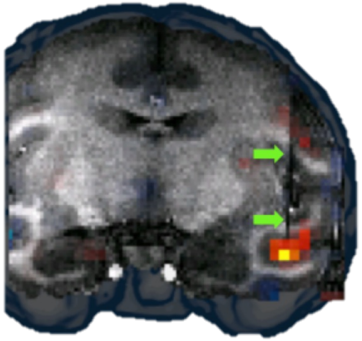
Visual responses: understanding local circuits through global mapping

microwire bundle in face patch AF



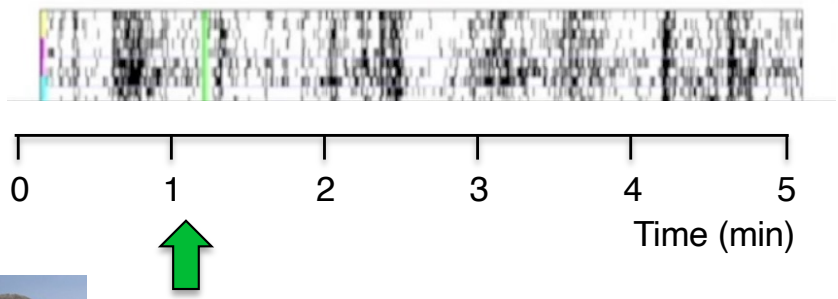


neurons in area AF are “face cells”

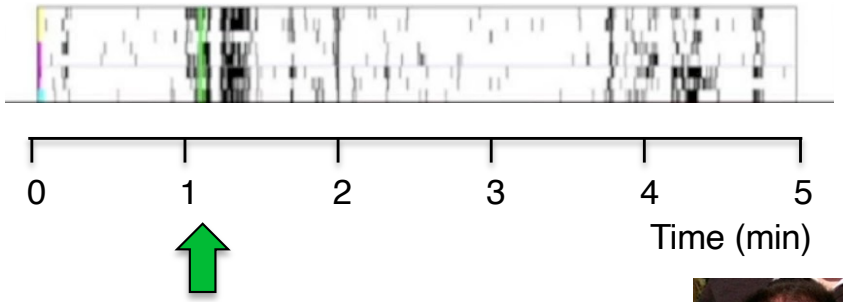


How do individual neurons in face patch AF respond during natural viewing?

Cell 102a

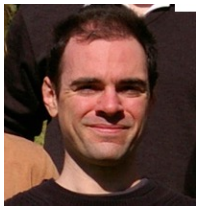


Cell 114a



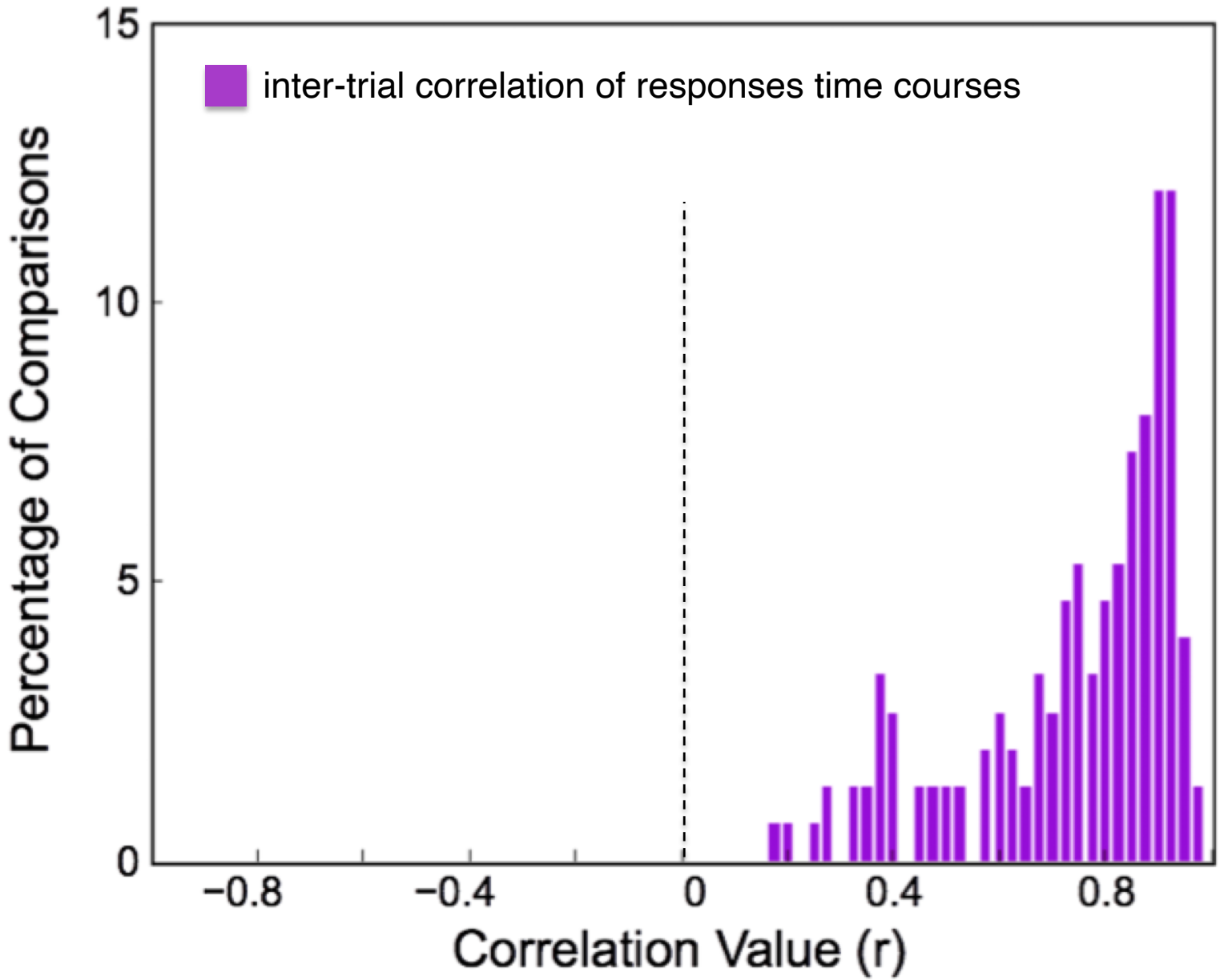
Brian Russ

McMahon, Russ, Elnaiem, Kurnikova, Leopold (2015)



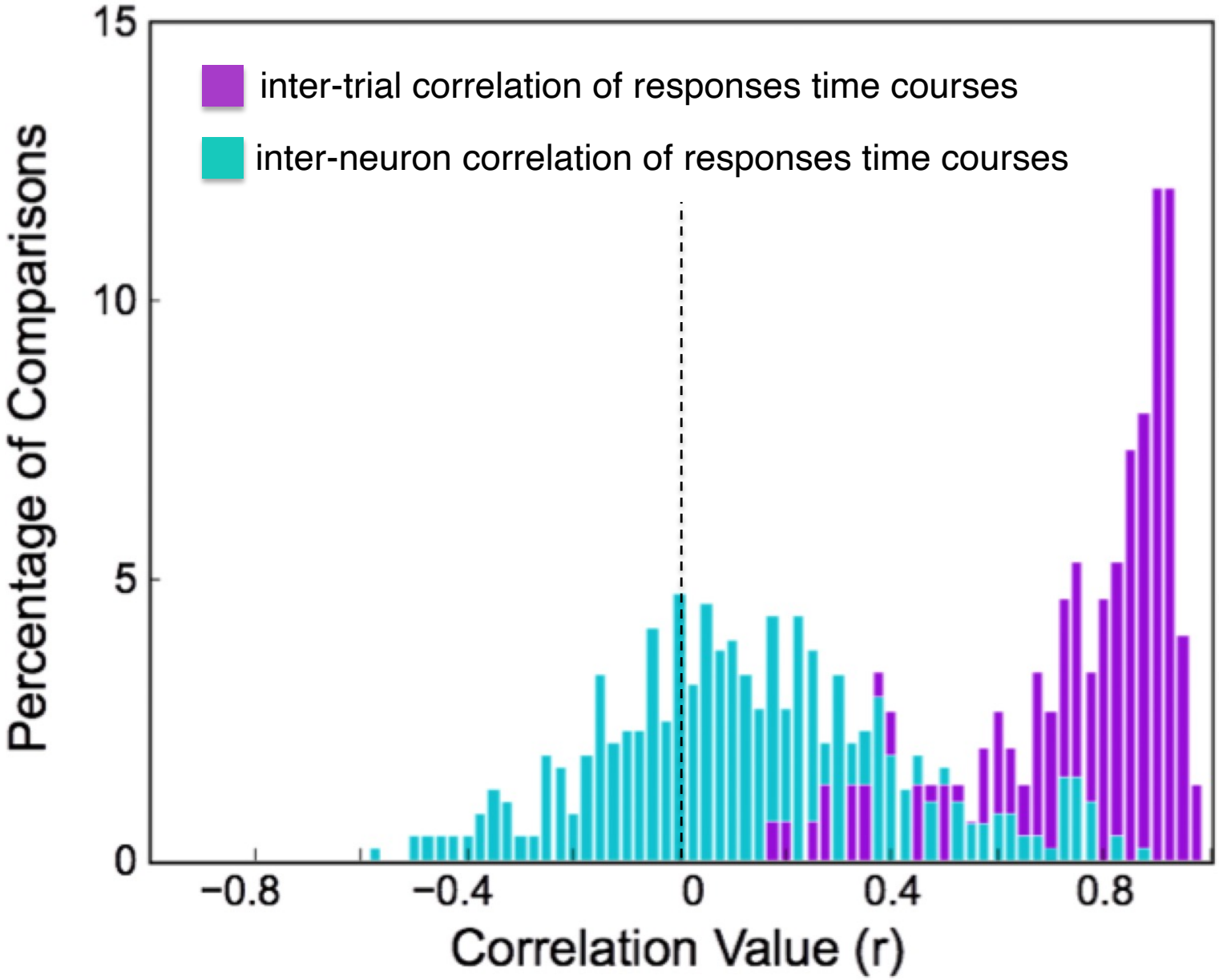
David McMahon

High reliability across trials for a given neuron but…

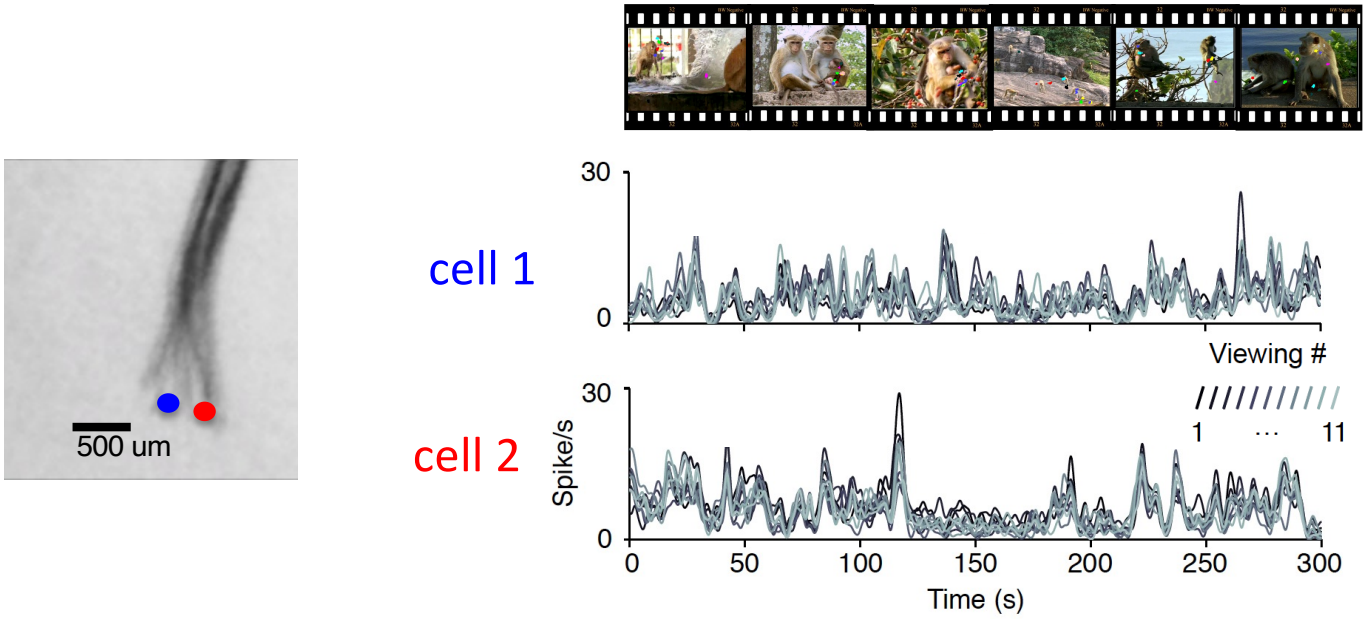


High reliability across trials for a given neuron but…

very low response correlation between neurons!



Why do adjacent neurons in a face patch respond so differently?

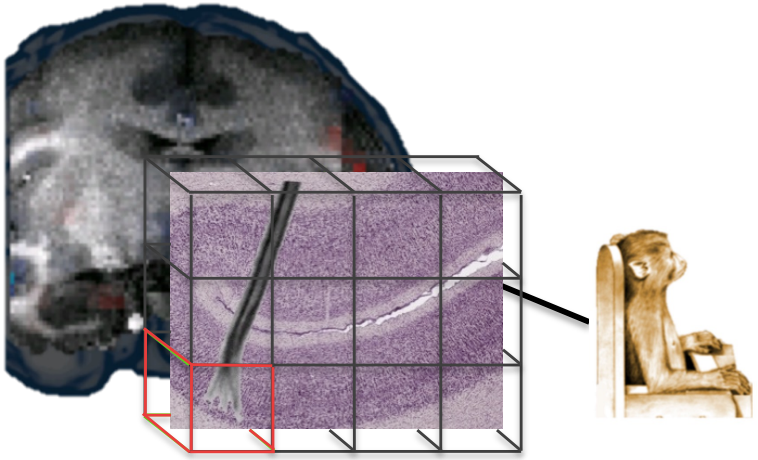


Possibility 1:
Response differences reflect the internal workings of a cortical column ("distribution of labor" hypothesis)

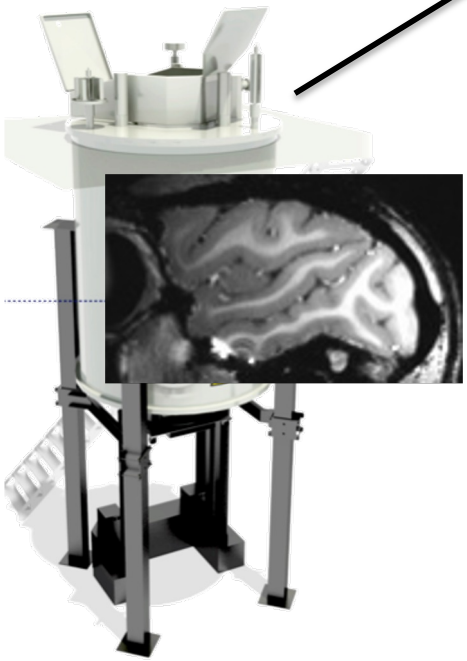
Possibility 2:
Response differences reflect contributions of specific long-range connections ("selective inputs" hypothesis)

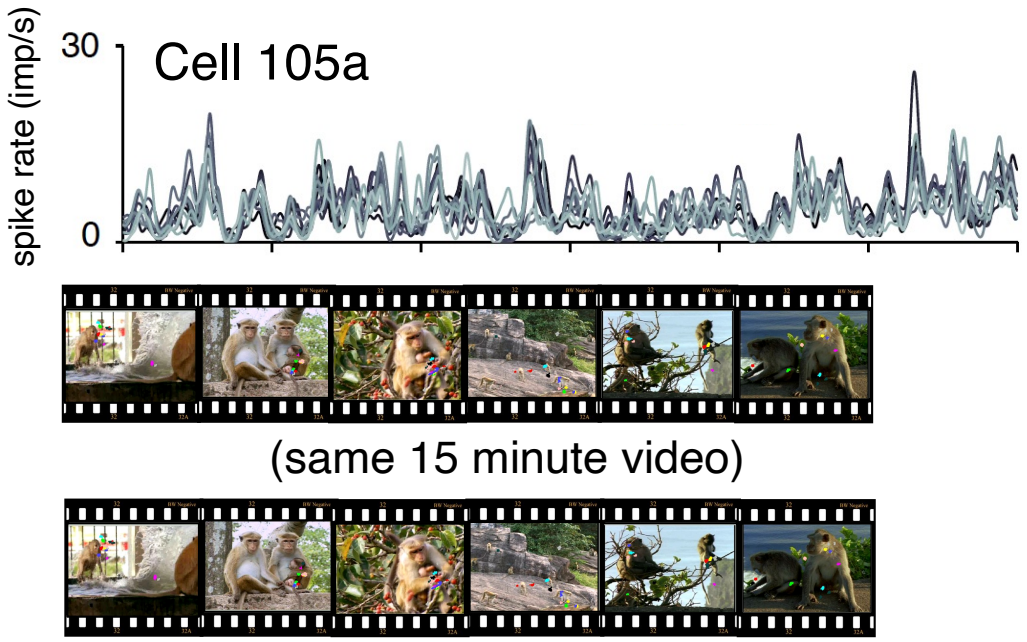
Using whole brain fMRI as a readout of single cells

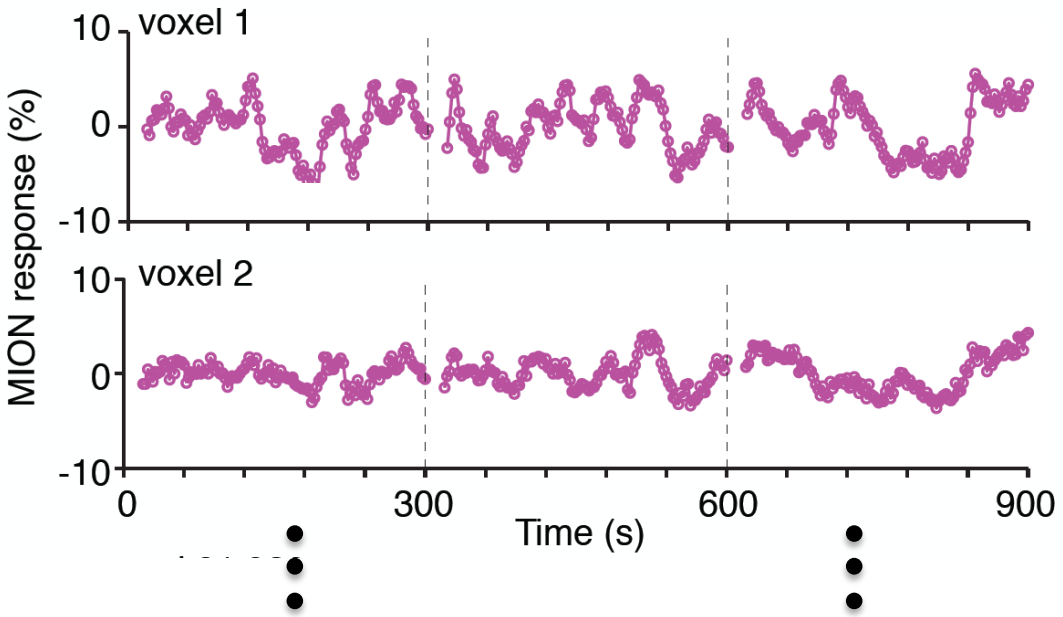
single units in face patch



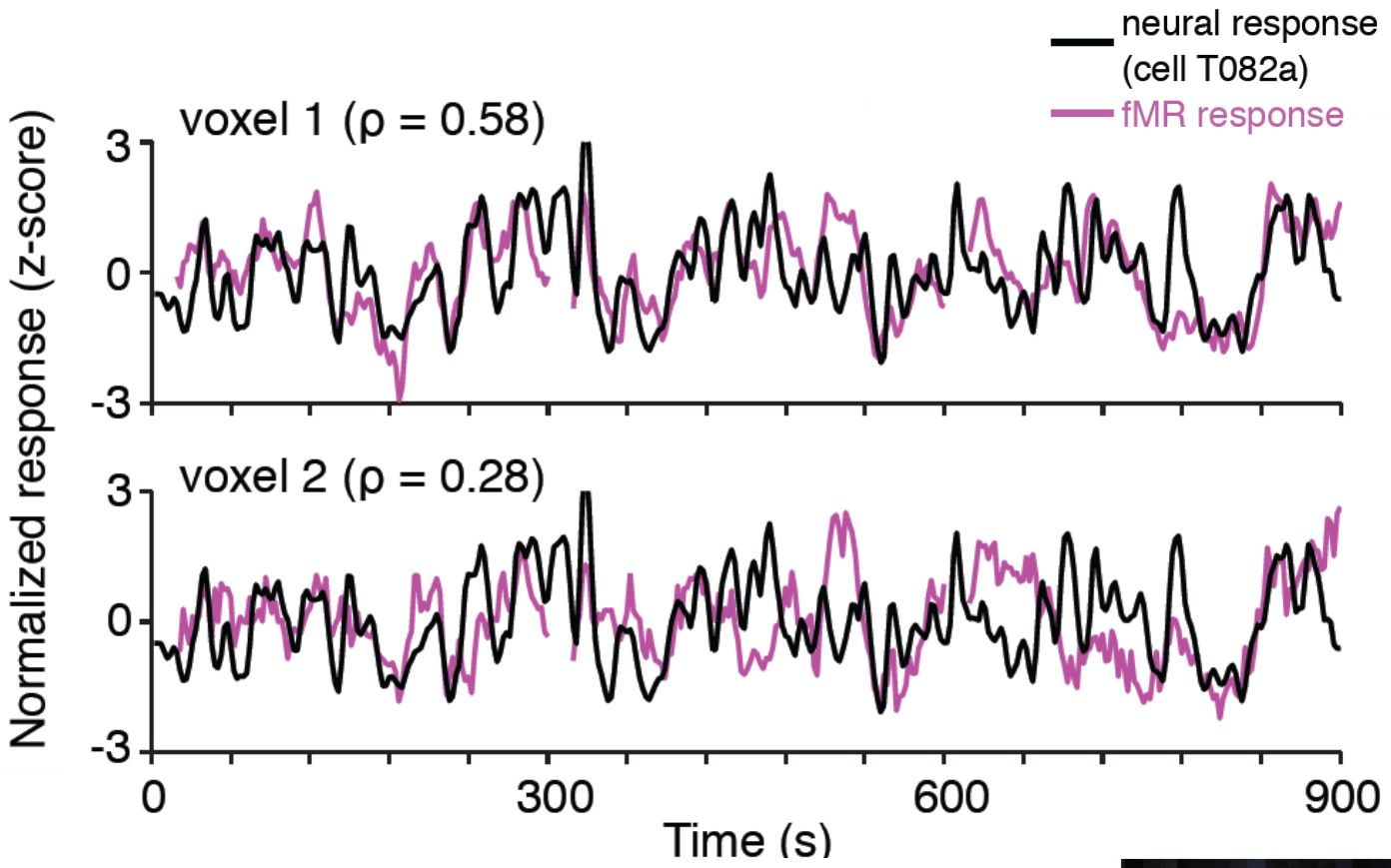
whole-brain fMRI



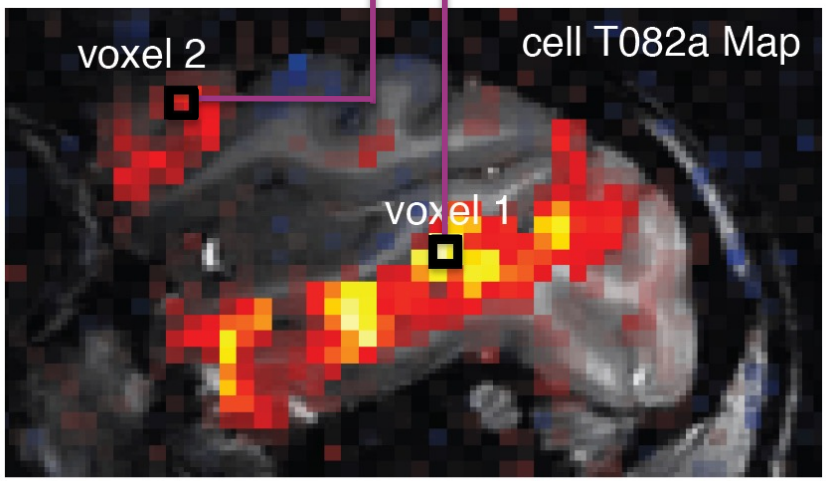




Using whole brain fMRI as a readout of single cells



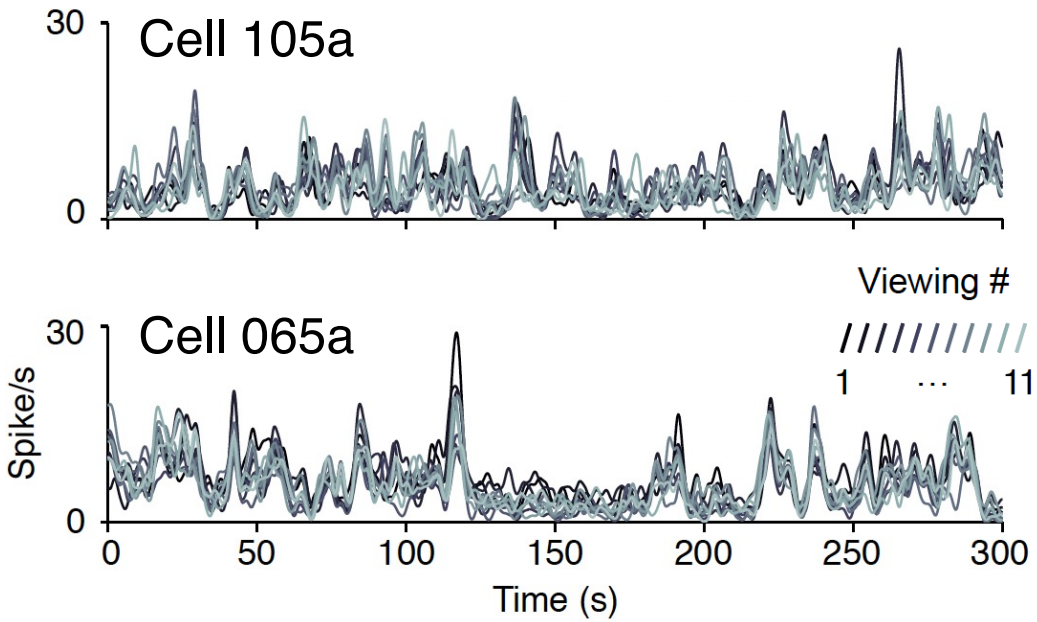
compute statistical relationship (e.g. correlation coefficient)

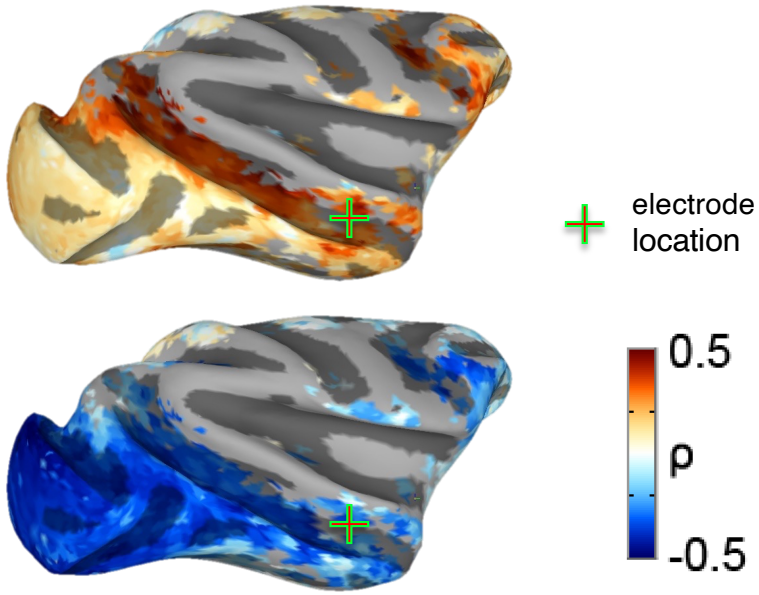


Soo Hyun Park

- cell-specific correlation map
- "smart" dimensionality expansion of single unit time courses

Examples of single-unit fMRI maps



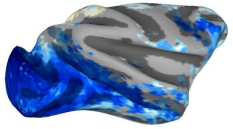


Soo Hyun Park

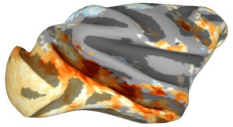
Functional maps from simultaneously recorded neurons in face patch AF population

- each map from isolated single cell (total volume ~500 μm)

cell T065a

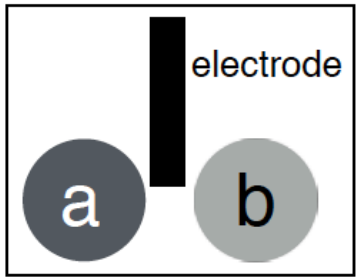


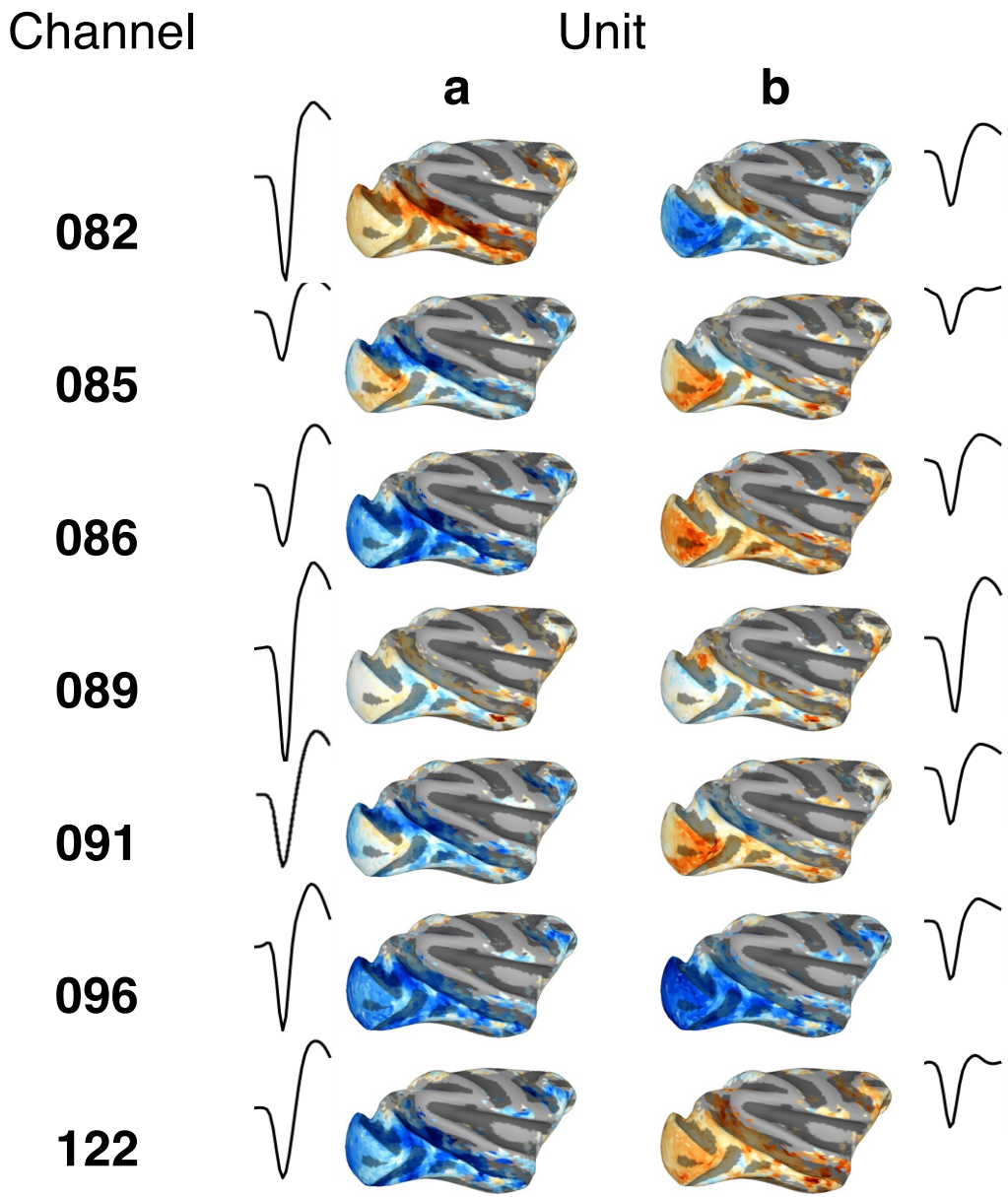
cell T082a



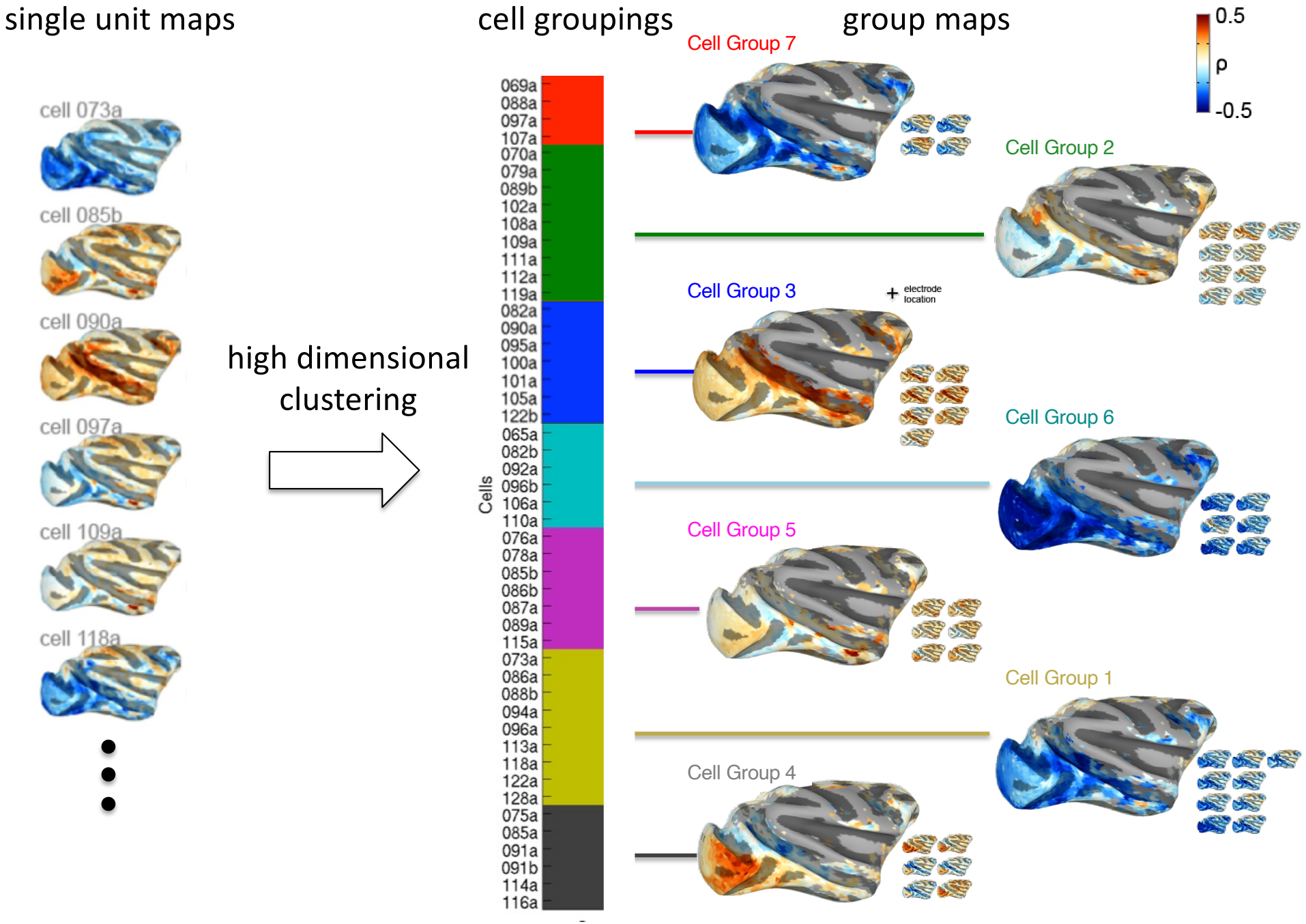
Can single unit fMRI mapping aid in classifying neural function?

Simultaneously recorded neurons from the same microwires





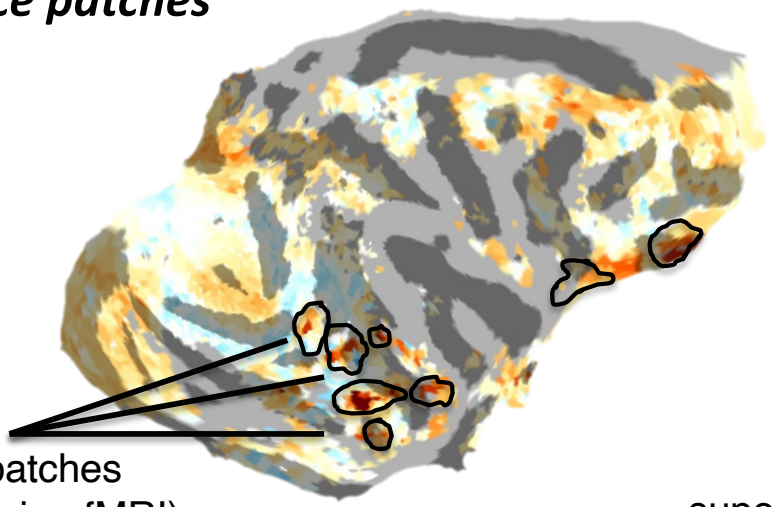
Grouping neurons based on fMRI maps



Comparing flattened average maps for four of the **cell groups**

5

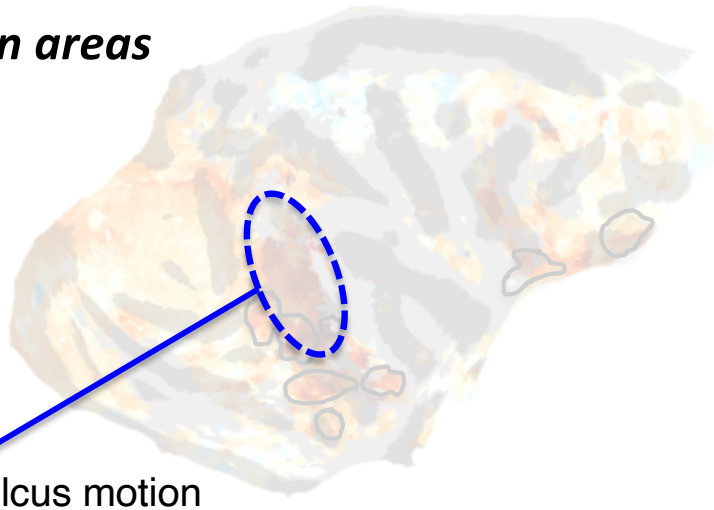
Only face patches



face patches
(block design fMRI)

3

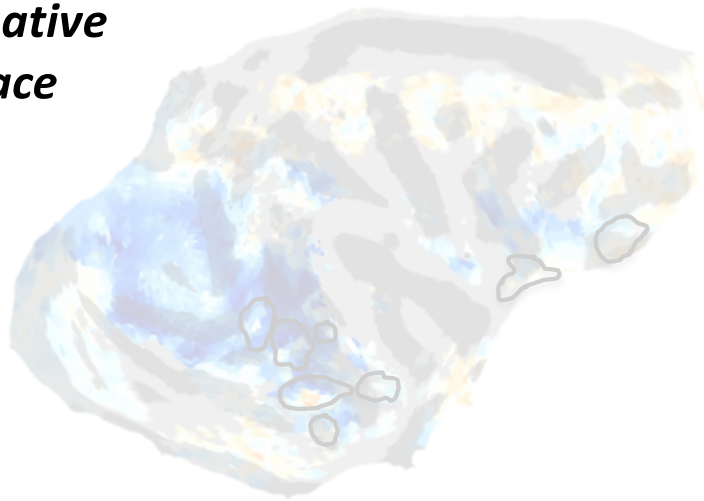
Face patches +
STS motion areas



superior temporal sulcus motion
areas (e.g. MT, MST, FST)

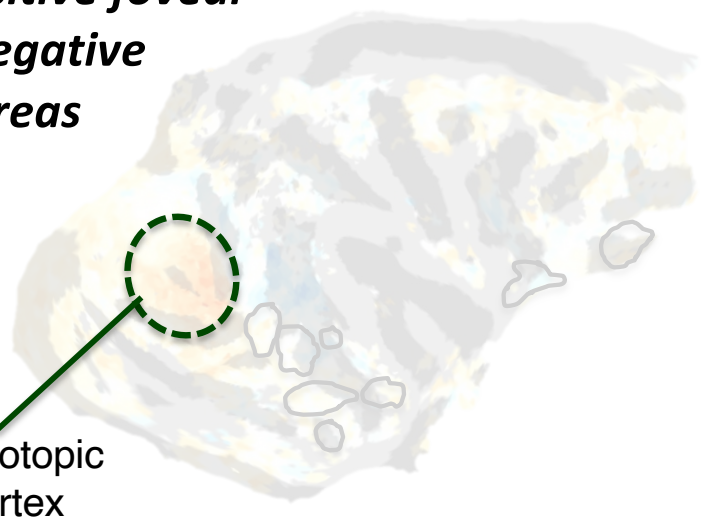
1

Broad negative
(sparing face
patches)



4

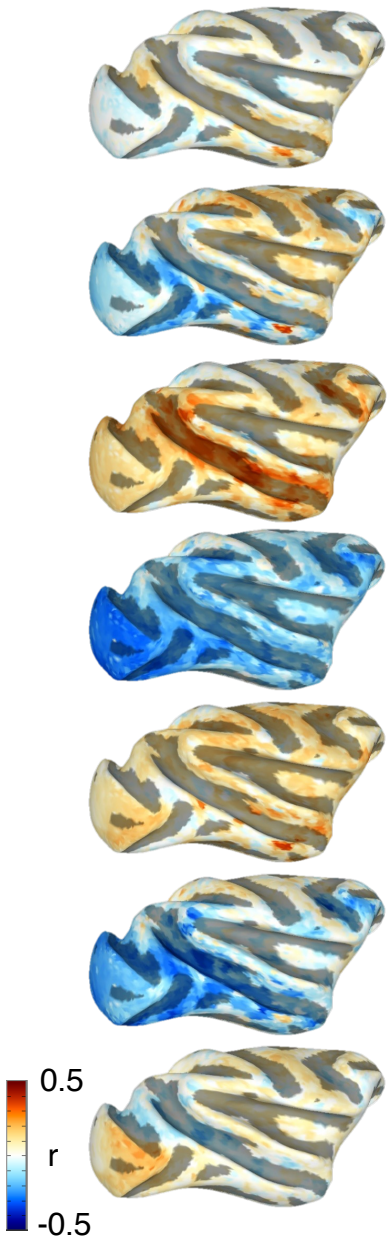
Weak positive foveal
V1 and negative
motion areas



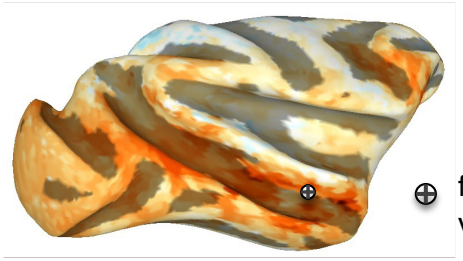
foveal retinotopic
visual cortex

Group maps

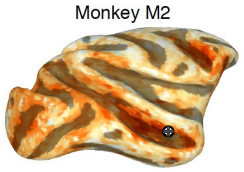
What about the local fMRI and LFP signals?



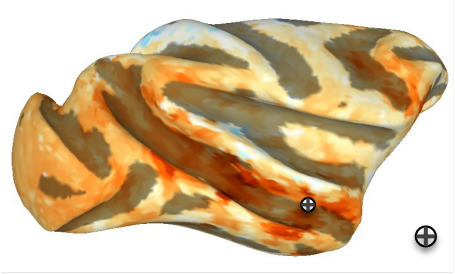
fMRI correlation: seed voxel



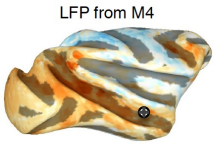
fMRI seed voxel location

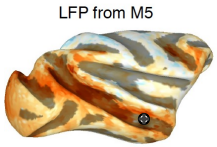


Local Field Potential: gamma power

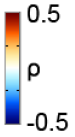


gamma LFP location



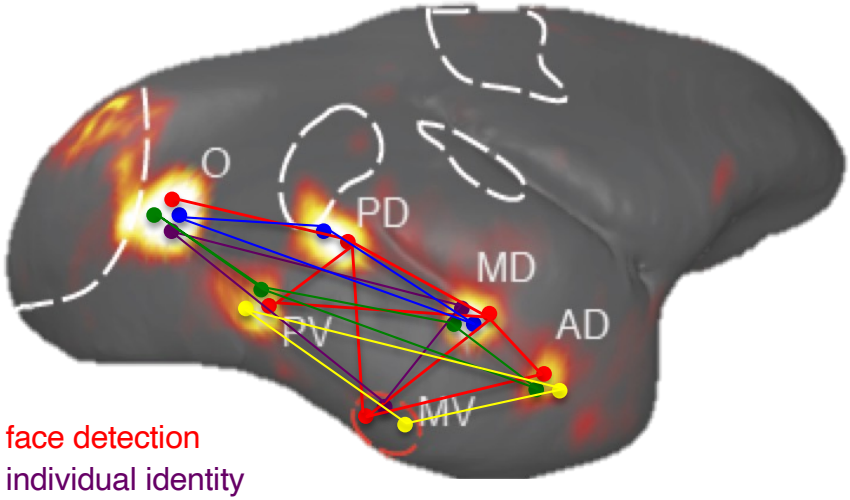


Group 3 single units



- *One group map* (~14% of recorded single units) matches functional maps based on the the fMRI seed voxel and gamma LFP power

Functional units distinct but not localized?



face detection
individual identity
face and head movement
reading attentional state
emotional expression

- spatial concentrations of broad selectivity (i.e. patches)
- units with different expertise (selectivity) interspersed within each area
- units with similar expertise have selective long-range communication (connections)
- **functionally coherent modules are confined in their location, but not strictly segregated**

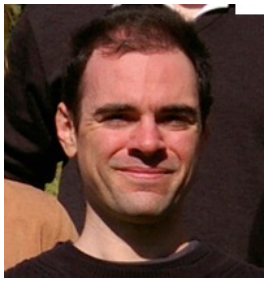
Summary

- Experiments in nonhuman primates have fundamentally shaped our current understanding of the human brain
- The great advantage of fMRI is whole brain readout of activity, for monkeys as well as humans.
- The combination of this readout with established and emerging methods will continue to be of great neuroscientific value.
- The long term value of fMRI will depend, in part, on the extent to which functional specialization is spatially segregated in the brain – question of the century.

Collaborators

Brian Russ

Soo Hyun Park



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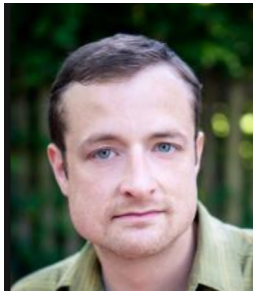

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