KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

Module:
Biological Foundations of Mental Health

Week 4:
Biological basis of learning, memory and cognition

Dr Sam Cooke

Topic 3:
The effects of activity, experience and deprivation on the nervous system
Part 2 of 5

Part 2

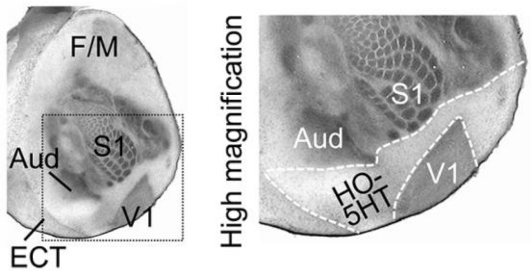
Part 2

Segregating inputs through Hebbian plasticity: how does activity shape the visual system?

Primary sensory regions of the neocortex

Primary sensory areas provide constrained experimental systems to test the effects of experience/deprivation.

Whisker barrels are columnar anatomical specialisations in primary somatosensory cortex of rodents that are dedicated to input from a single whisker.



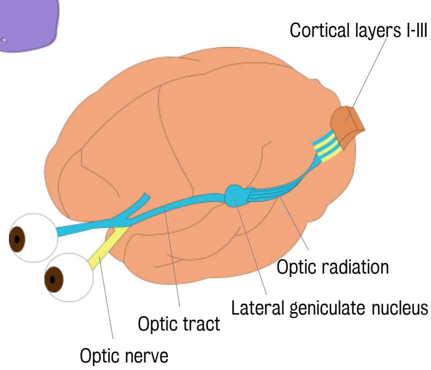
These regions are the best studied and understood due to the following:

1. they receive relatively unprocessed sensory information relayed from the relevant sensory apparatus via few intermediaries.
2. they provide a general model of neocortical function.
3. their structure and function are well understood and they often exhibit visible specialisations that reflect spatial recapitulations of the sensory world.

Zembrzycki et al., 2015

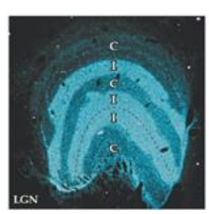
Tracking ocular dominance

Ocular dominance columns exist in the primary visual cortex of most highly binocular mammals.



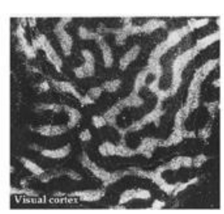
Autoradiographic tracing of functional segregation using trans-synaptic tracers.

Section of LGN



Layers dedicated to contralateral (C) and ipsilateral (I) eye

Above the primary visual cortex



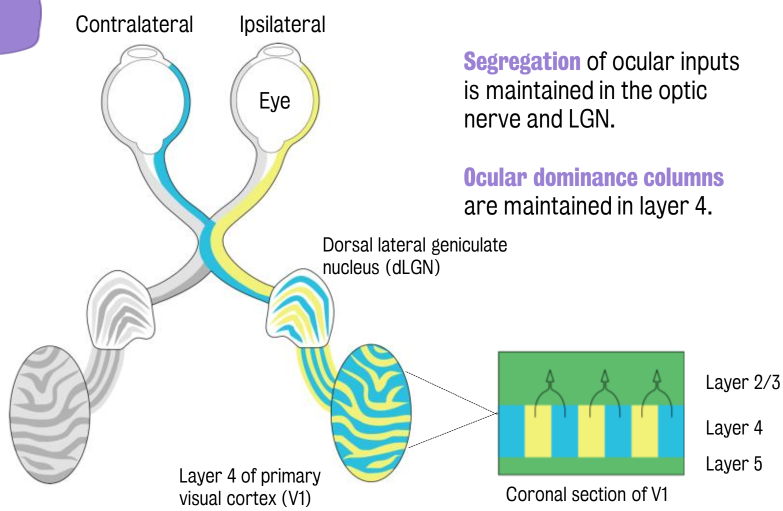
Interdigitated zones dedicated to one eye or the other across layer 4

Transverse view of primary visual cortex

White matter projections; zones restricted to layer 4

Early visual system

The early visual system integrates ocular inputs to form binocular representation.



Segregation of ocular inputs is maintained in the optic nerve and LGN.

Ocular dominance columns are maintained in layer 4.

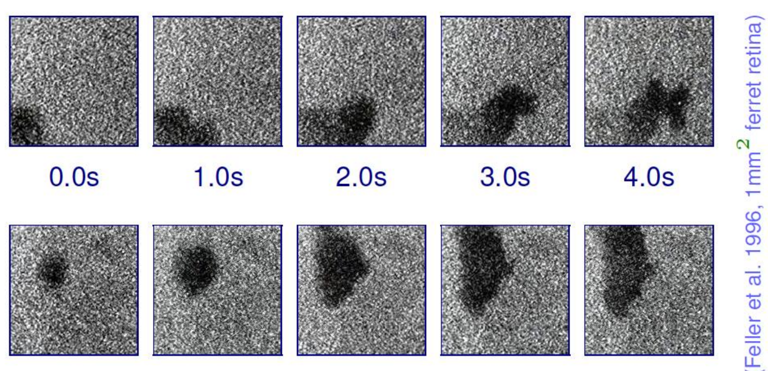
Through Hebbian plasticity:

- segregation into ocular dominance columns occurs in layer 4 of V1
- integration into binocular representations occurs in layer 2/3 of V1

Retinal waves

Does functional segregation arise from genetic programming or does neuronal activity play a critical role in development?

Calcium imaging reveals that retinal neurons produce spontaneous activity and that waves of this activity pass across the retina.



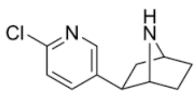
Retinal waves occur before the eyes of many species open.

Feller et al., 1996

Methods to inactivate the retina

What are the consequences of inactivating the retina and preventing the occurrence of this activity prior to eye opening?

Epibatidine

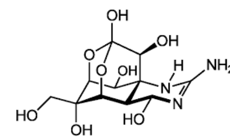


Derived from the poison dart frog

Acetylcholine receptor antagonist

Block neural activity

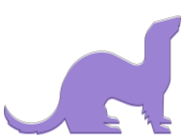
Tetrodotoxin – TTX

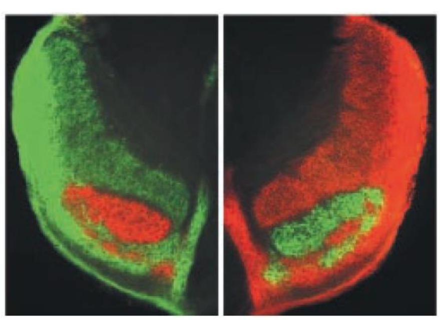


Derived from the pufferfish

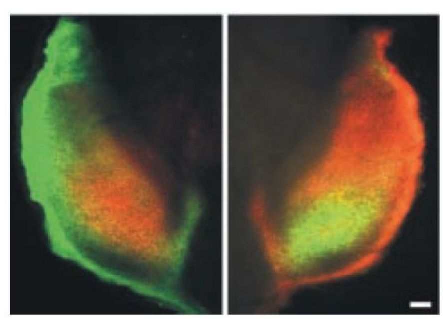
Blocks voltage-gated sodium channels

Binocular inactivation of the retina (ferret)





Normal activity pre-eye-opening (postnatal day 1-10)

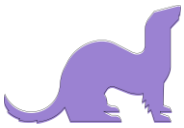


Retina inactivated before eye opening (postnatal day 1-10); epibatidine or TTX

Binocular inactivation of the retina prevents normal LGN segregation of ipsilateral and contralateral zones.

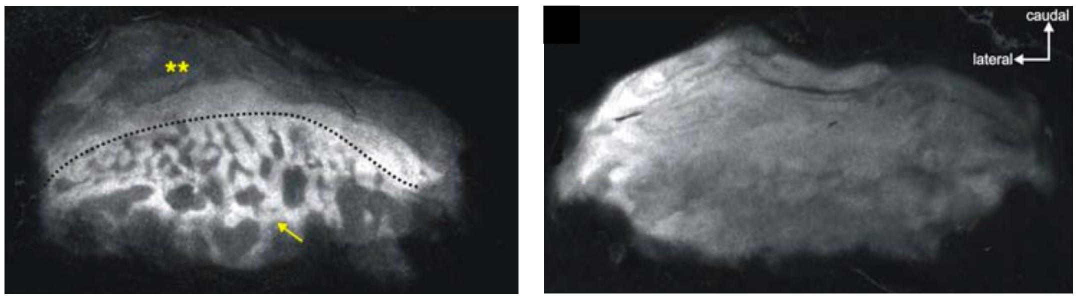
Huberman et al., 2003

Inactivation of the retina (ferret)



Normal activity pre-eye opening (postnatal day 1-10)

Retina inactivated before eye opening (postnatal day 1-10); epibatidine or TTX

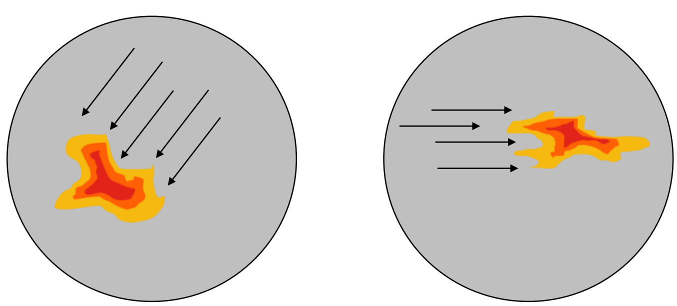


Inactivation of the retina prevents segregation of ocular dominance columns in V1.

Huberman et al., 2006

Spontaneous activity correlation

How does lack of synchronous retinal activity contribute to segregation of ocular dominance layers and columns?

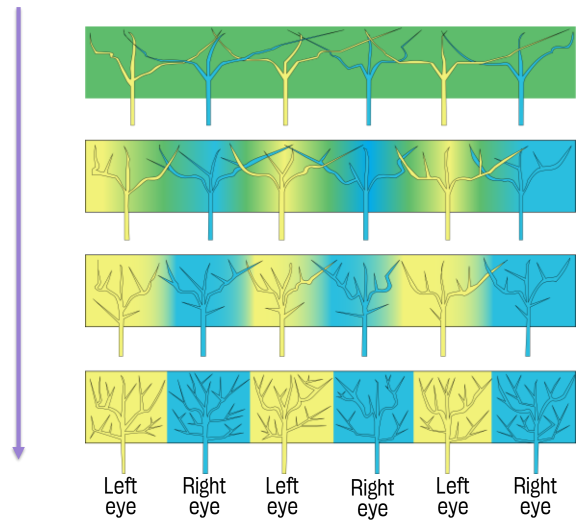


Spontaneous activity is not correlated between the two eyes, forcing Hebbian plasticity to segregate ocular dominance zones.

Hebbian plasticity and columns

How does Hebbian plasticity result in ocular dominance columns?

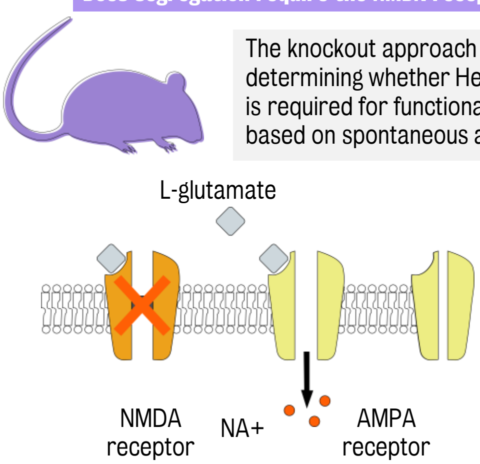
Activity-dependent plasticity prior to eye opening segregates inputs with uncorrelated spontaneous activity



Hebbian plasticity and columns

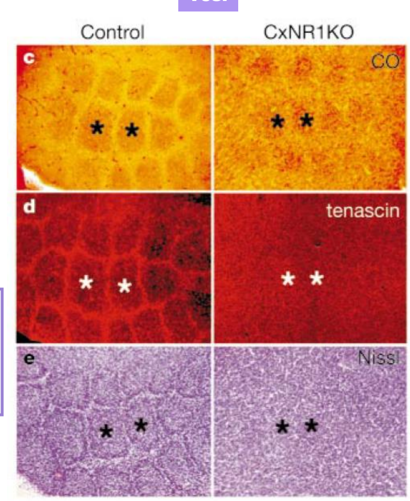
Does segregation require the NMDA receptor in cortical neurons?

The knockout approach is critical in determining whether Hebbian plasticity is required for functional segregation based on spontaneous activity.



Mice that do not express NMDA receptors in the neocortex have severely ill-defined whisker barrels.

Yes.



The requirement for NMDA receptors is further evidence that Hebbian plasticity plays a key role.

Iwasato et al. 2000

Summary

- ocular dominance columns are zones of cortex that only respond to input through one eye or another. They are present in the primary visual cortex of many species (eg cat/human). Functional segregation also exists in the visual thalamus.
- in many species, the eyes open some time after birth, but ocular dominance columns still emerge during this period.
- spontaneous neural activity can be recorded in the retinas prior to eye opening, known as retinal waves. Similar spontaneous activity can be detected in the visual thalamus. Retinal waves are not correlated between the two eyes.
- inactivation of the retinas, to prevent retinal waves, prevents the formation of discrete ocular dominance columns.
- evidence suggests that the blockade of NMDA receptors also prevents segregation of ocular dominance columns in visual cortex and whisker barrels in the somatosensory cortex.
- Hebbian synaptic plasticity is hypothesised to progressively sharpen the boundaries between ocular dominance columns by weakening connections between neurons that are uncorrelated in activity (ie responsive to opposite eyes) and strengthen connections between neurons that are correlated (ie responsive to waves in the same retina).

References

[1] Feller et al. (1996) Requirement for Cholinergic Synaptic Transmission in the Propagation of Spontaneous Retinal Waves. Science. 272 (5265) 1182-1187.

[2] Huberman A. et al. (2003) Eye-specific retinogeniculate segregation independent of normal neuronal activity. Science. 300(5621):994-8.

[3] Huberman A. et al. (2006) Spontaneous retinal activity mediates development of ocular dominance columns and binocular receptive fields in v1. Neuron. 52(2):247-54.

[4] Iwasato T. et al. (2000) Cortex-restricted disruption of NMDAR1 impairs neuronal patterns in the barrel cortex. Nature. 406(6797):726-31.

[5] Zembrzycki A. et al. (2015) Genetic mechanisms control the linear scaling between related cortical primary and higher order sensory areas. Elife. 4. pii: e11416.

End of part 2