Week 4: EARLY VISUAL PATHWAYS

1) Anatomical and physiological techniques
2) Retinal structure and function
3) ON and OFF channels
4) Anatomy and physiology of the early visual pathways

- Basic terminology
- Diagrams, sketches
- Historical milestones and trends
- Controversies and usage of terms

Parts of this lecture owe to a key historical overview:

NEURAL NETWORKS VS. NEURON DOCTRINE

19th century debate on brain:

Neuron doctrine:
Cells are the independent functional units of the brain.

Neural networks:
Assemblies of cells are the minimal functional units.

Cajal was a proponent of the neuron doctrine, basing his arguments in part on studies using the Golgi method of cell staining.

Golgi favored the reticular theory (i.e., “net” or “net-like” theory).

EYE OF THE BEHOLDER

THEME 1: Knowledge of the visual system has often been determined by (advances in or limitations of) observational techniques.

e.g., Golgi stain marks almost an entire neuron, but only “one out of N” on average (depending on variations of method).

This technique isolates individual cells for observation.

THEME 2: Data is interpreted within theories. Note that Golgi and Cajal “saw” different things when they looked at the same slides under a microscope.

ANATOMY AND PHYSIOLOGY

anatomy:     physiology:
geometry     dynamics
structure    function

Some measurement techniques can be applied, with some modification, to either anatomy or physiology:

staining:
- histological (anatomy) or metabolic (physiology)

imaging:
- magnetic resonance imaging (MRI) (anatomy)
- functional magnetic resonance imaging (fMRI) (physiology)
ANATOMICAL TECHNIQUES

*Multiple scales* or grains of observation:

- **Gross anatomy**, using dissection, MRI, etc.
- **Local circuit***, using staining, etc.
- **Cytoarchitecture** (cell parts), using scanning microscopy, etc.

*E.g., section and stain to reveal cell bodies, connections, fiber passages.*

MORE ANATOMICAL TECHNIQUES

**Cytochrome oxidase** (mitochondrial enzyme) staining reveals structures of similar cells (e.g. “puffs” or “blobs”) in contiguous areas of cortex.

**Note:** The “grain” of the structures revealed is “between” those of local circuits and gross anatomy (inter-cortical-area connectivity).

Measurement that may be used primarily for answering “anatomical” questions may contain elements of physiological technique, as when a stain is taken up in vivo in proportion to cell activity.

E.g. How are the cells that are primarily sensitive to *monocular* (left eye, right eye) or *binocular* visual inputs physically arrayed in cortex?

PHYSIOLOGICAL TECHNIQUES

**2-deoxyglucose** method: taken up by cells when metabolically active, as when stimulated by a “preferred” visual input. This radioactive marker “fools” the cell; it is taken up like glucose, but cannot be excreted. **Note:** Time scale of minutes needed.

*Radioactively tagged amino acids* can be transynaptically transported at known rates. **Autoradiography** then reveals connectivity across gross structures (e.g. retinal ganglion cell to LGN cell).

**Antidromic firing:** potentials can travel in either direction along an axon (!), so axons synapsing at a known location can be “backfired” to determine the (distal) location of the cell body belonging to that axon.

PHYSIOLOGY: HOW ALIVE?

If the evolutionary advantage (function) of neural activity relates to control of behavior, then ask:

- Is activity measured *in vitro*, or in an intact animal?
- Is the animal paralyzed? ... anesthetized? ... alert? ... simultaneously performing some psychophysical task?
**ELECTRODE RECORDING**

**Single electrode recording:**
*intracellular* (can measure local, graded potentials) or *exocellular* (“AC” conduction can pick up action potentials over some distance.)

**Multiple electrode recording**

*How accurately can location of electrode(s) be determined?*  
*When* can location be determined?

**NOTE:** “Awake, behaving” preparation sacrifices knowledge of precise electrode location (and, often, cell type) for better assessment of function.

(Location can to a certain extent be “recovered” by subsequent histology.)

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**OPTICAL RECORDING**

The reflectance and transmissivity of neural tissue varies -- slightly, but measurably -- as a function of mean activation in a region.

Activity in (several) superficial layers can thus be “imaged,” with or without the use of voltage sensitive dyes.

Blasdel, 1992

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**MORE TECHNIQUES**

**Neurochemistry:** Chemical analogs or antagonists of neurotransmitters can force or block firing of whole classes of cells at once.

**Lesions:** Experimenter-induced lesions can often be precisely localized in physiological studies.

**Human clinical:** psychophysical studies of patients with accidental or medically-mandated operative lesions, e.g. “split-brain” patients.

**Monoclonal antibodies:** These can be used to lesion highly selective structures (e.g. only cells in a lamina sensitive to specific molecules.)

**Functional magnetic resonance imaging (FMRI):** Measure activity-dependent blood flow rate (spatial, temporal resolution...)

**Always ask yourself:** What is the spatial and temporal resolution of the measurement? How “ecologically valid” is it?

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**METHODS OF TAXONOMY OF NEURONS**

**Cell morphology:**
- Cell body size
- Size and shape of dendritic arborization
- Axon length

**Conduction velocity of axons**

**Degree of depolarization or hyperpolarization**

**Chemical sensitivities to neurotransmitter analogs, antagonists,…**

**Staining** (Some cells just look different from others, even if functional reason is unknown.)

**Receptive field characteristics** (More on this topic later!)

**Columnar, laminar, or map structure**

**Question:** When and why is the process of making a taxonomy carried out in a science?
APPROACHING PHYSIOLOGICAL READINGS

Try to get used to “reading” diagrams like this with computational questions in mind. E.g:

1) Are there different types of bipolar cells? If so, how many? Why?
2) Why have two layers of horizontal connectivity in retina?

Note “horizontal” and “vertical” organization . . . interleaved (and, possibly, interacting) lattices.

KSJ4, Fig 26-6

A RETINA -- NOT A PHOTOMETER

Note that even a photoreceptor’s potential can be affected by “remote” quantum catches!

The “surround” antagonism is central to retina’s mission.

KSJ4, Fig 26-10

POINTS TO PONDER

Receptors are hyperpolarized by blockage of Na+ channels that are open in the dark.

Synapse of receptors to bipolars is not thresholded. (Rate of transmitter release is proportional to degree of depolarization.)

A single transmitter (glutamate) inhibits ON-center bipolars, and excites OFF-center bipolars.

There are no action potentials in the distal (outer plexiform) synaptic layer, where receptors, horizontals, and bipolars communicate.

Consider this w/r/t “standard” assumptions in many network models (e.g. McCulloch-Pitts neuron) that threshold cell potential to compute “firing rate.” This issue gets worse later.

Great retina site: http://retina.umh.es/Webvision/index.html

CENTER-SURROUND GANGLION CELLS

ON-center | OFF-center
---|---
Central spot |  
Peripheral spot |  
Central illumination |  
Surround illumination |  
Diffuse illumination |  

Note: OFF cells tend to have higher tonic levels of activity; not indicated here.

KSJ4, Fig 26-7
**CENTER/SURROUND ORGANIZATION**

**ON and OFF populations** with center/surround organization were first noticed in mammalian ganglion cells.

Origin of ON and OFF was traced to bipolars.

ON and OFF “pathways” extend through LGN.
What about V1?

**Note:** The words ON and OFF have both spatial and temporal significance . . .

which took years to sort out owing to limitations of multibeam ophthalmoscope, which could not produce a rapid onset of a low luminance spot!

**ORIGINS OF CENTER/SURROUND OPPONENCY**

Learn to “read” diagrams like this one:

A single transmitter, glutamate, has opposite effects (excitatory, inhibitory) on synapses of different kinds (ribbon, basal).

(Difference in synapse type is not indicated graphically in this figure.)

**DUMBING DOWN**

Quoting from an earlier edition KSJ3:

“Rods and cones contact different populations of bipolar cells at synapses with distinctive morphologies* . . .”

Cones contact:
OFF-center bipolars at basal (flat) synapses
ON-center bipolars at ribbon (invaginating) synapses.

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**RETINAL CONTROVERSY**

The 3rd edition of KSJ includes this diagram.

Note that the possibility of cross-talk from ON bipolars to OFF ganglion cells (and vice versa) is indicated by dashed connections.

This is consistent with a theory developed by Gaudiano concerning rapid signaling of luminance increments and decrements.

**BONUS QUESTION:** Does the absence of this dashed connection in the 4th edition mean that retinal cross-talk has been ruled out?
Paolo Gaudiano received the first CNS Ph.D. ever awarded and is a former CNS professor.

Gaudiano’s modeling analysis indicates that:
1) if anything like a shunting “front end” exists in retina, and
2) given certain psychophysical data concerning responses to luminance increments and decrements
then: there MUST be “cross-talk” between the ON and OFF channels at some point in the pathways. (The key point is that the very factorization of pattern and energy that is touted as such an advantage for spatial pattern processing, in turn, guarantees that the simple shunting network cannot be very sensitive to large and rapid temporal fluctuations of the same underlying spatial pattern.)

Gaudiano’s hypothesis was that this occurred from bipolars to ganglion cells, but it could, in principle, be later.

I have a number of Gaudiano’s papers, and others are readily available. He is also “reachable” via email, if any of you would like to pursue this matter further.

**ON and OFF**

Brief history of “ON” and “OFF”

Adrian, 1928
First to isolate a single neuron's response. Devised concept of “receptive field” (literally, the area on the skin which, when stimulated, results in cell's firing)

Hartline, 1938 (Limulus)
Spikes generated only at (temporal) onset or offset of stimulation

**ARTHROPOD COMPOUND EYE**

Hartline: Evidence for (spatial) lateral inhibition (Nobel Prize)

[Image: http://www.mbl.edu/animals/Limulus/vision/compound.eye2.jpg]

**LIMULUS PSYCHOPHYSICS**

Aside: Hartline “spent his life studying vision in a blind animal!”

But see: Barlow
**ON AND OFF IN SPACE AND TIME**

Kuffler (1953) was the first to report center-surround responses from ganglion cells of *mammalian* retina.

Cartoon of responses:

- **ON-center cell activity, light at (a)**
- **ON-center cell activity, light at (b)**
- **OFF-center cell activity, light at (c)**
- **OFF-center cell activity, light at (d)**

Limitations of apparatus: A multibeam ophthalmoscope can only turn small spots of light on or off; cannot “flash” a dark spot!

**LAMINAR STRATIFICATION**

ON and OFF retinal ganglion cells of cat have dendrites that branch in different laminae (“stratification”).

**INTERLEAVED LATTICES**

Cat retina: Ganglion cells

A, B & C: α cells; D, E, F: β cells (2X magnification)

α and β: morphological classes corresponding (very) roughly to magno/parvo B & E: ON-cells; C & F: OFF-cells; A & D both (from S & W).

**ON AGAIN, OFF AGAIN**

The ON and OFF systems each provide a lattice-like coverage of the entire visual field.

Q1: Why have both ON and OFF systems?

Q2: Are they “independent” channels? (i.e., is there “cross-talk” … in retina? … in cortex? What happens to ON and OFF signals in “later” cortical areas, where one never hears of “ON” or “OFF” signals?)

Q3: What is the relation of the designations ON and OFF to center-surround organization?

(Part of) A: Blockage of ON bipolars by a neurotransmitter analog leaves the center-surround organization of ganglion OFF cells “largely unaffected.” (Slaughter & Miller, 1981)
1. **Anatomy of early visual pathways**

   The LGN is often said to be a “relay station”.

   Arguments for:
   1) Position: it connects to the retina and to area V1 (primary visual cortex).
   2) It performs relatively simple processing.

   Argument against::
   Receives *feedback from V1*; in some species 80-90% of inputs to LGN are extraretinal in origin. Why? Attention??

2. **Physiology of early visual pathways**

3. **Processing strategies**

4. **Parting thoughts**

5. **Your responsibilities**

with thanks to Piers Howe for development of some of what follows.

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**INPUT INTO V1**

Projections of *magno and parvo* cells of LGN arrive at specific *sublaminas* of V1.

- Magno: 4Cα
- Parvo: 4Cβ and 4A

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**EARLY PATHWAYS**

- **lateral geniculate nucleus (LGN)**
- **V1 striate cortex**

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**KSJ4, Fig 27-4**

**KSJ4, Fig 27-16**
Orientation columns: cells in a vertical penetration tend to respond to similar orientations.

Ocular dominance columns: Input from each eye often remains segregated (at least in input layers).

Hypercolumn: A hypercolumn contains all the apparatus needed to process input from a specific retinal location: ocular dominance columns, each with a complete set of orientation columns as well as several “puffs” (Wong-Wiley) or “blobs” (Livingstone & Hubel) (regions of high cytochrome oxidase staining).

REST OF V1

Note: The diagram reproduced in the previous panel seems to suggest that the location of pinwheel centers is “between” cytochrome oxidase blobs.

Such may not be the case. There are a number of technical issues regarding how one measures the location of pinwheels that are beyond the scope of CN 530.

For more on this, you can take CN 780 with Prof. Eric Schwartz, or ask Jon Polimeni . . . who helped to develop the content of the next dozen panels.

PINWHEELS

Pinwheel representation of orientation columns: Note “smooth” variation and vortex singularity. (Scale: 1 X 1 X 2 mm)

. . . averaging over many cells!

ORIENTATION COLUMNS AND HYPERCOLUMNS

Figure 34. Our current model of the modular organization of macaque striate cortex (modified from Hubel and Wiesel, 1977).

Figure 5. Orientation preferences of units in a single 5-mm-long penetration in layers 2 and 3 of macaque parafoveal striate cortex. The orientation preference changes in a remarkably regular way, with only two reversals in the entire 5 mm. The rectangles indicate blobs [cytochrome oxidase “puffs”], where there is no orientation preference, and the sequence continues linearly as if the blob were not there.
An alternative hypothesis about the relation of orientation tuning “layout” with respect to the location of the blobs.

Note that “pinwheel” centers coincide with blob locations.

Using optical recording technique, one sees pinwheel centers displaced from cytochrome oxidase blobs.
FINDING EDGES IN SCALE SPACE

This image stolen from scale space tutorial available at:
http://www.nada.kth.se/~tony/cern-review/cern-html/

BLURRING OF ORIENTATION DATA

Finding the “average” of orientation tuning is tricky.

Research in Eric Schwartz’s lab indicates that the effective blurring region for averaging orientation tuning in optical recording is on the order of 300 microns.

Reasons include:
1) Photon scatter in cortical tissue.
2) Optics of macroscope lens.
3) Signal-to-noise issues in processing data.

These facts have important implications re: the “reall” location of pinwheel centers w/r/t blobs.

For details: Contact Eric and/or see CN 780 course materials.

Note that in the previous panel:
1) Corresponding edges at two adjacent scales may be *shifted* in location.
2) Edges that exist in one scale *may not exist at all* at the next larger scale.
2. PHYSIOLOGY OF EARLY VISUAL PATHWAYS

*Midget (M) and parasol (P) cells of retina input to parvocellular (P) and magnocellular (M) pathways, respectively!*

The pathways are often said* to have qualitatively different functional roles:

**P pathway**: form, fine stereopsis and color

**M pathway**: motion and coarse stereopsis

* *a hypothesis, not yet proven*

KSJ4,  
Fig 27-6

Determination of the roles of *magno* and *parvo* streams is one of the core issues in visual neuroscience today.

One simple hypothesis is that magno and parvo are really not that different (apart from sensitivity to wavelength), with *magno* favoring higher temporal frequencies and lower spatial frequencies while *parvo* can resolve higher spatial frequencies but lower temporal frequencies.

There are conflicting views of both:

1) the degree of differentiation vs. overlap of function, and
2) the degree of anatomical interaction and physiological cross-talk between the pathways.

There is much psychophysics on e.g., “form-motion interactions” that rules out a clean separation of function.

There is some degree of cross-talk at a physiological level, though the “amount” of cross-talk is hard to quantify. Why?!

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**M AND P PATHWAYS**

**Magnocellular pathway**

- Larger receptive fields
- Less responsive to high spatial frequencies
- Wavelength insensitive
- Transient responses to stimuli
- Higher sensitivity to luminance contrast
- Faster response to change

**Parvocellular pathway**

- Smaller receptive fields
- More responsive to high spatial frequencies
- Wavelength sensitive
- Sustained responses to stimuli
- Lower sensitivity to luminance contrast
- Slower response to change
HISTORICAL NOTE

Certain older sources refer to “X” and “Y” cells, rather than to magno and parvo.

X and Y refer to CAT only.
Magno and parvo refer to primate brains.

X
“linear”
medium velocity axons
sustained response
small receptive fields

Y
“nonlinear”
rapid velocity axons
transient response
large receptive fields

Note: While X and Y are superficially similar to magno and parvo characteristics, respectively, there are important differences.

More generally: Any anatomical or physiological feature may be more or less specific to an individual species (e.g., macaque, owl monkey, . . .)

Moral: Note which species is being referred to!
INTERDISCIPLINARY NOMENCLATURE

Bonus question: What is the difference between a cortical pathway and a channel?

Answer: “pathway” is an anatomical term, whereas “channel” is purely a functional term.

A psychophysicist might speak of “spatial frequency channels,” without making any claims at all about anatomically distinct pathways for processing different spatial frequencies.

The issue of “how many (spatial frequency) channels?” then becomes a question of how many basis functions are needed to span the space of psychophysically measured performance . . . under blah-blah-blah assumptions . . .

However, in practice the terms “pathways” and “channels” (and “streams”) are often used loosely.

BASIC CORTICAL CELL RECEPTIVE FIELDS (V1)

Unoriented -- layer 4 or “blob”

Simple cell -- oriented
  odd symmetric*
  distinct excitatory and inhibitory subregions

Simple cell -- oriented
  even symmetric*
  distinct excitatory and inhibitory subregions

Complex cell -- oriented
  no distinct excitatory and inhibitory subregions

* Many, and possibly most, simple cells are neither odd nor even.

ENDSTOPPED CELLS

Complex and (even) “simple” cells may be endstopped. How can you tell?

response:

weak

moderate

strong

zero*

* Perhaps the response is only severely reduced from maximum.

Single and Double Endstopping

* This nomenclature is from Starbucks not from neurophysiology.
Hubel and Wiesel’s original nomenclature referred to a presumed hierarchy of simple, complex, and hypercomplex cells.

The latter are now generally referred to as “end-stopped complex cells.”

Meanwhile, endstopping has been observed in some simple cells.

The interconnected circuitry of the various cell types makes the idea of going “from” simple to complex to hypercomplex suspect.

MORE PHYSIOLOGY: RECEPTIVE FIELDS

What does the phrase “receptive field” mean? . . . to a neurophysiologist? . . . to neural network modelers?

“Receptive field” is a functional, not an anatomical concept.

“The receptive field of a ganglion cell (or any other cell in the visual pathways) is that area of the retina where stimulation of photoreceptors with light causes either an increase or decrease of the ganglion cell’s firing rate.”

[emphasis added] (K, S, & J., 3rd Ed., p. 409*)

*Note: This definition is absent in the 4th edition! Why??!

RECEPTIVE FIELDS, MORE OR LESS

Note: Receptive field regions (or “sub-regions”) may be excitatory or inhibitory.

Q: How can an inhibitory receptive field region be measured?

A1: With difficulty, if a cell’s spontaneous firing rate is low.

A2: With more difficulty, if the inhibition is “silent” i.e., purely shunting, whereby no hyperpolarization occurs, and there must be excitatory input provided in order for the inhibition to be “noticed” by the experimenter.

RECEPTIVE FIELD ATTRIBUTES

In practice, we speak of attributes of a receptive field, not just its location in retinal coordinates. E.g., What about a RF’s center-surround organization? contrast sensitivity? orientational tuning? directional selectivity? etc.

Contextual modulation of RF attributes: E.g. “disappearance” of OFF-surround of ganglion cells at low light levels.

Temporal characteristics:

a) sensitivity to flicker rate, speed, etc.

b) rate of adaptation (to contrast, motion, etc.)

c) dynamics of tuning to dimensions of sensitivity (e.g. orientation, motion direction, etc.)
SPACE-TIME RECEPTIVE FIELDS, I

“Traditionally, the receptive field of a neuron is defined as the area of visual field within which visual stimulation influences neural responses. This classical notion no longer provides an adequate framework for understanding visual receptive fields. We must consider an additional dimension of time, and define receptive fields in the joint domain of space and time. For many cells in the visual cortex, there is no such thing as a unique spatial receptive field.” [emphasis added]

[IZumi Ohzawa]

Go to Ohzawa's excellent site:

Space-Time Receptive Fields of Visual Neurons

SPACE-TIME RECEPTIVE FIELDS, II

LGN cell: “ON-center, OFF-surround” (?)

Demos on this page downloaded from:
http://www.bpe.es.osaka-u.ac.jp/ohzawa-lab/teaching/AA_RFtutorial.html

Go there to learn about the reverse correlation technique.

TEMPORAL ASPECTS OF RECEPTIVE FIELDS

Some simple cell RFs are (apparently) simple:

with thanks for demo to Dario Ringach
http://manuelita.psych.ucla.edu/~dario/

NONCLASSICAL RECEPTIVE FIELDS

More on contextual modulation --
Identified RF attributes grow in complexity each year.
E.g., Cells of MST have been called “differential geometers:” “Center-surround” for radial expansion and contraction.

Also, cells exist that fire vigorously whenever a contrastive pattern moves horizontally to the right within a relatively clearly defined circular region, and that will not respond to movement in any direction anywhere else within the visual field.

But motion of the entire visual field horizontally to the right can null the response of the cell, even though the preferred pattern motion occurs within its “classical receptive field.”
FOOD FOR MENTAL INDIGESTION

The idea of “nonclassical receptive fields” is a bit tricky.

Do some cells have classical receptive fields, while others have nonclassical receptive fields?

Or . . .

Are all cells that used to be thought of as having classical receptive fields now thought of as also having nonclassical receptive fields?

Or

Is there just one unified way that we should think about receptive fields, which is a “nonclassical” way, compared to how we used to think?

RECEPTIVE FIELD SELECTIVITY

Barlow (1953) (rabbit) found cells that respond to small but not large stimuli; he devised the concept of “trigger feature.”

Lettvin, Maturana, McCulloch & Pitts (1959) “What the frog’s eye tells the frog’s brain.” discovered four classes of cells in frog’s retina (classified by function and morphology.)

- Boundary detectors
- Movement-gated-dark-convex-boundary (i.e., ____ detectors.)
- Moving or changing contrast detectors
- Dimming detectors

Lettvin was “laughed off the stage” (Schiller, 1986).

3. PROCESSING STRATEGIES

Processing strategies for which physiological evidence exists:

- **Topography** (retinotopic maps)
- **Space-variant processing** (cortical magnification factor)
- **Hierarchy** -- and “heterarchy”
- **Laminae** (layers) (functional significance?)
- **Feedback** -- within and between laminae and across cortical areas (time scales?)
- **Parallelism** (“branching” and “massive”)
- **Columns** and **hypercolumns**
- **Opponency** (and opponent channels)
- **Multiple scales** (channels) for spatial frequency tuning

Open question: How does the brain utilize these different strategies? Why are these different strategies needed?

4. PARTING THOUGHTS

1) Utility of data:
   Q: Given the complexity of the visual system only through LGN (tip of iceberg), how can psychophysical data be related to cell physiology?

2) What are valid degrees of abstraction for neural modeling?
   McCulloch-Pitts neuron? Integrate and fire neurons? Dendritic level (e.g. Genesis)? Field theory for maps? Waves of activation (e.g. fMRI)?

   A combination of the above?
FURTHER PARTING THOUGHTS

3) Uncertainty:

Same response:

\[
\begin{array}{cc}
\text{luminance} & \text{space} \\
\text{luminance} & \text{space}
\end{array}
\]

E.g. low amplitude, centered vs. high amplitude, displaced stimulus

Note: Uncertainty is an issue cells’ selectivities for orientation, scale, direction of motion, etc., as we shall see.

STILL MORE PARTING THOUGHTS

4) Sensitivity: What does it mean for a cell to be sensitive to some input dimension (e.g. contrast, wavelength, orientation, direction, speed)?

a) Weaker form: (Too weak?) Change along that dimension of stimulation sometimes changes response.

b) Stronger form: Under appropriate controls, monotonic (stronger still: linear) relation of response magnitude with stimulus variation can be shown for some range.

Functional significance? Even though a cell’s response varies systematically with, e.g., stimulus speed, that does not necessarily mean that the cell’s function is to signal speed. There may be factors of spatial or temporal frequency that affect the cells response to, e.g., stimulus onset, and that happen to covary with stimulus speed.

5. YOUR RESPONSIBILITIES

There will not be another anatomical/physiological lecture in CN530, though physiological data will be addressed in many places in upcoming lectures.

You are responsible for covering physiological material from required readings at a level of detail exemplified in this lecture.

Pay particular attention to material on:
- general function of major processing areas (e.g. LGN, V1, V2, V4.)
- motion-sensitive cells
- binocularly tuned cells
- anatomical and physiological evidence for functional pathways (e.g. form, motion, color pathways etc).