Cognitive Neuroscience:
Brain Mechanisms of Memory and Cognition
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NST II Neuroscience (M5) / Psychology 2005
Lecture 1 (Monday 17 January)
Cerebral cortex; two visual streams

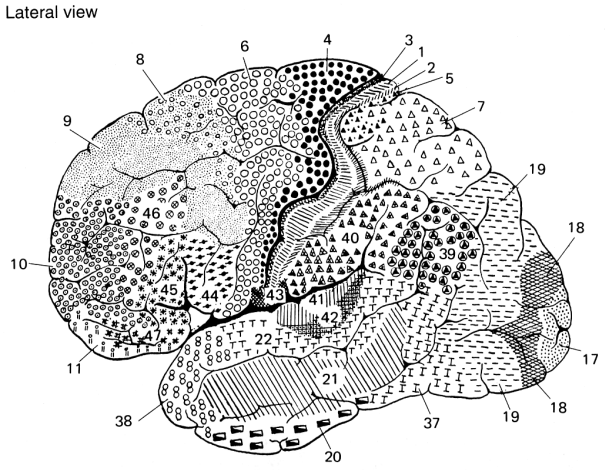
Objectives

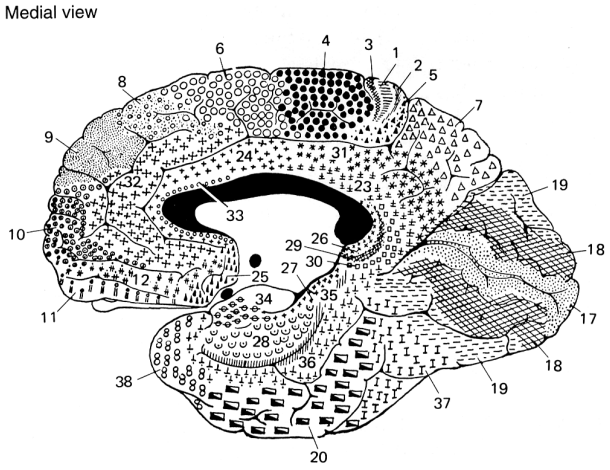
We will begin with a brief summary of the structure of the cerebral cortex, and consider cortical plasticity at a cellular and functional level. Next, we will consider the significance of concurrent (parallel) information processing using the visual system as an example (the dorsal and ventral visual cortical 'streams'). We will draw on evidence from lesion studies, electrophysiology, and functional imaging, and discuss the relevance of double dissociations. We will then focus on visual object processing in the ventral stream.

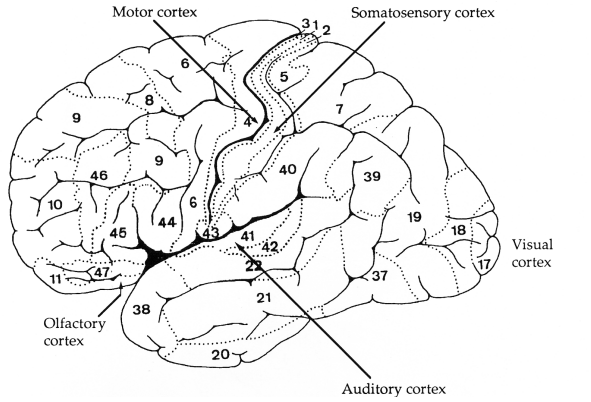
Cerebral cortex

Gross anatomy; modularity of function; experimental techniques

The cerebral cortex in humans is predominantly 6-layered *neocortex*. It is grey matter (comprising the cell bodies of neurons, as distinct from white matter comprising myelinated axons) convoluted to form *gyri* (folds) and *sulci* (fissures). It can be divided on cytoarchitectonic (cytoarchitectural) grounds into different areas. Human cortex is divided into Brodmann's areas (Brodmann, 1909; numbering of areas is arbitrary); similar systems exist for monkeys (von Bonin & Bailey, 1947) and rats (e.g. Zilles, 1985; Paxinos & Watson, 1998).







Brodmann's (1909) areas of the human cerebral cortex. Bottom left figure from Fuster (1995).

*The numbers are arbitrary. Anterior is to the left. The **frontal** lobe is everything anterior to the central sulcus (the large groove dividing area 4 [motor] from area 3 [somatosensory]), and is next to the frontal bone. The **occipital** lobe is at the back (areas 17, 18, 19), by the occiput. The **temporal** lobe is the bit below the lateral sulcus that extends down to the temporal bone (including areas 41, 42, 22, 21, 20, and so on). The **parietal** lobe is the rest, next to the parietal bone (including areas 1, 2, 3, 5, 7, 40, and so on).*

The cortex is divided into *sensory*, *motor* and *association* areas. All are functionally organized on *modular* principles, though the functions of sensory and motor areas have been fairly well established in comparison to those of association areas.

This modularity has been established using evidence from naturally and artificially brain-damaged human patients, experimental brain lesions in animals, and electrophysiological techniques (recording and stimulation). More recently, it has become

possible to disable human brain regions temporarily without neurosurgery using transcranial magnetic stimulation (TMS), and *functional imaging* techniques have come into widespread use.

One is *functional magnetic resonance imaging* (fMRI). MRI scanners apply a large static magnetic field to tissue, aligning things that have magnetic properties, such as protons. They then apply radio-frequency pulses to disrupt this alignment and measure the signal the nuclear 'magnets' emit as they return ('relax') to the aligned state. Generally, MRI uses protons as the magnets; the way the protons relax depends on their local chemical environment (e.g. water versus fat). These differences are used to generate structural MR images. Functional MRI is similar, but it makes use of the fact that local magnetic field, and hence the proton relaxation signal, is altered by the presence of deoxyhaemoglobin (a paramagnetic substance) much more than by oxyhaemoglobin. When a brain region is 'active', local blood flow increases (bringing in fresh oxyhaemoglobin and reducing the deoxyhaemoglobin concentration) more than O_2 extraction by the brain increases (which has the opposite effect); the scanner detects the decrease in deoxyhaemoglobin as an increased signal. The technique is therefore called blood oxygen level dependent (BOLD) fMRI. Anybody can be scanned, repeatedly if necessary, as long as they aren't claustrophobic, don't mind the noise, and have no magnetic metal in them. Experimenters have to use special equipment containing no magnetic metal to test subjects.

Another imaging technique is *positron emission tomography* (PET), which measures gamma-ray emission from any substance that can be labelled with a positron (anti-electron) emitter and injected intravenously. When positrons are emitted, they encounter electrons and annihilate to produce two gamma rays heading in opposite directions. The PET scanner detects these and works out where the annihilation occurred (which is up to a couple of millimetres from where the positron was emitted). Water ($H_2{}^{15}O$) and a glucose analogue (fluorodeoxyglucose, ^{18}F-DG) are two commonly-labelled molecules, which measure blood flow and glucose utilization respectively, but drugs can be labelled to calculate neurotransmitter binding. PET scanners are quiet, the subject doesn't have to lie in a narrow tunnel, and there are no problems with having metal around, but the radiation prohibits repeated scanning of the same person and premenopausal women are generally not allowed to serve as subjects for fear of egg damage.

To differentiate task-related activation from 'background', functional imaging experiments typically employ a subtractive design, in which subjects are scanned in two conditions differing only in the critical experimental factor.

Microanatomy of cortex

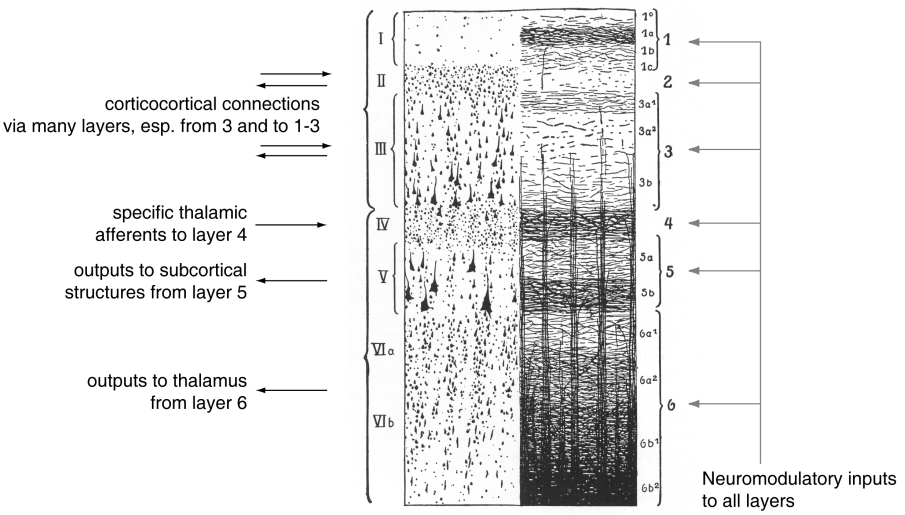
Neocortex comprises six layers; the main principles of organization are

- specific sensory thalamic inputs (afferents) to layer 4;
- outputs (efferents) to subcortical structures from *pyramidal cells* of layer 5;
- short- and long-range corticocortical connections, originating particularly in layer 3. There are many, often reciprocal, connections between cortical areas within one hemisphere and between the two hemispheres (originating from several layers, 2–6, and crossing in the commissure known as the *corpus callosum*);
- diffuse neuromodulator inputs from the brainstem reticular formation to all layers.

Cortical areas differ in the prominence of these layers (this was how Brodmann classified them). For example, primary sensory cortex has a prominent layer 4, where thalamic afferents arrive, and primary motor cortex has a prominent layer 5, where corticospinal pyramidal cell bodies sit.

In addition to pyramidal cells, which are typically glutamatergic (therefore excitatory), there are many types of *local circuit* neurons, including spiny stellate neurons (excitatory), basket, chandelier, and double bouquet cells (all GABAergic and therefore inhibitory), clutch cells (inhibitory), and bipolar cells, which frequently use neuropeptides such as cholecystokinin (CCK) and vasoactive intestinal polypeptide

Modified from Fuster (1995).



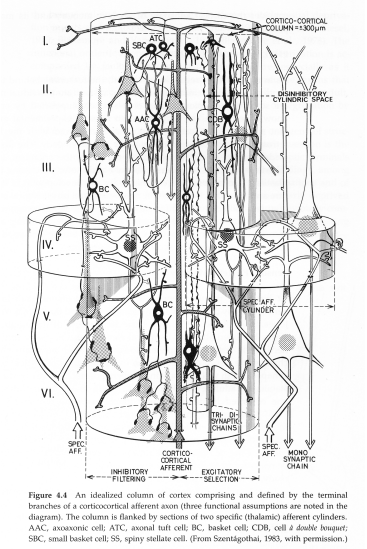


Figure 4.4 An idealized column of cortex comprising and defined by the terminal branches of a corticocortical afferent axon (three functional assumptions are noted in the diagram). The column is flanked by sections of two specific (thalamic) afferent cylinders. AAC, axoaxonic cell; ATC, axonal tuft cell; BC, basket cell; CDB, cell *à double bouquet*; SBC, small basket cell; SS, spiny stellate cell. (From Szentágothai, 1983, with permission.)

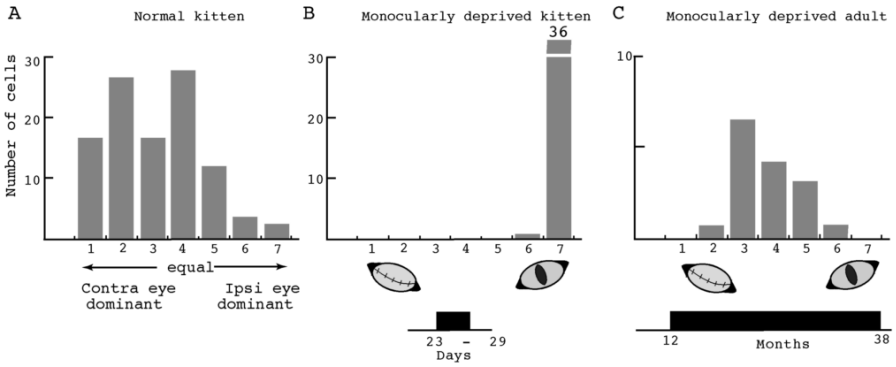
(VIP) as transmitters. GABAergic interneurons play an important role in synchronizing activity across cortical areas and probably perform local calculations as well. Interestingly, VIP is a potent vasodilator and a regulator of glial cell metabolism (Magistretti *et al.*, 2000); bipolar cells may be responsible for regulating blood flow and energy delivery to metabolically active areas of cortex. The point of listing all these is to emphasize that the cortex is complex tissue! (See figure.)

The basic unit of cortical processing is the *column*, 50–80 μm across and perpendicular to the cortical surface. Columns may be defined in several ways (e.g. around a pyramidal cell, around a thalamic afferent). They are easily detectable in primary sensory cortex. In primary visual cortex (V1), for example, columns respond to a line stimulus of a particular orientation. Outside sensory cortex, the columnar organization is harder to establish, but neocortex is similar across regions so it is suspected that columnar organization extends to regions whose functions we understand less well.

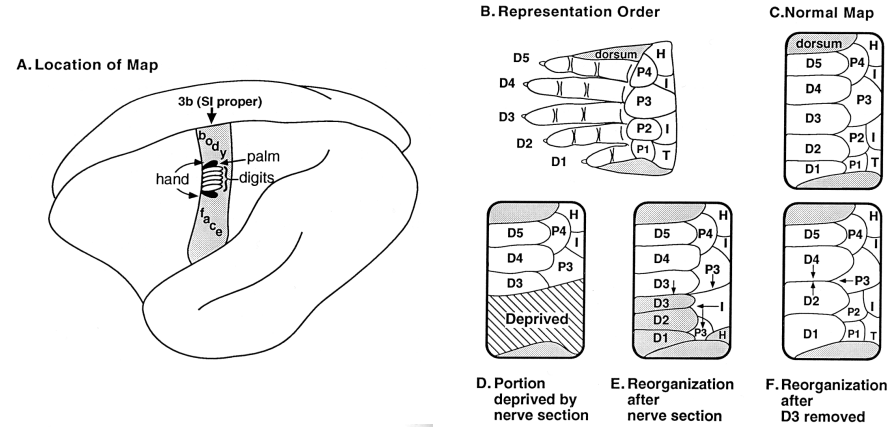
Cortical plasticity

Central to the function of the cerebral cortex is its ability to change its response to a given stimulus: this is *plasticity*, and is the basis of all long-term forms of memory. Cerebral cortex exhibits substantial plasticity during development; classic demonstrations include the finding that kittens who do not see vertical (or horizontal) lines during a critical postnatal period subsequently lack visual cortical cells that respond to that orientation (Blakemore & Cooper, 1970). Similarly, if visual input from one eye is lost, its cortical representation shrinks at the expense of that of the other eye (Wiesel & Hubel, 1963). This dramatic plasticity is not present in the adult cat; the creation of new synapses is much less frequent in the adult than during development (see Bourgeois *et al.*, 2000). However, adult cortex is plastic too: visual, auditory, somatotopic, and motor cortical maps can all reorganize. For example, amputation or denervation of a digit leads to loss of its cortical representation and expansion of adjacent somatosensory representations into the cortical area previously used by that digit, while training monkeys to perform a task involving a few fingers can expand the cortical representations of those fingers (Kaas, 1995; 2000). Pairing a tone conditioned stimulus (CS) with electric shock leads to auditory cortex receptive field plasticity that increases the response to the CS at the expense of other frequencies (Weinberger, 1995).

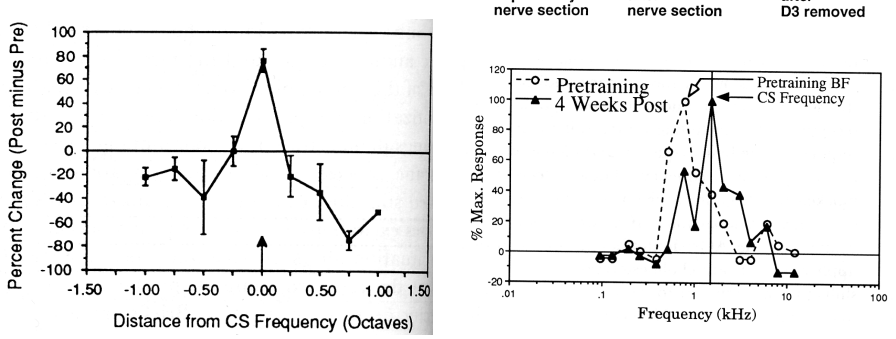
How is plasticity implemented? Cortical neurons implement a version of Hebb's (1949) rule. Simply stated, *neurons that fire together, wire together*. One such mechanism is synaptic long-term potentiation (LTP; Bliss & Lømo, 1973; Iriki *et al.*, 1989), through which synapses become stronger (i.e. release more transmitter and / or are more sensitive to it). LTP occurs when presynaptic neuronal activity coincides with strong postsynaptic depolarization beyond a threshold value (a threshold that is usually higher than that required to trigger action potentials). Conversely, presynaptic activity in the absence of postsynaptic activity may, at times, lead to



Visual cortex: monocular deprivation during critical periods. Data from Hubel & Wiesel (1970)2}.



Somatosensory cortex: nerve section and amputation. Figure from Kaas (1995).



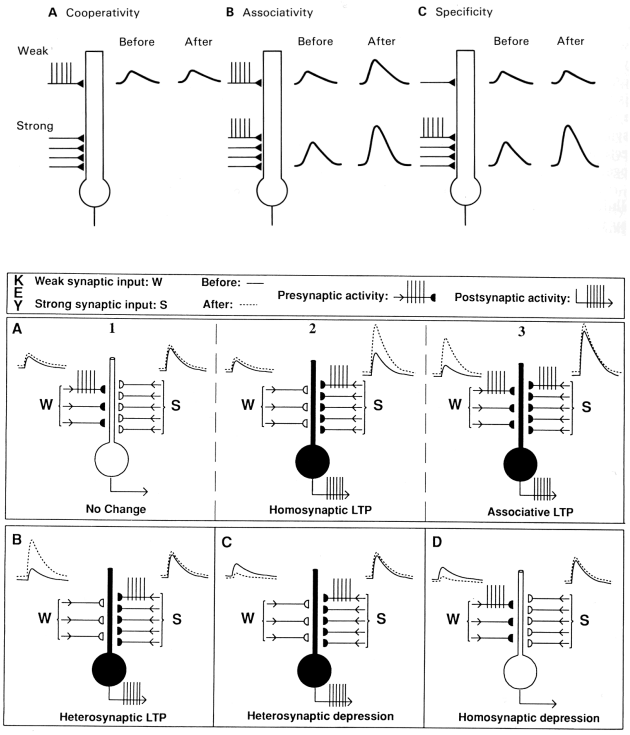
Auditory cortex: pairing a tone conditioned stimulus (CS) with electric shock. BF: best frequency that the neuron(s) responded to before training. Figure from Weinberger (1995).

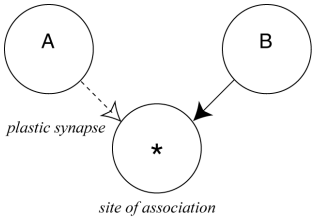
long-term depression (LTD) of that synapse. Since increases in synaptic strength must be balanced, in the long term, by decreases (e.g. at other synapses) — certainly to avoid overexcitation of the kind seen in epilepsy, and probably to keep the cortical network in a state where it can usefully learn — cortical and other neurons also exhibit *metaplasticity*, or activity-dependent plasticity of synaptic plasticity (Bear *et al.*, 1987; Bear, 1995; Abraham *et al.*, 2001; Royer & Pare, 2003). For example, if several synapses onto a cell undergo LTP, the cell will become less capable of supporting LTP subsequently, and more likely to exhibit LTD in response to presynaptic activity.

Cortical processing and function

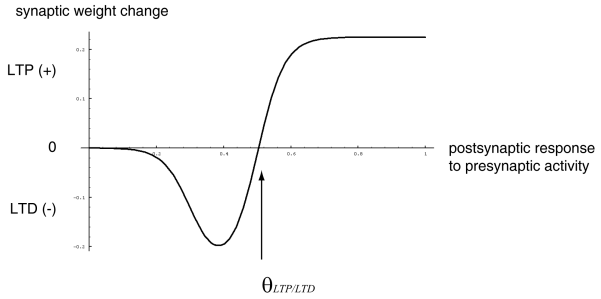
Singer (1995) suggests that one general property of sensory and motor cortex is to detect consistent relations among incoming signals (that is, 'features'). As the number of possible combinations of sensory signals is essentially infinite, he suggests that the cortex uses two strategies: (1) to *hard-wire* neurons, using feedforward connections, to detect features and relations that are particularly frequent and / or important; (2) to use high-speed *dynamic grouping* systems, based on reciprocal corticocortical connections, that can create a representation of any given sensory input by combining responses from hard-wired neurons. The 'vertical line detectors' in kitten visual cortex are a good example of hard-wired feature detectors. More complex feature detectors (e.g. face-sensitive neurons) in higher-order visual processing areas may be, too; they depend on simple feature analysis in primary visual cortex. (We will cover dynamic grouping in more detail when we consider the *binding problem*.)

In addition to this: (3) the cortex may exhibit use-dependent plasticity so that dynamic groups can be represented more permanently as new features or objects; (4)





Top left: *associative LTP (from Kandel et al., 1991)8}.* ***Bottom left:*** *use-dependent synaptic plasticity in general (from Fuster, 1995).* ***Top right:*** *associating representations.* ***Bottom right:*** *metaplasticity, after Bienenstock et al. (1982)7}.*



According to the Bienenstock-Cooper-Munro theory, this threshold increases when the postsynaptic cell has been active recently (and decreases when it hasn't).

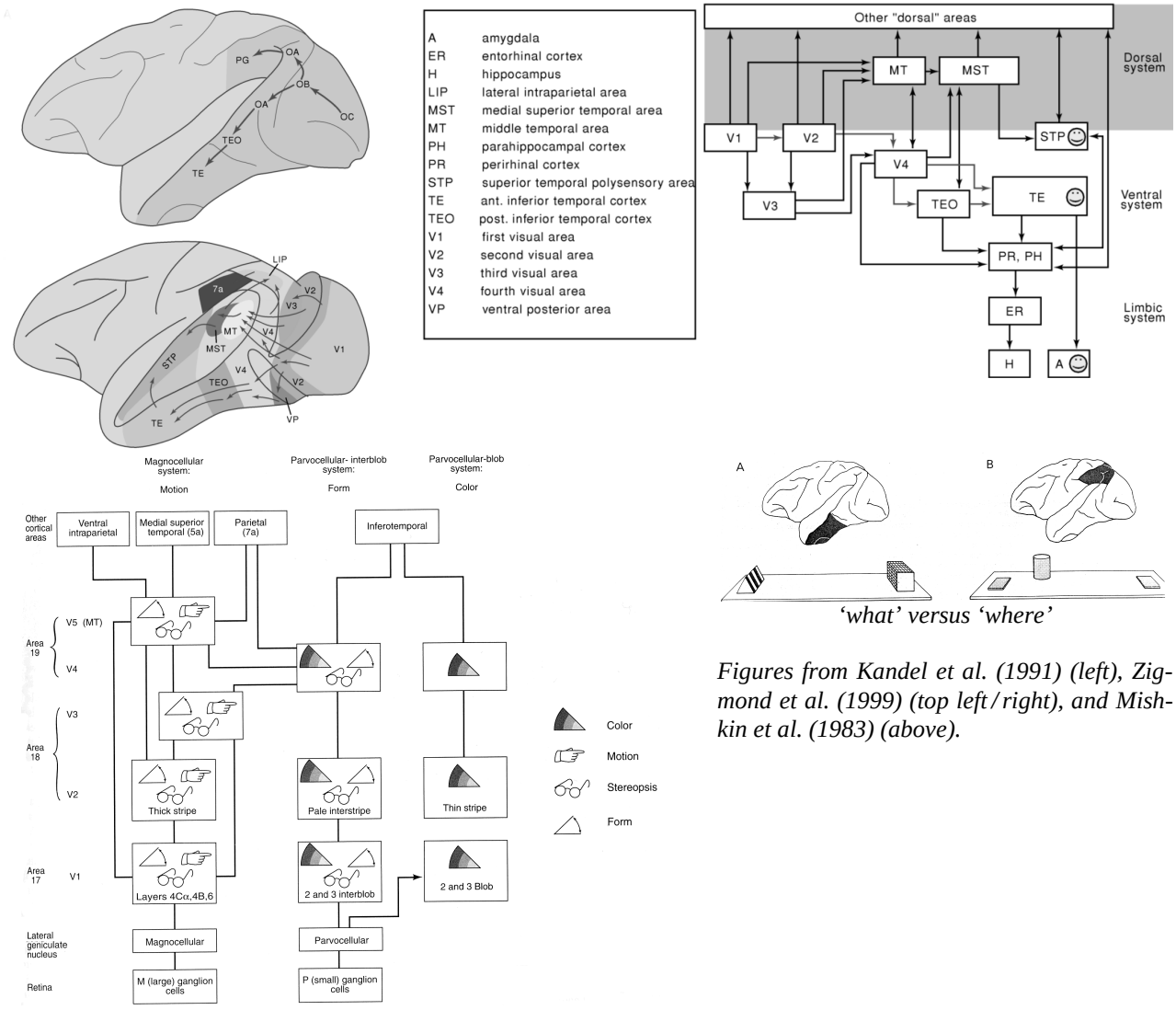
neuromodulators may influence cortical processing in several ways, such as by permitting plasticity (Weinberger, 1995; 1998); and, related to this, (5) different areas interact to alter processing at many levels. For example, top-down attentional processes can alter the responses of primary and secondary visual cortex to visual stimuli (Moran & Desimone, 1985; Luck & Hillyard, 2000; Maunsell & McAdams, 2000) and mental imagery involves activation of visual sensory cortical areas (Farah, 2000).

If all this gives you the impression that we don't understand the cell-level detail of cortical information processing very well, you'd be right. So let's move on to specific cortical regions.

Multiple maps and processing streams in striate and prestriate cortex

There are at least three distinct *retinotopic* maps in primate visual cortex, with topographic, point-to-point correspondence between retinal and cortical location. These are V1 (= striate cortex = primary visual cortex = Brodmann's area 17), V2, and V3 (both prestriate cortex, Brodmann's area 18). The map in V2 is a mirror image of that in V1, and both V2 and V3 receive input from V1. There is a cortical *magnification* of the central, foveal region of the retina. The thirty-or-so visual areas in primate cortex are best described as hierarchical (see figure) but information flow is not just 'bottom-up'; there are important *back projections* from V2 and V3 to V1.

Information processing in the visual pathways occurs in distinct streams, based on properties of the different types of neurons involved in early stages of visual processing. There is *parallel (concurrent) processing;* that is, information is processed simultaneously in several distinct streams, though there may be interactions between streams. (This is probably true of all sensory pathways.) Even in the retina, different populations of neurons encode different aspects of visual information (see also 1B, Psychology / Vision and Neuroscience / M4 lectures): *P* (*parvocellular;* L. parvus = small) retinal ganglion cells have small receptive fields and a sustained response to light; they subserve high-acuity vision and the resolution of fine spatial detail. *M* (*magnocellular*; L. magnus = large) retinal ganglion cells have large receptive fields and transient responses to light; they are especially suitable for the analysis of movement. These distinctions are reflected in cortex. Very approximately:



Figures from Kandel et al. (1991) (left), Zigmond et al. (1999) (top left/right), and Mishkin et al. (1983) (above).

- P (retina) → parvocellular layers of the lateral geniculate nucleus of the thalamus (LGN) → interblob regions (of V1) → interstripe regions (V2) → V4 and ventral cortical areas… *form (orientation; inc. binocular disparity)*
- P (retina) → parvocellular layers (LGN) → blobs (V1) → thin stripes (V2) → V4… *colour (wavelength)*
- M (retina) → magnocellular layers (LGN) → V1 → thick stripes (V2) and area MT… *motion (velocity; inc. binocular disparity)*

Though there is substantial segregation of processing by this stage, there are also interactions between sensory processing modules to effect functions such as depth and motion perception, form perception, colour perception and colour constancy.

Evidence for this segregation of processing comes from several sources, including monkey single-cell electrophysiological studies, neuropsychological studies of humans and monkeys, and functional imaging. The neuropsychological evidence includes the existence of patients with akinetopsia (inability to detect movement) and achromatopsia (inability to detect colour) — see Cognitive Neuropsychology lectures (and McCarthy & Warrington, 1990). PET studies have demonstrated that colourless, moving displays cause significant regional cerebral blood flow increases in human V5 (equivalent to monkey area MT) relative to a static display. In contrast, coloured 'Mondrian' displays activate V4 relative to a colourless but equiluminous and otherwise identical display (Zeki *et al.*, 1991). These double dissociations have been extended into higher visual processing systems.

Beyond the occipital cortex: the two visual streams — 'what' (ventral) and 'where' / 'how' (dorsal)

Higher visual cortical processing can be roughly divided into areas that are concerned with the analysis of objects (form, colour, etc.), and areas that are concerned with their spatial location and movement. The former appears to be mediated by a ventral stream, and the latter by a dorsal stream (Ungerleider & Mishkin, 1982). It was previously known that visual agnosia commonly follows damage to posterior cortex in humans (see Cognitive Neuropsychology lectures). Removal of large parts of temporal cortex produced a complex syndrome that included visual agnosia (Klüver & Bucy, 1939), and this could be duplicated by damage restricted to inferior temporal cortex. Lesions of area TE, in inferior temporal cortex, impaired monkeys' ability to discriminate objects visually (though they could still discriminate them using touch; this ability depended on somatosensory association cortex). Ungerleider and Mishkin (see Mishkin *et al.*, 1983) found that removal of posterior parietal cortex produced impairments when monkeys were required to discriminate objects on the basis of their spatial location (Pohl, 1973; Mishkin *et al.*, 1982). This double dissociation provided the basis for distinguishing 'what' and 'where' processing, based respectively in the ventral and dorsal streams; this dissociation is in general supported by functional imaging studies (see Ungerleider, 1995).

Anatomical properties of the ventral pathway

V1 extracts information about edges, brightness, and wavelength of stimuli from the inputs it receives from the LGN; this is passed to **V2.** From there, information passes to **V4** and to a posterior inferior temporal area (termed **TEO** in monkeys) just anterior to V4 (see figure above). Information is often retinotopic at this level. From here, information passes to area **TE** in anterior inferior temporal cortex. Together, TEO and TE comprise inferior temporal cortex (called IT). Here, there is less of a retinotopic representation. Subsequently, information passes forward again to the **temporal pole** and **perirhinal cortex** (Brodmann's area 36). These regions are connected to the hippocampal formation in the medial temporal lobe.

In addition to this posterior→anterior progression…

- there are many feedback projections to more posterior regions, including V1;
- there are other 'forward' projections to regions of the frontal lobes;
- there are side projections to a superior temporal polysensory (STP) region on the superior temporal sulcus, which also receives inputs from the dorsal stream;
- there are subcortical projections to the basal ganglia, amygdala, and the thalamic pulvinar nucleus;
- there are interconnections with related regions of the contralateral hemisphere (particularly further along the pathway).

Electrophysiological properties of the ventral pathway

Analysis of the 'trigger features' to which neurons respond has helped to define the functions of these more advanced visual processing centres. All regions in the ventral stream respond to some feature relevant to objects. As one moves forward along the ventral stream:

- the receptive fields (RFs) get larger (and there's less of a retinotopic representation). There is progressively greater representation of both visual fields in each hemisphere.
- Trigger features, such as edges, are consistent over much greater areas of visual space. (Taking this with the previous point implies that the neurons come to respond to object features with less regard to where the object is on the retina — invariance in response to retinal translation.)
- Trigger features are more specific and complex (e.g. for biologically-significant objects such as faces and body movements).
- Mnemonic factors become more important at the more anterior stages of the pathway, as we shall see later.

V2 cells are similar in many ways to V1 cells in responding selectively to trigger features such as orientation, width, length, and wavelength of a bar.

V4 cells are *jointly* tuned to features, such as length *and* width of a bar, and they respond to these features over larger receptive fields. They exhibit conjoint wavelength selectivity. The optimal trigger stimuli are often more complex than those in V1 or V2 (for example, irregular borders, edge conjunctions, and concentric areas of contrast). They exhibit antagonist effects such as 'silent surrounds' — areas around an RF which only affect the activity of the cell if the surround is stimulated at the same time as the RF. They exhibit *colour constancy* — i.e. they respond to the colour of objects based on the reflectancy of the object relative to its surrounds, not the actual wavelength of the light coming from the object. (This requires complex processing: the brain must infer the wavelength of the illuminating light by considering large portions of a visual scene.) They exhibit attentional effects (see later lectures).

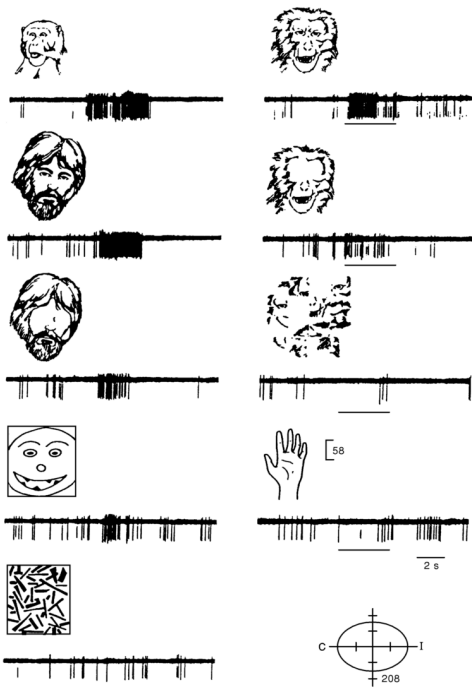
TEO and TE cells have very complex response requirements. It is difficult to trigger the neuron to fire in response to a subset of features of their preferred complex stimulus. Neurons exist that respond to objects such as bottles, food stimuli, and faces. Occasionally, neurons fire to a set of stimuli with no obvious common characteristics. It is unlikely that there are 'grandmother neurons' (this term refers to a hypothetical neuron that fires only in response to an extremely specific visual stimulus, namely one's own grandmother). Instead, visual stimuli are probably represented by networks or ensembles of neurons: the network that represents one object overlaps to some extend with the network that represents another, so that individual neurons participate in several such networks and contribute to representing several different objects. Neurons with similar properties are often 'clumped' together, which may represent columnar organization of cortex.

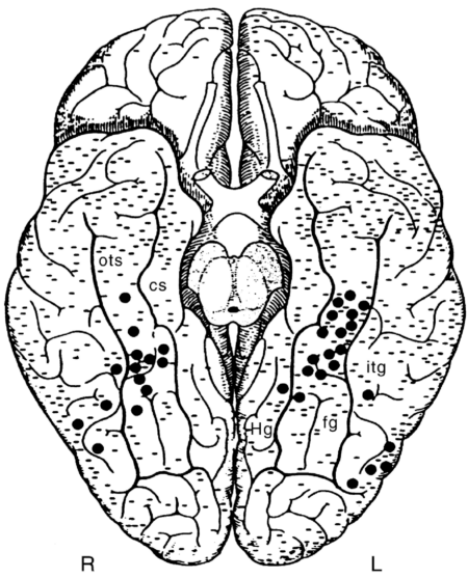
Receptive fields may be huge (e.g. 20°), enabling a cell to generalize a particular object preference across a wide area of space (responding to an object as it changes retinal position, spatial location, and depth). This spatial invariance is consistent with a role for IT in object recognition.

IT (TEO / TE) cells exhibit a variety of memory effects (see later lectures), e.g. a waning response to repeated presentation of an object, or firing when an object has disappeared.

Face-responsive neurons

Some neurons in areas TE and STP appear to be highly specific in their ability to respond to faces. They do not, generally, fire in response to other complex objects, or to components of the face reconfigured randomly. The response to a face is invariant over many transformations (e.g. different shading or colouring, or the face's position





***Left:** a face-responsive neuron in monkey area STP. **Below:** face-responsive regions in human ventral occipito-temporal cortex. Figures from Zigmond et al. (1999).*

in space).

Some neurons are selective for specific features of faces — often particular configurations of the eyes and nose. Responses can be influenced by the orientation of the face: some neurons respond selectively to frontal views, while others respond to profile views. Similarly, the face's gaze direction can influence responding; this can be quite sophisticated. (For example, some neurons respond to frontal views of faces if the eyes are not visible, or are pointed towards the subject, and also to faces that are turned slightly away if the eyes are still pointed towards the subject, but not to other combinations — i.e. they respond to visual indications that the face is looking at the subject. This is of clear behavioural relevance!) Neuronal responses can also be tuned by facial expression, and by particular facial identity (generalizing over a range of expressions). There is evidence for anatomical separation of some of these types of cell; for example, 'expression' and 'gaze' units are found more often in the superior temporal sulcus, while 'identity' units are more often found in area TE.

It is controversial whether face processing uses a different form of information processing, or different cortical circuitry, from objects in general. Faces are obviously of special biological and social significance, and are complex visual objects. There are 'face units' even in baby monkeys (Rodman *et al.*, 1993), so these cells may represent inborn templates for the detection of faces. The existence of a specific visual agnosia for faces, *prosopagnosia*, in humans (see Cognitive Neuropsychology lectures) that follows ventral occipitotemporal or temporal cortical lesions also suggests that there may be something special about faces. In PET studies of humans, scrambled pictures of faces activate posterior regions of cortex but only intact faces activate anterior temporal cortex (see Ungerleider, 1995). Electrophysiological studies of humans (chronic implanted electrodes used as part of the work-up for neurosurgery to treat epilepsy) have revealed 'clumps' of face-selective regions ventral occipitotemporal cortex (see Farah *et al.*, 1999). However, lesions of superior temporal sulcus in monkeys do not appear to produce a specific prosopagnosia; it is unclear whether this reflects a different degree of segregation of face and non-face processing in the two species or whether a 'critical locus' has yet to be found. There is debate as to whether face recognition represents a specific case of a general type of information processing (see Farah *et al.*, 1999), and about the degree to which the representation of faces (and other types of object) are modular or distributed in the brain (see Cohen & Tong, 2001).

Conclusion

In this lecture, we have discussed general properties of cortex and analysed evidence for one half of the Ungerleider–Mishkin hypothesis, concerned with object perception and the ventral stream of information processing. The next lecture will analyse different forms of spatial processing in the dorsal stream.

Sample essay questions

- Discuss the concepts of concurrent processing and modularity in the cerebral cortex with special reference to the visual system. What is their functional significance?
- What do single unit electrophysiological studies contribute to our understanding of the inferotemporal cortex? How have they helped us to understand visual agnosia?
- Are faces special in neural processing terms? Give reasons for your answer.

Suggested reading

General books for the course

- Zigmond *et al.* (1999) is perhaps the closest to a textbook for this course.
- Gazzaniga (1995) and Gazzaniga (2000) — these reference works are more like collections of research reviews textbooks, but they're excellent summaries of contemporary cognitive neuroscience research.

Cortex and plasticity

- Singer (1995) — excellent overview of the potential contribution of synaptic plasticity to cortical function.
- Fuster (1995) — book giving a lucid personal view of cortical memory (of different kinds).
- Crick & Asanuma (1986) — lots of detail on cellular variety in cortex; a little tedious.

- Bear (1987), Bear *et al.* (1995), Abraham & Bear (1996), Burrone & Murthy (2003) — models, molecular mechanisms and reviews of synaptic metaplasticity.
- Kaas (2000) — recent summary of sensory / motor map plasticity in adult cortex.
- Weinberger (1995; 1998) — classical conditioning to tones induces auditory cortex plasticity that needs ACh.

Visual streams

- Farah *et al.* (1999) — chapter 52 in Zigmond *et al.* (1999), concentrating on the ventral stream.
- Sacks (1995) — entertaining read; includes the case of a painter with acquired achromatopsia.
- Ungerleider (1995) — applicable to much of this course.
- Mishkin *et al.* (1983) — an early statement of the 'two streams' hypothesis.
- DeYoe & van Essen (1988) or van Essen & DeYoe (1995) — low-level look at visual processing streams.
- Cohen & Tong (2001) — faces, prosopagnosia, modular *v.* distributed representations of objects.
- Gauther & Nelson (2001) — critical review of face-processing studies and their design.
- Zeki (1993) — history and experiment in visual neuroscience.

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Don't read all these! Concentrate on the *Suggested Reading* list.

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