The Shape of the Eye:

Why the Eye is Round

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ABSTRACT

The most striking characteristic about the eye is that it is a round, spherical structure. This chapter explores the optical, mechanical, structural, phylogenic, and ontogenic reasons why eyes are round. This exploration is used as a starting point to describe how the different features of the eye are related to each other and how the roundness is maintained by the inflow and outflow of fluid in the eye.

INTRODUCTION

If you look up into the night sky at the constellation of the Big Dipper and have 20/30 or better visual acuity and adequate night vision, you will see that the next-to-the-last-star in the handle of the dipper is actually two stars that are quite close together. One star is brighter than the other. The brighter star is called *Mizar*, and the fainter *Alcor.* It is easy to fall into the trap described by the ancient Arabic proverb that, “He sees Alcor, but not the full moon.” The lesson here is that the most outstanding fact about eyes is not something arcane, but the obvious fact that eyes are round; that is, eyes are spheres. Therefore, this first chapter will focus on the fact that eyes are round. Why should eyes be round? What does it tell us about how eyes are constructed and how they work? Not only is this shape similar in different animals but the variation in size of the vertebrate eye, from tree shrew to whale, is much smaller in proportion than the variation in size of these creatures. I will also describe how different features of the eye (shown in Figure 1) are related to each other and how the roundness is maintained and controlled by the formation, flow, and removal of fluid in the eye.

WHY ARE THINGS ROUND?

When I first thought about the roundness of eyes, I realized I didn’t know why anything was round. So, I made a list of other round objects to help organize my thought process. My list consisted of the sun, the earth, the moon, oranges, frog urinary bladders, basketballs, and rocks. As you can see, the list consists of both organic, animate and inorganic, inanimate objects.

Inanimate Objects

Before we start with the inanimate objects on the list, we first need to understand the concept of *equilibrium*. Consider your textbook, unopened, on a desk. Even though it is static, there are at least two forces at work, making it that way. It is actually in dynamic equilibrium, subject at every instant, to opposing forces which balance it. Gravity is pulling the book down toward the center of the earth. The desk is pushing it up, preventing it from moving. All objects that appear static are actually in this balancing act of opposing forces. If one of the forces were stronger, it would change the object rapidly, until an opposing force balanced it, and then the object would again be at a new equilibrium. Objects change so rapidly when out of equilibrium that we are not likely to catch sight of them during that time.

What forces are balancing in these inanimate objects? How do those forces determine the shapes of these objects? In the sun, gravity pulls the gases of the sun together, pushing all its material toward its center. The inward pull of gravity raises the temperature which raises the pressure of the gas in the sun until the outward pressure of the gas balances the inward pull of gravity. Both the inward pull of gravity and the outward push of gas pressure are *isotropic*. That is, they are equally effective in all directions. That is why the sun is round. If one of these forces were not isotropic, then the sun would not be round. Sometimes there are other pressures. If a star is rapidly rotating, or has a strong magnetic field, then the gas pressure is weaker along that axis. The gas collapses along that axis, and the star becomes a flattened disk. The weaker pressure along the axis balances the weaker gravitational force of the thin mass in the thickness of the disk, whereas the stronger pressure along the radius of the disk balances the larger gravitational force of the larger amount of mass in the radial direction. Thus, round objects exist when forces are *isotropic* and non-round objects when forces are not isotropic.

In the earth, the gravitational force pushing inward is balanced by the outward push of the strength of the rocks, a result of the push of electrons against each other in adjacent atoms. Both these forces are isotropic, and so the earth is round. In a basketball, the air pressure pushing outward is balanced by the tension on the fabric pushing inward. Again, both these forces are isotropic and so the basketball is round.

Animate Objects

In inanimate objects, a round configuration results from a balance of *isotropic* forces, that is, forces experienced equally in all directions. But what determines the shapes of living things? The Zoologist and classical scholar, D'Arcy Thompson attempted to answer this puzzling phenomena in his book, "On Growth and Form" published in 1917. Although you may not be familiar with his publication, there is a good chance that you have seen reproductions of his drawings. His exquisite illustrations of forms of radiolaria or how the shapes of animals change from one species to another have been prolifically copied. The seminal point of Thompson's book was that genes do not set the blueprint of the shape of an organism, but they set the rules of how the organism interacts with its environment. It is then this dynamic interaction between the organism and its environment that produces the structure.

For example, the *final* shape of the long bones in the arms and legs is dependent on forces between osseous cells and the forces of their environment. Since bone is alive, material is constantly being added and removed from biochemical reactions by cells within the bone. When a bone is bent, fluid flows inside the bone. The negative and positive ions in this fluid flow at different rates generating an electrical voltage. This voltage affects the cells in the bone so that their enzymes add more calcium on the electrically negative side of the bend, and remove more calcium on the electrically positive side of the bend. As a result, the bone is resculpted into a straighter shape. Bone is very strong at resisting compressive forces pushing inward on both ends. It is weak at resisting tensile forces pulling outward from both ends. The resculpting adds material where the bone is in compression and more material is needed. It removes material where the bone is in tension and excess material is wasted. Thus, the genes, through their complex programming of cells and their enzymes, have set the rule: add material where it is needed and remove material where it is not needed. The genes have set the rule of how the bone interacts with the environment. That rule and its interaction with the environment then generates the straight shape of the bone.

Such interactions also sculpt the eye and its surrounding tissues. In congenital glaucoma, the increased pressure in the eye stimulates the entire eye to develop to a larger size than normal. When an eye with retinal blastoma has to be enucleated at an early age to prevent the cancer from spreading, the bones of that orbit do not grow as large as the other orbit because the pressure of the eye is needed to stimulate their normal growth.

For the living things in my list, how much shape is determined solely by the genes and how much by the rules of interaction with the environment set by the genes? I have my own guesses about oranges and frog urinary bladders. What are your guesses? To answer these questions you must ask yourself “What forces are balancing to determine the shape?” and “What is the mechanism of feedback between the world and the tissue?”

WHY ARE EYES ROUND?

Optical Properties

My first guess was that since the most important function of the eye is to form our image of the world there must be an optical reason why eyes are round.

The eye focuses light onto the retina. Most people think that this focusing is performed by the lens in the eye. However, light is bent most sharply when it passes through an interface of materials of different refractive indices. In the eye, the difference in refractive index is much larger at the air/tissue interface of the cornea, (the clear front surface of the eye), than at the fluid/tissue/fluid interface of the lens. Thus, 2/3 of the focusing of light is done by the cornea and only 1/3 by the lens. The lens does the fine tuning of the focusing of the image. The cornea controls the overall quality of the image. It is problems of the cornea that produce nearsightedness, farsightedness, or astigmatism that can be corrected by glasses or contact lenses.

Is the eye round to achieve the best optical image on the retina, where the light is detected and transformed into electrical signals? There a number of different aberrations, ways in which the focus of images on the retina are not perfect. Important deviations include *spherical aberration* (where a light ray in the center of the cornea reaches a focus that is closer to the cornea than a ray at the periphery of the cornea) and *chromatic aberration* (where a ray of blue light reaches a focus that is closed to the cornea rather than a ray of red light). Another aberration is that the cornea focuses images onto a spherical surface rather than a flat surface. Moreover, this spherical surface has a different radius for vertical and horizontal images on the cornea. The retina of the eye is a spherical surface whose radius is a good compromise between those two different radii. This looks like a good reason why eyes might be round, but actually, it is only a very small effect.

In fact, the image of the world on the retina does not need to be in very good focus across the entire retina. Brown notes that "the optical characteristics of the eye . . . are nicely matched to the receptors [photoreceptors] and neural components." Only a very small part of the retina, the fovea, requires light to be accurately focused. This is because the neural components of the retina that sense light only have high resolution in the fovea. There are about 100 million photoreceptors, rods and cones, in the eye that convert light into electrical signals. There are 1 million retinal ganglion nerve cells that carry the information out of the eye into the brain. This enormous number of nerve cells is about 1/3 of all the afferent nerve fibers bringing information into the brain. But even with this large number of nerve cells there are still 100 photoreceptors for each nerve cell. Hence, the light from every photoreceptor does not individually reach the brain. Only in the fovea is there is a 1:1 coupling between photoreceptors and nerve cells. Away from the fovea, the output from many photoreceptors is processed and blended together into far fewer nerve cells that reach the brain. Thus, throughout most of the retina the neural pixels (picture elements) are coarse. In most of the retina, the eye sacrifices spatial resolution for enhanced sensitivity at low light levels as well as enhanced resolution of how the light level is changing in time.

The spatial resolution is high only in the fovea which senses an area that is about two degrees (2^{o}) across, only four times the diameter of the full moon. Everything else in your image of the world is fuzzy. The look of the world, its sharp edges and beautiful colors, is an illusion generated high up in the neural pathway located in the visual cortex in the back of your head. The eye is not like a camera. It is more like an electronic information sampling system. The brain moves the high resolution, clear image, fovea to sample interesting features such as an ornate edge or a flashing light. It samples phenomena that look interesting. What you see depends primarily on what you saw before and what you are thinking now. This information is combined into the fiction of a clear, stable world.

A sharp, clear image is not needed across most of the retina because the neural elements there that detect light do not have a high spatial resolution. A coarse image is a nice match to the coarse neural elements. Most of the retina provides a wide angle, low resolution detection system to spot potential predators. The spherical retina may provide a useful detector for such system. Sharp, clear images are only needed in the fovea, a region 3 mm in diameter. A spherical shape is not needed to produce a clear image over such a small target. For example, when light is dim, at the bottom of the ocean or late at night on the land, animals have developed long cylindrical eyes with large, fast (high f ratio) lenses that maintain focus and clear images to the central area of their flattened retinas.

Thus, it does not seem as roundness is a necessity for optical efficiency.

Eye Movement

I used to ask scientists at eye research conferences why they thought eyes were round. Inevitably, the answer that I received was that eyes were round because this was the best shape for rapid and accurate eye movements. It's mechanically easy to rotate a round eye in a round socket to aim it at any direction. Spheres also have the lowest moment of inertia for their mass and thus require the least force to move.

Is this the reason why eyes are round? In his classic book on the vertebrate eye Walls notes that the "primitive function of the eye muscles was not to aim the eye at objects at all [but] . . . designed to give the eyeball the attributes of a gyroscopically-stabilized ship, for the purpose of maintaining a constancy of the visual field despite chance buffetings and twistings of an animal's body by water currents and so on."

Let's examine the evolutionary sequence. Fishes lack the fovea needed for sharp vision. They do not need to aim their eyes accurately so they do not follow objects with their eyes. Amphibians also have limited eye movement capabilities. Neckless frogs turn their entire bodies in order to change their direction of gaze. Reptiles show variation in their eye movement. Some, like the Gila monster, have eyes that are fixed in their head. Others, like the chameleon, can use one eye to look forward and the other to look backward at the same time. Birds, the descendants of dinosaurs, have better vision than humans. Some birds have extended, high resolution areas on their retinas that cover a huge field of view. Other birds have more pigments in their photoreceptors for enhanced color resolution or extra structures to deliver more oxygen to the retina. Yet, their eyes are fixed and immobile. It is only mammals that have rapid and accurate movements.

This idea of roundness to facilitate eye motion, which seems obvious to many scientists, when considered in more detail, seems less convincing. The evolutionary record is whispering to us that eyes were round before they moved rapidly or accurately. Thus, it does not seem as if the eye is round *primarily* for eye movement reasons.

Hollow

Perhaps it is the hollow inside which is significant. A spherical shell, inflated with fluid, can provide a clear optical pathway to the retina unobstructed by bones and ligaments. The spherical shape also provides the shortest, therefore the quickest, pathways for oxygen and nutrients to reach the interior structures of the eye and for wastes to leave them. A convoluted interior space, with serpentine passageways, would reduce the efficiency of such diffusion.

But the eye has not taken full advantage of this unobstructed interior space. Except in the core of the fovea, one layer of blood vessels that nourish the retina and two layers of synapses of nerve cells, lie in front of the photoreceptors. Light passes through these cells to reach the photoreceptors. These obstructions affect the image on the retina. You have probably observed this blood flow. On a clear day, when you look at a bright blue sky (but not the sun which can cause severe and permanent damage) you can see tiny white specks darting around. This image is called the *blue entoptic phenomenon*. The white specks are white blood cells moving in front of the photoreceptors. The photoreceptors become adapted to the more numerous red blood cells shadowed against the blue sky, but then detect and respond to the occasional white blood cell. Experimentally, the speed of the white dots on a computer screen has been matched with the speed of these white specks to measure relative retinal microcirculation. To calibrate the system, a few volunteers wore a neck cuff to reduce the circulation to head so that the speed of the dots on the computer screen could be related quantitatively to the blood flow in the retina.

The eye has taken some, but not complete advantage of this hollow space. Thus, it does not appear that the eye is round *primarily* for structural reasons to create a hollow space.

Phylogeny and/or Ontogeny

Walls notes "the great German anatomist Froriep once likened the 'sudden' appearance of the vertebrate eye in evolution to the birth of Atena, fully-grown and fully-armed, from the brow of Zeus." There are no intermediate anatomical adaptations. Animals either have eyes that form images or spots that detect the amount of light. Perhaps roundness is a consequence of evolutionary pressures that produced the vertebrate eye. This idea is supported by the anatomical evidence found in the eyes of the cephalopods such as squid and octopus. Their eyes evolved separately from the vertebrate eye yet except for some small differences, their anatomy is strikingly similar. One of the few differences is that the cephalopod eye has nerves which travel from the back of the photoreceptors, rather than the front of them, so that they do not interfere with the light pathway to the photoreceptors.

Tripathi notes “the final resemblance between the two types of eye [cephalopod and vertebrate]. . .makes this one of the most striking cases of convergence in evolutionary history.” Convergence means that similar adaptive pressures led to similar anatomical structures. Perhaps, those pressures also dictated the roundness of the eye.

Maybe the answer lies not in phylogeny, the evolutionary history of a species, but in ontogeny, the developmental history of each new individual. The structures of the eye need to be axis-symmetric along the line of rotation that brings light through the eye into the retina. Perhaps, developmental processes that form spherical structures are the embryo’s path of least resistance to form such axis-symmetric structures.

Although speculation on both species specific evolution or individual development is both interesting as well as attractive, the hard evidence in support of these ideas is lacking. Thus, it does not seem that the eye is round *primarily* for phylogenic or ontogenic reasons.

Conclusion

Neither optical, nor movement, nor structural, nor evolutionary, nor developmental reasons seem to be the primary reason why the eye is round.

PRESSURE

Although we don’t understand *why* the eye is round, we do understand *how* it is round. As explained earlier, the roundness of the eye reflects a balance of two opposing forces. The outward force exerted by the pressure of the fluid inside the eye is balanced by the inward tension in the shell of the eye.

Surface Tension

The tension in the outer layers of the eye is called surface tension. If we were to make a small cut on the eye, the surface tension would be the force pulling the two sides of the cut away from each other. For a given pressure inside, the sphere is the shape that has the lowest surface tension. Containers for gas under pressure of any shape other than spherical require stronger walls. In the inorganic world, it is harder to manufacture spheres than cylinders, thus, most gas containers are cylinders. However, the material of these cylinders must be made twice as strong as would be needed for a sphere to hold the same pressure of gas.

In a cylinder, the surface tension across a cut in a curved direction is equal to that for a sphere of the same radius under the same pressure, but the surface tension for a cut in the long direction has twice the surface tension. This is the reason that the skin of frankfurters always tears in the long direction when cooked. The surface tension is twice as great in the lengthwise direction. Since the frankfurter skin is equally strong in both directions, it always breaks along the long direction where the force tearing at it is twice that of the force tearing at it in the curved direction.

Pressure in the Eye

The fluid that flows in the eye is called the *aqueous humor*. It flows out of the ciliary body, passes in front of the lens, moves through the pupil, and circulates in the space behind the cornea. As discussed earlier, the outward force from the fluid pressure of the aqueous humor inside the eye is *isotropic*, felt equally in all directions. The inward force of the surface tension in the outer shell of eye is also *isotropic*. The balance between these inward and outward forces determines the spherical shape of the eye.

Since the force of the fluid pressure inside the eye is isotropic, a pressure increase in one part of the eye causes a pressure increase everywhere throughout the eye. In glaucoma, the pressure increase in the aqueous humor in the front of the eye is transmitted to the back of the eye. Although the pressure increase is caused by events in the front of the eye, the damage to vision is due to the effects of this pressure in the back of the eye. The increased pressure crimps the retinal nerve and blood flow, killing retinal ganglion cells either by cutting off the transport of essential materials along the inside of their axons, or the blood supply that nourishes them from the outside. The loss of vision results from the death of these nerve cells.

The hardness of the eye to touch is not determined by the toughness of the fabric of the eye, but by the fluid pressure inside the eye. When the pressure is high, the eye is hard. When the pressure is low, the eye is soft.

However, this is not the whole story. There is an additional factor. I have always felt that when my bicycle tires are old, no matter how much I pump them up, they never feel quite as hard as new tires. In the eye too, when the fabric is compromised, the shape and hardness of the eye changes. For example, the shape of the cornea changes in keratoconus where the collagen in the cornea is weakened. In pathological myopia, there is a slow mechanical yielding of the fabric, and the eye steadily enlarges in time.

AQUEOUS FLOW

Balance of Inflow and Outflow

The eye is round because it is inflated by the pressure from the fluid inside. Is that what is necessary to maintain its shape, that is, to fill it once with aqueous humor under pressure? Nothing lasts forever. For example my bicycle tires lose about 20% of their air every week. In order to maintain the pressure in the eye we need to push fluid in and have it leak out in a very precise system. At first thought, it seems unbelievably wasteful to push fluid into the eye just to let it leak out again but it’s actually the most basic biological trick to expend energy for the sake of control. Balancing the inflow and outflow of aqueous humor provides a way to maintain and control the pressure inside the eye.

Soon we'll see in detail how the aqueous humor is produced and how it leaks out of the eye. The important point to remember here is that there is a balance of inflow and outflow. If the inflow was greater than the outflow, the fluid inside the eye would continually increase, and the eye would burst. If the inflow were less than the outflow, the fluid inside the eye would continually decrease, and the eye would collapse.

The flow of aqueous humor out of the eye is driven by the pressure inside the eye. The resistance to the flow of aqueous out of the eye determines the intraocular pressure inside the eye. If it is hard for the aqueous humor to leave the eye, then more aqueous accumulates in the eye. This increases the pressure within the eye which forces more aqueous out. The pressure continues to increase until the aqueous flow out of the eye equals the aqueous flow into the eye. The pressure at which this balance occurs is determined by the resistance to the outflow of aqueous humor leaving the eye. Thus, there is always a balance in the amount of aqueous entering and leaving the eye.

Inflow

The aqueous humor is generated by the *ciliary body*, a wiggly layer of tissue two cells thick, along the edge of the ciliary muscle in the inside angle of the eye a little back from where the clear cornea merges into the white sclera. From the ciliary body, the aqueous humor flows into the posterior chamber behind the lens. Then it passes through the pupil into the anterior chamber in front of the lens.

Outflow

The aqueous humor in the anterior chamber leaves the eye by passing through a series of structures in the angle of the eye inside of where the cornea merges with the sclera. On its way out of the eye, the aqueous flows through a coarse filter and then a fine filter called the trabecular meshwork. Then it flows through a layer of cells and into a tube called Schlemm's canal that circles the cornea. From the canal it flows through collecting channels that bring it to the veins. It is not known which of these structures offers the most resistance to the flow. Some recent evidence suggests that the cells that line Schlemm's canal offer the most resistance to the flow and thus determine the intraocular pressure inside the eye.

THE CILIARY BODY

Structure

Aqueous humor is produced by two layers of epithelial cells in the ciliary body. A layer of pigmented cells is attached to a membrane that borders the capillaries. Inside of this is a layer of unpigmented cells that borders the posterior chamber. Fluid flows from the plasma in the capillaries, through these two layers of cells, into the posterior chamber.

In science, we use numbers to get a feeling for places that we can never touch with our fingertips. We will now use *Reynolds, Peclet* and *concentration* numbers to gain a better understanding of the nature of the production of aqueous humor from these cells of the ciliary body.

Numbers in Science

There seems to be quite a misunderstanding about how numbers are used in science. Numbers are used only for qualitative purposes. Numbers are never used for quantitative purposes. What an oxymoron!

Let me illustrate this with an example. What do you think is the average density of the sun? The average density, the sun's mass divided by its volume, is about 1.4 gm/cm^3. The importance of this number is that the density of coal is about 3 gm/cm^3 and the density of iron is about 8 gm/cm^3. Thus, knowing the average density of the sun immediately tells us that the sun cannot be a burning ball of coal or a red hot ball of iron. In fact, the light coming from the sun has strong spectral lines of carbon and iron, so it would not be unreasonable to think that the sun was made of coal or iron. Yet, the number of the density tells us that the sun must be made out of something else.

The importance of the number of the average density of the sun is not that we know that it is 1.414 gm/cm^3 rather than 1.415 gm/cm^3, but that in relationship to other facts, namely the density of other materials, this number tells us something. It gives us the qualitative information that the sun is not made out of coal or iron. This is how numbers are used in science, to reach qualitative conclusions about the nature of things.

Let's now use some numbers to get a feel of what it's like to be in the ciliary body where the aqueous humor is produced.

Reynolds Number

The wind flowing toward a beachball is deflected by its curved surface. The air curves around the beachball. It continues its curvy path after it flows past the beachball. This tendency of objects in motion to remain in motion is called inertia. The beachball changes the flow of the air most near its surface and has little effect on the air some distance away. There is friction as the nearer and more distant streams of air scrape against each other. This friction is called viscosity.

The Reynolds number is the ratio of inertia to viscosity. When the Reynolds number is small, then a fluid flow is dominated by viscous friction. The flow is viscous, smooth, and regular. For example, a pearl in honey has a Reynolds number of about 0.01. When the Reynolds number is large, then a fluid flow is dominated by inertia. The flow is fast, disorderly, and turbulent. For example, a rowboat in a lake has a Reynolds number of about 10,000.

The Reynolds number for the flow of aqueous humor through the cells of the ciliary body is about 0.00001. This is the same Reynolds number that you would have if you were in a swimming pool filled with molasses and were told not to move any part of your body faster than 1 cm/minute. Thus, the flow of aqueous through these cells is smooth, laminar and stately. It is like the squishy motion of a macrophage slipping between endothelial cells that you may have seen in movies taken through microscopes. It is not like the flow of water out of your kitchen faucet, gurgling with disordered turbulence at Reynolds numbers of 10,000-100,000.

From our first number, the Reynolds number, we have learned to picture aqueous production as thick and regular, dominated by friction rather than by inertia.

Peclet Number

Place a drop of black ink into a clear mountain stream. The drop will spread in the water. This is called diffusion. The drop will also be carried downstream. This is called advection. The osmotic Peclet number is the ratio of diffusion to advection. When the Peclet number is small, the flow is dominated by advection. The ink drop will be swiftly carried a long way downstream before it has time to spread. When the Peclet number is large, the flow is dominated by diffusion. In this case, the ink drop will spread much faster than travel downstream.

The Peclet number inside the cells of the ciliary body is about 100. The motion of molecules inside the cell is dominated by diffusion. A molecule soon wanders from any one part of the cell to any other part of cell, precluding the necessity for a conveyer belt. It is not necessary to mechanically grab molecules and carry them from one part of the cell to another. Just wait a little while and the molecule will diffuse. This is true for all cells except for nerve cells with long axons where diffusion is not efficient. In such nerve cells energy from ATP drags carrier molecules along complementary tracks. However the micro situation inside the ciliary body differs from both the nerve cell situation and our macro environment where all types of clever mechanical devices are needed to move things from one place to another. Sometimes membranes wall off compartments within a cell and reduce the efficiency of the diffusion of molecules. Molecules are then carried by proteins across those membranes from one compartment to another.

Thus, from this second number we have learned that diffusion, rather than the mechanical transport of our macroscopic world, is the mechanism that moves molecules around in the cells of the ciliary body.

Concentration Number

Another useful number is the concentration number of ions such as sodium, potassium, and chloride in the intracellular and extracellular solutions. The concentration of a solution of sodium chloride adjusted to match the osmolarity of plasma, called isotonic saline, is about 300 milli-moles/liter. Molecular weight units, such as moles per liter, are helpful for computing the amounts that must be weighed out on a scale in order to mix a solution with a given concentration. These units are not helpful to form a physical picture of these solutions.

A more useful unit of concentration is the number of water molecules for each ion. The number of ions in solution is similar in isotonic saline, the blood plasma, the aqueous humor, the solution in the cells in the ciliary body, and the solution in the spaces between those cells. In each of these solutions there are about 150 molecules of water for each ion. You can now picture a few cubes of solution, each with about 1 ion and about a 150 water molecules. You can now understand why these ions are close enough to interact a little, but not too much. The interactions between the ions change the osmotic force by about 10% from that which would be generated if the ions did not interact with each other.

Thus, from our third number we have learned that both within and outside the cell, there are about 150 molecules of water for each ion of sodium, potassium, and chloride.

Fluid Transport

How do the cells in the ciliary body produce the aqueous humor? Proteins in the cell membranes of these cells could clutch water molecules and push them across the cell membrane. But these cells do something more clever, more subtle, and more efficient. If one ion is transported across the cell membrane it will change the concentration on the other side. This change in concentration will osmotically induce the flow of water. How much water? In these solutions 1 ion is balanced by 150 molecules of water. Therefore, the movement of 1 ion will induce the movement of 150 molecules of water.

So, why pump 150 molecules of water, if you can induce the same fluid flow by pumping 1 ion? That is exactly how these cells generate the flow of aqueous humor. They transport ions across the cell membrane. The fluid that forms the aqueous humor is then osmotically driven by the changes in concentration caused by these ions.

For this elegant scheme to work, the water permeability of the cell membrane must be much larger than its ion permeability. This is needed so that the water easily flows across to join the ion that has been transported to the other side of the membrane and so that the ion does not freely cross back across the membrane. In order to move 150 water molecules for each ion, the permeability of the cell membrane to water needs to be about 150 times that of its permeability to ions, which is indeed the case.

The location of the small spaces whose concentrations have been altered by the transport of ions is not known. They could be up against the front surfaces of the cells or in between them.

The flow of aqueous humor through the cells in the ciliary body is prodigious. In the usual units, the flow is about 1 μliter/min/cm^2. A more meaningful question is to ask how long it takes for each cell to transport a volume of aqueous equal to its own cellular volume. Each cell transports its own volume in 2 minutes. The fluid floods through these cells.

Ion Transport

The transport of ions is complex. Outside cells, the movement of ions is driven by differences in electrical voltage and concentration. Across the cell membranes, ions are moved by proteins. Some of these proteins use energy from ATP to move the ions uphill against their electrical and concentration gradients. Some of these proteins bind a few different ions at a time, and then move them into and out of the cell. Some of these proteins are like big holes that allow many ions through at any one time.

As mentioned previously, cells use energy to pump ions out, and then let them leak back in again. This is not futile. By controlling the pump and leak, cells control the movement of ions and the voltage across the cell membrane.

A typical epithelial cell, like those in the ciliary body, has about 1,000,000 sodium potassium ATPase protein molecules in its cell membrane. There are so many of these molecules that they are quite close together on the cell surface, about 10 nm apart. About 30 times a second, each of these molecules uses the energy from ATP to move a few sodium ions out of the cell and a few potassium ions into the cell.

However, the ions leak back across the cell membrane in a very different way. Each cell has about 100 ion channel protein molecules in the cell membrane. There are so few of these molecules that they are quite far apart on the cell surface, about 1,000 nm apart. About 10 times a second, for about 1/200 of a second, each of these channels opens and 30,000 ions leak through.

Thus, the pump is very different from the leak of ions across the cell membrane. The pump works by using energy to move a few ions at a time, at many places, on the cell surface. The leak works passively to move many ions at a time, across a few places, on the cell surface.

The leak of ions through the ion channels is well separated in space and time on the cell surface. This makes it possible to measure the flow of ions through an individual channel. A piece of cell membrane, small enough to contain only one ion channel, is sealed in a micropipette called a patch clamp. The electronics are sensitive enough to resolve the picoampere current through an individual ion channel in such a patch when it opens for a brief time. The much smaller currents through the proteins that pump ions are too small to measure this way.

The proteins for the pump and leak are on different sides of the cells in the ciliary body. The ions pumped across one side of the cell leak across the other side of the cell. Thus, there is a net transport of ions. The pigmented and unpigmented layers of cells in the ciliary body transport ions in opposite directions. This is a complex machine, and how it works to produce the aqueous humor is not clear.

Active or Passive

The ciliary body of an animal can be removed and mounted in a chamber. The current measured due to the flow of the ions transported is about 8 μAmps/cm^2. Since each ion will drag about 150 water molecules with it, we can use that current measurement to compute the rate of aqueous production. The result is that the ion transport accounts for only 2% of the aqueous production! It has been suggested that the failure of ciliary body to pump fluid in these experiments is due to the fact that the tissue has been damaged in the dissection or that the capillaries are collapsed in the mounting so that fluid does not reach the cells for them to transport. Perhaps the ion flows are recirculated so that the net ionic current is not a complete measure of the amount of fluid transport.

However, the fact remains, that in most of the experiments of isolated ciliary tissue or isolated animal eyes, the ciliary body does not secrete aqueous humor. This has led some scientists to argue that the aqueous humor is produced by the filtration of fluid under pressure from the plasma across the ciliary body rather than by fluid transport driven by active ion transport.

It is hard to believe that the aqueous humor is generated by passive filtration from the plasma. Aqueous humor has different concentrations of ions and other substances than the plasma. This suggests that those ions and substances were actively pumped into the aqueous humor. The ciliary epithelium has features that are present in other epithelia that are known to move fluid by the active transport of ions. These features include ruffled edges to enlarge the area of the cell membrane and a large number of mitochondria to provide energy in the form of ATP for ion transport. It would be hard to understand why such specializations for ion transport would not be present in a tissue that was not transporting ions and fluid.

It's puzzling that the production of the aqueous humor by the ciliary body has been so difficult to demonstrate in these experiments.

LARGE SCALE AQUEOUS MOTIONS

The aqueous humor emerges from the posterior chamber, through the pupil, into the anterior chamber. The fluid in the anterior chamber can be stained with fluorescein dye. At this larger scale, the Peclet number is small, so the dye does not diffuse rapidly enough to stain the new, emerging aqueous. Thus the flow of the new, clear aqueous can be followed from the posterior into the anterior chamber. Even at this scale, the Reynolds number is still low. Thus, the "jet" of aqueous emerging through the pupil has the form of an expanding ball. This is very different from the thin cone of water in the high Reynolds number jet that emerges from your kitchen faucet.

The interior of the eye is warmer than the air outside. Warm aqueous rises and cool aqueous falls. Thus, there is also a vertical convective circulation of aqueous humor. This circulation can sometimes be seen in the motion of small particles in the eye.

CONTROL OF INTRAOCULAR PRESSURE

Intraocular pressure is determined by the balance of the aqueous inflow and outflow. How is that balance set and maintained? Many variables can act to alter that balance.

Like other somatic phenomena, there is a circadian rhythm in the pressure: it is low at 7 AM and high at 7 PM.

Diseases alter the pressure. In glaucoma the increased resistance to the outflow of aqueous humor increases the pressure within the eye.

Osmotic agents, such as alcohol, suck additional fluid from the eye. Increased outflow of fluid lowers the pressure.

Pharmacological agents that mimic or inhibit neurotransmitters can also change the pressure. The physiological implications of the effects of these agents are rarely discussed in the literature. Does it mean that synapses are involved in either the sensing of intraocular pressure or control of aqueous production or aqueous outflow? If there is a neural circuit, is it local, through the spinal cord, or all the way upstairs to the brain?

SUMMARY

Eyes are round. We don't really understand why eyes are round. The roundness might involve their optical properties or their ability to move rapidly and accurately. However, the evidence in support of these reasons seems weak. Still less evidence suggests that roundness arises from the need to maintain a clear interior space or is a result of the evolution of eyes in vertebrate species or their individual developmental history.

If we don't know *why* eyes are round, we know *how* they are round. They are round because they are inflated from within by pressure of the aqueous humor, the fluid in the eye.

The balance of the inflow and outflow of the aqueous humor determines the pressure within the eye. We're not sure how the aqueous is produced. We're not sure which structures determine the resistance to the outflow of the aqueous from the eye. We don't understand the factors that control the intraocular pressure during the day, or how they are altered in the course of certain diseases.

It's sobering to realize how little we know about the most salient features of the eye.

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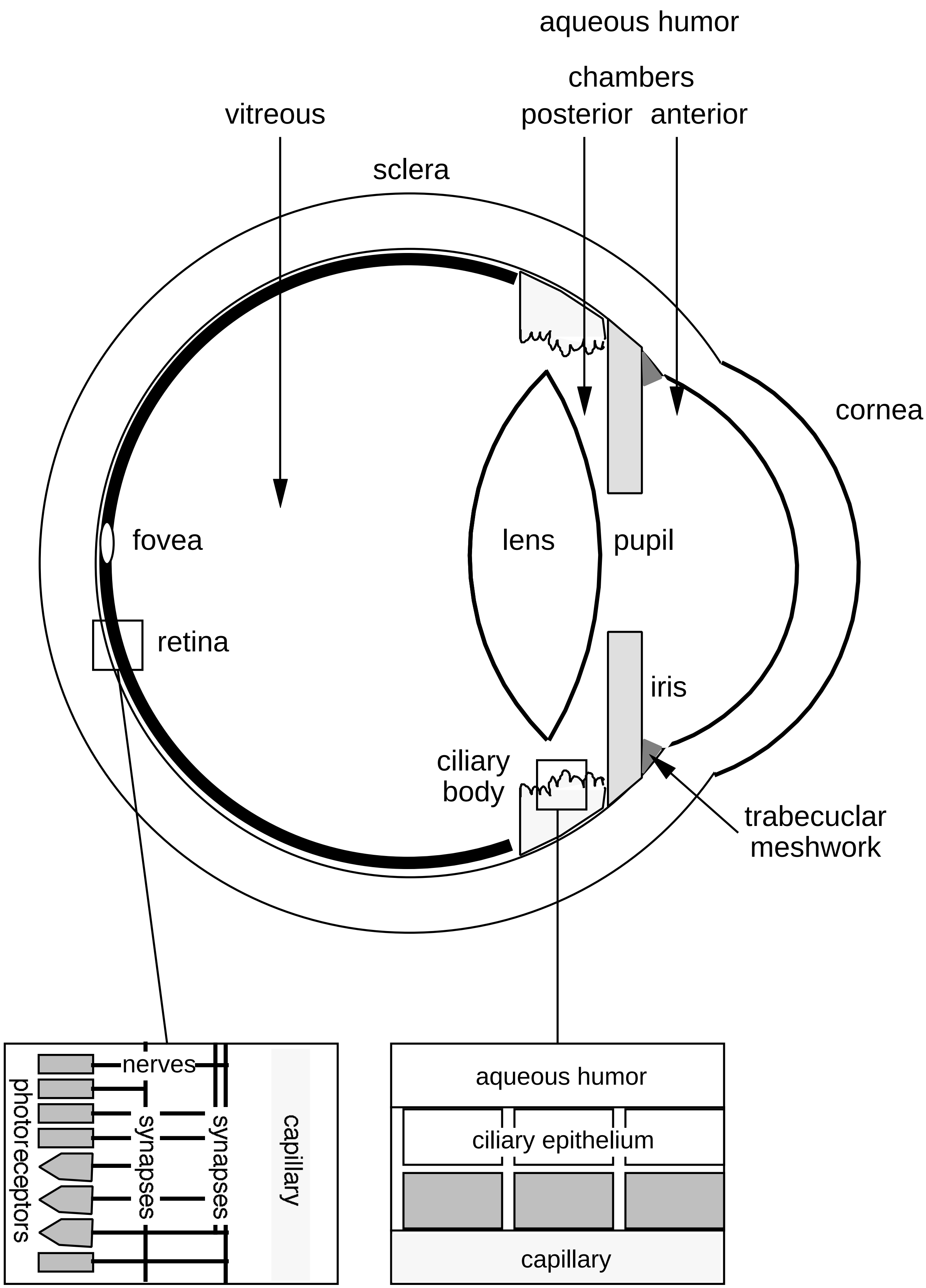
FIGURE LEGENDS

Figure 1. The eye.


aqueous humor
chambers
posterior
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vitreous
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fovea
lens
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retina
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nerves
photoreceptors
synapses
synapses
capillary
aqueous humor
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capillary