Introduction to Neuroscience

Visual Processing by the Retina
Vision
Different visions

• Many different versions of the eye, e.g.
  – Horseshoe crab
  – Compound eyes
  – Mammalian eye
Structure of the human eye
Fig. 2.8. A man would need a compound eye of at least 1 m diameter to get the same angular resolution as his lens eye. (From Kirschfeld 1976.)
Retinal Development

- Ectoderm
- Cell classes and molecules as the brain
- Why is it there?
Retina layout

Cajal
Retinal Organization I

- choriocapillaris
- Bruch’s membrane
- retinal pigment epithelium
- outer segments
- inner segments
- outer limiting membrane
- outer nuclear layer
- fiber layer
- outer synaptic layer
- inner nuclear layer
- inner synaptic layer
- ganglion cell layer
- optic fiber layer
- inner limiting membrane

100 µm

source: Boycott and Dowling, 1969
Retinal Organization II
Currently, there are no studies of Berson and colleagues, who used vital dyes. It also allows, in the more recent work, physiological methods that are less capricious than the Golgi, because they target primarily visual microinjection [20, 21]. This method has been used in the rabbit. The studies of cat and monkey show that when seen by the Golgi method, a total of 29 types of neurons have been published from the monkey [14, 25]. Less has been done for green fluorescent protein, and particle-mediated transfection techniques have been used to fill cells: photofilling, flow injection, and cell-mediated transfection. We are searching for completeness by using four mechanistically independent methods for filling cells: photofilling, flow injection, and cell-mediated transfection. However, it is possible that some neurons may have been missed.
• Sensory, “simple” closed system
• Multi-layered neural system
• Non-trivial computations
• Relatively easy to record from
• Important concepts discovered in the retina
Photoreceptors: Rods and Cones

Rods to Cones ratio ~ 20:1
Slow integration time in rods (~100 ms), faster in cones
Photoreceptors

Frog

Fish

Turtle

Human
Photoreceptors in Mouse retina

rods

cone

10 µm
Distribution of photoreceptors in the human retina

After, 1935
Ophthalmic view of the retina

Human retina

fovea

optic nerve
Fovea cross-section (human)
Blood vessels around the fovea
How photoreceptors work
Translating light into electricity

- Dark current of Na+ and K+ ions
- Cells are depolarized without light
- Light shuts down the Na+ current
Biochemical circuit of vision

- $\sim10^8$ Rhodopsins per photoreceptor
- Each excited rhodopsin diffuses in the membrane and catalyzes a change in $\sim100$ molecules of the regulatory transducin protein that activates a Phosphodiesterase molecule, which ends up breaking $\sim10^4-10^5$ cGMP/s.
Rhodopsin noise is very low

Spontaneous rate of rhodopsin transition is 1 per 1000 years per molecule (compared to 1/yr for retinal), which gives ~2 events/min/cell
Reliable response of rods to single photons

Rieke & Baylor, Rev Mod Phys, 1998
Photoreceptor detections of single photons

agreement indicates that the neural circuitry processing the rod responses acts effectively noiselessly (Barlow, 1977). Indeed the dynamics of the initial step in the processing of the single-photon response can be predicted based on the rod signal and noise spectra and an optimal design argument (Bialek and Owen, 1991).

VI. REPRODUCIBILITY OF THE SINGLE-PHOTON RESPONSE

Reliable photon counting requires that the detector's responses to the same input vary little from trial to trial, so that the responses to each absorbed photon have a similar size and shape. The rod meets this requirement. If we repeatedly present a rod with a very dim flash of nominally fixed intensity, there are large intertrial fluctuations in the response due to variability in the number of absorbed photons, but there is little variability in the rod's response to a single absorbed photon. This reproducibility of the elementary response allows the rod to encode accurately the number of absorbed photons.

Reproducibility of the rod's elementary response can be demonstrated by presenting the rod with a series of dim flashes as in Fig. 4(d) and analyzing the statistics of the resulting responses. Figure 7(a) shows a simple statistical measure — a histogram of the maximum response amplitudes. The stepped curve is the experimental data and the smooth curve is the theoretical prediction. Figure 7(b) shows the time-dependent ensemble variance of a series of dim flash responses and of single-photon responses alone. The variance in darkness has been subtracted in each case. The curve labeled ''all responses'' is calculated from all 349 responses contributing to the histogram in (a). The curve labeled ''singles only'' is calculated only for responses with amplitudes between 0.3 and 1.2 pA; most of these are responses to a single-absorbed photon. Thus the variance of the single-photon response is much smaller than the variance introduced by the Poisson statistics of photon absorption; this low variability of the elementary response allows for accurate photon counting.

Figure 8. Possible mechanisms responsible for the reproducibility of the rod's elementary response. (a) Saturation. Saturation of an element of the transduction cascade downstream of rhodopsin (e.g., closure of all channels) could reduce variability in the elementary response by making the current insensitive to fluctuations in the time course of rhodopsin's activity. (b) Feedback. A downstream activation product of rhodopsin could act as a feedback signal, causing rhodopsin to shut off once the elementary response had reached an appropriate amplitude. (c) Multistep rhodopsin deactivation. The rhodopsin molecule's catalytic activity might be reduced by a series of transitions, each of which reduced the activity by a small amount and occurred after a stochastic, first-order delay. In spite of variations in the timing of the transitions (e.g., three traces shown), the integrated catalytic activity would be more constant than that in the case where a single transition terminates rhodopsin's activity.

Figure 7. Reproducibility of the rod's elementary response. (a) Histogram of the response amplitudes from an experiment such as that in Fig. 4(d) in which 349 responses were collected. The peak centered around 0 pA is from trials in which no photons were effectively absorbed, and the peak around 0.6 pA from the single-photon responses. The smooth curve fitted to the experimental histogram is calculated assuming the noise in darkness and the noise in the single-photon response amplitude are independent and additive and that the number of photons absorbed per trial is described by Poisson statistics. This fit provides an estimate of the standard deviation and the mean of the elementary response amplitude; in this cell the mean was 3.9 times greater than the standard deviation. (b) Time-dependent ensemble variance of a series of dim flash responses and of single-photon responses alone. The variance in darkness has been subtracted in each case. The curve labeled ''all responses'' is calculated from all 349 responses contributing to the histogram in (a). The curve labeled ''singles only'' is calculated only for responses with amplitudes between 0.3 and 1.2 pA; most of these are responses to a single-absorbed photon. Thus the variance of the single-photon response is much smaller than the variance introduced by the Poisson statistics of photon absorption; this low variability of the elementary response allows for accurate photon counting. (c) Expected distribution of single-photon response amplitudes if rhodopsin's catalytic activity shuts off in a first-order, memoryless transition and the amplitude of the response is proportional to rhodopsin's lifetime. This exponential distribution is compared to the measured distribution of the single-photon response amplitudes from the experiment in (a).
We can see single photons

Figure 2.2: Probability of seeing calculated from Eq. (2.2), with the threshold photon count $K = 6$, compared with the experimental results from Hecht, Shlaer and Pirenne. For each observer we can find the value of $\theta$ that provides the best fit, and then plot all the data on a common scale as shown here. Error bars are computed on the assumption that each trial is independent, which probably generates error bars that are slightly too small.

The first nontrivial result of these experiments is that human perception of dim light flashes really is probabilistic. No matter how hard we try, there is a range of light intensities in which our perceptions fluctuate from flash to flash of the same intensity, seeing one and missing another. Quantitatively, the plot of probability of seeing vs log(intensity) is fit very well by the predictions from the Poisson statistics of photon arrivals. In particular, Hecht, Shlaer and Pirenne found a beautiful fit in the range from $K = 5$ to $K = 7$; subjects of different age had very different values for $\theta$ (as must be true if light transmission through the eye gets worse with age) but similar values of $K$. In Fig 2.2 I've shown all three observers' data fit to $K = 6$, along with error bars (absent in the original paper); although one could do better by allowing each person to have a different value of $\theta$, it's not clear that this would be supported by the statistics. The different values of $\theta$, however, are quite important.

Details aside, the frequency of seeing experiment brings forward a beautiful

After Hecht et al, 1943
Color vision is based on 2 or 3 receptors
Variety of photo absorbing tools
Cones vs. Rods...

- Cones response is much faster and transient.
- Seems that Rods are more reliable in transmitting signals to their cones (which is why they are useful in the dark).
- Rods saturate at bright lights and cones do not.. (very high rates of regeneration of rhodopsin).
Bipolar cells

Bipolar cell types primate retina

- DB-diffuse types
- MB-midget types
- BB-blue cone type
- GBB-giant bistratified type
- RB-rod bipolar
Bipolar cells pathways
Ganglion cells

Light

$E_{Rb}$

Light

$E_{x}$

Off-center bipolar cell

Off-center ganglion cell

On-center ganglion cell

On-center bipolar cell

To optic nerve

Cone

Action potentials
Ganglion cells mostly encode differential signals

Kuffler, 1953
Midget and Parasol cells
Some types of ganglion cells in cat retina
Retinal computation
B  Parvocellular receptive fields

C  Magnocellular receptive fields
Position, shape & function of ganglion cells are related
Retinal organization

- Random layout of different types
- Exclusion zone for cells of same type

Rockill et al. PNAS 2000
Mosaics of Ganglion receptive fields in the primate retina

Shlens et al 2009
Classes of Horizontal cells in primate retina
Horizontal cell coverage & connectivity in the primate retina (H1)

Packer & Dacey, J vision, 2002
Many types of Amacrine cells (and they do cool things)
Direction Selective
Retinal Ganglion cells

![Diagram of Direction Selective Retinal Ganglion Cells]

- Postsynaptic model
- Inhibitory-NULL presynaptic model
- Excitatory-PREF presynaptic model
Dendritic visual computation in Amacrine cells

Detwiller & Denk, 1999
Basic mammalian retinal architecture
Retinal Coding
Mathematical models of Ganglion cell responses
Decoding visual information from the retina

A

1 cell (A)

2 cells (A,B)

... 

14 cells (A-N)

A

B

C

D

E

F

G

H

I

J

K

L

M

N

3.5

4.0

4.5

Time (s)

Warland et al. 1997
Decoding from more cells…

Einat Granot-Atedgi (MSc thesis)
Retinal adaptation

- Photoreceptors adaptation to light level relies on Ca2+ buildup
- Ganglion cell adaptation to light level relies on photoreceptor adaptation as well as interneuron, synaptic, and ganglion cell adaptation
Detectable light spot after dark adaptation

Retinal Contrast Adaptation

Figure 6. Contrast Adaptation in the Light Response of Salamander Retinal Ganglion Cells

(A) Firing events in response to uniform random flicker (see Figure 5A) of the same mean intensity but varying contrast. The contrast, $C$, measured as the standard deviation of the Gaussian intensity distribution in units of the mean, is indicated on the right. The two stimulus traces (top) show the time course of the light intensity for the two extreme values of contrast, $C = 0.023$ and $C = 0.35$. Note that the waveforms are identical except for the magnitude of fluctuations about the mean intensity.

(B) The average firing rate of a ganglion cell following a change in the contrast of uniform random flicker (from Smirnakis et al., 1997). Every 100 s, the contrast $C$ alternated between 0.09 and 0.35. A sample intensity waveform is shown at the top, but each stimulus trial used a different random sequence. The firing rate was computed from the average spike count over 100 trials in 5 s time bins.

(C) The average firing rate of a ganglion cell following a change in the spatial pattern of random flicker (from Smirnakis et al., 1997). Every 60 s, the stimulus pattern alternated between a uniform field and a checkerboard of 0.272 mm square size. The uniform field and each square of the checkerboard were modulated by independent random flicker sequences, all with the same mean and a contrast $C = 0.24$. The firing rate was computed from the average spike count over 50 trials in 2 s time bins. Note that following adaptation to the checkerboard, the response is more sensitive to the uniform field, and vice versa, following adaptation to the uniform field, the response is more sensitive to the checkerboard.

Such adaptation to contrast is a well-known phenomenon in human psychophysics. For example, after prolonged viewing of a high-contrast grating, our sensitivity is reduced in a low-contrast environment. For some cells, the threshold for firing appears to vary in proportion to the contrast for detection of similar gratings is much reduced (Blake-More and Campbell, 1969). The loss of sensitivity under high-contrast conditions and subsequent recovery under low-contrast conditions requires several seconds fluctuations (Figure 6A). After a shift back to low contrast, the retina's sensitivity gradually recovers to the initial state.

These adjustments in sensitivity are relatively slow contrast adaptation have been observed in the responses of neurons in the visual cortex (Albrecht et al., 1984; Ohzawa et al., 1985; Allison et al., 1993; Carandini and Ferster, 1997). These changes have been thought to arise in cortical circuitry, because adapting stimuli presented to one eye can have some effect on test stimuli presented to the other eye. However, recent work shows that such gradual contrast adaptation also occurs in the retina and substantially modifies the light response of retinal ganglion cells. These changes are revealed in experiments where a flickering visual stimulus suddenly changes from low contrast to high contrast of the same mean intensity (Donner et al., 1991; Smirnakis et al., 1997). Following such a switch, the retina gradually reduces its sensitivity. When this adaptation is complete, one finds that in the high-contrast environment larger intensity transients are required to trigger a ganglion cell response than in the low-contrast environment. For some cells, the threshold for firing appears to vary in proportion to the contrast for detection of similar gratings is much reduced (Blake-More and Campbell, 1969). The loss of sensitivity under high-contrast conditions and subsequent recovery under low-contrast conditions requires several seconds fluctuations (Figure 6A). After a shift back to low contrast, the retina's sensitivity gradually recovers to the initial state.

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Population activity of ganglion cells
Typical correlations between pairs of ganglion cells is weak

Schneidman et al 2006
Redundancy of ganglion cells

Puchalla et al 2005
Retinal networks are strongly correlated

Schneidman et al 2006
Activity waves in development

Meister et al 1994
Calcium waves during development

Feller et al 1996
Neuronal shape depends on local Calcium signals

Fig. 8. Live confocal imaging of a GFP-expressing chick retinal ganglion cell during embryonic development. Removing extracellular calcium causes shrinkage of the dendritic arbor.
From the retina to the brain
saccades
Fixational eye movements
Movement prediction

Berry et al. Nature 1999
Omitted Stimulus Response

Schwarz et al, Nat Neuro, 2007
Light Sensitive Ganglion Cells

Diversity of photoreceptor distribution

Roorda & Williams, Nature, 1999
Augmented vision? adding a new photoreceptor

Eye Smarter than Scientists Believed: Neural Computations in Circuits of the Retina

A

B

C

Gollisch+Meister 2010
Upward motion sensitive cells

Kim et al, 2008
Human primary visual pathway
Output to LGN

![Graph showing the number of cells in various parts of the visual system including retina and visual cortex.]
Principles of sensory coding?

• Receptor types and layout
• Natural scene statistics
• Optimal coding
• Redundancy reduction vs. error-correction
• Predictive coding
• Throwing information?