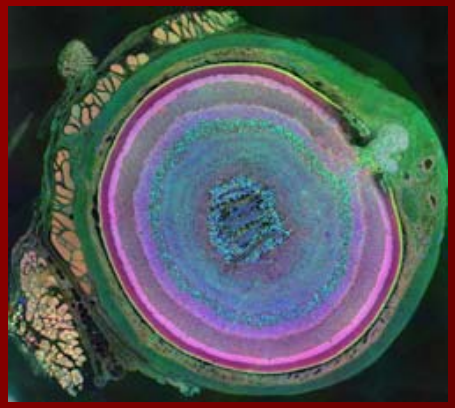
# CLINICAL VISUAL OPTICS
# OPTO 223: WEEK VI

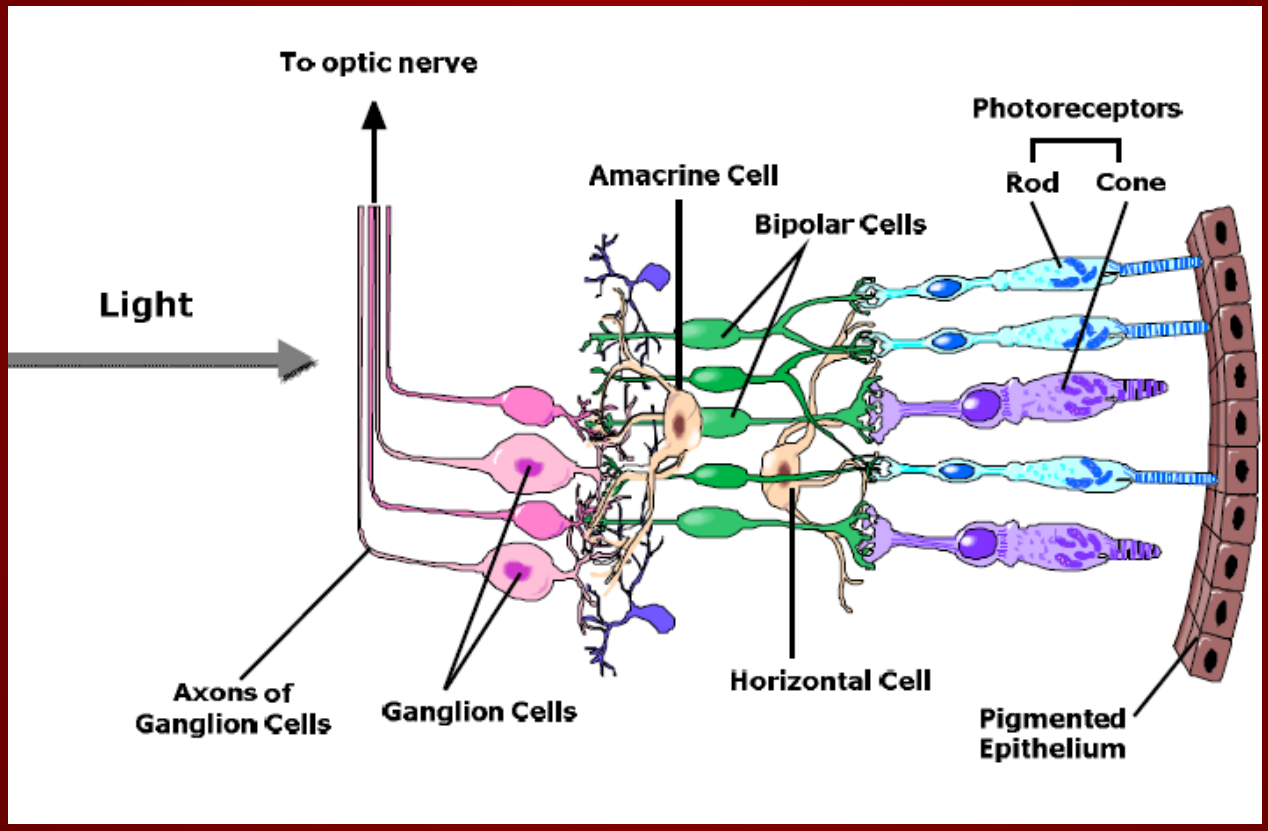
Dr Salwa Alsaleh

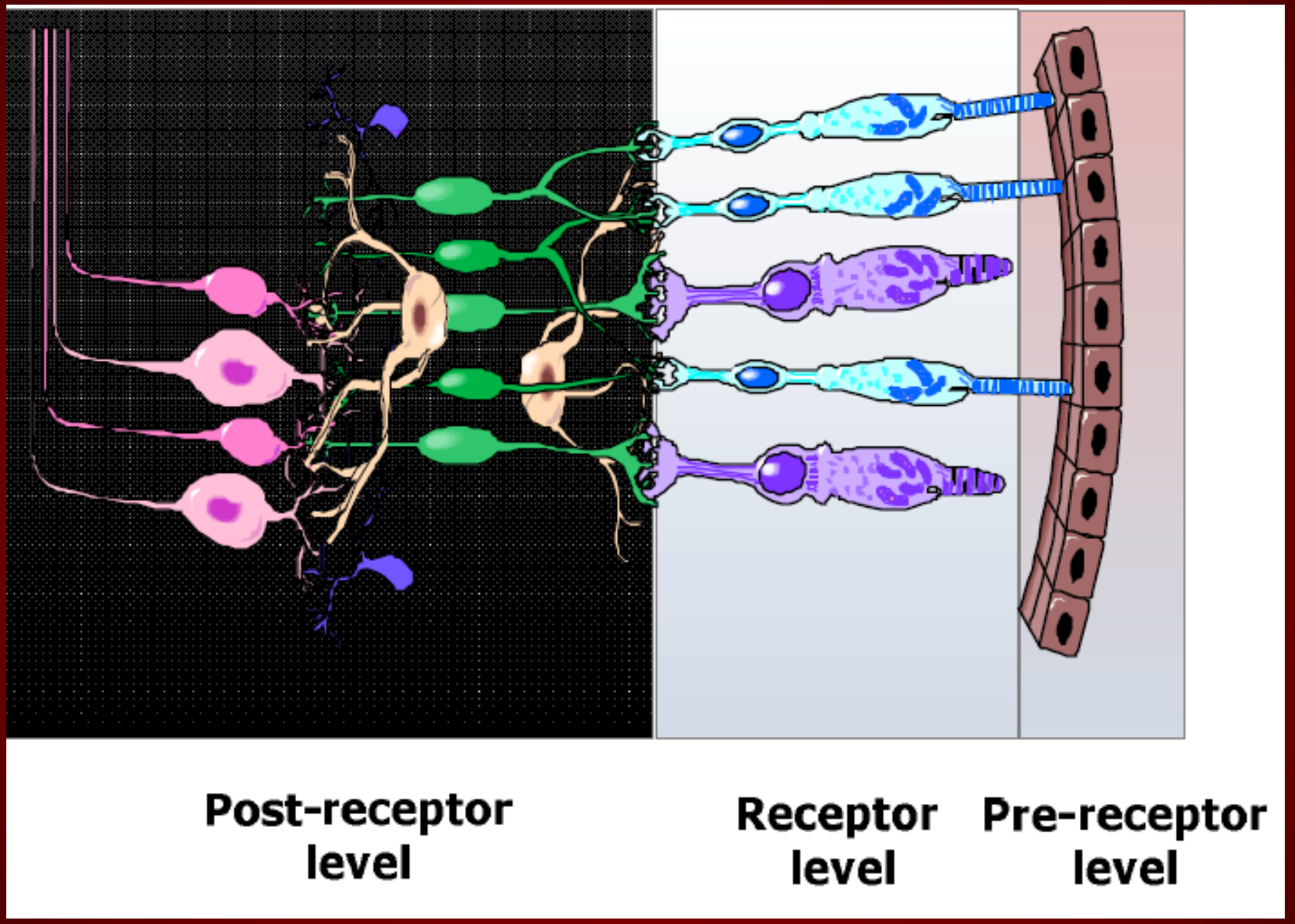
# WEEK IV : OUTLINE

- **Retinal electrophysiology review**
- Electrophysiological vision tests:
- ERG test
- VECP test



# REVIEW OF RETINAL ANATOMY





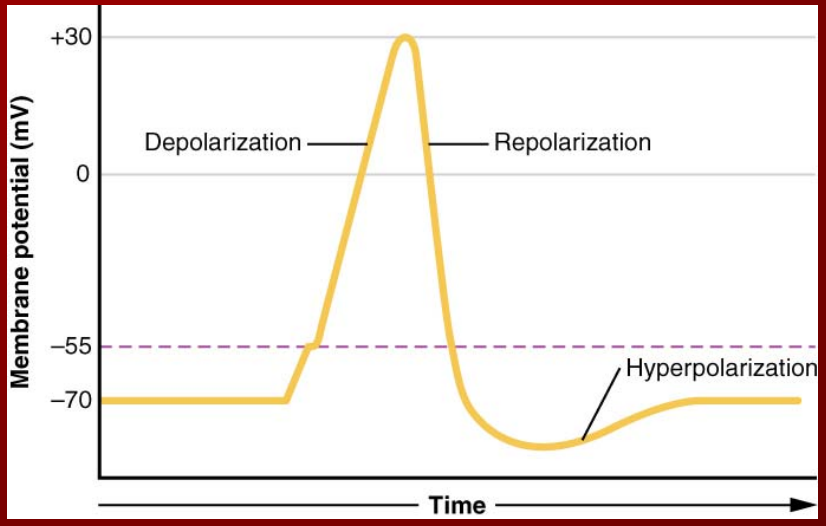
Post-receptor level

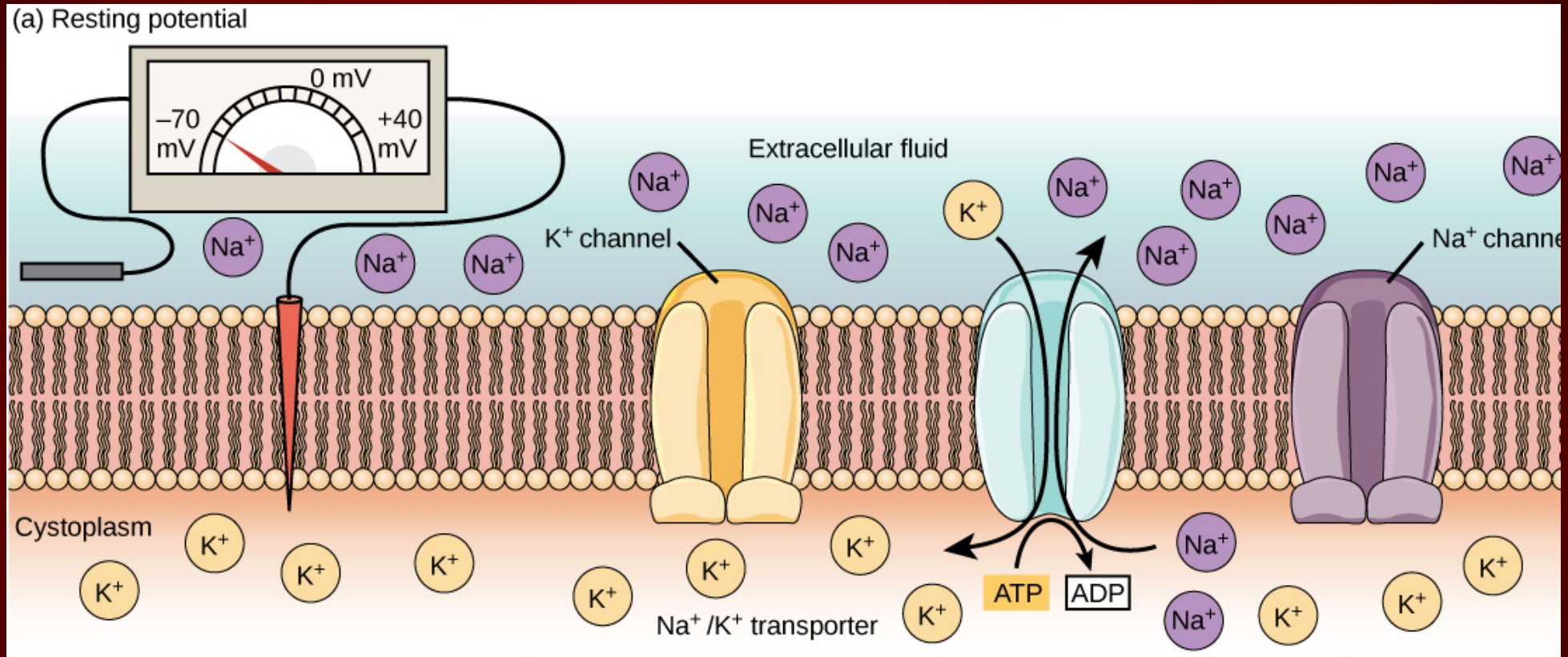
Receptor level

Pre-receptor level

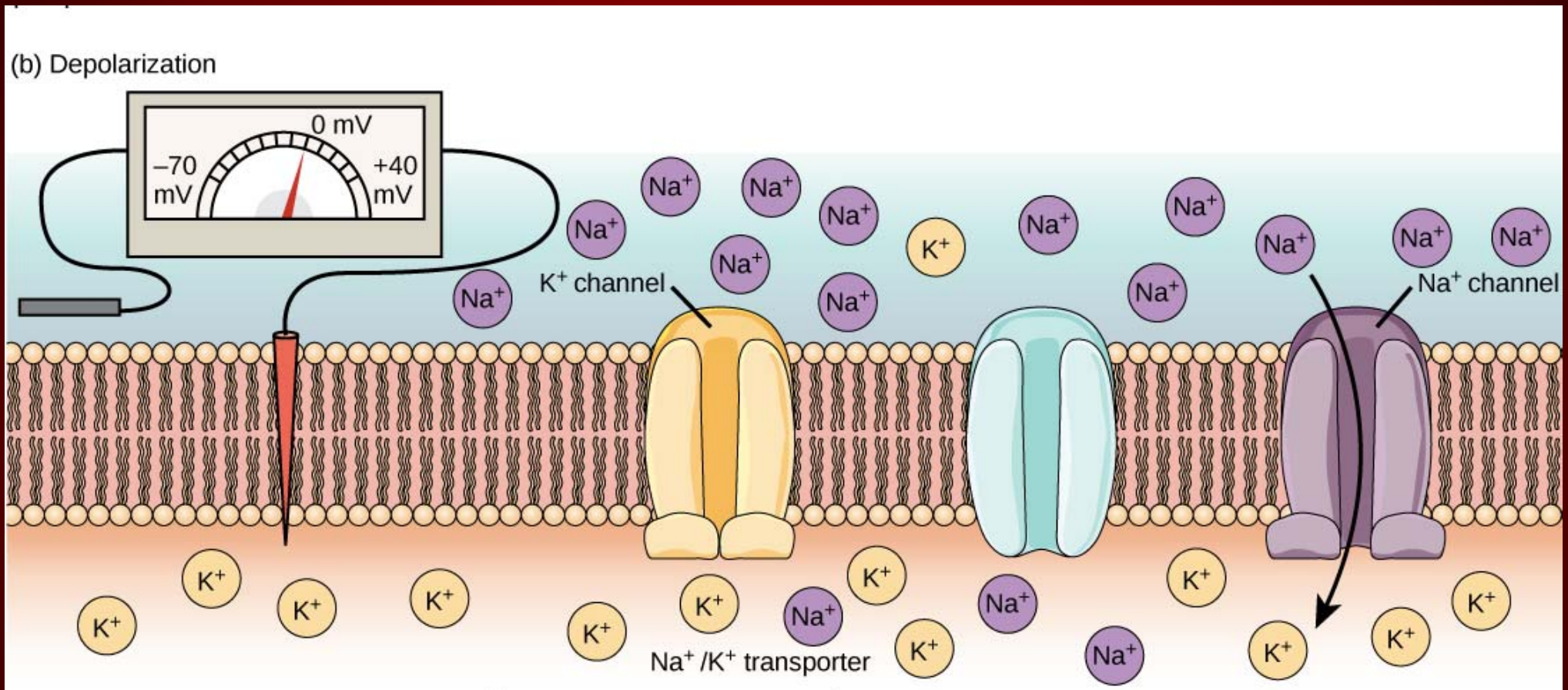
# HYPERPOLARIZATION AND DEPOLARIZATION

- **Hyperpolarization** is a change in a cell's membrane potential that makes it more negative. It is the opposite of a **depolarization**. It inhibits action potentials by increasing the stimulus required to move the membrane potential to the action potential threshold.

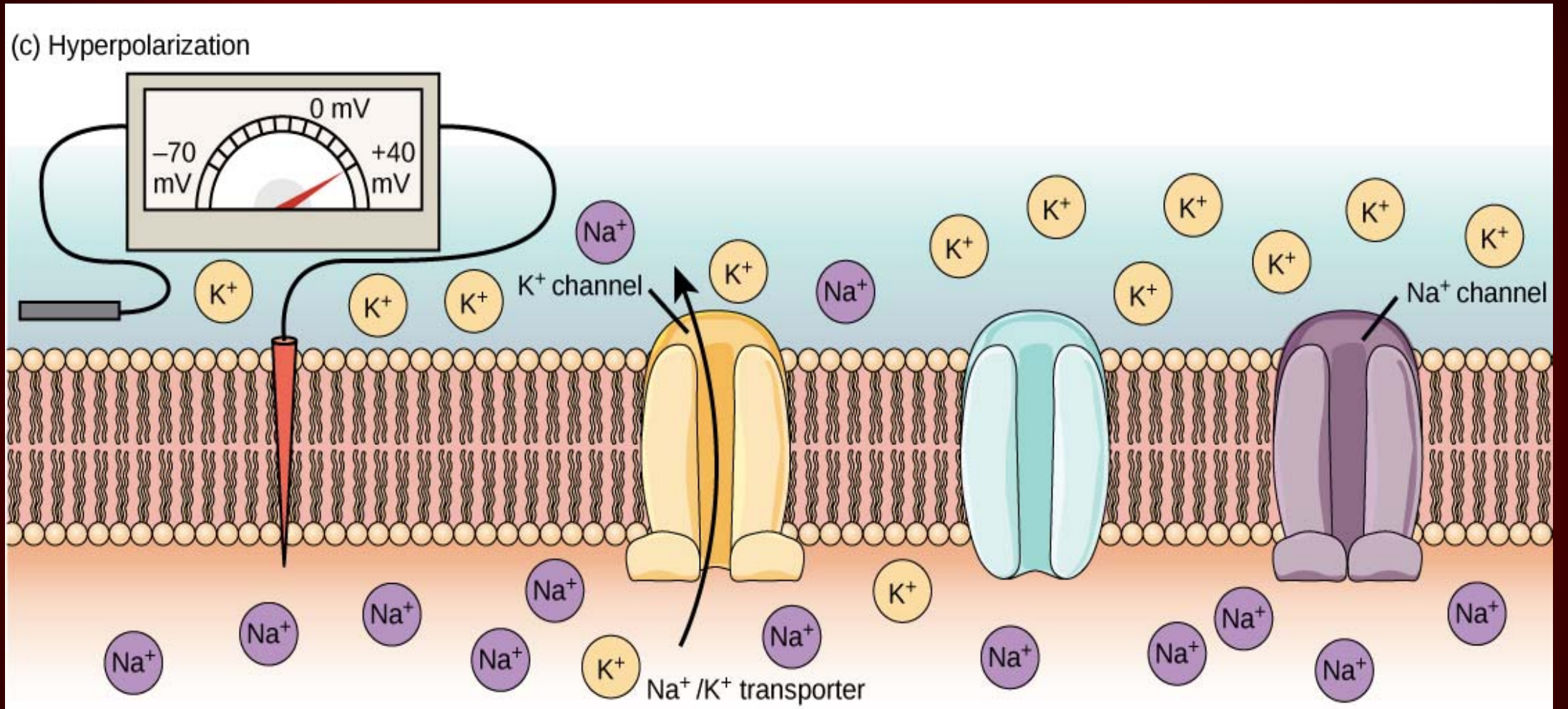





At the resting potential, all voltage-gated $Na^+$ channels and most voltage-gated $K^+$ channels are closed. The $Na^+/K^+$ transporter pumps $K^+$ ions into the cell and $Na^+$ ions out.




In response to a depolarization, some $Na^+$ channels open, allowing $Na^+$ ions to enter the cell. The membrane starts to depolarize (the charge across the membrane lessens). If the threshold of excitation is reached, all the $Na^+$ channels open.




At the peak action potential, $Na^+$ channels close while $K^+$ channels open. $K^+$ leaves the cell, and the membrane eventually becomes hyperpolarized.

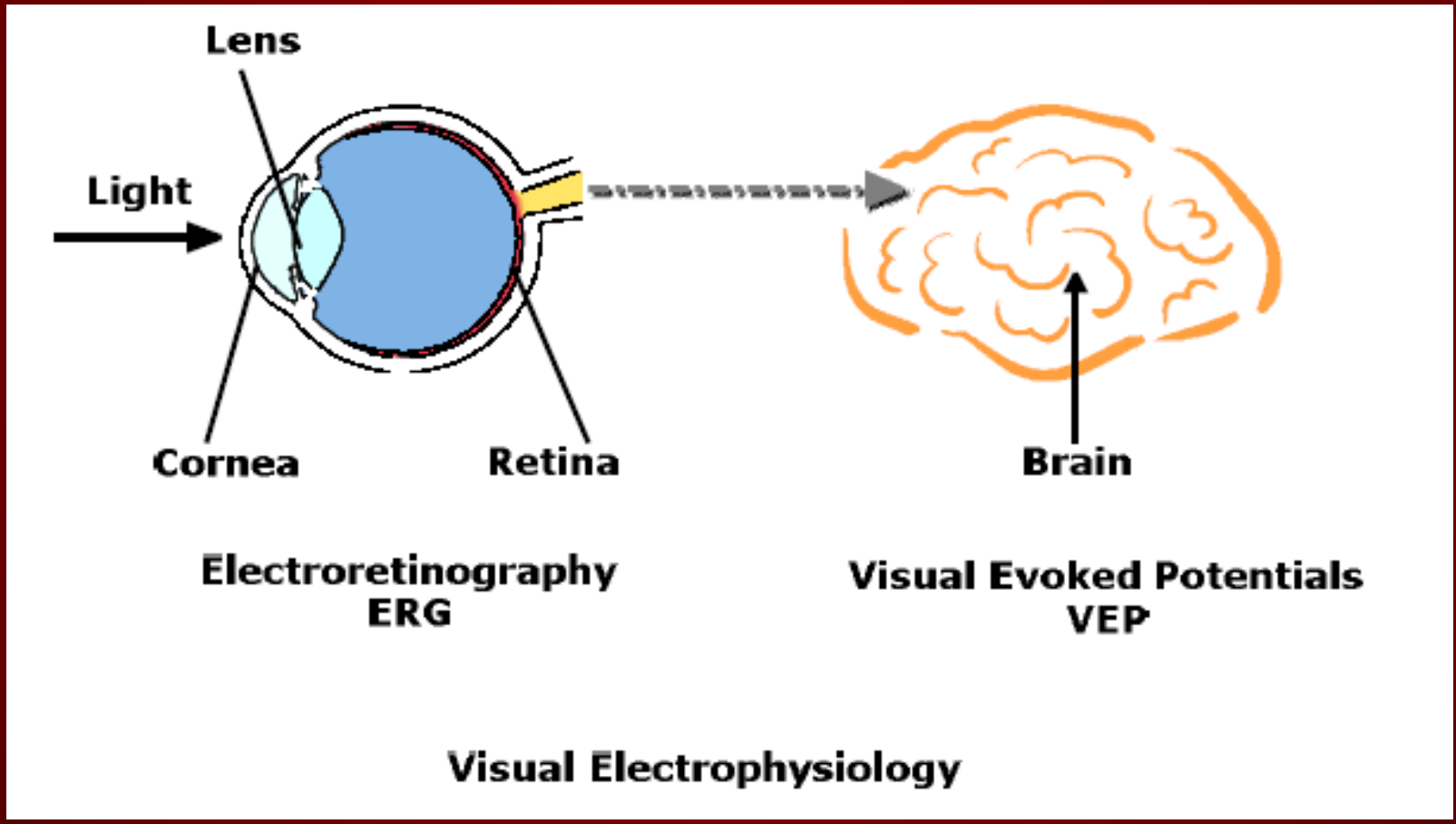
# RETINAL ELECTROPHYSIOLOGY

- **►Receptor level : hyperpolarisation**
- **►Post-receptor level**
- Bipolar cells : depolarisation or hyperpolarisation
- Horizontal cells : hyperpolarisation
- Amacrine cells : transitory hyperpolarisation
- Ganglionar cells : depolarisation or hyperpolarisation
- **►Pre-receptor level : depolarisation after hyperpolarisation**

# ELECTROPHYSIOLOGICAL VISION TEST

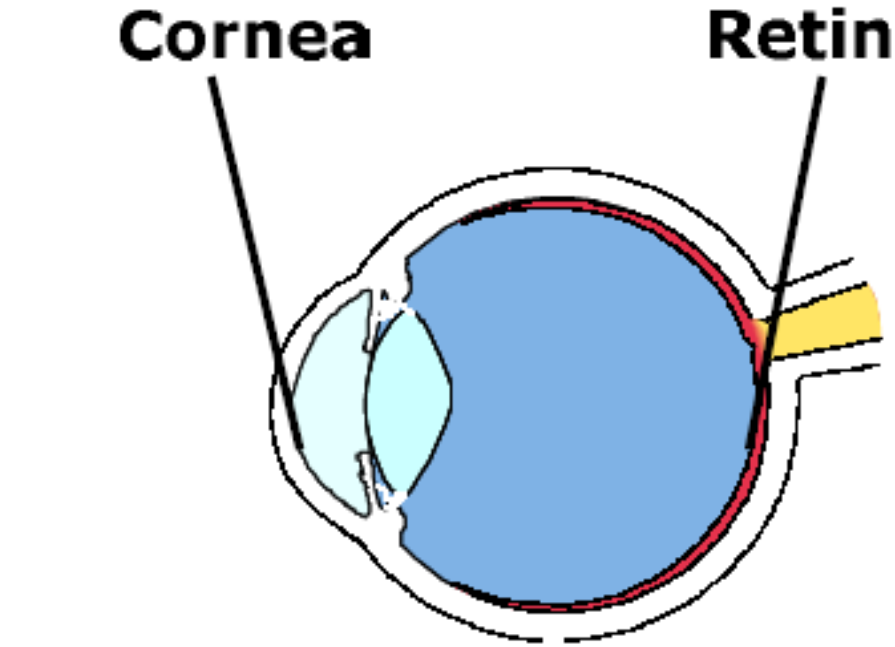
- Electrophysiological tests of vision are diagnostic tests for the retina  that ureses one  or more of the electrophysiological steps of vision processes, e.g. photoreceptors interaction with incoming light.
- These tests are important in diagnosing several retinal dysfunctions or to detect toxicological effects of some agents on the retina.
- There are many electrophysiological tests, we shall only disscuss 2 main ones.

# ERG & VEP

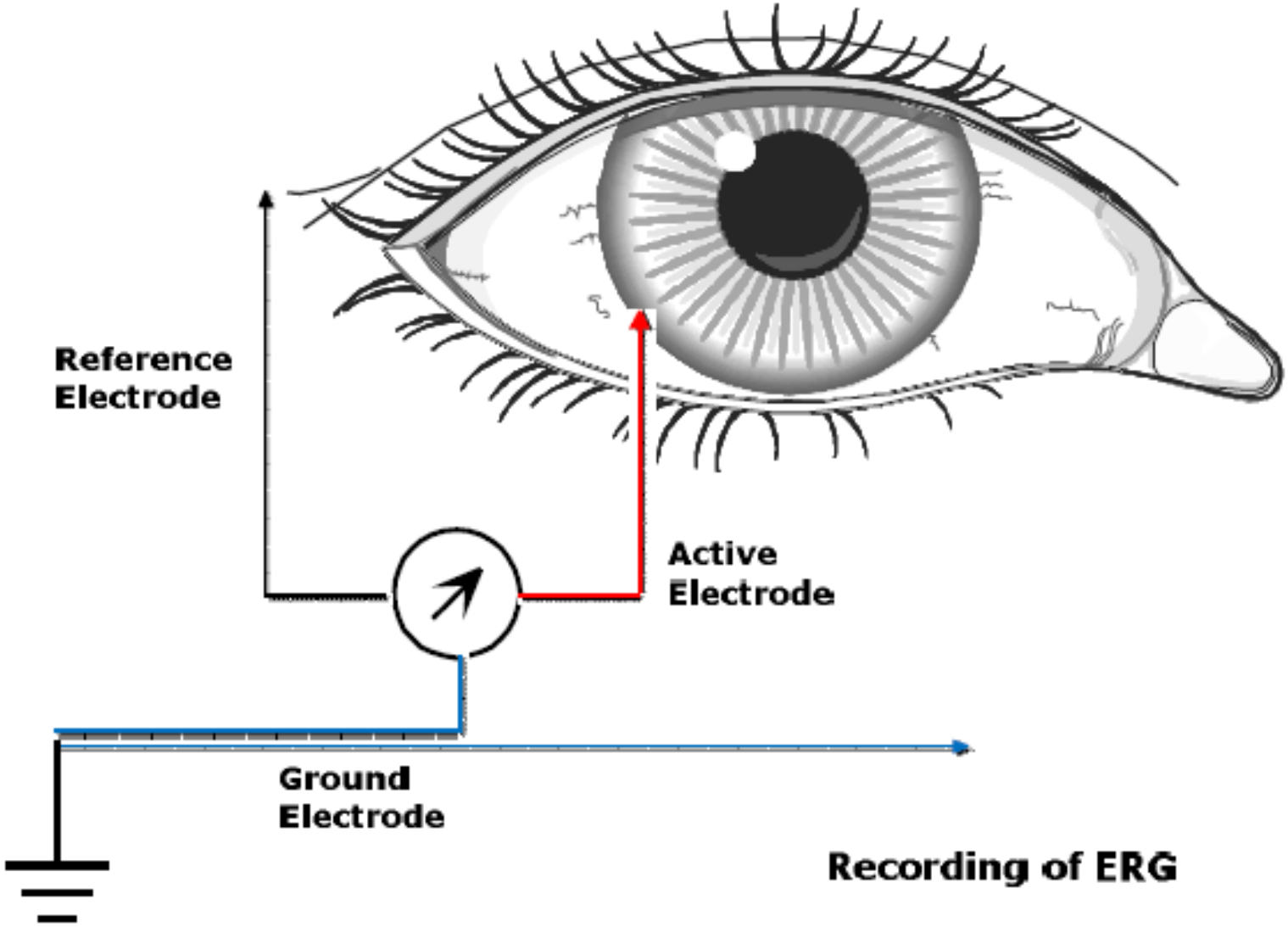

Lens
Light
Cornea
Retina
Brain
Electroretinography
ERG
Visual Evoked Potentials
VEP
Visual Electrophysiology

# ELECTRORETINOGRAPHY (ERG)

- The electroretinogram (ERG) is a diagnostic test that measures the electrical activity generated by neural and non-neuronal cells in the retina in response to a light stimulus. The electrical response is a result of a retinal potential generated by light-induced changes in the flux of transretinal ions, primarily sodium and potassium. Most often, ERGs are obtained using electrodes embedded in a corneal contact lens, which measure a summation of retinal electrical activity at the corneal surface.




Propagation of electric field after polarisation


Reference Electrode
Active Electrode
Ground Electrode
Recording of ERG

# COMPONENTS OF ERG

- **a-wave**: initial corneal-negative deflection, derived from the cones and rods of the outer photoreceptor layers
- This wave reflects the hyperpolarization of the photoreceptors due to closure of sodium ion channels in the outer-segment membrane. Absorption of light triggers the rhodopsin to activate transducin, a G-protein. This leads to the activation of cyclic guanosine monophosphate phosphodiesterase (cGMP PDE) eventually leading to a reduction in the level of cGMP within the photoreceptor. This leads to closure of the sodium ion channels resulting in a decrease of inwardly directed sodium ions, or a hyperpolarization of the cell. The a-wave amplitude is measured from baseline to the trough of the a-wave.

# COMPONENTS OF ERG

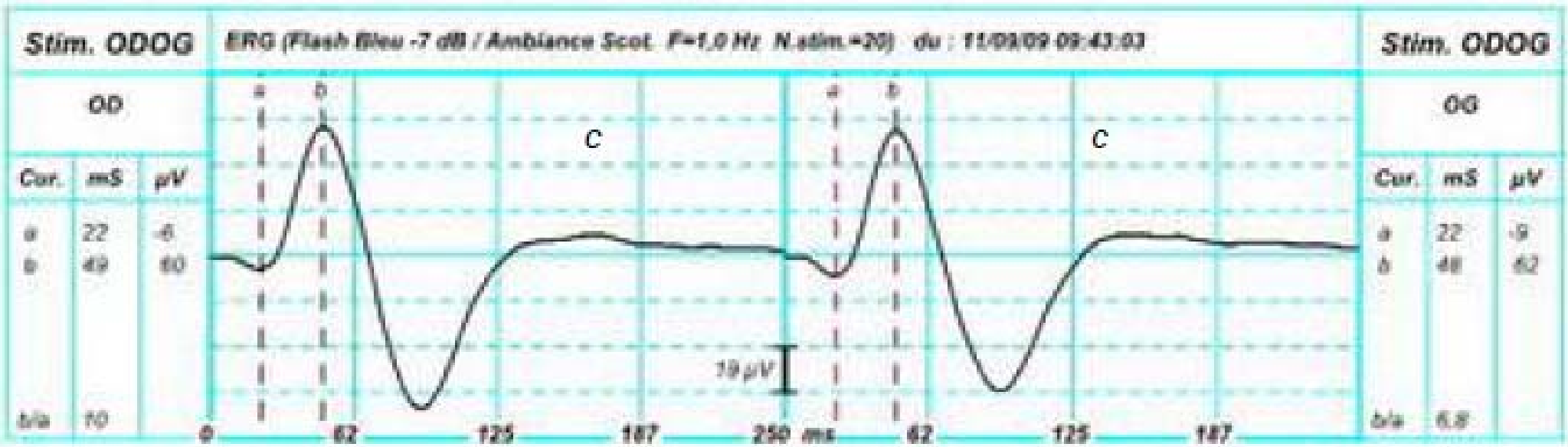
- **b-wave:** corneal-positive deflection; derived from the inner retina, predominantly Muller and ON-bipolar cells
- The hyperpolarization of the photoreceptor cells results in a decrease in the amount of neurotransmitter released, which subsequently leads to a depolarization of the post-synaptic bipolar cells. The bipolar-cell depolarization increases the level of extracellular potassium, subsequently generating a transretinal current. It is this transretinal current that depolarizes the radially oriented Muller cells and generates the corneal-positive deflection. The b-wave amplitude is generally measured from the trough of the a-wave to the peak of the b-wave. This wave is the most common component of the ERG used in clinical and experimental analysis of human retinal function.

# COMPONENTS OF ERG

- **c-wave:** derived from the retinal pigment epithelium and photoreceptors
- The c-wave is a reflection of the resulting change in the transepithelial potential due to the hyperpolarization at the apical membrane of the RPE cells and the hyperpolarization of the distal portion of the Muller cells. The c-wave generally peaks within 2 to 10 seconds following a light stimulus, depending on flash intensity and duration. Due to the c-wave response developing over several seconds, it is susceptible to influences from electrode drift, eye movements, and blinks

# COMPONENTS OF ERG

- **Latency of response** refers to the onset of the stimulus to the beginning of the a-wave.
- **Implicit time** is a measure of the time interval from onset of the stimulus to the peak of the b-wave.




**a-wave :** receptor level
**b-wave :** post-receptor level
**c-wave :** pre-receptor level

Other waves :
Oscillatory potentials (OP)
Early Receptor Potential (ERP)

# TYPES OF RECORDING ELECTRODES

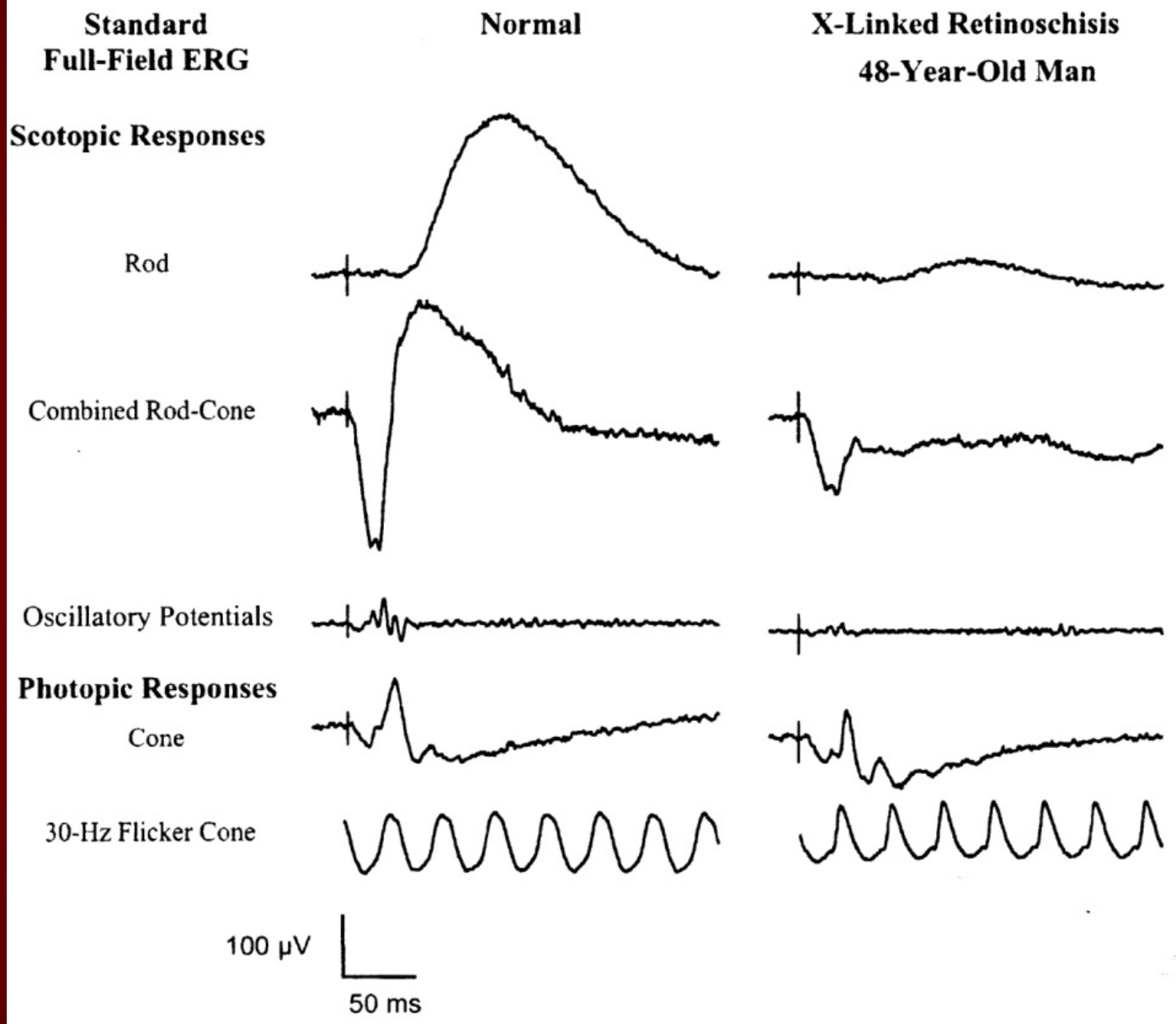
- **Burian-Allen Electrode**- (commonly used electrode for flash ERG) variable lens sizes consisting of an annular ring of stainless steel surrounding the central polymethylmethacrylate (PMMA) contact-lens core with a lid speculum
- **Dawson-Trick-Litzkow Electrode**- low-mass conductive Mylar thread consisting of individual fibers impregnated with metallic silver
- **ERG-Jet Electrode**- a disposable plastic lens with a gold-plated peripheral circumference

# TYPES OF RECORDING ELECTRODES

- **Mylar Electrode**- aluminized or gold-coated Mylar
- **Skin Electrode**- may be used as a replacement for corneal electrodes by placing an electrode on the skin over the infraorbital ridge near lower eyelid; due to decreased amplitudes and variable responses, the skin electrode is primarily used for screening purposes onl
- **Cotton-Wick Electrode**- Burian-Allen electrode shell fitted with a cotton wick which is useful for minimizing light-induced artifact
- **Hawlina-Konec Electrode-** Teflon-insulated thin metal wire (silver, gold, platinum) with three central windows, 3 mm in length, molded to fit into the lower conjunctival sac.

# NORMAL ERG RESPONSES

- The rod and cone photoreceptor function responses can be separated using a variety of ERG techniques. Scotopic (rod) responses are isolated by dark-adaptation for a minimum of 20 minutes per ISCEV standards followed by a short wavelength stimulus as a single flash or 10 Hz flicker. Although the resulting response has rod and cone components, the rod component is dominant and the primary contributor to the increased amplitude and increased implicit time.
  Photopic (cone) responses can be obtained either before or after dark-adaptation.
- Since rods cannot follow a flicker stimulus greater than 20 Hz, cone photoreceptor function is primarily measured under light-adapted conditions for at least 10 minutes with either single flash (stimulus wavelength greater than 680 nm) or 30 Hz flicker stimulus. Photopic responses result in small b-wave amplitudes with a short latency (30-32 ms), whereas scotopic (rod) conditions produce much larger b-wave amplitudes with a longer latency (60 ms).


Standard
Full-Field ERG
Normal
X-Linked Retinoschisis
48-Year-Old Man
Scotopic Responses
Rod
Combined Rod-Cone
Oscillatory Potentials
Photopic Responses
Cone
30-Hz Flicker Cone
100 μV
50 ms

# FACTORS AFFECTING THE ERG

- Duration of stimulus
  Size of retinal area illuminated
  Interval between stimuli
  Size of pupil
  Systemic circulation and drugs
  Development of Retina
  Clarity of Ocular Media
  Age, Sex, and Refractive Error
  Anesthesia
  Diurnal Fluctuations

# ABNORMALITIES IN SOME DISEASE STATES

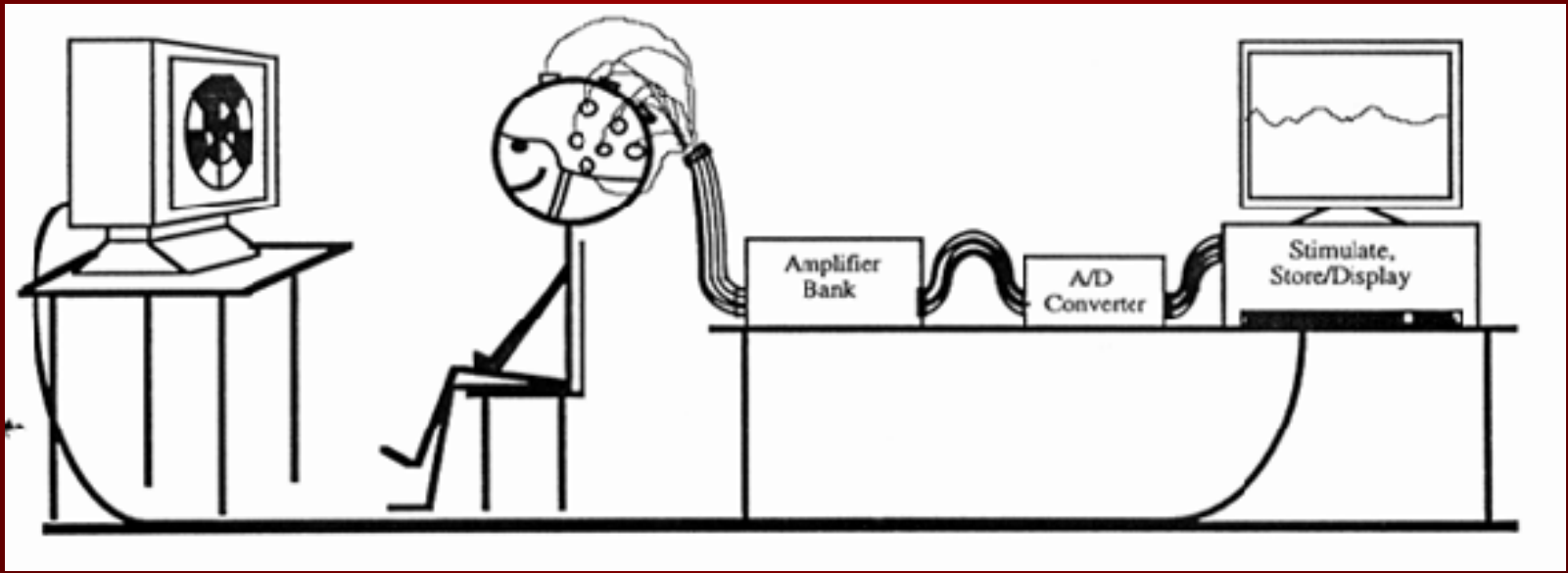
| Disease entity | full-field ERG findings |
| --- | --- |
| Multiple evanescent white dot syndrome (MEWDS) | initially depressed a- and b-wave responses with return to normal values |
| Vitamin A deficiency | marked rod dysfunction and elevated threshold of rods and cones on dark adaptation |
| Cone dystrophy | markedly depressed photopic response and less affected scotopic response |
| Cancer associated retinopathy (CAR) | significantly reduced a-wave and b-wave amplitudes |
| Melanoma associated retinopathy (MAR) | extinguished rod responses, normal a-wave, reduced b-wave (electronegative ERG) |
| Retinitis pigmentosa | minimal or sub-normal a- and b-wave amplitudes (response primarily from cone system) |
| Congenital Achromatopsia (typical (rod) monochromat) | non-detectable cone response, normal or subnormal rod response |
| Congenital Achromatopsia (atypical (cone) monochromat) | normal ERG responses |
| Congenital Red-Green Color Deficiency | normal ERG responses |
| Congenital Hereditary Stationary Night Blindness (Schubert-Bornschein type) | normal scotopic a-wave with selectively reduced b-wave; implicit time of b-wave is approximately the same under scotopic and photopic conditions |
| Oguchi disease | normal photopic responses with predominantly reduced scotopic b-wave amplitudes |
| Fundus Albipunctatus | reduced scotopic amplitudes which improve to normal values after longer (variable) perior of dark adaptation |
| Fleck Retina of Kandori | reduced b-wave amplitudes relative to a-wave in scotopic and photopic conditions |
| Stargardt Macular Dystrophy (Fundus Flavimaculatus) | extent of reduced a- and b-wave amplitudes depends on extent of fundus pigmentary changes; longer duration of dark-adaptation may be necessary for scotopic amplitudes to reach normal values |
| Best Vitelliform Macular Dystrophy | normal ERG responses with an abnormal EOG |
| Pattern dystrophies | normal ERG responses |
| North Carolina Macular Dystrophy | normal ERG responses |

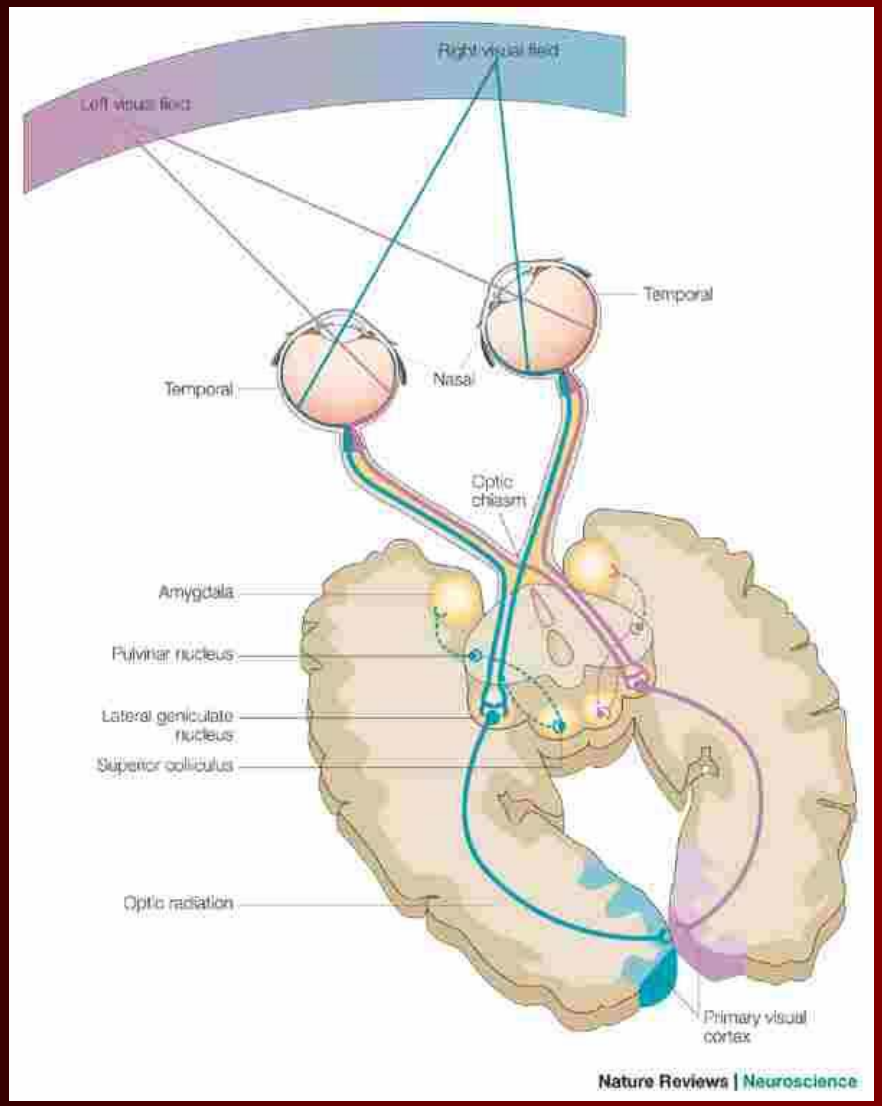
# VISUAL EVOKED POTENTIAL (VEP)

- Record of gross electrical signal generated at **visual (occipital) cortex** in response to visual stimulation

- The **amplitude** of VEP-3 to 25 microvolt is **considerably smaller** than that of ERG, which can be as large as 100 microvolt

- Averaged and amplified record of action potentials in visual cortex
- VEP is the only objective technique available to assess clinically the functional state of the visual system **beyond the retinal ganglion cells.**





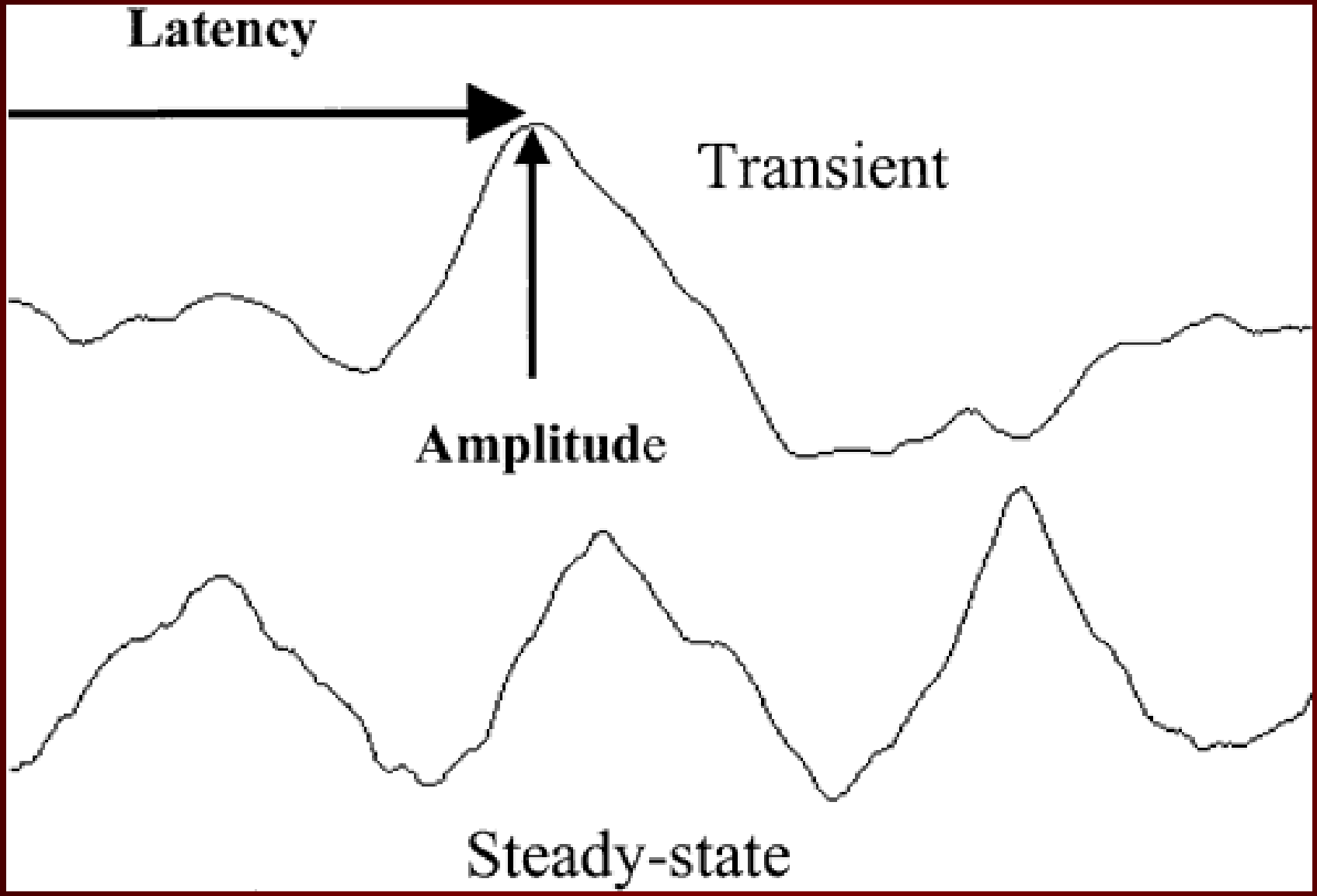

**VEP abnormality**

**Visual pathway abnormality**

# STEADY-STATE VEP & TRANSIENT VEP

- At rapid rates of stimulation the waveform becomes sinusoidal – **STEADY STATE VEP** Not used routinely due to inferior information on latency

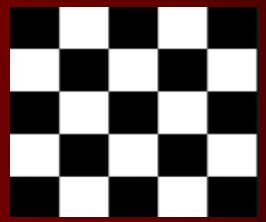
- Low rates of stimulation – discrete deflections. Known as **TRANSIENT VEP**This is commonly employed


Latency
Transient
Amplitude
Steady-state

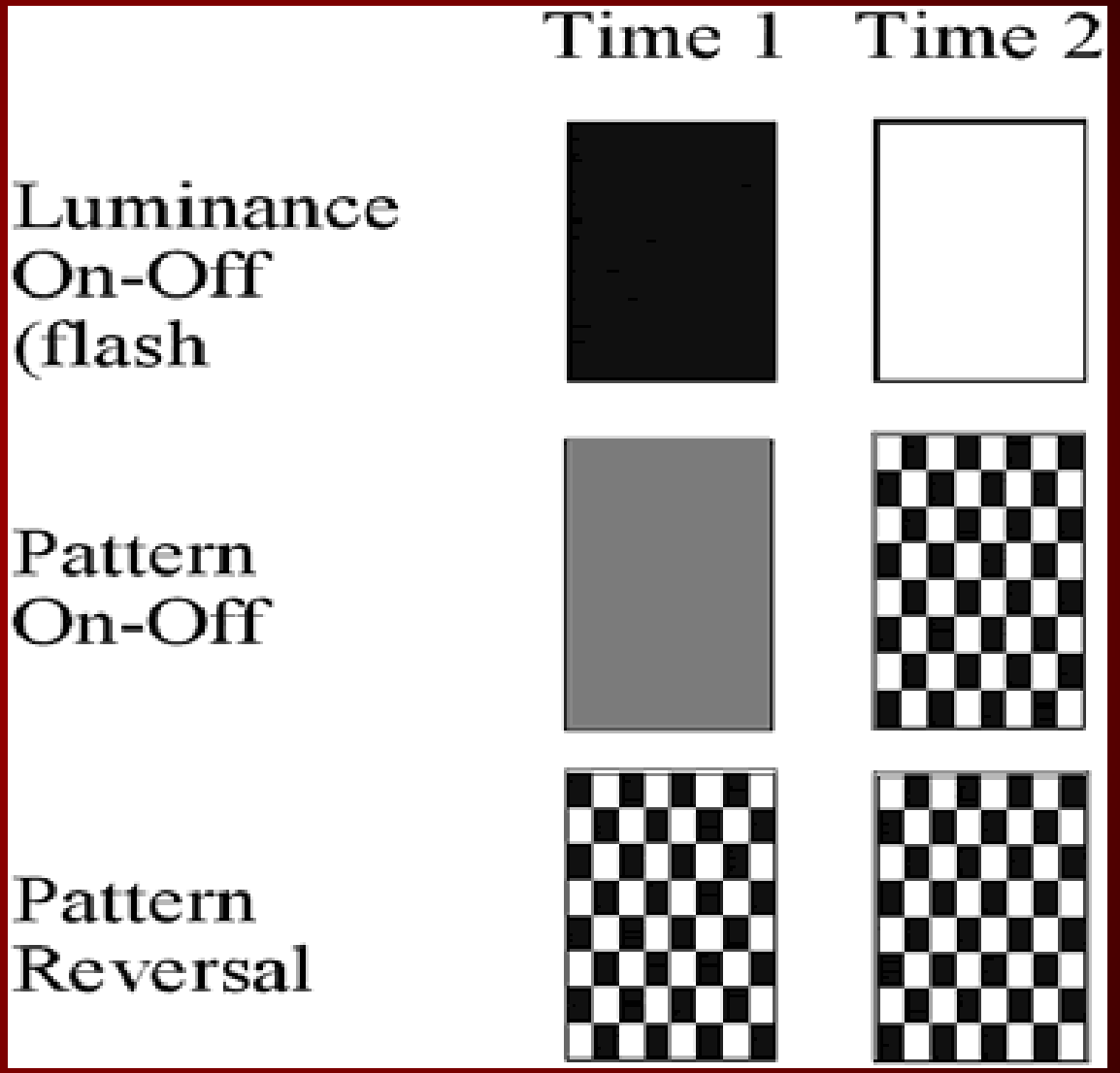
# VEP STIMULI

- FLASH : Occipital cortex is relatively insensitive to flash

- PATTERN: Cortex is sensitive to edges of contrast



# TYPES OF VEP


Time 1
Time 2
Luminance
On-Off
(flash
Pattern
On-Off
Pattern
Reversal

# FLASH VEP

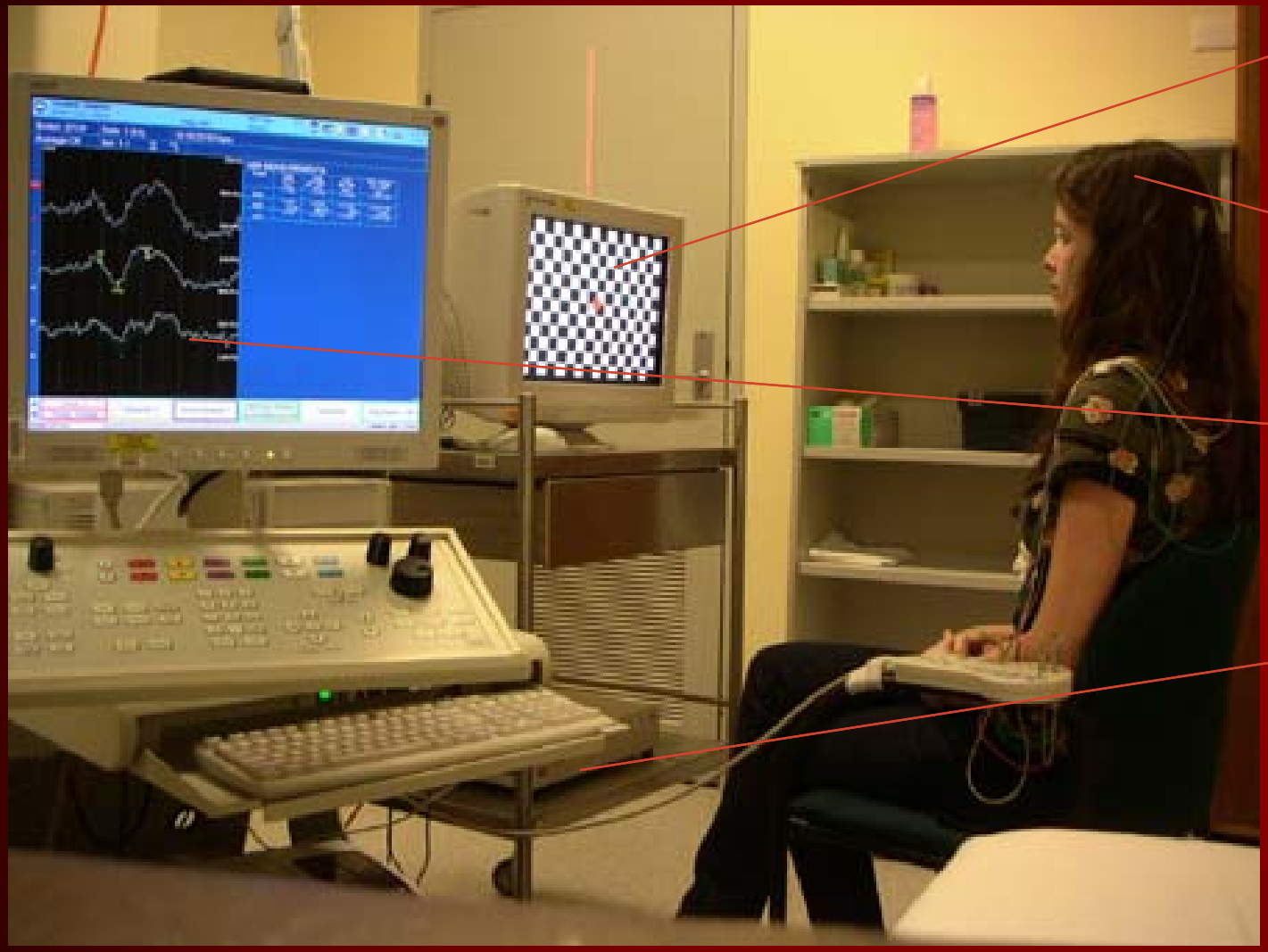
- Response to **diffusely flashing light stimulus** that subtends a visual field of 20 degrees
- Cruder response than pattern VEP
- Merely indicates that light has been perceived by cortex
- Indications – media haze, infants,poor patient cooperation

# PATTERN REVERSAL VEP

- Response to a **patterned stimulus** - checkerboard or square and sine wave gratings
- Frequency of gratings is decribed in CPD- cycles per degree
- For check pattern visual angle subtended by a single check is used
- Preferred technique for most clinical purposes, gives an estimate of form sense and thus visual acuity

# PATTERN ONSET/OFFSET VEP

- A pattern is abruptly **exchanged** with an equilluminant diffuse background
- More intersubject variability than pattern reversal VEP
- Useful in detection of pts with malingering , pts with nystagmus



Visual stimulus

Scalp electrodes

Computer, read-out system

Amplifier

# TECHNIQUE OF RECORDING VEP

- Undilated pupil
- Monocular recording
- Refractive correction
- Relaxed position
- 1m distance from monitor

# COMPONENTS OF VEP

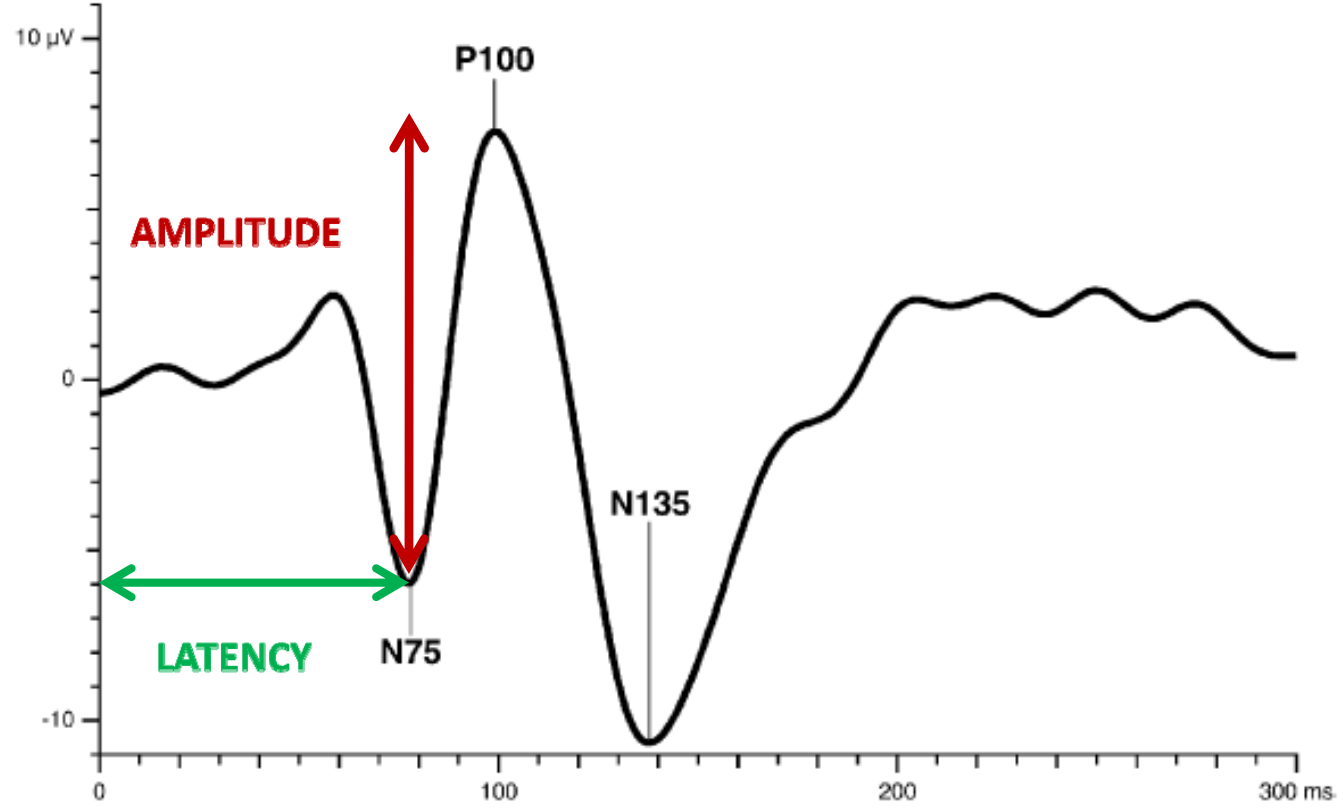



*Figure 2.* A normal pattern reversal VEP.

# NORMAL VEP DATA

- P 100 LATENCY ( m sec ) = 102 ± 5
- R-L difference ( msec) = 1.3 ± 2.0
- Amplitude (μV) =10 ± 4.2
- Duration = 63 ± 8.7

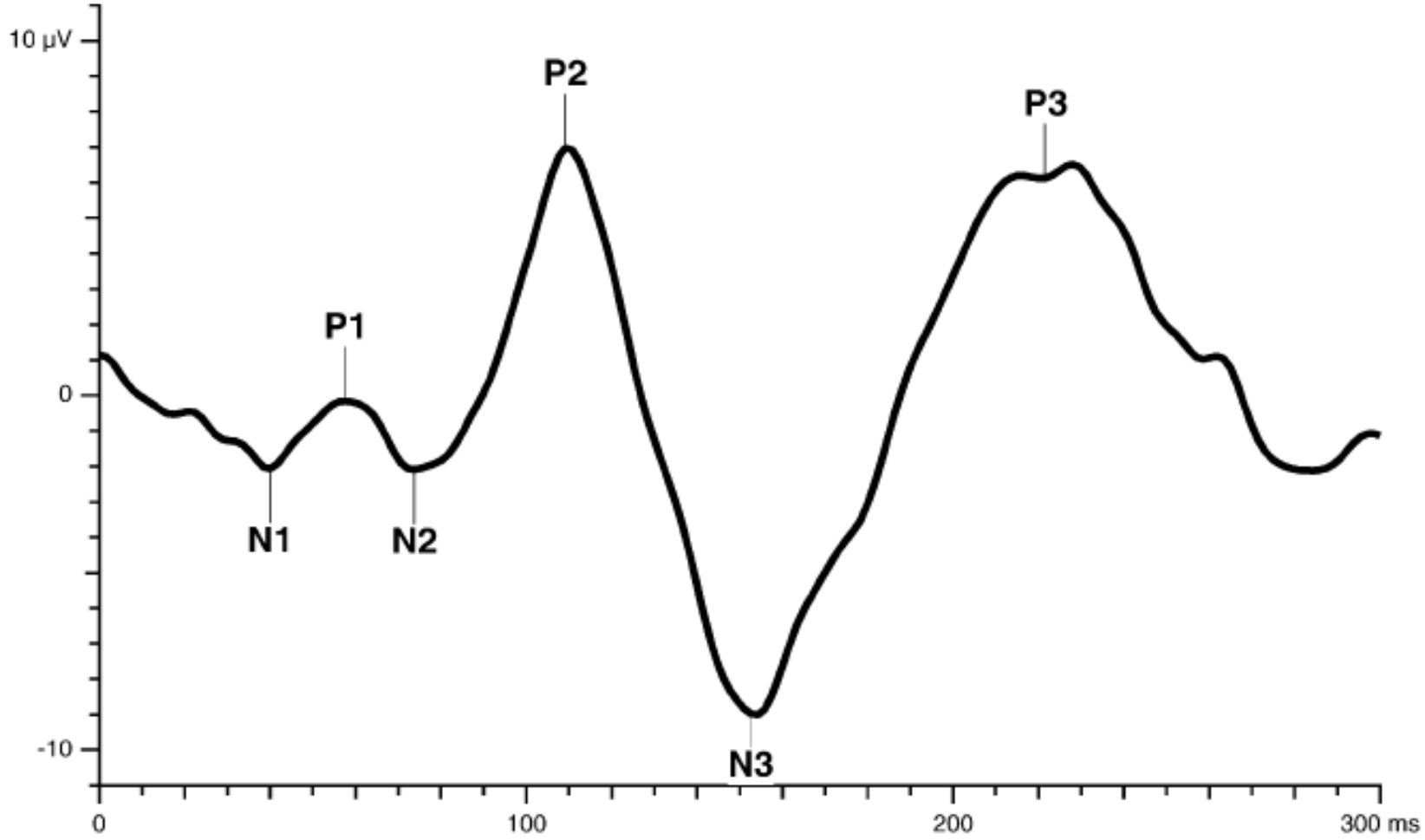
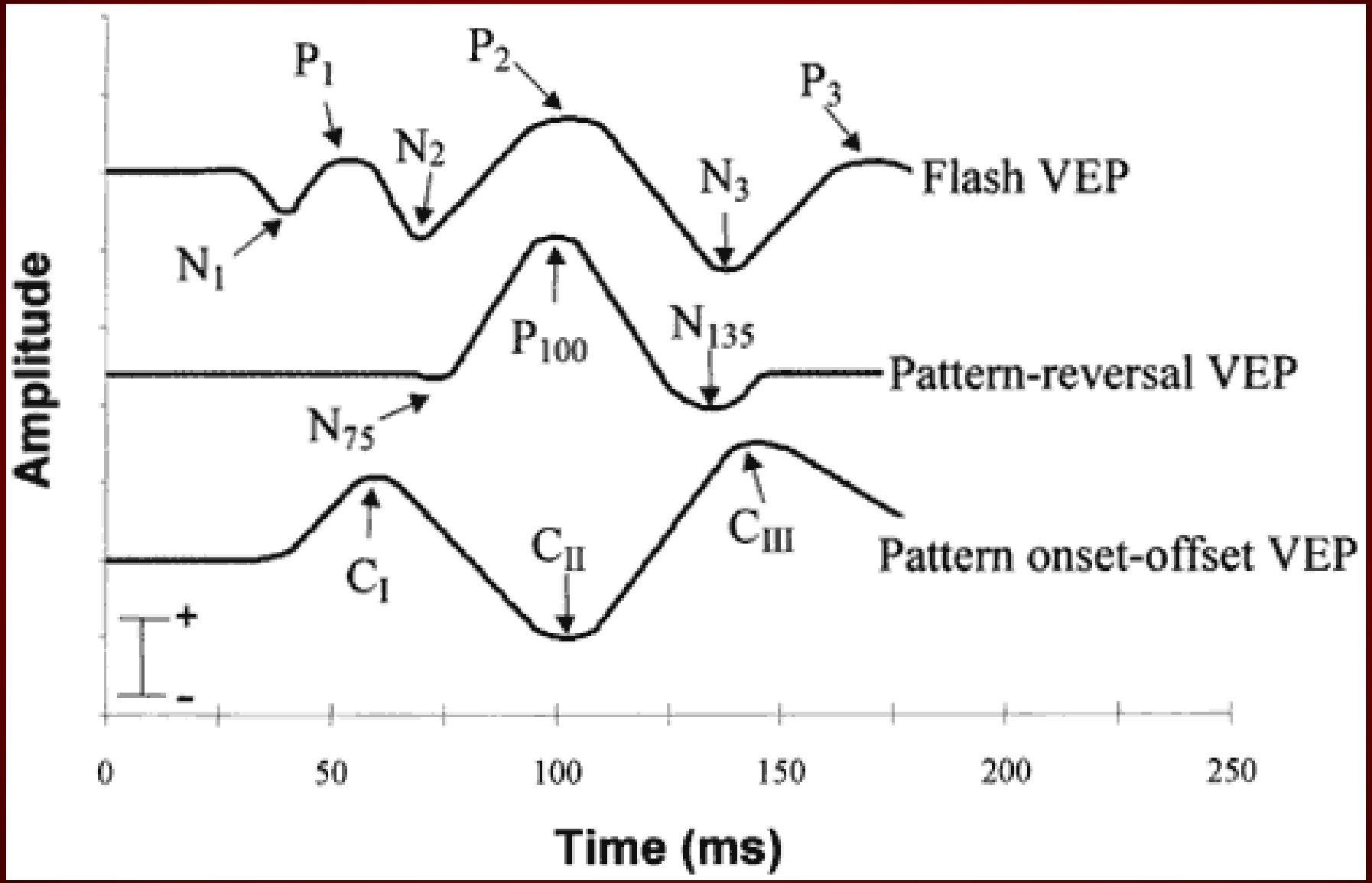



*Figure 4.* A normal flash VEP.


P1
P2
P3
N2
N3
N1
Flash VEP
P100
N135
N75
Pattern-reversal VEP
CI
CII
CIII
Pattern onset-offset VEP
+
-
Amplitude
0
50
100
150
200
250
Time (ms)

# REMARKS

- If **acuity** of the patient is in question , the **amplitude** is more important
- If detection of a **lesion in visual pathway** is in question , **latency** is more important
- Latency is more reliable than amplitude (Variabilty – 5% as compared to 25%)
- Presence of reduced amplitude is non specific, gains importance only on serial testing
- B/L symmetry is seen both with flash and pattern VEP , thus an **asymmetrical response** is more indicative of an abnormality

# FACTORS INFLUENCING VEP

- **SIZE OF STIMULUS** – Decrease in size of stimulus increases amplitude of VEP
- Position of electrodes on scalp
- **AGE**- amplitude decreases with age
- **ATTENTION OF PATIENT** – If subject looks to side of stimulus , there is rapid fall in size of response

# CLINICAL APPLICATIONS OF VEP

- **DELAYED LATENCY:**
- Demyelinating optic neuritis
- Neurotransmitter disorders
- Glaucoma
- Uncorrected refractive error
- Ageing

# CLINICAL APPLICATIONS OF VEP

- **REDUCED AMPLITUDE:**
- Optic atrophy
- Toxic agent
- Compressive
- Uncorrected refractive error
- Ambylopia

# EXAMPLE: GLAUCOMA

- Decreases in pattern VEP amplitude and prolonged VEP latencies are found in many patients with glaucoma and some glaucoma suspects
- **Steady-state VEPs** appear to be more sensitive for detecting glaucomatous damage thantransient responses

# EXAMPLE 2: MULTIPLE SCLEROSIS

Increased latency of P100

Even when no defect in visual acuity , colour vision or field of vision.

About 96% of pts with MS have delayed latency

# END OF LECTURE IV

- Further reading for this week includes more electrophysiological tests other than ERG and VEP. Moreover, more medical applications of ERG and VEP.

- Homework III: Case presentations of different patients with ERG or VEP test results.

- Have a nice week !!