Neuroimaging group
Marseille
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Sub-millimeter resolution fMRI in awake behaving monkeys at 3 Tesla

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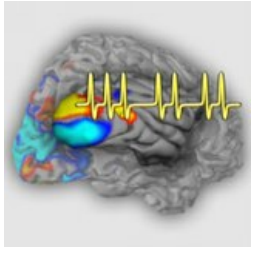


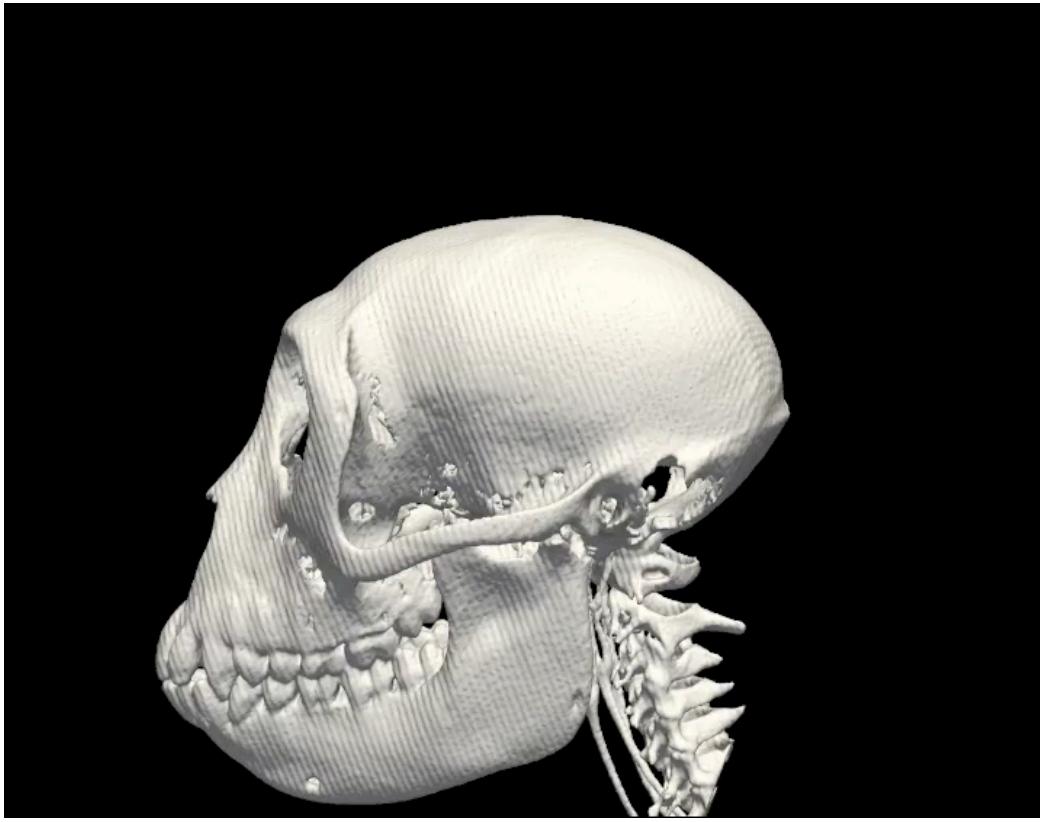
Overview talk

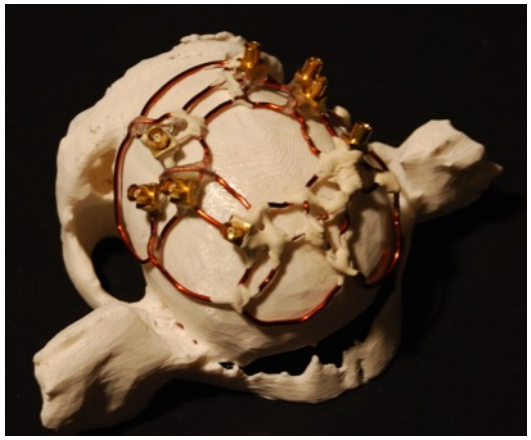
- Implanted phased array coils in macaques allows sub-mm imaging at 3T.
- Proof of principle: thin/thick/pale stripes in V2
- New view on retinotopic organization dorsal visual cortex
- ‘columns’ all over the place?
- High resolution imaging in cognitive tasks

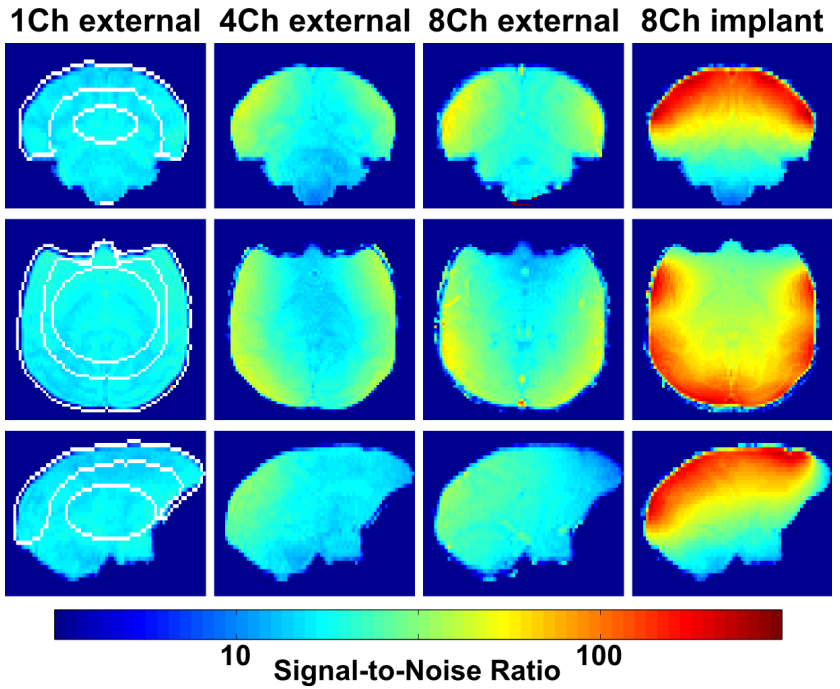
Implant phased array coils

8-Ch Coil: CT scan skull

3D printed recording wells: CT scan skull + coil.







+ **Increase in SNR**
+ **Full brain coverage**
+ **Accelerated imaging**
+ **multi-band**

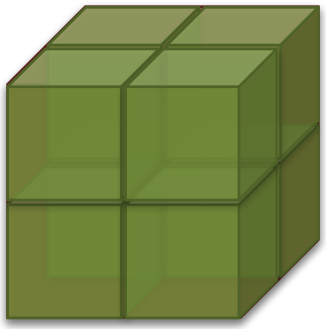
Janssens et al., Neuroimage 2012

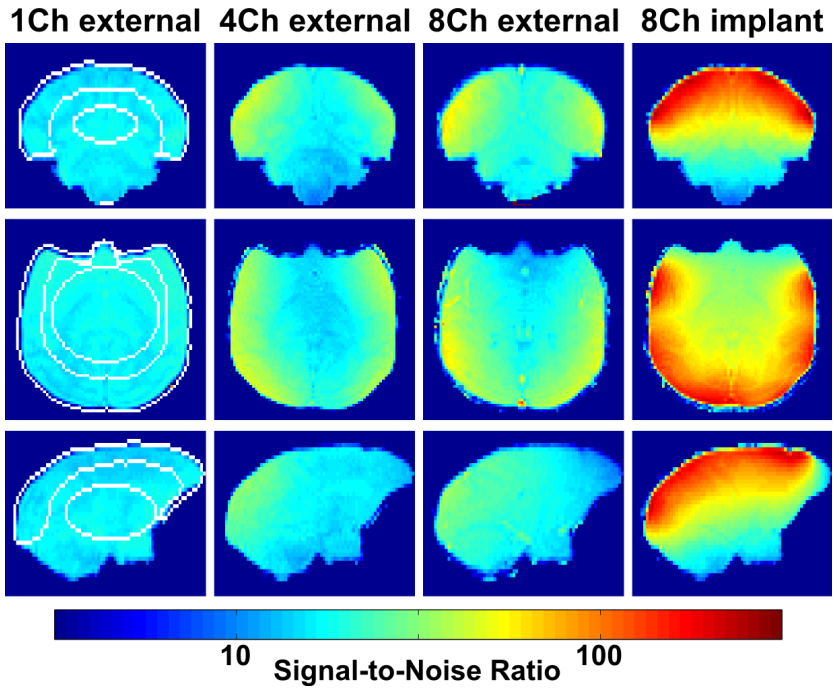
High-resolution fMRI using implanted coils

$$SNR_{accel.} = \frac{1}{\sqrt{R}} \cdot g^{-1} \cdot SNR_{non-accel.}$$

Cortical SNR gain :	4
Acceleration gain: √(3/2)	1.2
G-factor gain:	×1.7
	8.2

1 mm isotropic ⟹ 0.5 mm isotropic





Monkey fMRI

Contrast agents (MION)

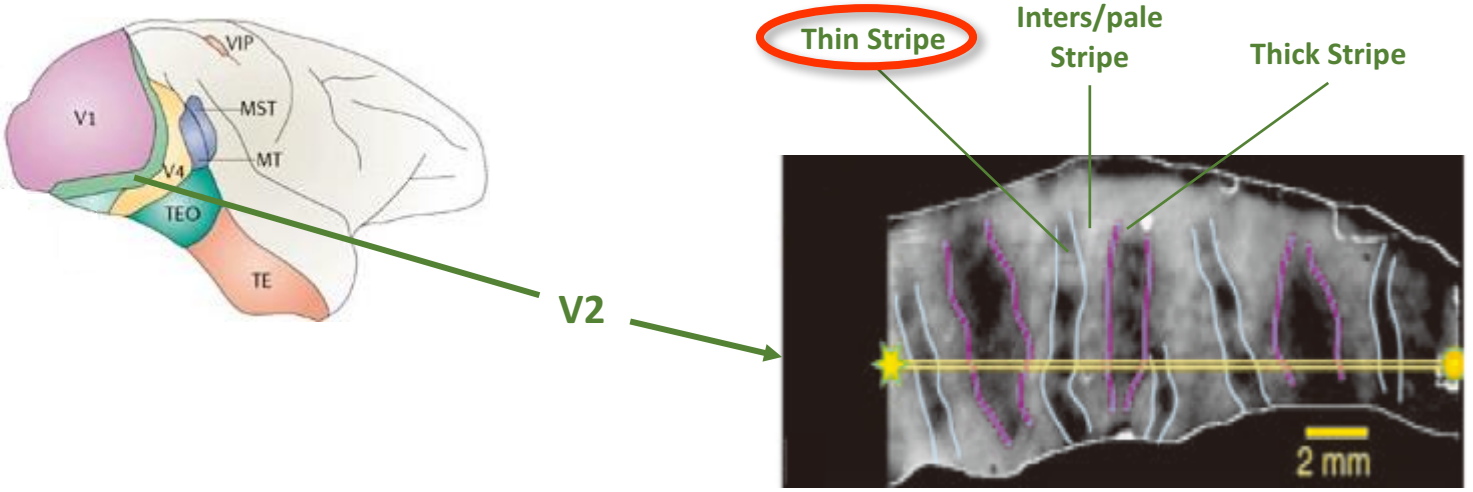
- Cerebral blood volume-weighted(CBV) signals instead of BOLD
- 3~-fold gain of CNR at 3T

Vanduffel et al., Neuron 2001

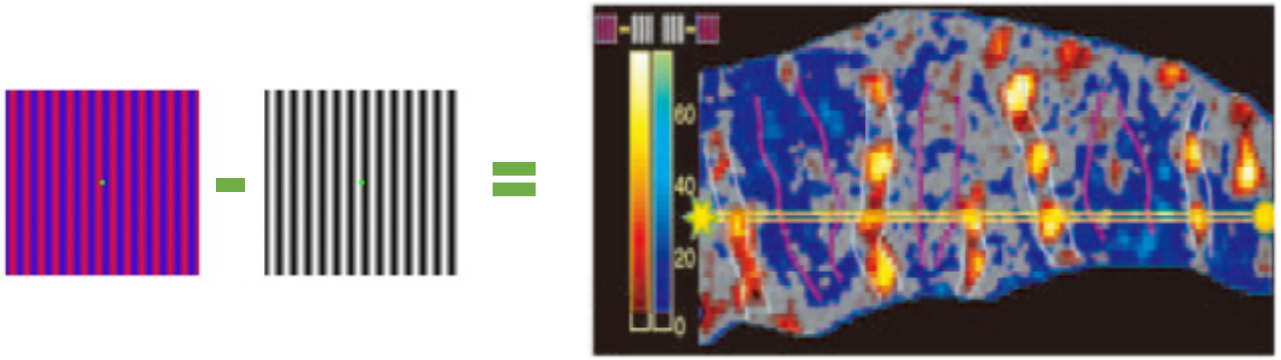
1. Proof of principle:

V2 stripes: thick, thin and inter-stripes

Test High-Resolution MRI:
Visualization of Color-Biased Stripes in Monkey V2



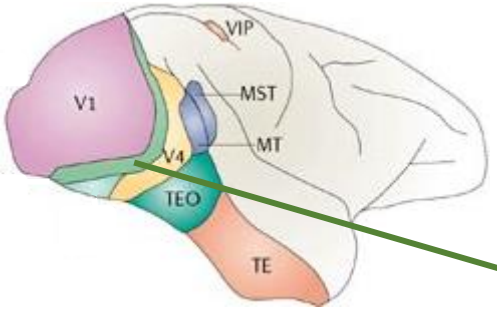
Cytochrome Oxidase Stain



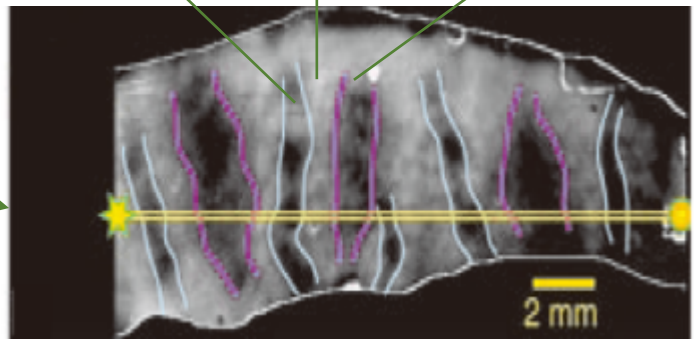
2L-DG

Tootell et al. (2004)

Test High-Resolution MRI:
Visualization of Disparity-Biased Stripes in Monkey V2

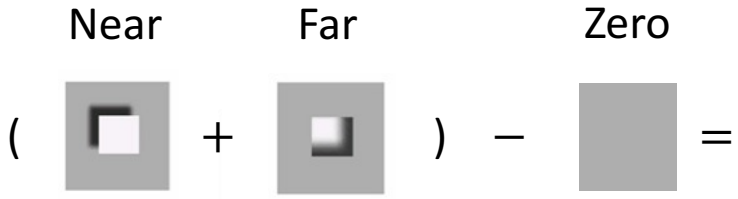


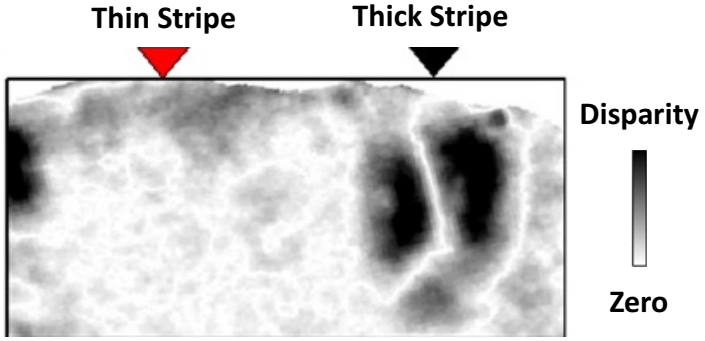
V2



Cytochrome Oxidase Stain

Tootell et al. (2004)

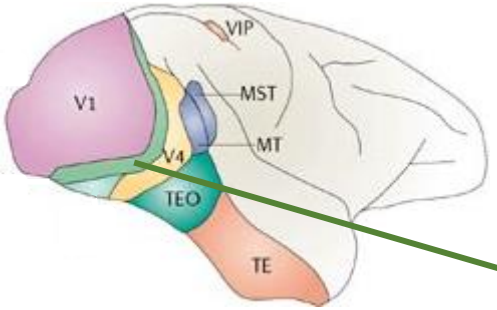




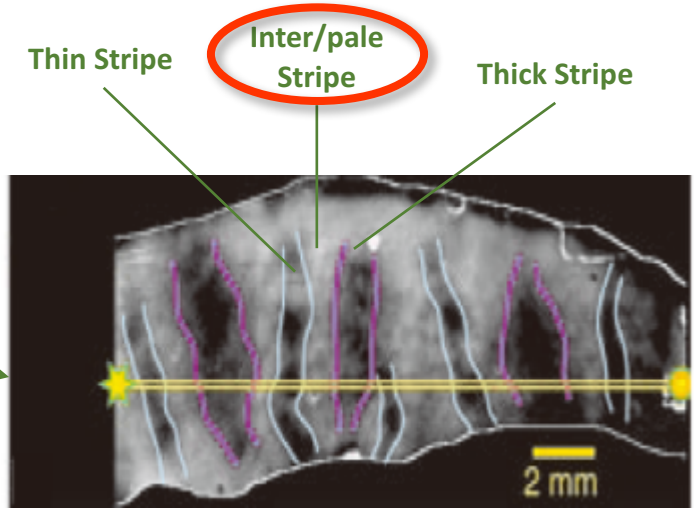
Intrinsic signal optical imaging

Chen et al. (2008)

Test High-Resolution MRI:
Visualization of High Myelinated Stripes in Monkey V2



V2



Cytochrome Oxidase Stain

Tootell et al. (2004)

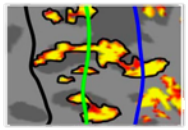
	Luxol Stain	Gallyas Stain
Inter/pale Stripe	Lower myelin densities	Higher myelin densities

Horton J.C., Hocking D.R. (1997)

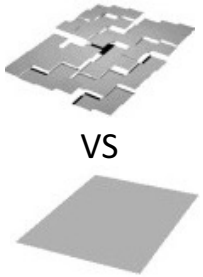
Test High-Resolution MRI:
Previous fMRI Study: Visualization of 2 Kinds of Stripes in Human V2

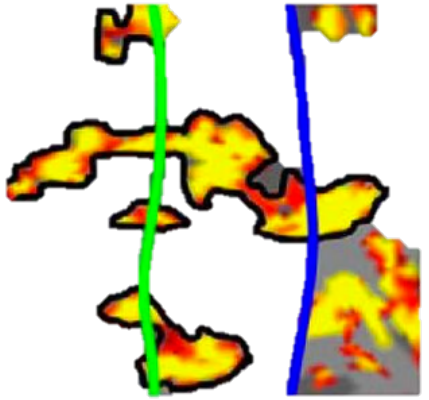
Color

V1



Disparity

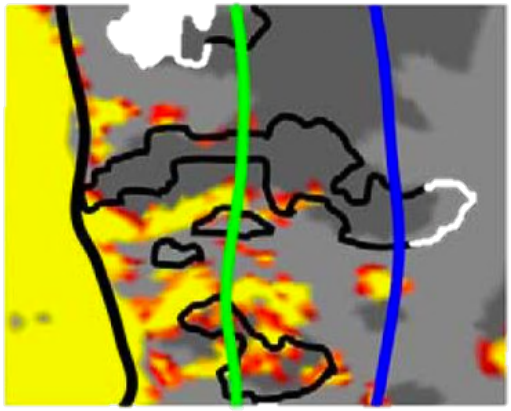




Co-registration

Color Stripes

Disparity Stripes



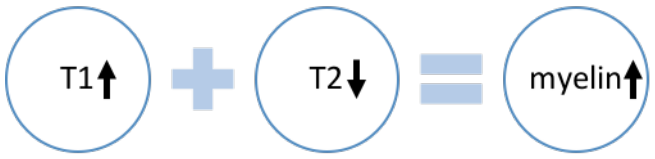
- Human fMRI study
- High field (7T)
- 1 mm isotropic voxels

Nasr S. et al. JN 2016

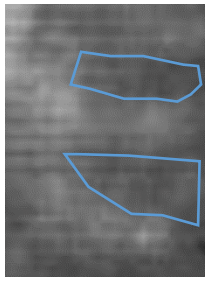
Challenge

	Macaque	Human
Widths	1 - 1.5 mm	1 - 3 mm
Distance between stripes of the same kind	~4 mm	4 - 8 mm

Addition: Pale Stripes Visualization



MRI



Pale stripe

Pale stripe

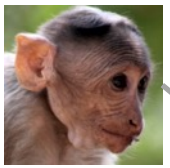
Higher myelinated

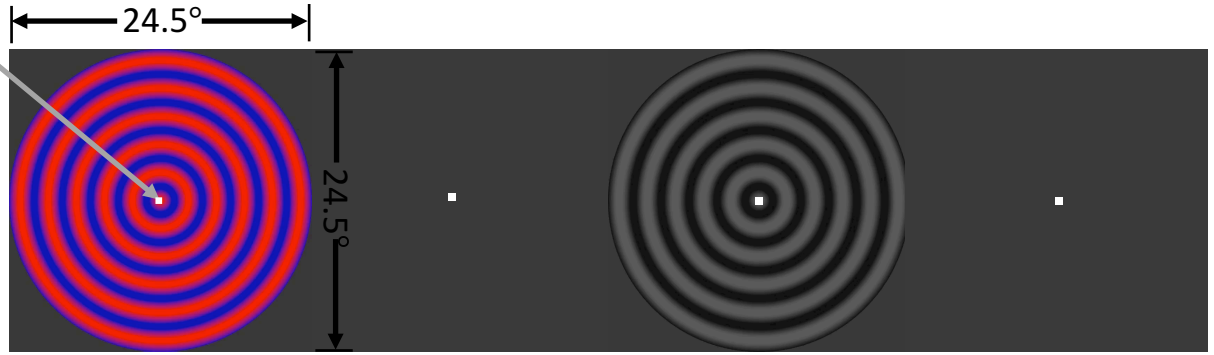
Lower myelinated

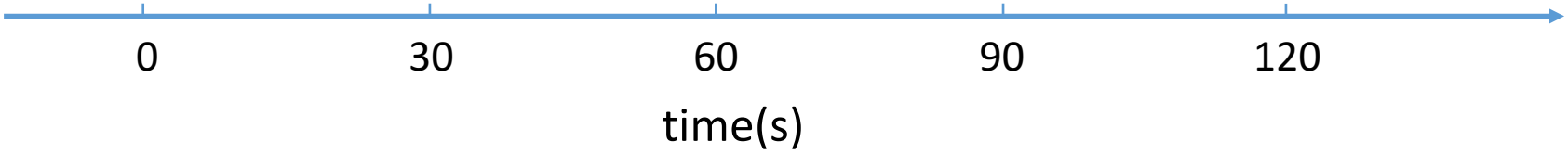
Gallyas Myelin Stain

Horton J.C., Hocking D.R. (1997)

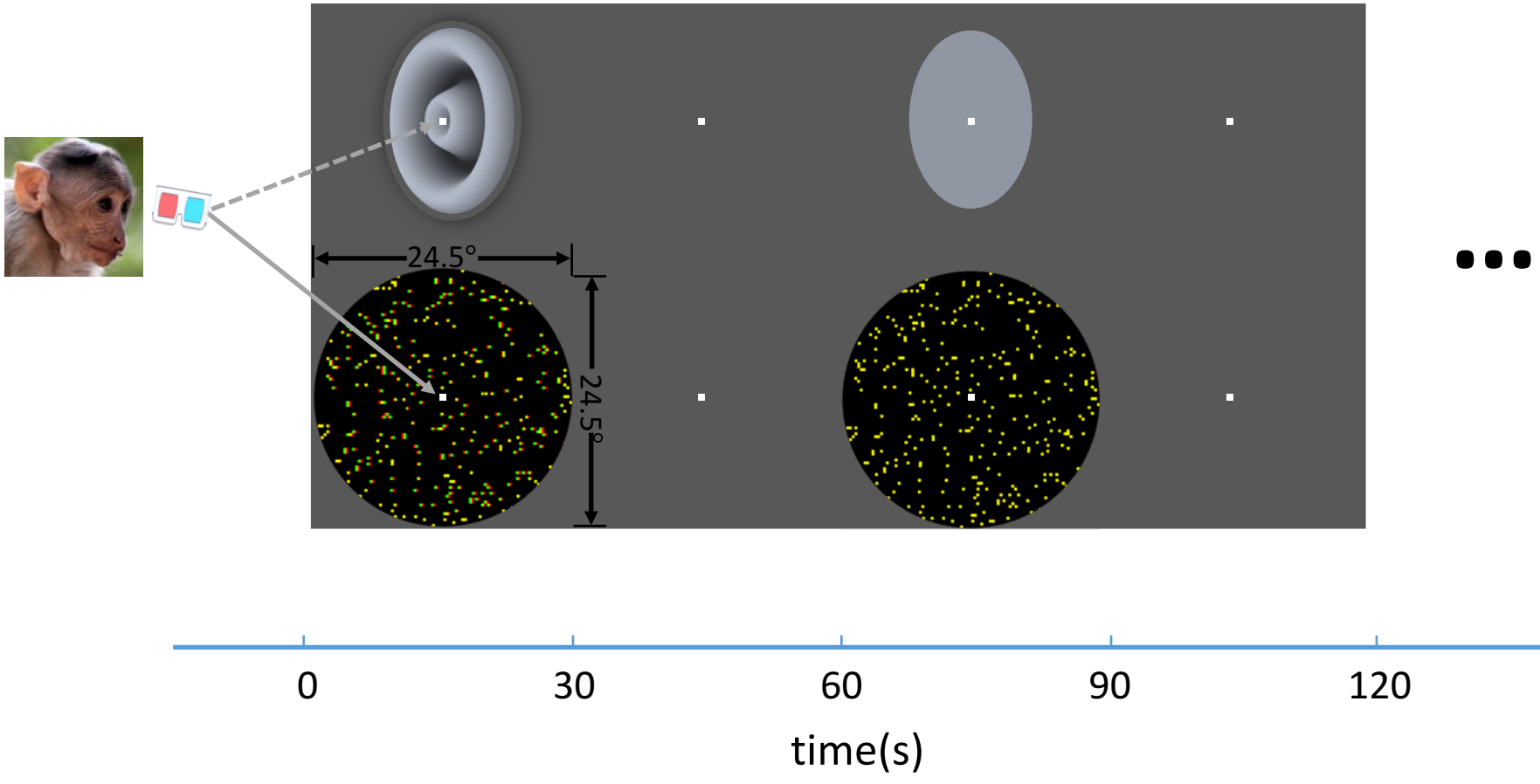
Experimental Task
(Color stripes visualization)





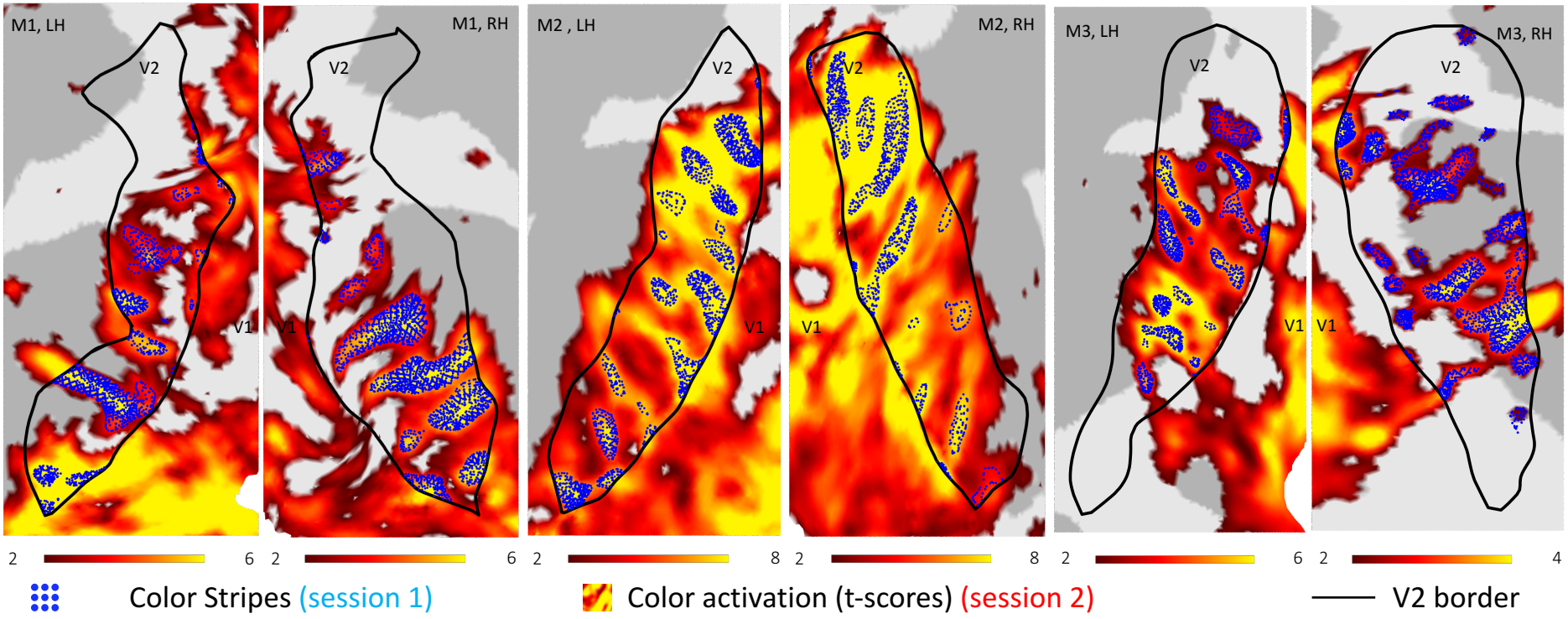


Experimental Task
(Disparity stripes visualization)



Reliability Test of Color-biased thin stripes in V2

co-registration of color stripes defined by session 1 and color activation from session 2 in V2



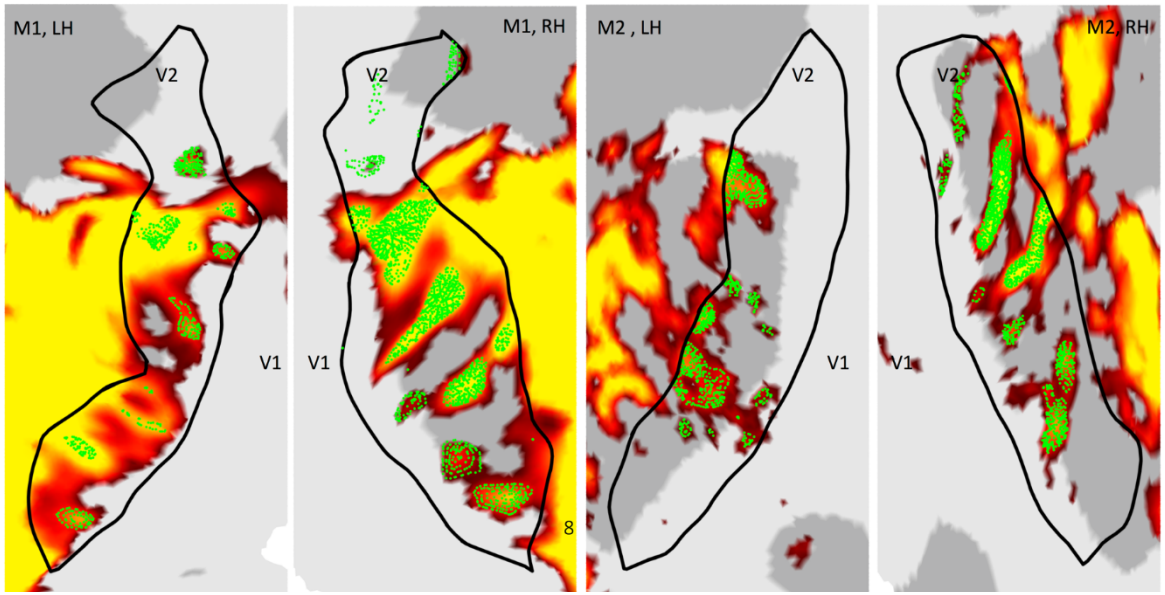
The Spearman correlation coefficient between fMRI signal changes of different sessions

	M1	M2	M3
LH	0.58	0.62	0.91
RH	0.77	0.55	0.80

* All of them are highly significant ($p < 10^{-5}$).

Li et al., CC2018

Disparity-biased thick stripes in V2



The Spearman correlation coefficient between fMRI signal changes of different sessions

	M1	M2
LH	0.93	0.51
RH	0.83	0.46

* All of them are highly significant ($p < 10^{-5}$).

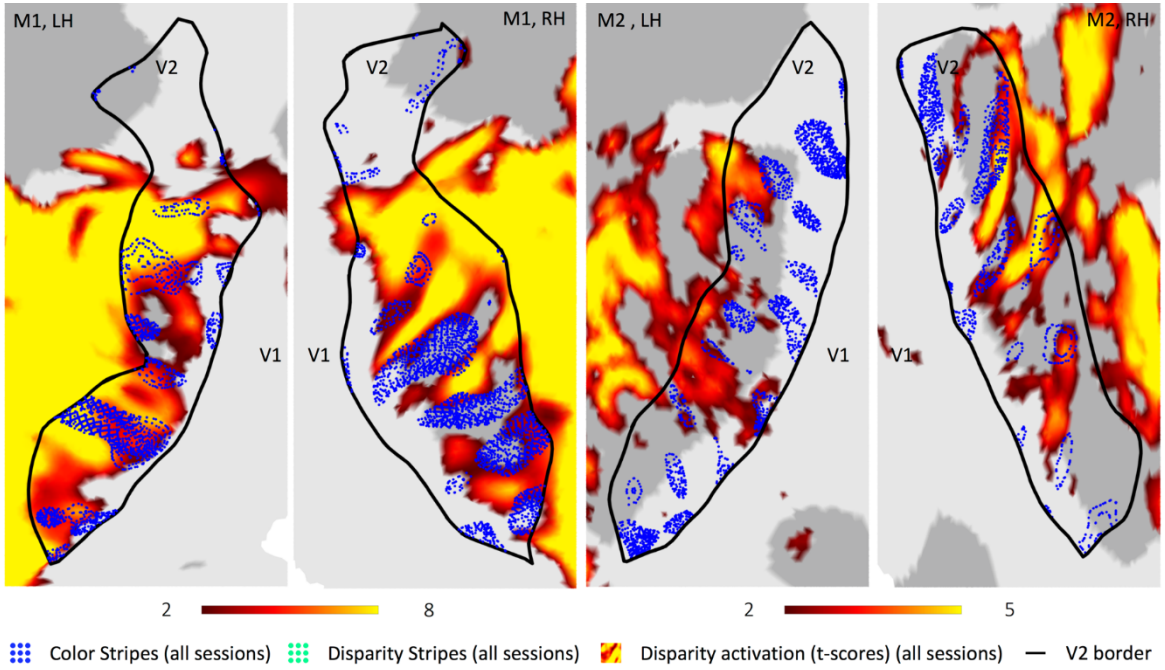
Li et al., CC2018

Disparity-biased thick stripes in V2

The Spearman correlation coefficient between color and disparity activation

M1	LH	-0.23
	RH	-0.46
M2	LH	-0.60
	RH	-0.41

* All of them are highly significant ($p < 10^{-6}$).

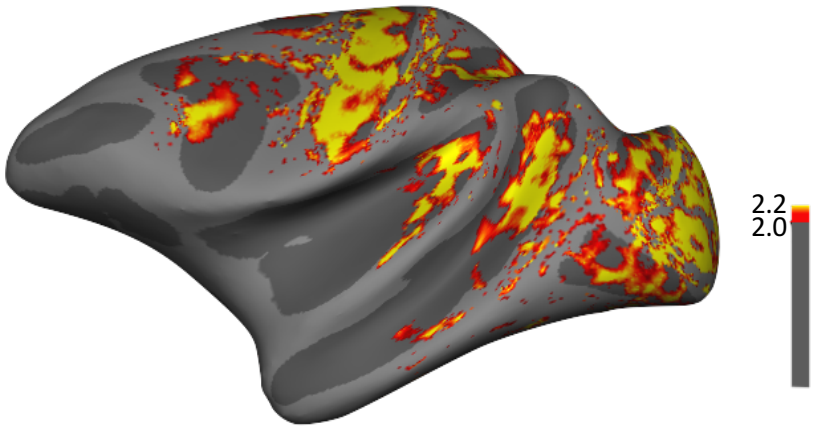


Li et al., CC2018

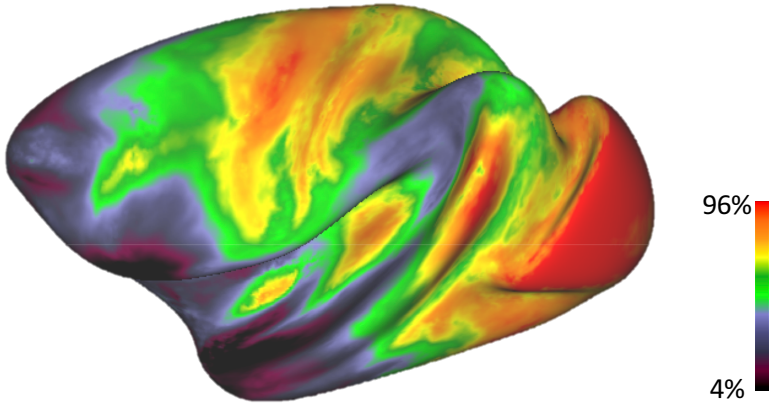
Pale Stripes Visualization

- Myelination mapping
- 0.4 mm isotropic
- 2 anesthetized subjects (M1 and M2)
- Single loop receiving coil
- T1 weighted / T2 weighted ratio (Glasser et al., 2012)

M1, LH



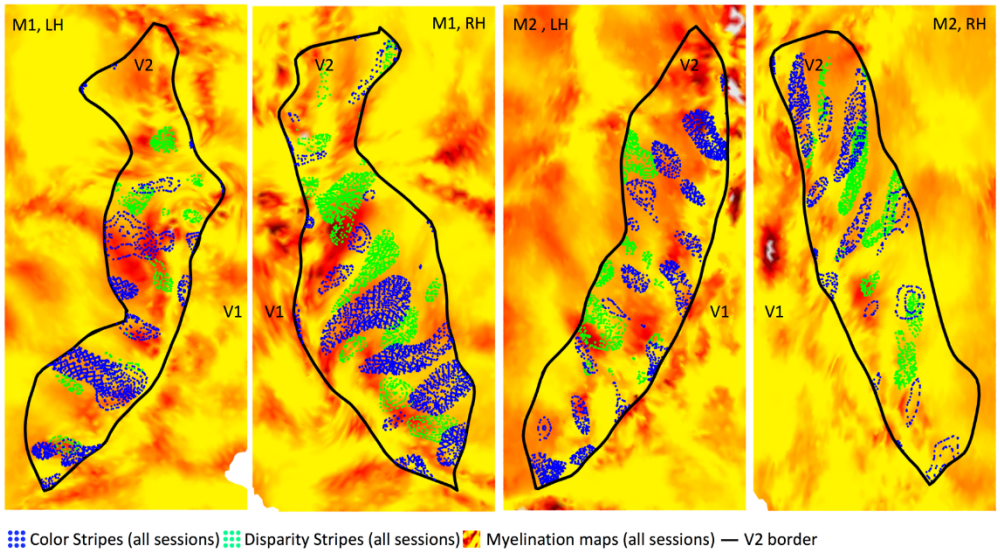
Previous Macaque Myelination Map Study



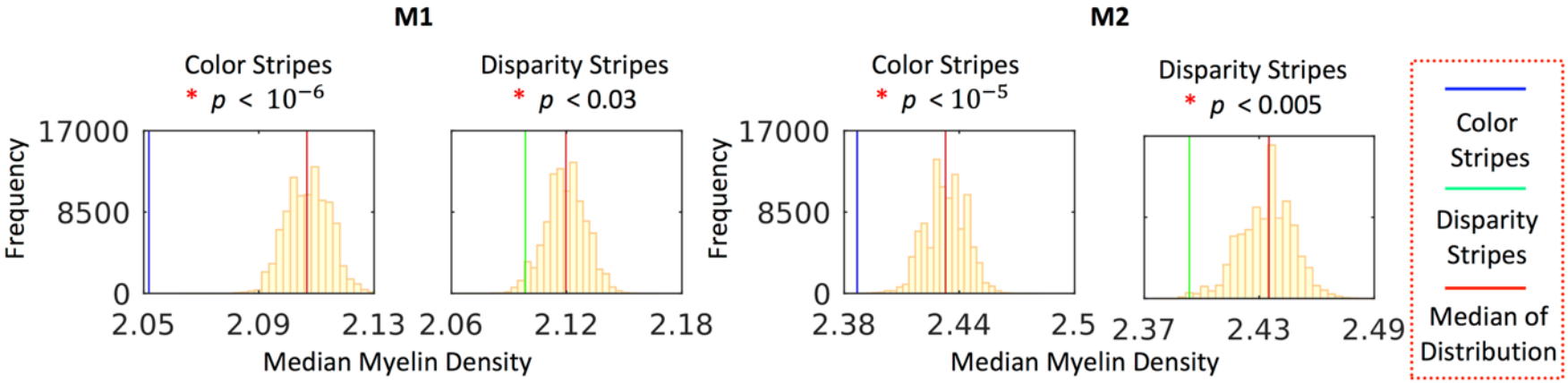
Glasser et al. 2011

Higher myelinated interstripes in V2

Co-registration of cc and myelin maps in V2



Significant higher probability to find color and disparity stripes in low myelinated areas



Li et al., CC2018

Conclusion: in retinotopically defined V2

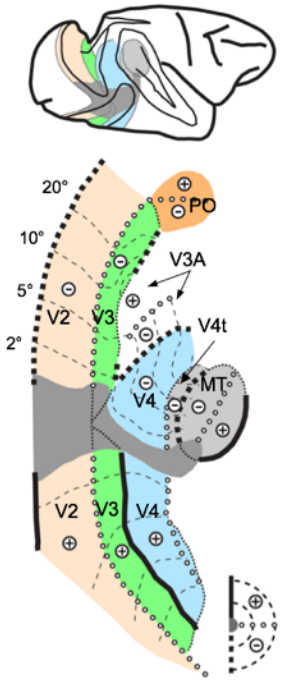
- **Thin color stripes**
- **Thick disparity stripes**
  - reproducible across monkeys and across scan sessions
- **Higher myelinated inter-stripes** are largely separated from color- and disparity-selective stripes >< Dumoulin (higher myelination in thick stripes).

- High-resolution 3T fMRI can be reliably used to study **in-vivo submillimeter-scale functional organizations** of the primate brain

2. Revise ‘textbook’ retinotopic knowledge:

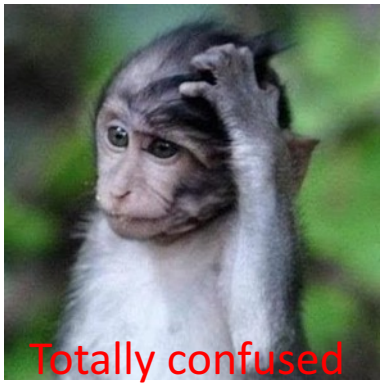
controversies about the topographic organization of V3 and V4

Macaque monkey models

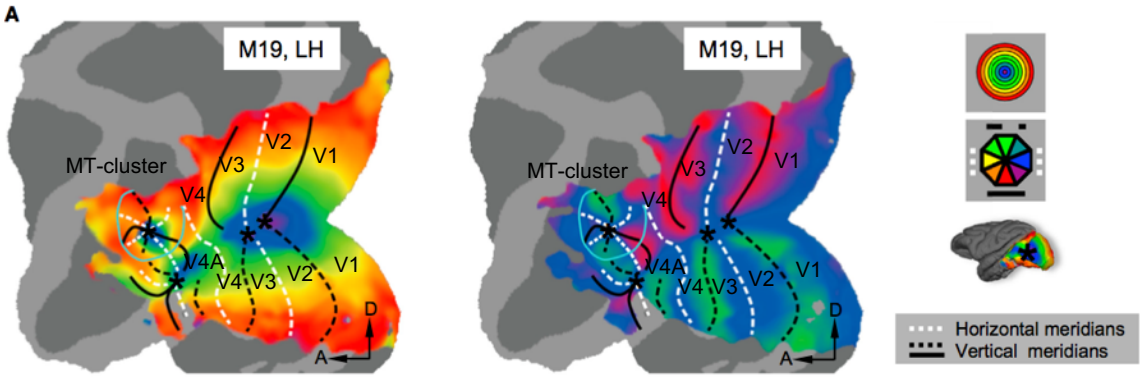


Gattass et al., 1988[6]
Gattass et al., 2015[1]

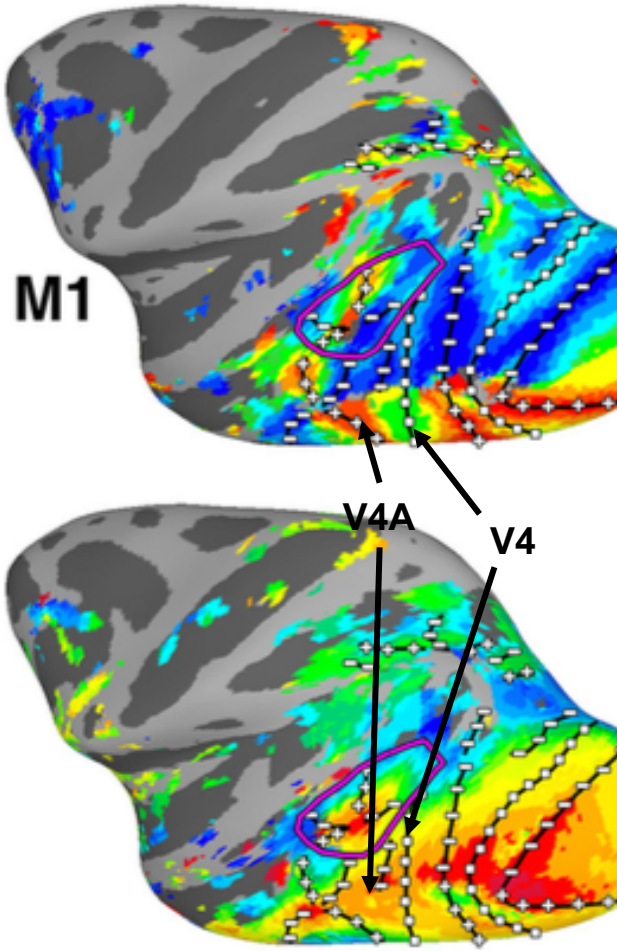
New World monkey models



controversies about the topographic organization of V3 and V4



Vanduffel et al., Neuron 2014



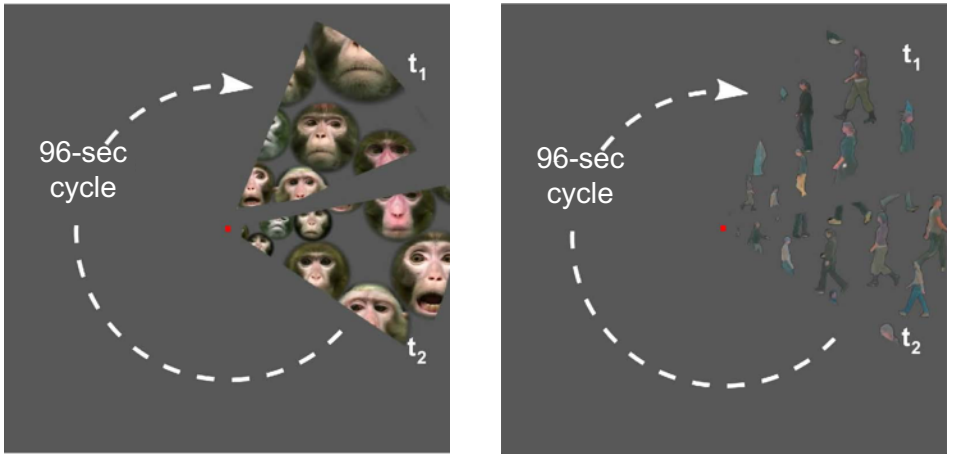
Arcaro and Livingstone, JN2017

Methods

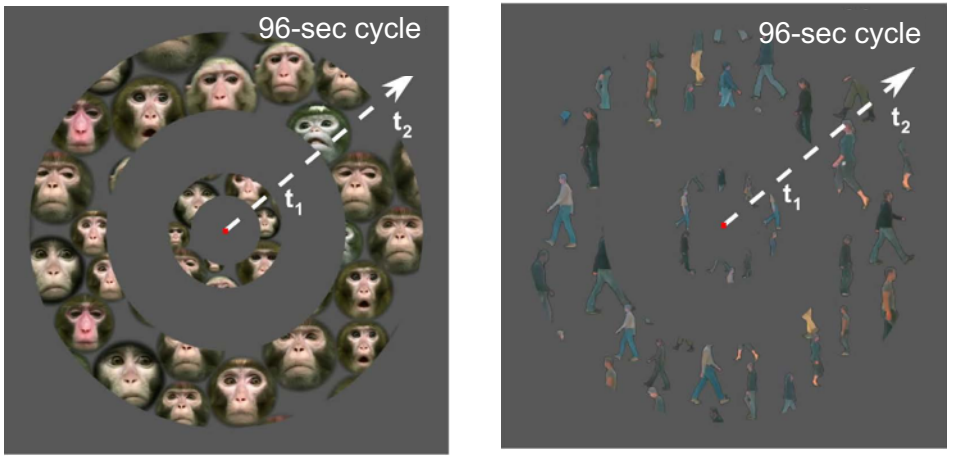
Retinotopic stimuli

0.6 mm isotropic voxels
TR = 3000 ms,
TE = 21 ms,
acceleration factor = 2,
flip angle (α) = 90°,
MB = 2
acquisition matrix = 140 × 140 × 48

Polar angle
(clockwise & counter-clockwise rotating wedges)

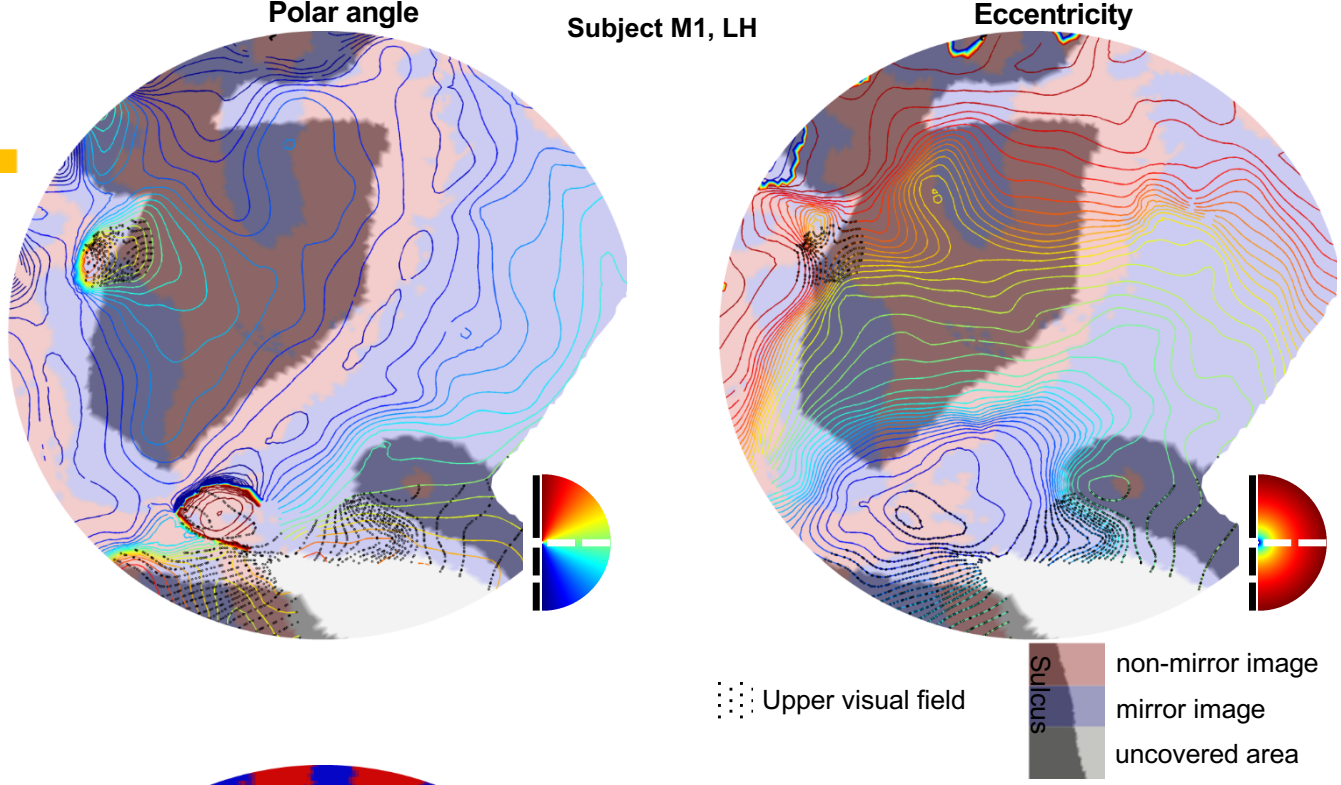


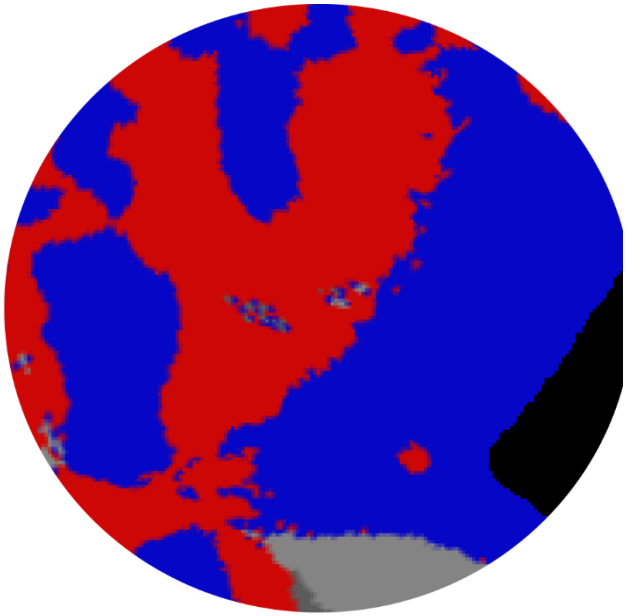
Eccentricity
(dilating and contracting annuli)

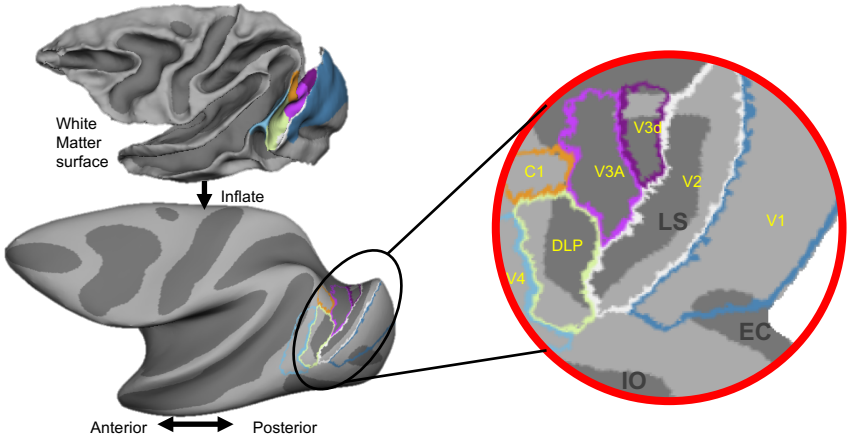


- Every stimulus traverses visual field between 0.25° and 12.25° of visual angle

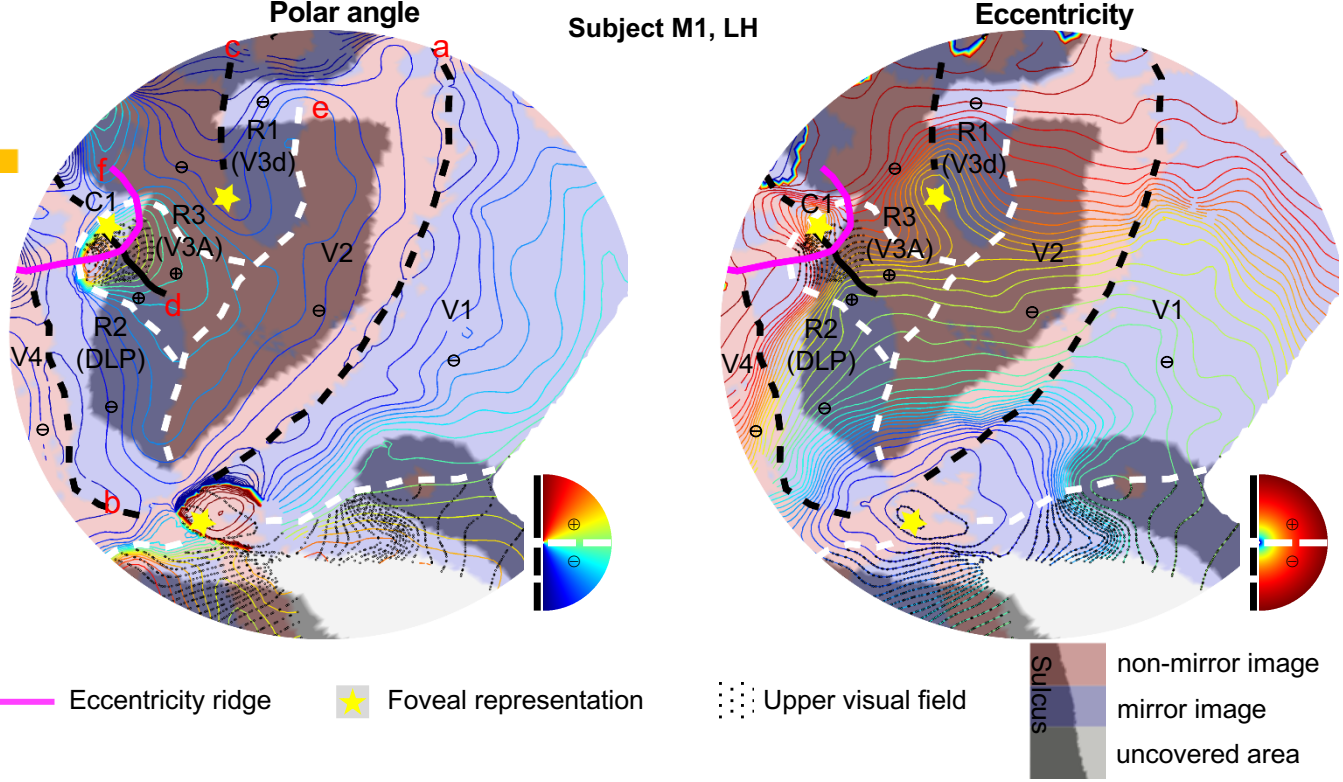
Results


Polar angle
Subject M1, LH
Eccentricity
Upper visual field
Sulcus
non-mirror image
mirror image
uncovered area




White
Matter
surface
Inflate
Anterior
Posterior
V3d
C1
V3A
V2
LS
V1
DLP
V4
EC
IO

Results

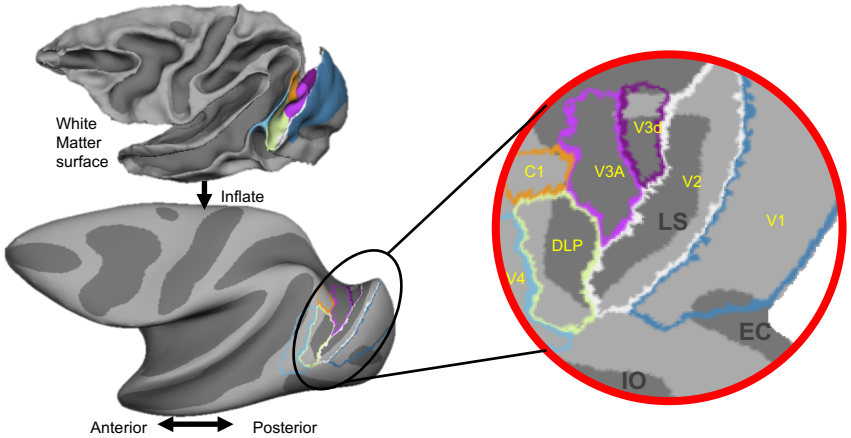


0.6 mm isotropic

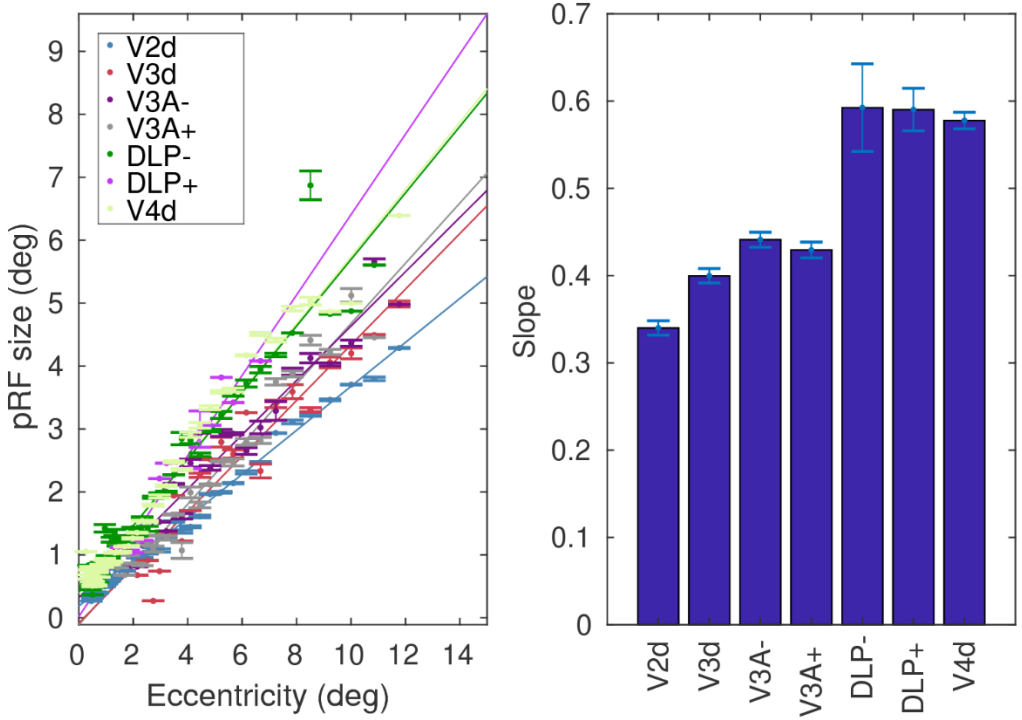
polar angle

eccentricity

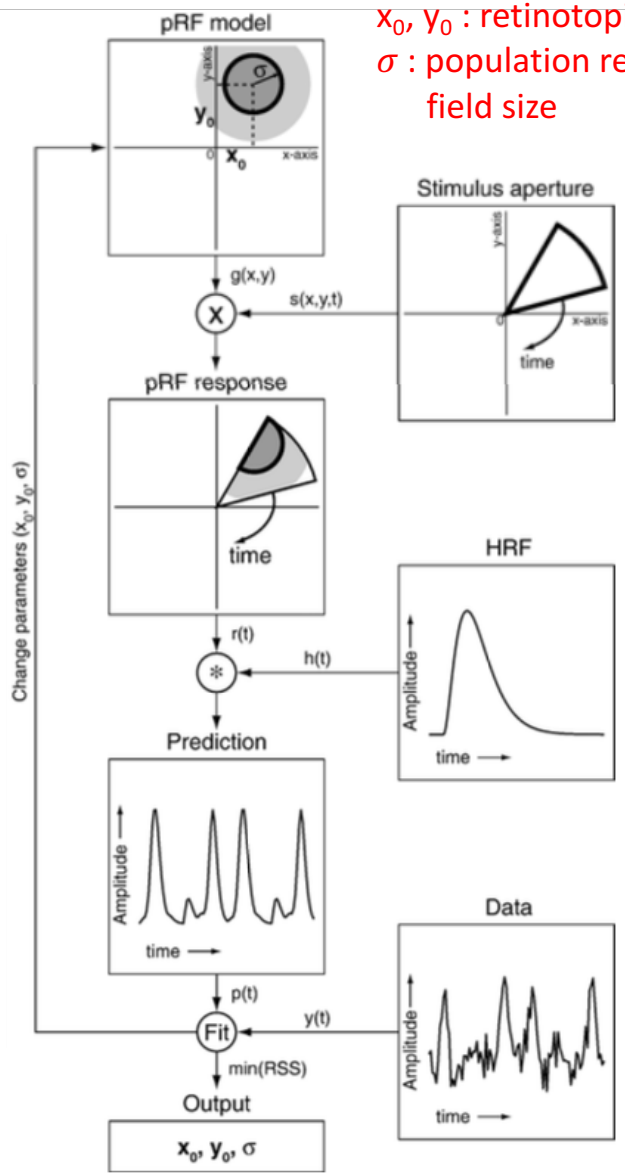
field map



Population receptive field size

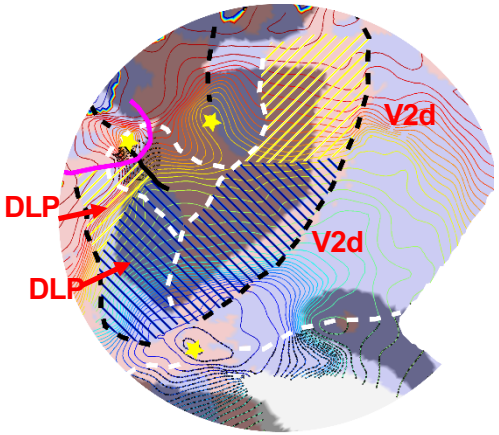


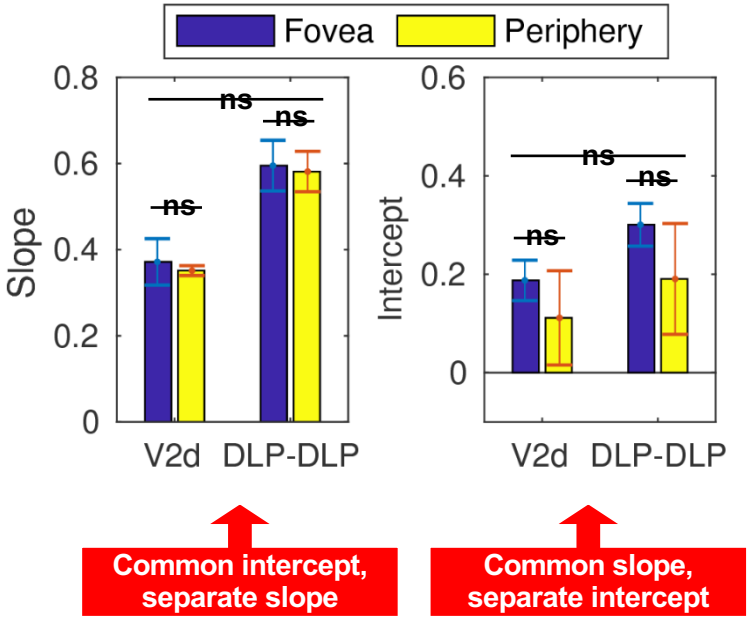
x_0, y_0 : retinotopic location
σ : population receptive field size



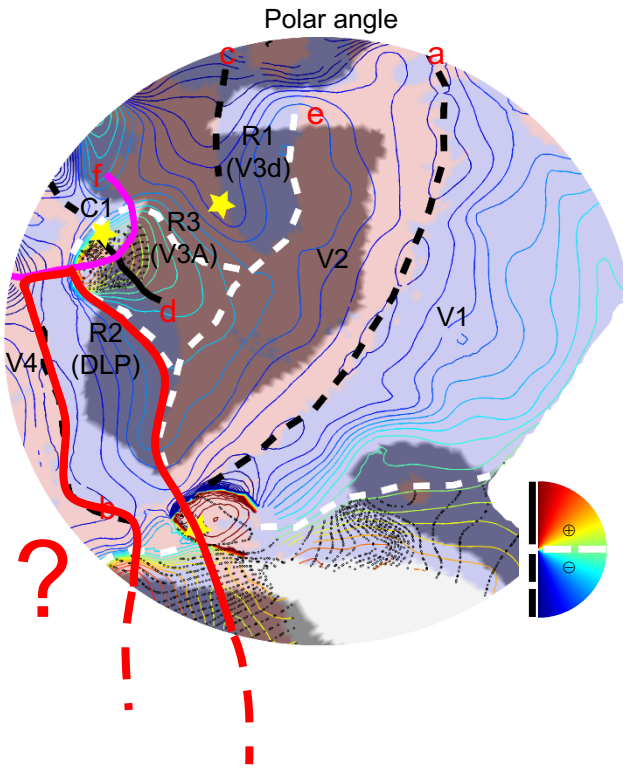
Dumoulin, S. O., et al., neuroimage, *2008*

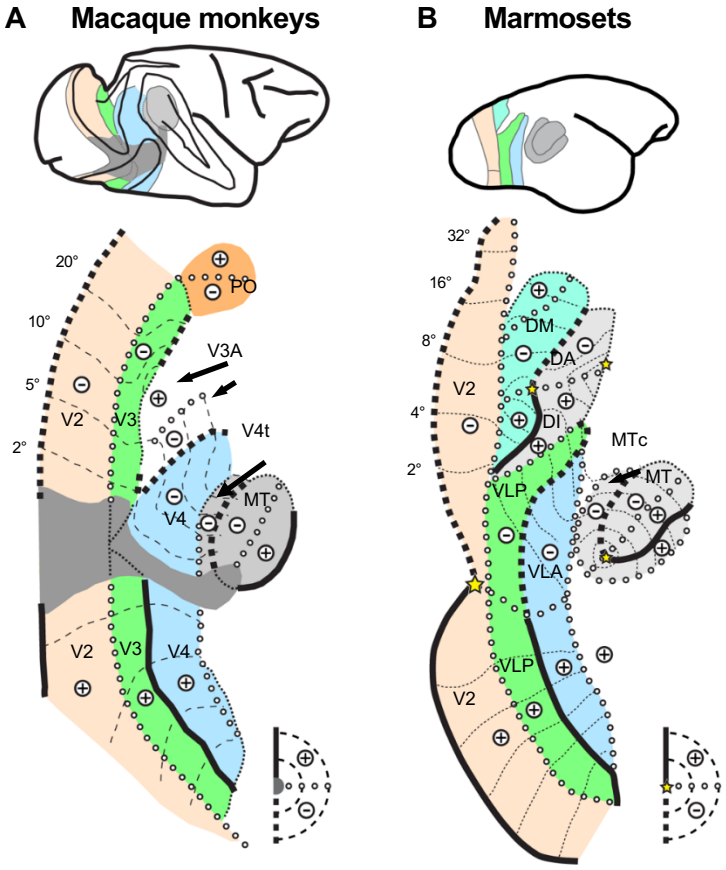
Population receptive field size differences between R2 (DLP) and R1 (V3d)



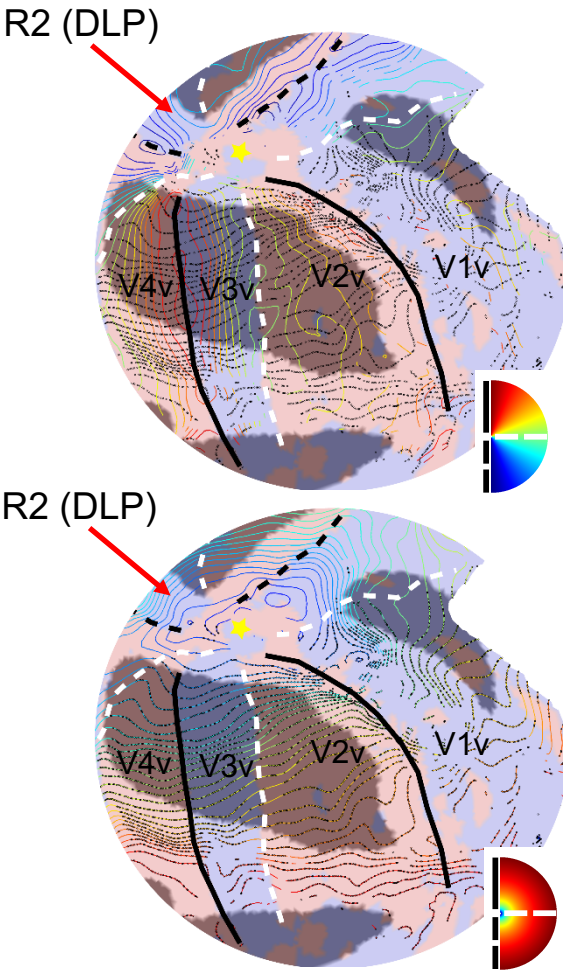


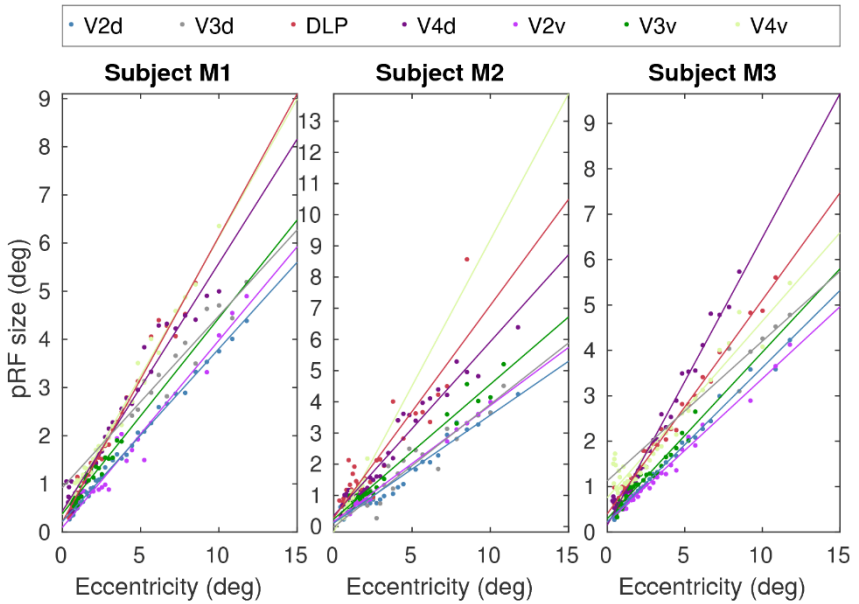
Does R2 (DLP) fit the New World monkey model for third tier areas?

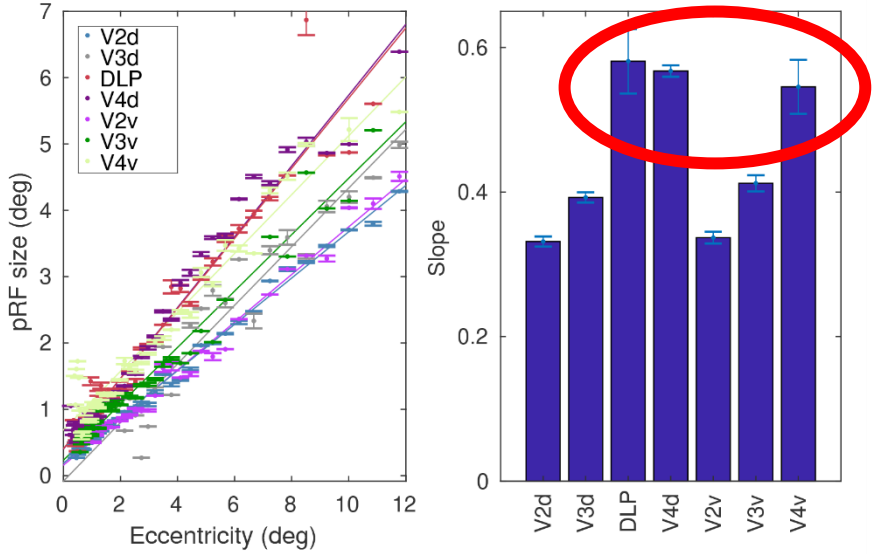




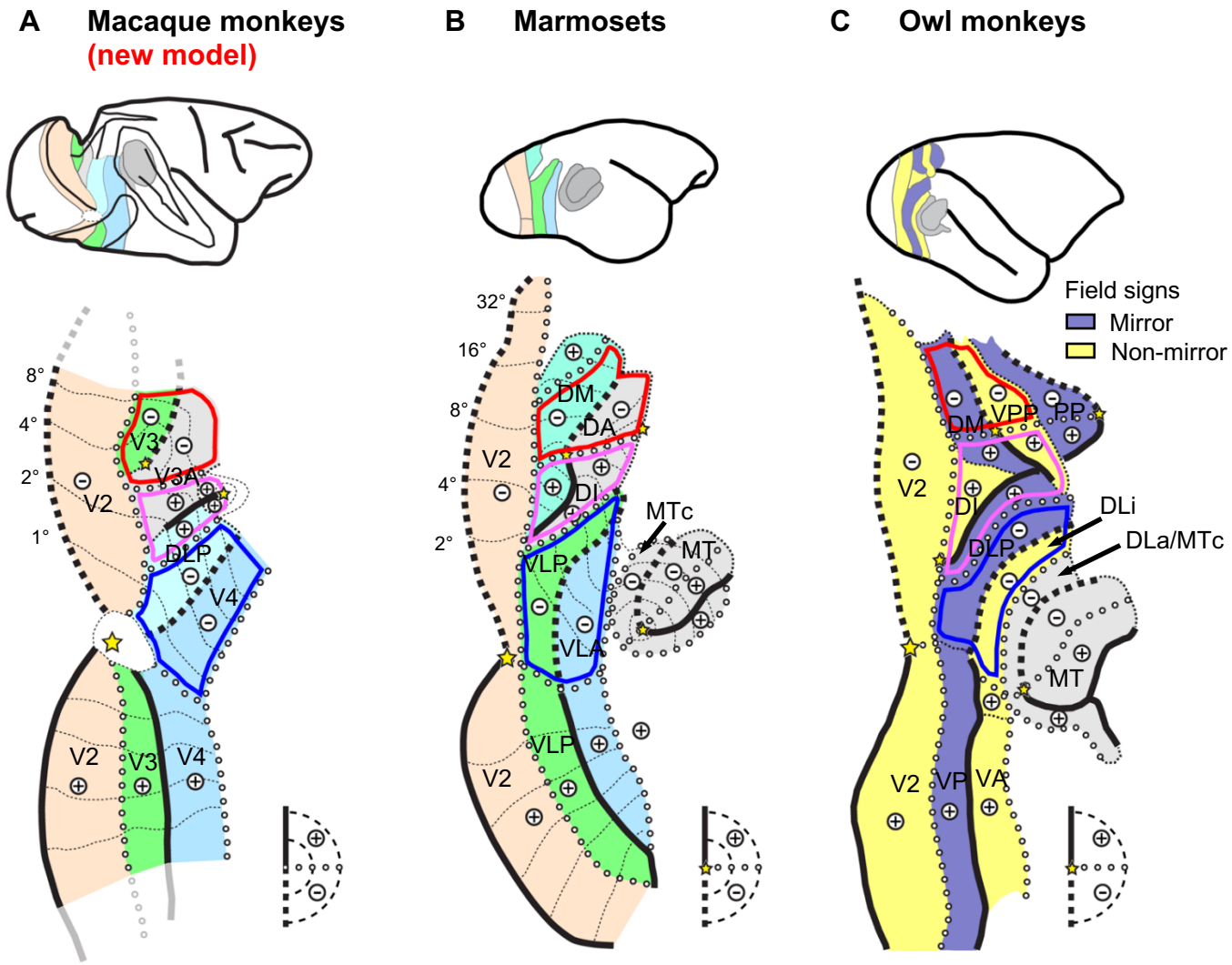
Does R2 (DLP) fit the New World monkey model for third tier areas?







Discussion: Comparisons with New World monkeys



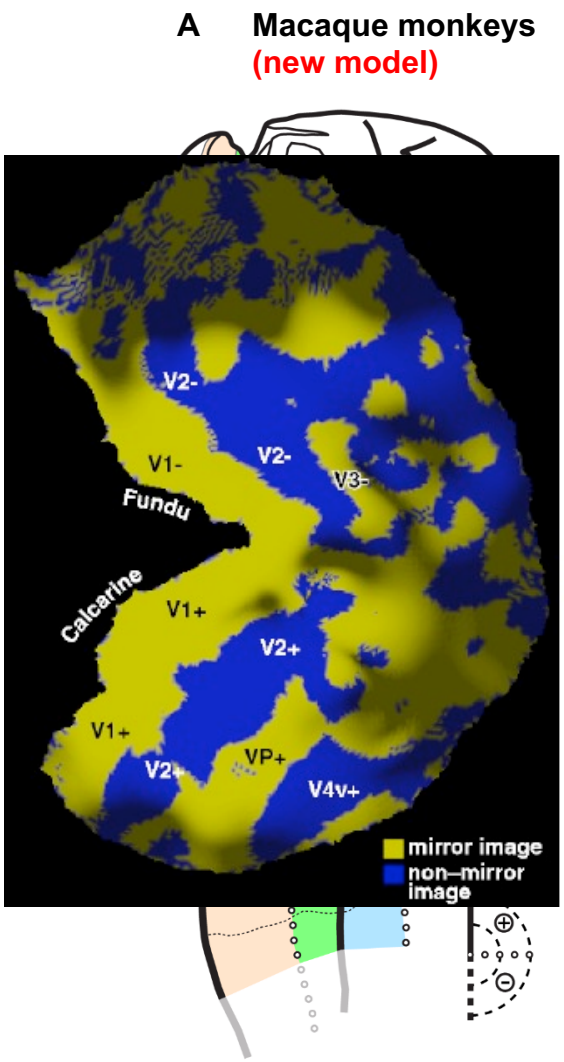
Zhu and Vanduffel PNAS 2019

Conclusion

A new model of the dorsal third and fourth tier areas in macaque monkeys

- **V3d** is reduced in size, similar as DM- in New World monkeys.
- Area **V3A**
- Area **DLP** a fourth tier area

- **The overall organization of these areas is remarkably similar between Old and New World monkeys, suggesting that this organization is evolutionarily preserved.**
- **Also in Human?**

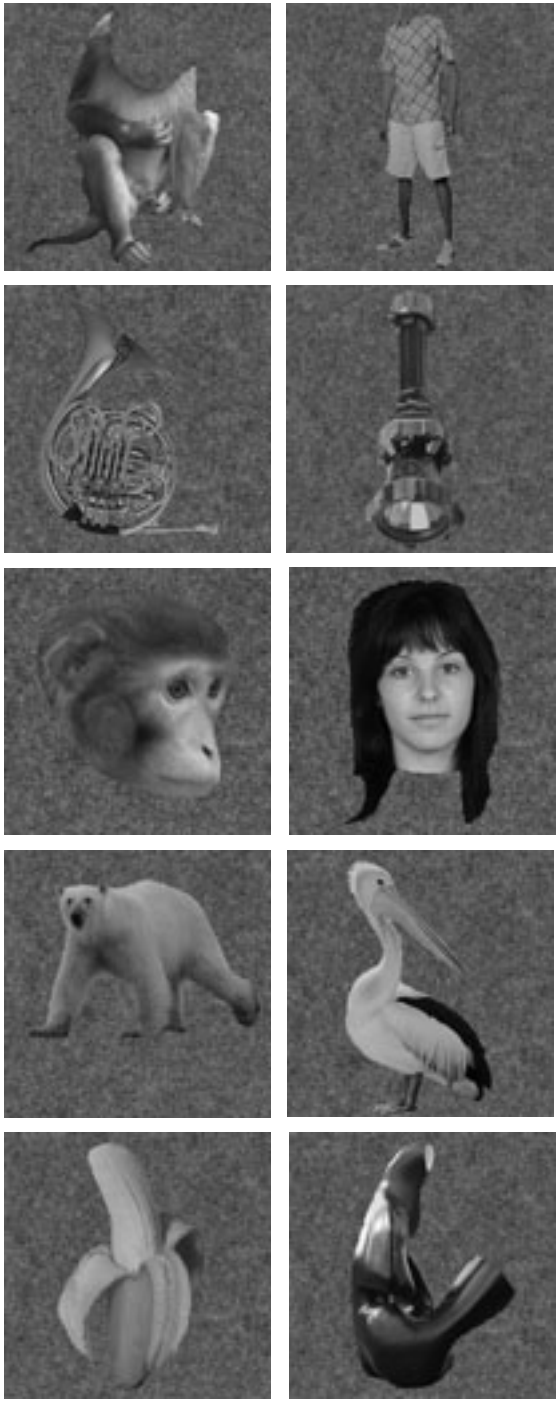


Sereno et al. Science 1995

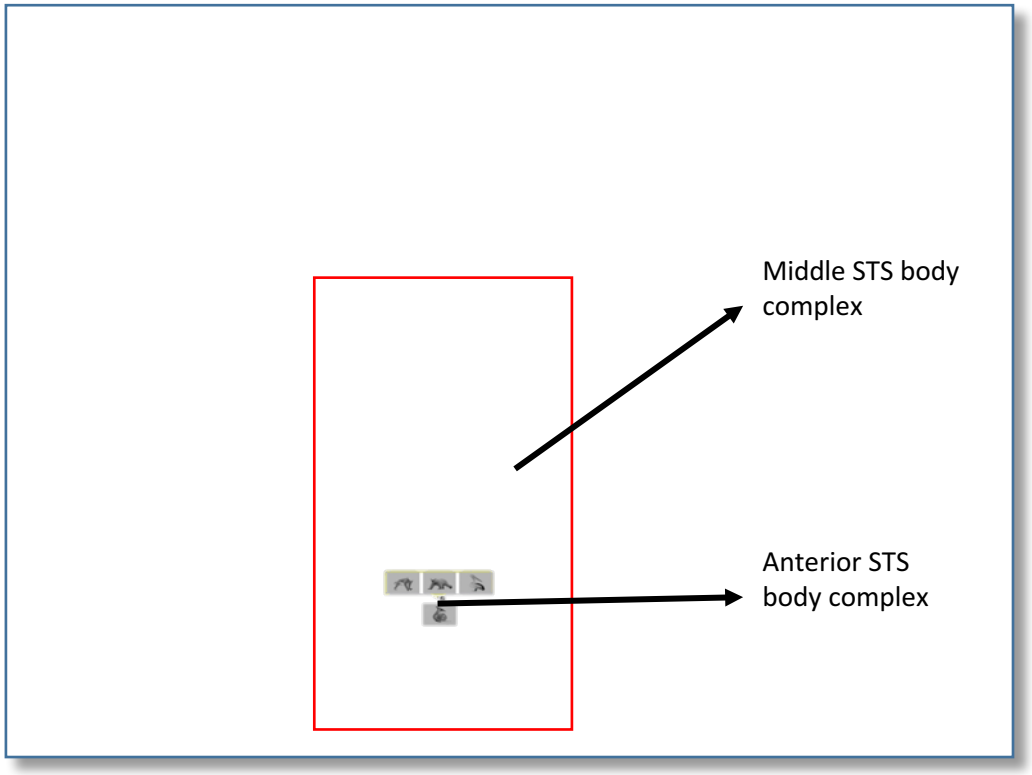
3. The fun part: new ‘columns’ in extrastriate cortex?

Stimuli

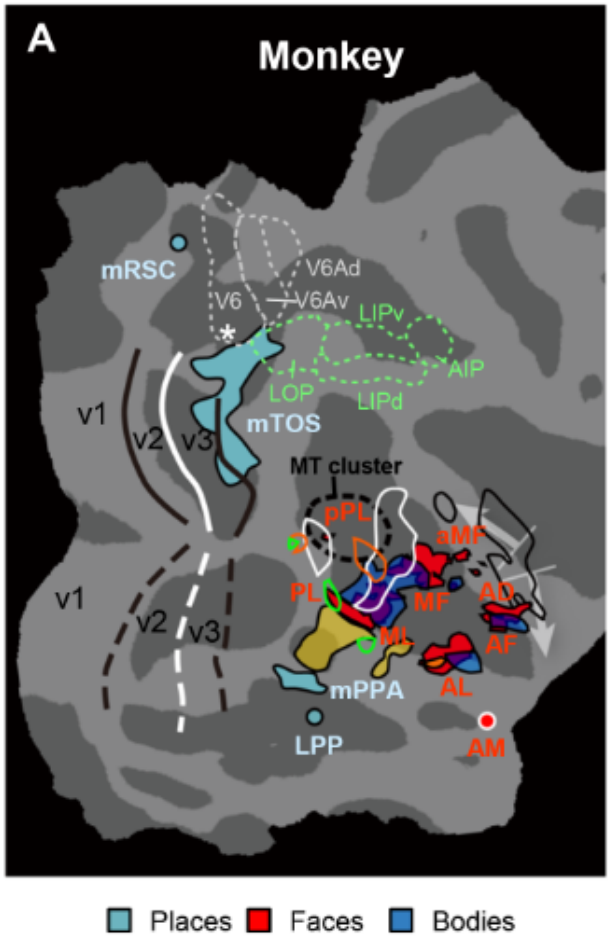
- 10 categories (each consisting of 20 stimuli):
  - headless monkey bodies;
  - headless human bodies;
  - monkey faces;
  - human faces;
  - objects (matched for the monkey bodies);
  - objects (matched for the human bodies);
  - 4-legged mammals;
  - birds;
  - fruits;
  - sculptures;
- Embedded into pink noise pattern;
  - similar spatial frequency to natural images;



‘Body areas’ at low resolution



Popivanov et al., NeuroImage 2012



Vanduffel et al. Neuron 2014

- HERE A NUMBER OF UNPUBLISHED SLIDES FOLLOWED

Conclusion

- **Very fine grained body & face activations**
- **Body: crescent-like organization**, surprisingly similar to the fine-grained organization of human EBA.
- mostly corresponding to **peripheral** eccentricity representations as in humans.
- **Face**: **next to body** activations corresponding to **more foveal** eccentricity representations. They also form a **crescent-like** band surrounding PITd body activations.
- **Several new body and face patches (columns?) were found consistently in anterior IT, STS and even IPS**.

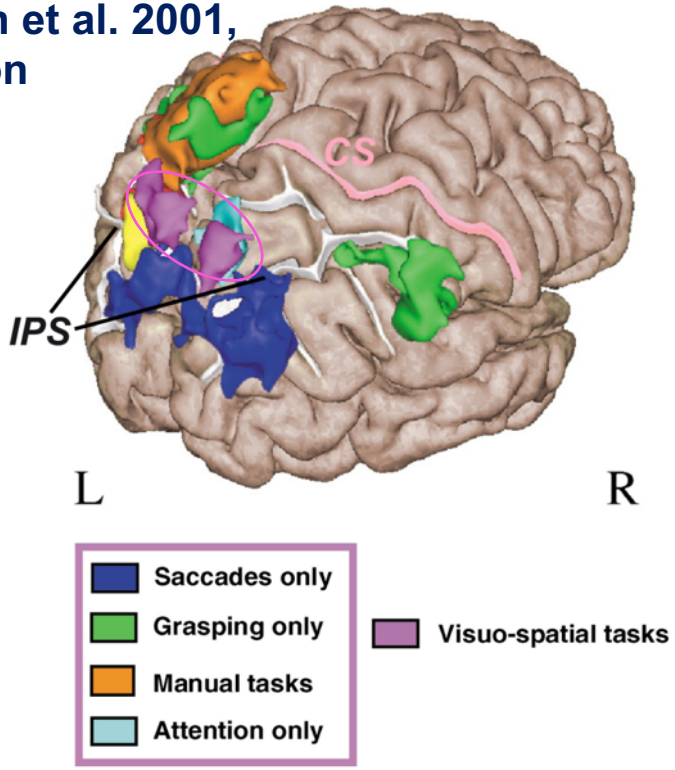
→ columns in visual, parietal and frontal cortex: syntax?
→ human?

4. But also cognitive paradigms: from human to monkey!

I- A region in Human

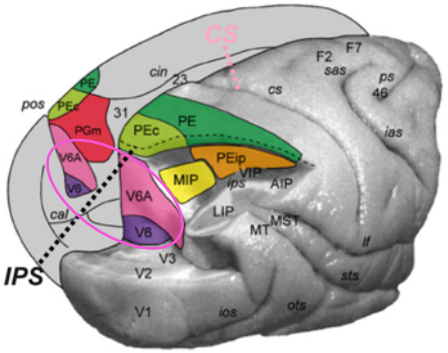
SPL is activated by visuo-spatial tasks

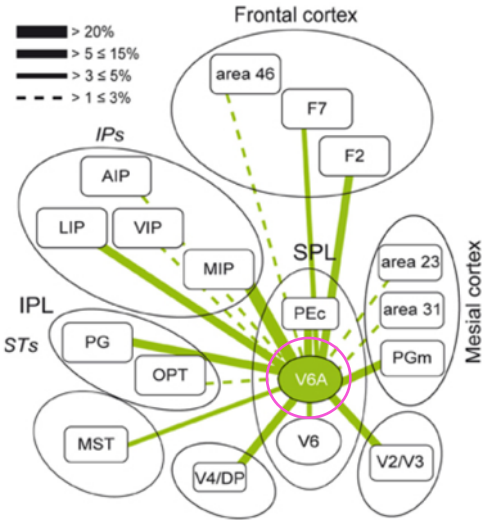
Simon et al. 2001, Neuron



SPL

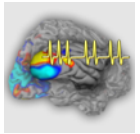
Single cell data in MONKEY have shown similar properties for **V6A**, **Galletti et al. 2011, Plos one**





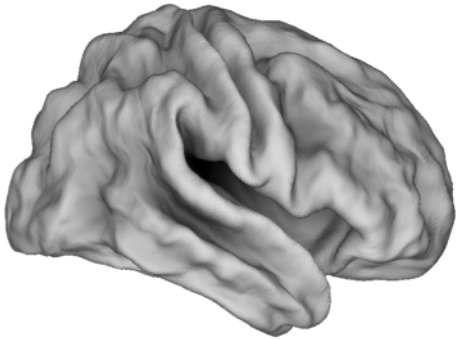
→ are they functionally homologous?

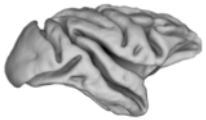
→ **Using a data driven approach**

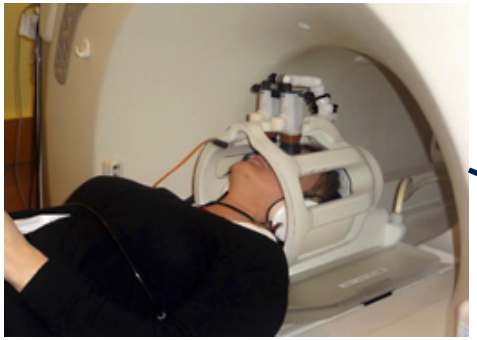


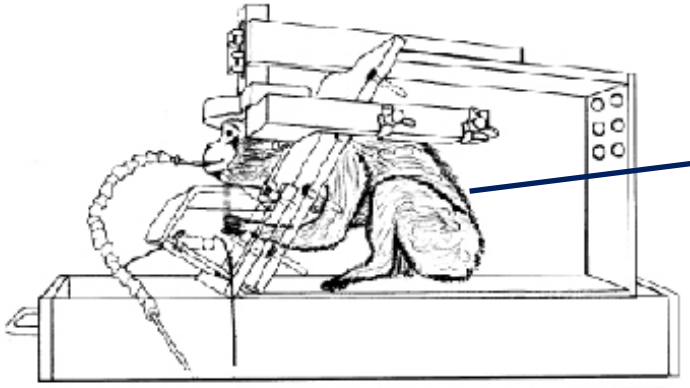
II-1 Methods

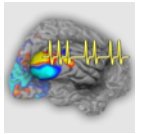
fMRI in both species, while they are actively engaged in the same covert selective spatial attention task



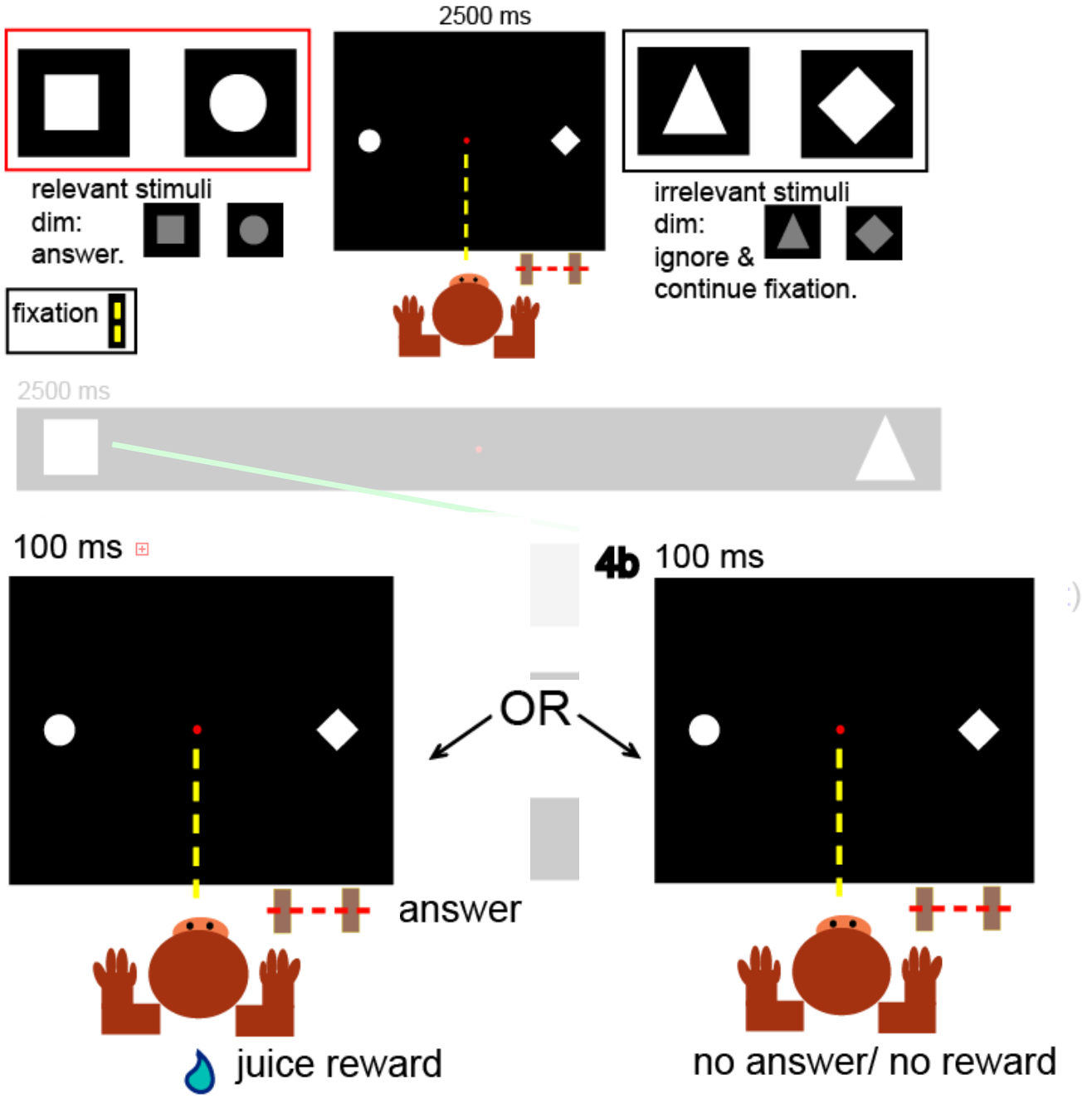




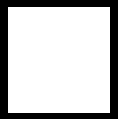




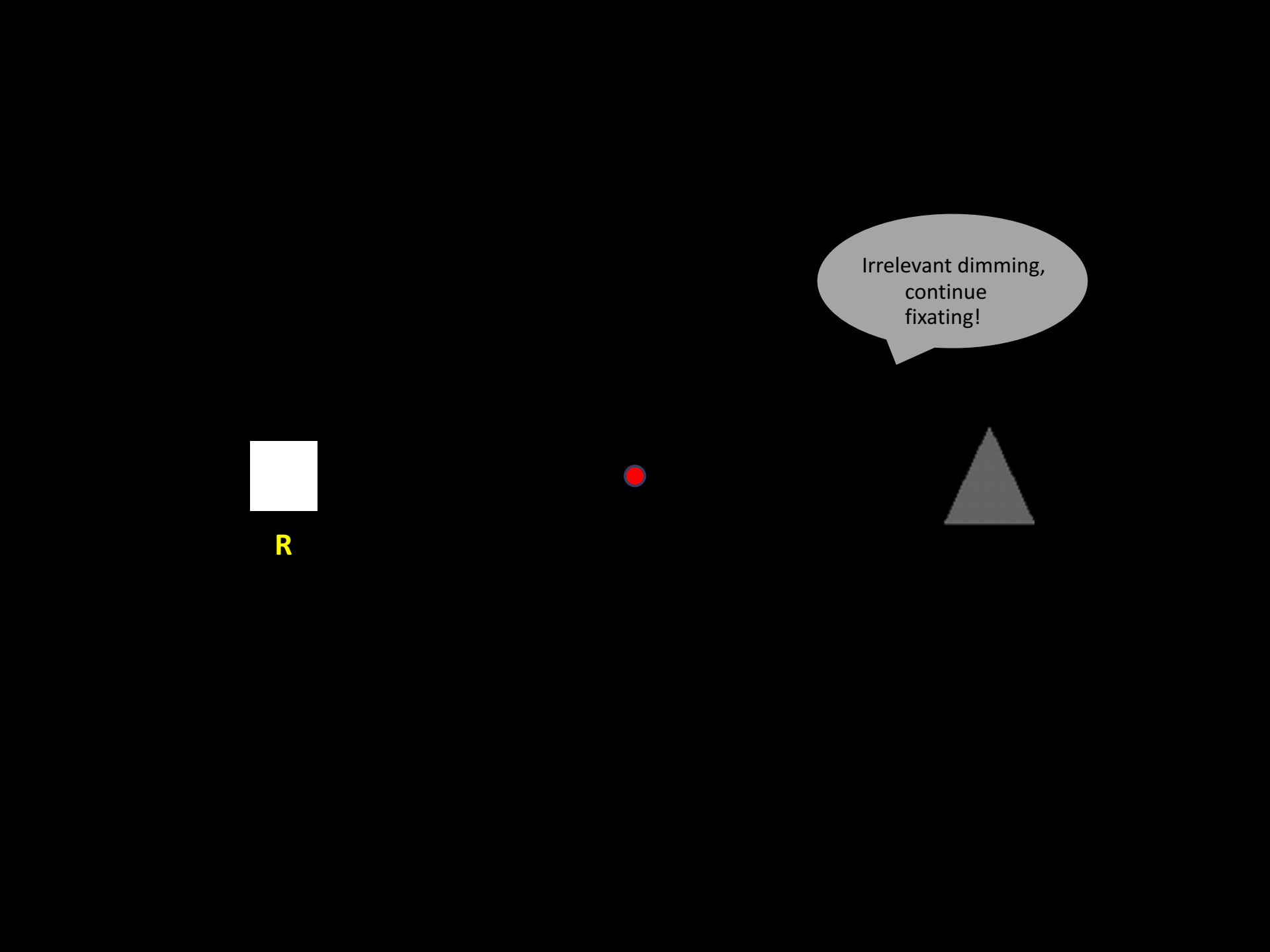
II-3
Task

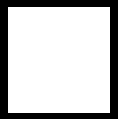


adapted from: Molenberghs et al. 2007, Cortex



R

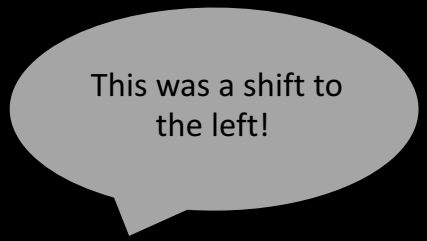

Irrelevant dimming, continue fixating!
R

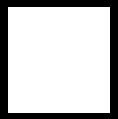


R

R

This was a shift to the right!



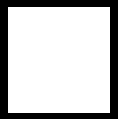


R

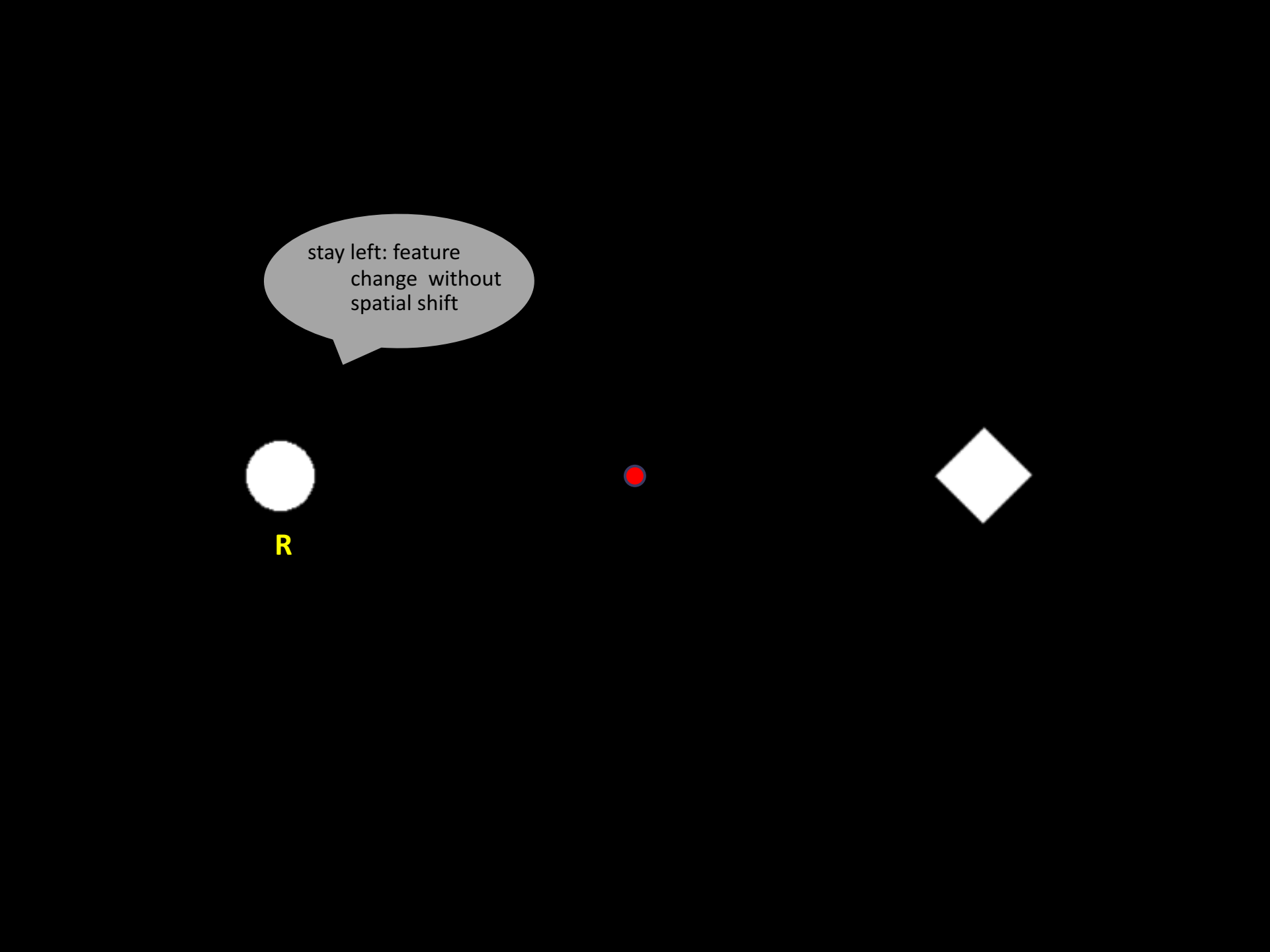
relevant dimming,
answer →


or

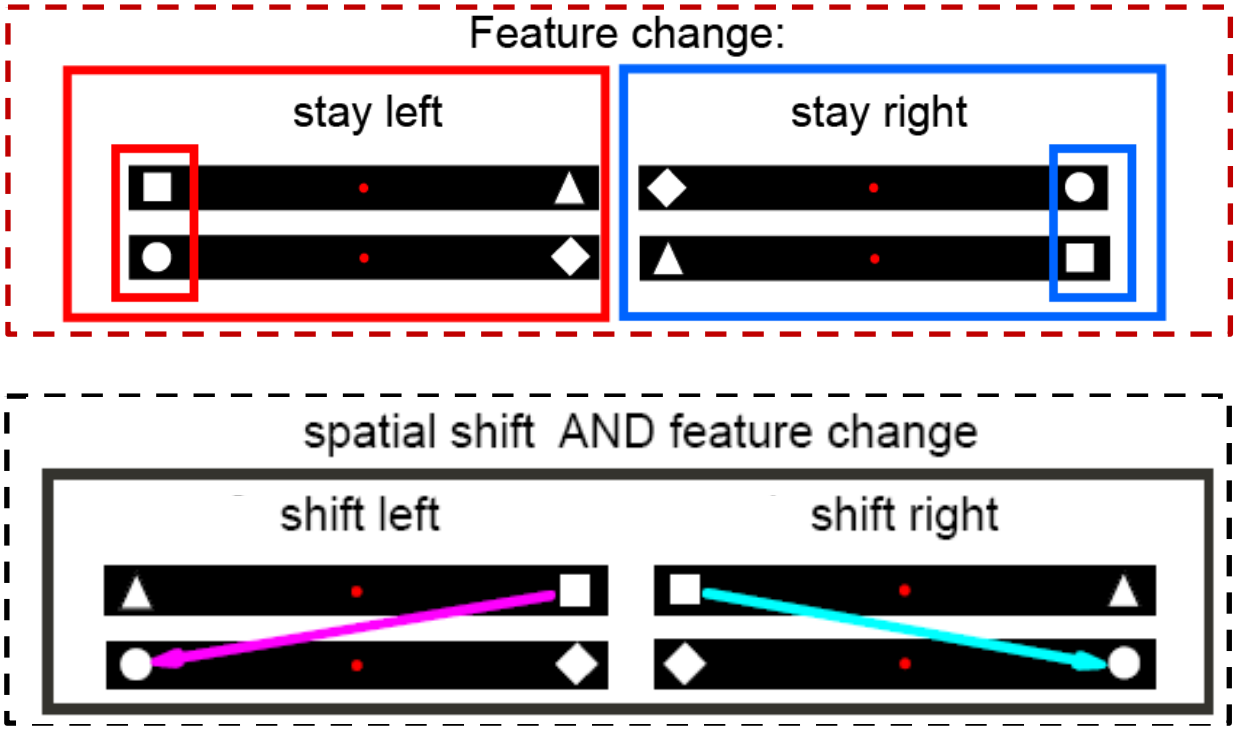

R



R

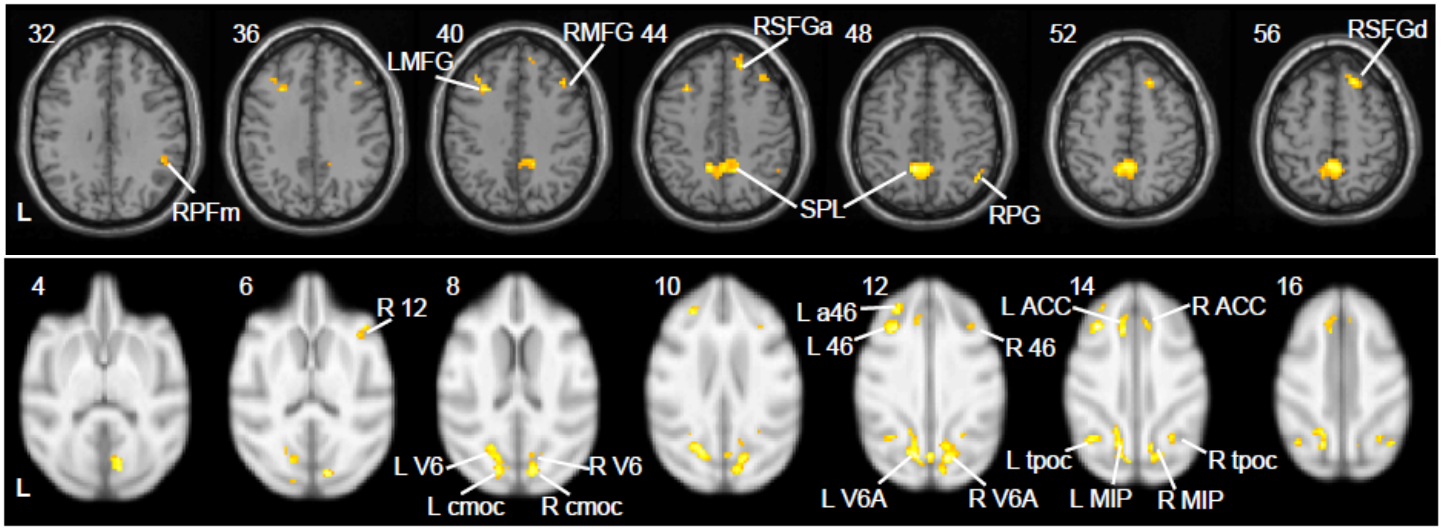

stay left: feature change without spatial shift
R

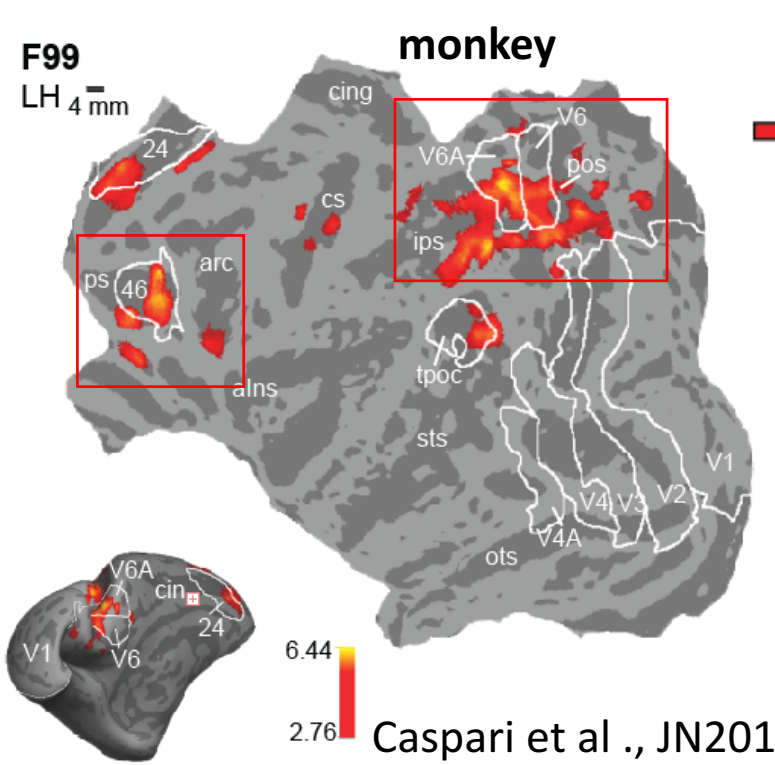
II-5 Data Analysis- GLM contrast



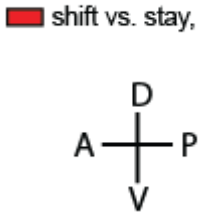
Contrast 3:
shift (left & right)
vs. stay (left & right)

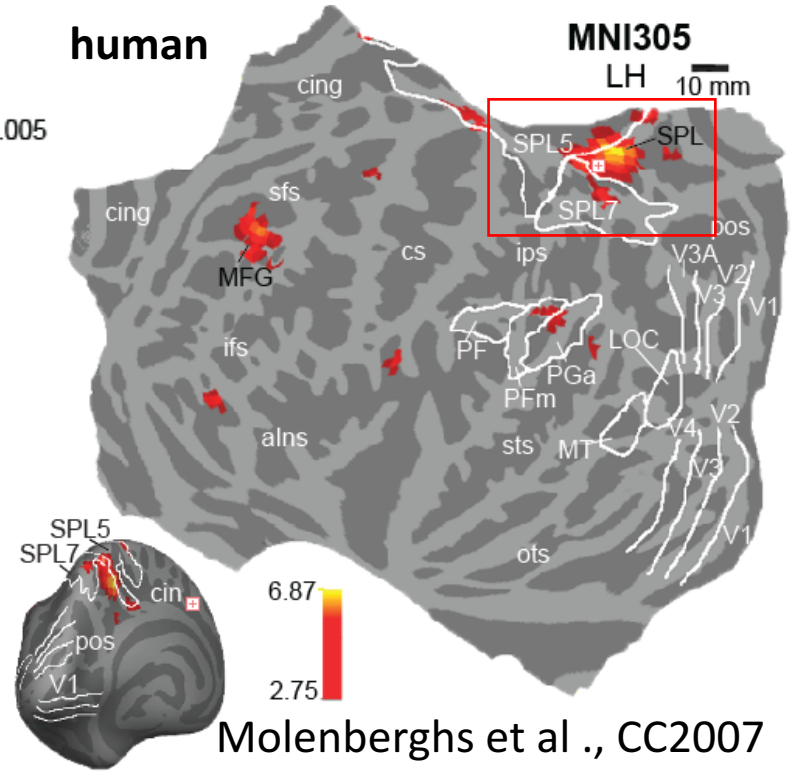
III- 2 Results: GLM contrast shift vs. stay





Caspari et al ., JN2015





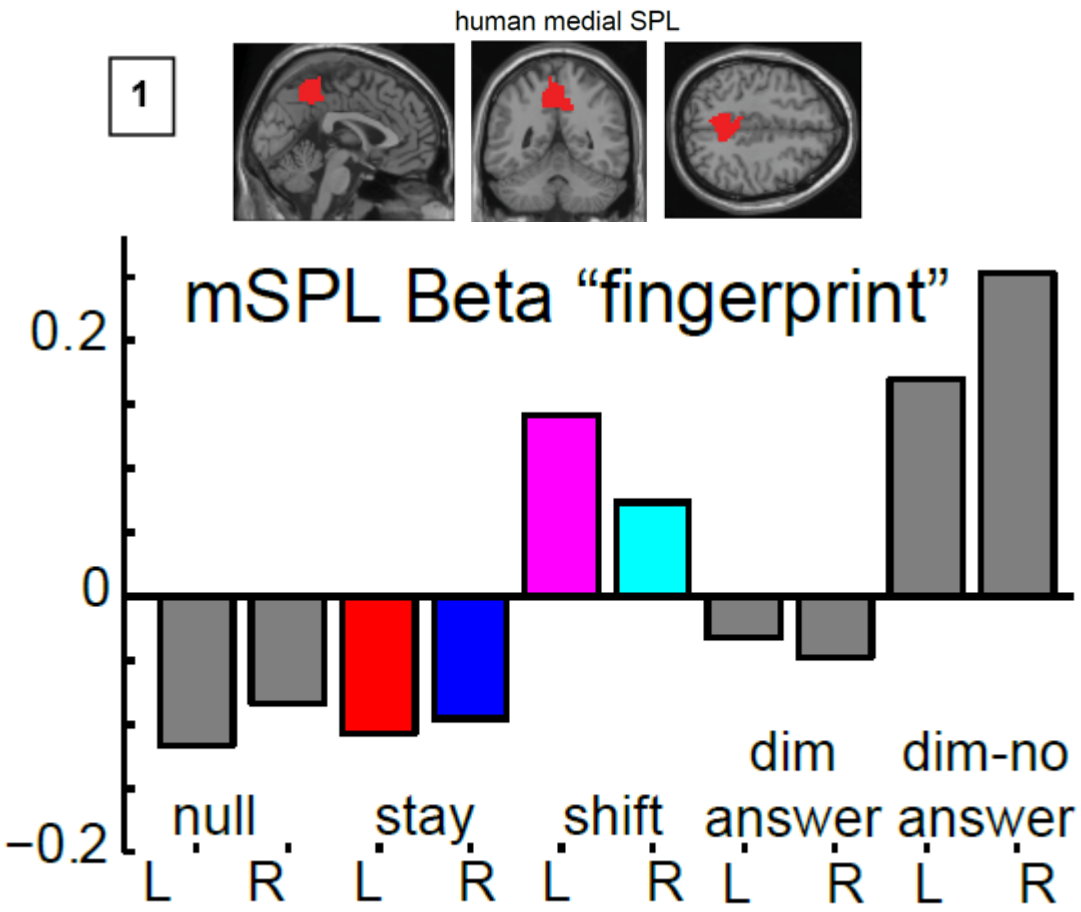
Molenberghs et al ., CC2007

- Correlating beta-values across species
  - (ROI→ voxel) or
  - (voxel → voxels)
- **Inter species beta correlation (ISBC)**

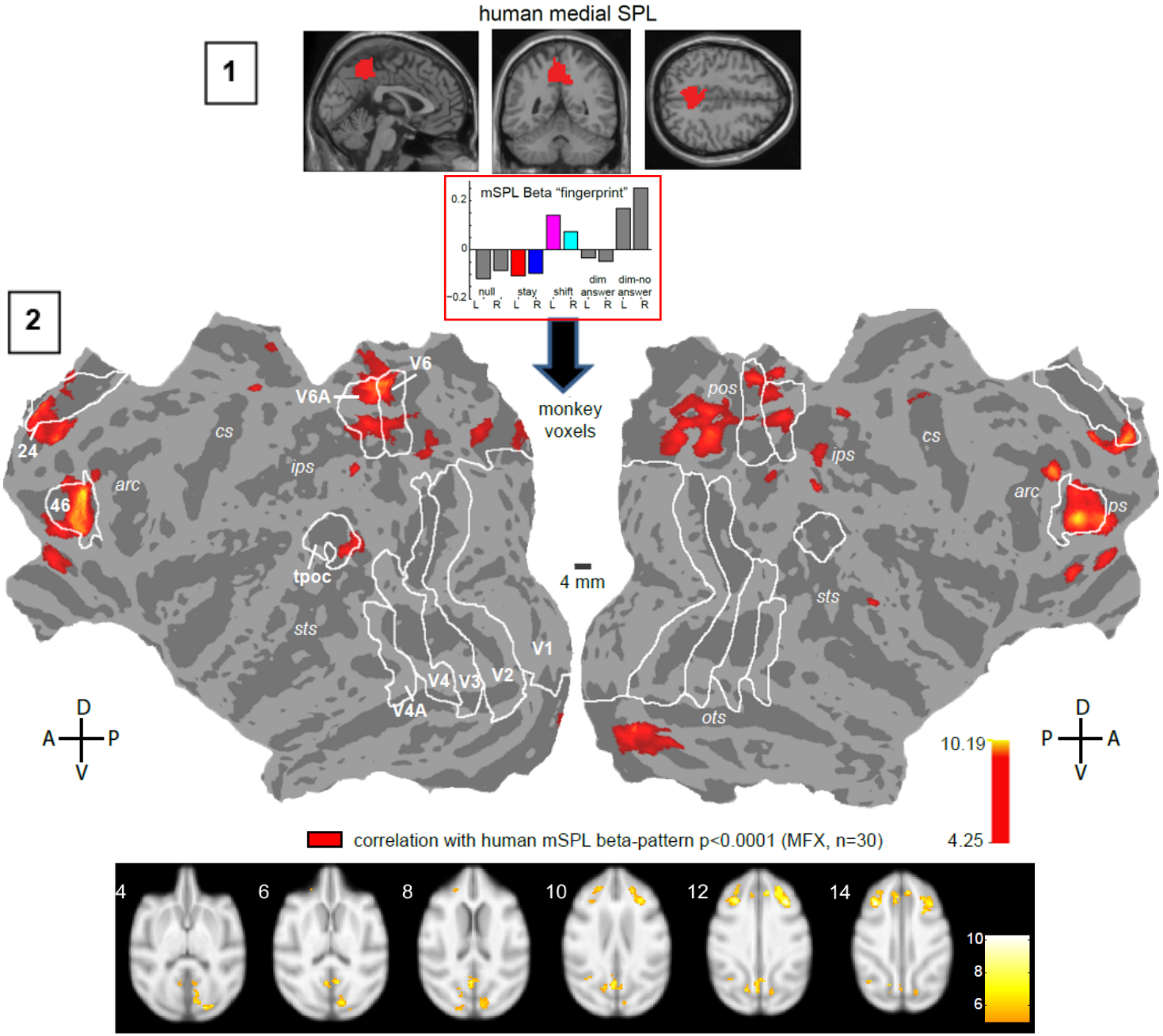
- → temporal structure of the paradigm is not relevant as in interspecies activity correlation (ISAC) – as we did in Mantini et al. Nat. Methods 2012

- → useful for comparing task-based activations where subjects determine the pace of the experiment

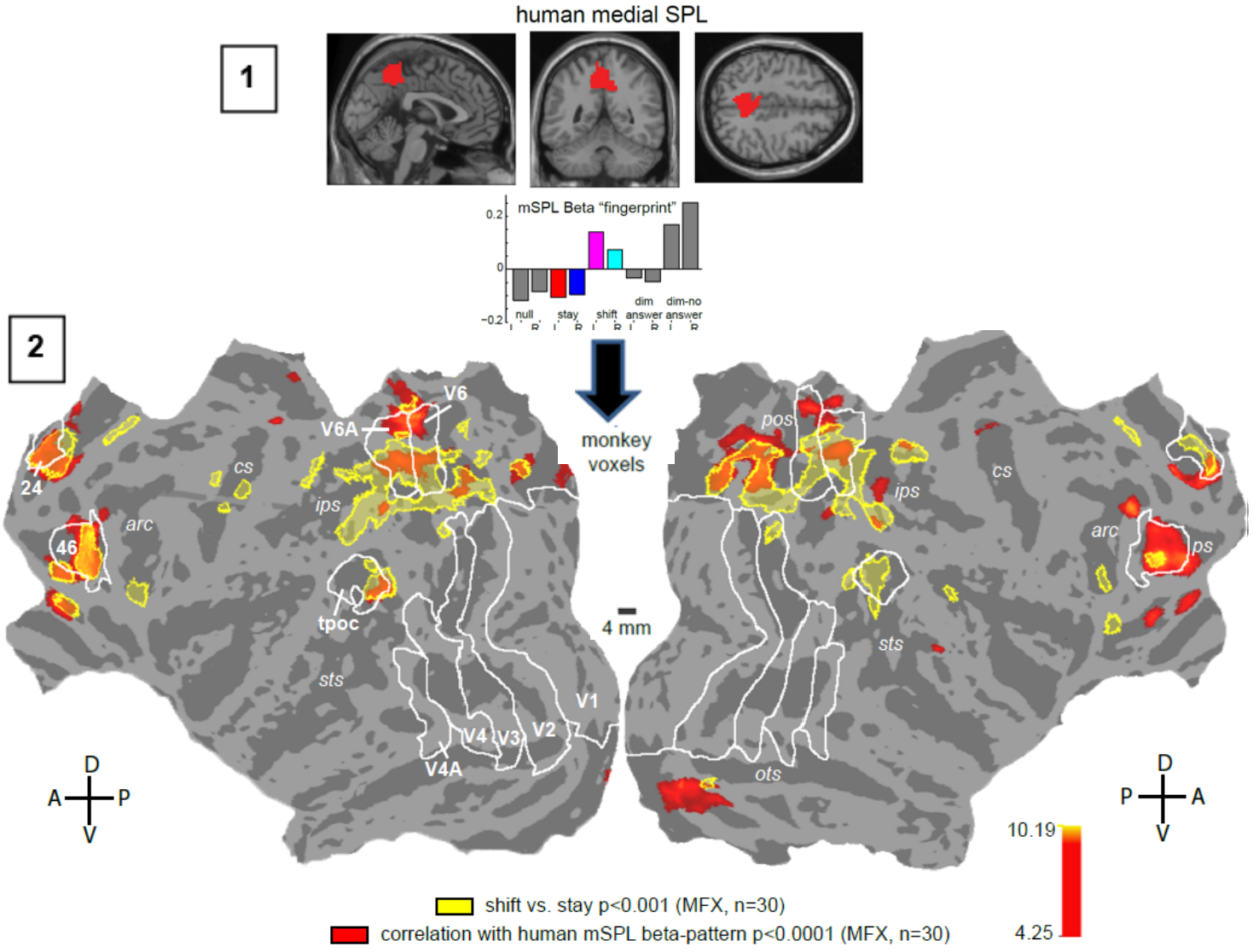
III- 3A Results: Inter-Species Beta-Correlation (ISBC) with single voxels in monkey



III- 3A Results: ISBC with single voxels in monkey



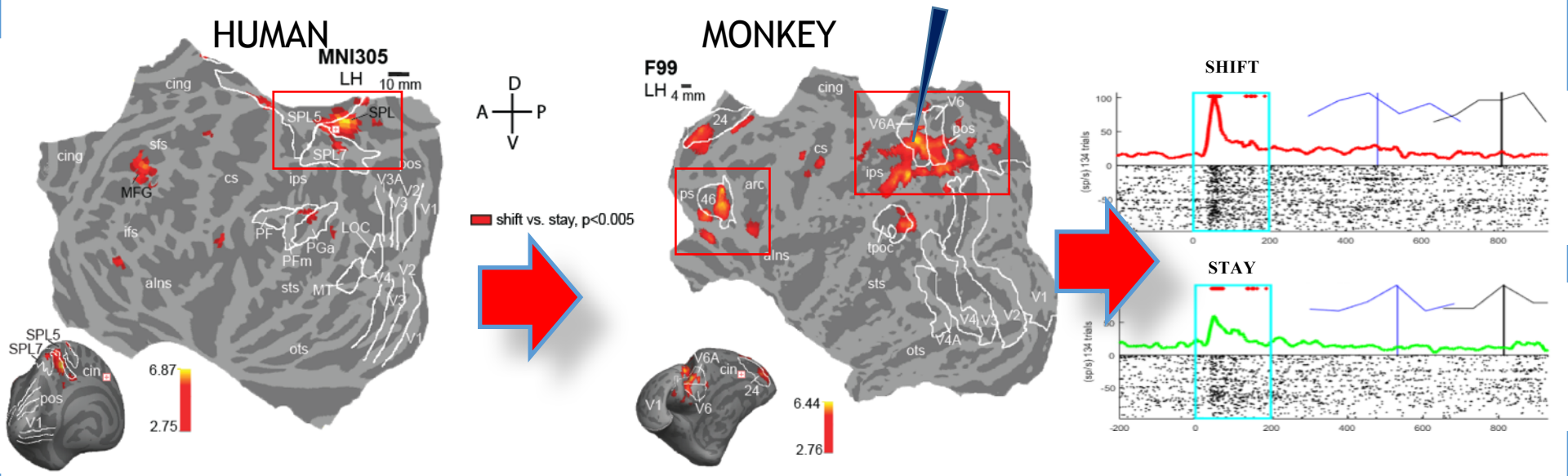
III- 3B Results: correspondence of ISBC with GLM



Human fMRI → Monkey fMRI → **Single Unit Activity** → optogenetics

Example: cognitive processing **Shift in covert selective attention shifts**

fMRI-guided shift selective neuron in monkey



Work in progress by Marina De Vitis

conclusions

Different methods to perform comparative fMRI:

- With spatial assumptions: e.g. GLM
- Without spatial assumptions
  - ISAC: same temporal order of ‘events’ required
  - ISBC: temporal order of events not relevant: ideally suited for comparative task studies
- Ongoing:
  - Representational similarities across species
  - correlating electrophysiological measures with fMRI (within and across species)

Thanks!

Human Brain Project

KU LEUVEN

fwo

Belgian Science Policy Office

belspo