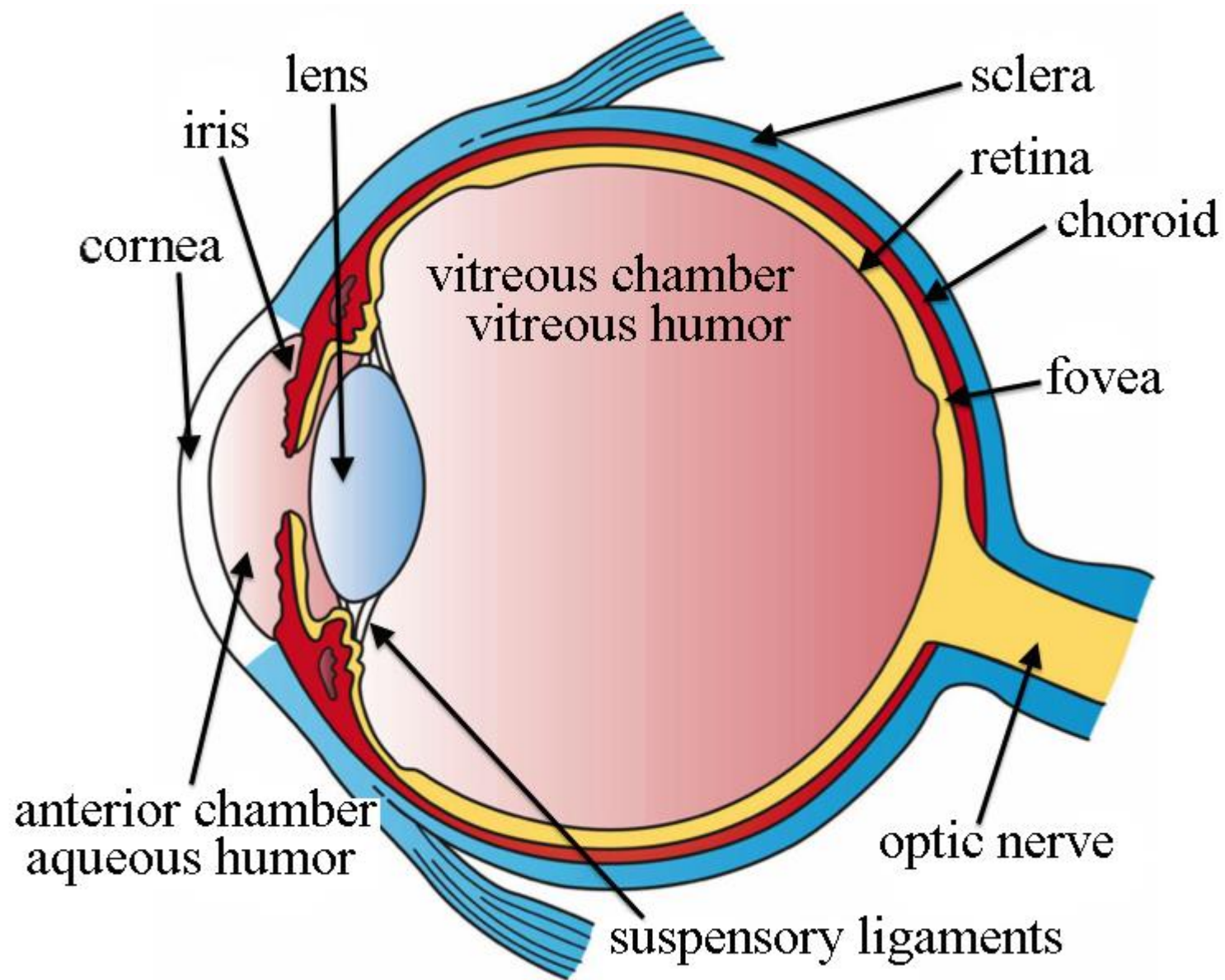


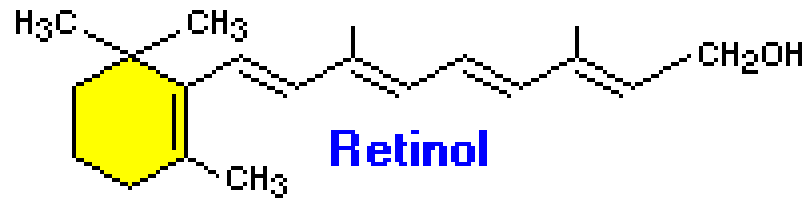
# Biochemistry of vision

Ahmed Salem, MD, PhD, FRCR



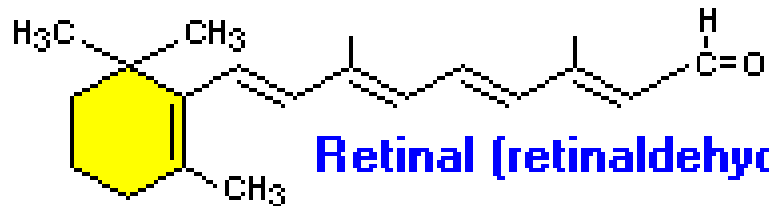
# Vitamin A intro

- Vitamin A is needed by the retina in the form of a specific metabolite called **retinal** (vit A aldehyde) this is light absorbing
  - Necessary for low-light (scotopic) & colour vision
- Vitamin A also functions in a very different role as an irreversibly oxidized form of **retinol** (vit A alcohol) known as **retinoic acid** (vit A acid) which is an important hormone-like growth factor for epithelial and other cells
- **Vitamin A is present in 3 forms:**
  - Retinal
  - Retinol
  - Retinoic acid
- Beta carotene is a pro-vitamin which is yellow to orange fat soluble pigment → vitamin A activity of beta carotene is 1/12 of retinol



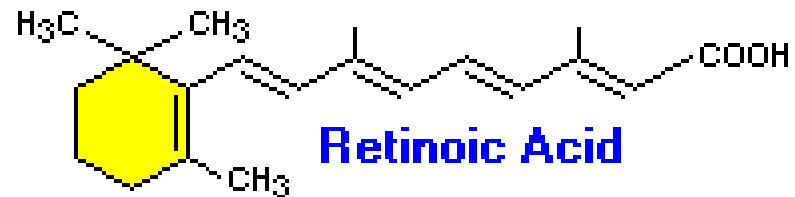
**Retinol**

**Function:** reproductive system



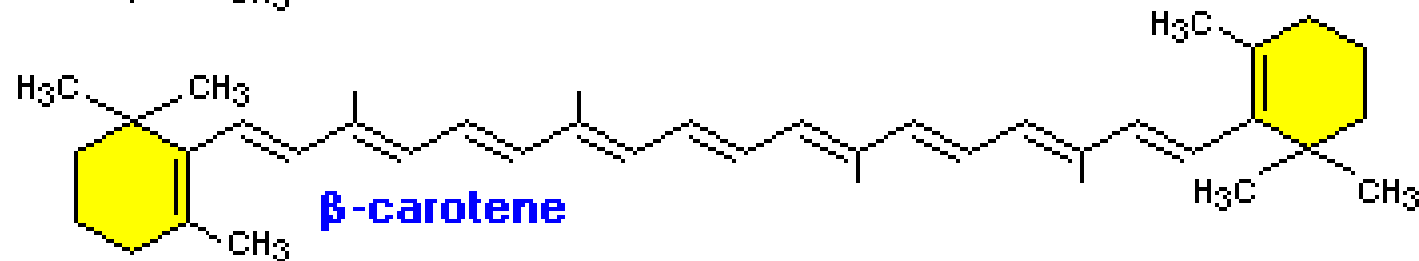
**Retinal (retinaldehyde)**

**Function:** vision



**Retinoic Acid**

**Function:** growth & differentiation



**β-carotene**

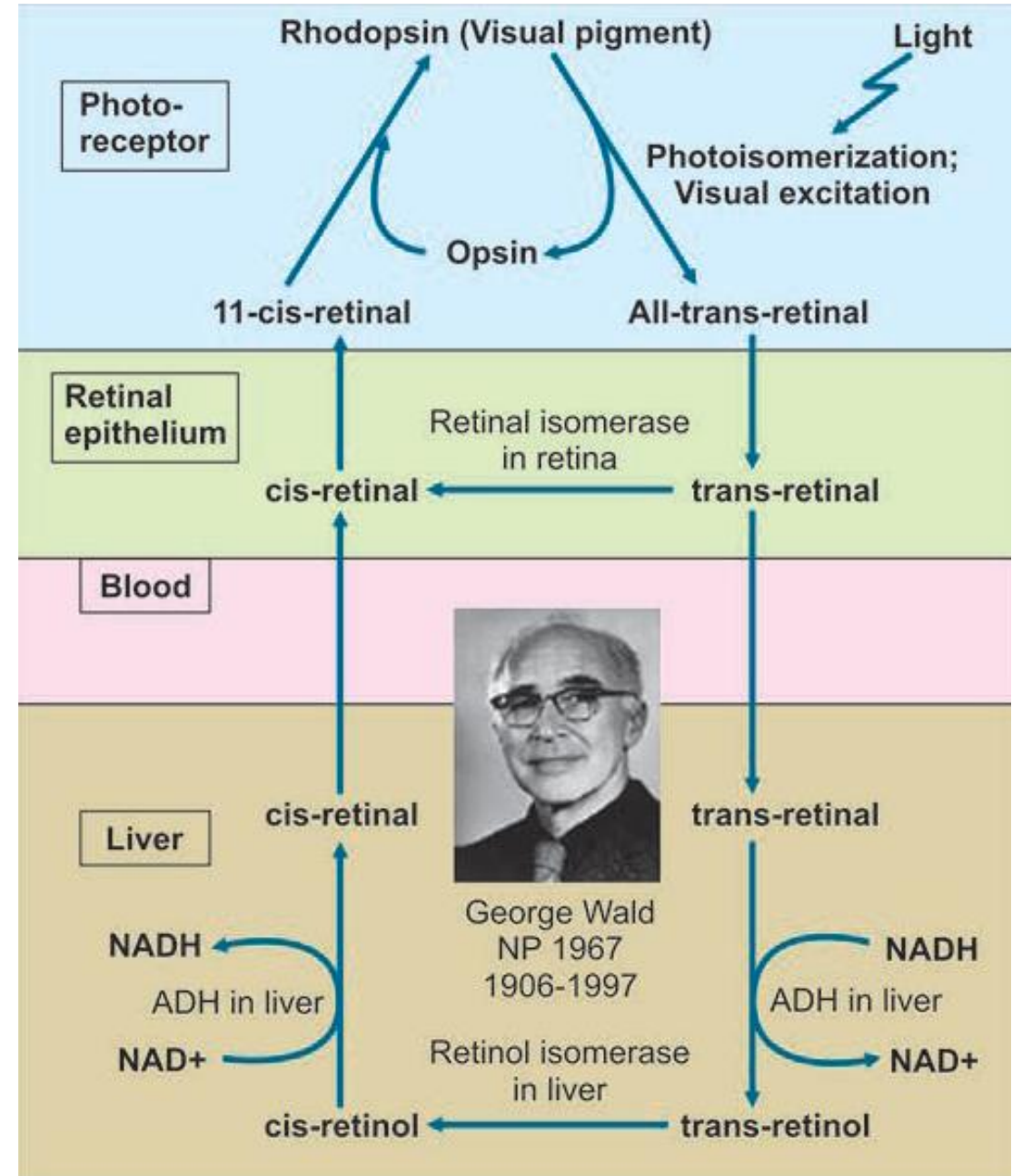
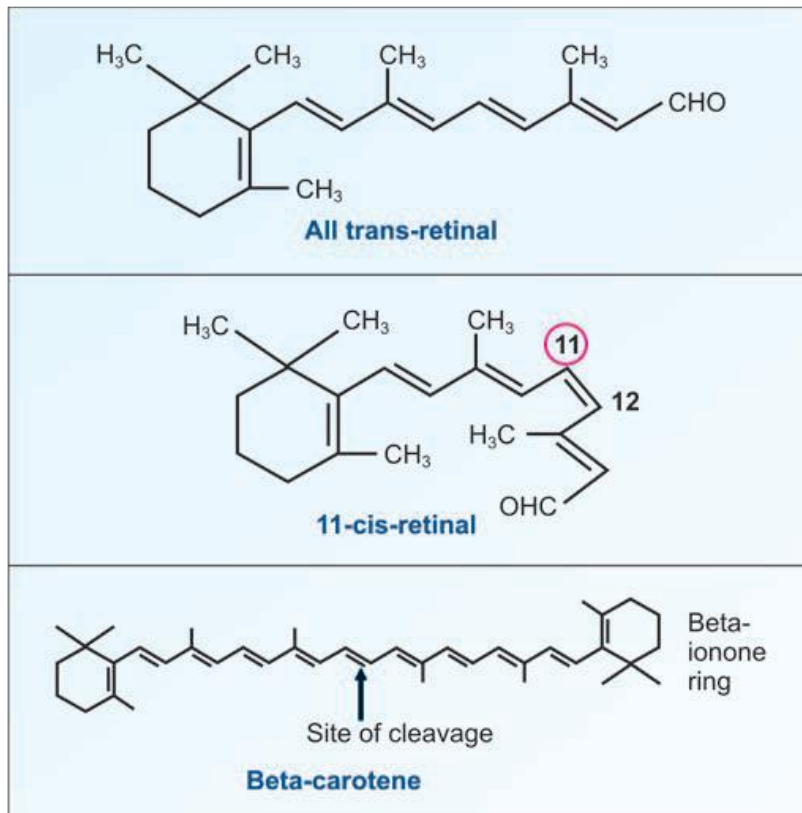
**Function:** pigment + anti-oxidant properties

# Vitamin A info

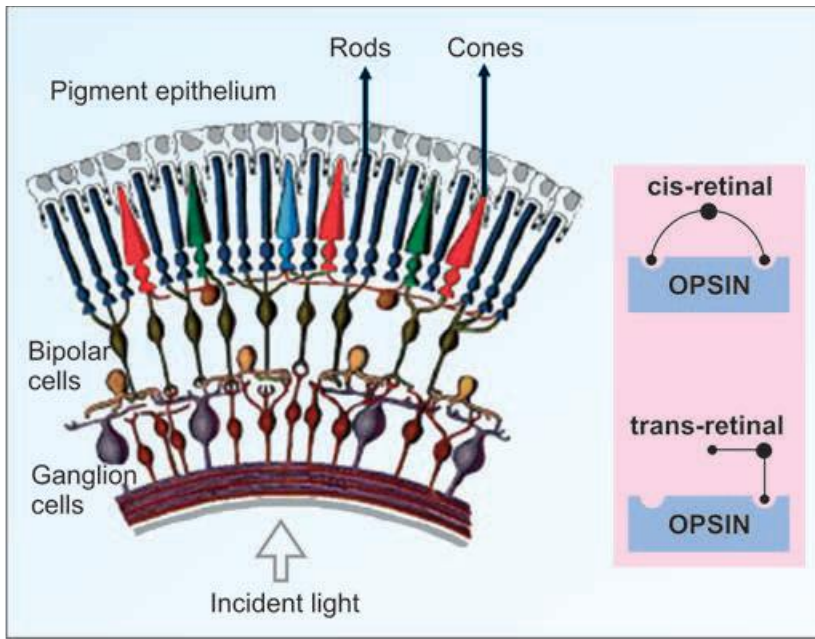
- Retenoids:
  - Source: animal tissues as cod liver oil, liver, kidney, butter
  
- Carotenoids: in both animal and plant sources as carrots

# Role of vitamin A in vision

- 11-cis retinal is reversibly associated with the protein opsin in the rod cells of the retina → **visual pigment (rhodopsin)**

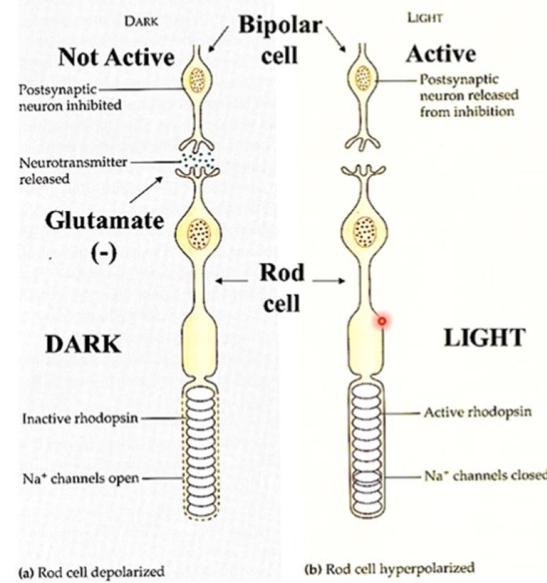


# Generation of Nerve Impulse



## Metabolism in the Retina

### Principles of Phototransduction



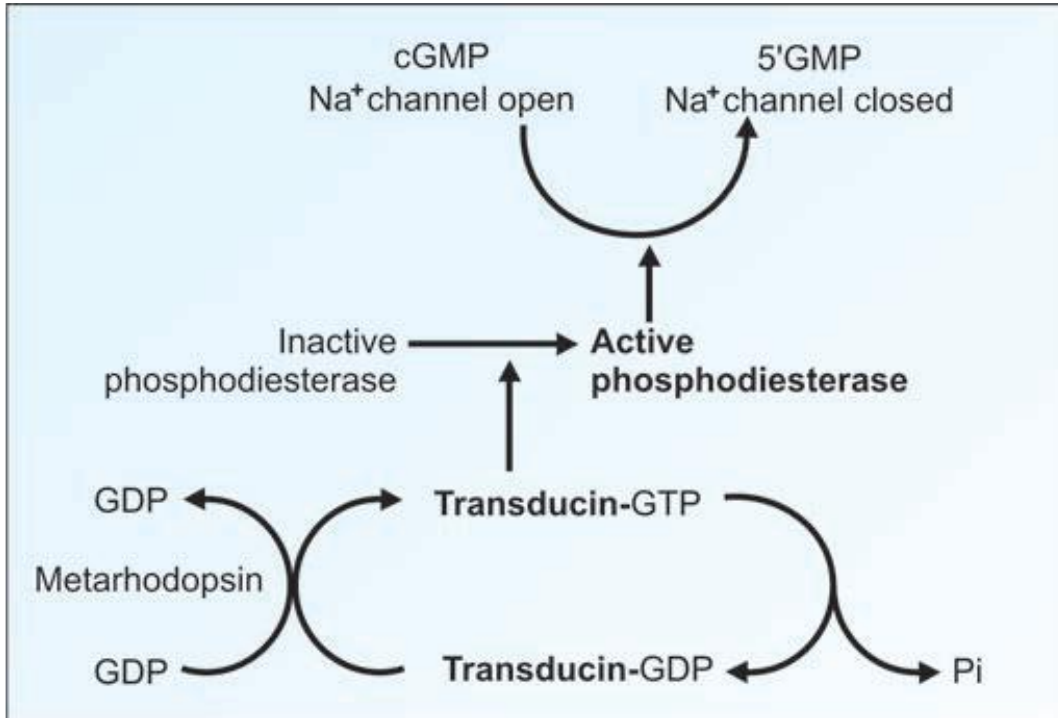
cGMP keeps the ion-channel gates open!

Open gates = depolarization!

Released glutamate inhibits bipolar neurons

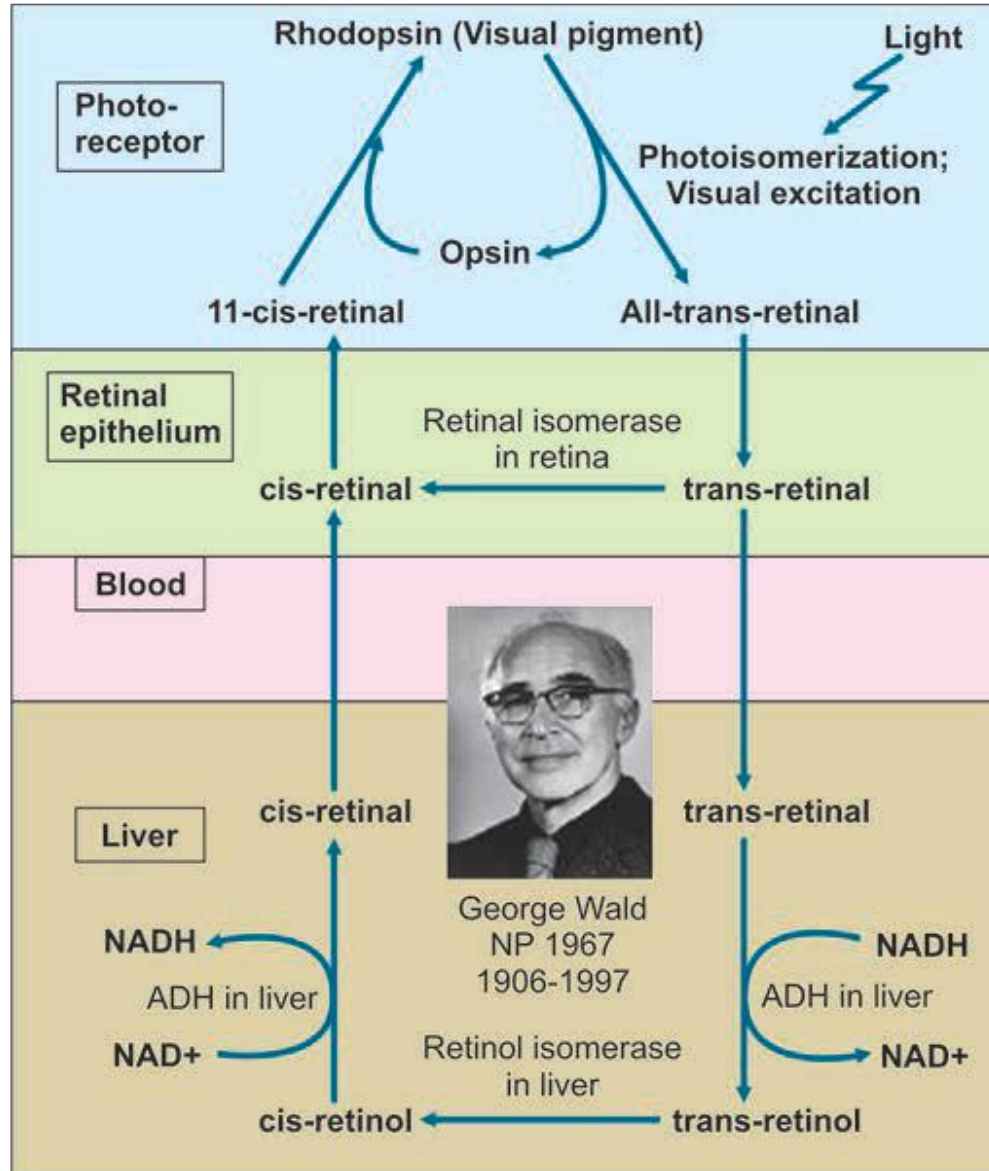
When it is **dark**, lots of cGMP → cGMP bound to rod membrane and gates kept open → inflow of cations → **depolarized** membrane → glutamate neurotransmitter release

When it is **light**, cGMP is lacking → gates are closed → no inflow of cations → **hyperpolarized** membrane → no glutamate neurotransmitters released





# Regeneration of 11-cis-retinal



Zinc



# Dark Adaptation Mechanism

- Bright light depletes stores of rhodopsin in rods
- Therefore when a person shifts suddenly from bright light to a dimly lit area, there is difficulty in seeing
- After a few minutes, rhodopsin is resynthesized and vision is improved. This period is called **dark adaptation time**
  - It is increased in vitamin A deficiency
    - Rhodopsin present in rods is made up of 11-cis-retinal + opsin
    - Deficiency of cis-retinal will lead to increase in dark adaptation time and night blindness
- In humans → contains about 120-200 million rods, each of which carries 40-120 million molecules of rhodopsin
- The number of rods is more in cats, mice and owls

# Cones for colour vision

- Cones are responsible for vision in bright light as well as colour vision
- They contain the photosensitive protein, conopsin
- There are 3 types of cones, each is characterized by a different conopsin, that is maximally sensitive to either blue (cyanopsin), green (iodopsin) or red (porphyropsin)
- In cone proteins also, 11-cis-retinal is the Chromophore
- Reduction in number of cones or the cone proteins, will lead to colour blindness
- One eye contains about 6 million cones

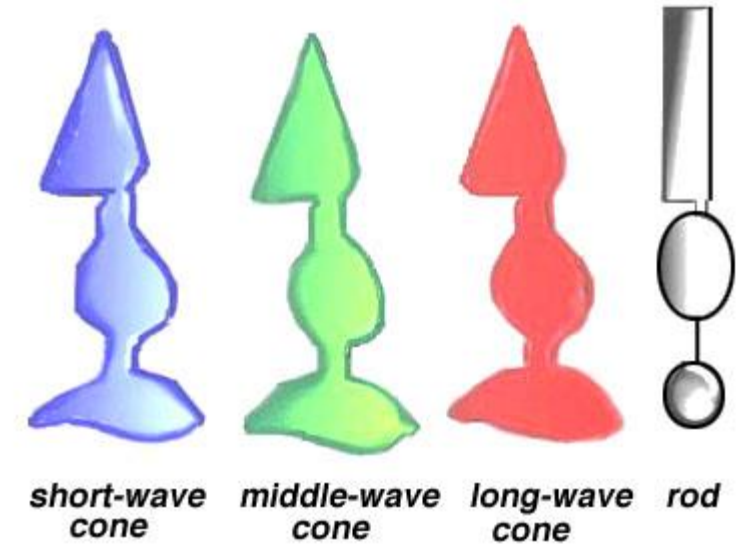
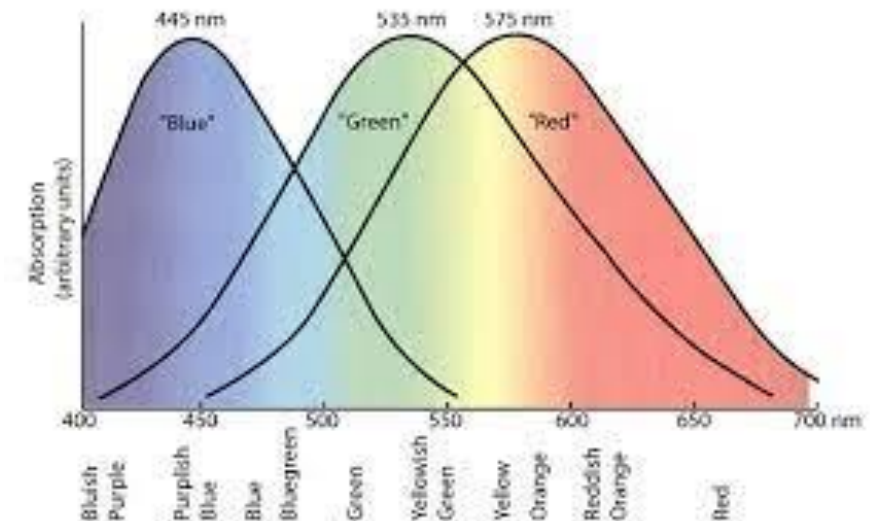


Fig. 13. There are four photoreceptor types in the human retina. Short-wavelength cones (blue), medium wavelength cones (green), long wavelength cones (red) and rods.



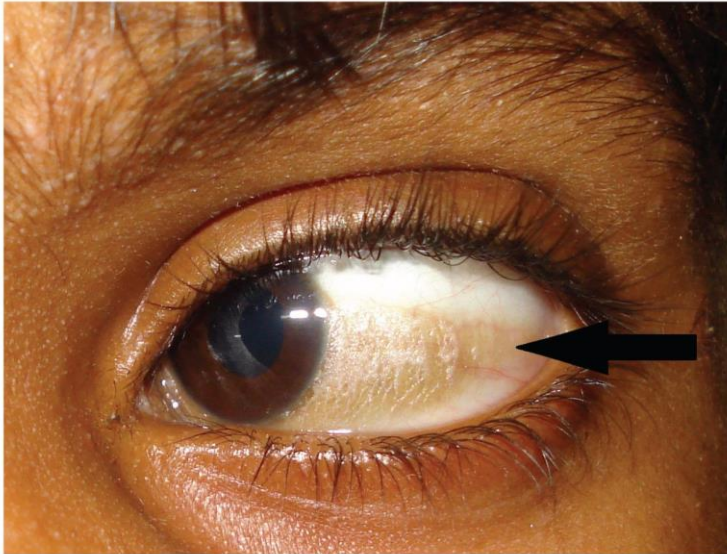
# Colours have profound influence in life

- About one-third of grey matter of the brain is involved in the processing of visual information
- About 70% of information inputs to the brain are visual

## For info only

- The optimists view the world through “rose-coloured” eyes
- When sad, a person is in a “blue” mood
- Saffron colour has tranquilizing effect, especially in agitated persons
- Mice living in red light are most active, while in green/blue light, they are least active

# Deficiency manifestations of Vitamin A



- **Night Blindness or Nyctalopia**

- Visual acuity is diminished in dim light
- The patient cannot read or drive a car in poor light
- The dark adaptation time is increased

- Xerophthalmia (conjunctiva is dry and thick)

- Bitot's Spots (greyish-white triangular plaques firmly adherent to the conjunctiva)

- Keratomalacia (softening of the cornea)

→ **Preventable blindness**

- About 40% of blindness is preventable (vit A is most common cause of preventable blindness)
- Vitamin A deficiency is a major public health problem

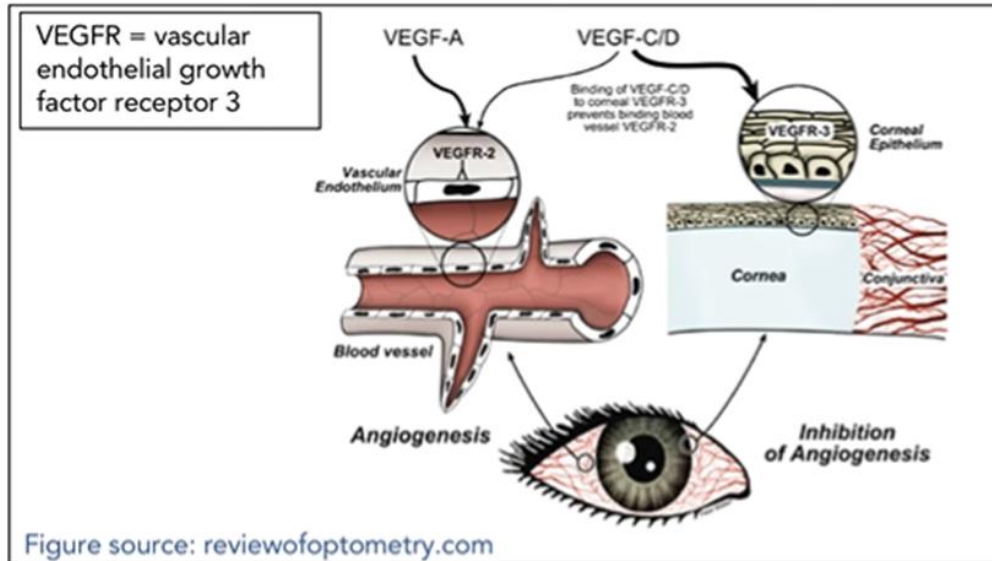


# How does cornea stay clear

## How does the cornea stay clear?

The cornea must stay clear in order to diffract light. This is achieved through two mechanisms:

[1] Avascular state maintained by VEGFR-3 to prevent angiogenesis



[2] ATP-driven water pump that controls the water content and clarity

## How does the cornea generate ATP?

### Glucose Metabolism in the Cornea

Glycolysis (30%)

30% glucose metabolised through aerobic and anaerobic (lactate mediated) glycolysis

Hexose Monophosphate Pathway (60%)

60% glucose metabolized by HMP pathway. Note that this pathway produces NADPH (a reducing agent)



# How does the cornea protect itself from reactive oxygen species?

## How does the cornea protect itself from ROS?

The cornea is prone to reactive oxygen species (ROS) due to exposure towards atmospheric oxygen

ROS cause damage through:

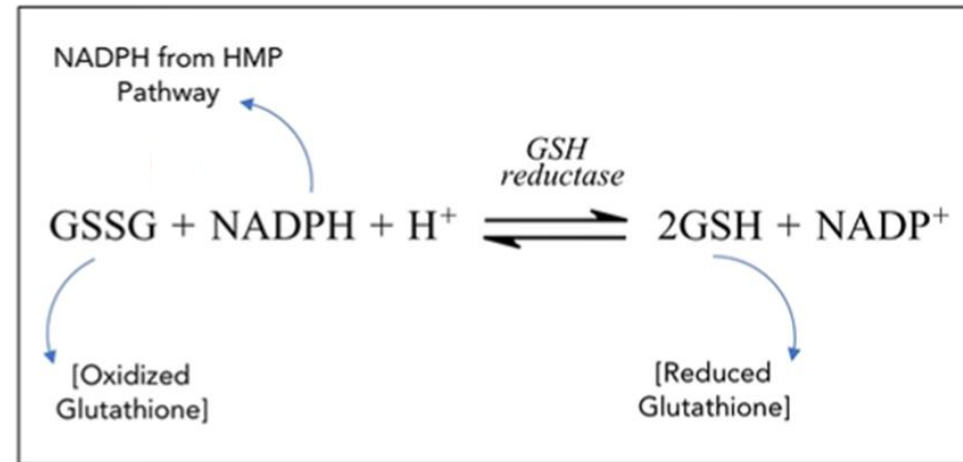
1. Lipid peroxidation
2. Protein oxidation

The cornea protects itself by **neutralizing ROS** using **NADPH** (produced from HMP pathway) which enhances the work of **glutathione (GSH)**

## How does NADPH enhance GSH to neutralize ROS?

If an oxidant comes along, GSH takes the blow and gets oxidized. But too much oxidants may lead us to GSH deficiency

Therefore we need to **increase GSH production** by reducing GSSG through NADPH + GSH reductase



GSH = glutathione, GSSG = glutathione disulfide

Figure adapted from: Devlin, TM. 2011. *Textbook of biochemistry*. John Wiley & Sons

# Biochemistry of the lens

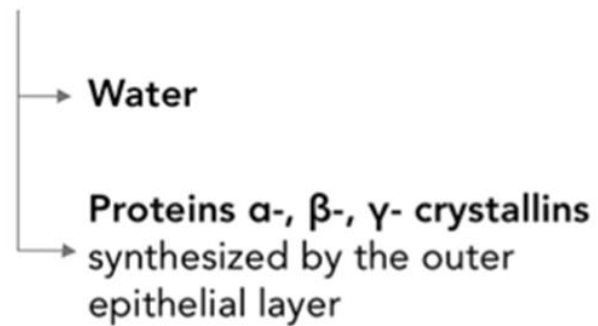
## How does the lens stay clear?

Main function is to **maintain clear crystallin state**

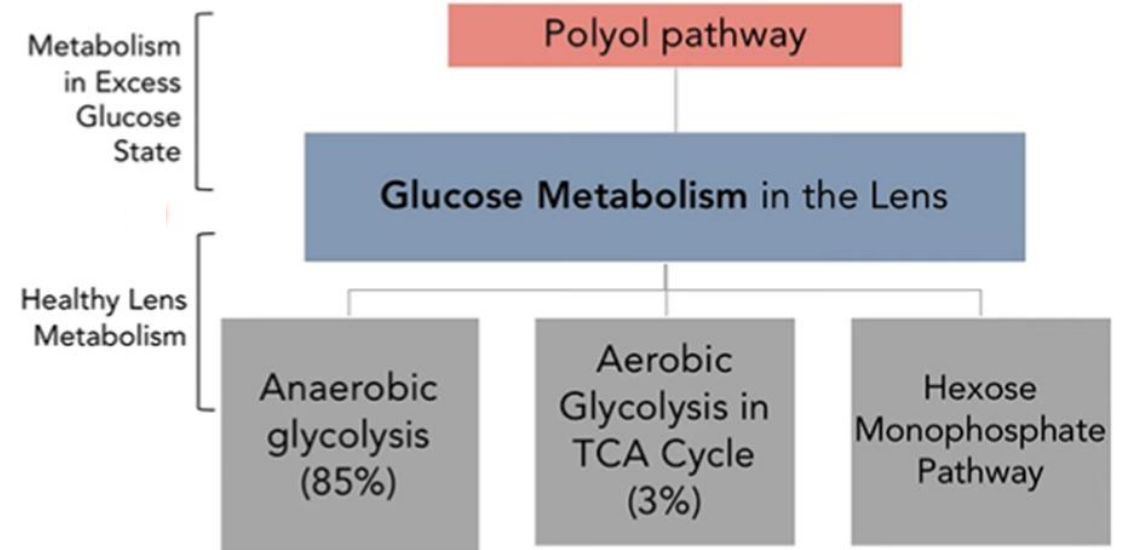
Osmotic balance regulated through **Na<sup>+</sup>/K<sup>+</sup> ATPase**

Lens is **avascular** and is nourished by vitreous humour

### Main components of the lens:



## How does the lens generate ATP?

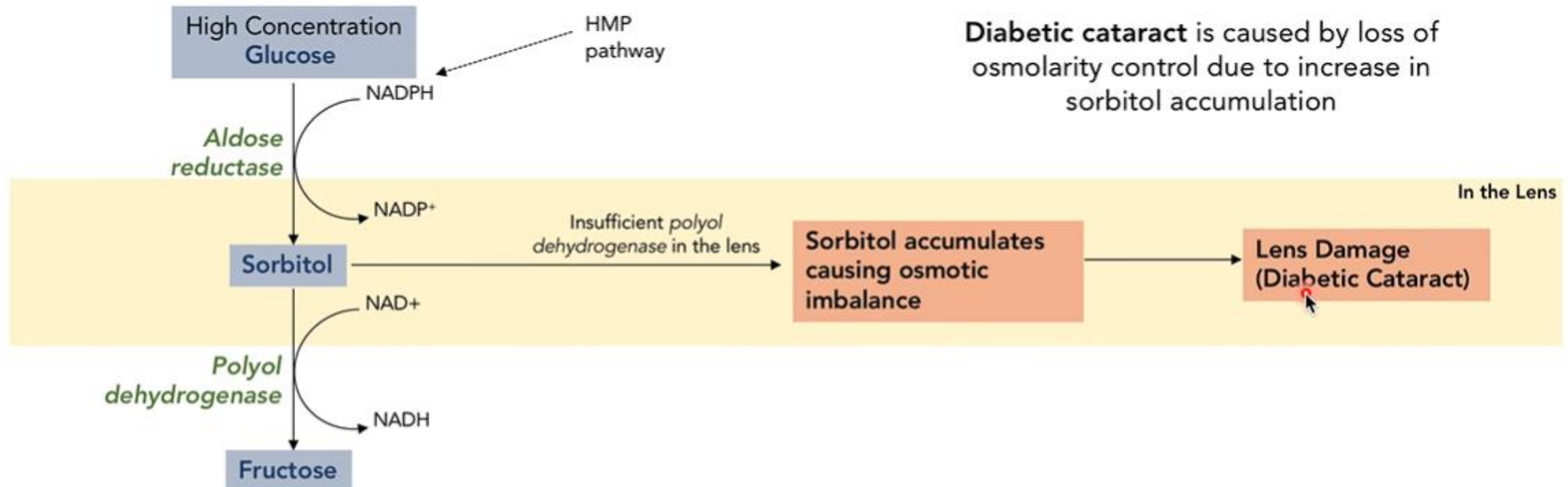


# Diabetic cataract

## How is the polyol pathway activated?

The polyol pathway converts **glucose to fructose**

In the lens, the polyol pathway is activated in conditions of excess glucose (eg: diabetes)



## How does polyol pathway cause diabetic cataract?

**Cataract is a disorder of lens opacity**

**Senile cataract** is caused by age-related changes in crystallin structure

**Diabetic cataract** is caused by loss of osmolarity control due to increase in sorbitol accumulation

# Conclusions

- Vitamin A is very important for vision
- Cornea needs to protect itself from reactive oxygen species
- Lens: polyol pathway important in diabetic cataract