

MOLECULAR PHYSIOLOGY

Biochemistry of vision

P. D. Gupta
Atmiya Institute of Gerontology
'Yogidham'
Kalawad Road
Rajkot

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Keywords

Vision; Signal transduction; Nigt blindness; Vitamin A deficiency

Vision

Different levels of vision correlate to the different types of eyes found in various animal species. The simplest eye, a sort of, photo receptor is that of planarians, flatworms. When light is shone on the cup containing photoreceptor cells, the observable behaviour of the planarian is to turn away from the light source and seek a dark place under an object, an adaptation that protects it from predators. However, the human eye is very complicated and when light is shone on the eye, through various physical and chemical reactions in the photoreceptor cells (retina) by signal transduction pathway brain is able to recognize the image.

Functional aspect of the human eyes

The human eye is the most important sense organ. As you focus on each word in this sentence, your eyes swing back and forth 100 times a second, and every second the retina performs 10 billion computer-like calculations. The eyes can perceive more than 1 million simultaneous visual impressions, and able to discriminate among nearly 8 million gradations of colour, can distinguish about 500 different shades of gray, and take in more information than the world's largest telescope. Each time the eye blinks over 200 muscles move and you blink 25 times a minute or over 6 million times each year. The retina inside the eye covers about 650 square millimeters and contains some 137 million light-sensitive cells; 130 million rod cells for black and white vision and 7 million cone cells for colour vision. To focus all this the muscles of the eye move 100,000 times a day. An eye weighs 1.25 ounces. By the age of 60, our eyes have been exposed to more light energy than would be released by a nuclear blast at onetime. Sight accounts for 90 to 95 percent of all sensory perceptions.

The human eye sees everything upside down, but the brain turns it right side up, with an average field of vision encompassing a 200-degree wide angle. Ears and nose continue to grow entire life but eyes are of the same size from birth to death. A bird's eye takes up about 50 percent of its head; human eyes take up about 5 percent the head. To be comparable to a bird's eyes, human eyes would have to be the size of baseballs. If one goes blind on one eye, he will loose only one-fifth of the vision but lose all depth perception. The only part of the human body that has no blood supply is the cornea and the lens; it takes its oxygen directly from the air.

Newborn babies are not blind but have approximately 20/50 vision and can easily discriminate between degrees of brightness. The daughters of a mother who is colourblind and a father who has normal vision will have normal vision, however the sons will be colourblind. While 7 men in 100 have some form of colourblindness, only 1 woman in 1,000 suffers from it. The most common form of colour blindness is a red-green deficiency. People are the only animals in the world who cry tears. Onion tears are caused by an irritant in onions known to brominate molecules, which react with the water on the eye to, produce an acid, which the eye removes by producing tears. Those stars and colours you see when you close and rub your eyes are called phosphenes.

While reading a page of print, the eyes do not move continually across the page. They move in a series of jumps, called "fixations," from one clump of words to the next. Though more comfortable with daylight, given enough time to adjust, the human eye can, for a time, see almost as well as an owl's. The sensitivity of the human eye is so keen that on a clear, moonless night, a person standing on a mountain can see a match being struck as far as 50 miles away. Much to their amazement, astronauts in orbit were able to see the wakes of ships.

When you have a black eye, you have a bilateral periorbital hematoma. The pupil of the eye expands as much as 45 percent when a person looks at something pleasing.

Structurally the eye is a complex organ wrapped in three layers of tissue as shown in the Fig.1.

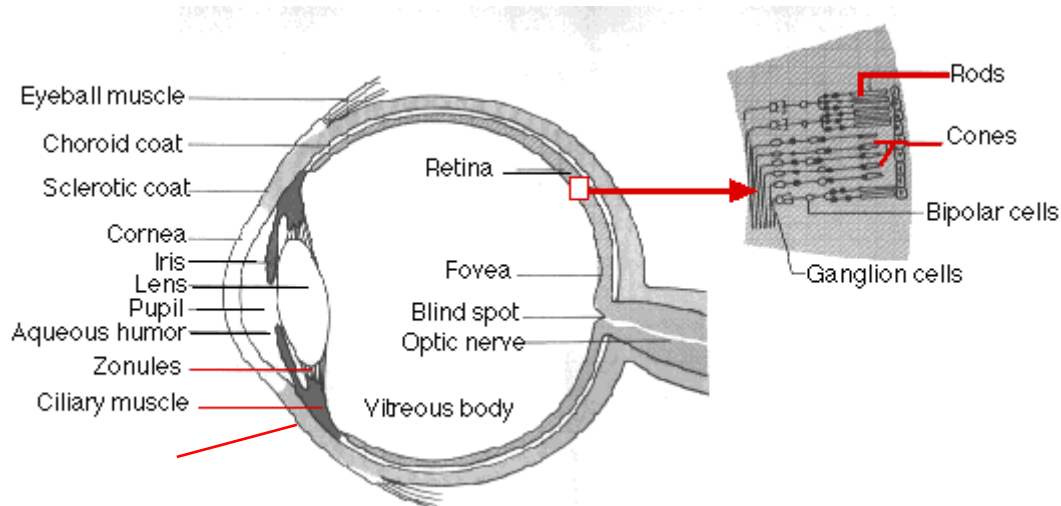


Fig. 1: Cross sectional view of the human eye. Inset shows details of retinal structures

1. The sclerotic coat: This tough layer creates the "white" of the eye except in the front where it forms the transparent cornea. The cornea admits light to the interior of the eye and bends the light rays so that they can be brought to a focus.

The surface of the cornea is kept moist and dust-free by secretions from the tear glands. Just behind the cornea the iris and lens are situated which, divide the eye into two main chambers:

- the front chamber is filled with a watery liquid, the aqueous humor.
- the rear chamber is filled with a jelly like material, the vitreous body.

The lens is located just behind the iris. It is held in position by zonules extending from an encircling ring of muscle. When this ciliary muscle is relaxed, its diameter increases, the zonules are put under tension, and the lens is flattened; contracted, its diameter is reduced, the zonules relax, and the lens becomes more spherical. These changes enable the eye to adjust its focus between far objects and near objects as shown in Figs. 1 and 2.

2. The choroid coat: This middle layer is deeply pigmented with melanin. It reduces reflection of stray light within the eye. The choroid coat forms the iris in the front of the eye. This, too, is pigmented and is responsible for eye "colour". The size of its opening, the pupil, is variable and under the control of the autonomic nervous system. In dim light (or when danger threatens), the pupil opens wider letting more light into the eye. In bright light the pupil closes down. This not only reduces the amount of light entering the eye but also improves its image-forming ability.

- Farsightedness — If the eyeball is too short or the lens too flat or inflexible, the

light rays entering the eye — particularly those from nearby objects — will not be brought to a focus by the time they strike the retina. Eyeglasses with convex lenses can correct the problem. Farsightedness is called hypermetropia.

- Nearsightedness — If the eyeball is too long or the lens too spherical, the image of distant objects is brought to a focus in front of the retina and is out of focus again before the light strikes the retina. Nearby objects can be seen more easily. Eyeglasses with concave lenses correct this problem by diverging the light rays before they enter the eye. Nearsightedness is called myopia.
- Cataracts — One or both lenses often become cloudy as one ages. When cataract seriously interferes with seeing, the cloudy lens is easily removed and a plastic one substituted. The entire process can be done in a few minutes as an outpatient under local anaesthesia.

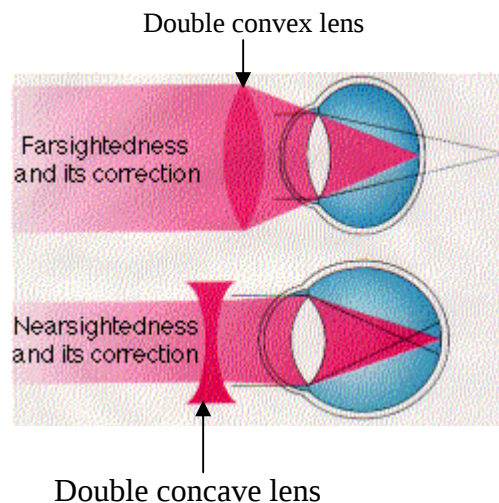


Fig. 2: The path of light without glasses is shown when the image is formed beyond the retina. With glasses, the correction is made and the image exactly falls on retina, thus one can see clearly. The lenses of modern eyeglasses are not so simple in shape as those shown here but function in the same way

3. The retina: The retina is the inner layer of the eye and not only simply a sheet of photocells, but in fact, the retina really is a part of the brain and grows out from it during embryonic development. It contains the light receptors, the rods and cones (and thus serves as the "film" of the eye). The retina also has many interneurons that process the signals arising in the rods and cones before passing them back to the brain (Fig. 1).

The retina infects a tiny brain center that carries out complex information processing before sending signals back along the optic nerve. The retina contains a layer of photoreceptors (specialized, light-sensitive cells) that lines the interior of the eyeball. These photoreceptors make the adjustments that are responsible for adaptation to varying degrees of light. There are two types of photoreceptors — cones and rods. The rods in the retina (of which there are around 100 million) detect the degree of light entering the eye (Fig. 3).

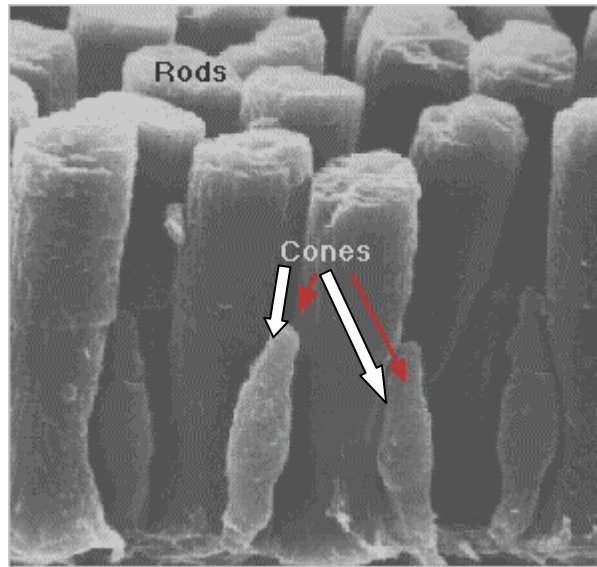


Fig. 3: Scanning electron micrograph shows rods and cones in the retina of the tiger salamander

Rods contain the pigment rhodopsin, or visual purple, which is generated within the cells, becomes temporarily bleached by bright light. Therefore rod cells only work in low light as at high illumination the reduced level of this photosensitive pigment leads to a very low sensitivity. The speed at which rhodopsin adjusts to darkness depends on a sufficient supply of vitamin A in the body. Humans cannot make rhodopsin, instead they use an external source, β -carotene, which is found in food in order to synthesise it.

Cone cells (of which there are around 3 million) are concentrated in the center of the retina (the region called the macula), also sensitive to light levels but retain their function up to high illumination via use of the pigment iodopsin. Detection of colour is a function of the three types of cone cells present within the retina; between them they cover the visible spectrum. This is because each type is sensitive to a different range of wavelengths with maximums corresponding to red (long), green (medium) or blue (short) (Fig. 4).

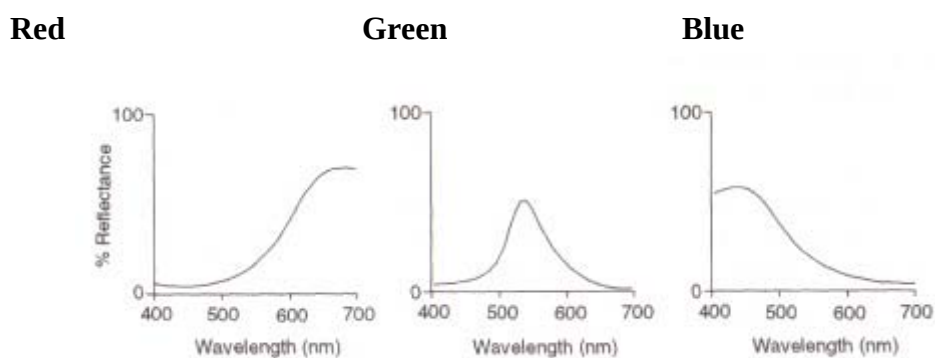


Fig. 4: Maximum of (from left) red, green and blue cone cells, respectively

Cones distinguish fine detail and colour, while rods, which predominate around the edges of the retina, are sensitive to the intensity of light and do most of the work in dim light.

Four kinds of light-sensitive receptors are found in the retina: One on rods and three kinds of cones, each "tuned" to absorb light from a portion of the spectrum of visible light.

- cones that absorb long-wavelength light (red)
- cones that absorb middle-wavelength light (green)
- cones that absorb short-wavelength light (blue)

Each type of receptor has its own special pigment for absorbing light. Each consists of a transmembrane protein called opsin coupled to the prosthetic group retinal. Retinal is a derivative of vitamin A (which explains why night blindness is one sign of vitamin A deficiency) and is used by all four types of receptors.

The amino acid sequences of each of the four types of opsin are similar, but the differences account for their differences in absorption spectrum. The retina also contains a complex array of interneurons bipolar cells and ganglion cells that together form a path from the rods and cones to the brain a complex array of other interneurons that form synapses with the bipolar and ganglion cells and modify their activity.

Ganglion cells are always active. Even in the dark they generate signals of action potentials and conduct them back to the brain along the optic nerve. Vision is based on the modulation of these nerve impulses. There is indirect relationship between visual stimulus and an action potential that is found in the senses of hearing, taste, and smell. In fact, action potentials are not even generated in the rods and cones.

Rod vision

Rhodopsin is the light-absorbing pigment of the rods. It is incorporated in the membranes of disks that are neatly stacked (some 2000 of them) in the outer portion of the rod (This arrangement is reminiscent of the organization of thylakoids, another light-absorbing device in chloroplasts in green plants) (Fig. 5a).

The electron micrograph (Fig. 5b) shows the rod cells of the kangaroo rat. The outer segments of the rods contain the orderly stacks of membranes that incorporate rhodopsin. The inner portion contains many mitochondria. The two parts of the rod are connected by a stalk (arrow) that has the same structure as a primary cilium.

Although the disks are initially formed from the plasma membrane, they become separated from it. Thus signals generated in the disks must be transmitted by a chemical mediator (a "second messenger" called cyclic GMP (cGMP)) to alter the potential of the plasma membrane of the rod.

Rhodopsin consists of an opsin of 348 amino acids coupled to retinal. The opsin has 7 segments of alpha helix that pass back and forth through the lipid bilayer of the disk membrane.

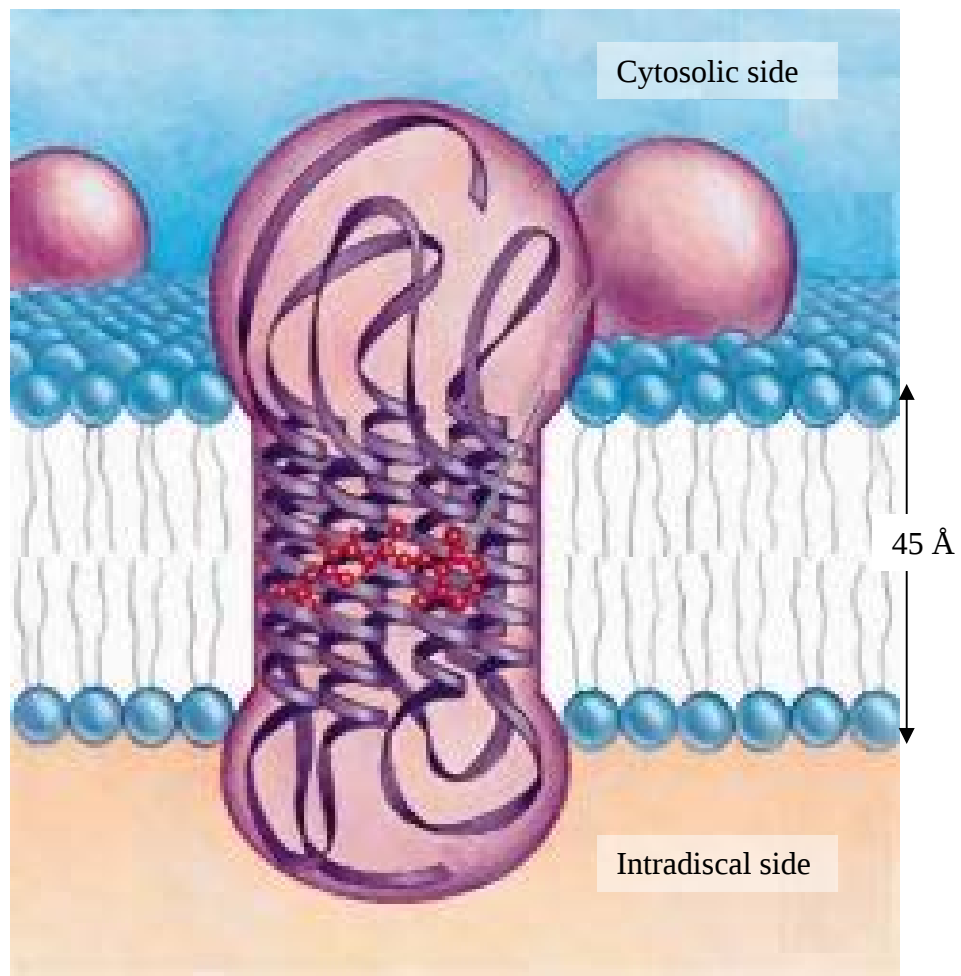


Fig. 5a: The presence and position of rhodopsin pigment in the plasma membrane of rod cells

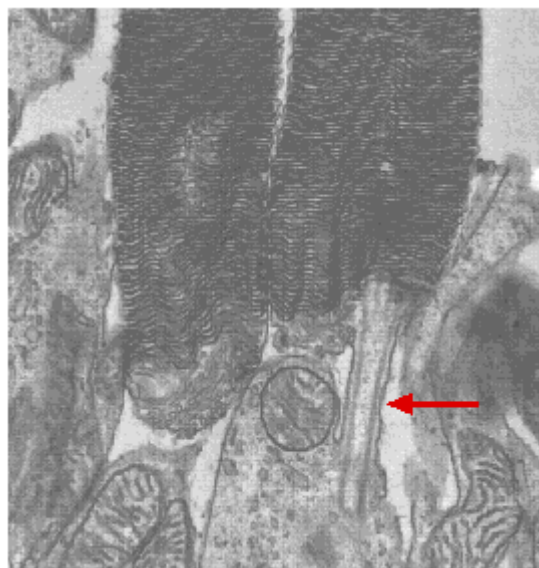


Fig. 5b: Transmission electron micrograph of retina

Retinal consists of a system of alternating single and double bonds. In the dark, the hydrogen atoms attached to the #11 and #12 carbon atoms of retinal (**arrows**) point in the same direction producing a kink in the molecule (Figs. 6 and 7). This configuration is designated *cis*. When light is absorbed by retinal, the molecule straightens out forming the all- *trans* isomer. This physical change in retinal triggers the following chain of events culminating in a change in the pattern of impulses sent back along the optic nerve.

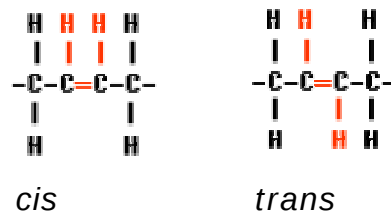


Fig. 6

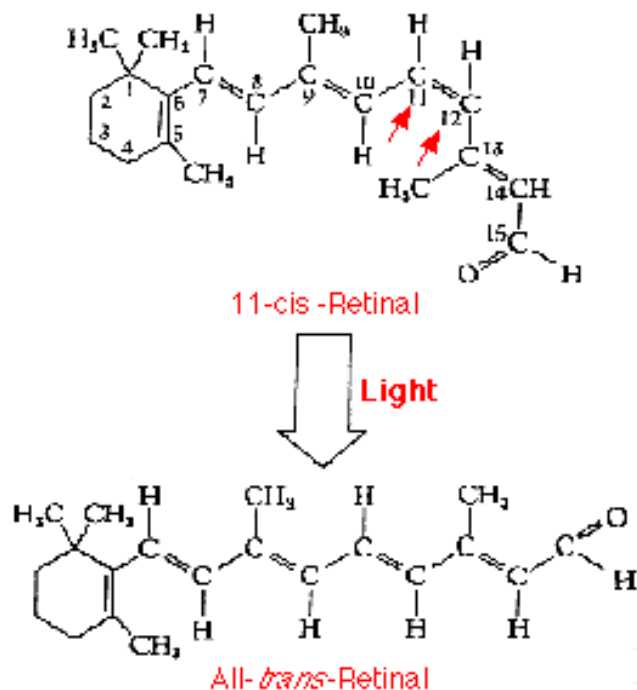


Fig. 7: Retinals (*cis* and *trans*) under the influence of light

Formation of all- *trans* retinal activates its opsin. Activated rhodopsin, in turn, activates many molecules of a protein complex called transducin (Transducin is one of many types of G-protein-coupled receptors — GPCRs). Transducin activates an enzyme that breaks down cyclic GMP.

The drop in cGMP closes Na^+ and Ca^{2+} channels in the plasma membrane of the rod. Because these positive ions can no longer enter (while Ca^{2+} can still leave), the interior of the cell becomes more negative (hyperpolarized) increasing its membrane potential from -40 to as much as -80 mV.

This slows the release of a neurotransmitter at the synapse of the rod. However, because this transmitter is inhibitory, the effect is a "double-negative" one, i.e. positive. Interneurons are

relieved of their normal inhibition. This, in turn, relieves the inhibition of the spontaneous firing of the ganglion cells to which they are connected.

Rod vision is acute but coarse. Rods do not provide a sharp image for several reasons. Adjacent rods are connected by gap junctions and so share their changes in membrane potential. Several nearby rods often share a single circuit to one ganglion cell. A single rod can send signals to several different ganglion cells.

So if only a single rod is stimulated, the brain has no way of determining exactly where on the retina it was. However, rods are extremely sensitive to light. A single photon (the minimum unit of light) absorbed by a small cluster of adjacent rods is sufficient to send a signal to the brain. So although rods provide us with a relatively grainy, colourless image, they permit us to detect light that is over a billion times dimmer than what we see on a bright sunny day.

Cone vision

Human peripheral vision is almost completely rod based! The implication then is that we cannot see colour at the edges of our vision. Although cones operate only in relatively bright light, they provide us with our sharpest images and enable us to see colours. Most of the 3 million cones in each retina are confined to a small region just opposite the lens called the fovea. So our sharpest and colourful images are limited to a small area of view. Because we can quickly direct our eyes to anything in view that interests us, we tend not to be aware of just how poor our peripheral vision is.

The three types of cones provide us the basis of colour vision. Cones are "tuned" to different portions of the visible spectrum (Fig. 4).

- red absorbing cones; those that absorb best at the relatively long wavelengths peaking at 565 nm.
- green absorbing cones with a peak absorption at 535 nm.
- blue absorbing cones with a peak absorption at 440 nm.

Retinal is the prosthetic group for each pigment. Differences in the amino acid sequence of their opsins account for the differences in absorption. The response of cones is not all-or-none. Light of a given wavelength (colour), say 500 nm (green), stimulates all three types of cones, but the green-absorbing cones will be stimulated most strongly. Like rods, the absorption of light does not trigger action potentials but modulates the membrane potential of the cones.

Signal transduction

The photoreceptor cells in the retina are of two types: rods and cones. The rods are more sensitive to light but are not involved in distinguishing colour. They function in night vision and then only in black and white. Cones require greater amounts of light to be stimulated and are, therefore, not initiated in night vision. However, they are involved in distinguishing colours.

The human retina has approximately 125 million rod cells and approximately 6 million cone cells. The rods and cones account for nearly 70 percent of all receptors in the body,

emphasizing the importance of vision in a human's perception of the environment. The numbers of photoreceptors are partly correlated with nocturnal or diurnal habits of the species, with nocturnal mammals having a maximum number of rods.

In humans the highest density of rods is at the lateral regions of the retina. Rods are completely absent from the fovea, the center of the visual field. This is why it is harder to see a dim star at night if you look at it directly than if you look at the star at an angle, allowing the starlight to be focused onto rod populated regions of the retina. However, the sharpest day vision is achieved by looking directly at an object because the cones are most dense in the fovea, approximately 150 thousand cones per square millimeter. Some birds actually have more than one million cones per square millimeter, enabling species such as hawks to spot mice from very high altitudes.

Photoreceptor cells have an outer segment with folded membrane stacks with embedded visual pigments. Retinal is the light-absorbing molecule synthesized from vitamin A and bonded to opsin, a membrane protein in the photoreceptor. The opsins vary in structure from one type of photoreceptor to another. The light-absorbing ability of retinal is affected by the specific identity of the opsin partner.

The chemical response of retinal to light triggers a chain of metabolic events, which causes a change in membrane voltage of the photoreceptor cells. The light hyperpolarizes the membrane by decreasing its permeability to sodium ions, so there are fewer neurotransmitters being released by the cells in light than in dark. Therefore a decrease in chemical signals to cells with which photoreceptors synapse serves as a message that the photoreceptors have been stimulated by light.

The axons of rods and cones synapse with neurons, bipolar cells, which synapse with ganglion cells. The horizontal cells and amacrine cells help integrate information before it is transmitted to the brain.

The axons of the ganglion cells form optic nerves that meet at the optic chiasma near the center of the base of the cerebral cortex. The nerve tracts are arranged so that what is in the left field of view of both eyes is transmitted to the right side of the brain (and vice versa).

The signals from the rods and cones follow two pathways: the vertical pathway and the lateral pathway. In the vertical pathway, the information goes directly from receptor cells to the bipolar cells and then to the ganglion cells. In the lateral pathway, the horizontal cells carry signals from one photoreceptor to other receptor cells and several bipolar cells. When the rods or cones stimulate horizontal cells, these in turn stimulate nearby receptors but inhibit more distant receptor and bipolar cells that are not illuminated. This process, termed lateral inhibition, sharpens the edges of our field of vision and enhances contrasts in images.

The information received by the brain is highly distorted. Although the anatomy and physiology of vision has been extensively studied, there is still much to learn about how the brain can convert a coded set of spots, lines, and movements to perceptions and recognition of objects.

Night blindness

Historically, nyctalopia (Greek for "night blindness") also known as moon blindness, a temporary night blindness believed to be caused by sleeping in moonlight in the tropics. However, now nyctalopia is a condition of the eyes in which vision is normal in daylight or other strong light but is abnormally weak or completely lost at night or in dim light, thus making it difficult or impossible to see in the dark. It is a symptom of several eye diseases. Night blindness may exist from birth, or be caused by injury or malnutrition. The rod cells, one of two light-sensitive areas of the retina of the eye, are impaired in their capacity to produce a chemical compound called rhodopsin, or visual purple, that is necessary for the perception of objects in dim light. Consequently, the visual threshold, or the minimum intensity of light necessary for sight, is greatly increased.

Why are we unable to see in the dark?

The rods and cones are present around a small yellow-pigmented spot called *fovea centralis* that is the area of greatest visual acuity of the eye. At the centre of the fovea, the sensory layer is composed entirely of cones. The cones become fewer towards the periphery. At the outer edges only rods are present. The cones help to distinguish very fine details. The rods do not have the ability to separate small details of the visual image. So in the visual field of the eye, an area of lesser sharpness surrounds a small central area of great sharpness. Just in front of the *fovea centralis* is the pupil, which is a contractile opening in the iris (pigmented diaphragm). The pupil regulates the amount of light falling on the eye. The pupil generally dilates in the dark and constricts in brightness.

Every object the eye perceives acts as a source of light. Generally in the dark the intensity of the source of light is lesser than the light minimum (minimum amount of light energy which can induce a visual sensation). Therefore we cannot see till we get used to the darkness. Moreover since only the rod cells are stimulated in dim light we are unable to discriminate colours and also far less quanta of light falls on the retina, out of which a fraction falling on just one or two rods is sufficient to initiate a visual response. Dim objects can be seen at night on the peripheral part of the retina when they are invisible to the central part. The seeing mechanism in the dark involves a resynthesis of rhodopsin (Fig. 8). Visual purple is bleached by the action of light and is reformed by the rod cells under conditions of darkness. So it takes time for the pigment to begin to form. When the pigment is formed the eyes are sensitive to low levels of illumination and the eyes are said to be dark adapted.

Under normal circumstances, there is a routine and rapid process of rhodopsin synthesis in the dark, because equilibrium is maintained in the retina such that the rate of breakdown of rhodopsin is equal to the rate of its synthesis. Vitamin A plays a major role for dark-adaptation. But if there is a deficiency of vitamin A, the rate of re-synthesis is delayed or there is a delay in the dark adaptation. This is the defect in night blindness (Fig. 9).

The protein rhodopsin contains the protonated retinal-Schiff's base complex, which naturally lies in the inter-membrane pocket formed by the seven trans-membrane β -helical receptors. There are many flat discs of rhodopsin within the outer segment of a rod cell, which upon light detection undergo a photo-isomeric change from rhodopsin (11-*cis*) to all-*trans* retinal. After the photoisomerisation cascade which, occurs via 5 short lived intermediates (Fig. 7), *trans* retinal diffuses away and is converted back into 11-*cis* retinal before re-entry into the cycle. This process occurs via reduction to all-*trans* retinol followed by oxidation

/isomerisation in the dark. Photoexcited rhodopsin (4th of the 5 intermediates) triggers an enzymatic cascade process resulting in the hydrolysis of GMP. This in turn closes cation-specific channels within the rod cell membrane, which are naturally open to influx of Na^+ in the dark, and due to the effect of hyperpolarisation, the inner synaptic body sends a nerve signal to other neurons in the retina. Finally the light-induced lowering of calcium levels aids recovery of excited neurons to a passive, "dark" state and the cycle starts again upon detection of light. The photoreceptors of cone cells are also seven β -helical receptors with 11-*cis*-retinal as their chromophore. The detection range varies from green to red as the three non-polar hydroxyl-containing residues near retinal are sequentially replaced with polar ones.

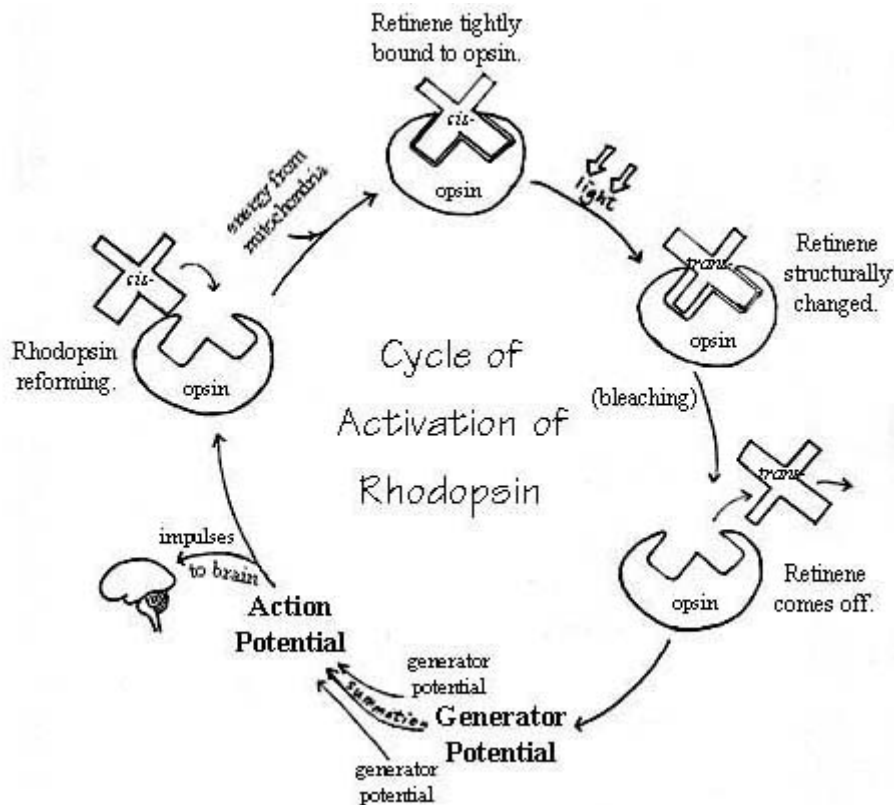


Fig. 8: Rhodopsin activation cycle

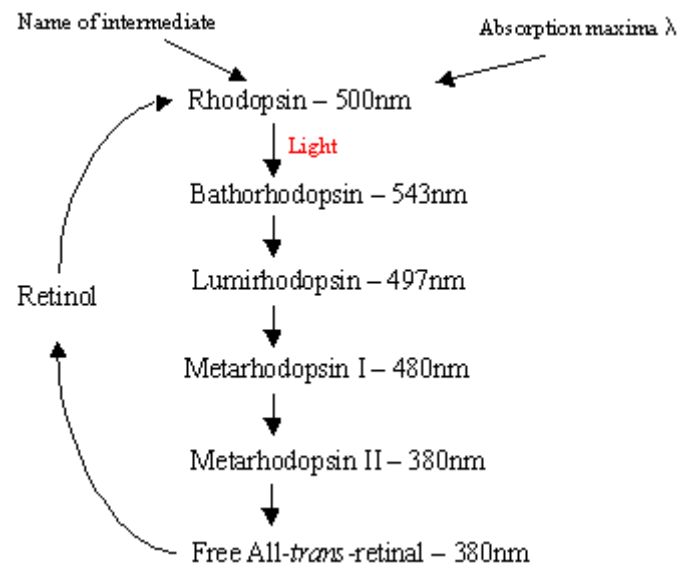
How does the mechanism of bacteriorhodopsin (Fig. 10) found in halobacteria differ from that of rhodopsin found in rod cells of the human eye? This time the protonated retinal-Schiff's base complex naturally blocks a channel through the membrane otherwise formed by two adjacent chambers. The protonated *trans* complex donates a proton to Asp-85 which then allows exit of that same proton to the extracellular side. Photoisomerisation to the 13-*cis* structure allows the Schiff's base to pick up a proton from the Asp-96 residue on the cytosolic side. Upon reorientation of the *cis* form to the *trans*, the cycle of isomerisation and proton pumping continues.

Eyes need Vitamin A

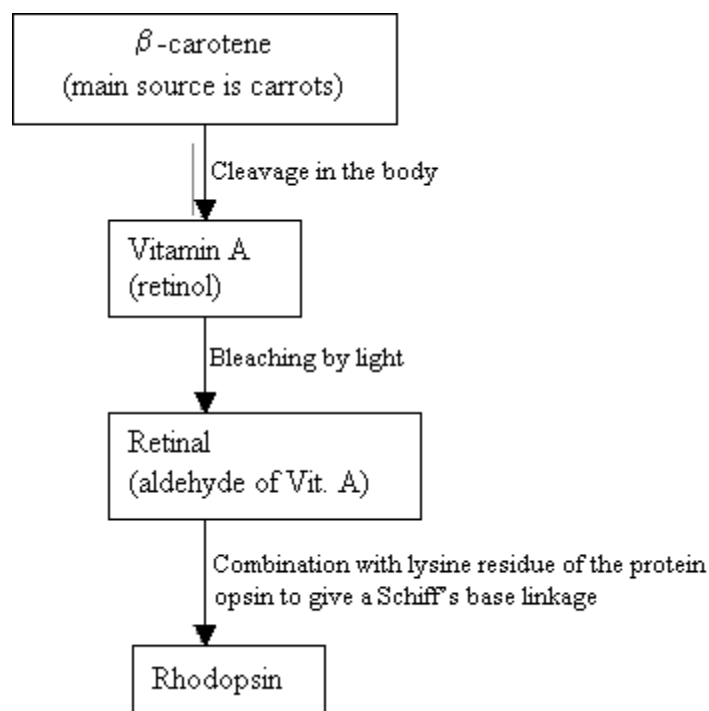
Night blindness is a complex subject. Doctors now know that it can result from nutritional factors, genetics, uncorrected nearsightedness or an eye disease such as cataracts, macular

degeneration or retinitis pigmentosa. And anything that affects vitamin A metabolism, such as liver disease, intestinal surgery, malabsorption or alcoholism, can also cause the problem.

Step 1



Step 2



Step 3

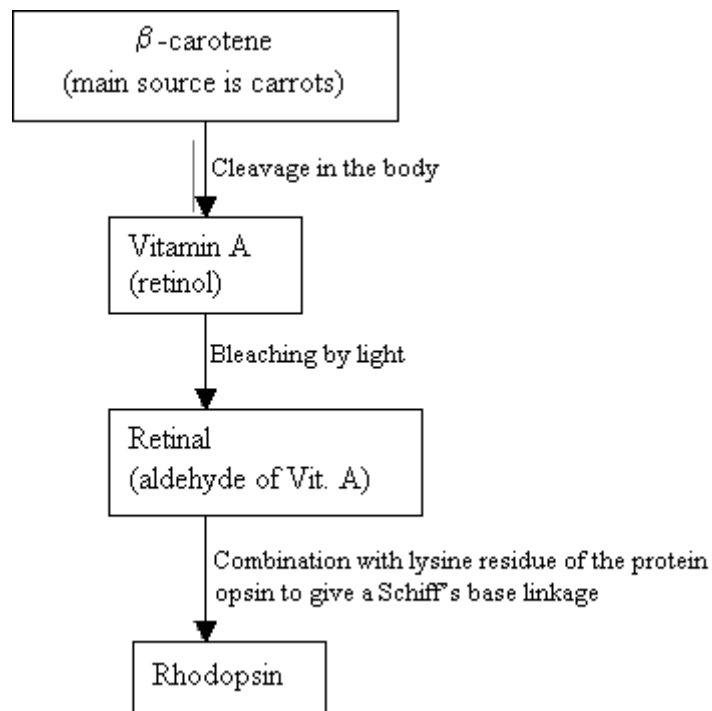


Fig. 9: Flowchart - Synthesis of rhodopsin

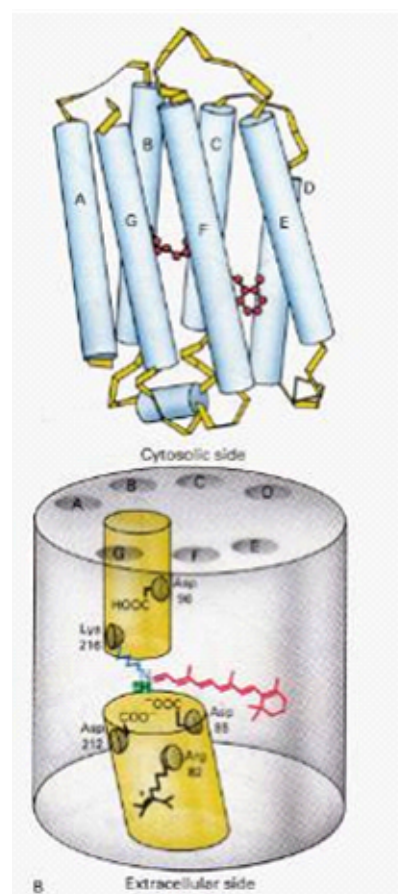


Fig. 10: Molecular modeling of the structure of bacteriodopsin

Vitamin A deficiency and night blindness

Vitamin A (retinol) deficiency to the very high prevalence of [night blindness](#) is observed in children of developing countries such as India and Bangladesh.

Vitamin A deficiency causes deterioration of light sensitive cells ([rods](#)) essential for vision in low lighting. Its deficiency also can extensively damage the eye's clear front surface ([cornea](#)) when eye tissue begins to dry out and shrivel away to create total blindness.

Vitamin A reduces night blindness

As part of ongoing research, Sommer and his team gave oral vitamin A supplementation to 10,000 children twice yearly, at a cost of two cents per dose. It was found that night blindness decreased by one-third in children who received vitamin A.

Vitamin A decreases childhood deaths

Sommer's team also documented startling evidence that childhood deaths were greatly decreased with the simple introduction of vitamin A supplementation. This finding is thought to be related to vitamin A's essential role in supporting tissue health in other parts of the body and immune responses in the presence of childhood diseases such as measles.

Vitamin A increases survival rate of new mothers

As is often the case with a radical new breakthrough, the medical community at first dismissed Sommer's discoveries. In follow up studies in Indonesia, however, Sommer and his team continued to record astonishing results that included a 40% reduction of deaths with vitamin A supplementation among women giving birth.

Vitamin A deficiency

Vitamin A was the first fat-soluble vitamin to be isolated. It was discovered in 1913 as a result of its ability to prevent night blindness and xerophthalmia (a drying and hardening of the mucous membrane that lines the eyelids). In 1932, β -carotene (pro-vitamin A) was discovered to be the precursor to vitamin A and it is sometimes referred to as provitamin A. Vitamin A belongs to a class of compounds called retinoids, which only occur in animal products. Retinoids with vitamin A activity occur in nature in three different forms: a) the alcohol, retinol, b) the aldehyde, retinal or retinaldehyde, and c) the acid, retinoic acid. Vitamin A requires fats as well as minerals in order to be properly absorbed from the digestive tract. Substantial amounts of vitamin A are stored in the liver, and therefore, it does not need to be supplied in the diet on a daily basis.

β -carotene, which is also called pro-vitamin A, is found exclusively in plant (fruit and vegetable) sources. β -carotene consists of two molecules of vitamin A linked head to head (A-A). Enzymes in the intestinal tract split β -carotene into two molecules of vitamin A whenever the body needs it.

The Nurses' Health Study has evaluated the health over 72,000 postmenopausal women 34 to 77 years old for a variety of reasons. One group of investigators evaluated the relationship between high vitamin A intake from foods and supplements and the risk of hip fracture among 72,337 postmenopausal women. Women in the highest group of vitamin A intake (3000 mcg/day of retinol equivalents [RE]) had a significantly elevated relative risk of a hip fracture compared to women in the group with the lowest intake of vitamin A (<1250 mcg/day of RE). Women using estrogens postmenopausally demonstrated a decrease in this risk and the use of β -carotene did not contribute significantly to the fracture risk.

Women are not the only individuals affected by high doses of vitamin A. Researchers have found that the risk of bone fractures was more prevalent among men with higher serum levels of vitamin A.

Vitamin A deficiency exists when the chronic failure to eat sufficient amounts of vitamin A or β -carotene results in levels of blood-serum vitamin A that are below a defined range. β -carotene is a form of pre-vitamin A, which is readily converted to vitamin A in the body. Night blindness is the first symptom of vitamin A deficiency. Prolonged and severe vitamin A deficiency can produce total and irreversible blindness.

Vitamin A (called retinol in mammals) is a fat-soluble vitamin. The recommended dietary allowance (RDA) for vitamin A is 1.0 mg/day for the adult man and 0.8 mg/day for the adult woman. Since β -carotene is converted to vitamin A in the body, the body's requirement for vitamin A can be supplied entirely by β -carotene. Six mg of β -carotene are considered to be the equivalent of 1 mg of vitamin A. The best sources of vitamin A are eggs, milk, butter, liver, and fish, such as herring, sardines, and tuna. Beef is a poor source of vitamin A. Plants does not contain vitamin A, but they do contain β -carotene and other carotenoids. The best sources of β -carotene are dark-green, orange, and yellow vegetables; spinach, carrots, oranges, and sweet potatoes are excellent examples. Cereals are poor sources of β -carotene.

Vitamin A is used for two functions in the body. Used in the eye, it is a component of the eye's light-sensitive parts, containing rods and cones that allow for night-vision or for seeing in dim-light circumstances. Vitamin A (retinol) occurs in the rods. Another form of Vitamin A, retinoic acid, is used in the body for regulating the development of various tissues, such as the cells of the skin, and the lining of the lungs and intestines. Vitamin A is important during embryological development, since, without vitamin A, the fertilized egg cannot develop into a fetus.

Vitamin A deficiency occurs with the chronic consumption of diets that are deficient in both vitamin A and beta-carotene. When vitamin A deficiency exists in the developed world, it tends to happen in alcoholics or in people with diseases that affect the intestine's ability to absorb fat. Examples of such diseases are celiac disease (chronic nutritional disorder), cystic fibrosis, and cholestasis (bile-flow failure or interference). Vitamin A deficiency occurred in infants during the early 1900s in Denmark. The deficiency resulted when milk fat was made into butter for export, leaving the by-product (skimmed milk) for infant feeding. Vitamin A deficiency has taken place in infants in impoverished populations in India, where the only foods fed to the infants were low in β -carotene. Vitamin A deficiency is also common in areas like Southeast Asia, where polished rice, which lacks the vitamin, is a major part of the diet.

The earliest symptom of vitamin A deficiency is night blindness. Prolonged deficiency results in drying of the conjunctiva (the mucous membrane that lines the inner surface of the eyelids and extends over the forepart of the eyeball). With continued vitamin A deficiency, the drying extends to the cornea (xerophthalmia). The cornea eventually shrivels up and becomes ulcerated (keratinomalacia). Superficial, foamy gray triangular spots may appear in the white of the eye (Bitot's spots). Finally, inflammation and infection occur in the interior of the eye, resulting in total and irreversible blindness.

Vitamin A status is measured by tests for retinol. Blood-serum retinol concentrations of 30-60 mg/dl are considered in the normal range. Levels that fall below this range indicate vitamin A deficiency. Night blindness is measured by a technique called electroretinography. Xerophthalmia, keratinomalacia and Bitot's spots are diagnosed visually by trained medical personnel.

Vitamin A deficiency can be prevented or treated by taking vitamin supplements or by getting injections of the vitamin. The specific doses given are oral retinyl palmitate (110 mg), retinyl acetate (66 mg), or injected retinyl palmitate (55 mg) administered on each of two successive days, and once a few weeks later if symptoms are not relieved. The prognosis for correcting night blindness is excellent. Xerophthalmia can be corrected with vitamin A therapy. Ulcerations, tissue death, and total blindness, caused by severe vitamin A deficiency, cannot be treated with vitamin A.

Vitamin A toxicity warning

Vitamin A can be toxic at abnormally high dosages. While vitamin A supplementation can be beneficial, never take unusually high dosages without supervision or direction from a medical doctor. Bone loss and defects are among the many symptoms that can occur with development of hypercalcemia, a condition that can result when vitamin A supplementation is 10 times higher than the recommended daily requirement of 5000 I/U.

Molecular biology of night blindness

The genetic locus for incomplete congenital stationary night blindness (CSNB2) has been identified as the CACNA1f gene, encoding the alpha 1F calcium channel subunit, a member of the L-type family of calcium channels. The electroretinogram associated with CSNB2 implicates alpha 1F in synaptic transmission between retinal photoreceptors and bipolar cells. Lastly, we present evidence for L-type alpha 1D calcium channel subunits in cone terminals of the mouse retina. The presence of alpha 1D channels in cones may explain the residual visual abilities of individuals with CSNB2.

Gene for autosomal dominant congenital stationary night blindness maps to the same region as the gene for the β -subunit of the rod photoreceptor cGMP phosphodiesterase (PDEB) in chromosome 4p16.3. Interestingly the gene for the β -subunit of the rod photoreceptor cGMP-specific phosphodiesterase maps to the very same chromosomal region. Autosomal recessive form of congenital night blindness is associated with a negative ERG waveform.

Naturally occurring point mutations in the opsin gene cause the retinal diseases retinitis pigmentosa and congenital night blindness. Although these diseases involve similar mutations in very close locations in rhodopsin, their progression is very different, with

retinitis pigmentosa being severe and causing retinal degeneration. We report on the expression and characterization of the recently found T94I mutation associated with congenital night blindness, in the second transmembrane helix of rhodopsin, and mutations at the same site.

The reported results, together with previously published data on the other two known congenital night blindness mutants, suggest that the molecular mechanism underlying this disease may not be structural misfolding, as proposed for retinitis pigmentosa mutants, but abnormal functioning of the receptor by decreased thermal stability and/or constitutive activity.

Recently, a mutation (Gly38Asp) was identified in the α -subunit of rod transducin in members of the Nougaret pedigree affected with dominantly inherited stationary night blindness. Although the Nougaret form of stationary night blindness has been cited as a prototype of absent rod function with normal cone function, our findings, based on the genealogically and genotypically documented descendants of Jean Nougaret, show that rod function is present, although subnormal, and that there is slight impairment of cone function. The data also suggest that these abnormalities can be simulated by light-adapting the normal retina, compatible with the proposal that the rod transducin encoded by the mutant gene is constitutively active and that the night blindness results from partial desensitization of rods caused by the constitutive activity.

Incomplete X-linked congenital stationary night blindness (CSNB) is a clinically variable condition which has been shown to be caused by mutations in the calcium-channel CACNA1F gene.

Although the patients shared a common CACNA1F mutation, there was considerable variability in the clinical expression of the incomplete CSNB phenotype. These findings suggest the presence of other genetic factors modifying the phenotype of this disorder.

X-linked congenital stationary night blindness (CSNB) is a nonprogressive retinal disorder characterized by disturbed or absent night vision; its clinical features may also include myopia, nystagmus, and impaired visual acuity. X-linked CSNB is clinically heterogeneous, and it may also be genetically heterogeneous.

Genetic and clinical analyses of this set of 32 families with X-linked CSNB, together with the family studies reported in the literature, strongly suggest that two loci, one for complete (CSNB1) and one for incomplete (CSNB2) X-linked CSNB, can account for all reported mapping information. The predicted polypeptide is a glycosylphosphatidylinositol (GPI)-anchored extracellular protein with 11 typical and 2 cysteine-rich, leucine-rich repeat (LRRs). This motif is important for protein-protein interactions and members of the LRR superfamily are involved in cell adhesion and axon guidance. Future functional analysis of nyctalopin might therefore give insight into the fine-regulation of cell-cell contacts in the retina.

Conclusion

True night blindness is rare. Most of what people call night blindness is either a lack of vitamin A in the diet or a failure to understand the night blind spot. Unaided night vision even now in the 21st century is still the subject of some controversy.

For best night vision

Be sure you are getting enough vitamin A or its precursor β -carotene in your diet (needed for the visual purple).

Green leafy stuff is best, followed by vegetables that have an orange colour. Yes that includes carrots but spinach or dark leaf lettuce is better. It is possible to get too much vitamin A especially as a supplement.

Keep up your general health. Smoking is also very bad for night vision, as are most illegal drugs and some prescription drugs.

Keep your blood sugar level as even as possible. No meal skipping. Six small meals are better than three large meals. For carbohydrates favour starches (potatoes, rice, and bread) over simple sugars (sweets, alcohol).

Use dark neutral gray sunglasses, that pass no more than 15% in full sun, when outside during the day.