遺伝子発現パターンを指標にした霊長類大脳皮質視覚野の比較解剖学

July/24/2015

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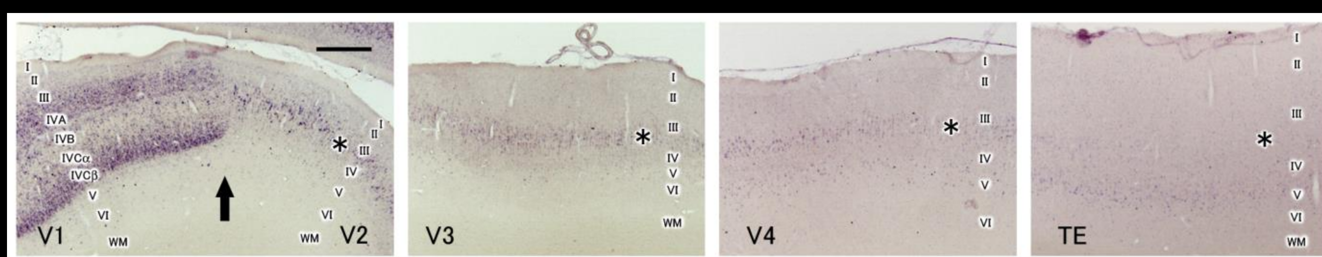
of Neuroscience and Technology (ZIINT)

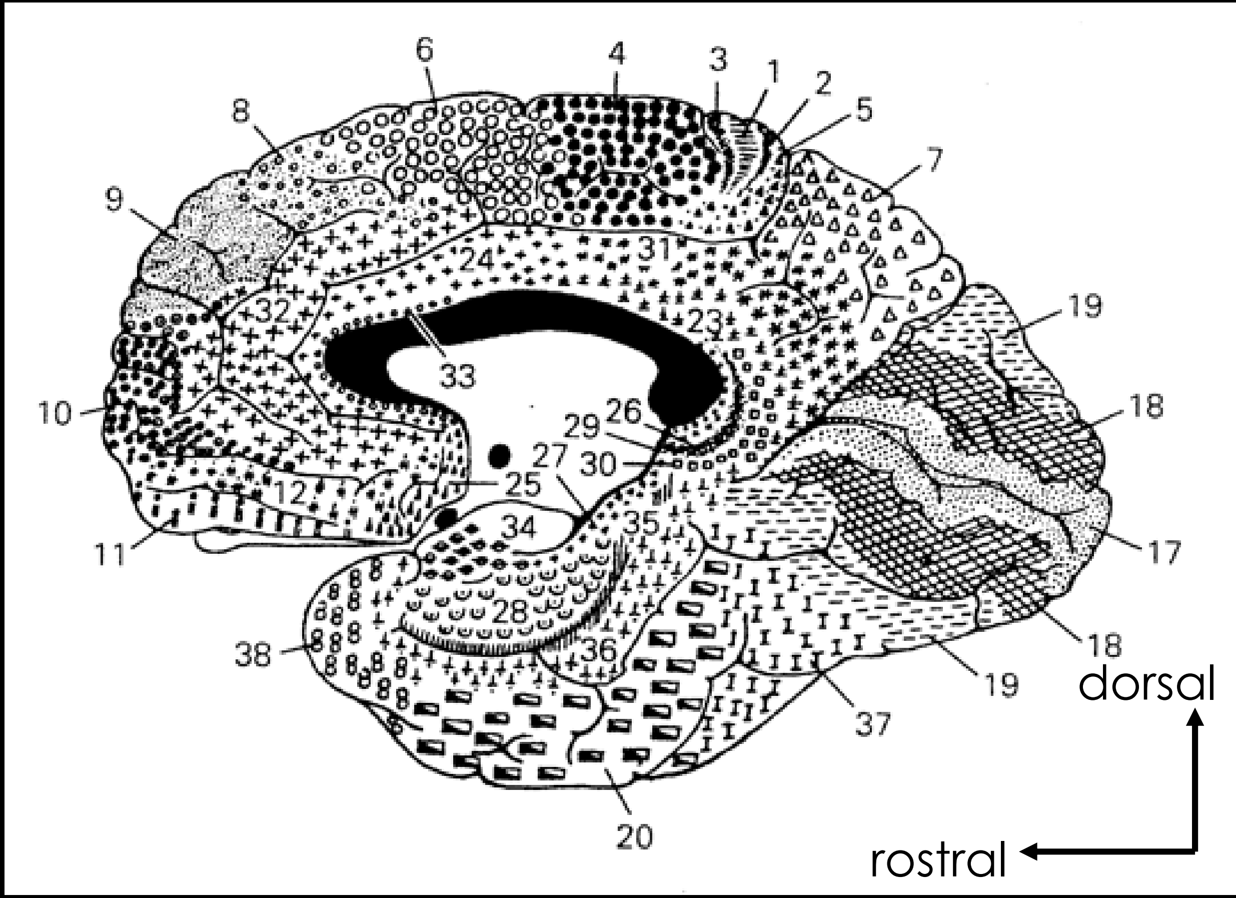
Part 1.

Unique mRNA expression of *OCC1* in primate visual cortex.



INTRODUCTION

Brodmann's "cortical area"



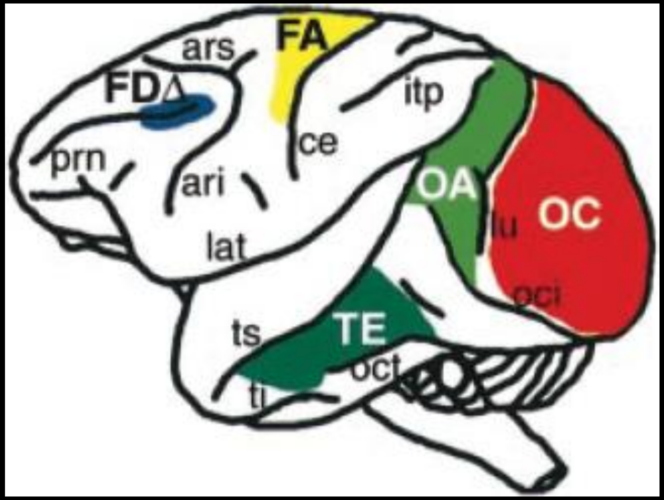
INTRODUCTION

Cerebral cortex used to be referred as “isocortex”, based on the homogeneous structure.

↓

However, it has been shown that cerebral cortex is heterogeneous in various ways, e.g. dendritic field and the degree of plasticity.

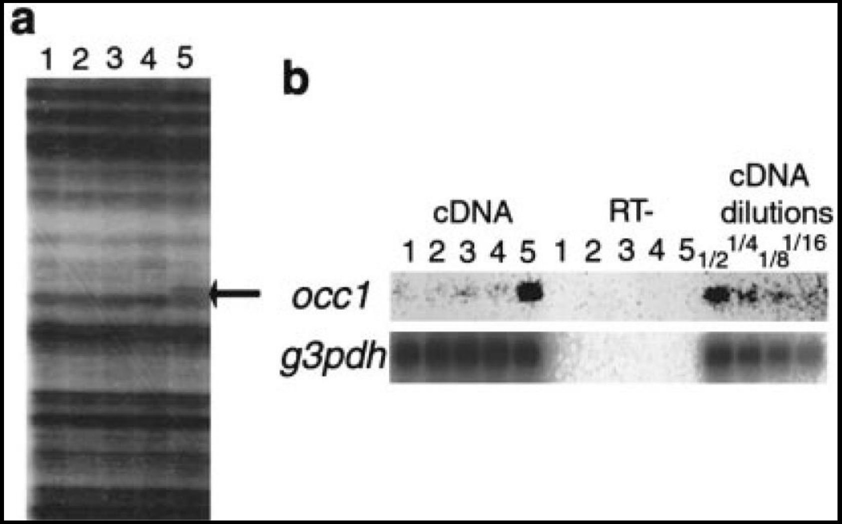
We explored how primate cerebral cortex is heterogeneous in terms of gene expression.



1: FD△ (prefrontal cortex)
2: FA (primary motor cortex)
3: TE (temporal cortex)
4: OA (parietal cortex)
5: OC (occipital cortex)

Differential Display

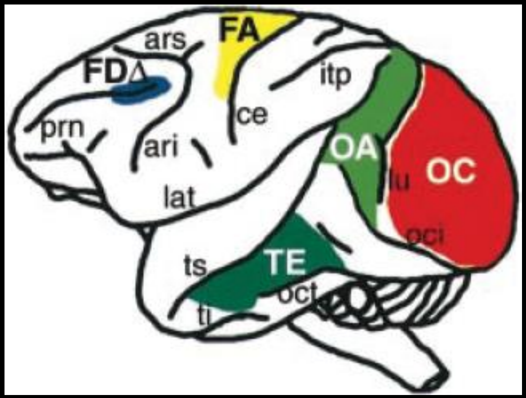
RT-PCR

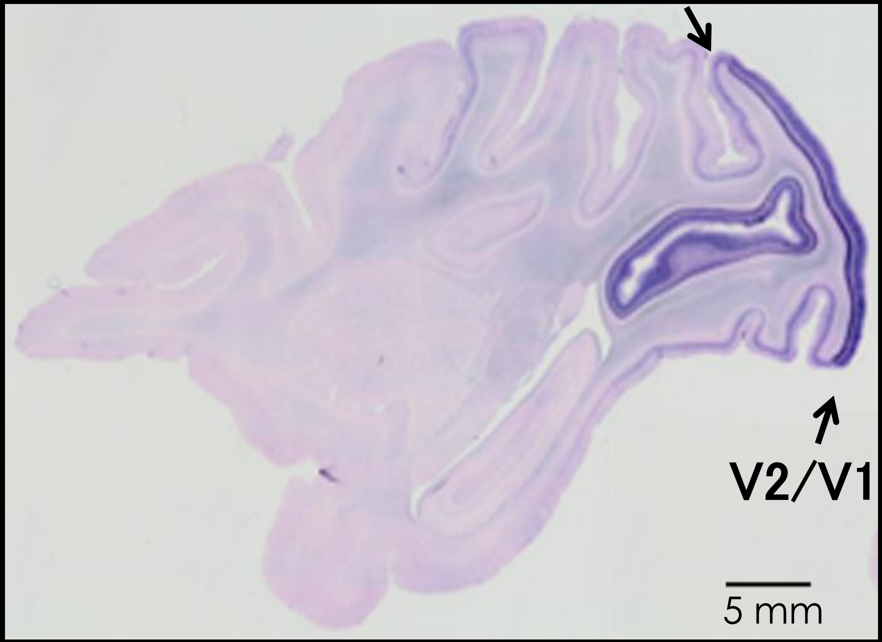


***OCC1* is expressed preferentially in the occipital cortex of primates!**

Tochitani, et al. (2001) *Eur J Neurosci*

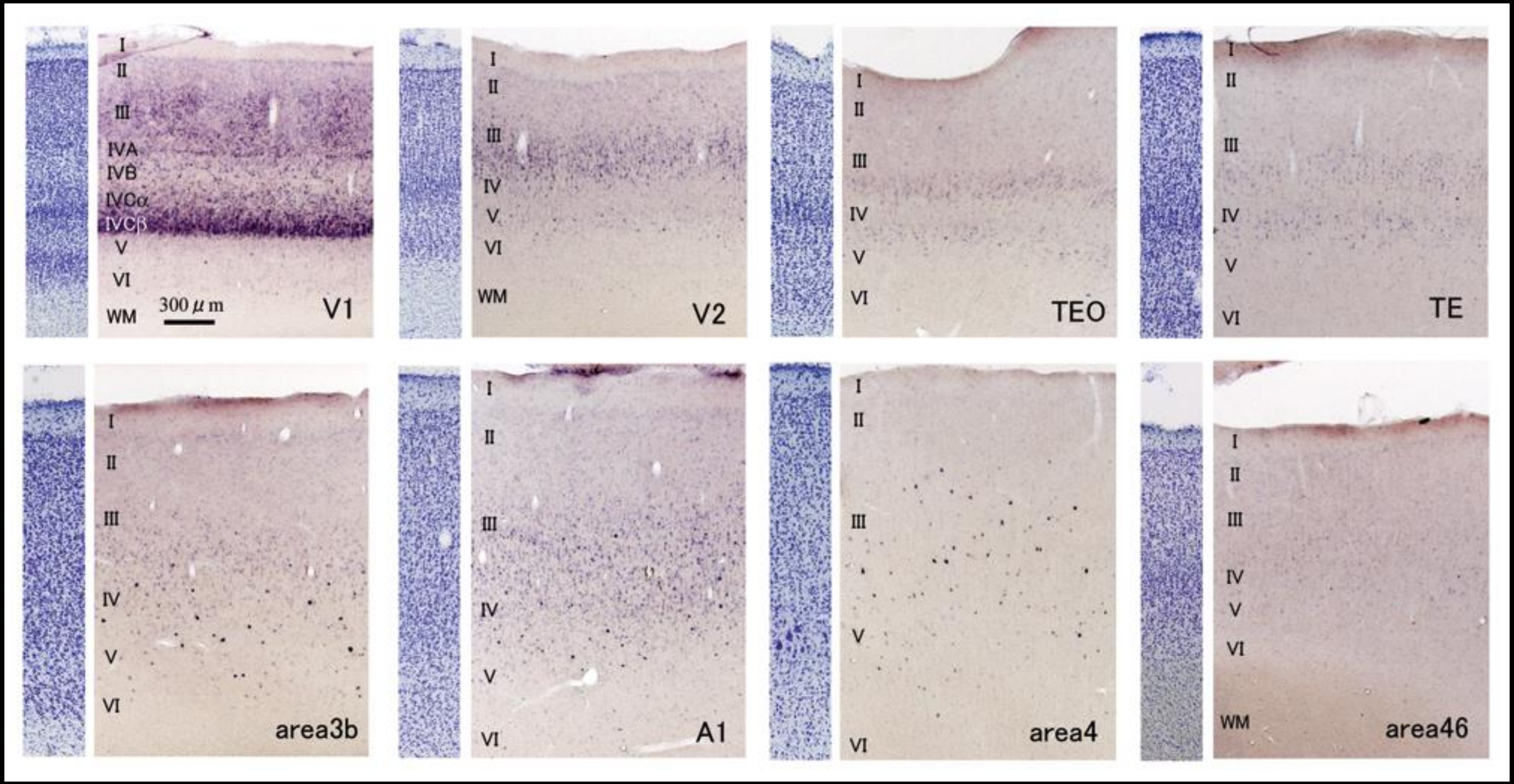
OCC1 gene is expressed preferentially in macaque V1.





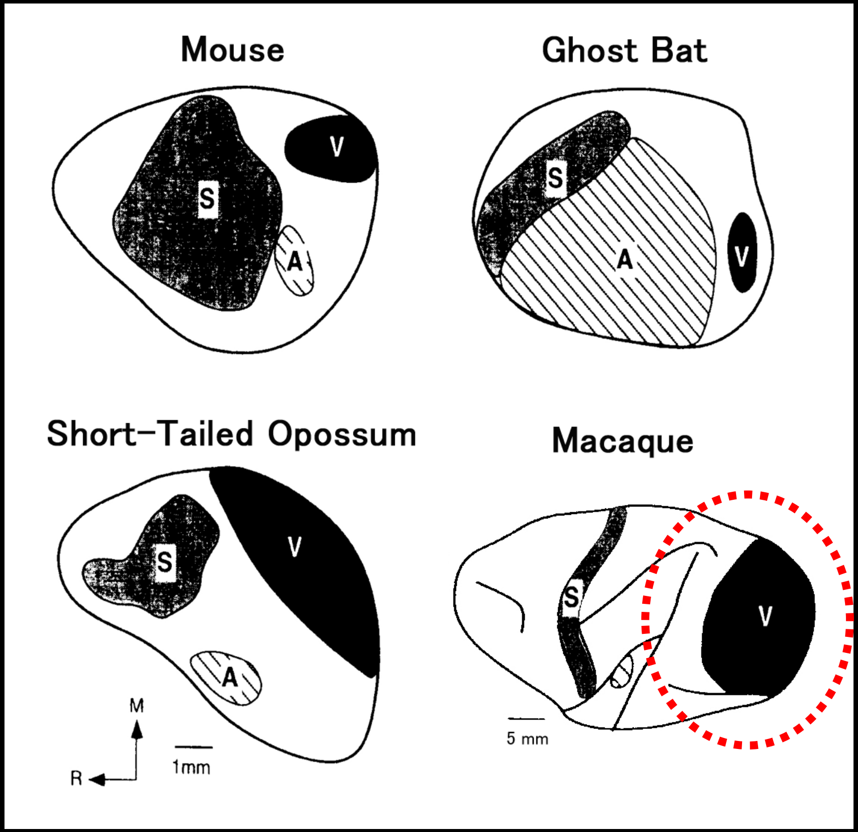
Tochitani, et al. (2001) *Eur J Neurosci*

OCC1 gene is expressed preferentially in macaque V1.



Takahata, et al. (2006) *Cereb Cortex*

Visual pathway is especially well-developed in primates.



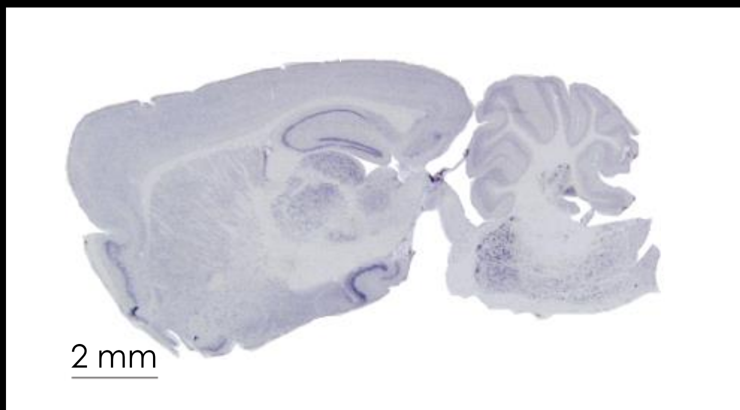
Krubitzer, (2000)

S: Somatosensory Cortex
A: Auditory Cortex
V: Visual Cortex

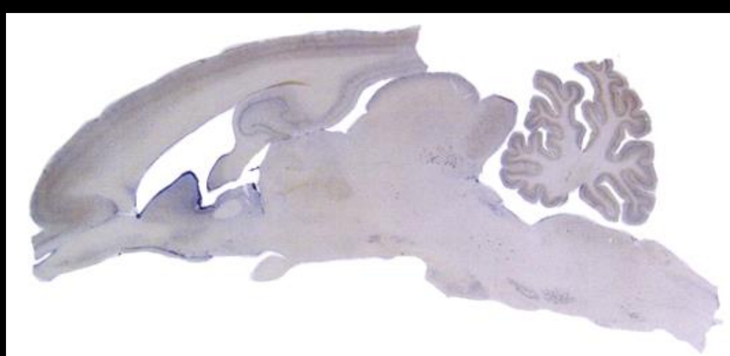
What about expression pattern of *OCC1* in other species?

OCC1 expression is not abundant in V1 of non-primate mammals.

Mouse



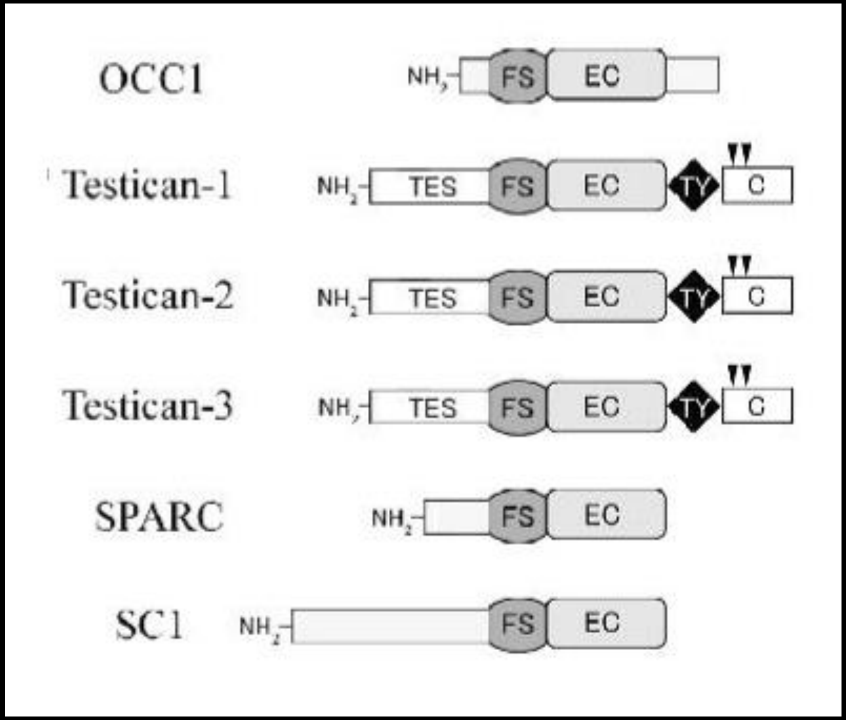
Rabbit



Ferret

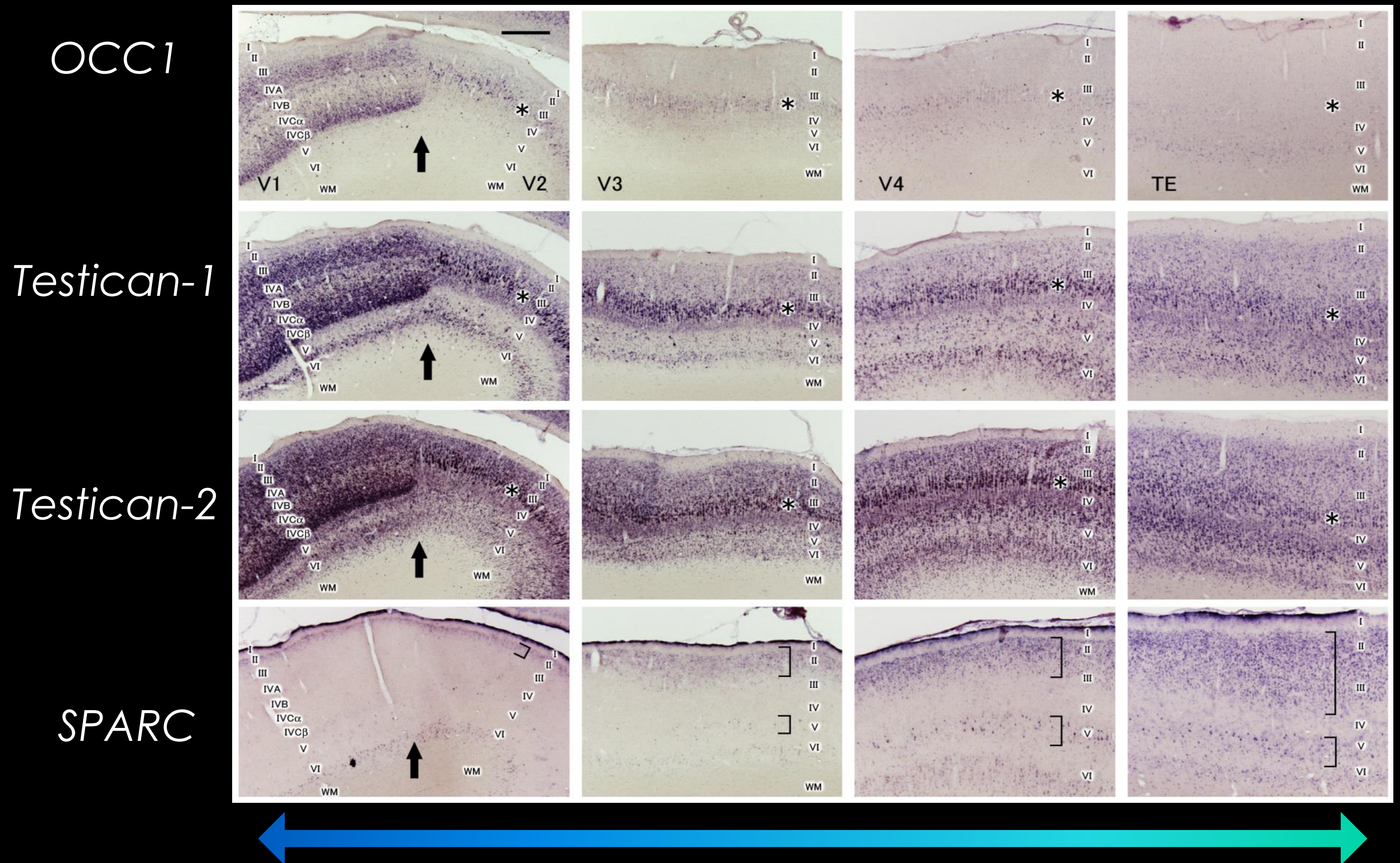
Takahata et al. (2006) *Cereb Cortex*

OCC1 and its related genes encode extracellular matrix proteins.



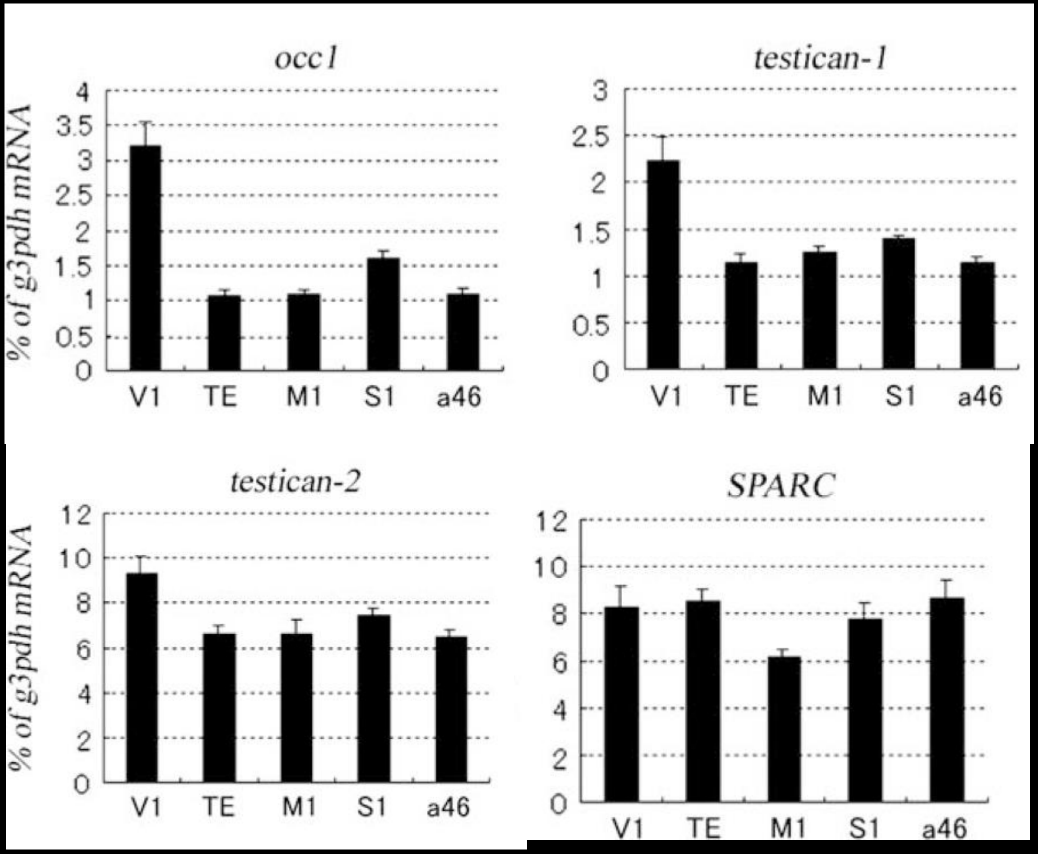
What are expression patterns of *OCC1*-related genes?

There is a gradient between V1 and TE in the mRNA expression of *OCC1* and several other related genes.



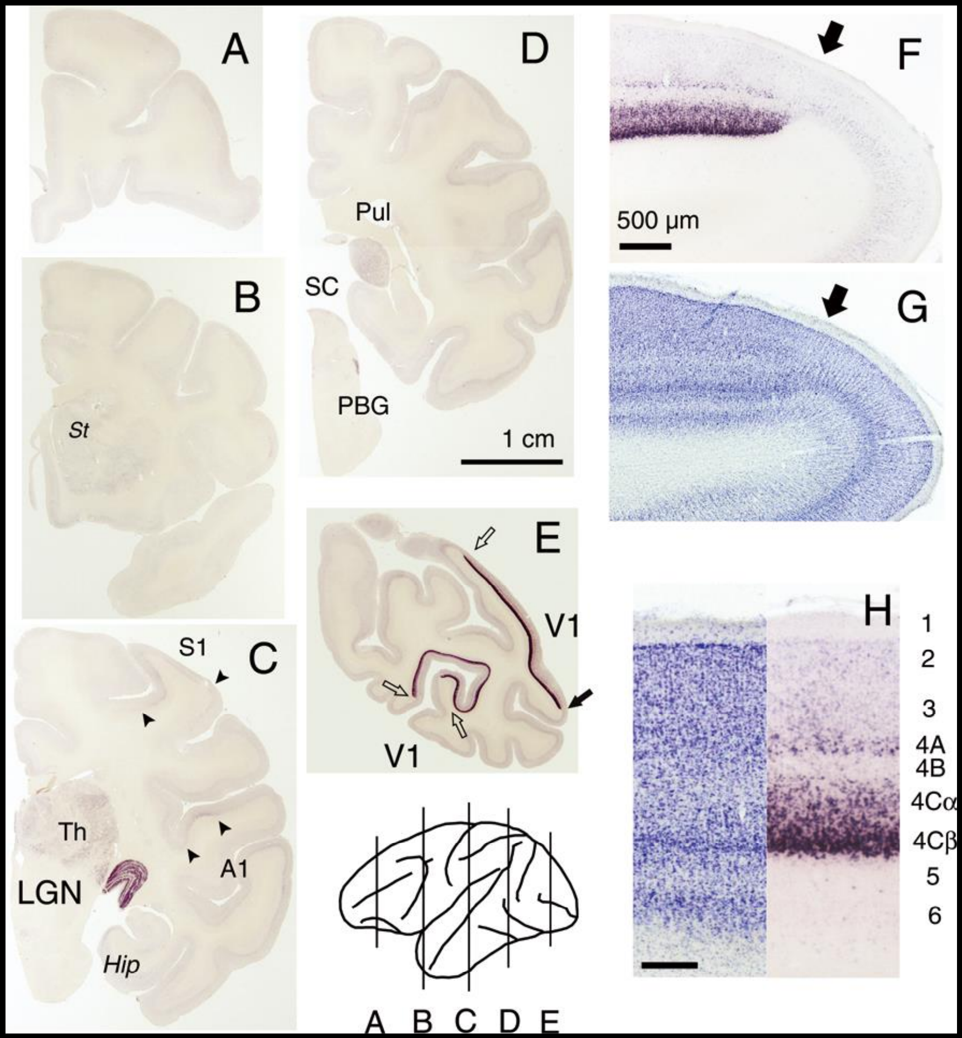
Takahata et.al. *Cereb Cortex* (2009)

Quantification of the mRNA expression of OCC1-related genes in 5 cortical areas (qRT-PCR)



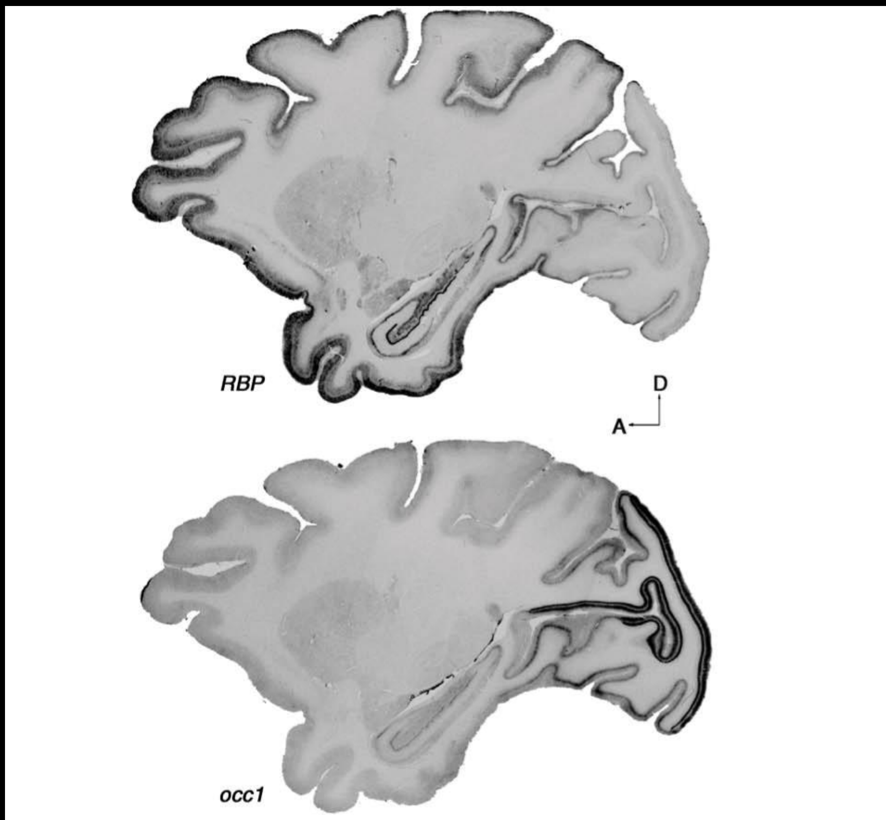
Takahata et.al. *Cereb Cortex* (2009)

5-HT1B (and 2A) receptors are also preferentially expressed in macaque V1

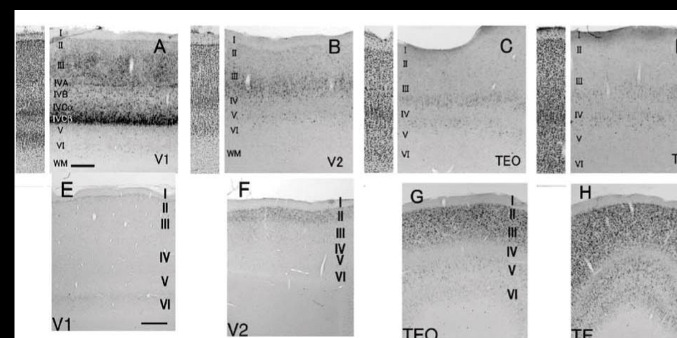


Watakabe. *et.al.*
Cereb Cortex
(2009)

RBP (*retinol binding-protein*) and some other genes are expressed in a complimentary pattern to *OCC1*.



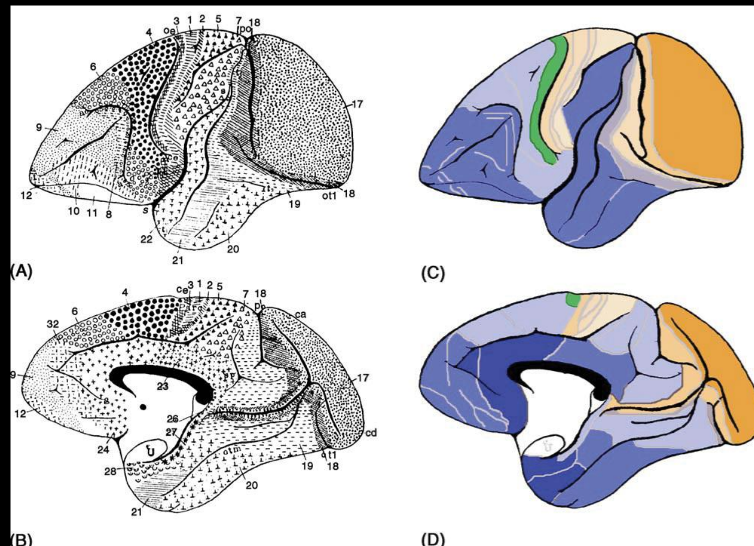
OCC1



RBP

Komatsu. *et.al.* (2005) *Cereb Cortex*
Yamamori and Rockland (2006) *Neurosci. Res.*

Heterogeneous gene expression in cerebral cortex of primates



Yamamori and Rockland (2006) *Neurosci. Res.*

Association areas ⟷ **V1**

TE | TEO | V4 | V3 | V2

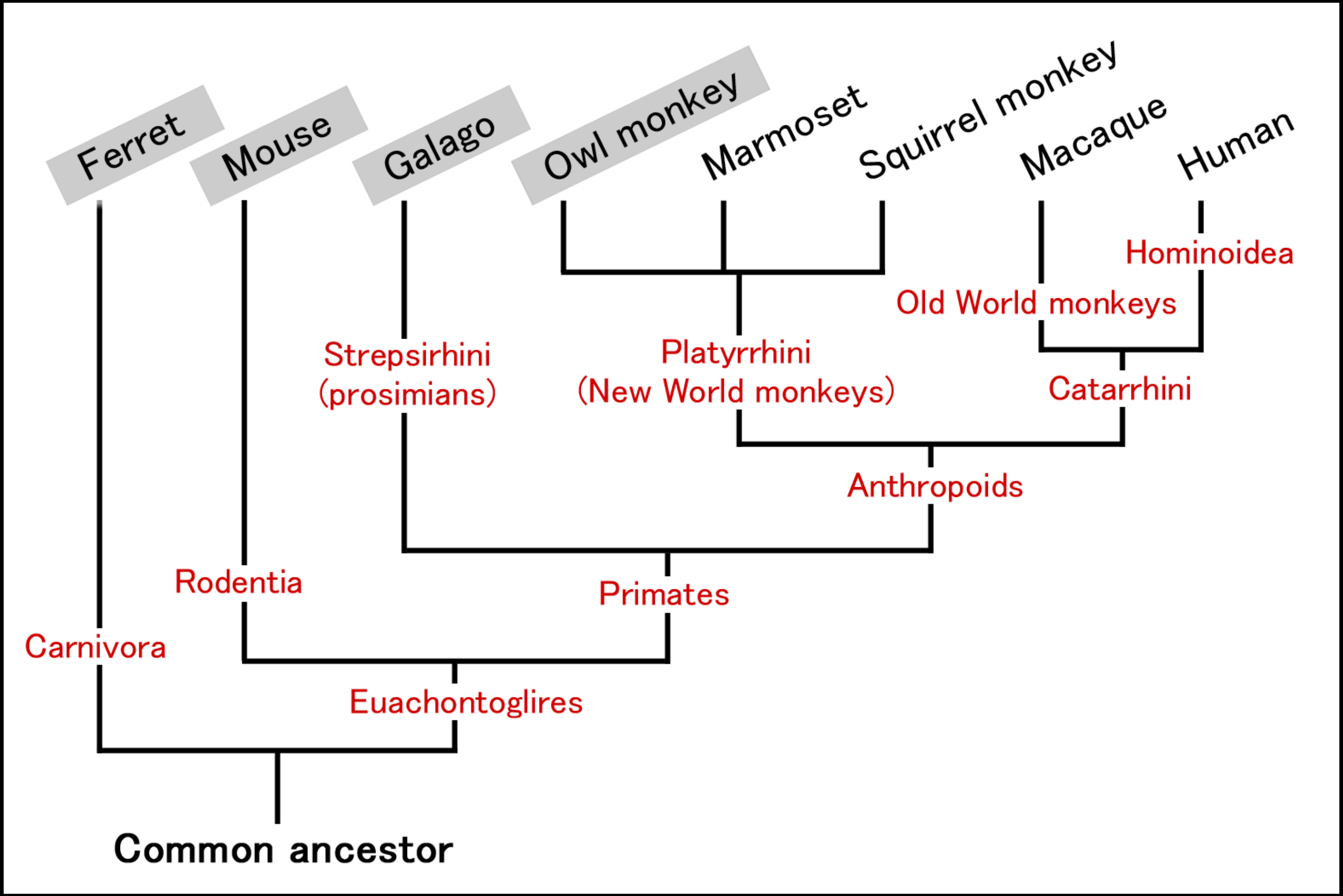
A2 | A1

S2 | S1

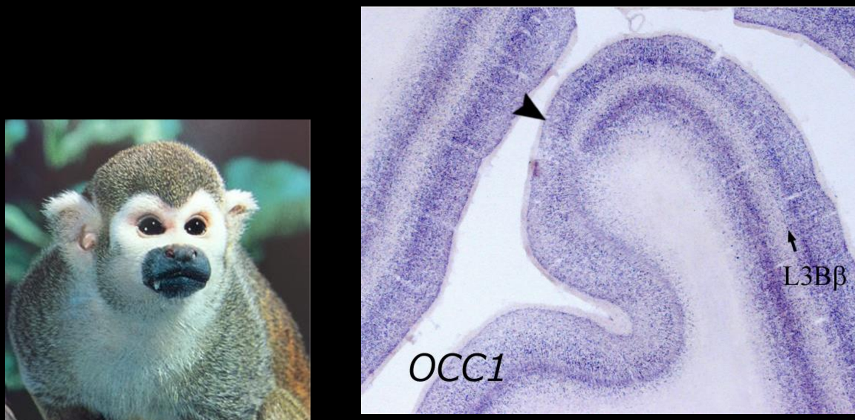
e.g. RBP, SPARC, PNMA1, SLIT1

e.g. OCC1, TES-1, TES-2, 5-HT1B, 5-HT2A

How much extent is V1-selective gene expression conserved?

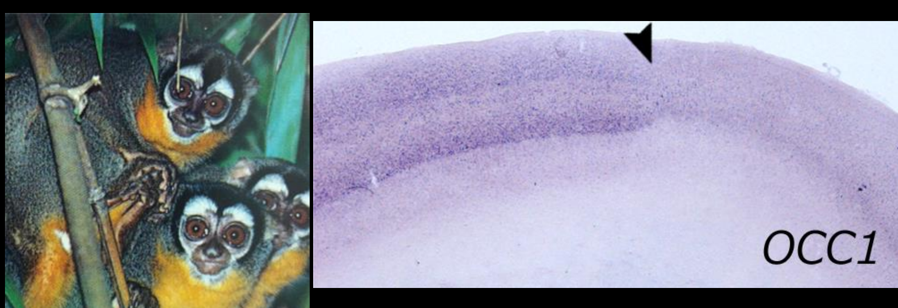


V1-selective gene expression is observed in New World and prosimian primates, but they are less conspicuous than macaques.

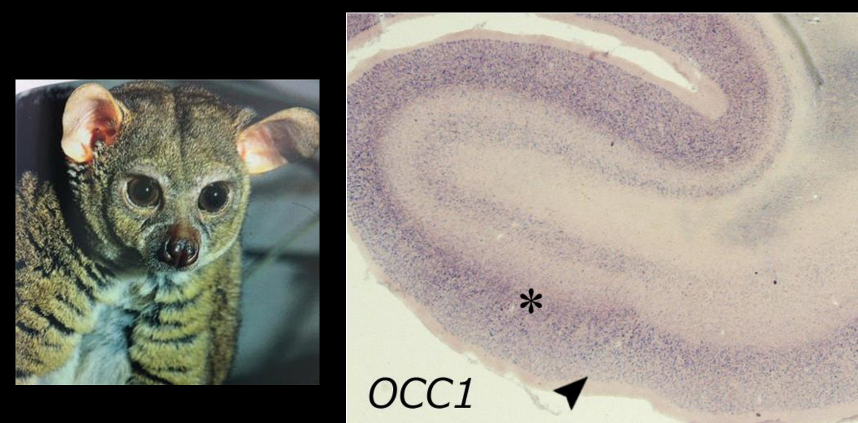


SQIRREL MONKEY

MARMOSET



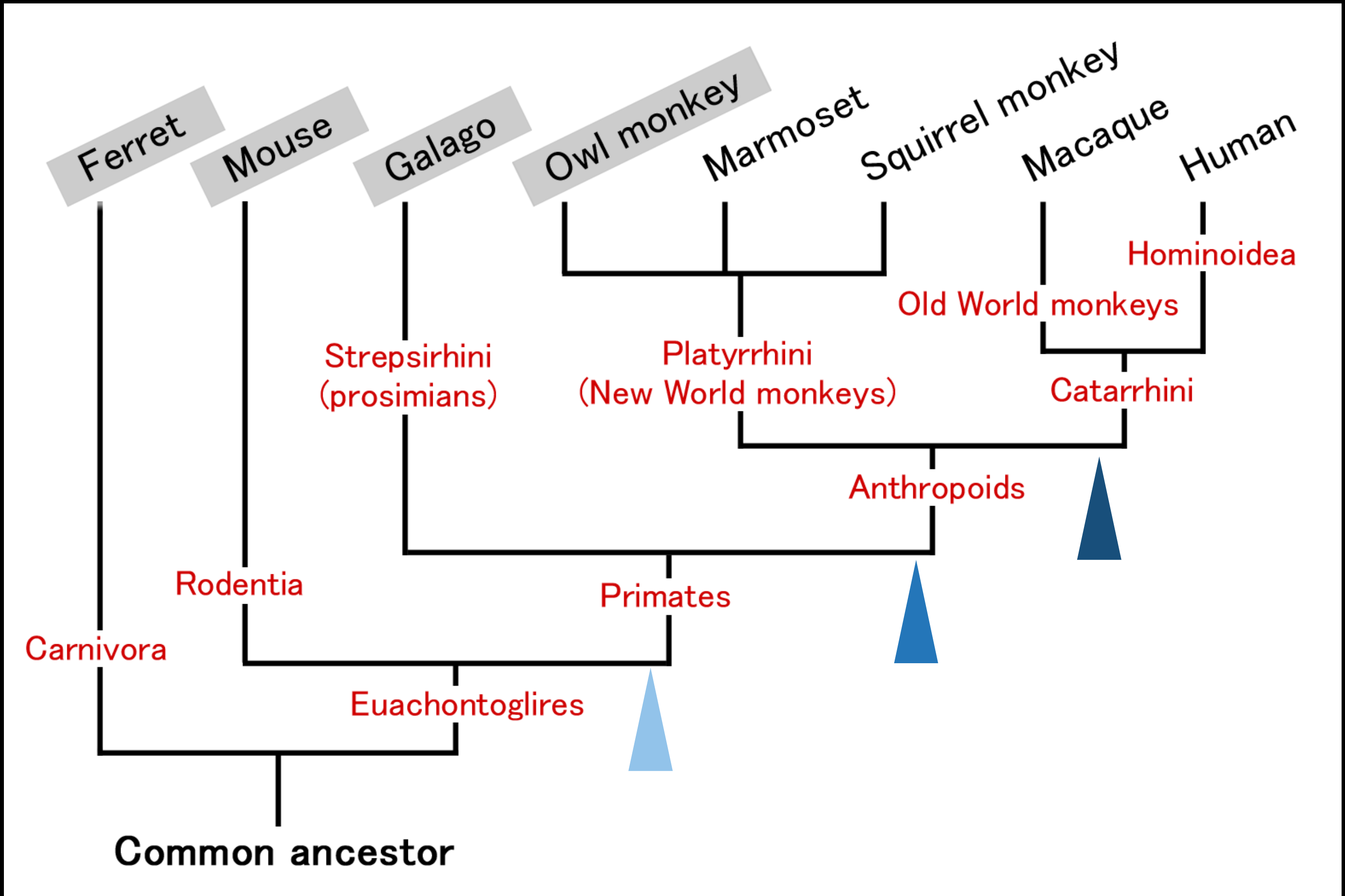
OWL MONKEY



GALAGO

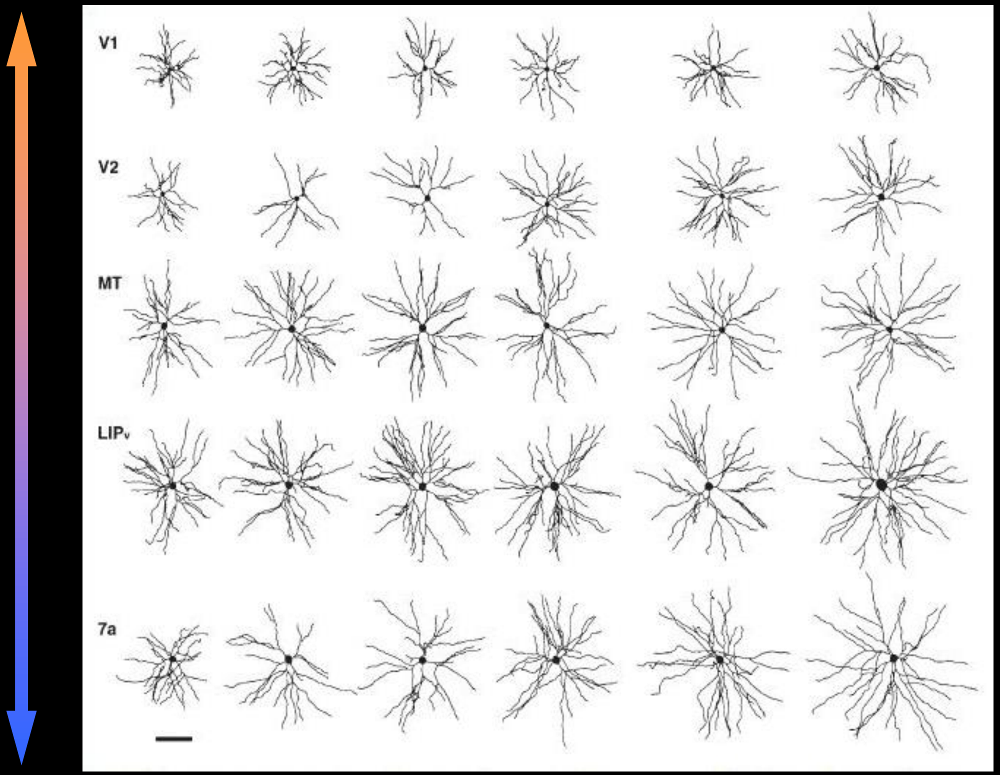
Takahata et.al. *Cereb Cortex* (2012)

V1-selective gene expression can only be observed in primates, and the closer relatives of humans shows more conspicuous pattern.



Takahata et.al. *Cereb Cortex* (2012)

There is a gradient in dendritic field size among cortical areas.



Elston (1997) *Cereb Cortex*

Possible importance of area-selective gene expression

Area difference of gene expression

↓

Area difference of dendrite extension

↓

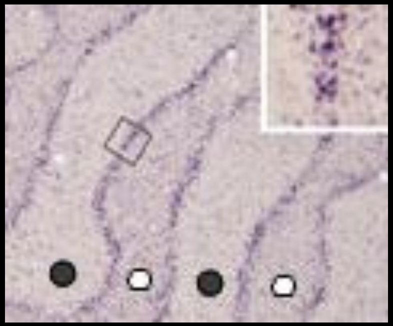
Area difference of receptive field

↓

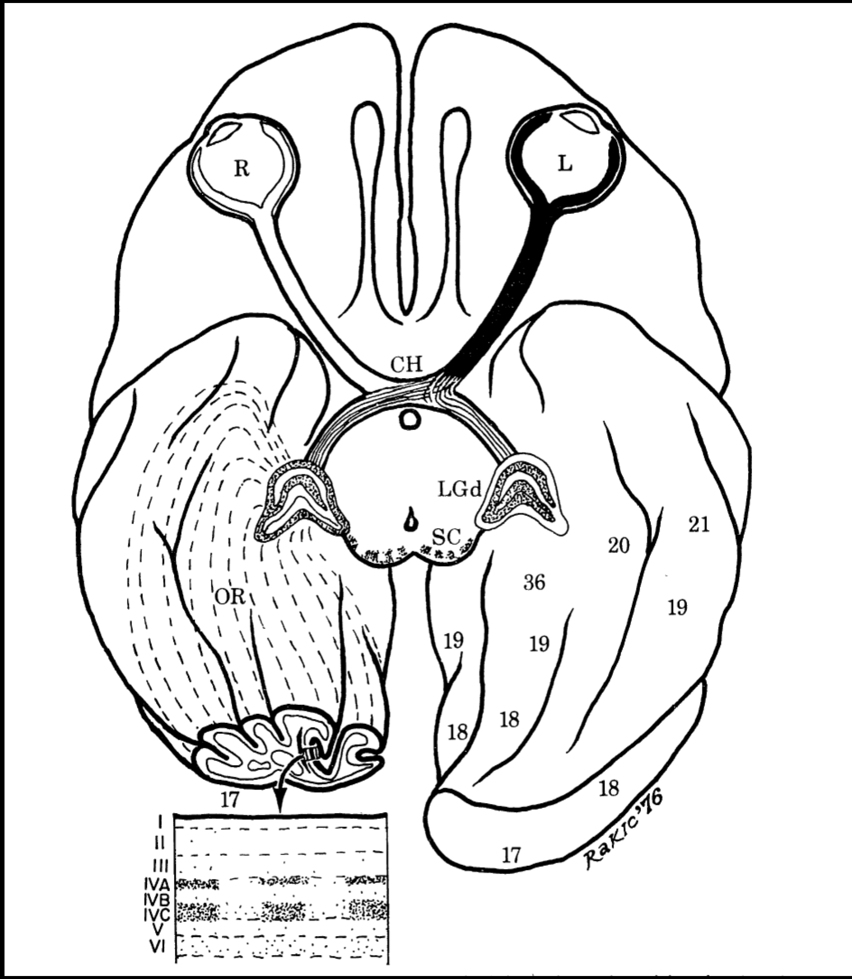
Hierarchy of primate visual cortices

Part 2.

Discovery of border strips in macaque V1 through immediate-early gene expression patterns.



Ocular dominance columns are most studied in macaques.



Rakic (1977) *Philos Trans R Soc Lond B Biol Sci*

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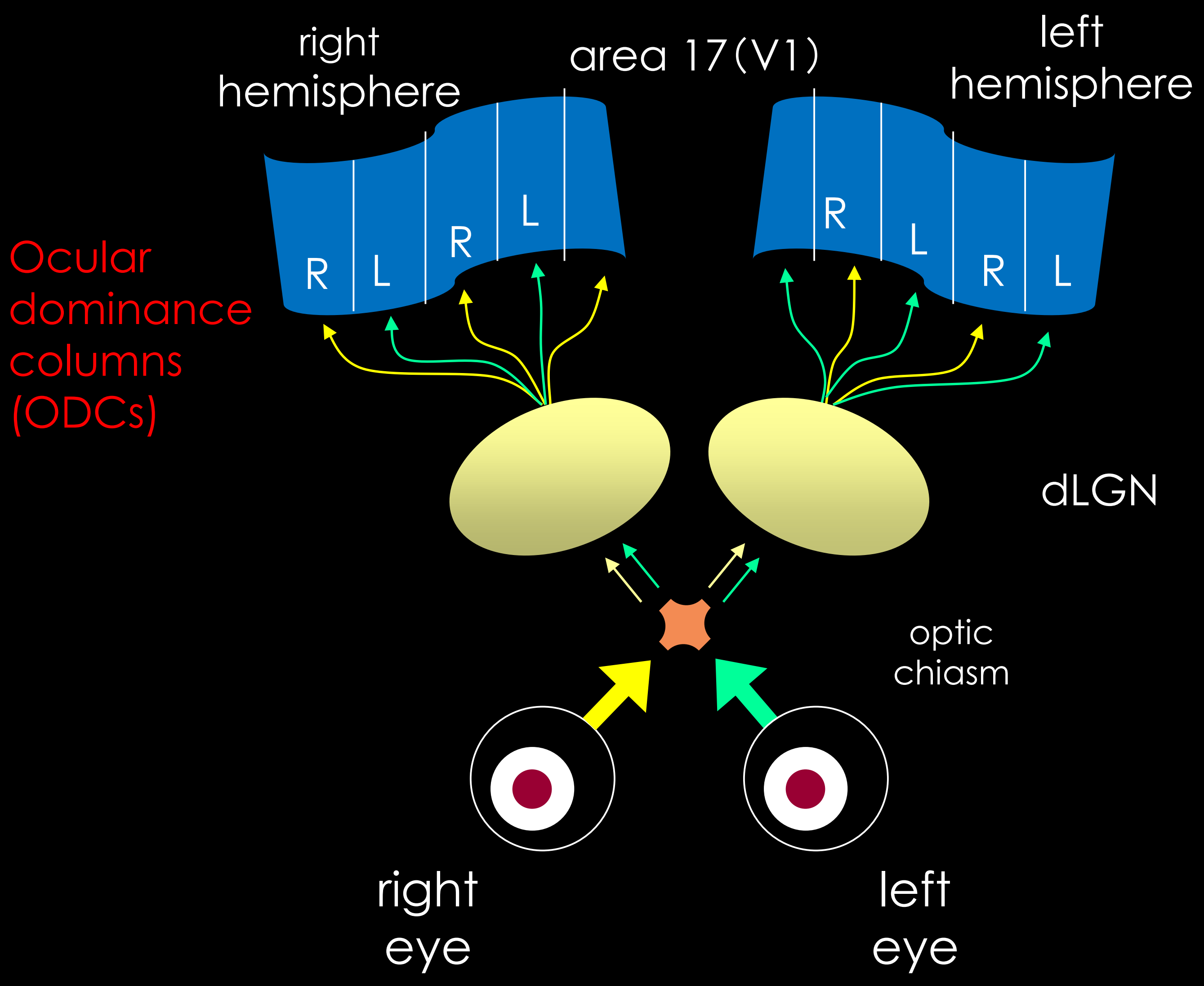

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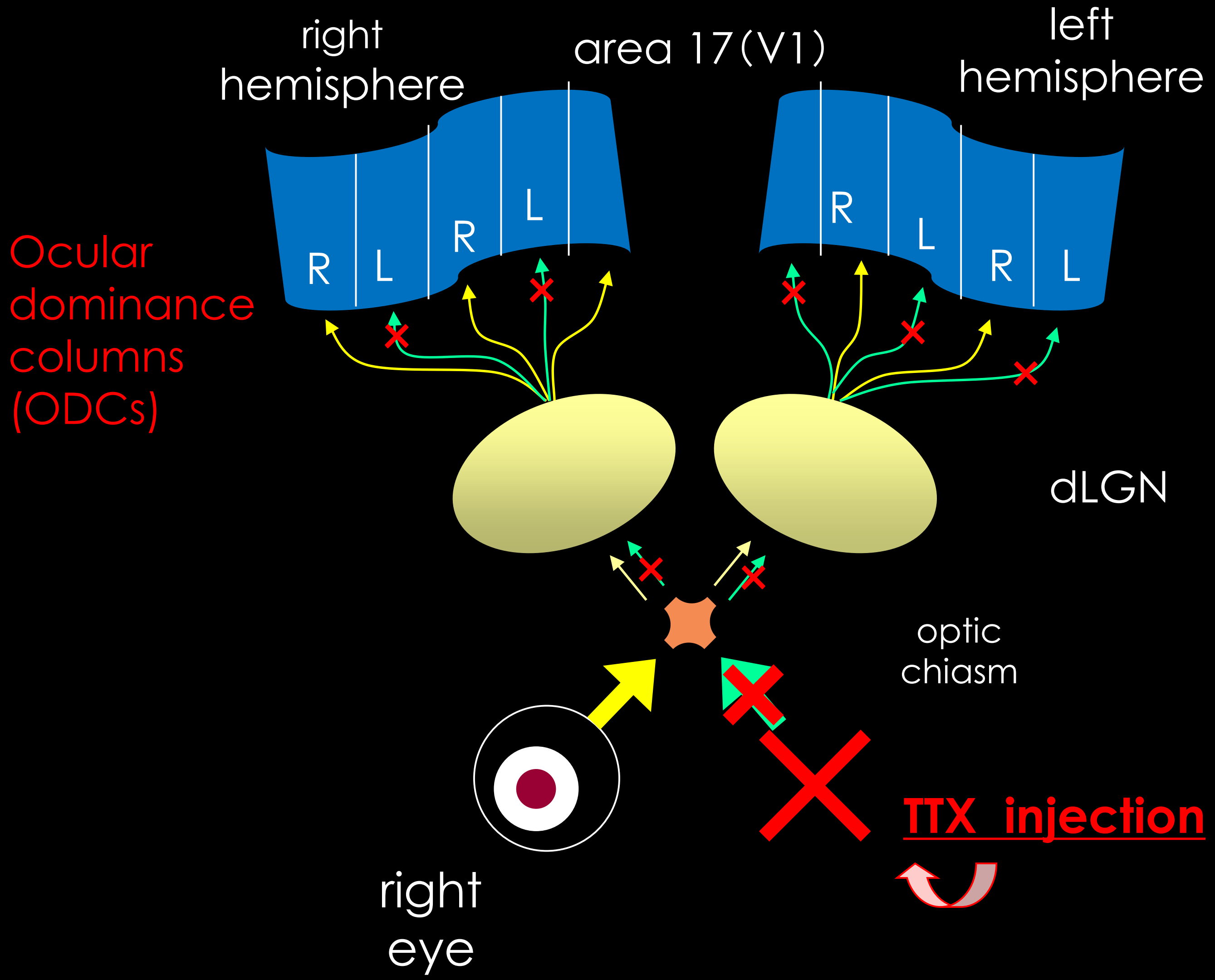

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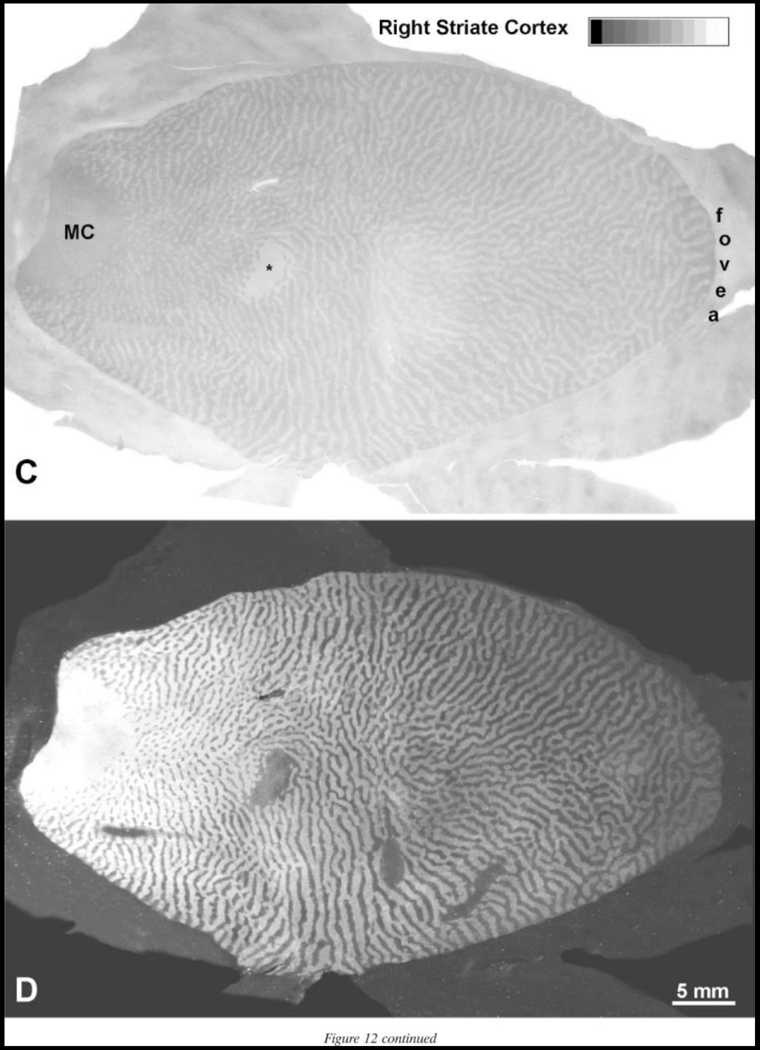
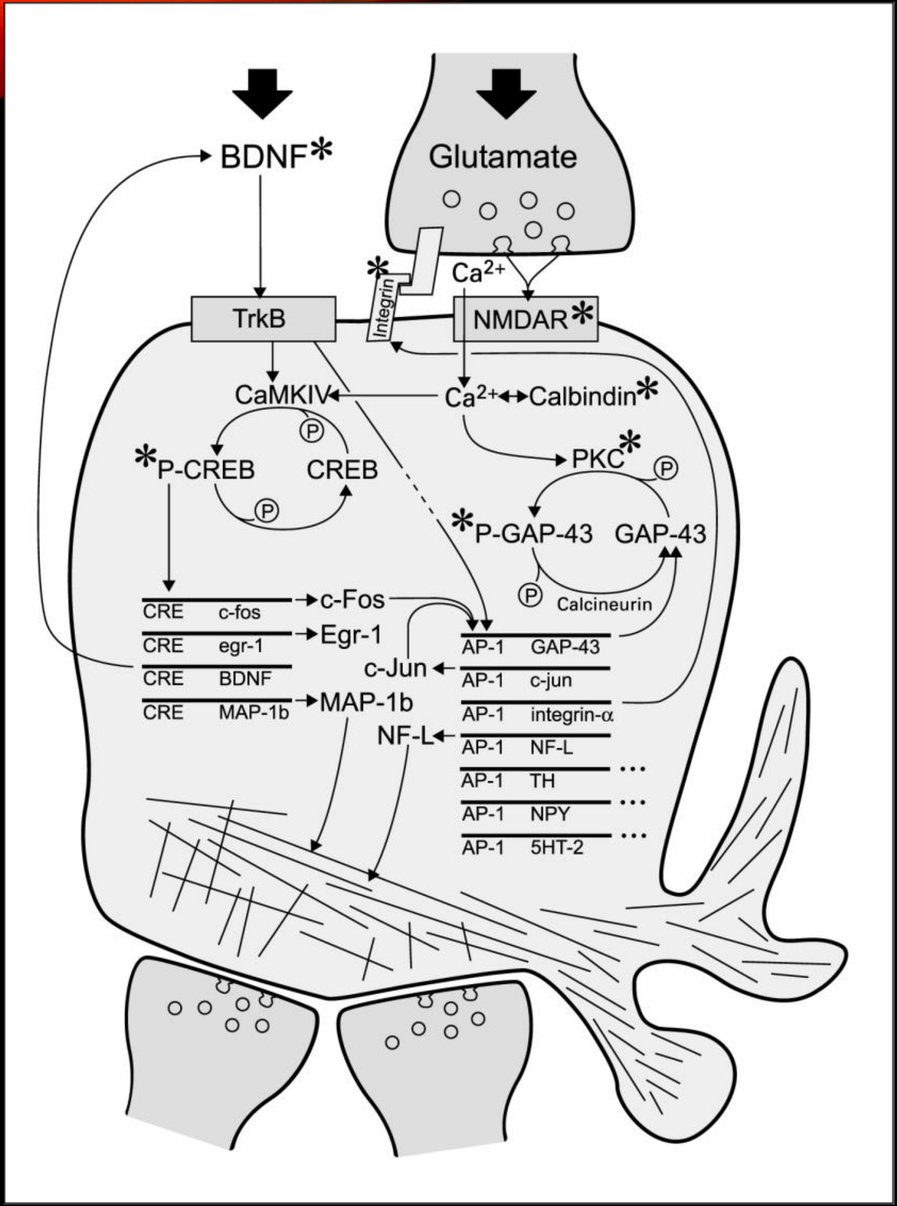


CO histochemistry

[^{3}H] Proline

Horton and Hocking (1998) *J Neurosci*

macaque V1

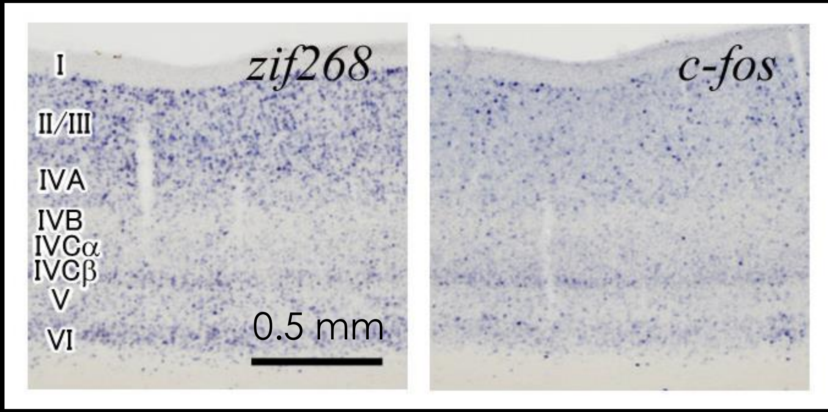


The expression of immediate-early genes are regulated by neuronal activity.

Illing, (2001) *Audiol Neurootol*

Ocular dominance columns can be studied by examining immediate-early gene expression.

Normal binocular vision (macaque)



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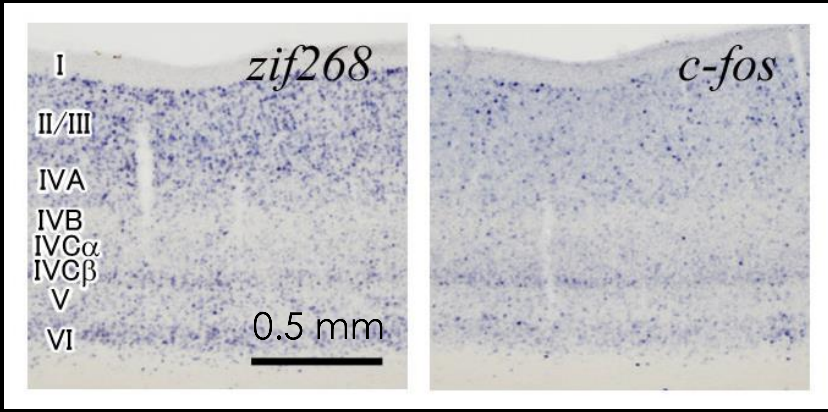
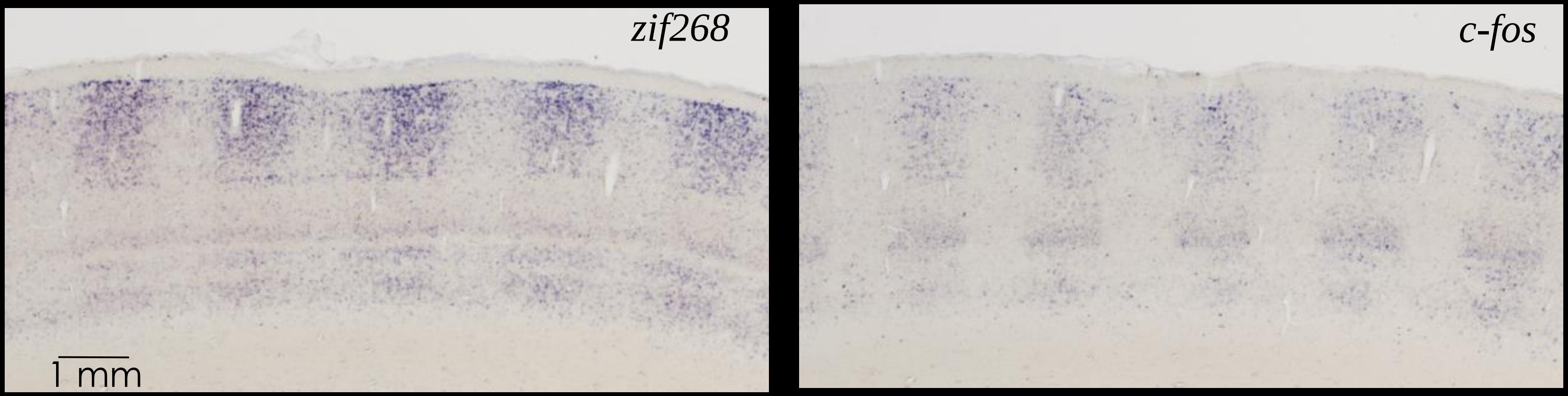
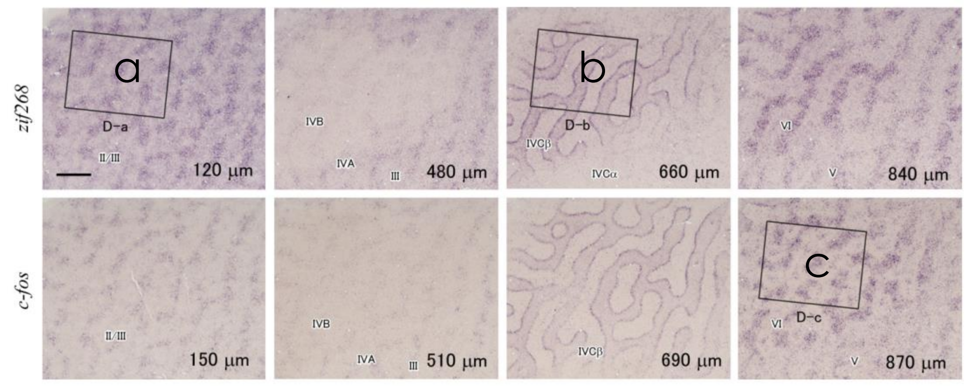


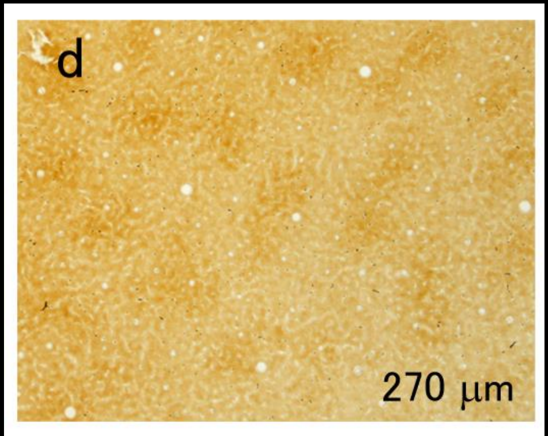
21 days TTX (macaque)

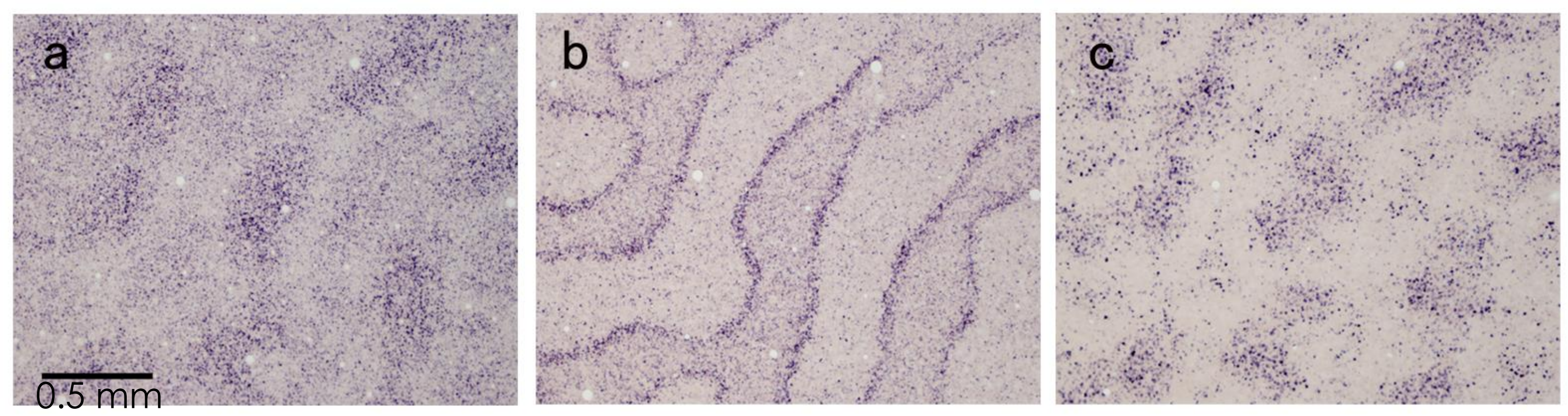


1h TTX
(macaque)



blob

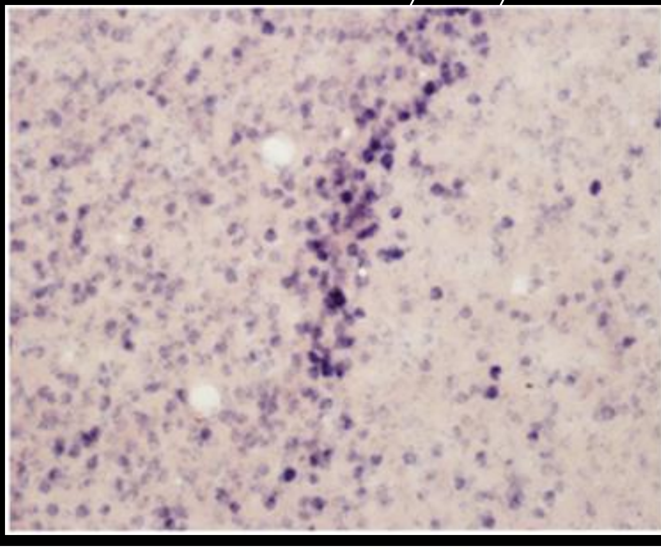




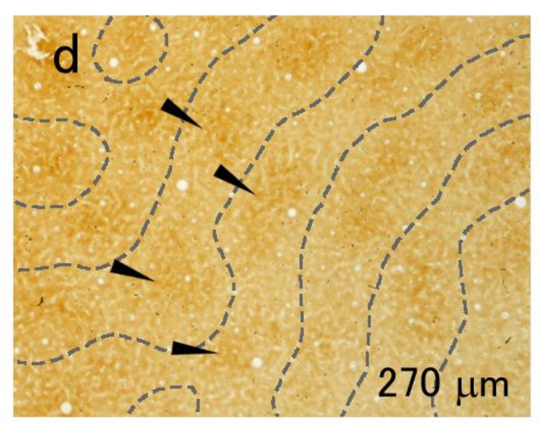
Takahata, et al., (2009) *Proc Natl Acad Sci USA*

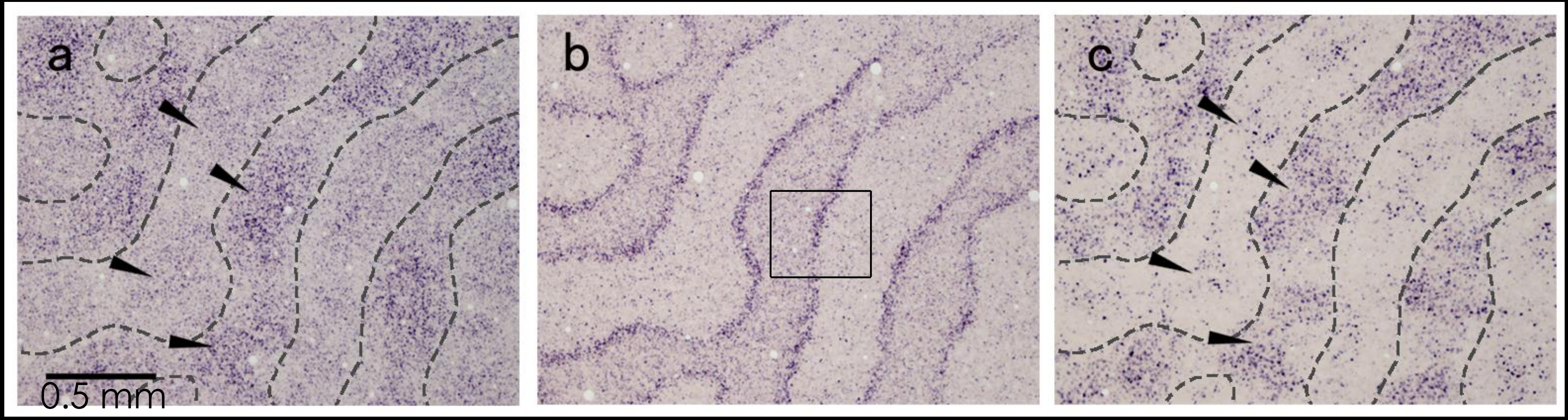
border strip

1h TTX (macaque)



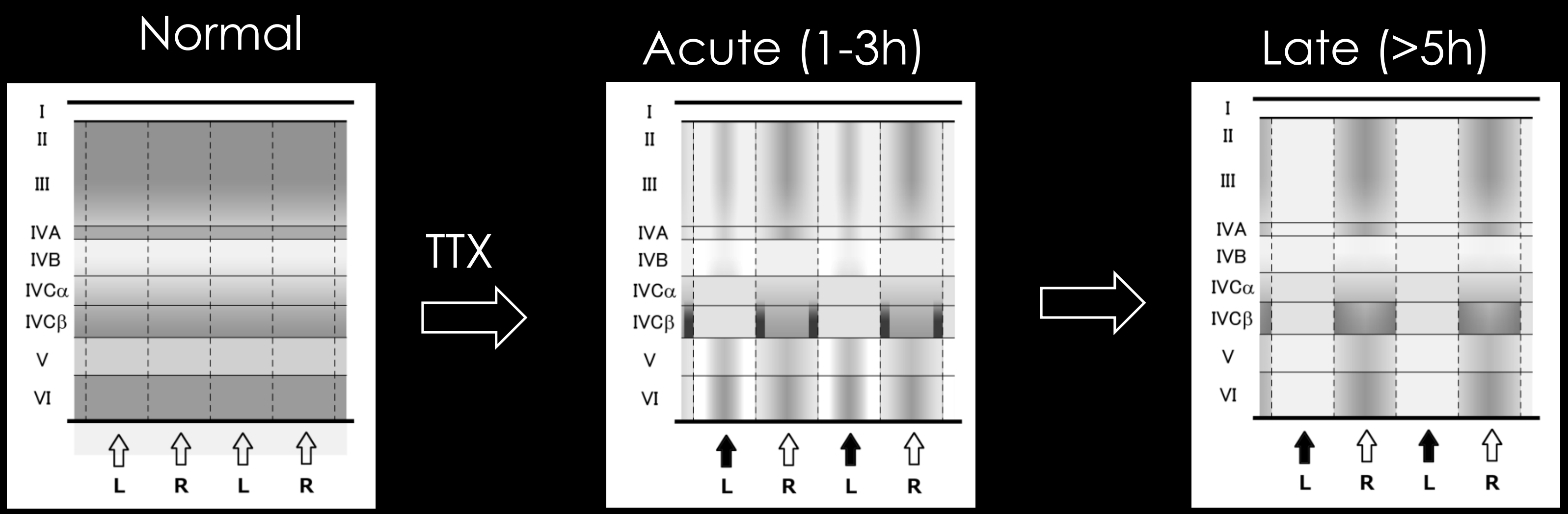
blob





Takahata, et al., (2009) *Proc Natl Acad Sci USA*

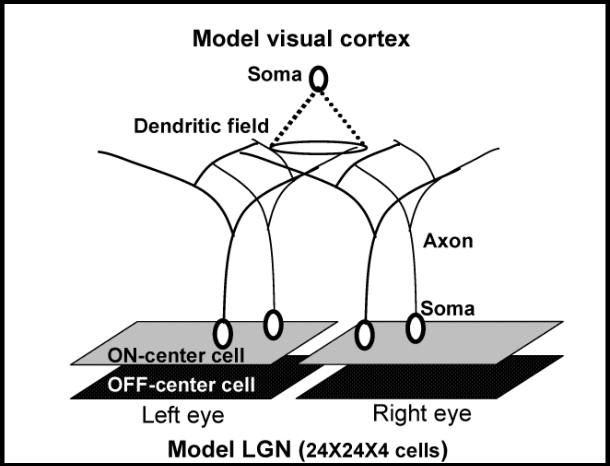
Schematic changes of gene expression changes after monocular inactivation.

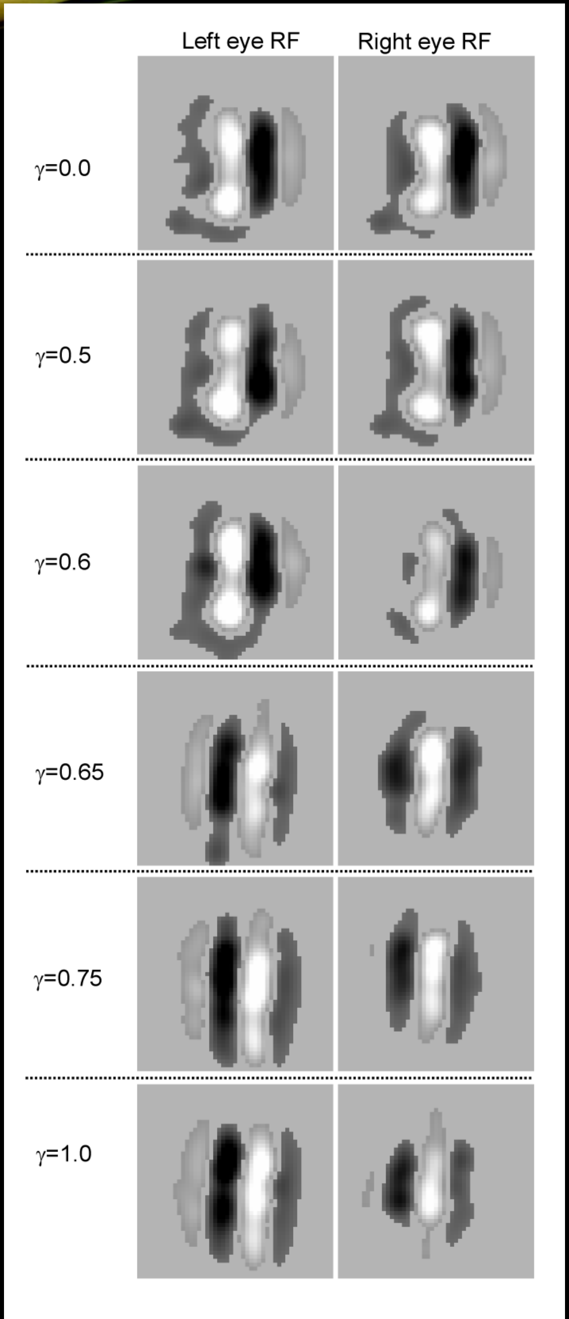


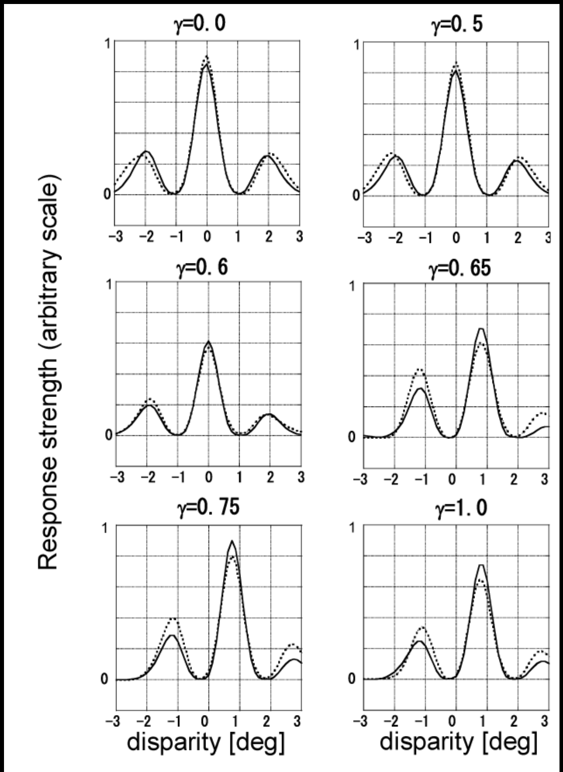
Takahata, et al., (2009) *Proc Natl Acad Sci USA*

What is functional importance of border strips?

Lateral inhibition between the two eyes is required to form “binocular-disparity coding neurons.”

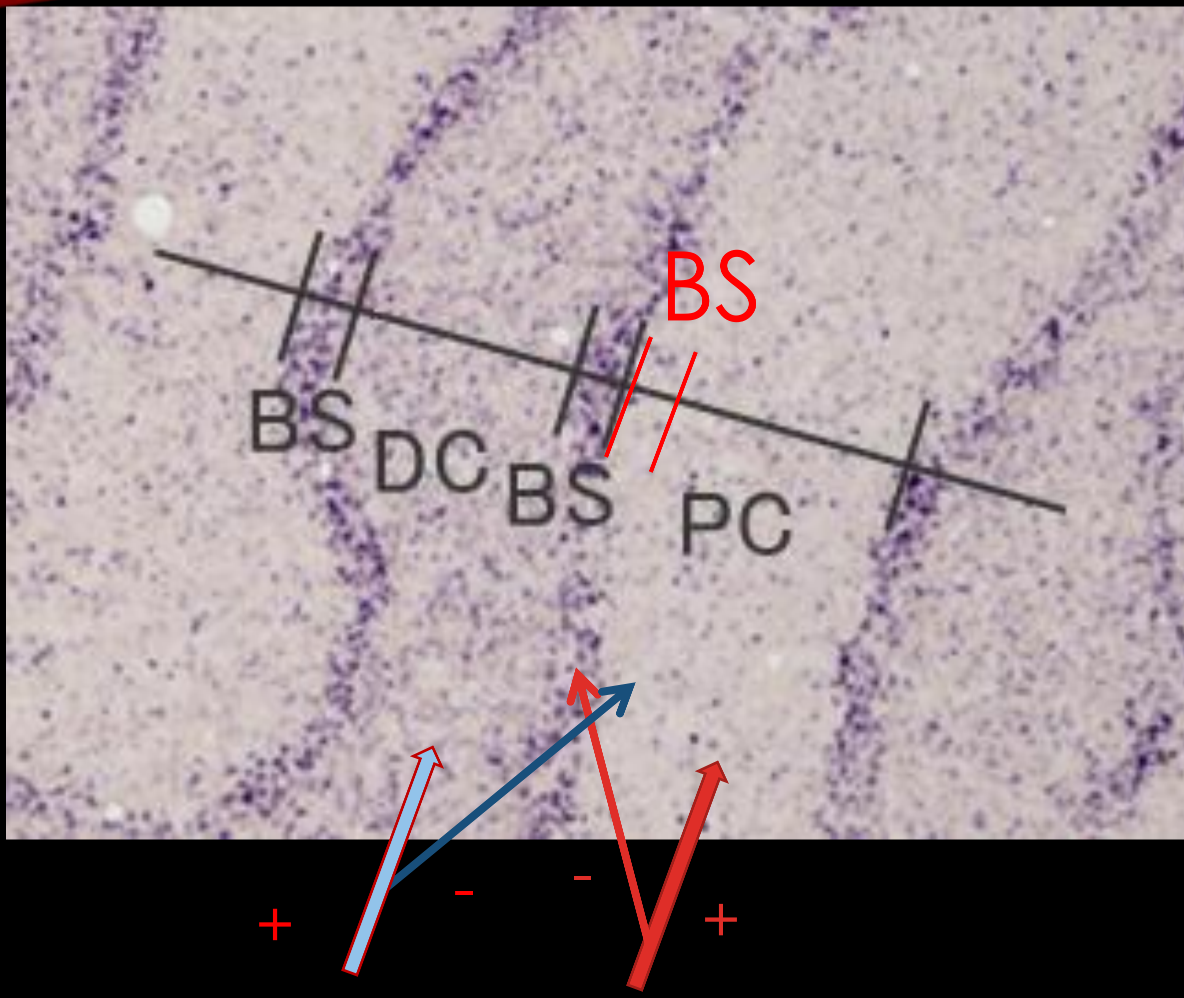






Kikuchi, et al. (2009) *Info Engin*

macaque, 1h TTX, layer IV, *zif268*



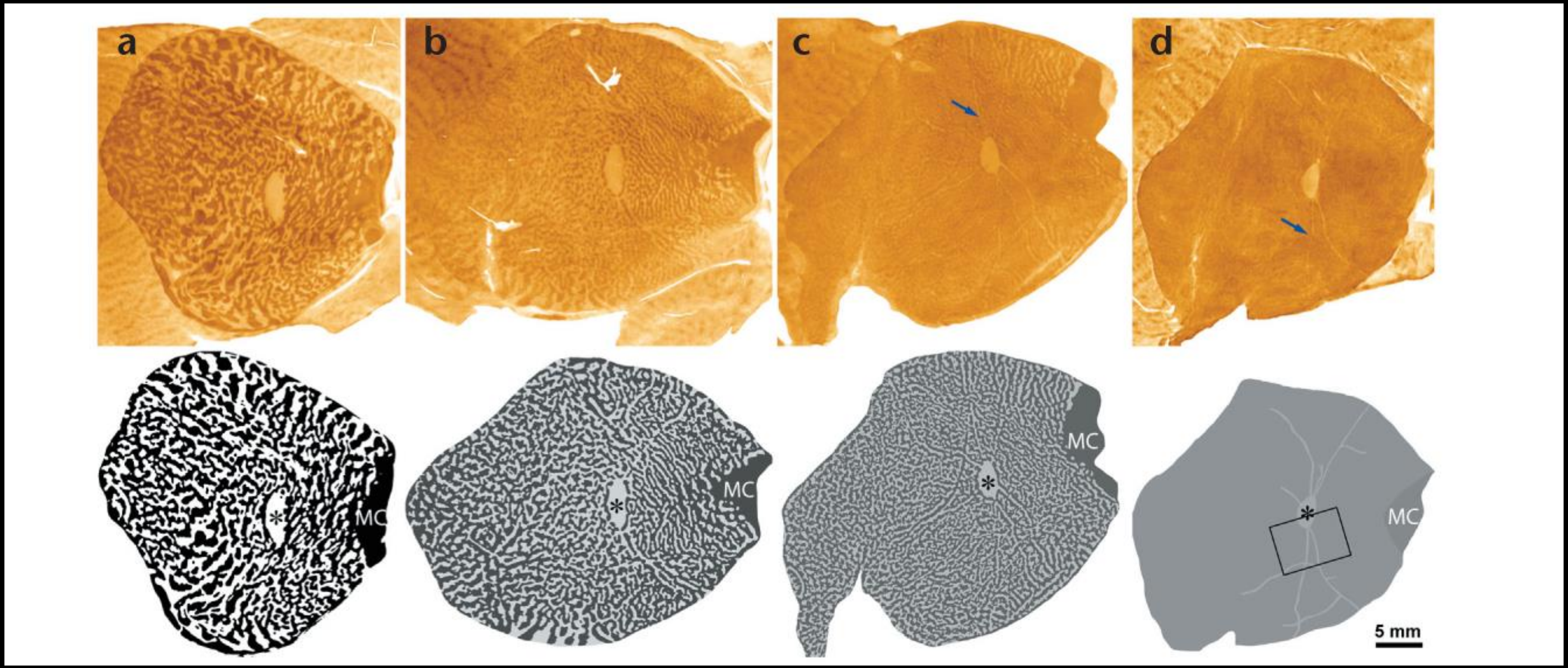
DC: dark column
PC: pale column
BS: border strip

This circuit may contribute to induce binocular-disparity coding neurons?

Part 3.

Cross species comparison of ocular dominance columns.

Ocular dominance columns in New World monkeys.

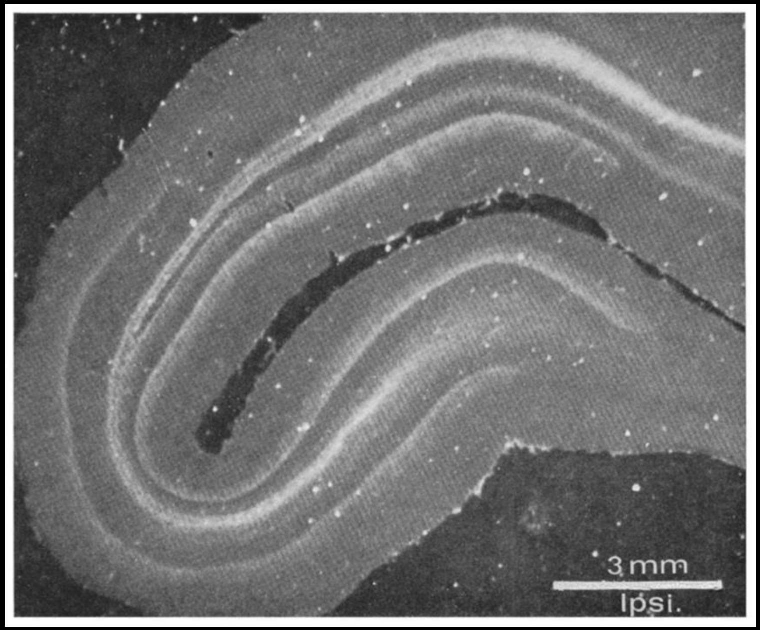


Squirrel monkey

Adams and Horton (2003) *Nat Neurosci*

Ocular dominance columns in New World monkeys.

Owl monkey



Kaas and Casagrande, (1976) *Brain Res*

Ocular dominance columns in New World monkeys.

marmoset

Brain Research, 488 (1989) 376–380
Elsevier

BRE 23526

Loss of ocular dominance columns with maturity in the monkey, *Callithrix jacchus*

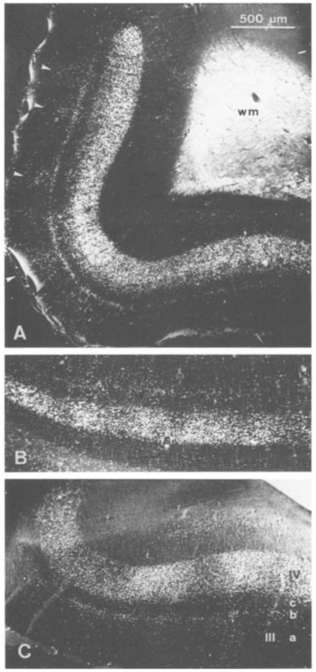
W.B. Spatz

Department of Oto-Rhino-Laryngology, Morphological Brain Research, Freiburg (F.R.G.)

(Accepted 14 February 1989)

Key words: Marmoset monkey; Primary visual cortex; Ocular dominance column; Postnatal ontogenesis

Previous studies have shown that adult marmosets lack ocular dominance columns (ODC) in area 17, but that ODCs can be demonstrated upon visual deprivation. The present results, obtained by transneuronal transport of WGA-HRP, indicate that ODCs normally develop in juvenile marmosets but disappear before the animal reaches maturity. The findings suggest that formation of ODCs during ontogenesis, and their persistence through adulthood, are different developmental processes depending on different mechanisms.

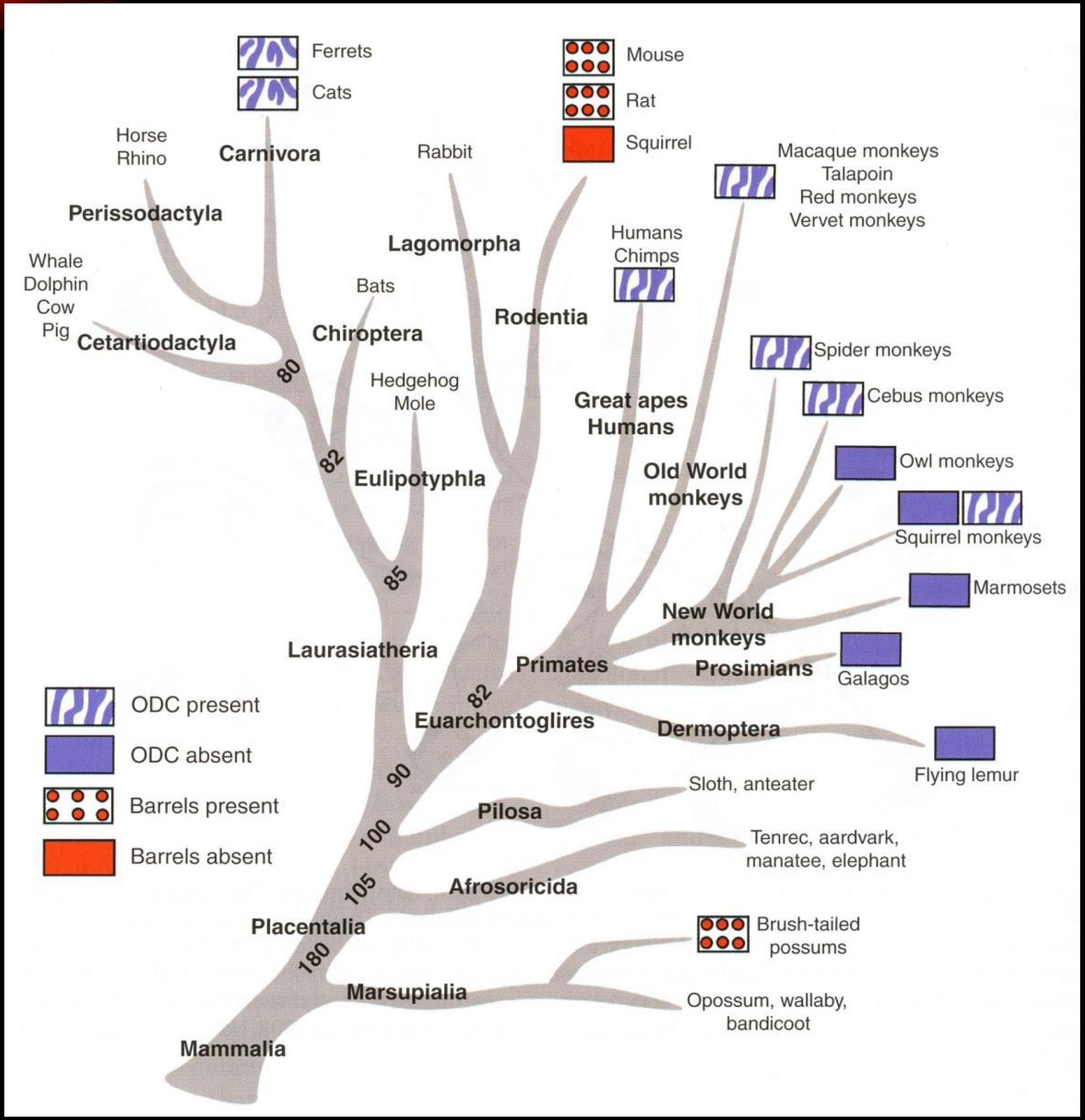


11 mo

9 mo

3 mo

Spatz, (1989) *Brain Res*


Ferrets
Cats
Mouse
Rat
Squirrel
Horse
Rhino
Carnivora
Rabbit
Macaque monkeys
Talapoin
Red monkeys
Vervet monkeys
Perissodactyla
Lagomorpha
Humans
Chimps
Whale
Dolphin
Cow
Pig
Bats
Rodentia
Cetartiodactyla
Chiroptera
Spider monkeys
80
Hedgehog
Mole
Great apes
Humans
Cebus monkeys
82
Eulipotyphla
Old World
monkeys
Owl monkeys
Squirrel monkeys
85
Marmosets
New World
monkeys
Laurasiatheria
Primates
Prosimians
Galagos
82
ODC present
Euarchontoglires
Dermoptera
ODC absent
90
Flying lemur
Sloth, anteater
Barrels present
100
Pilosa
Barrels absent
Tenrec, aardvark,
manatee, elephant
105
Afrosoricida
Placentalia
Brush-tailed
possums
180
Marsupialia
Opossum, wallaby,
bandicoot
Mammalia

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Phil. Trans. R. Soc. B (2005) **360**, 837–862
doi:10.1098/rstb.2005.1623
Published online 29 April 2005

The cortical column: a structure without a function

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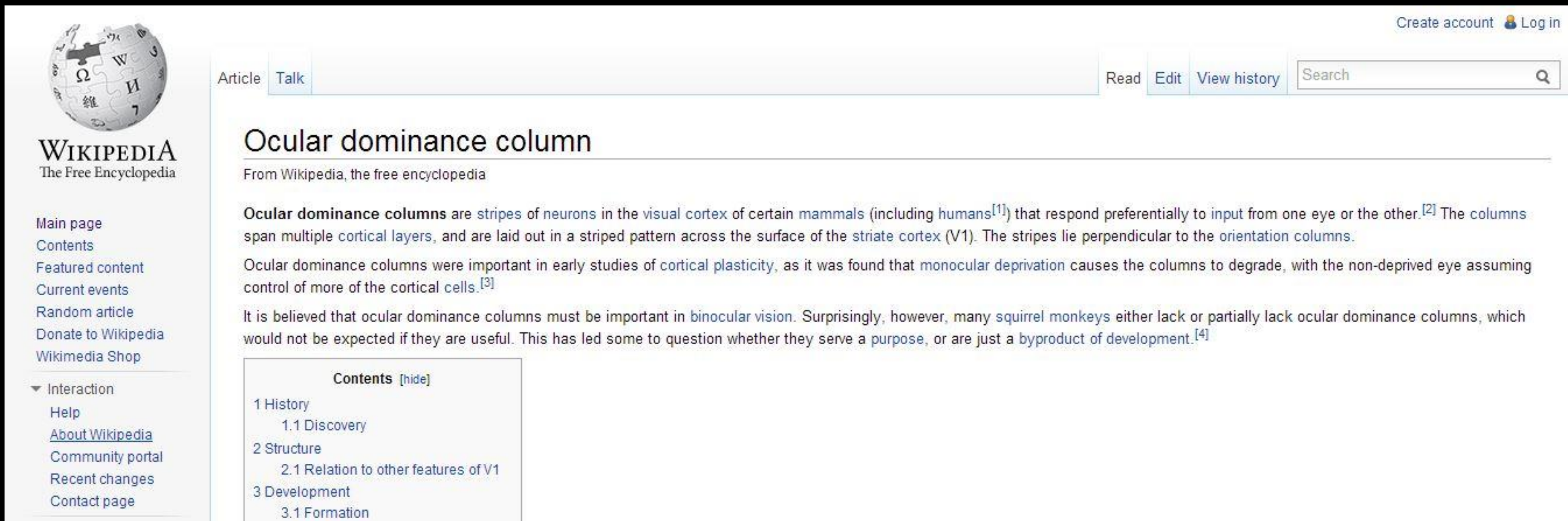
This year, the field of neuroscience celebrates the 50th anniversary of Mountcastle's discovery of the cortical column. In this review, we summarize half a century of research and come to the disappointing realization that the column may have no function. Originally, it was described as a discrete structure, spanning the layers of the somatosensory cortex, which contains cells responsive to only a single modality, such as deep joint receptors or cutaneous receptors. Subsequently, examples of columns have been uncovered in numerous cortical areas, expanding the original concept to embrace a variety of different structures and principles. A 'column' now refers to cells in any vertical cluster that share the same tuning for any given receptive field attribute. In striate cortex, for example, cells with the same eye preference are grouped into ocular dominance columns. Unaccountably, ocular dominance columns are present in some species, but not others. In principle, it should be possible to determine their function by searching for species differences in visual performance that correlate with their presence or absence. Unfortunately, this approach has been to no avail; no visual faculty has emerged that appears to require ocular dominance columns. Moreover, recent evidence has shown that the expression of ocular dominance columns can be highly variable among members of the same species, or even in different portions of the visual cortex in the same individual. These observations deal a fatal blow to the idea that ocular dominance columns serve a purpose. More broadly, the term 'column' also denotes the periodic termination of anatomical projections within or between cortical areas. In many instances, periodic projections have a consistent relationship with some architectural feature, such as the cytochrome oxidase patches in V1 or the stripes in V2. These tissue compartments appear to divide cells with different receptive field properties into distinct processing streams. However, it is unclear what advantage, if any, is conveyed by this form of columnar segregation. Although the column is an attractive concept, it has failed as a unifying principle for understanding cortical function. Unravelling the organization of the cerebral cortex will require a painstaking description of the circuits, projections and response properties peculiar to cells in each of its various areas.

Keywords: spandrel; barrel; angioscotoma; retinal wave; pinwheel; macaque

Horton and Adams (2005) *Phil Trans R Soc B*



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Ocular dominance column

From Wikipedia, the free encyclopedia

Ocular dominance columns are stripes of neurons in the visual cortex of certain mammals (including humans[1]) that respond preferentially to input from one eye or the other.[2] The columns span multiple cortical layers, and are laid out in a striped pattern across the surface of the striate cortex (V1). The stripes lie perpendicular to the orientation columns.

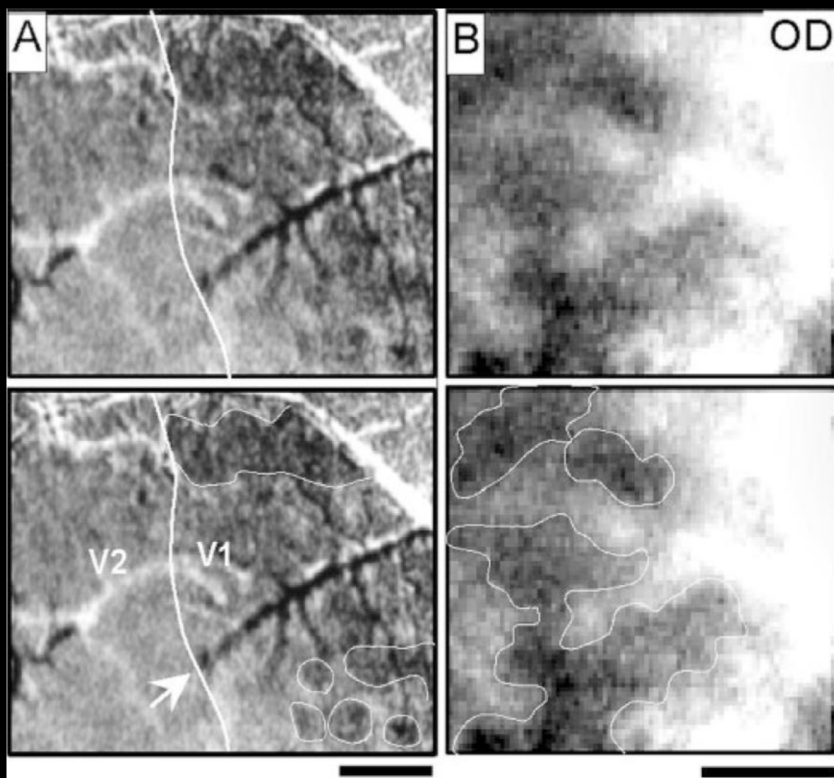
Ocular dominance columns were important in early studies of cortical plasticity, as it was found that monocular deprivation causes the columns to degrade, with the non-deprived eye assuming control of more of the cortical cells.[3]

It is believed that ocular dominance columns must be important in binocular vision. Surprisingly, however, many squirrel monkeys either lack or partially lack ocular dominance columns, which would not be expected if they are useful. This has led some to question whether they serve a purpose, or are just a byproduct of development.[4]

Contents [hide]

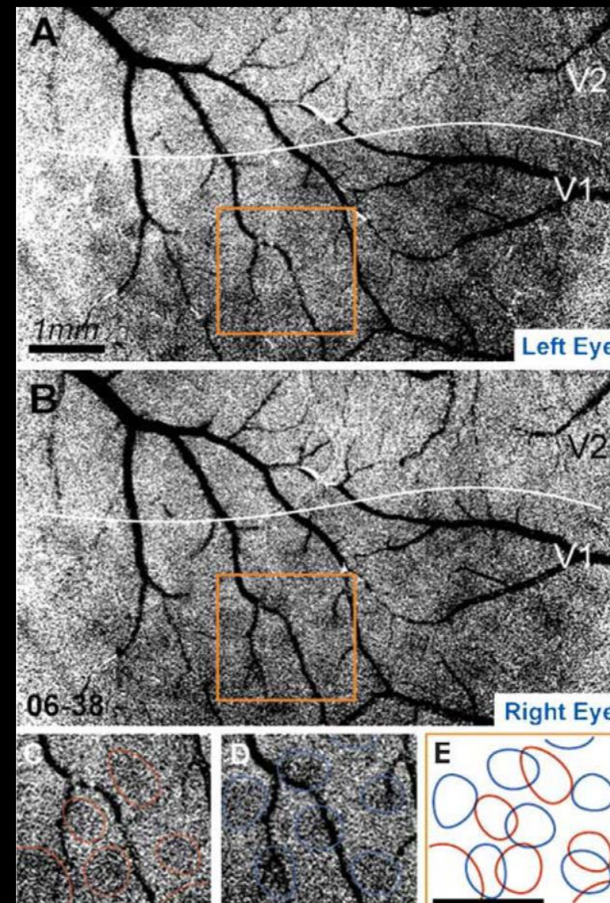
"Surprisingly, however, many squirrel monkeys, either lack or partially lack ocular dominance columns, which would not be expected if they are useful. This has led some to question whether they serve a purpose, or are just a byproduct of development."

However, recent studies imply that New World monkeys possess ocular dominance columns as well.



Marmoset

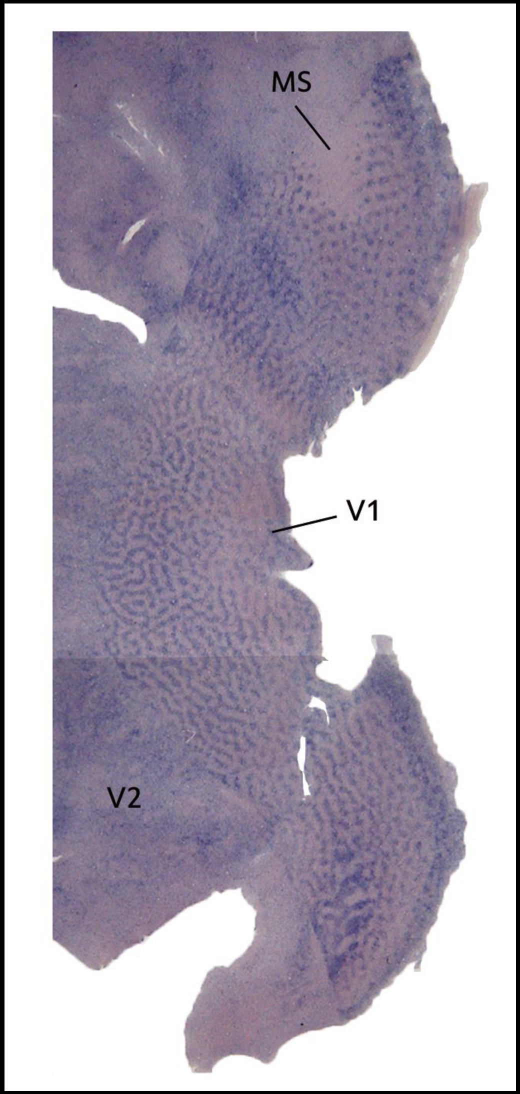
Roe, et al. (2005) *Anat Rec A*



Owl monkey

Kaskan et al. (2007) *Front Neurosci*

Expression of immediate-early gene clearly represent ocular dominance columns in owl monkeys!

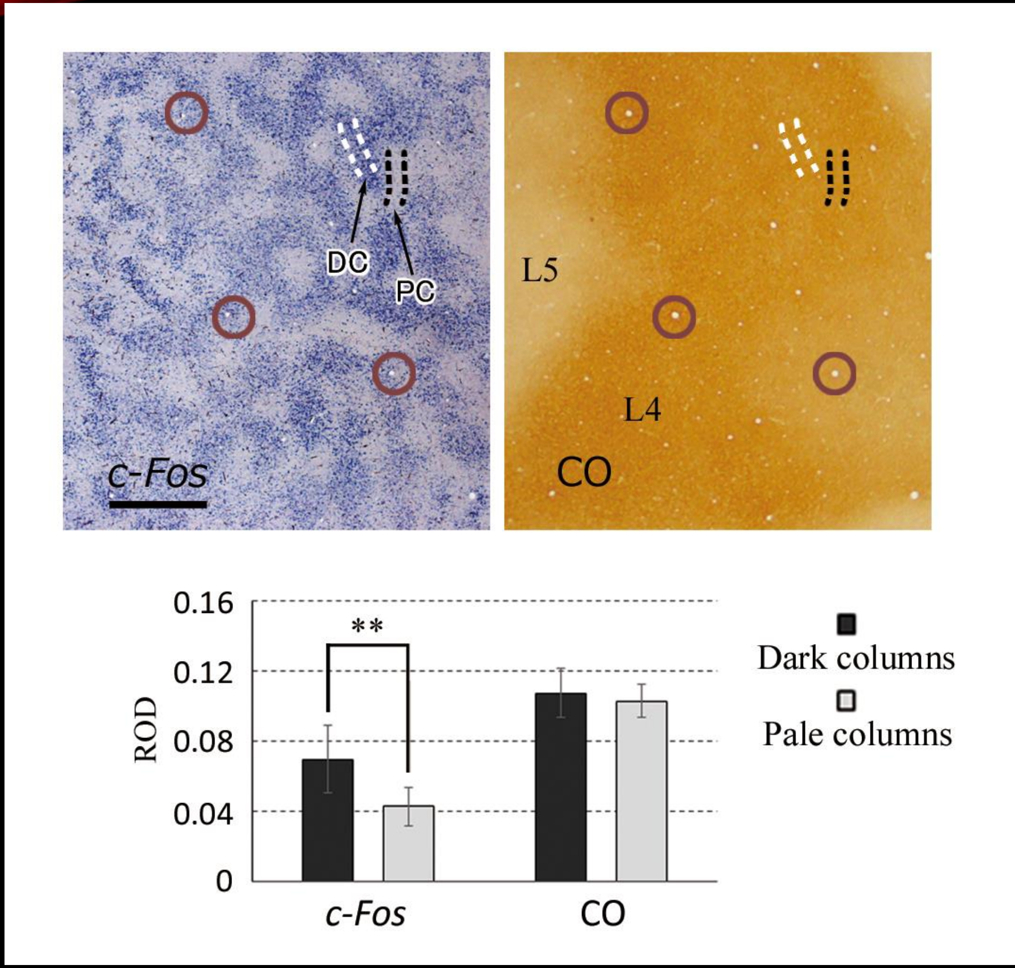


Layer 2/3

Layer 4

Owl monkey, V1, 24 h-monocular inactivation, ISH for c-FOS

Takahata, et al., (2014) *Proc Natl Acad Sci USA*

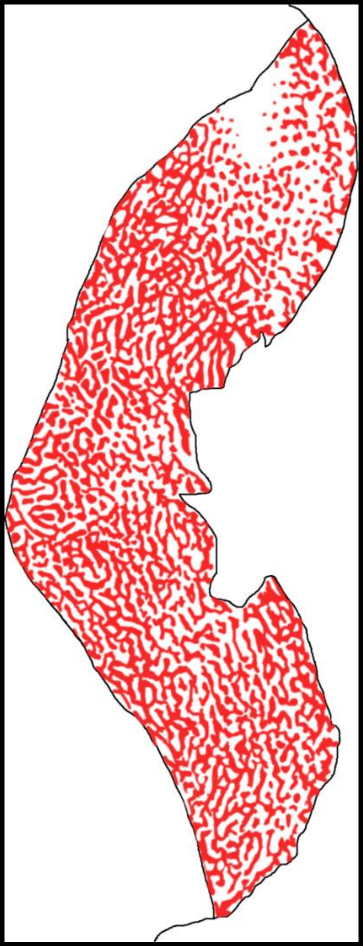


Takahata, et al. (2014)
Proc Natl Acad Sci USA

Obviously, CO staining is not good enough to conclude absence of ODCs.

Patchy or stripe-like representation of ODCs can be explained by computer simulation.

Owl monkey



Macaque

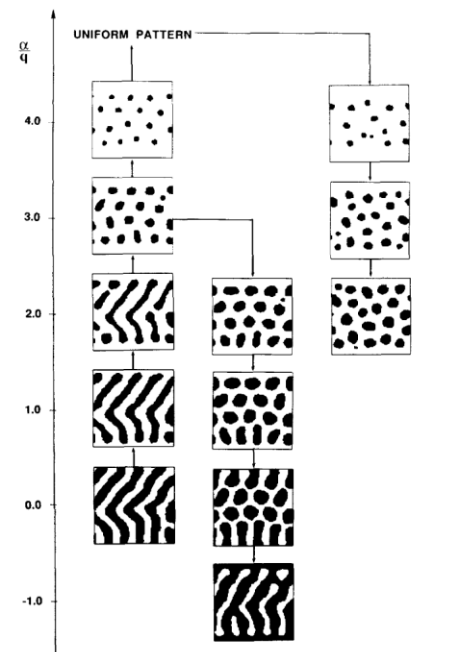
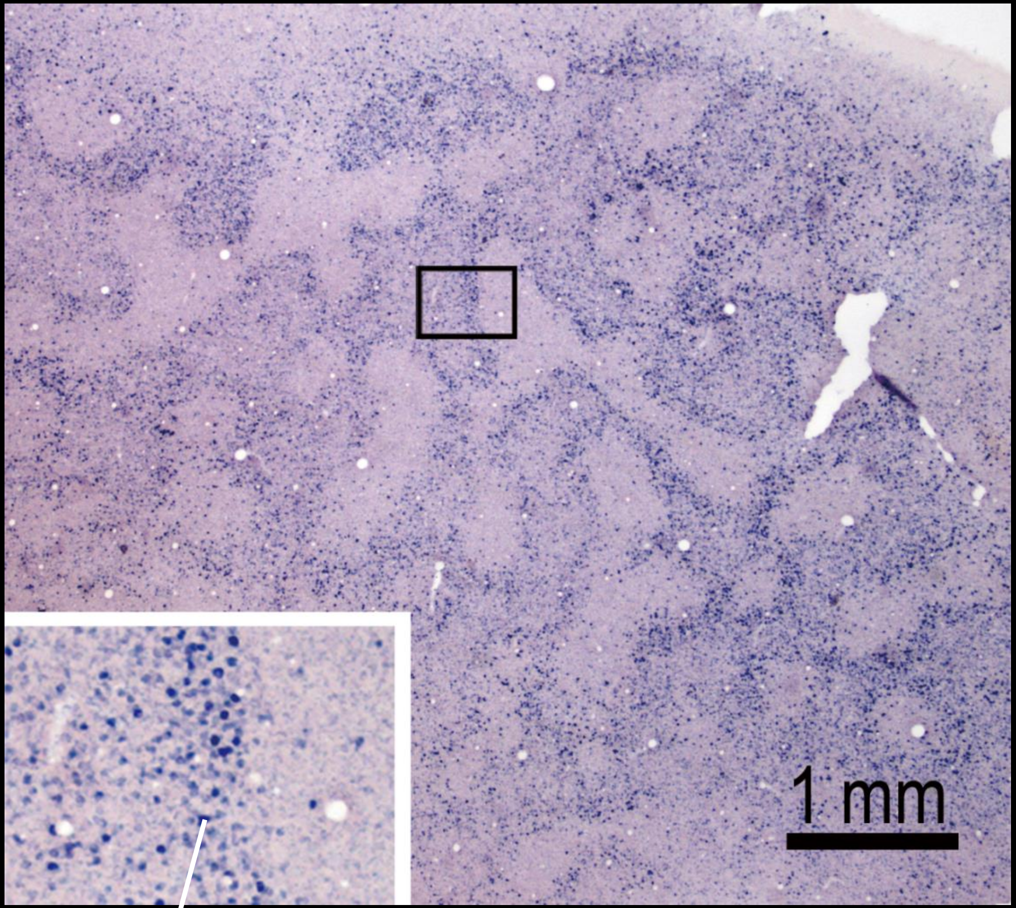


Fig. 5. Computer-simulated ocular dominance patterns for various imbalanced activities. Parameter values are as follows: $r = 0.0$, $\beta = 10.0$, $\kappa = 5.0$. The vertical axis gives the value of α/q. Arrows show the directions in which α/q is changed in the simulations. Note a kind of hysteresis; the emerging patterns depend upon the preceeding sequence of patterns. Therefore, two different patterns, the blob and stripe, are obtained even at the same $\alpha/q = 1.0$ since their initial patterns are different. An asymmetric stripe pattern remains during the increase from 0 to a large α/q value. But on the way back, a blob-lattice pattern is maintained up to a small α/q value

Tanaka (1991) Theory of ocular dominance column formation: Mathematical basis and computer simulation. *Biol Cyber*

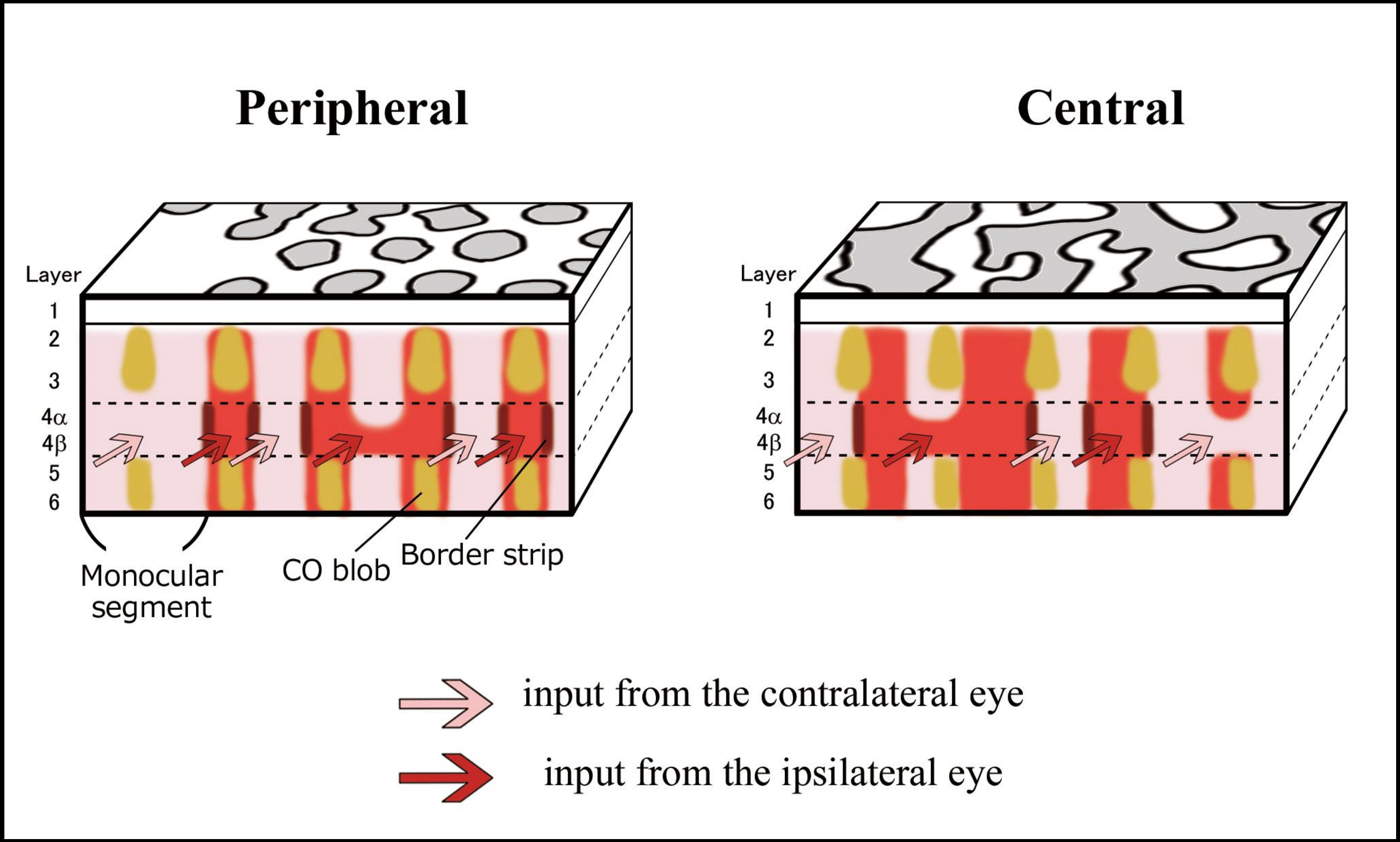
Border strip-like structure was also observed in owl monkeys.

Owl monkey (1 hour-MI)



Takahata, et al. (2014)
Proc Natl Acad Sci USA

Summary of ocular dominance representations in owl monkey V1.

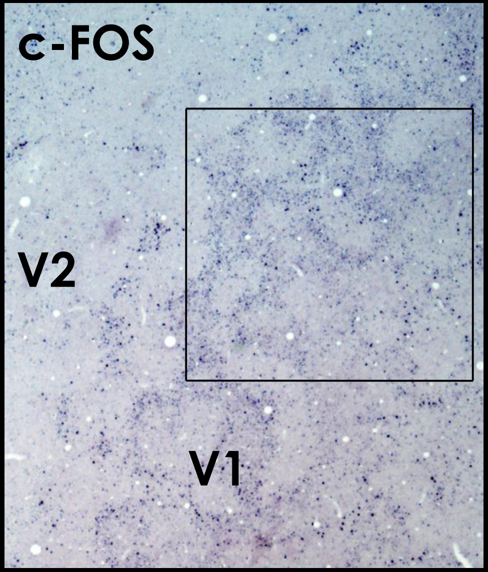


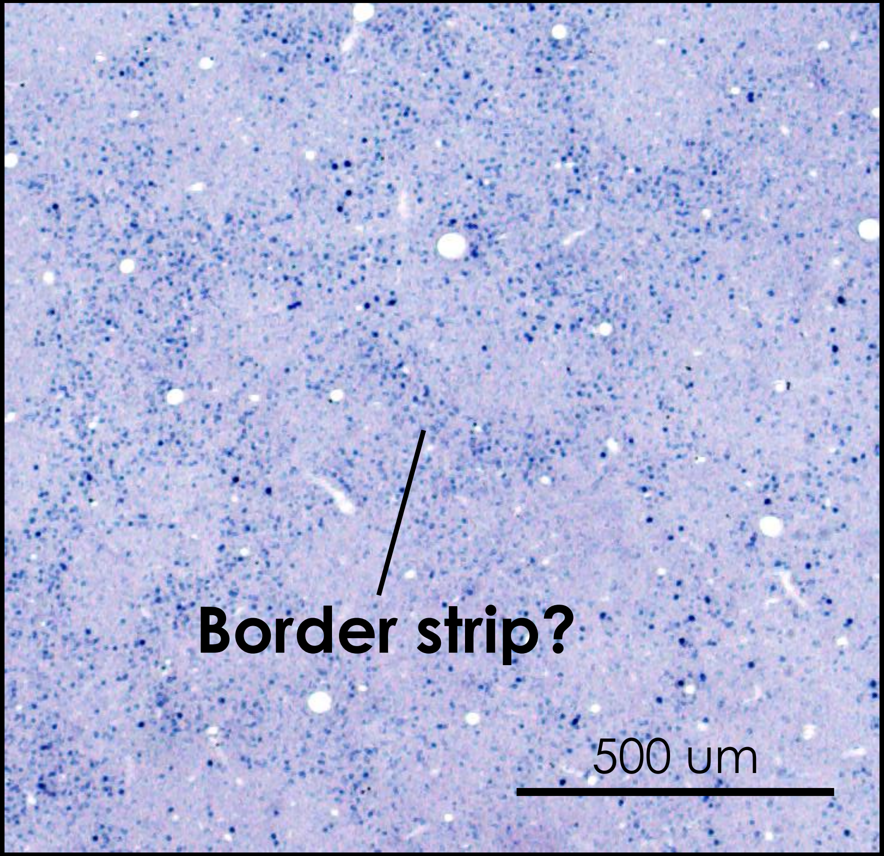
Takahata, et al. (2014) *Proc Natl Acad Sci USA*

ODCs and border strips were observed in galagos as well.

Galago (1 hour-MI)

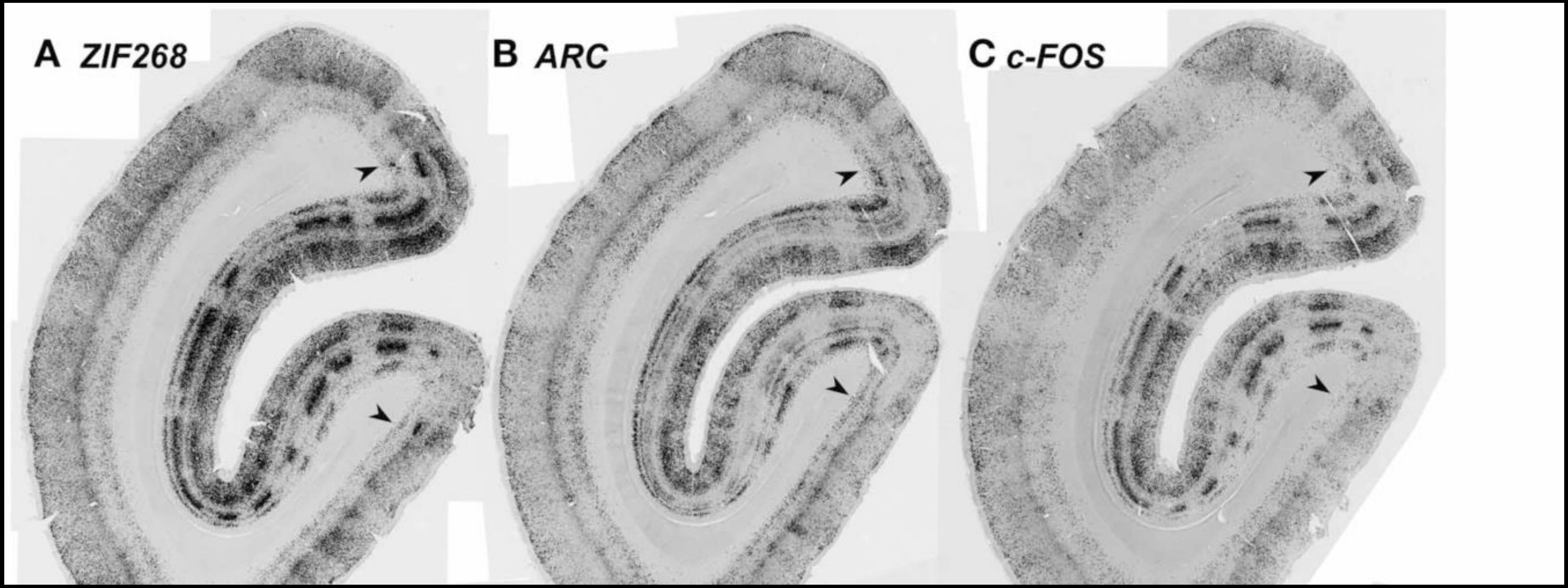
contralateral to blocked eye





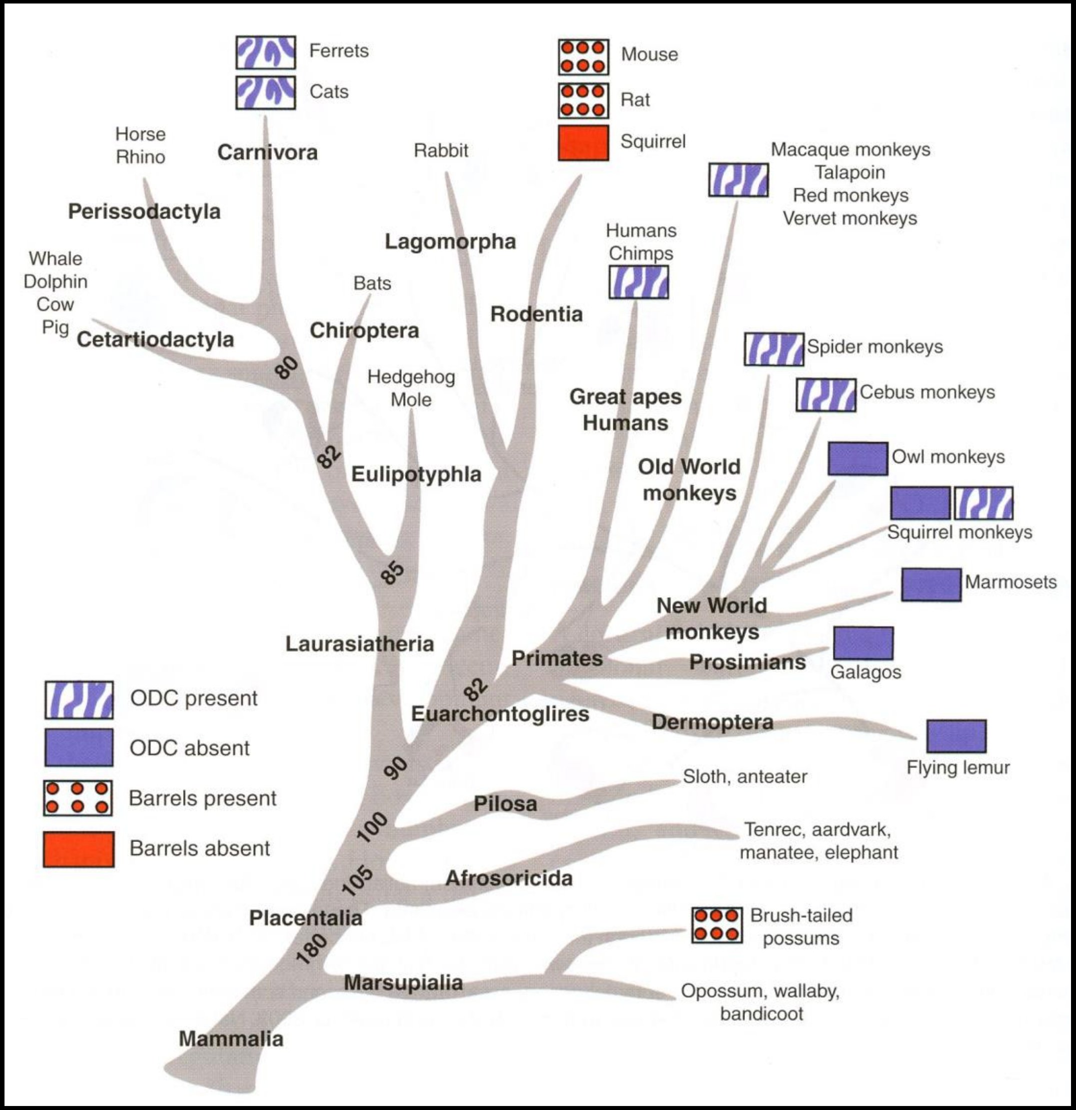
ODCs can be revealed by immediate-early gene expression in marmosets as well.

Marmoset, V1

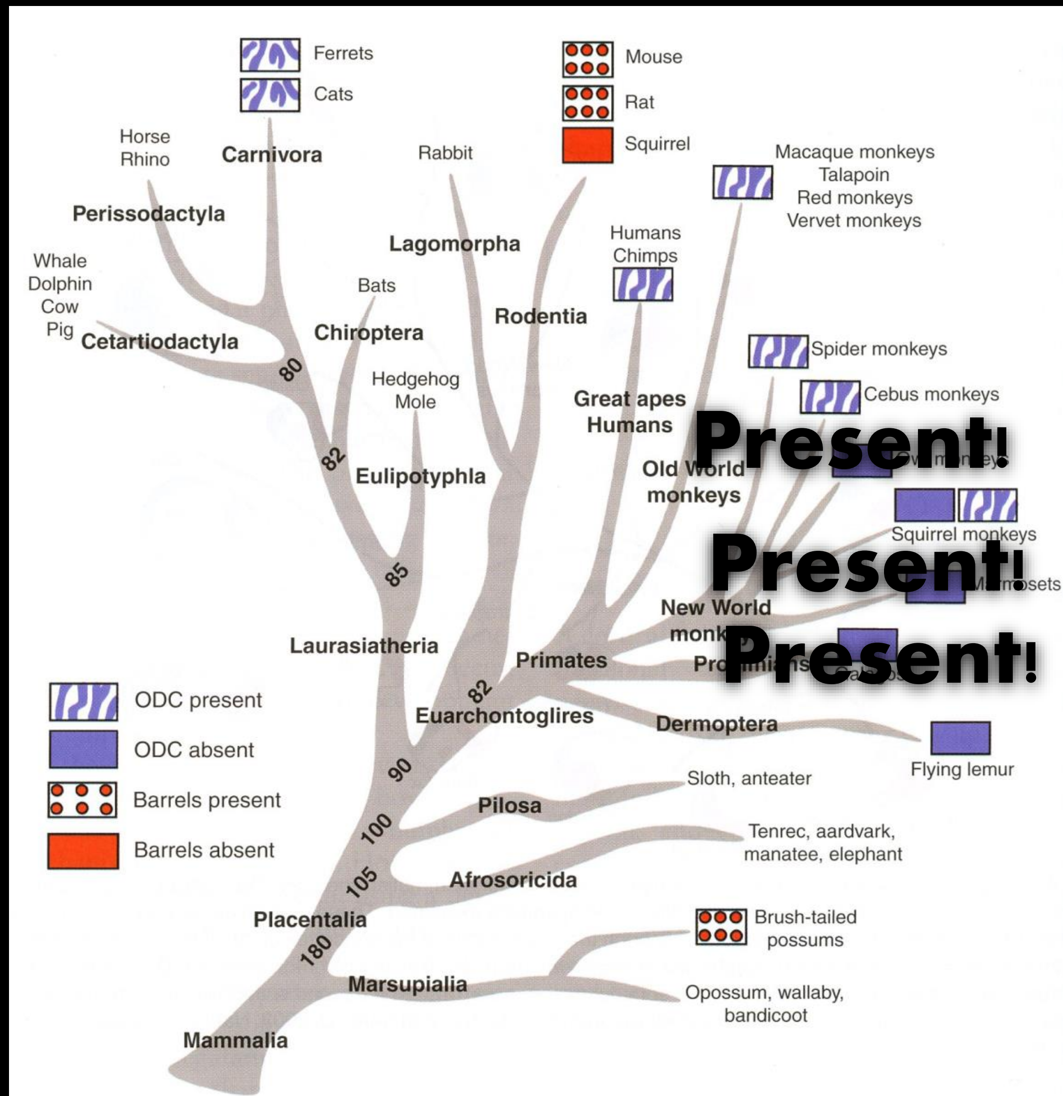


Nakagami, et al. (2013) *Front Neural Circuits*

Previously, ODCs were thought to only present in a few primate species.



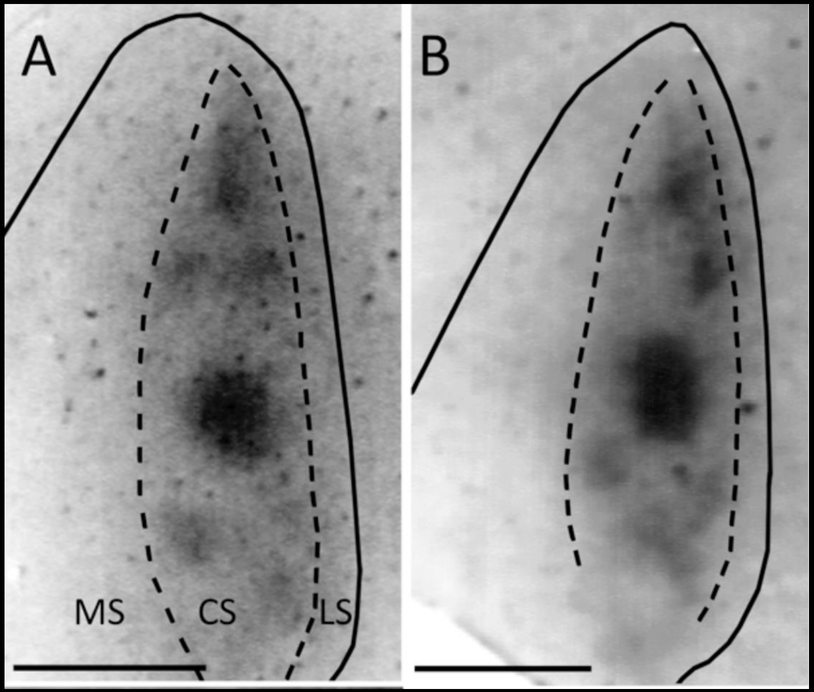
However, recent studies suggest that they are universal in primates.



Dr. Olavarria told that he showed ODC-like patches in rat V1.

Jaime Olavarria, MD., Ph.D., University of Washington

Rat

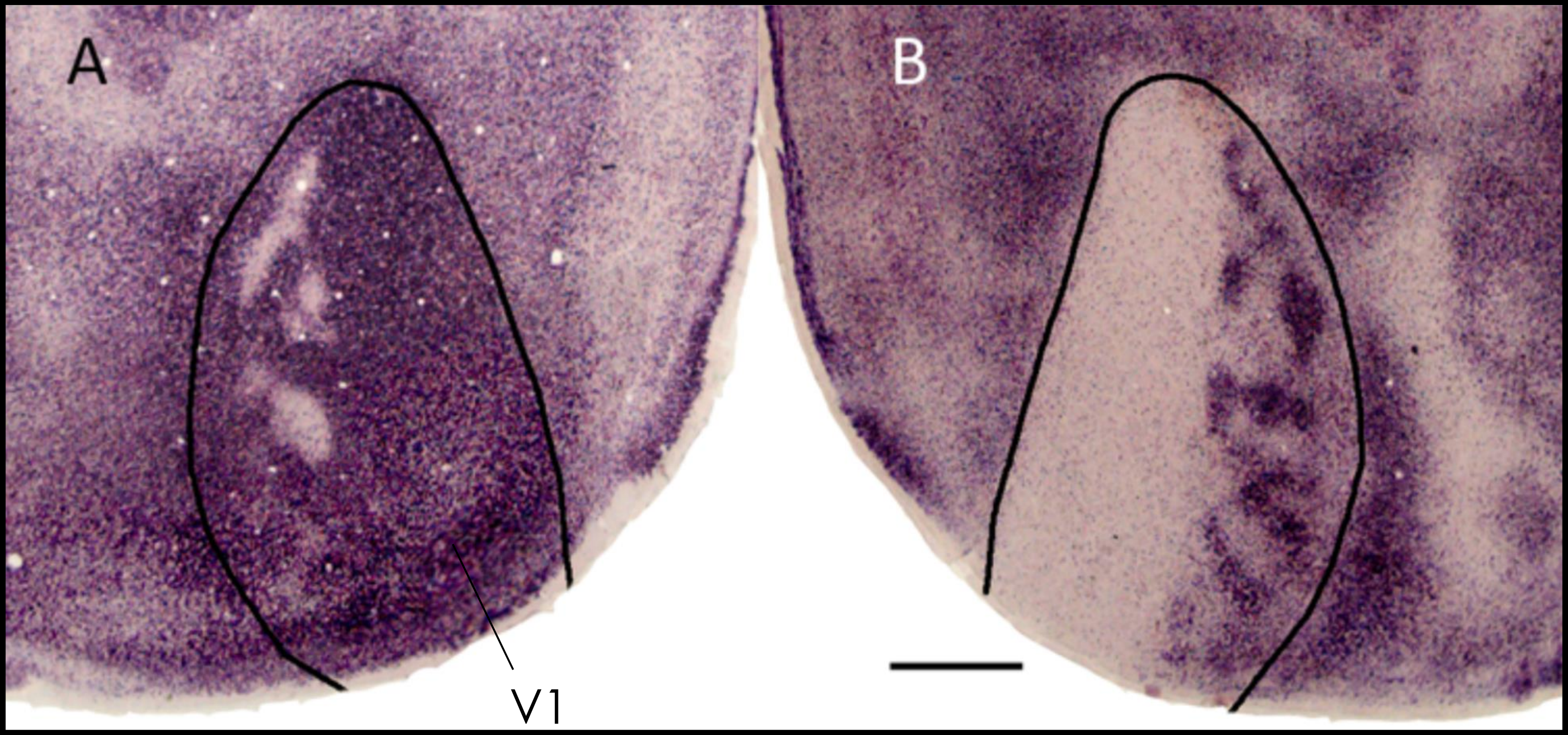


WGA-HRP injection

ODC-like pattern was even observed in rats!

Rat (24 hour-MI)

ipsilateral to the blocked eye | contralateral to the blocked eye



Laing, Turecek, Takahata, Olavarria, **(2014) "Eye-specific domains correlate with patchy callosal connections in visual cortex of Long Evans rats."** *Cereb Cortex*

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Ocular dominance column

From Wikipedia, the free encyclopedia

Ocular dominance columns are stripes of neurons in the visual cortex of certain mammals (including humans[1]) that respond preferentially to input from one eye or the other.[2] The columns span multiple cortical layers, and are laid out in a striped pattern across the surface of the striate cortex (V1). The stripes lie perpendicular to the orientation columns.

Ocular dominance columns were important in early studies of cortical plasticity, as it was found that monocular deprivation causes the columns to degrade, with the non-deprived eye assuming control of more of the cortical cells.[3]

It is believed that ocular dominance columns must be important in binocular vision. Surprisingly, however, many squirrel monkeys either lack or partially lack ocular dominance columns, which would not be expected if they are useful. This has led some to question whether they serve a purpose, or are just a byproduct of development.[4]

Contents [hide]

"Notably, they are also absent in many animals with binocular vision, such as rats."

Currently dominant paradigm

① A portion of New World monkeys do not have ocular dominance columns.

② However, all of New World monkeys are capable of stereopsis.

↓

③ Therefore, ocular dominance columns are not functionally important.

My data suggests that ① is likely wrong.
Consequently, ③ is also skeptical.

Functional significance of ocular dominance columns should be reconsidered!

Next Questions:

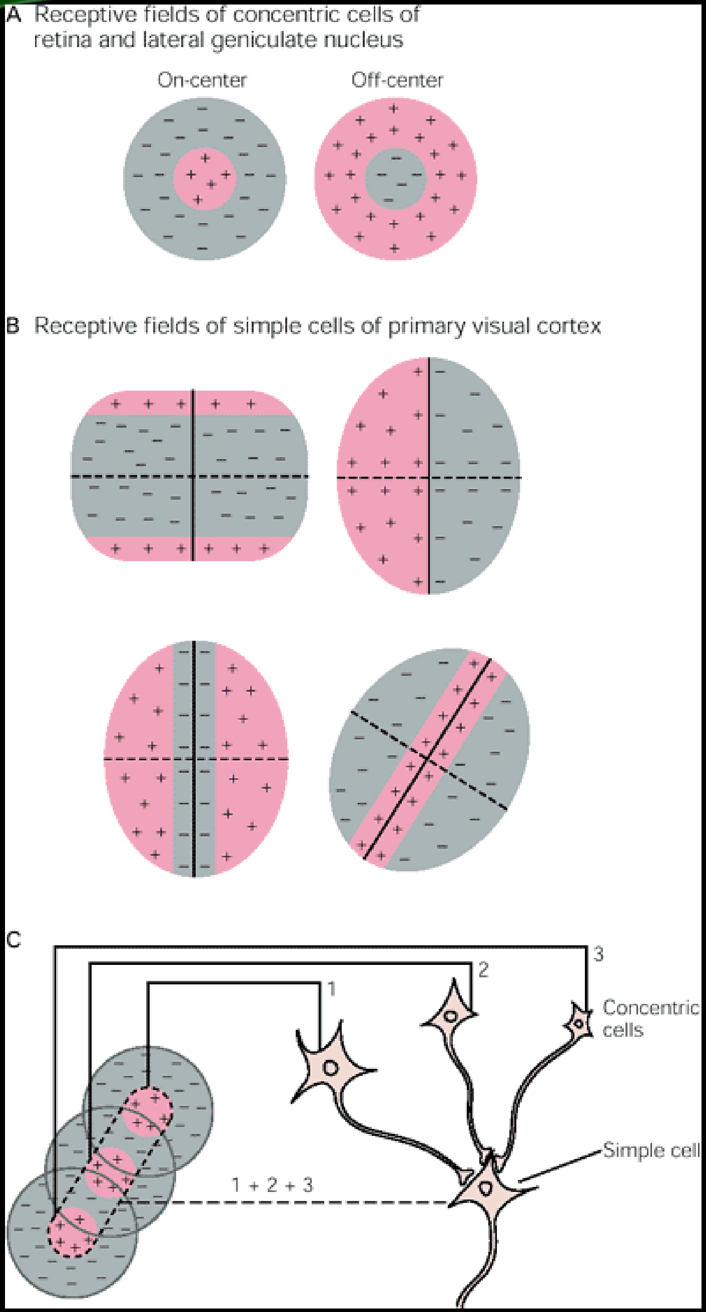
How are ocular dominance important?

Why do ocular dominance columns exist?

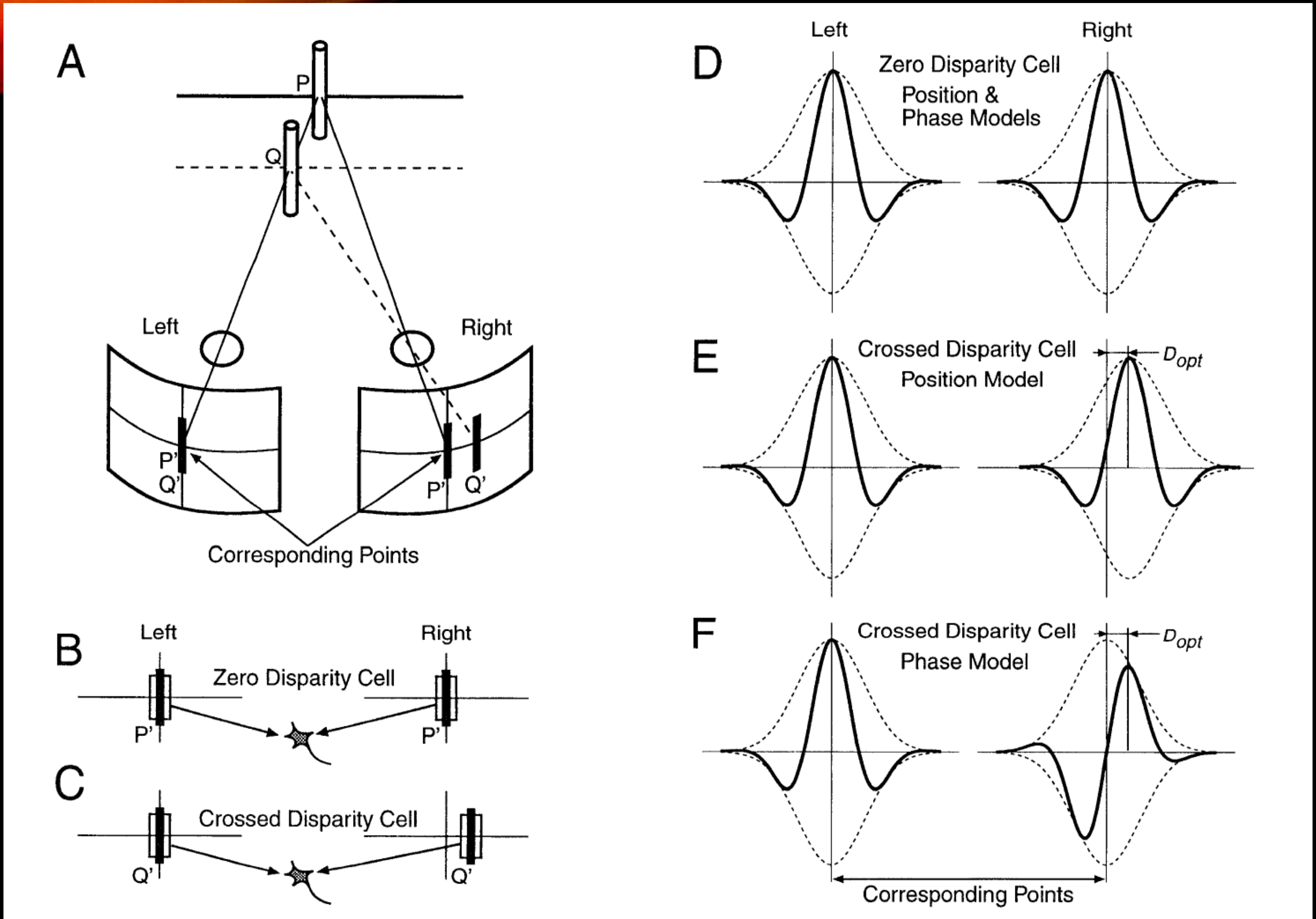
↓

Think about relationship with other modalities

1. In order to achieve depth coding, ocular segregation is necessary at the first (and second) synapses.

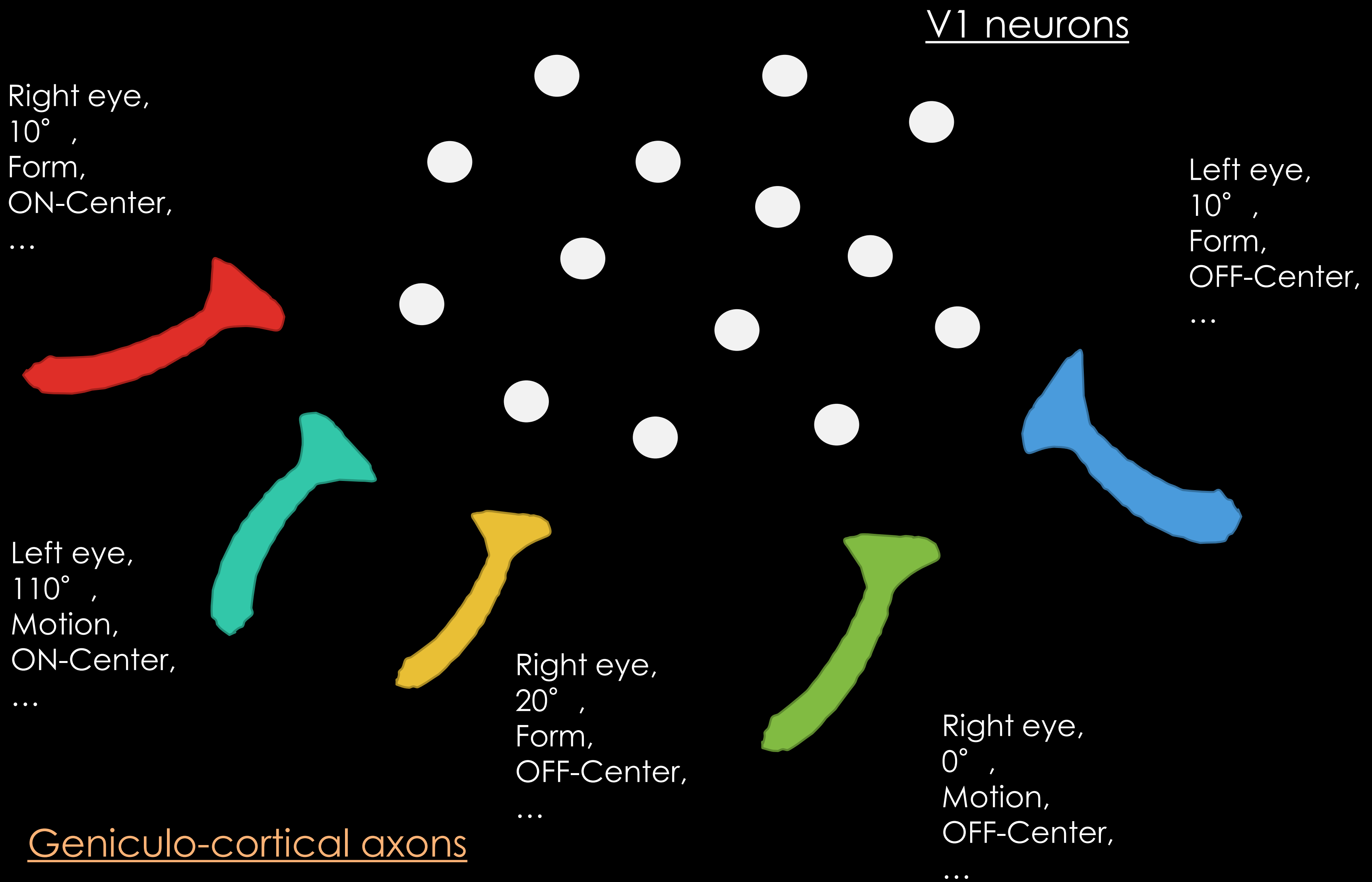


Principles of Neural Science: IVth Edition

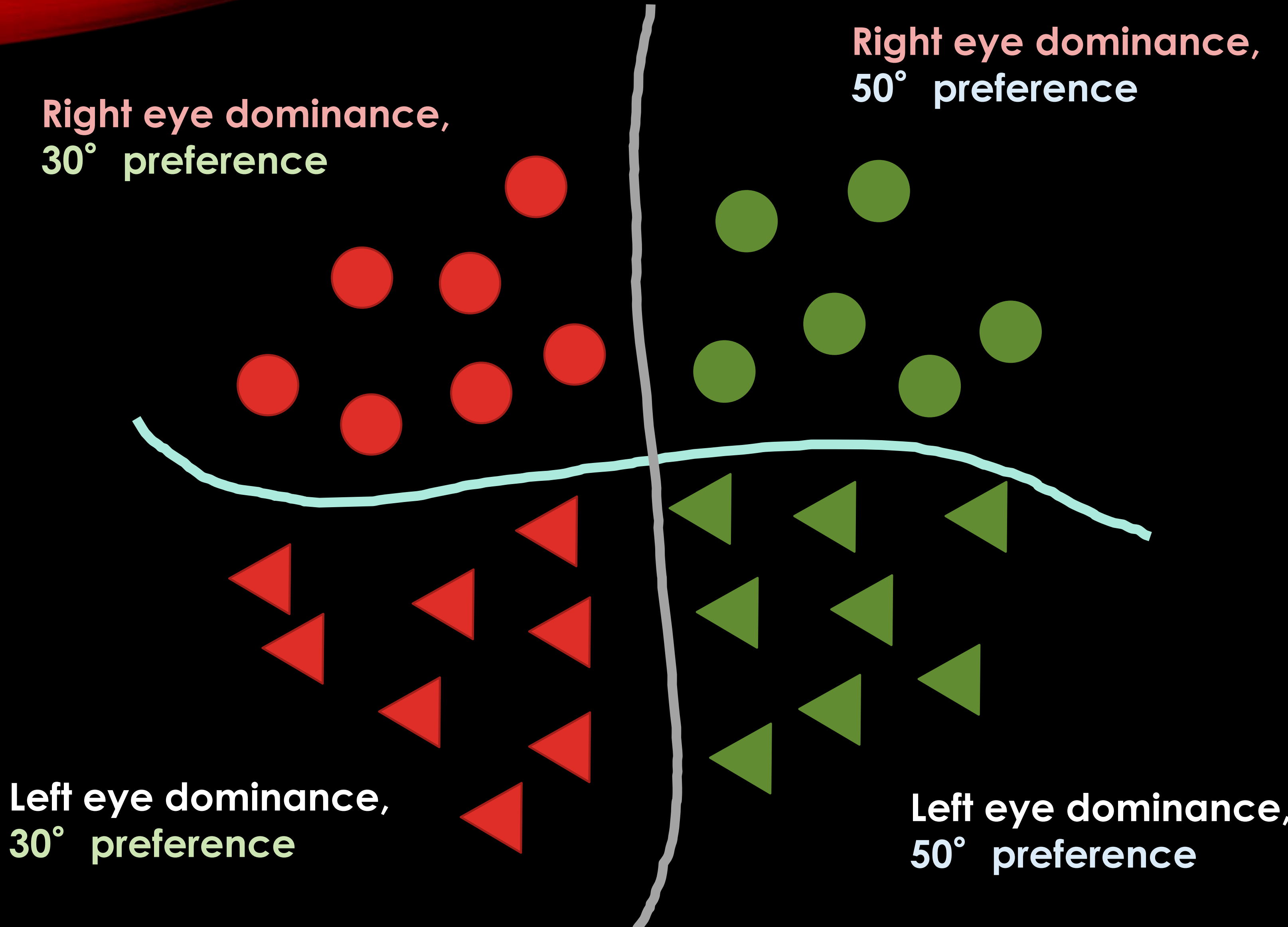


Ohzawa, DeAngelis and Freeman (1996) Encoding of binocular disparity by simple cells in the cat’s visual cortex. *J Neurophysiol*

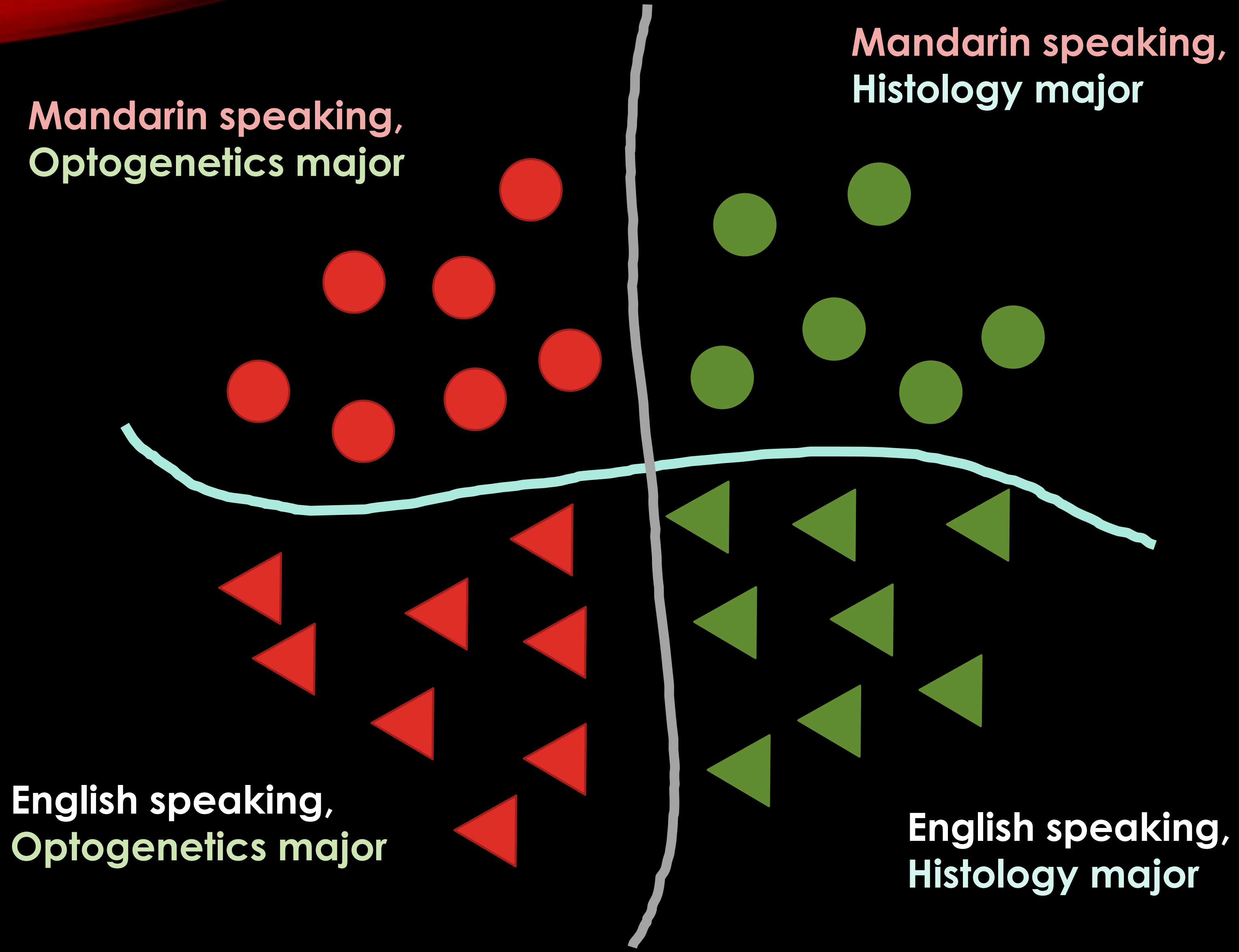
2. Same (similar) profile attracts each other, and tends to make clusters.



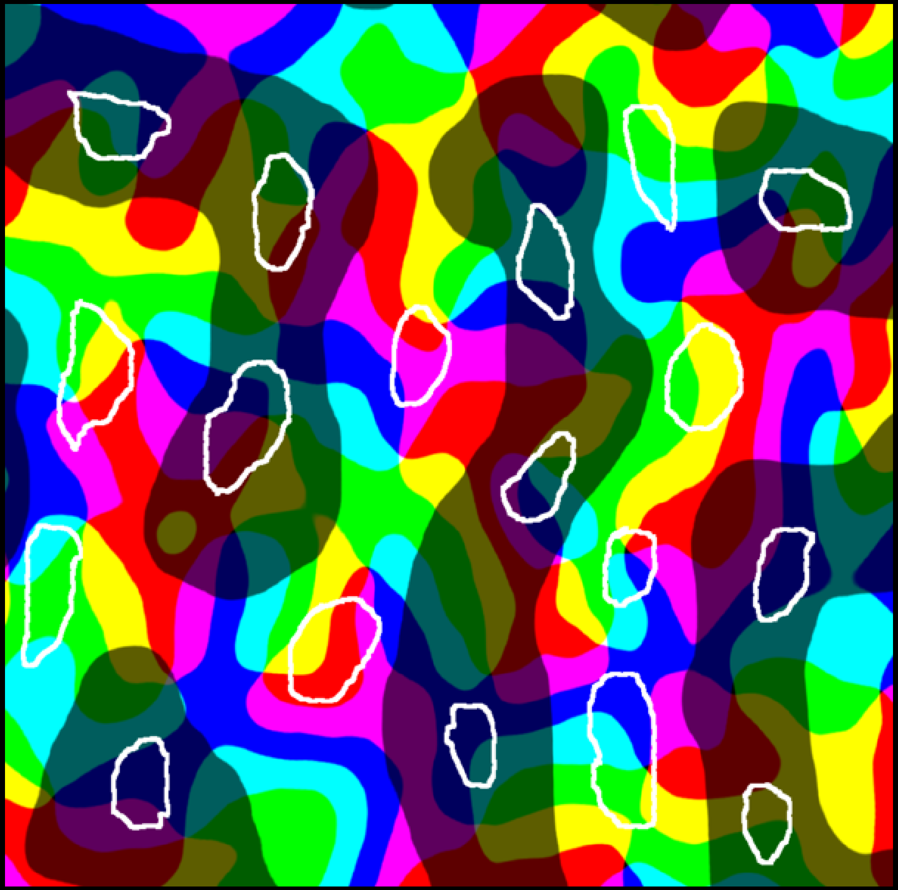
1. Same (similar) profile attracts each other, and tends to make clusters.



1. Same (similar) profile attracts each other, and tends to make clusters.



ODCs and orientation columns tend to cross at a vertical angle.



Dark/bright: ODCs
Color: orientation columns
White: CO blobs

It has been suggested that neurons tend to locate and connect so that they can minimize economy.

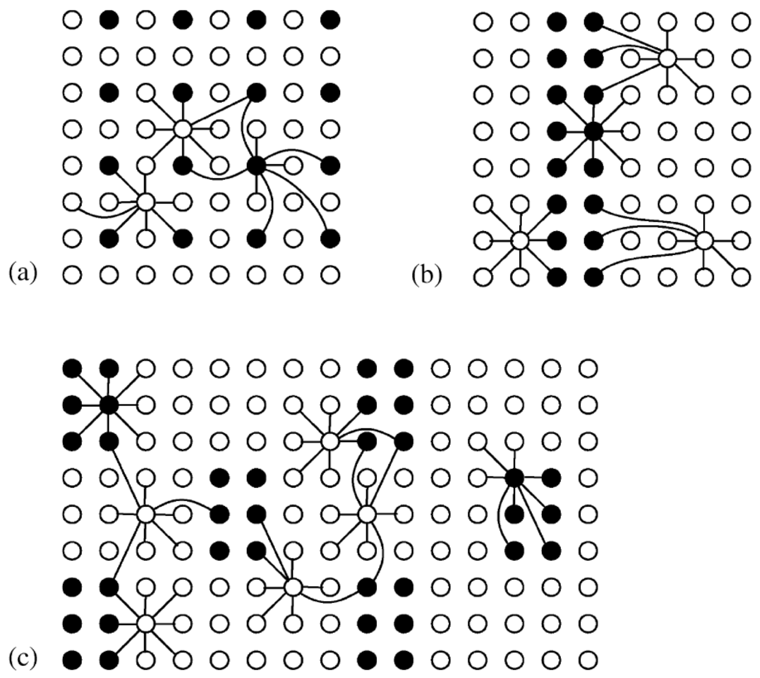
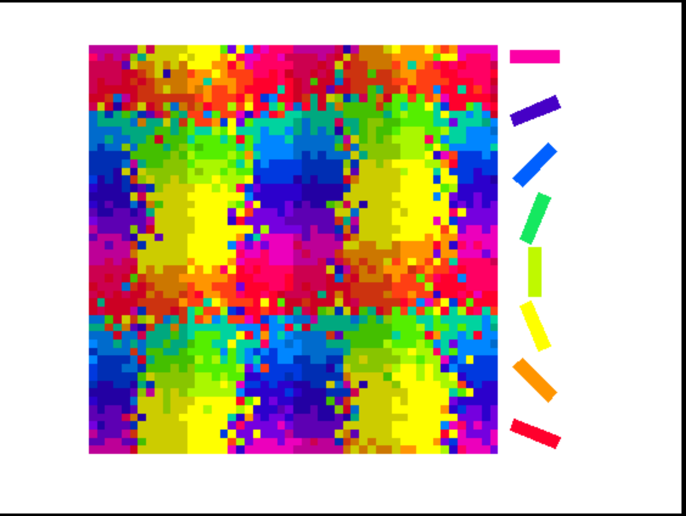


Fig. 5. Ocular dominance patterns for $f_L = \frac{1}{4}$ and $N_s = 5$, $N_o = 3$. Realizations of the (a) *Salt and Pepper* ($l \approx 11.26$) and (b) *Stripes* ($l \approx 11.49$) are suboptimal. (c) A realization of the *L-Patch* phase gives minimal wire length ($l \approx 10.67$).

Chlokovskii and Koulakov. (2000) *Physica A*

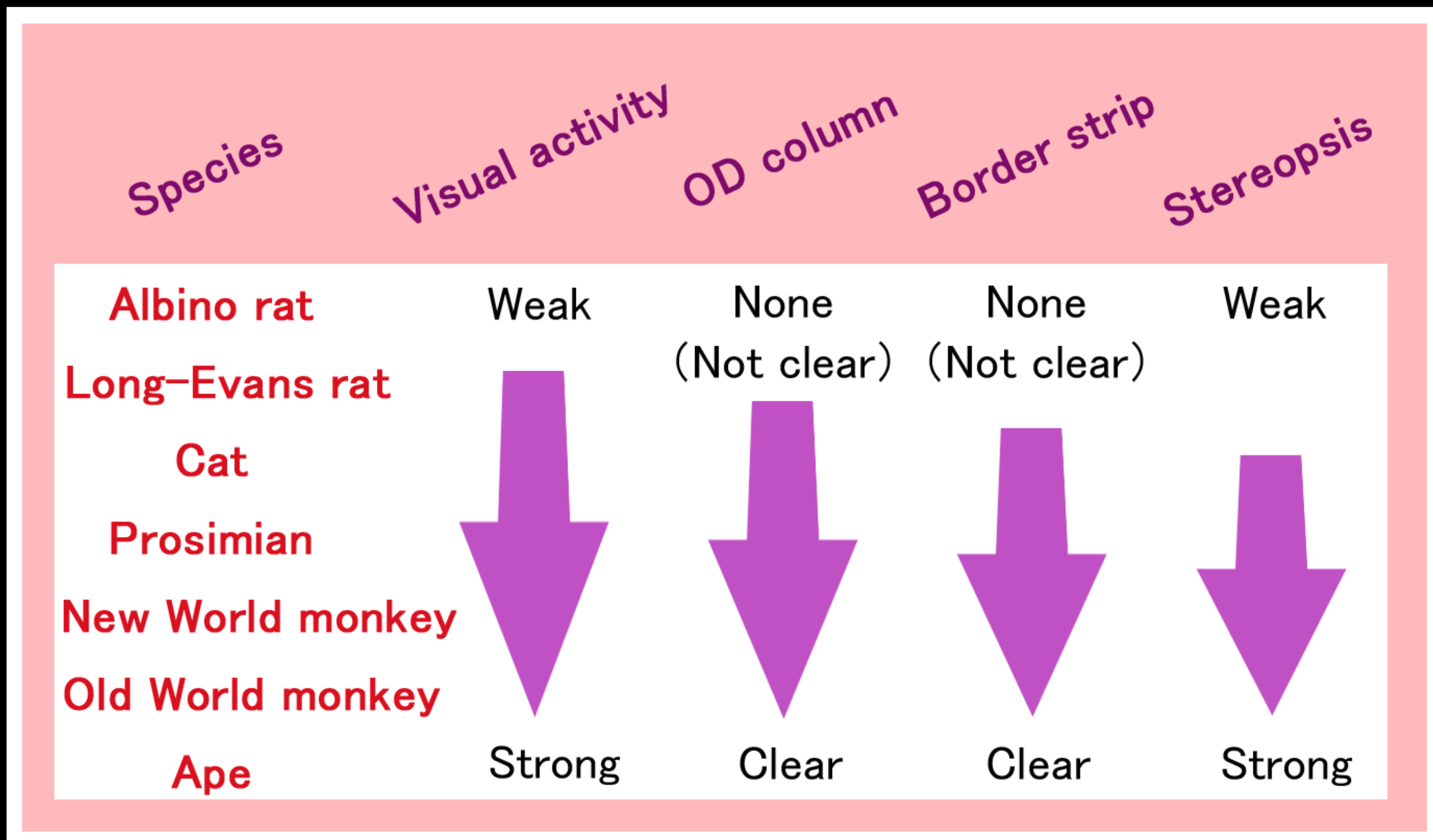
It has been suggested that neurons tend to locate and connect so that they can minimize economy.



The pattern of preferred orientation and ocular dominance combined on the same picture, which is obtained in a computer simulation minimizing the total length of connections. The preferred orientation is coded by color. The left-eye dominated areas are shown by a darker color.

Koulakov, A
(Cold Spring Harbor Laboratory)

ODCs may contribute to stereopsis via border strip circuit.

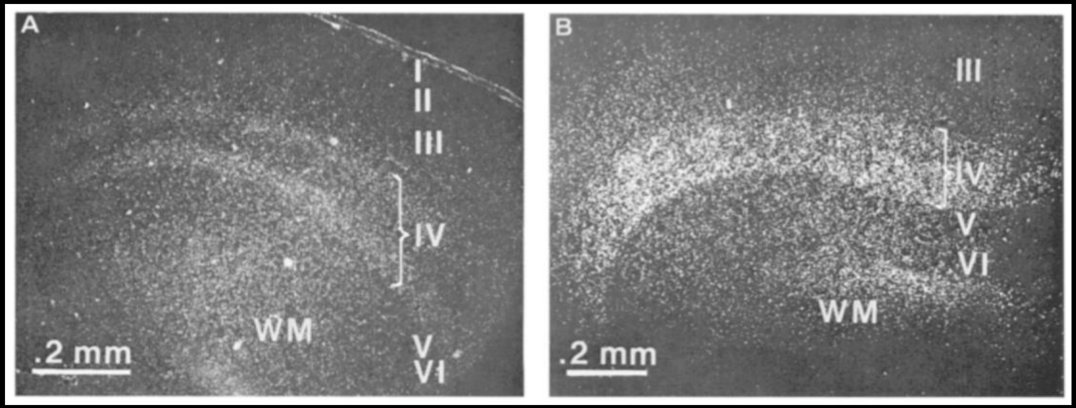


Part 4.

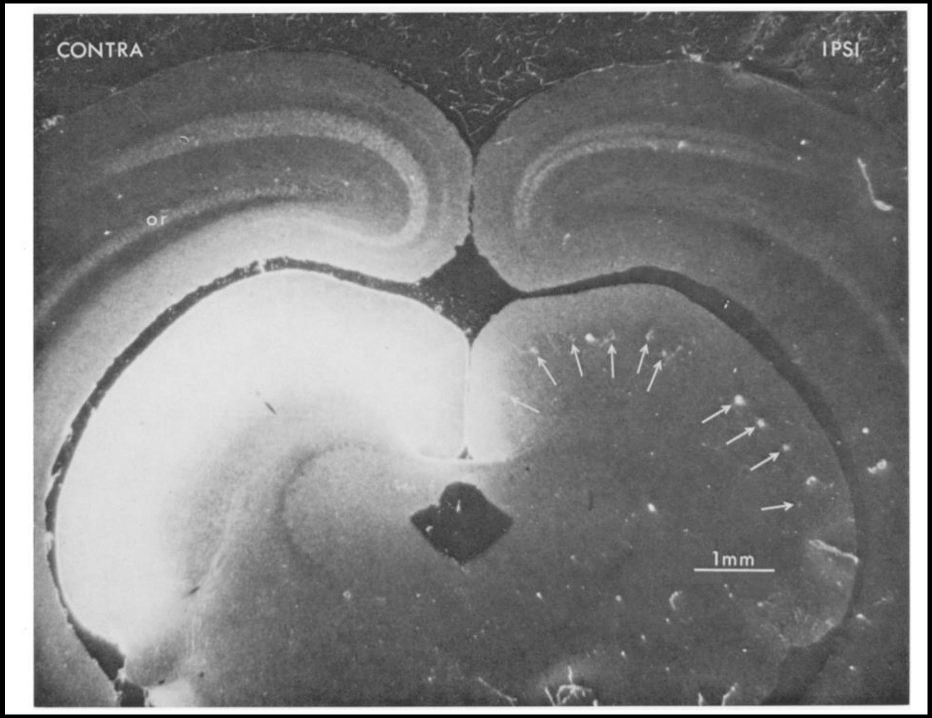
Ocular dominance layers?

Tree shrew (*Tupaia belangeri*)

It has been suggested that right and left eye inputs are segregated into layers, not columns in tree shrews.

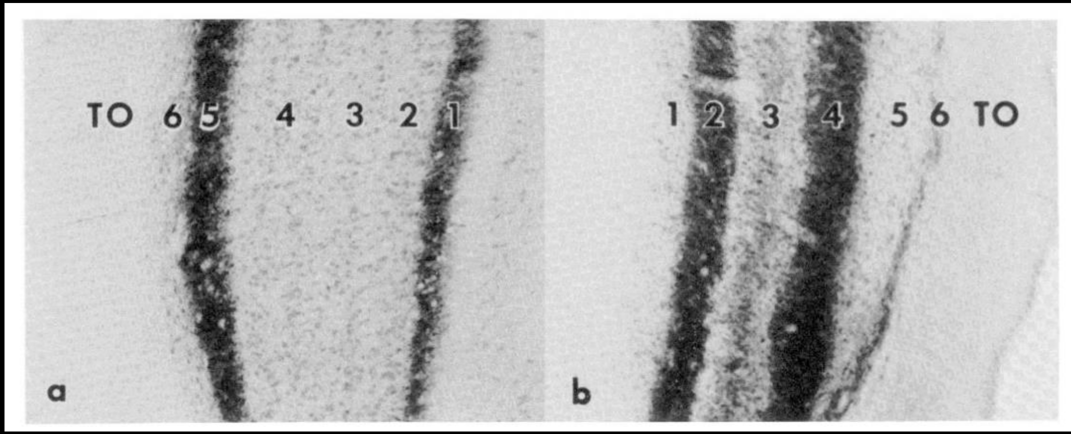


Casagrande and Harting (1975) *Brain Res*

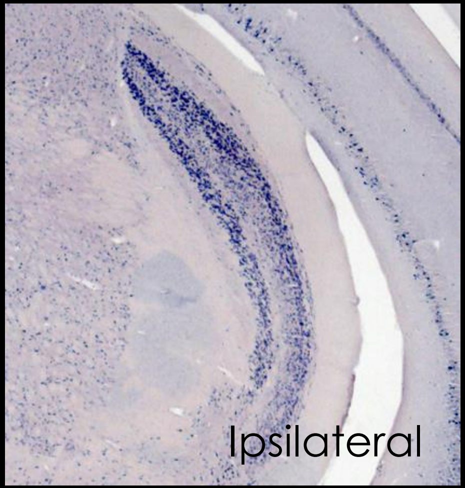


Hubel (1975) *Brain Res*

Right and left eye inputs are clearly segregated into layers in LGN of tree shrews.

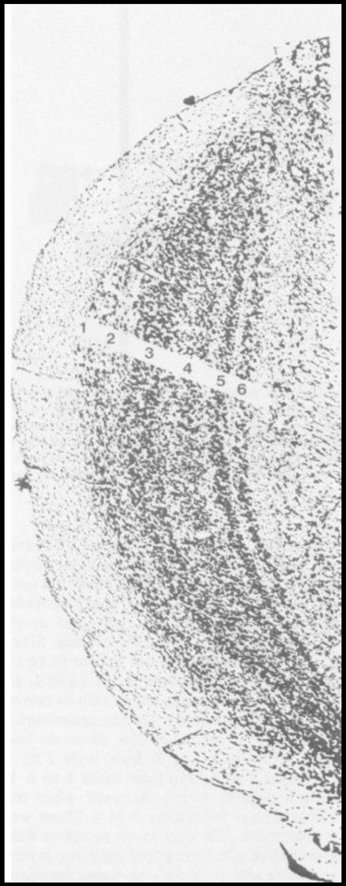


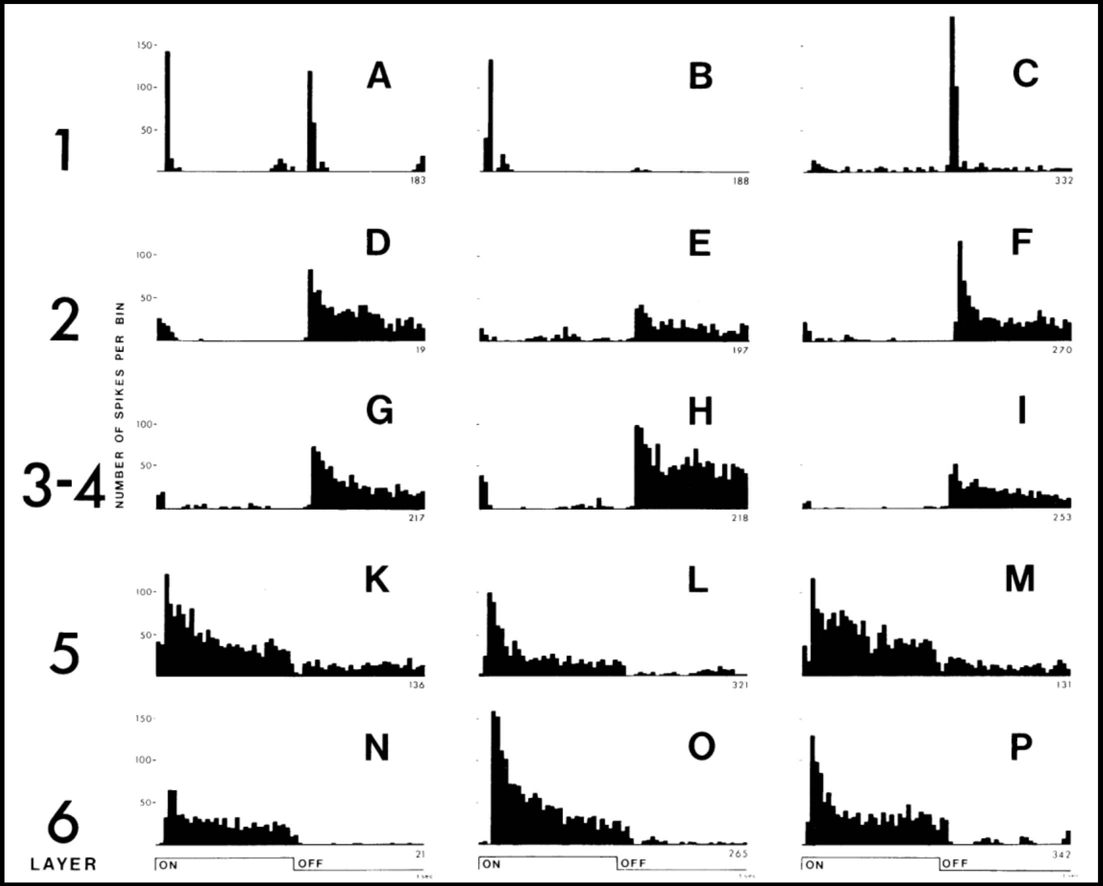
Conley, et al. (1984)
J Neurosci



c-Fos

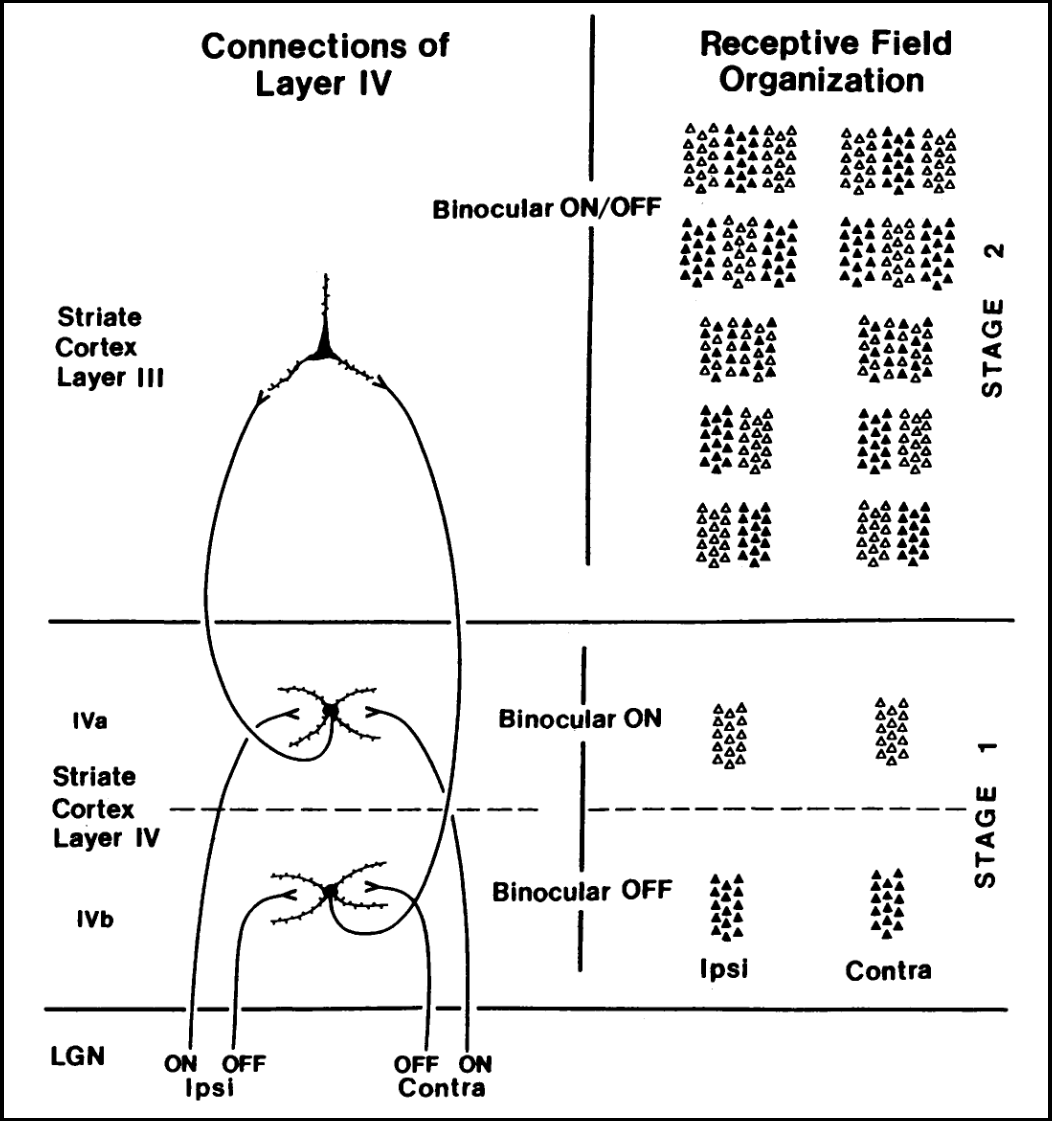
LGN layers are segregated by ON-Center/OFF-Center neurons, as well as ocular dominance.





Conway and Schiller (1983) Laminar organization of tree shrew dorsal lateral geniculate nucleus. *J Neurophysiol*

ON-Center/OFF-Center segregation is maintained in V1 layers.



Fitzpatrick and Raczkowski (1990)
Proc Natl Acad Sci USA

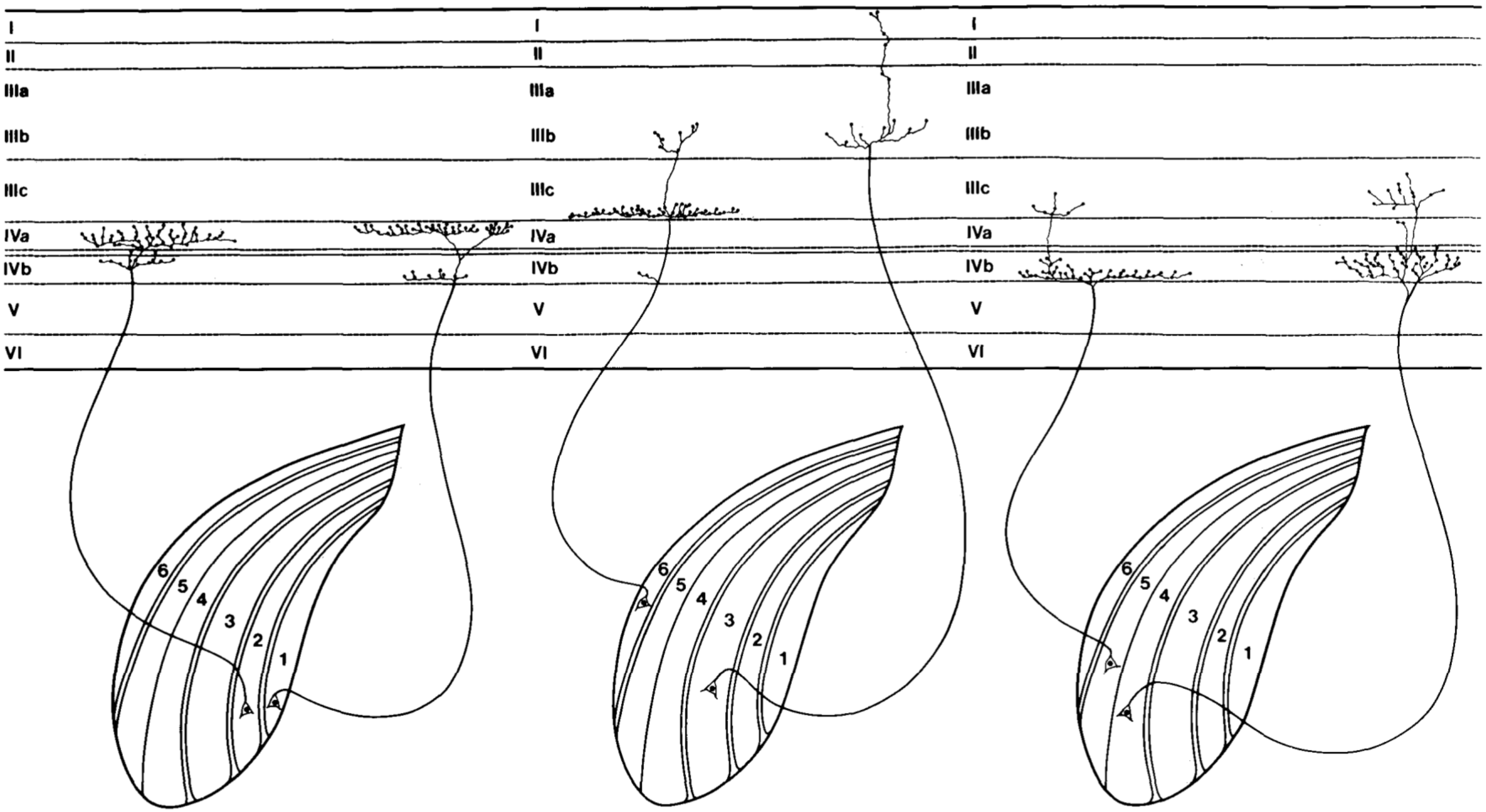
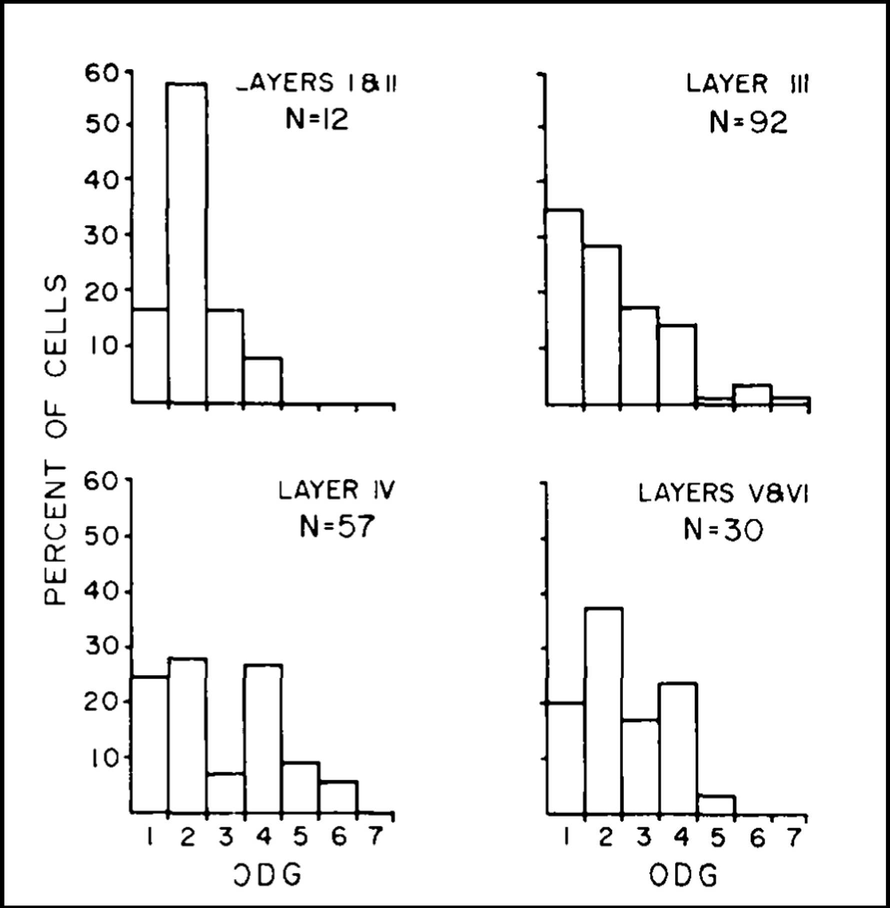
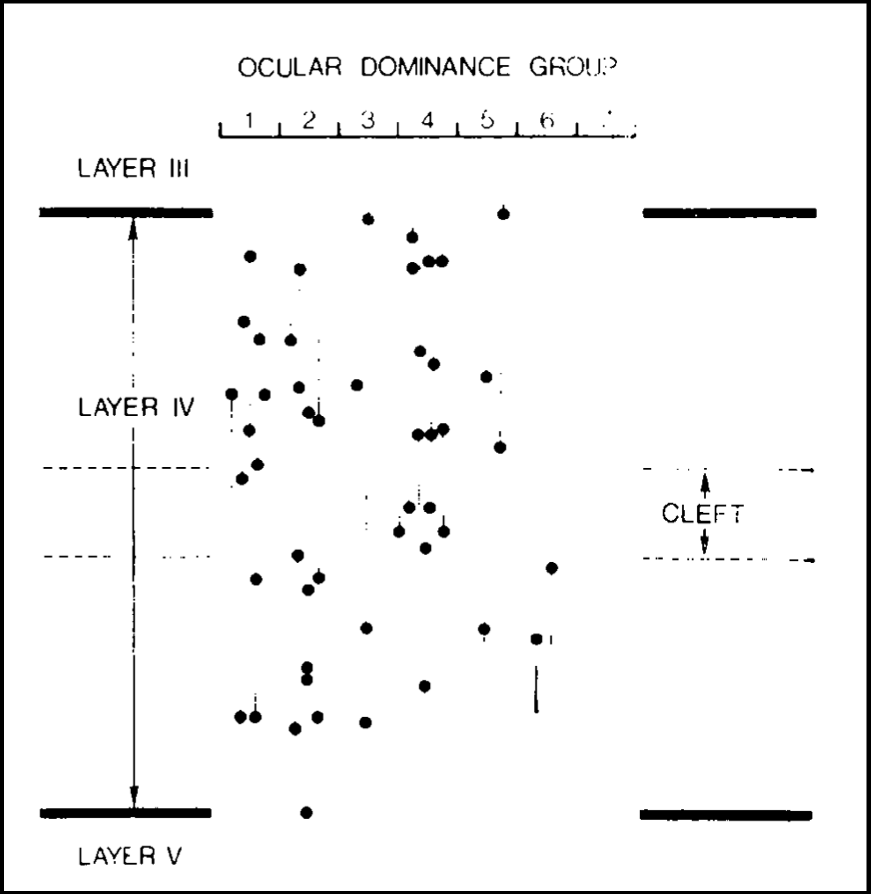


Figure 22. Summary diagram of the major and minor projections of each of the six lateral geniculate layers.

Conley, Fitzpatrick and Diamond (1984) *J Neurosci*

Most of the V1 neurons are contralaterally-biased binocular neurons.





Humphrey, Albano and Norton (1977) *Brain Res*

Summary

- ODCs likely globally exist in all primate species.
- There is border strip in V1 layer 4 that is conserved in primate species.
- Even rats have ODCs.
- Tree shrews have weird arrangement of ocular dominance and ON-Center/OFF-Center neuron classes.
- Do not accept all the descriptions in textbooks or Wikipedia.

Possible Future Directions

- Examine orientation domains by IEG expression in various species.

- Examine orientation domains after monocular deprivation in juvenile animals.

- Examine OD domains after orientation deprivation in juvenile animals.

Part 5.

Zhejiang University, Interdisciplinary Institute of Neuroscience and Technology

Top 5 universities in China

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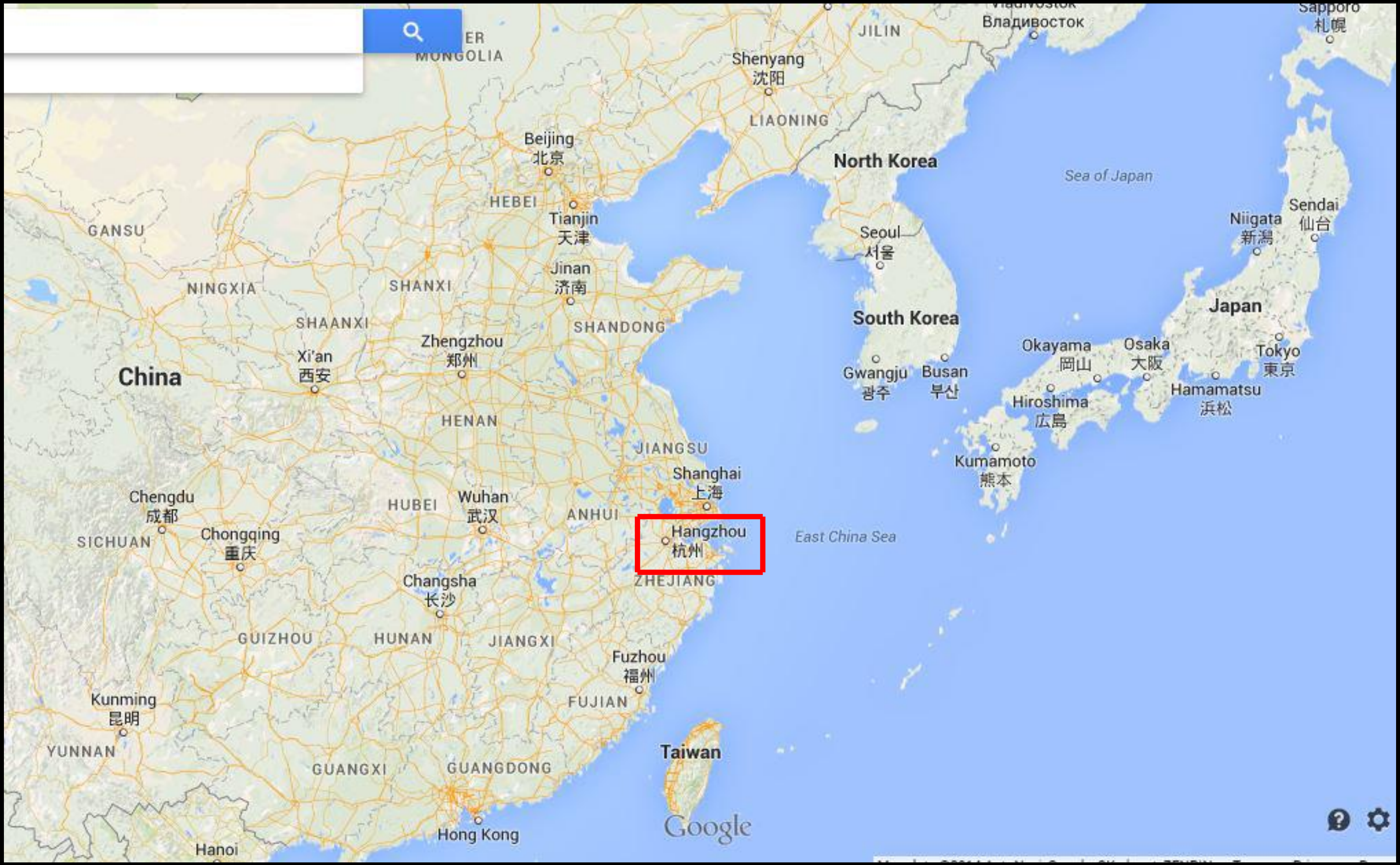
南京大学　　浙江大学

浙江省・杭州市



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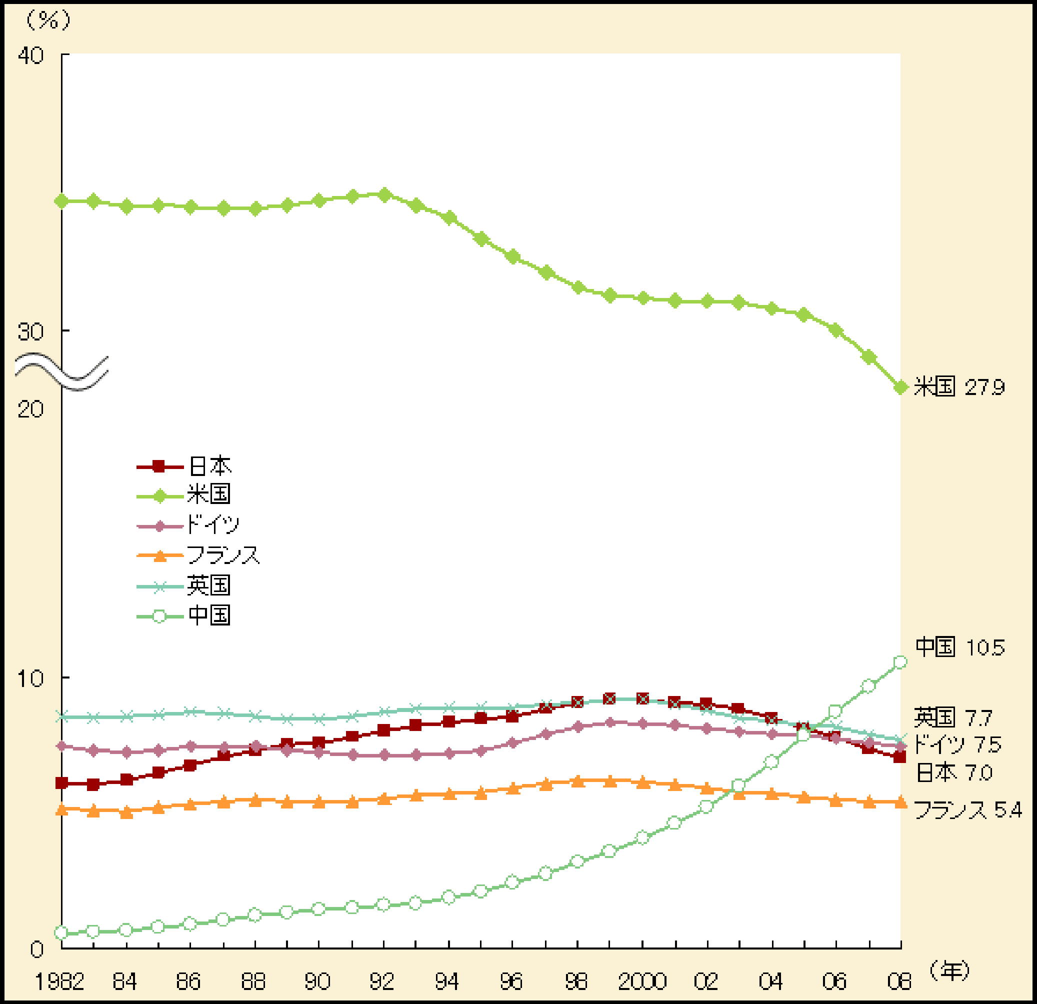

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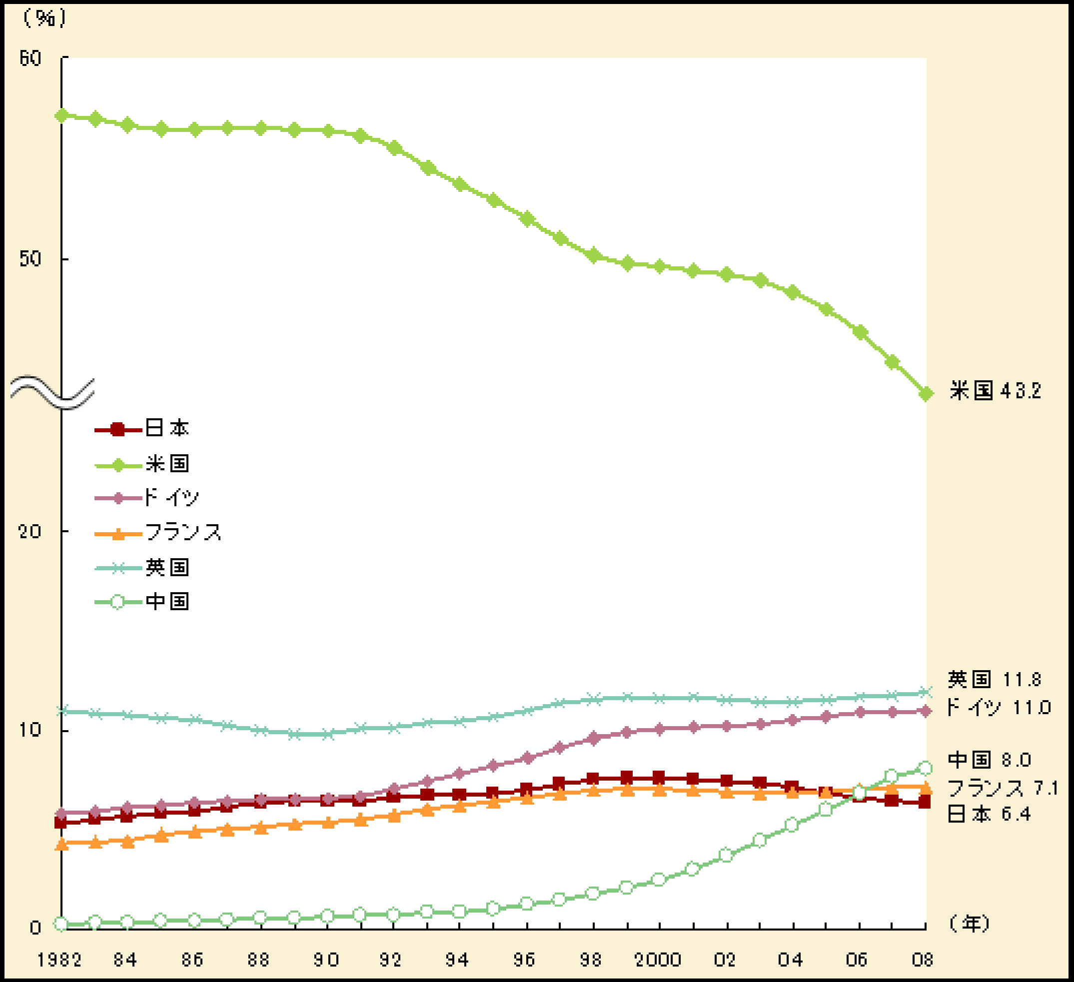

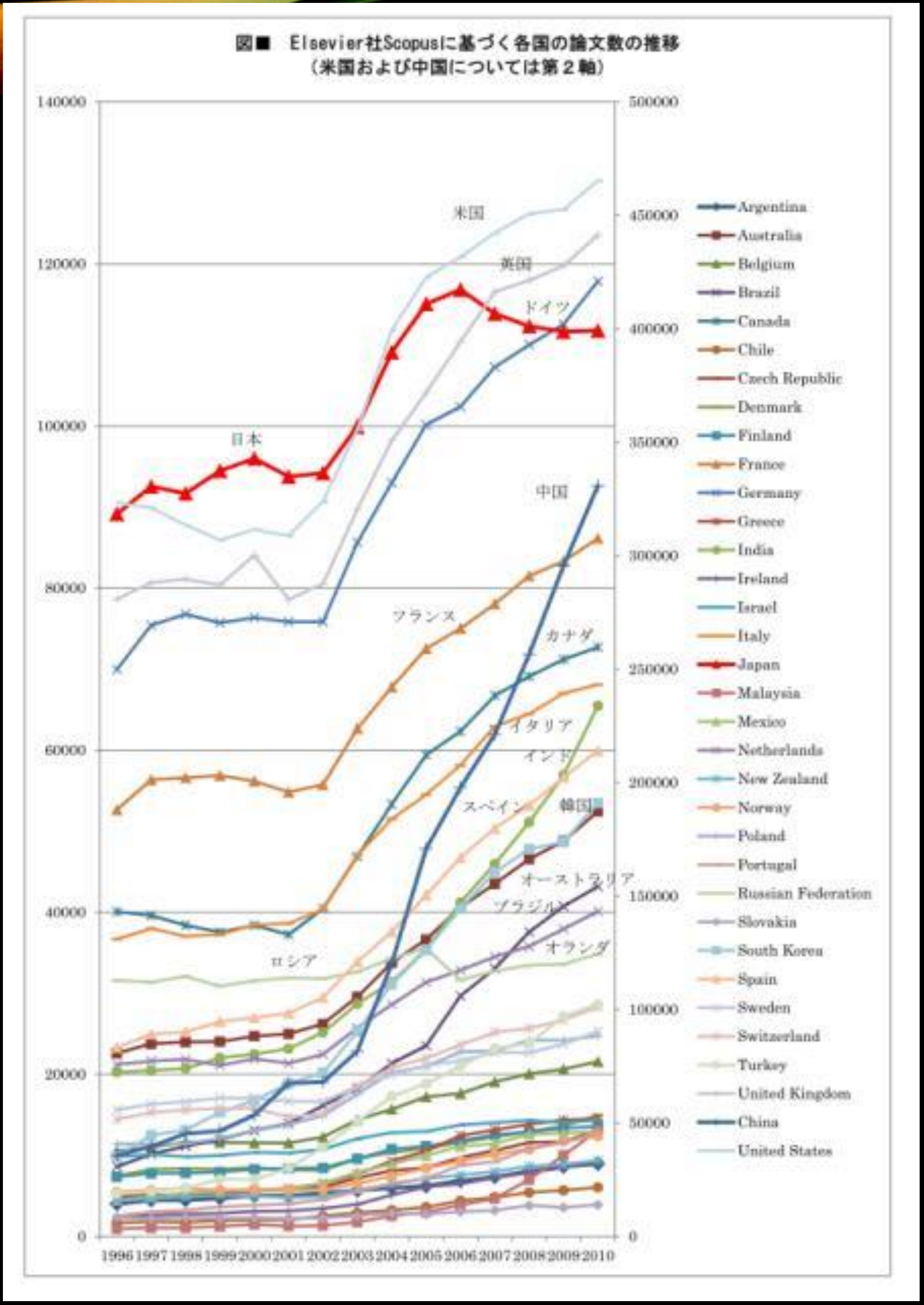

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Slovakia
South Korea
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Sweden
Switzerland
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United Kingdom
China
United States

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Professor of Psychology, Biomedical Engineering, and Radiology & Radiological Sciences

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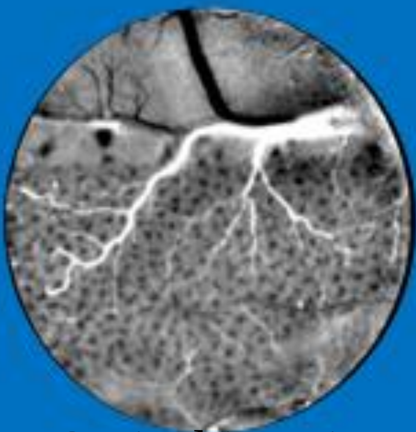
Overview of Interests

Zhejiang University Interdisciplinary Institute of Neuroscience and Technology (ZIINT)

浙江大学系统神经与认知科学研究院



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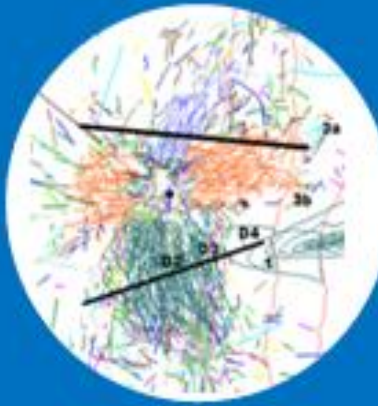
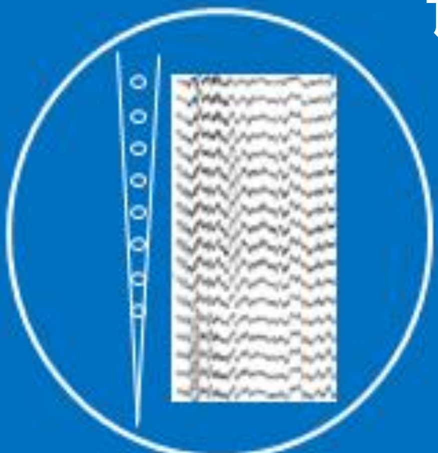
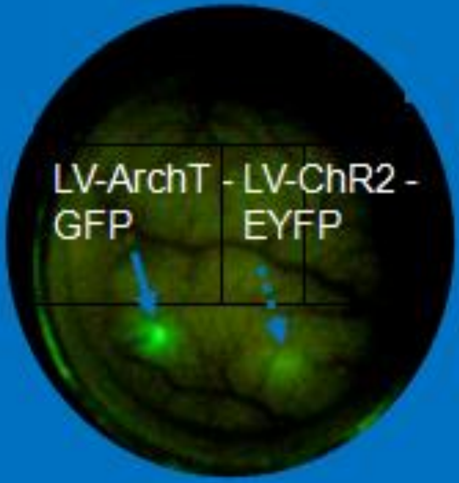


Anatomy



Electrophysiology

MRI



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Computer Cluster

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(director)
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Chen
3D vision, MRI

Xiaodong
Chen
Visuo-Vestibular

Lynn
Ho
Neurvascular
Coupling

Ye
Li
Cortical Lineage
2 Photon

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Hailan
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Attention

Xiongjie
Yu
Audition
Auditory Attention

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….more to come!

これからの研究計画

１・サル胎児大脳皮質で領野特異的遺伝子の探索をする

２・サル大脳皮質領野特異的遺伝子の転写調節因子を探索する

３・眼優位性カラムと方位選択性カラムの相互作用を調べる

↓

霊長類大脳皮質に特有な生理・解剖学的特徴を明らかにする。

そしてその特徴を生み出す遺伝的基盤を明らかにする。

Acknowledgements

電気通信大学
- 田中　繁　教授

基礎生物学研究所
- 山森　哲雄　教授

沼津高等専門学校
- 宮下　真伸　准教授

Vanderbilt University
- Dr. Jon H. Kaas
- Dr. Troy A. Hackett
- Dr. Vivien A. Casagrande
- Dr. Anna W. Roe

University of Louisville
- Dr. Heywood M. Petry

University of Washington
- Dr. Jaime F. Olavarria

- Animals