• PNS and CNS responses to injury
• Plasticity during early development: ferret re-wired
• Adult neurogenesis
• Somatosensory cortex: Plasticity after nerve, spinal cord, or thalamic injury
• Motor cortex: Plasticity after ischemic injury
• Visual cortex: Topographic plasticity following experimental retinal injury.
• Species differences?
• Topographic plasticity following macula degeneration.
• Human cortical plasticity fMRI: ‘natural experiments’
• Perceptual learning
Three types of nervous system repair or regeneration

A. Peripheral nerve regeneration

B. Repair in CNS at and around site of injury—hypertrophic glia form scar.

C. Neuronal replacement in CNS due to neural stem cells
Dr. Henry Head’s Peripheral Regeneration Experiment

(A) Site of cut
External cutaneous nerve
Site of cut
Superficial radial nerve

(B) Blood vessel

NEUROSCIENCE, Fourth Edition, Figure 25.3

NEUROSCIENCE, Fourth Edition, Figure 25.4

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Molecular and cellular signals promoting peripheral nerve (PNS) regeneration
CNS Repair?

Proximal to injury

Injury to CNS axon

Distal to injury

Oligodendrocytes

Prolonged clearing of myelin debris

Inhibitory factors disrupt axon extension

Astrocytes

(A)

Site of nerve damage

Sciatic nerve graft

Optic nerves

Superior colliculus

Time

NEUROSCIENCE, Fourth Edition, Figure 25.10
Re-innervation of muscles after motor nerve damage
Figure 23.10 Changes to synapses during early postnatal life in the mammalian PNS
Mammalian Adult Neurogenesis

(A) Diagram of the brain showing neurogenesis processes. Key components include:
- Olfactory bulb
- Corpus callosum
- Cerebral cortex
- Cerebellum
- Lateral wall of lateral ventricle
- RMS (rostral migratory stream)
- Proliferating precursors in the anterior subventricular zone

(B) Close-up view of the hippocampus:
- CA1 and CA3 regions
- Molecular layer
- Dentate gyrus
- Hippocampal formation

1. Proliferation
2. Translocation
3. Differentiation

NEUROSCIENCE, Fourth Edition, Figure 25.12
Adult Neurogenesis in goldfish and songbirds

NEUROSCIENCE, Fourth Edition, Figure 25.11

Mouse Anterior Subventricular Zone

Transit amplifying cells: asymmetrical division
Plasticity after Perinatal to Adult Injury:

• **Experimental Models**
  Re-wired ferrets
  Intro to: Peripheral nerve, spinal cord, thalamic, or cortical injury models
  Somatic-sensory plasticity: spinal cord and thalamic injury
  Motor cortex plasticity: stroke and training
  Topographic plasticity following retinal injury cats, mice, monkey, man. Methods and mechanisms
  Unilateral cortical damage and human map plasticity

• **Early Human Damage** (not shown)
  Ischemia, periventricular stroke, infections, teratogens, congenital blindness
‘Re-wired’ Ferret: Sur and colleagues. Ferrets are born very altricial and thus provide a unique opportunity to examine perinatal cortical plasticity.
Ferret Visual Cortex Development: thalamo-cortical pathways

Unilateral deafening of pup combined with unilateral lesion of LGN.

Consequence: Retinal afferents ‘find’ vacant MGN and then synapse. MGN neurons follow normal developmental process to innervate primary auditory cortex, AI.
AI becomes visual cortex. A quasi-topographic map is formed, neurons develop near normal orientation selectivity, and ferrets can use this cortex to make visual discriminations. Re-wired AI develops clustered horizontal connections like normal V1.
• **The behavioural role of retinal projections routed to the auditory pathway.** a, Pathway from the retina to the visual thalamus, including LGN and the lateral posterior nucleus (LP), and to the superior colliculus (SC) in the control hemisphere (right); and to the LGN/LP and medial geniculate nucleus (MGN) in the rewired hemisphere (left).

• **The SC and adjacent brachium (b) of the inferior colliculus (IC) were ablated neonatally in the left hemisphere.**

• **b, Apparatus for experiment 1.** Dashed lines denote the borders of the left and right monocular fields and the direction of central gaze.

• Animals were rewarded at the right spout after a light in the left monocular field, and at the left spout after a sound from a central speaker.

• Subsequently, their responses to light in the centre or the right monocular field were tested. Animals initiated trials by standing in the start box with their muzzle between an infrared LED and a photodiode detector.
Adult Cortical Plasticity

~20 years ago, adult cortex was viewed as static, containing fixed sensory (and motor) maps. Early experiments reinforced the idea of critical periods for cortical development and plasticity after which the resultant cortical maps were largely immutable.

Since then, multiple lines of research have demonstrated a remarkable capacity for cortical reorganization following peripheral nerve injury, focal cortical lesions, as well as resulting from behavioral training (perceptual learning).

Somatosensory cortical plasticity after nerve injury: Merzenich, Kaas, and others.

Somatosensory plasticity following spinal cord injury: Kaas and others

Somatosensory cortical plasticity as a result of training: Merzenick et al

Visual Cortex training: perceptual learning effects: Ungerleider et al.

Visual cortex plasticity after eye damage/removal: Chino and others

As well as numerous studies that examined massive re-organization following perinatal injury and restricted reorganization after adult injury.
Area 3b map re-organization after digit amputation

Area 3b map re-organization after VPL lesion
Long-term re-organization of Somatosensory Thalamus
Thalamic but not Cortical Re-organization
Review: Somatosensory Ascending Pathways
Cortical Organization following Dorsal Column Transection
Possible Mechanisms Underlying Cortical Plasticity after Injury

- Growth factors
- Extracellular matrix
- Neurotransmitters
- Axonal sprouting
- Synaptogenesis
- Unmasking of ‘overlapping’ inputs
- Growth of new pathways?
- Adult neurogenesis?
- ???
Location of area 3b in a macaque monkey brain (left) and outline of the somatotopy (right) in area 3b.

A photomicrograph showing a fluorescent electrode track in a section of the cortex cut tangentially to the surface through area 3b of monkey MCh73.

A–C, Coronal sections of the thalamus through the VP nucleus of monkey MCh75 (A, B) and MCh21 (C) showing electrolytic lesions (arrows) made to help align microelectrode recording results with histological features revealed in sections.


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Black circles indicate sites with response to **light cutaneous touch** on the skin, dotted circles with responses to hairs, open circles with responses to **taps**. Larger circles indicate better responses and smaller circles weaker responses. Triangles mark the sites with weak responses to **hard taps**, making it difficult to define the receptive field with certainty. Multiple dots indicate sites with multiple or split receptive fields. The crosses mark the sites where neurons did not respond to any stimulation. Stars mark the sites where electrolytic lesions were made. D, Dorsal; M, medial; C, caudal.
Locations of all the receptive fields on the face that were recorded for neurons in the reorganized cortex medial to the normal hand–face border in monkey MCh75 (Fig. 4 A).

Photomicrograph of a section of the flattened cortex of monkey MCh75 stained for myelin. The myelin-light septum (arrow) marking the hand–face border is clearly visible. Left and right dotted lines respectively mark the fundus and the lip of the posterior bank of the central sulcus. R, Rostral; M, medial. Scale bar, 2 mm.
Receptive fields of neurons in two penetrations through the posterior bank of the central sulcus in monkey MCh75. The penetrations illustrated here correspond to those marked by the black and the open arrowheads in Figure 4 and use the same color codes. The receptive fields of neurons at the sites marked by letters are shown on the figurines on the left. Note that at many sites the receptive fields split with responses elicited by touch on the hand/arm as well as chin. The receptive fields on the hand are large, often extending over multiple digits, unlike those in normal animals.
The organization of the hand representation in monkey MCh75. No clear somatotopy with distinct borders between digits was found although a lateral to medial D1–D3 trend was present. The white arrow marks the position of the septum that demarcates the hand–face border (Fig. 5). The arrowheads mark the penetrations for which detailed receptive fields are shown in Figure 7.
A, Somatotopy in right area 3b and the bordering cortex in monkey MCh73.

The border marked by the white arrow is the normal hand–face border revealed in sections of the flattened cortex stained for myelin (Fig. 11). Note the expansion of the face-responsive regions into the deafferented hand area.
Somatotopy in the left area 3b and the bordering cortex in monkey MCh21. The white arrow on the top marks the expected location of the normal hand–face border as estimated from the location of the tip of the intra-parietal sulcus (Fig. 15). Note the expansion of the face responsive regions into the deafferented hand, arm and occiput areas.

Receptive fields on the face were also seen in the medial most region intermingled with the leg and the foot representations.

Somatotopy in area 3b of monkey MAc19 before and immediately after lesion of the dorsal columns. A, Cytochrome oxidase-stained section of the flattened cortex through area 3b showing electrolytic microlesions made during the experiment (arrows and double arrow) and some visible electrode tracks (arrowheads). B, A myelin-stained section of the flattened cortex showing the hand–face border (white arrow) and the border between D1 and D2 (blue arrowhead).

C, Locations of neurons with receptive fields on the face, hand and arm encountered in area 3b and the adjacent cortex before lesion of the dorsal columns of the spinal cord, and

(D) immediately after lesion of the contralateral dorsal columns of the spinal cord. Only a few neurons responded to the taps on the hand or arm perhaps because of sparing of some of the dorsal column fibers.
Methods for longitudinal fMRI and cross-model imaging alignment. A, The placement of the topmost (red box) of the four oblique image slices, which covers the cortical region around the central sulcus (CS), is shown on coronal image. B, Field of view of the top oblique image slice is indicated by the red box placed on top of the schematic illustration of the functional organization of somatosensory areas (areas 3a, 3b, and 1) around the CS. LS, Lateral sulcus; STS, superior temporal sulcus.

C, D, T2-weighted structural MRI images obtained from two separate imaging sessions. CS and LS (green lines), surface and trans-cortical veins (black lines and dots) were used as landmarks (red and green arrows) for image alignment.

E, Corresponding blood vessel map of the image field of view obtained from the same animal. Corresponding alignment landmarks are also shown. This blood vessel map was used for both optical imaging (OIS) and electrophysiology experiments. a, Anterior; l, lateral; m, medial; p, posterior.
Longitudinal fMRI mapping of digit activations to tactile stimulus before and after unilateral partial dorsal column lesion in monkey SM-O. A–F, fMRI activations of the individual digits D1–D5 in response to tactile stimulation before the lesion and a color-coded composite map of all five digit activations. Dotted line in F indicates the approximate border between area 3b and area 1. G–L, fMRI activations of the individual digits D1–D5 and a composite map of all five digits at 4 weeks after lesion. M–R, fMRI activations at 8 weeks after lesion. S, Plot of activation center shifts (in millimeters) of each digit as a function of time after lesion.

Longitudinal fMRI mapping of digit activations to tactile stimulus before and after unilateral partial dorsal column lesion in monkey SM-C.

Longitudinal fMRI mapping of digit activations to tactile stimulus before and after unilateral partial dorsal column lesion in monkey SM-R.
Spatial correspondence of fMRI, OI, and electrophysiology maps of digit activation after dorsal column lesion in contralateral and ipsilateral areas 3b and 1 in monkeys SM-O and SM-D. A, E, Overlay of pre-lesion fMRI and post-lesion electrophysiology maps of digits. Color outlines indicate location and size of fMRI activations, whereas color patches present location and size of neuronal responses. B, F, Spatial comparison of post-lesion fMRI and post-lesion electrophysiology digit maps. C, G, Spatial comparison of post-lesion OI and post-lesion electrophysiology digit maps. D, H, Overlay of electrophysiology maps of digits D1–D4 in the ipsilateral area 3b and area 1 of the same animals.

Schematic summary of dynamic functional reorganization of digit representations in area 3b after dorsal column section. Different color patches indicate the locations and relative sizes of fMRI activations to tactile stimulation of distal finger tips in pre-lesion (left column), 4 weeks after lesion (left middle column), and 8 weeks after lesion (right middle column). Red dots indicate the centers of pre-lesion digit activation centers. Dotted black lines indicate the center line of digit activations before lesion. Arrows represent the trends of activation shifts. Orange patches (right column) show the digit representation regions identified with neuronal firing properties. Black dots indicate the microelectrode penetration sites.
Figure 5. Neuron response properties and somatotopic representations in area 3b after task-specific recovery from DCLs show similarities to normal. (A) Area 3b somatotopic organization based on receptive field mapping from multielectrode arrays (Blackrock Microsystems) for a normal monkey (left), a monkey with an incomplete lesion (middle), and a monkey with a nearly complete lesion (right). Dashed lines indicate estimated borders of area 3b based on receptive fields and histological reconstructions of flattened cortex sections. Representations of the dorsal hand are not specified, but receptive fields representing multiple hand or arm locations are indicated with gradient shading (Mixed receptive fields [RFs]).

Expected somatotopic organization is found after task-specific recovery from an incomplete lesion (middle) at C6 that preserved many of the afferents from digits 1 and 2. Digits 1 and 2 appear to be represented in more territory than digits 3–5, and responsive regions include mixed RFs.

After task-specific recovery from a nearly complete lesion (right) at C4, more regions of area 3b were unresponsive to touch on the hand (X) or weakly responsive (open circles), but reactivated cortex was largely somatotopically organized.

(B) Peristimulus time histograms (PSTH) of example neuronal activity in (contralateral) area 3b indicates responsiveness to tactile stimulation on digit 3 in cases without lesion (left), with incomplete lesion (middle), and nearly complete lesion (right). A red dot on each map in (A) marks the electrode location from which an example neuron in (B) was recorded. In (B), gray arrows mark the stimulus onset, and gray shading indicates stimulus duration in each trial (500 ms in the case with no lesion, 400 ms in the cases with lesions). Modified from Reed et al70 and Qi et al.19,69
Figure 6. Summary of differences before and after incomplete DCLs for different measures reflecting plasticity. All panels show schematics representing measures without lesions (pre-lesion, left), shortly after incomplete lesion (immediate, post-lesion, middle), and several weeks after incomplete lesion (~6 weeks, post-lesion, right). (A) Representative neuronal activities are shown to indicate decreased responsiveness shortly after lesion and recovery to near-normal levels over time. Conventions follow Figure 5.

(B) Schematics of area 3b cortical activation depict inactivation immediately after the lesion deprives the cortex of normal driving activity (gray hatching). The extent of cortical reactivation can vary based on characteristics of the lesion and other factors; when the lesion is incomplete responsiveness can return, but may be weaker (light shading). Representations may also show abnormal organization (multicolored hatching).

(C) Graphics of the movement to reach (gray) and grasp (black) a sugar pellet from a well depict impairment of performance on the reach-to-grasp task shortly after lesion and recovery of performance over time. (D) Drawings of coronal sections of cervical spinal cord before and after lesion (black) depict lack of spontaneous improvement of the lesion over several weeks. (E) Simplified schematic summarizes differences in measures relative to normal over time before and after incomplete lesion. Lines correspond to the color of the boxes shown for each of the panels (A–D). Lines would overlap, but are separated for visualization.

The spinal cord does not heal structurally after a DC lesion (red); however, functional improvements can be measured that indicate plasticity outside of the DCs underlies recovery to near-normal levels several weeks after incomplete DCL.
Adult Motor Plasticity

Motor Cortex plasticity following stroke: (Nudo et al.)

Focal infarct in M1 cortex produces a immediate loss of (hand) representation and subsequent shrinkage of adjacent hand representations.

Restraining of the ‘good’ hand prevented the loss of hand movement representation surrounding infarct.

The ‘lost’ hand movement representation also expanded into the adjacent cortex, previously represented movements of the elbow and shoulder.

Rehabilitation training also resulted in expansion of supplemental motor field representations. (new cortical connections also revealed).
Mechanisms of Adult Motor Cortex Plasticity

- Contralesional forelimb deficits in motor performance
- Ipsilesional forelimb altered motor performance (hyper-reliance in rats; deficits in humans)
Mechanisms of Adult Motor Cortex Plasticity

**Ipsilateral effects**
- Decreased dendritic branching
- Decreased spine density
- Increased dendritic branching
- Neural sprouting
- **Synaptogenesis**
- GABA$_A$ receptor downregulation
- NMDA receptor enhancement
- Neuronal hyperexcitability
- Facilitation of LTP
- Alteration of motor maps

**Contralateral effects**
- Increased cortical thickness
- Dendritic growth (up to day 18 post-lesion)
- Dendritic elimination (after day 18 post-lesion)
- Increased spine density (after day 18 post-lesion)
- **Synaptogenesis** (after day 18 post-lesion)
- GABA$_A$ receptor downregulation
- NMDA receptor enhancement
- Neuronal hyperexcitability

[Diagram of brain showing lesion core, perilesional region, and remote regions]
Adult Motor Cortex Plasticity:
Nudo et al.
Representation of distal forelimb representations in motor cortex after digit skill training as defined by intracortical microstimulation. Digit areas (red) expand after only 12 days of training.

Combination movements that reflect the individual kinematics that the monkey employs also expand their representations. (A) Pre-training map. (B) Post-training map. (C) Still images of squirrel monkey retrieving food pellets from small wells (Nudo et al., 1996a)
Differential effects of skill vs. use.

(A) ICMS-derived motor map (digit, red; wrist, green; elbow/shoulder, light blue) of a rat that learned a skilled reaching movement.

(B) ICMS-derived motor map of a rat that learned to press a bar. The two forelimb areas are outlined in white. The caudal forelimb area (CFA) is separated from the rostral forelimb area (RFA) by a band of head/neck representations (yellow). The hindlimb area (HLA) is shown in dark blue and nonresponsive sites in gray.

(C) Note the enlarged digit and wrist/forearm representations in the skilled reaching condition (SRC), and enlarged shoulder representation in the unskilled reaching condition (URC, bar press).

(D) In the CFA, synapses per neuron were significantly increased (*p < 0.05), but no changes occurred in RFA or HLA (Kleim et al., 2002a).
FIGURE 5| Functional map changes in forelimb (sFL) and hindlimb (sHL) somatosensory cortex after a focal infarct in mouse. Thalamic projections (arrows) and intracortical connections (double arrows) are also shown. (A) Normal somatosensory representation of sFL and sHL. (B) Within hours after focal infarct (gray), yellow areas show reduced sensory specificity, responding to both FL and HL stimulation. (C) Over the ensuing weeks, growth-promoting processes are triggered. Local axonal sprouting (double-headed arrows), dendritic spine expansion, and synaptogenesis occurs in the peri-infarct cortex. (D) Several weeks after stroke, specificity in sensory responses returns. Neurons that were formerly responsive to stimulation of hindlimb become responsive to forelimb stimulation (Murphy and Corbett, 2009).
Rewiring of corticocortical connections after ischemic infarct. (A) In normal healthy squirrel monkeys, the primary motor cortex (M1) has dense reciprocal connections with both the premotor cortex (PMv, PMd, SMA) as well as the primary somatosensory cortex (S1) and the second somatosensory area (S2). (B) In addition to M1, the ventral premotor cortex (PMv) has dense connections with a rostral area called pre-PMv. PMv has moderate connections with S2, but negligible connections with S1. (C) Several weeks after an ischemic infarct in M1, axons originating in PMv can be seen making sharp bends and avoiding the infarct area. (D) A low-magnification plot of axons within the section show that the axons originating from PMv course around the central sulcus. Substantial terminal bouton labeling (not shown) appears in S1 (areas 1 and 2). The blue line in (B) signifies the de novo pathway that forms after the lesion (Dancause et al., 2005).
Adult Visual Cortex Plasticity

Since somatosensory cortex can undergo large-scale topographic plasticity, is this a general feature of sensory cortex?

Mixed results:
Small, corresponding binocular retinal lesions in adults generally fail to reveal shifts of topographic maps into deafferented cortex. (cat, monkey, and human).

Unilateral enucleation combined with unilateral retinal lesions can reveal ‘filling-in’ of deafferented cortical field. (cat)

Conclusions: V1 may be unique in that binocular correspondence rules may limit the extent to which thalamocortical arbors and/or horizontal excitatory connections may spread into deafferented cortex.
Overview of hierarchy of plastic re-organization with retinal injury (Darian-Smith and Gilbert 1995)

Figure 1. Summary diagram of possible steps at which changes may occur along the visual pathway. Alterations in the cortical topographic map could, in theory, originate at the level of the retina, via the extension (or sprouting) of retinogeniculate projections (A), within the LGN as a result of lateral connections within that nucleus (B), in the cortex as a result of the spread (or sprouting) of thalamocortical arbors (C), through long-range horizontal connections formed by cortical pyramidal cells (D), or feedback connections from other cortical areas, such as area 18 (E).
Cortical not sub-cortical re-organization!

Figure 2. A. RF maps for cat #4 pre-lesion, immediately after lesioning, and several months later; and B. RFs for LGN of the same animal, 3 months postlesion. Insets in A show the dorsal view of the lateral gyrus of the cat’s visual cortex, with the circles representing electrode penetrations (recording sites) in visually responsive cortex (open circles) and unresponsive cortex (filled circles). These indicate that the silent region had shrunk from 7.5 mm along the anteroposterior axis immediately postlesion to 2 mm 3 months later. The gray rectangles represent RF sizes, orientations, and positions at each recording site. At each stage of recovery recordings were made at the same or similar sites, using cortical vasculature and dural landmarks as fiducial references. In the 3 month recovery recordings, RFs mapped at many cortical sites had shifted from positions within the zone of the scotoma to positions immediately outside it, as indicated by the arrows. Scale marker = 1°. B. Recording sites in LGN (left), made after cortical reorganization, are superimposed on a dorsal view reconstruction of the LGN. The Horseley-Clarke coordinates are shown. Open circles mark penetrations in visually responsive sites, and filled circles indicate penetrations along which significant stretches of visually unresponsive LGN were observed. The diameter of the visually unresponsive area was 1–1.5 mm, which approximates the normal representation of the lesioned retina. RFs mapped along these penetrations indicated a normal progression within the visual field, with no “bunching up” of RFs near the boundary of the lesion, and no significant change in the size of the RFs. For penetrations where RF positions could be mapped either side of the scotoma, visually unresponsive zones were encountered which extended for 1–1.5 mm. Scale marker = 1°.
Lack of LGN re-organization, but emergence of cortical responses, in deafferented cortex.
Receptive field shifts in the striate cortex

A Day #1-pre retinal lesion + 1 year

B Day #1-pre retinal lesion + 26 weeks

LF

RF
Figure 1 Intrinsic-signal imaging of the LPZ in mouse visual cortex after focal retinal lesions. (a) Layout of drifting grating stimuli (6 4 grid design subtending 90 60 degrees of visual space) used for mapping responses in the visual cortex. (b) Individual activity maps showing responses (dark patches) to moving gratings at different stimulus positions corresponding to the layout in (a)

Keck et al, 2008
Figure 2 Intrinsic imaging of functional recovery in mouse visual cortex after focal retinal lesions. (a–d) Repeated retinotopic mapping in two mice (a,c) on different days after induction of a focal retinal lesion that was induced on day 0. Cortical regions that were initially unresponsive to visual stimulation (white outline) progressively regained responsiveness. Note that the animal presented in a was mapped with a 7 x3 stimulus grid.
Figure 3 Structural reorganization in the visual cortex following retinal lesions. (a) Time line schematic of experimental protocol. (b) Apical dendritic stretch of a layer 5 pyramidal neuron from a mouse with a small retinal lesion imaged repeatedly over more than 2 months. Arrows point to positions of new (gray), disappearing (yellow) and stable spines (cyan). Filled and open arrows indicate present and absent spines, respectively. For clarity, axonal processes from other cells crossing the dendrite have been removed in these images. Scale bar represents 5 mm. (c) Spine turnover rate for different groups of mice. Note the strong and transient increase in spine turnover rate for cells located in the center of the LPZ (center of LPZ, early and middle time points compared with control,
Figure 4 Increased spine dynamics reflect functional reorganization. (a) Absence of visually evoked responses in the visual cortex of a mouse with complete binocular retinal lesions. Scale bar represents 300 mm. (b) Apical dendritic stretch of a layer 5 pyramidal neuron from a mouse with a complete retinal lesion imaged repeatedly over more than 2 months. Arrows indicate positions of new (gray), disappearing (yellow) and stable spines (cyan). Filled and open arrows indicate present and absent spines, respectively.
Figure 5 Number of new persistent spines increases with functional recovery.

(a) Examples of layer5 cell apical dendritic stretches with newly appearing persistent spines. Cyan arrows indicate stable spines and gray arrows indicate new persistent spines. Scale bars represent 2 mm.

(b) The number of new persistent spines as a fraction of spines initially present:
Dynamics and specificity of cortical map reorganization after retinal lesions Dimitrios et al. 2006

Fig. 1. Retinal lesions, RF topography, and single cell responses 4 weeks after lesion. (A) Fundus photographs of the left and right eyes of a cat with homonymous photo-coagulator lesions of 10° diameter centered to the area centralis in both eyes. (B) Tangential recordings along the medial bank and sample recording sites (1–12) 4 weeks after lesion. Dashed lines indicate the borders of the LPZ as determined for 10°-diameter lesions with zif268 in situ hybridization. (C) RF map of units recorded from B. Retinal lesion is shown in gray. Units recorded in the LPZ have ectopic RFs at the retinal lesion border. (D) Polar diagrams and post-stimulus time for selected units (stimulus onset at 500 ms). Is, impulses/s.
Fig. 2. RF positions and recording probability in control and lesioned animals. (A) Eccentricity of RF positions in the visual field from one control animal (black diamonds) and all experimental animals at 2 (blue square), 4 (green triangle), and 12 (red circle) weeks, and 1 year (magenta triangle) plotted in dependence of recording distance along the medial bank. The intersection between the regression lines indicates the border between LPZ and normal cortex.

(B) The probability of recording spiking cells from positions separated by 150–300 m within each 1 mm along the medial bank is shown for control, the 2-, 4-, and 12-week, and 1-year animals. All symbols and colors are as in A.
Fig. 3. Maintained and evoked activity in the LPZ at different recovery times. (A) **Maintained activity** in different zones of the LPZ. C, deafferented center; P, activity peak; B, border region; S, surround. Controls recorded at corresponding eccentricities and results from different survival times are shown. Error bars are SEM. Asterisks indicate significant deviations from the normal surround (P0.05). Is, impulses/s.

(B) Normalized maintained activity as a function of increasing recording distance along the medial bank (see Fig. 1B). **A peak of maintained activity is found progressively inside the LPZ at 2 and 4 weeks.** Color-coded dots indicate points where activity was significantly higher or lower compared with normal surround at respective survival times (P0.05).

(C) Normalized maximal response to a drifting grating of preferred orientation and direction of motion. Normalization, color coding, and symbols are as in B. Color-coded arrows indicate the **position of the first well defined RFs for different survival times.**
Fig. 4. Degree and limits of RF width and orientation tuning recovery. (A) RF widths from all recovery periods compared with normal RF widths recorded at corresponding eccentricities in control animals. Recording distance is defined as in Fig. 3B. Statistically significant differences at the 5% level are indicated by *; indicates significant differences of RFs in the LPZ from those in the normal surround at each given survival time (color coding is as in Figs. 2 and 3). Error bars are SEM. (B) Orientation tuning half-width with increasing recording distance along the medial bank and eccentricity in the visual field.
Rapid Axonal Sprouting and Pruning Accompany Functional Reorganization in Primary Visual Cortex

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Figure 3. Axonal Dynamics in LPZ

(A) Axonal tracing of Z stacks acquired through a depth of 200 mm. **Gray**, axon segments that remained unchanged compared to the previous time point; **yellow**, segments that were added; **red**, segments eliminated. Last panel shows the axons present at the end of the imaging session.

(B) Axon density (axonal length per unit of volume) for axons that had been added (yellow), pruned (red), and remained unchanged (gray) since the preceding imaging section. The total axonal density is shown in black.

(C) Axonal survival fraction. Axonal length still present from the initial axonal population (7 days) as a fraction of the total initial length.
Figure 4. Axon Pruning Modes and Bouton Turnover in LPZ (A) An axon branch previously shown in Figure 2 (arrow) present before (7 days) and after the lesion (0.25 day, imaged 4:30 to 9 hr post lesion) undergoes degeneration by 14 days. Note the beading and swelling (*) and detachment of portions of axonal shaft (arrowhead). By 28 days, remnants of the segment were no longer detected. (B) Retraction of a terminal branch (arrow) is shown in a segment from 0.25–35 days. (C) An axon segment showing an increase in bouton density immediately after the lesion (four white arrows) and two being eliminated (yellow arrowheads). (D) Bouton density.
Figure 5. Axonal Dynamics in Peri-LPZ (MA and MB) (A) Axonal tracing of Z stacks from MA acquired through a depth of 100 mm. (B) MB, description as in (A). (C) Axon density represented as axonal length per unit of volume from MB. Axon addition (yellow) and elimination (red) occurred at similar rates, resulting in a stable overall axon density (black).
**Figure 1 | Homonymous retinal lesions.** a, Left, picture of the right eye fundus 1–2 h after photocoagulation. The lesion appears pale white. Right, right eye cup after extraction and fixation. The lesion (white arrowhead) is scarred and hyperpigmented.
b, Top, haematoxylin–eosin stain of a section 15 mm thick through the right eye lesion in a. **Note the complete destruction of the photoreceptor layer, as well as the nearly complete obliteration of ganglion and inner nuclear cell layers.** Bottom left and right, edges of the haematoxylin-eosin stained section at higher magnification. c, Left, picture of the left eye fundus 1–2 h after photocoagulation. Right, overlay of the right and left fundi. Lesions are marked by white arrowheads. The left retina (smaller square overlay) was mirrored along the vertical axis and scaled to make the optic nerves overlap. **Black dots outline the left eye lesion and its homonymous location in the right eye, which lies almost entirely over the right eye lesion except for a small sliver of normal retina (black arrowhead).** This results in a partly homonymous left visual field scotoma.
d, **Eyes were stimulated separately with the full-field checkerboard stimulus** (see Methods) and activation maps (voxels with $P < 0.05$, uncorrected, cluster criterion 6) were overlaid on the right operculum of monkey O97 by using Brain Voyager (Brain Innovation B.V., Maastricht, The Netherlands).

Areas are coloured as follows: yellow, activation through the right eye; red, activation through the left eye; orange, activation map overlap; blue, no visual modulation through either eye. The dotted line marks the segment of the right-eye-LPZ border, where reorganization is expected to be maximal. This is the part of the right-eye-LPZ border that also belongs to the border of the binocular LPZ. The yellow region abutting the LPZ is the projection zone of the sliver of normal retina marked with the black arrowhead in (c, right).
Figure 2 | BOLD signal inside the LPZ remains at noise level and LPZ size does not change as a function of time after lesioning. a, Coherence map on the right operculum measured with the expanding-ring stimulus (see Methods) presented to the right eye of macaque E02 4 months after lesioning. The green area is the LPZ, a zone of low coherence surrounded by normal cortex. Note that noise level coherence is expected to be 0.28 and not zero (see Methods).

b, A cortical area of radius 3 cm centred near the fovea was flattened and the coherence map was overlaid. The monkey operculum is outlined by the calcarine, lunate and inferior occipital sulci. Regions of low coherence outside the operculum correspond to non-visual cortex or visual cortex too eccentric to be activated by our stimuli.

LPZ borders are shown at 0 days (LPZ0, black), 4 months (LPZ4, cyan) and 7.5 months (LPZ7, blue) after lesioning. LPZ size was, respectively, 158, 179 and 180mm\(^2\) and was larger, if anything, at later time points. Because the LPZ perimeter is about 50mm this corresponds approximately to an 0.5-mm outward shift of the LPZ border (within noise). A threshold coherence level of 0.4, 1 s.d. above noise level, was used to define the LPZ border at all time points.

c–e, Signal in LPZ0 recorded 7.5 months after lesioning.

c, Percentage modulation of the BOLD signal as a function of stimulus cycles. d, Average signal modulation per stimulus cycle (11 rings). e, Signal amplitude as a function of temporal frequency. Red marks the frequency of the visual stimulus. Note that the signal amplitude at the stimulus frequency does not differ significantly from the amplitude of noise present at other frequencies (P > 0.05). There is therefore no significant stimulus-driven modulation inside the LPZ0 even 7.5 months after lesioning.

f–h, Plots corresponding to c–e for a region of normal V1 cortex at similar eccentricity to that of the LPZ. Strong visual modulation is evident in all plots. IOS, inferior occipital sulcus; MT, middle temporal area. Error bars represent s.e.m.
Figure 3 | The profile of BOLD coherence across the LPZ border does not change as a function of time after lesioning. a, Flattened map of the right operculum of macaque E02 with coherence map overlaid, as in Fig. 2. A set of linear ROIs 0.5–1.0-mm thick, parallel to the LPZ border, was selected to span several millimetres on each side of the border. The white line represents the first ROI located inside the scotoma. ROIs are selected once on the anatomical scan and remain the same for all time points. They therefore provide an absolute, time-invariant, reference frame that can be used to gauge whether the profile of functional activity shifts over time.

b, Monkey E02, full-field stimulation paradigm. The mean coherence of each linear ROI is plotted against the mean distance of that ROI’s voxels from the line of zero displacement (represented by the dotted lines at point zero).

c, Equivalent plots to those in b for each monkey (from left to right: E02, A01, O97 and E01). Top row, retinotopic stimulation paradigm; bottom row, full-field stimulation paradigm. Error bars represent s.e.m. There is no consistent shift in position or change in slope of the coherence–distance curve over time (see also Supplementary Fig. 2). The position of the LPZ border is stable to within 1 mm. IOS, inferior occipital sulcus; MT, middle temporal area.
Figure 4 | Receptive field maps cannot be obtained and steady-state neural responses remain abnormal inside the LPZ. 

a, Coherence map overlaid on the flattened right operculum of monkey E02. Each linear trajectory (white, yellow and blue) represents 16 electrode locations from 1 of 3 experiments. Electrodes were 1 mm apart, starting near the lunate (electrode 1). Black arrowheads mark the last position yielding a multi-unit RF. Blue, yellow and white arrowheads mark the last position whose steady-state multi-unit activity was modulated more than 10% by the full-field stimulus. 
b, Multi-unit RF maps: RFs could not be mapped with spatially restricted stimuli beyond electrode 1 (experiment 1, data not shown), 7 (experiment 2) and 8 (experiment 3). RF location is accurate to 1–28 because of slow eye drifts. 
c, Multi-unit firing rate histograms averaging 48 cycles of full-field visual stimulation alternating with spatially uniform background intensity (electrode 3 inset). Multi-unit activity at steady state is higher during stimulation for electrodes 2–10 (outside the LPZ), but not for electrodes 11–16 (inside the LPZ). Electrode 10 falls on the BOLD-defined LPZ border. 

Brief ON and OFF firing transients persist inside the LPZ (11–16). These may arise through extra-classical receptive field? Transients arising in electrodes with good RF maps (electrodes 2–8) had a mean latency of 68±4 ms compared with 93±16 ms for electrodes near or inside the LPZ border (electrodes 9–16). 
d, Steady-state firing rate (blue) and coherence (red) modulation curves as a function of distance from the BOLD-defined LPZ border. Inside the LPZ the average event-rate modulation strength was 1.3%, with 95% confidence limits from 22.7 to 5.3%.
Figure 1 | ocular dominance columns and visual field map in primary visual cortex (V1). a | A medial view of the posterior right hemisphere of a postmortem human brain. Human V1 is located principally in the calcarine sulcus (CS), although its full extent frequently reaches the occipital pole on the ventrolateral surface. b | The white and grey matter surface measured using MRI in a living subject. c | Part of a flattened postmortem brain from a subject with an enucleated left eye, showing the right calcarine and surrounding cortex. The cytochrome oxidase staining forms light and dark bands that reveal the ocular dominance columns. The dark spot (arrow) is the projection zone from the left eye’s blind spot (optic disk). d | Calcarine and surrounding cortex computationally flattened from the structural MRI-derived surface mesh. The colour overlays identify the stimulus angle (left) or eccentricity (right) that most effectively stimulates each cortical location (measured using functional MRI). Angle and eccentricity (up to 12° from the fovea) are measured with respect to fixation.
Primary visual cortex (V1) neurons receive diverse inputs. a | A V1 neuron can receive input from the lateral geniculate nucleus (LGN), extrastriate cortex (V2, V3, middle temporal (MT) and other extrastriate sources), lateral connections between V1 neurons, and the pulvinar. In healthy V1, the reported receptive field (RF) size can vary fourfold depending on the nature of the mapping stimulus. b | The different inputs to V1 neurons have a wide range of RF sizes. The RF size of centre-surround LGN inputs (left) is small compared with the RF size of extrastriate sources (right). Extrastriate sources have RF sizes that vary and can be larger than 5° in diameter. V1 neurons can also receive input from other V1 neurons with RF centres separated by a degree or more. The variations in estimated RF size of V1 neurons probably result from different contributions from the pathways that deliver the input signals to the V1 neuron. c | From the V1 visual field map, it is possible to express estimates of the RF centre radius on the cortical surface. The radius of V1 RFs is often larger than 3 mm, and more than 10% of the neurons have a radius exceeding 5 mm. The surround influence generally extends beyond 7 mm.
Functional MRI responses in a subject with juvenile macular degeneration (JMD) (left) and a control (right). The JMD subject has a large central scotoma and spared vision in the lower peripheral field; the responses from the control subject were measured with a similar ‘artificial’ scotoma.

In the passive condition subjects passively viewed a visual stimulus presented in the peripheral visual field near the lower vertical meridian. In both subjects this produced a modest response in the anterior calcarine at the location corresponding to the position of the stimulus in the peripheral visual field (upper images; arrows).

In the active condition subjects were asked to remember the visual stimulus from trial to trial (lower images). In this condition, responses in the calcarine sulcus of the JMD subject spread significantly towards the occipital pole, and responses increased in other regions, such as the ventral surface.

In the control subject there was no significant expansion of the blood oxygen level-dependent signal towards the posterior calcarine sulcus. The colour bar indicates the amplitude of the blood oxygen level-dependent response (percent modulation), either in synchrony (red) or out of synchrony (blue) with the stimulus. Only modulations exceeding 0.3% coherence are shown.
The expected effect of retinal lesions on V1 responses. a | This schematic illustrates the diverse receptive fields of neurons expected to be found within a region of V1. b | The same receptive fields are shown with a transparent blue rectangle that indicates the lesion projection zone (LPZ) — the portion of the visual field that is blinded by a simulated retinal lesion. The retinal lesion is located in the centre of the receptive fields that are sampled from this part of the cortex. The effect of the retinal lesion is a reduction in the number of responsive neurons within the LPZ. Assuming that there is no cortical plasticity, we still expect some cells to continue to respond to signals placed on adjacent regions of spared retina (red circles). Such neurons will necessarily have receptive fields that are displaced (ectopic) from their pre-lesion position. There are fewer responsive neurons inside the LPZ post-lesion than pre-lesion, presumably because neurons with small receptive fields are silenced. Such data should be construed as supporting adult cortical plasticity only if the reduction in the number of responsive cells, and the change in the properties of the ectopic receptive fields, differs significantly from a model that assumes no plasticity.
Plasticity following macula degeneration

MD8

A) Diagram showing fovea and blind field with PRL and non-PRL regions.

B) Bar graph showing % signal change for PRL, nonPRL, and fovea.

C) Graph showing % signal change over time from block onset (seconds).
Plasticity following macula degeneration

MD1

A)

B)

C)

% signal change

PRL

nonPRL

stimulus > blank

blank > stimulus

PRL

nonPRL

% signal change

time from block onset (seconds)
Adult Visual Cortex Plasticity

Since somatosensory cortex can undergo large-scale topographic plasticity, is this a general feature of sensory cortex?

**Mixed results:**
Small, corresponding **binocular retinal lesions** in adults generally fail to reveal shifts of topographic maps into deafferented cortex. (cat, monkey, and human).

**Unilateral enucleation combined with unilateral retinal lesions** can reveal ‘filling-in’ of deafferented cortical field. (cat)

**Conclusions:** V1 may be unique in that binocular correspondence rules may limit the extent to which thalamocortical arbors and/or horizontal excitatory connections may spread into deafferented cortex.

OR…..
Figure 2. Polar angle retinotopy for C1. A, E, Color-coded polar angle maps from the left (A) and right (E) hemispheres displayed on partially inflated (left) and spherical (right) cortical surface models (posterior pole: white star). Visual area boundaries are marked by representations of the horizontal (dotted white) and vertical (solid white) meridian representations. B, F, Functional field maps depicting a back-projection of the retinotopic maps from the left (B) and right (F) hemispheres onto maps of C1’s visual field. Each circle in the FFMap is associated with a voxel in the brain that was maximally activated by a stimulus at the symbol’s location in the visual field. The color of the symbols is as for A and E. C, G, Polar histograms depicting the amount (in cubic millimeters) of brain tissue (voxels) in the left (C) and right (G) hemispheres representing different angular positions in the visual field of C1 (gray shading) and averaged for all healthy controls (light blue shading, dotted lines show SEM). D, H, Bar graphs depicting the total amount of tissue representing each visual hemifield in the left (D) and right (H) hemispheres of C1 (gray shading) and averaged for all healthy controls (light blue shading; error bars indicate SEM). L, Left; R, right; RH, right hemisphere; LH, left hemisphere.
Eccentricity maps for healthy control (C1).


**Figure 3.** Eccentricity maps for healthy control (C1). Color-coded eccentricity maps from the left (top) and right (bottom) hemispheres of C1 displayed on spherical cortical surface models (posterior pole: white star). Visual area boundaries are as in Figure 2, A and E. RH, Right hemisphere; LH, left hemisphere.
Figure 4. Polar angle retinotopy for patient with surgical ablation of epileptic focus in right hemisphere (P1). A–H, Figure layout is the same as in Figure 2, with the following exceptions. A, Black dashed outlines indicate approximate location of expanded ipsilateral representation. B, Black dashed outlines highlight inset showing expanded ipsilateral representation especially near fovea. B, F, Blue dashed outlines encircle the regions corresponding with the visual field perimetry in Figure 5B. E, Dark shading indicates regions of brain damage. Location of V1 in the right hemisphere was estimated by fundus of calcarine sulcus. RH, Right hemisphere; LH, left hemisphere.
Figure 5. Eccentricity maps and perimetry for P1. A, Figure panel layout is the same as in Figure 3, except that the black dashed outline and visual area boundaries are as in Figure 4A, E. B, VAP 10-2 test (based on the Humphrey 10-2 perimetry) performed binocularly (both eyes together). Gray scale indicates the relative visual sensitivity from 0 to 1. Blue dashed outline encircles the region corresponding with the FFMaps in Figure 4, B and F. L, Left field; R, right field; S, superior field; I, inferior field; RH, right hemisphere; LH, left hemisphere.
Figure 6. Polar angle retinotopy for patient with congenital cerebral malformation (P2). A–H, Figure layout is the same as in Figure 2, with the following exceptions. A, Black dashed outlines indicate the approximate location of expanded ipsilateral representation. B, Black dashed outlines highlight inset showing expanded ipsilateral representation especially near fovea. B, F, Blue dashed outlines encircle the regions corresponding with the visual field perimetry in Figure 7B. RH, Right hemisphere; LH, left hemisphere.
Eccentricity maps and microperimetry for P2.

Figure 7. Eccentricity maps and microperimetry for P2. A, Figure panel layout is the same as in Figure 3, except that the black dashed outline and visual area boundaries are as in Figure 6A, E. B, Monocular microperimetry plots (LE, left eye; RE, right eye) based on HFA modified 10-2 test presented with an OPKO microperimeter. The color scale for perimetry test points indicates the relative visual sensitivity, from 0 to 1. Perimetry data points are overlaid on SLO retinal images, which are oriented to correspond to visual field locations. Fixation scatter is indicated by group of yellow and blue symbols. Blue dashed outlines encircle the regions corresponding with the FFMaps in Figure 6, B and F. L, Left field; R, right field; S, superior field; I, inferior field; RH, right hemisphere; LH, left hemisphere.
Figure 8. Polar angle retinotopy for patient with a brain tumor in left hemisphere (P3). A–H, Figure layout is the same as in Figure 2, with the following exceptions. A, Extensive left hemisphere damage prevented construction of a cortical surface model, so three anatomical views of color-coded polar angle maps are displayed. White dashed outline shows the region of cortical damage. L, Left; R, right; S, superior; I, inferior; A, anterior; P, posterior; RH, right hemisphere; LH, left hemisphere. E, Black dashed outlines indicate the approximate location of expanded ipsilateral representation. F, Black dashed outlines highlight the inset showing expanded ipsilateral representation, especially near the vertical meridian. B, F, Blue dashed outlines encircle the regions corresponding with the visual field perimetry in Figure 9B.
Eccentricity maps and perimetry for P3.

Figure 9. Eccentricity maps and perimetry for P3. A, Figure panel layout is the same as in Figure 3, with the following exceptions. A, Top row, Extensive left hemisphere damage prevented construction of cortical surface model, so three views of anatomical color coded eccentricity maps are displayed. White dashed outline shows region of cortical damage. L, Left; R, right; S, superior; I, inferior; A, anterior; P, posterior. A, Bottom row, Black dashed outline and visual area boundaries as in Figure 8E. B, Monocular Humphrey 30–2 perimetry plots (LE, left eye; RE, right eye). Gray scale indicates the relative visual sensitivity, from 0 to 1. Blue dashed outlines encircle the regions corresponding with the FFMaps in Figure 8, B and F. L, Left field; R, right field; S, superior field; I, inferior field; RH, right hemisphere; LH, left hemisphere.

Fixation records for patients P1 and P2 with atypical cortical organization.

Patients with atypical cortical organization have larger ipsilateral field representations.

**Figure 11.** Patients with atypical cortical organization have larger ipsilateral field representations. **A, B,** Group-averaged polar histograms and bar graphs for hemispheres from patients with atypical retinotopic organization (red shading, n3), healthy controls (light blue shading, n12), and healthy controls with expanded VOIs including all of visual cortex (dark blue shading, n12). Black dashed lines in the inset in **A** and error bars in **B** show SEM. **C, D,** Group-averaged polar histograms and bar graphs for hemispheres from healthy controls (light blue shading, n 12), patients with typical retinotopic organization (yellow, n 22), and patients with typical retinotopic organization that have been normalized to match controls in the total volume of activation (dark yellow, n22). Note: different y-axis scales in **B** and **D** for the ipsilateral versus contralateral visual fields.
Figure 12. Conceptual model of interhemispheric suppression and effects of unilateral damage on apparent retinotopy.  

A, Schematic of the retino-geniculate afferent pattern into V1, including a naso-temporal overlap zone (highlighted by red lines) providing a source of ipsilateral visual field input to V1 in each hemisphere.  

B, Tonic suppression along the edge of each hemisphere (left V1 only shown for clarity) reduces the apparent number of retino-geniculate afferents (black dashed curve) along the naso-temporal overlap zone. Inset: the effect of a loss of suppression is an increase in the apparent number of afferents.  

C, Schematic model of flattened visual cortex highlighting the V1/V2 border at the representation of the ipsilateral field (thin contrasting colored strip). Compared with healthy visual cortex (top), unilateral damage (bottom) to the right hemisphere causes expansion of the visual field representation near the vertical meridian, including the ipsilateral field.
Summary

Adult Cortical Plasticity
  Visual cortex
  Somatosensory cortex
  Motor cortex

Perinatal animal plasticity
  Ocular dominance
  ‘Re-wired’ Ferrets

Human Cortical Plasticity
  Language development
  Auditory processing with early blindness

Plasticity vs. Vulnerability: The cost of plasticity
Conclusions

• Investigations in adults reveal the capacity and some mechanisms underlying cortical plasticity and re-organization.
• The consequences of early damage to the nervous system depend upon the timing, location, and extent of the injury.
• Although early damage may, in some circumstances, allow for maximal re-organization (recovery), prolific reorganization may lead to long term negative consequences.
The Gestalt rule of good continuation and the association field. In complex scenes observers tend to perceptually link or group line segments that lie along smooth contours. Upper left, observers perceptually link line segments a and c, and perceptually segregate those having a large change in orientation, such as line segments a and d (from Wertheimer, 1923). This reflects a geometry of collinear and co-circular interactions, known as the association field, represented in the right panel. The grey square in the center of the right panel represents the RF measured with a single oriented line segment, but the association field, as represented by the colored oriented line segments flanking the RF, mediates collinear and co-circular facilitatory interactions between multiple line segments lying along smooth contours, enabling neurons to be influenced by the properties of contours extending well outside their RFs. The colors of the line segments indicate the strength of the association field interactions at different positions, red being the strongest, light blue the weakest. Bottom left, the association field contributes to contour integration and contour saliency, where smooth contours tend to pop out from a complex background (adapted from Field et al, 1993).
Figure 2.
Contextual influences modifying neuronal responses. Left, A simple stimulus, such as a single oriented line segment, will elicit a response at one location, but by itself will produce no response at an adjoining location. This defines the boundaries of the RF. But if one line is placed within the RF and a second line at the adjoining location, the response of the neuron can be multiplied several fold. This interaction reflects the sensitivity of neurons for the continuity of contours extending for long distances outside the RF, and interrupting this continuity by introducing a cross-bar between the collinear lines blocks the contour related facilitation (Kapadia et al., 1995). Consequently, the response properties are highly nonlinear—one cannot predict the response to a complex stimulus consisting of multiple components from the response to the individual components. Right, the interaction between contour elements can be represented as a 2-dimensional map of facilitatory (blue) and inhibitory (red) influences relative to the response of a neuron to a line segment centered in the RF (white bar). (Kapadia et al., 2000). These interactions constitute the representation of the association field in V1.
Relationship between long range horizontal connections and cortical functional architecture. An individual superficial layer cortical pyramidal cell (top left) forms long range connections that extend many millimeters parallel to the cortical surface, enabling their neuronal targets to integrate information over an area of cortex representing an area of visual field much larger than their classical RFs. Labeling these connections with an adenovirus carrying the eGFP gene allows one to image the axons of a population of labeled cells with a confocal microscope (top right, surface view of labeled horizontal connections in V1). Combining this labeling technique with intrinsic signal optical imaging enables one to establish the relationship between the axon collateral clusters formed by the horizontal connections and the columnar functional architecture (bottom right), where short range connections contact a wide range of orientation columns but long range connections link columns of similar orientation preference (indicated by the histograms at bottom left). (From Gilbert, 2012; McGuire et al., 1991; Stettler et al., 2002)
Figure 4.
Changes in RFs and topography following retinal lesions and model of perceptual fill-in. Top row, a series of electrode penetrations in superficial layers of V1 shows topographic arrangement of RFs in the mapped cortical area. Binocular retinal lesions (dashed line) in this part of the visual field makes neurons in the center of the cortical lesion projection zone (LPZ) unresponsive to visual stimuli (sites denoted by X’s). However, even on the same day of making lesions, neurons with RFs just inside the LPZ boundary have shifted their RFs to positions outside the retinal scotoma (Cross hatched RFs, middle. Recordings made before and after placing lesions were located at the same cortical sites. The arrows start at the original RF position before the lesion and point towards the new RF position, for that cortical position, at the time of recording). Over the subsequent weeks (top right) the entire LPZ regains visually driven activity, with larger shifts in RF position (Darian-Smith and Gilbert, 1995). Middle row, the shifting RFs can be schematically represented as a remapping of cortical topography, with the initial LPZ shrinking the representation of the lesioned part of the retina and expanding the representation of the retinal loci surrounding the retinal scotoma. Bottom row, modeling the perceptual consequences of topographic remapping. The model assumes that each neuron is a labeled line for a given position and orientation, but by shifting its RF, is activated by stimuli outside the retinal scotoma, thereby mediating perceptual fill-in at positions within the scotoma.

Viewing an image, left, through a retina with areas of geographic atrophy and a salt and pepper loss of photoreceptors in between (which is meant to simulate visual field losses in adult macular degeneration), middle, it is difficult to identify the viewed object. But if one allows RFs to shift along the association field, maintaining their original orientation (Das and Gilbert, 1995), the image can be effectively filled in (right). Though locally distorted, the simulated process of fill-in mediated by cortical topographic reorganization allows the image to be readily identified (From Darian-Smith and Gilbert, 1995; Gilbert and Wiesel, 1992; McManus et al., 2008).
Figure 5.
Axonal sprouting and pruning in V1 of monkey MA induced by focal binocular lesions. Axonal tracing of 2-photon microscope Z stacks acquired through a depth of 200 um in the LPZ. Gray, axon segments that remained unchanged compared to the previous time point; yellow, segments that were added relative to the previous time point; red, segments eliminated after the previous time point. The last panel shows the axons present at the end of the sequence of imaging sessions (from Yamahachi et al., 2009).
Figure 6.
Specificity of perceptual learning. Left, training on a 3-line bisection task, where the observer has to determine whether the central line among 3 parallel lines is closer to the one on the left or right, leads to a decrease in the task threshold. The threshold in this task is the offset from the central position of the middle bar that is required to reliably see to which side the line is closer. The light gray bars indicate the thresholds before training and the dark gray bars the thresholds after training on the 3-line bisection task for the left and middle pair. Consistent with the specificity of perceptual learning, practice on this task does not transfer to a vernier discrimination task involving the same target line with a different context, a collinear line (middle). Specific training on the vernier task leads to substantial improvement in the threshold on that task (right, gray bar indicates threshold before and black bar after training on vernier task). (From Crist et al, 1997.)
Figure 7.
Perceptual learning and changes in V1 associated with a contour detection task. A patch of randomly oriented lines is presented in each of the two visual hemifields on either side of a fixation spot. Embedded in one patch is a linear contour consisting of a series of collinear line segments. The monkey is trained to make a saccade in the direction of the patch containing the embedded contour. In half the trials the contour lies over the RF recorded from a neuron in the superficial layers of V1. The perceptual saliency of the contour is measured as a function of the number of collinear line segments, with longer lines being more salient. In the initial period of training (first week) the monkey’s performance is shown in the psychometric curve (black dashed line) and the contour related facilitation in neuronal responses is shown in the neurometric curve (black solid line). Perceptual learning in the task is reflected in the change observed in the second week of training, with a shift up in both the psychometric (red dashed line) and neurometric (red solid line) curves. The effect is that the animal can reliably detect contours composed of fewer line segments, and there is a stronger contour related facilitation at the neuronal level (Li et al., 2008).
Figure 8.
Shape selectivity of neurons in V1 of monkeys trained on a shape discrimination task. Animals were trained to identify the shape of a contour embedded in a complex background after being given a shape cue. A1 and A2, the cue was presented in isolation (A1), and after a delay period in which stimuli of various geometries were presented (B1), the animal was shown the cue and a false target, each embedded in a complex background on opposite hemifields (C1). The task involved making a saccade towards the hemifield containing the cued target (C2). Over successive trials, during the delay period between presentation of the cue and the target (B1,B2), a computer algorithm searched for the shape that elicited the maximum response from the cell by placing line segments with various positions and orientations in the RF surround, gradually building up the optimum 3-line, 5-line and 7-line contours. Several shapes were used as cues: a circle, line and wave (A2). The response to different shapes are represented as heat maps (B2), with the color indicating the strength of response in the shape space, and the axes representing the position and orientation of the line segments at the ends of the contour. (From McManus et al., 2011)
Figure 9.
Influence of learning and of shape expectation on V1 shape selectivity. The examples shown illustrate heat maps of the stimulus-response profiles of three typical neurons, with dark red indicating the strongest neuronal responses to certain contour shapes measured in a delayed match-to-sample experiment (Figure 8). As the algorithm searches for the neuron’s optimal stimulus, it zeroes in on a particular portion of the shape space. The axes in the plots define a battery of geometric shapes of contours tested during the delay period (Figure 8; some shapes are illustrated as cartoons superimposed on the 2D map at corresponding points), with the top row graphs showing the best 3 line contours and the bottom row the best 5-line contours. The X-axis (α) represents the angle of orientation of the outermost flanking bar and the Y-axis (β) represents the position of the flanking bar relative to the bar centered in the RF. When the cue was a straight line (left pair), the optimum contour had a collinear profile, when the cue was a circle the neuron showed selectivity for co-circular line segments (middle pair), and when the cue was a wave shape (right pair), the optimum contour showed a reversal in curvature mirroring the wave-like profile of the cue. (from McManus et al., 2011)
Figure 10.
Learning on a visual search task. Subjects were required to find a target, the downward pointing triangle, which was presented at random positions from trial to trial in a 5×5 field of triangles of different orientations (left). Initial performance was at chance levels, but after practice the target popped out from the distracters and was reliably detected. The improvement in performance did not occur simultaneously at all stimulus positions, but instead occurred at one location at a time until subjects were able to detect the target at all positions in the array (right series from 1 to 27, with each circle representing a position in the array and the blackness of the circle indicating the performance level at that position). This suggested that the cortical representation of the target occurred at multiple locations within a retinotopically organized area. (From Sigman et al 2005).
Figure 11.
Effect of learning on a visual search task on patterns of cortical activation elicited by trained versus untrained stimuli. Shift of stimulus representation to early visual cortex after training human subjects in a visual search task. (A) The stimulus contained a number of Ts that were rotated by multiples of 90 degrees and distributed in the four quadrants of the visual field. The upside down T was the target. The task was to report the quadrant within which the target T appeared. (B) Differential activation between the trained and untrained conditions. The first row shows the front and back views of the brain; the second row, the left and right hemispheres; the third row, the ventral and dorsal (bottom and top) views. The untrained condition was more active (shown in green) than the trained condition over an extended network that mainly involved the parietal and frontal cortices and lateral occipital cortices. The trained condition was more active (shown in red) than the untrained condition in the middle occipital cortex, corresponding to early visual areas in retinotopic cortex including V1 (from Sigman et al., 2005).
Figure 12.
Experience dependent changes in the turnover of dendritic spines. A, retinal lesions cause an increase in spine turnover in the LPZ of mouse visual cortex. The blue arrows indicate stable spines, filled and open yellow arrows indicate disappearing spines, and open and filled grey arrows indicate newly appearing spines (Keck et al, 2008). B, similar changes have been observed in mice during motor skill learning, with the appearance of newly formed spines (red arrows) in motor cortex that correlates with the improvement in performance (from Yang et al, 2009).
Selected References


