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A Novel 3D Animation about Human Visual System: From Retina to Perception

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From Retina to Perception

by

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Acknowledgments

Thanks to Professor James Perkins, my inspiration for this thesis project is from his scientific visualization class. Thanks to Professor Craig Foster for answering tons of questions I had about Autodesk Maya. Thanks to my classmate Janette and her husband who helped me with narrating the animation. Also, thanks to Professor Michael Peres for letting me take the microscopy class with his photo science students, which inspired me a lot about vision and perception. I would also like to thank all my friends and family; I cannot complete the project study without you guys. It has been a great experience learning from everyone at RIT.

Abstract

Introduction to vision and perception has been a fundamental topic for students from varied majors in college. Students who study Biology, Cognitive Science, Neuroscience, and Visual Design, need to learn about the visual pathway before they dive into more specific research topics. This thesis intends to create a 3D animation to assist professors in explaining the complex process of the visual pathway. The target audience for this project is undergraduate students majoring in color science. My goal of this animation is to introduce students to the complicated anatomy of the retinal structure and the molecular pathway of the photoreceptors to demonstrate visual perception. Different functions and structures of rods and cone cells are highlighted, followed by a zoomed-in view of the rod membrane proteins to show the activation of the photoreceptor reaction cascade in the dark environment. This animation would enable the students to visualize different cell types and protein structures; thus, enhancing students' learning of the visual pathway.

Introduction

The most crucial part of my job as a medical illustrator is to solve communication challenges by translating complicated biomedical information into clear, accurate, and appealing visuals. To do that, I have to identify who my target audience is and then utilize different verbal or visual contents to effectively communicate with different audience groups. Since the target audience for my animation is undergraduate students who study color science or vision science, they need a more specific understanding of the visual system and how it functions. To achieve that goal, this thesis project focuses on a detailed presentation of the signaling pathway, which is the basis for all vision science research.

Various visual and neural media are involved in the signal transduction process through visual pathways. Rods and cones are two types of receptor cells that sit in the retina. Cones are centralized in the fovea of the retina. Rods play a crucial role in vision at a low-light level. Conversely, cones are in charge of color perception at high light levels. In 1942, researchers revealed that a rod cell can be activated by a single photon (Selig, et al., 1942) due to the photoreceptor protein named Rhodopsin. The Rhodopsin protein is a transmembrane protein that is found in rod cells. When light hits the retinal, it initiates a G-protein coupled cascade that closes cation-specific channels and finally leads to hyperpolarization of the rod cells (Wald, 1968). Hyperpolarized rods lower the release of glutamate which can excite the on-Bipolar cells (Dowling and Boycott, 1966). The signal will finally be received by the visual cortex of the brain. To clarify the relationship of each medium that participates in the story, I decided to create 5 different 3D scenes that can represent 5 biological structures which are the eyeball, retina, disc membrane, synapse, and brain. Structures at different scales are animated to clarify the relationship between them.

Background

During the scientific visualization class taught by Professor Perkins, I learned about the history of scientific visualization. Scientists from the biological field have been trying to visualize tiny structures that are not visible to naked eyes for a long time. Different techniques are developed to make small things visible. Taking blood cells as an example, both red blood cells (RBCs) and white blood cells (WBCs) are not visible to the human eye. To visualize RBCs and WBCs, a light microscope can be used. The human eye can resolve things with a diameter down to 10^{-4} meters, which is about the thickness of a human hair. Under a light microscope, structures like cells with diameters as low as approximately 10^{-7} meters to 10^{-6} meters can be seen. The protein structures were still impossible to be seen until the discovery of X-ray crystallography technology which pushed the limits of atomic resolution. However, there are many other biochemical components like adenovirus that cannot be seen with either a light microscope or X-ray crystallography. To visualize structures with a size falling in between the resolution gap of X-ray crystallography and light microscope, emerging technologies like Cryo-EM are developed (Stewart, et al., 1993). Cryo-EM also allows people to access the 3D structure of a protein.

An interesting point about the size of proteins is that molecules like proteins are smaller than the wavelength of visible light; thus, they cannot reflect light rays. In other words, not only the color of proteins but also the highlight and shadow of them are imaginary. Although the presentation of proteins in my thesis project is rendered with color and shadow, which aims to create a more appealing and aesthetic visual, realistically proteins do not have aspects like shadow or color due to the size when compared to the wavelength of light. “Invisible” structures like proteins also intrigued me to explore more about the boundary of visible forms and invisible forms within the scientific visualization field. Most of the time, only people who are doing research could have access to advanced technology like Cryo-EM and electron microscopes. It’s hard for the lay audience to picture what small biological molecules look like such that small molecules seem more “invisible” to them. Some of them might have a generic picture in mind about what a DNA molecule looks like, but the generic picture was too “loose” compared to the information that students have to absorb from classes. Along with my study about scientific visualization, I figured a more detailed description was needed for what things actually look like.

There is an increase in demand for scientific visualization products showing a more realistic and sophisticated rendering of proteins, cells, and organs for students to understand the science behind them. In this animation, I used 3D model data from the Protein Data Bank (www.rcsb.org) that was collected with the Cryo-EM technique. After downloading the PDB file from Protein Data Bank, I used UCSF Chimera (www.cgl.ucsf.edu/chimera) to visualize the protein structure and export it as an .obj file which is a common 3D format that most popular 3D software can recognize. There are also many great toolkits designed by scientists for molecular visualization such as Pymol (https://pymol.org/2/) and VMD (https://www.ks.uiuc.edu/Research/vmd/). Some plugins are also designed for Autodesk Maya, Cinema 4D, and Blender to make 3D visualization such as the embedded Python Molecular Viewer (ePMV - http://epmv.scripps.edu/). I didn't use ePMV at this time because I was switching computers from different labs at school and not all of them have the plugin installed such that it might be easier for me to keep all the files exported as .obj format and import them into 3D software manually.

Along with the development of imaging technology, scientists have made fundamental progress in the research of the visual pathway. Scientists have found that Rhodopsin is a transmembrane protein with 7 alpha-helices (Edward, et al., 1983). It consists of a protein called opsin that is attached to the light-absorbing component retinal. The photoexcited Rhodopsin then excites the transducin and phosphodiesterase protein (Kwok-Keung Fung and Stryer, 1980). This causes a reduction in Cyclic GMP level and the closure of the Calcium channel (Zimmerman, et al., 1985). After the closure of the Calcium channel, cations can no longer enter the rod cell through ligand-gated ion channels. The inner pore region of the rod cell becomes more negative due to the reduced influx of positive sodium ions. This causes the hyperpolarization of the Rod cell.

In a dark environment, photoreceptors can release glutamate that inhibits on-BC and excites off-BC via a chemical synapse. On the other hand, in a light environment, hyperpolarized rods would release less glutamate, thus no longer inhibiting on-BC. The on-BC would then transmit visual signals to the ganglion cell (Wald, 1968). The signal will finally be received by the visual cortex of the brain. In addition to the cell types mentioned above, horizontal cells can also participate in the visual transmitting pathway (Ramon-y-Cajal, 1933). Many other internal

circuits within the retina are in charge of visual perception, such as the cone circuit during different light levels, and the convergence circuit of rods and cones upon ganglion cells. I decided not to cover all of them in this animation. Students who want to learn more specific details can explore more about the information by themselves after class.

Working Process

For my thesis project, I worked closely with Mark Fairchild, PhD and Susan Farnand, PhD. Professor Fairchild and Professor Farnand work for the Munsell Color Science Laboratory at Rochester Institute of Technology. Professor Fairchild and Professor Farnand helped me by reviewing and finalizing my script as well as supporting me with more background knowledge of color perception which allows me to better understand what I would like to discuss in my animation. The script and storyboard were also reviewed by Professor Foster during his 3D animation class.

Initially, the script was written to allow me to create scenes for the animation. I decided to talk about the human eyes at the beginning to grasp the audience with something that everyone is familiar with. After the eyes, the next part of the script is about cells in the retina with a focus on the rods and cones. The third part of the script is about how the switching between light and dark environments affect rods and cones. After giving enough background, I mentioned the Rhodopsin protein in the rod cell and its activation cascade. After that, the neural pathway and activation of the brain cortex was briefly illustrated. Final full script can be found in the appendix.

The storyboard illustrations are created using Procreate software on an iPad. These illustrations are created by the size of 16” x 9” to fit into PowerPoint slides. The first two illustrations of the storyboard are designated to show an eyeball and its inner anatomical structure. The third and fourth illustrations of the storyboard are to demonstrate the structure of layered retina cells. Different colors were used to highlight rod and cone cells. The next two illustrations are zoomed in images showing only one rod cell and one cone cell with some small circles around them representing the neurotransmitters. After that is a sequence of illustrations designed to show the simplified steps that lead to rod cell hyperpolarization. These illustrations were all started with a lipid bilayer and protein structures referencing from the Protein Data Bank.

The last two illustrations were to represent chemical synapse and the brain cortex. The full storyboard can be read in the appendix.

According to my storyboard, the initial scene of my animation should be an eyeball and its inner structure. To give the eyeball a realistic look, I used a UV color map and a UV alpha map. The UV color map is to add an image of the iris to the surface of the eyeball and the alpha map is to create a visible vessel bump on the surface of the eyeball. To achieve that, I had to unwrap the UV in Maya UV tool kit and save the UV map as an image with a transparent background. After saving the UV map, I then imported the UV map image into Adobe Photoshop and drew the color map and alpha map on top of it. The color map and alpha map were then imported into Maya and linked with an Arnold material (Fig. 1). After applying the material to the eyeball model, both the blue-colored iris and the blood vessels are visible on the surface of the eyeball.

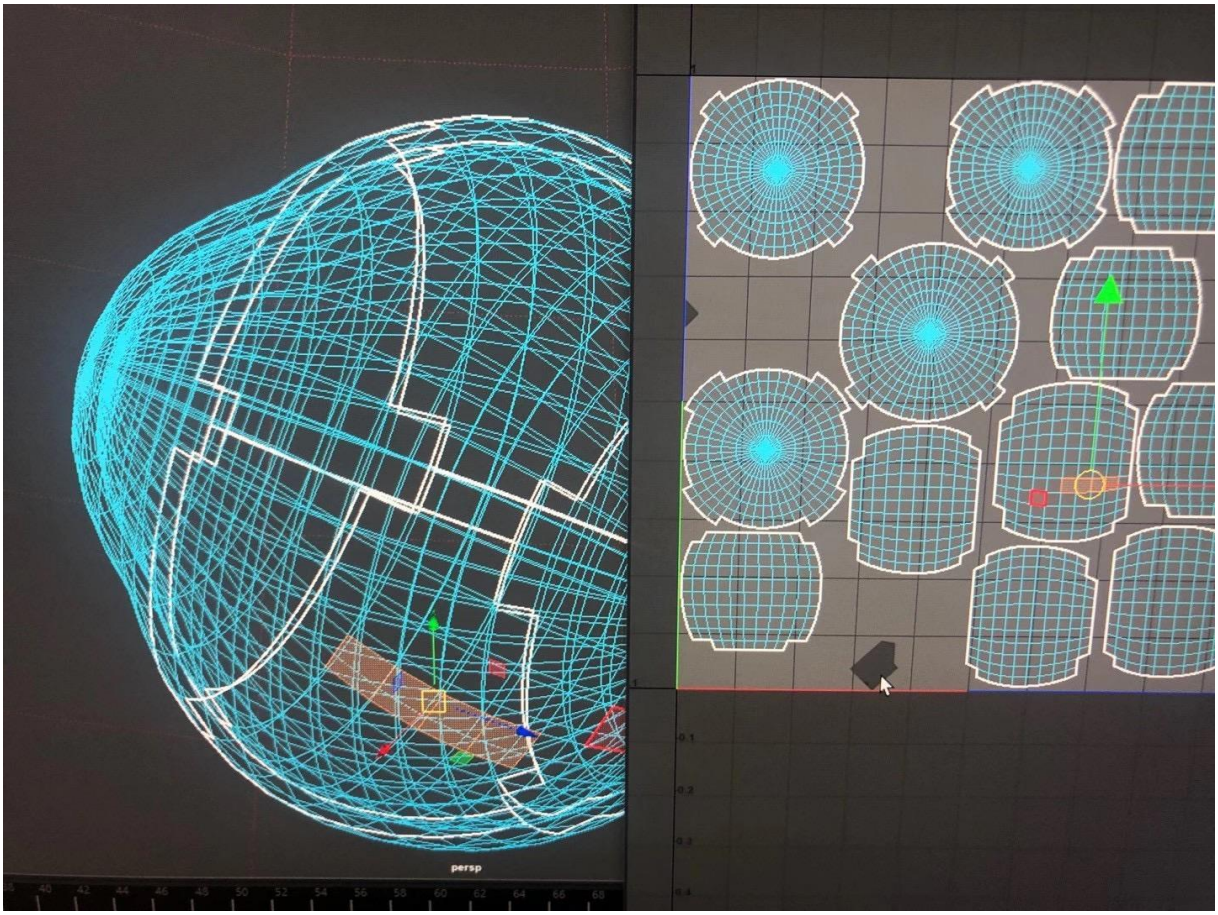


Figure 1. Screenshot of the cut UV map and 3D model of the eyeball

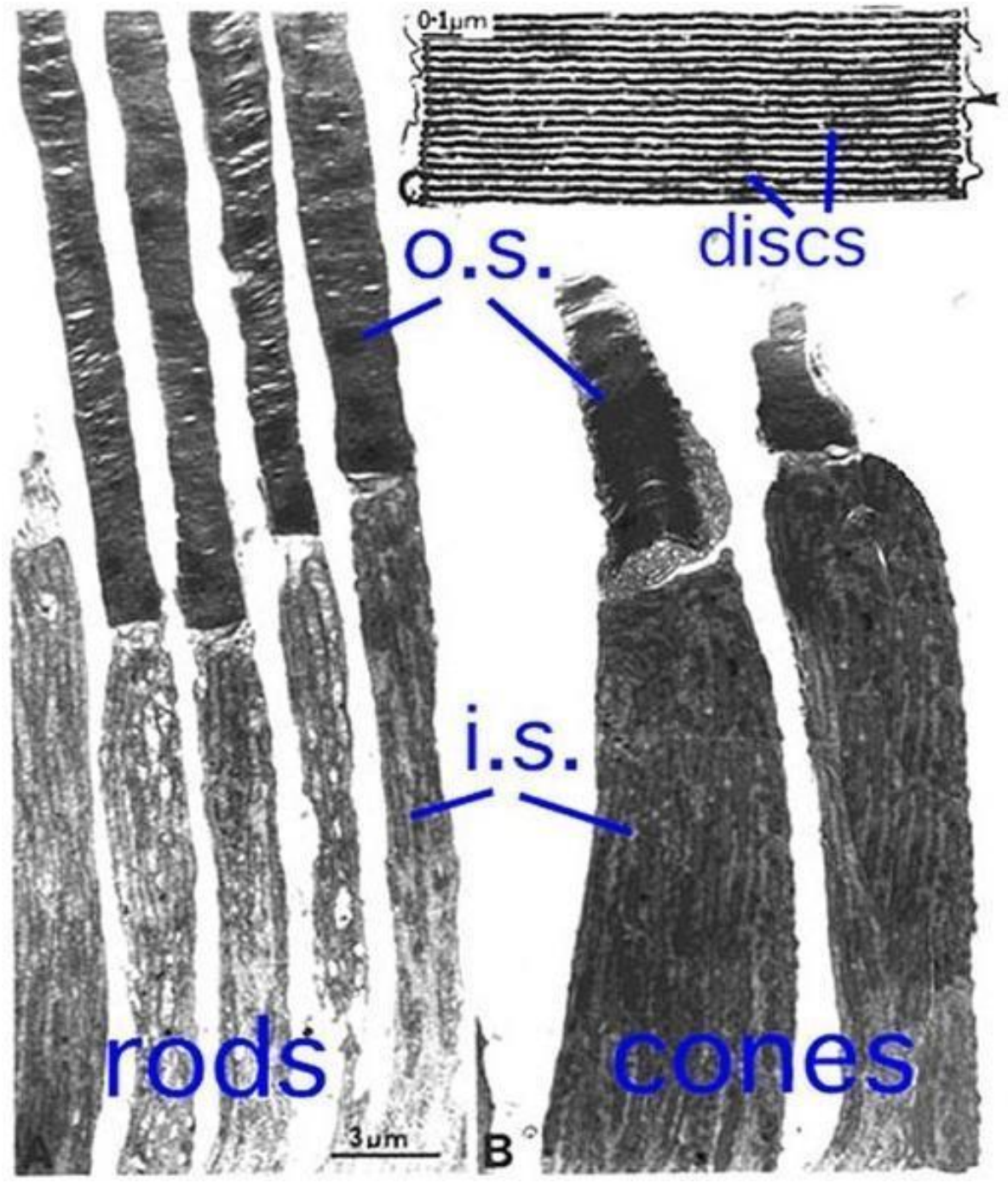


Figure 2. Low magnification electron micrograph of rods and cones (Kolb, et al., 2005)

The second scene of my animation shows the anatomy of the retina. To explain the organization of the retina cell types, I made a model of layered cells that represents a cut section of the retina under electron microscopy. I used a cloner tool in Maya to duplicate a single type of a cell into multiple layers of cells (Fig. 3).

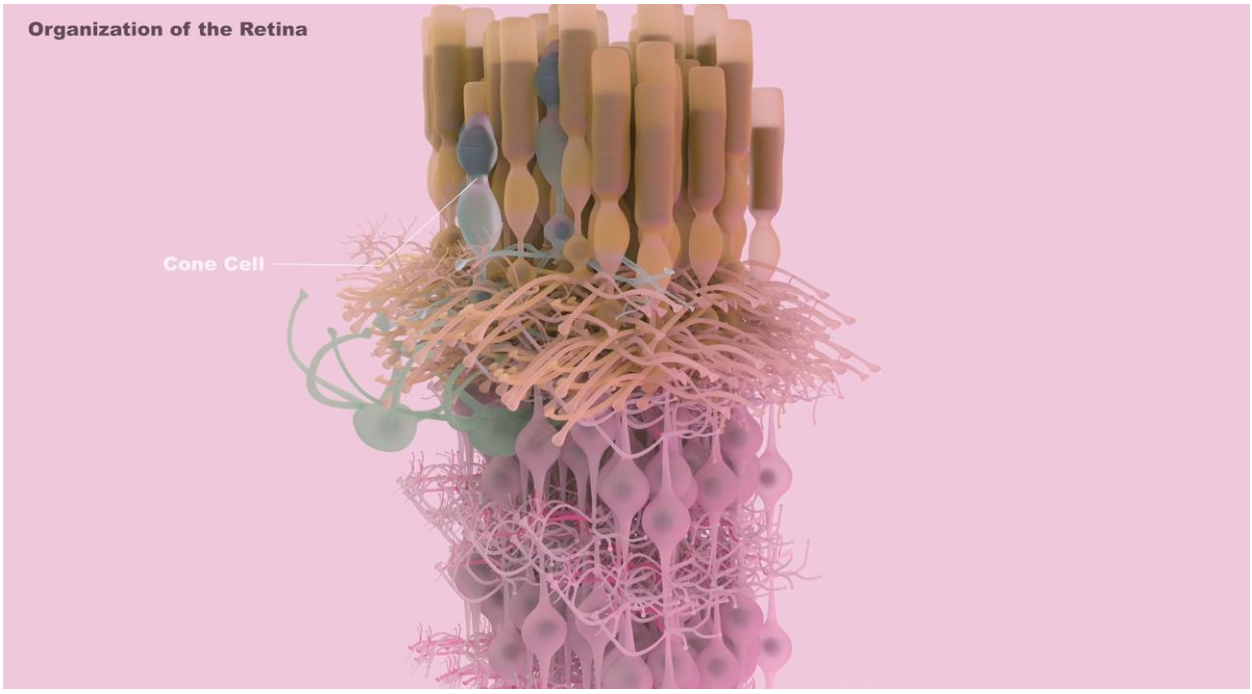


Figure 3. 3D model created in Maya showing different types of cells in the retina

The third scene is the rod cell membrane with different proteins embedded. I used UCSF Chimera as a scientific visualization tool. The molecule model can be saved as .obj format from UCSF Chimera. The 3D protein molecules were then imported into software AutoDesk Maya. The original protein model generated by UCSF chimera had too many vertices which would take too long for the 3D software to render. This would result in potential pressure in the creation process. I then used Blender to reduce the vertices by using the Merge Vertices by Distance tool to combine nearby vertices while maintaining the overall structure of the protein (Figs. 4 and 5).

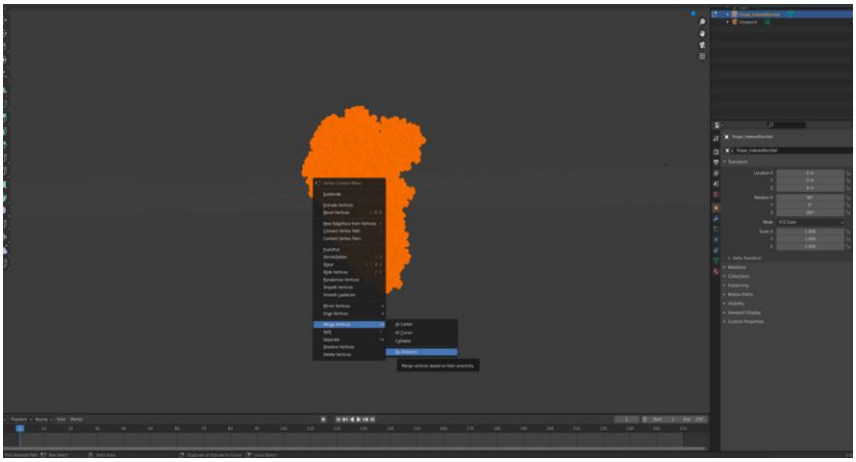


Figure 4. Screenshot of the Blender interface of how to decrease vertices of the original molecule model

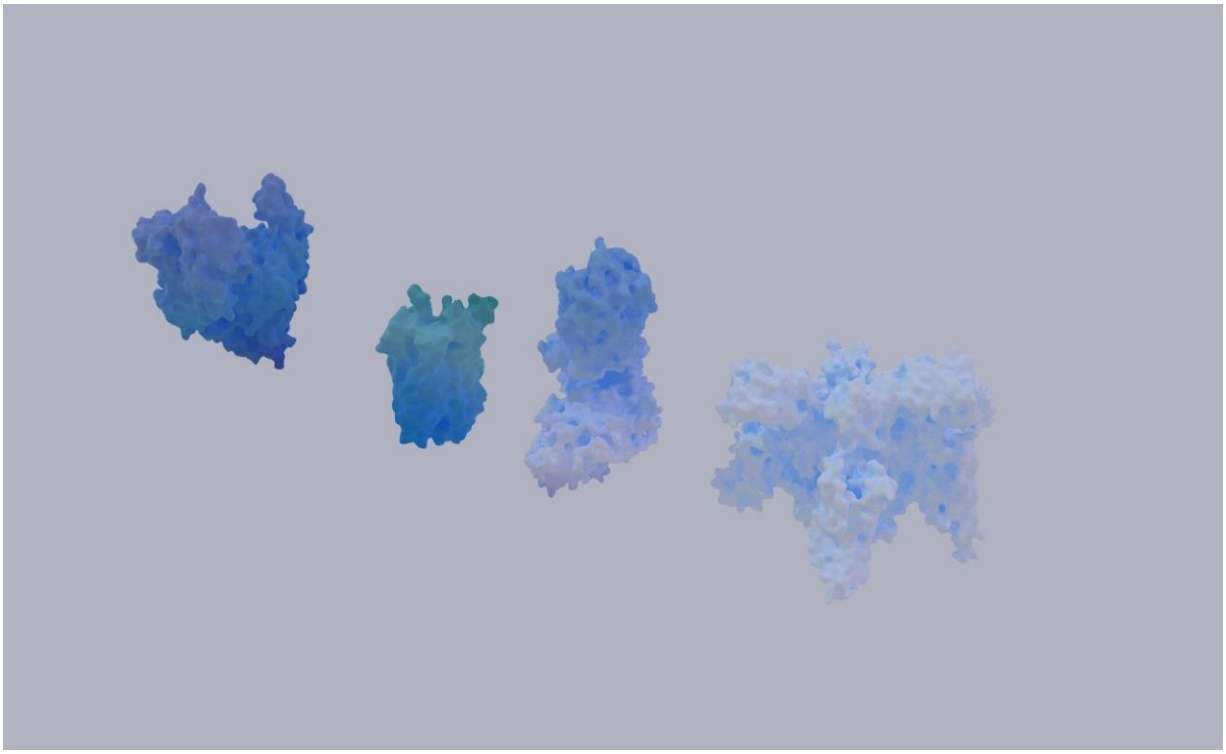


Figure 5. Low vertices 3D molecule models imported into Maya

After importing different proteins into Autodesk Maya, the next step was to create a schematic lipid bilayer with all the transmembrane proteins embedded. To determine the relative shape and size of the membrane to the protein structure and the relationship of the activation cascade, I did more research about the G protein-coupled receptors in the phototransduction pathway. Luckily, I found a research paper published by the Stanford medical school about the structure of the visual signaling complex between Transducin and Phosphodiesterase 6 (Fig. 6; Gao, et al., 2020). Thus, I could have a more accurate reference in creating the animation about the phototransduction pathway.

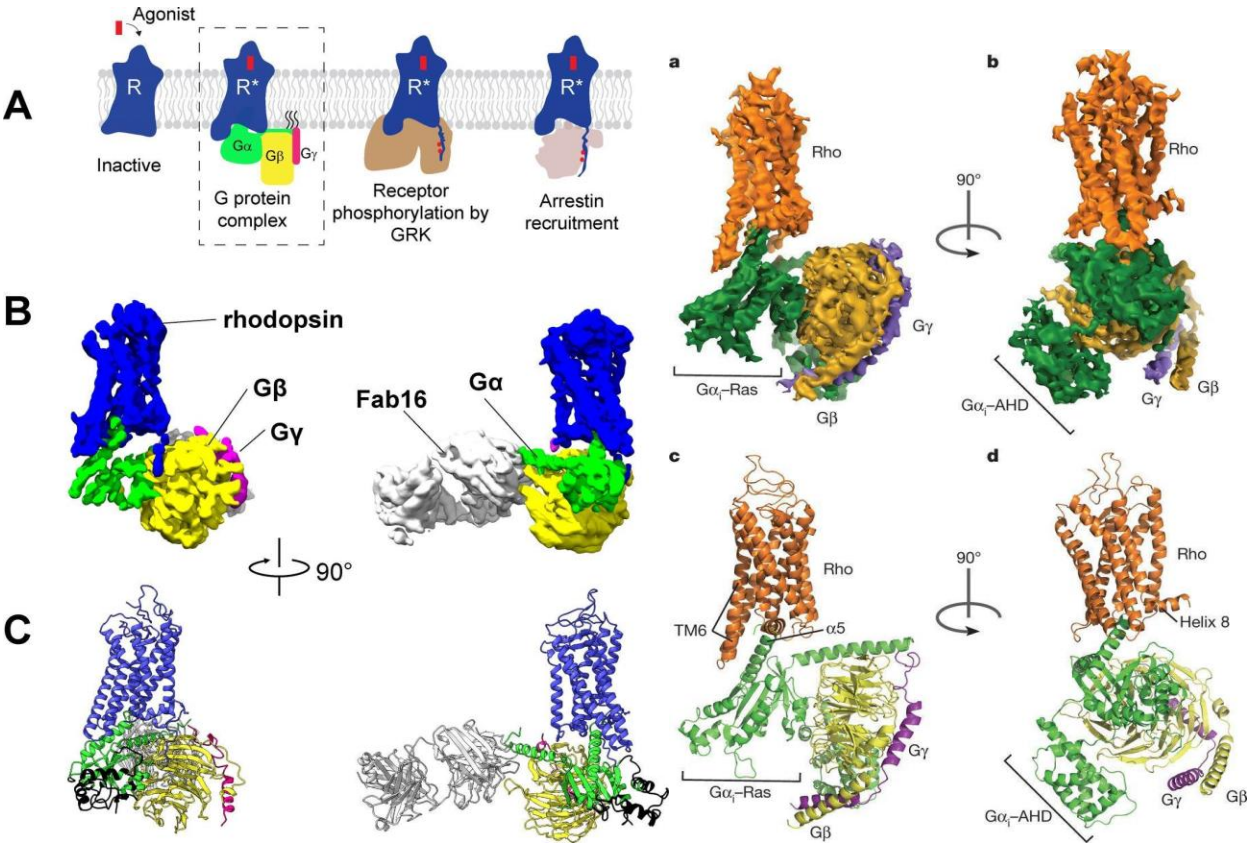
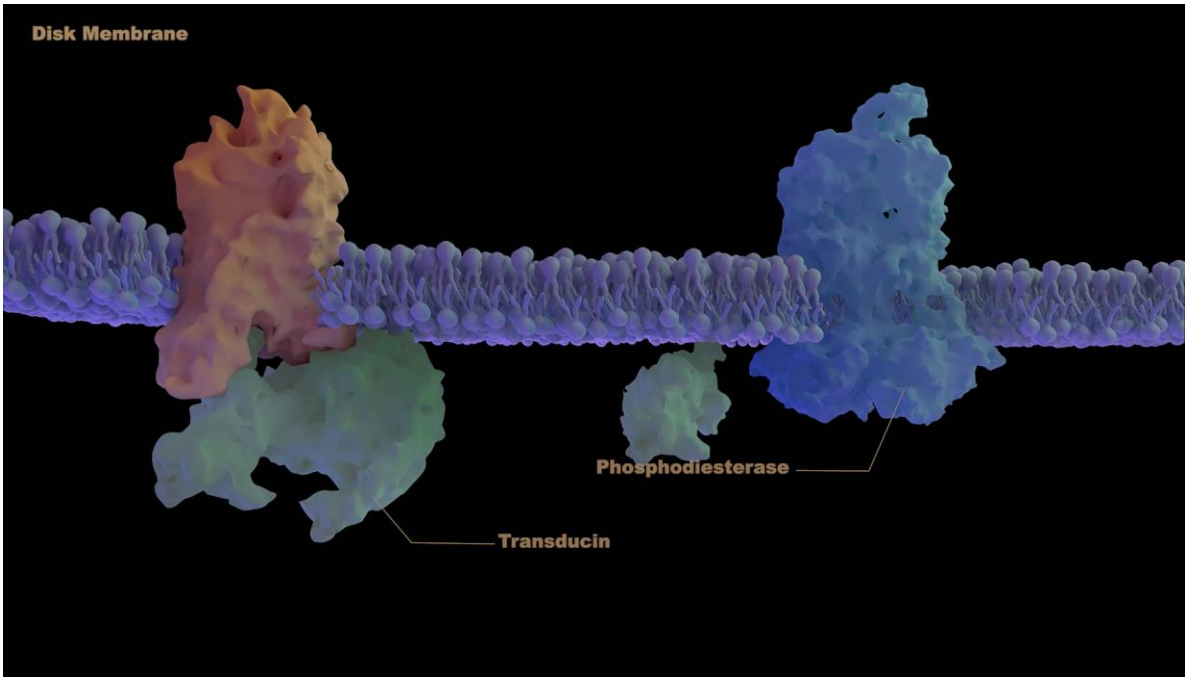


Figure 6. High resolution Rhodopsin, Transducin and PDE 6 molecules published by the Gao team in 2020 (Gao, et al., 2020)



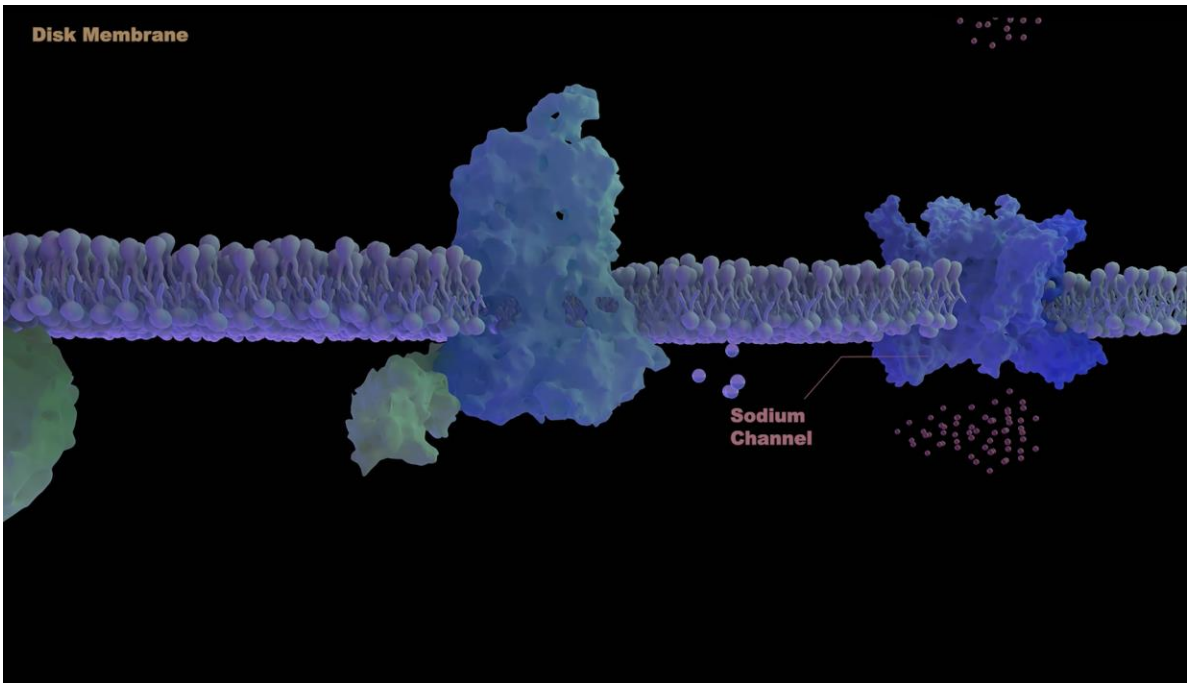


Figure 7. Protein models rendered in Maya with lipid bilayer

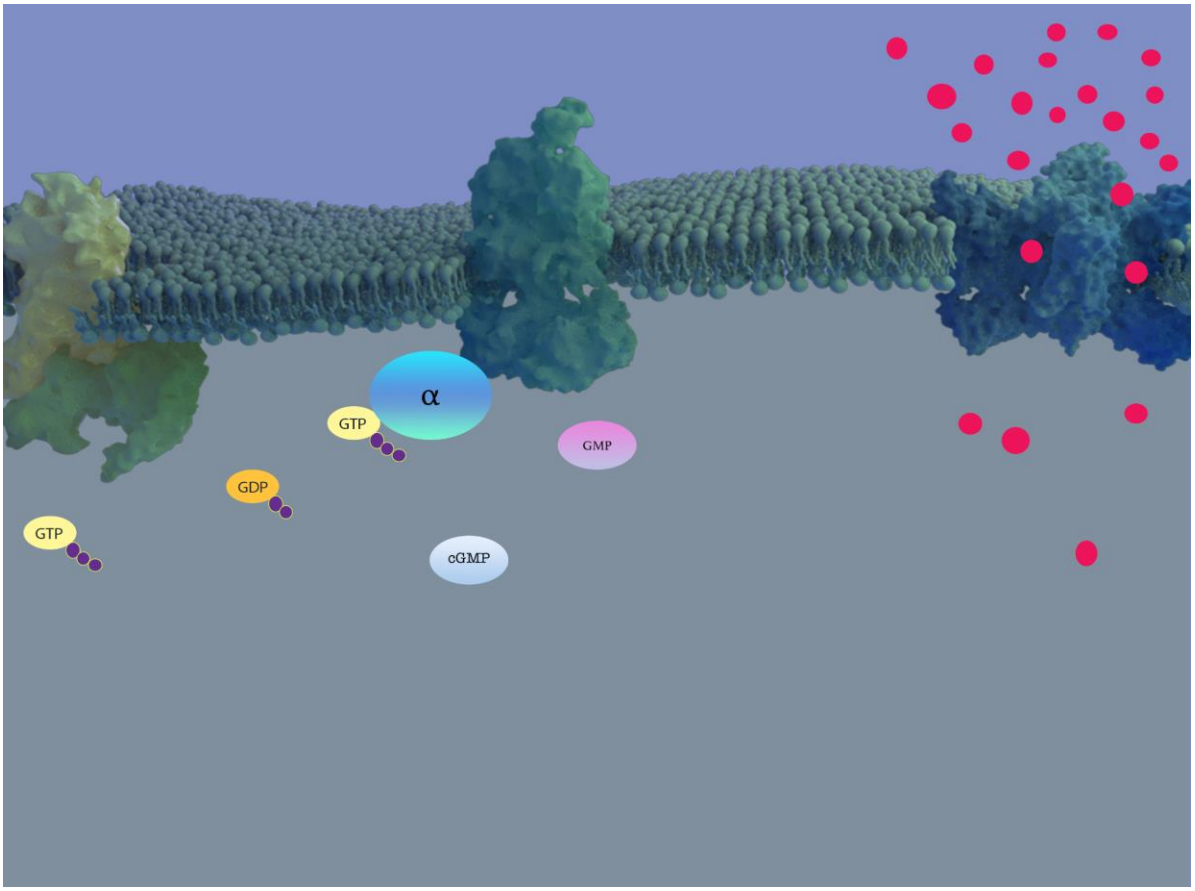


Figure 8. A diagram about how to animate small molecules in this animation

I also created a diagram (Fig. 8) showing a detailed story about how the G-protein coupled receptor was activated and how it would affect the sodium channel. However, it might be too complex to render all the small molecules in a realistic style. A simplified rendering of the small molecules might be sufficient for this purpose. I decided to use spheres with different colors to represent different small molecules in my animation. I choose to use a red sphere for sodium ion which is a commonly used color for sodium in scientific visualization. I also used a pink sphere to represent a small molecule cGMP and a blue sphere to represent hydrolyzed cGMP since blue would remind people of water which is related to the hydrolysis process.

For the last part of my animation, I choose to use a less realistic representation showing the 3D models of a chemical synapse, neuron firing, and the brain. Since this animation is more focused on the molecular pathway and retina cells, a simplified representation of these structures in the nervous system was chosen.

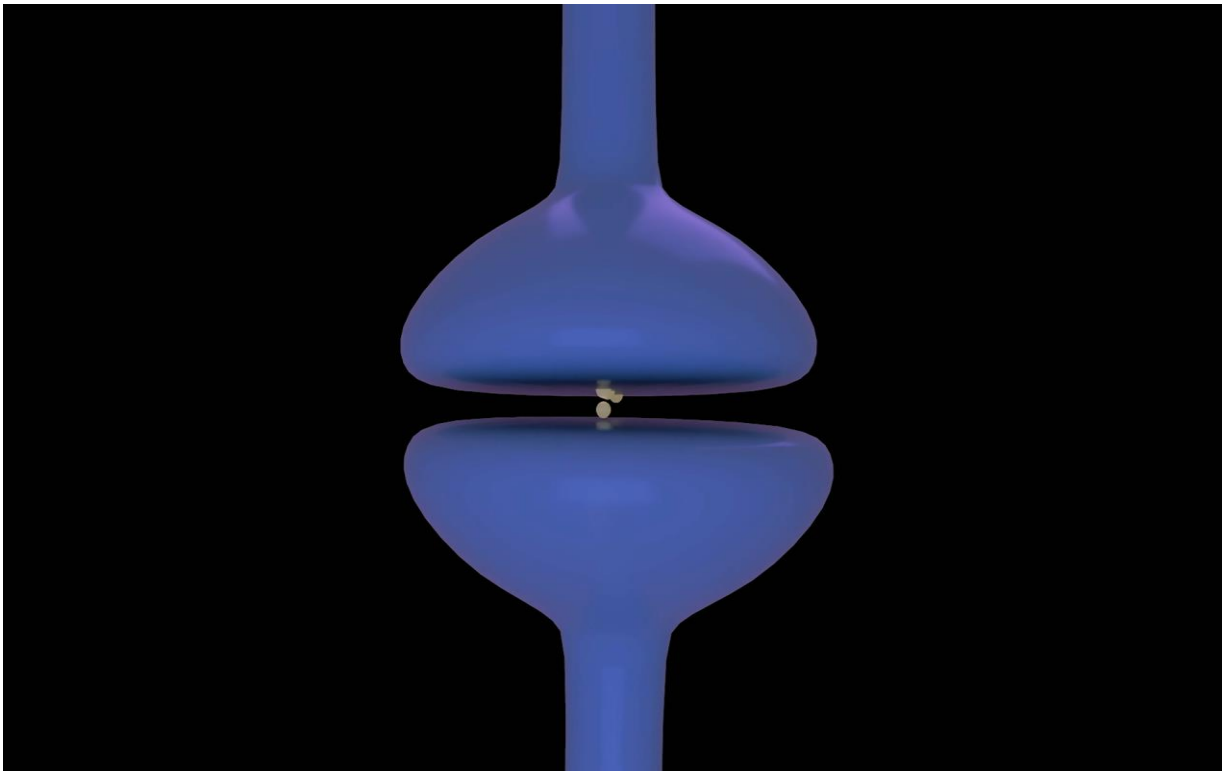


Figure 9. Model of chemical synapse showing the release of neurotransmitters

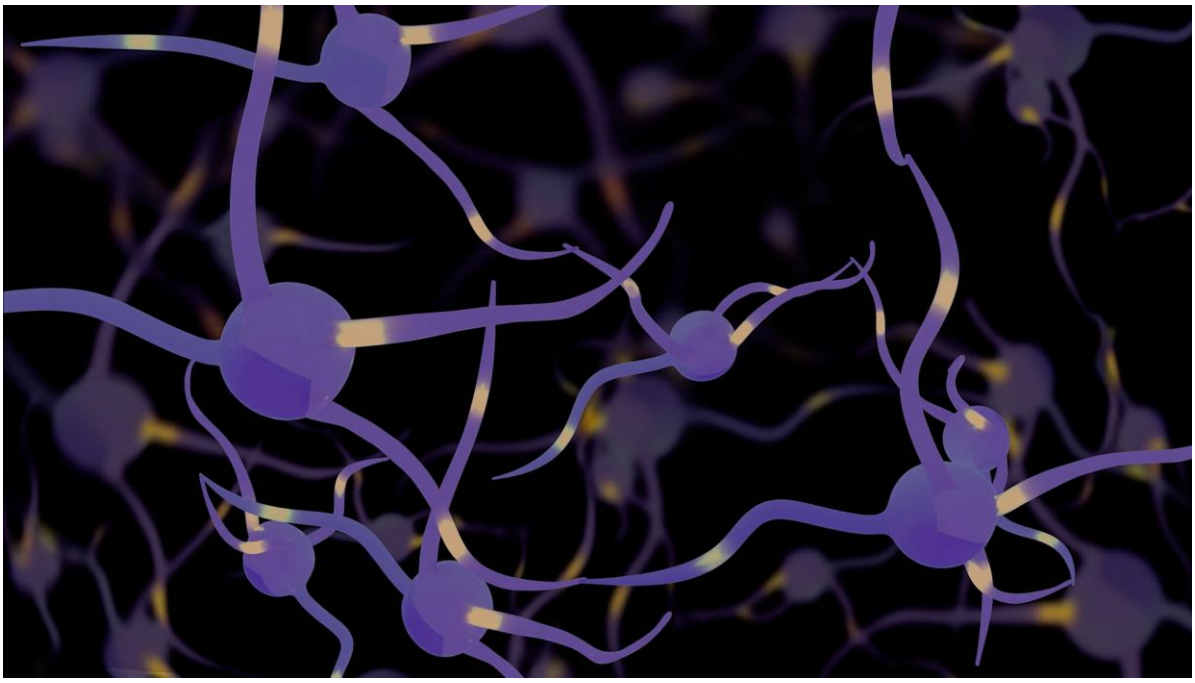


Figure 10. Screenshot of animation showing the process of neurons firing and transmitting

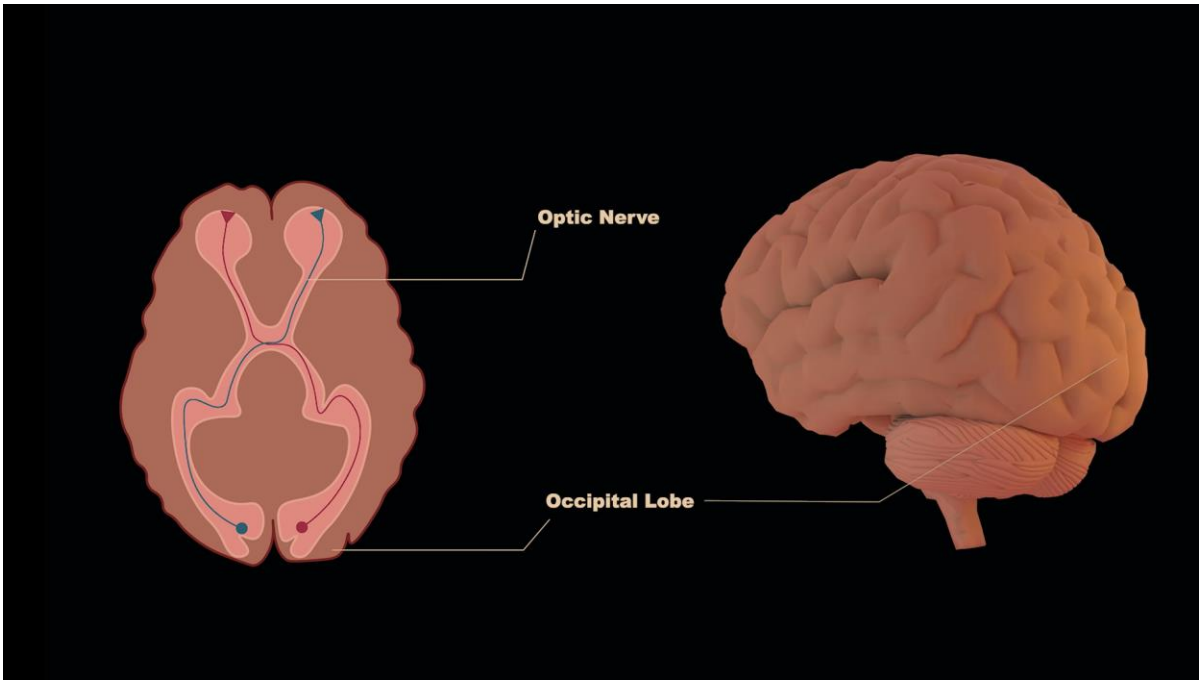
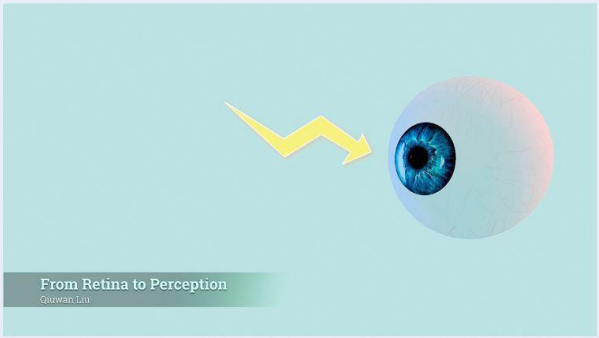
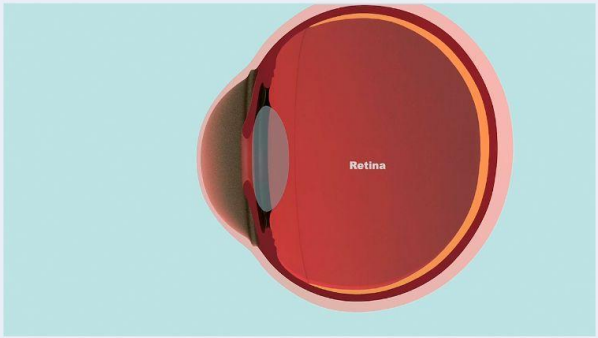


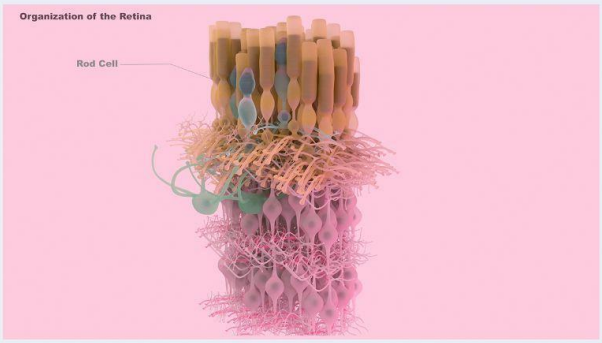
Figure 11. 2D diagram and 3D model showing the signal transduction to the visual cortex in the brain

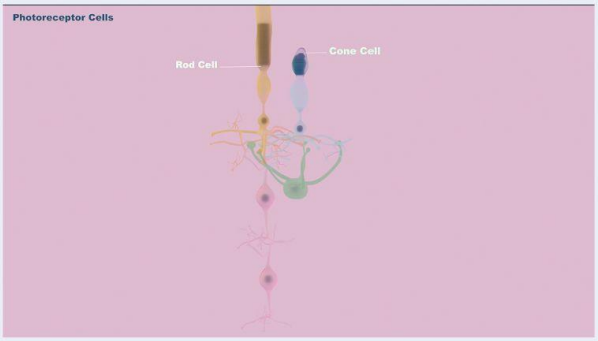
The final animation was rendered with 4K resolution. Since the target audience are college students, there might be a need for displacing the animation on larger screens or projectors at school. The animation is also uploaded to YouTube such that students can have access to it after class. A high-resolution animation can help students to see clear and sharp images on varied types of screens in class and help them to understand the class materials better.

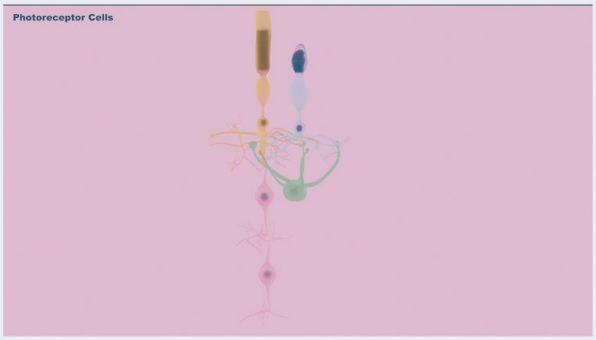
Final Animation

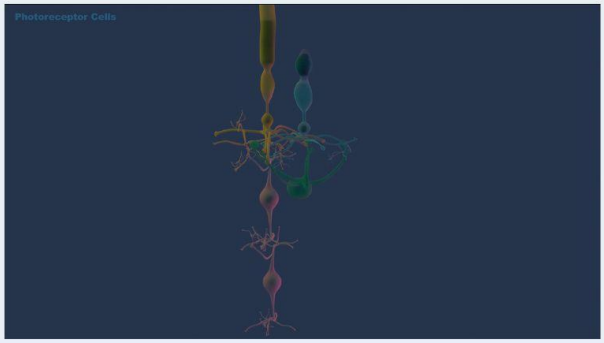


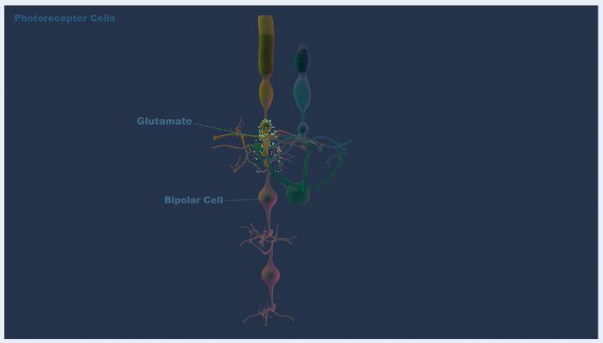




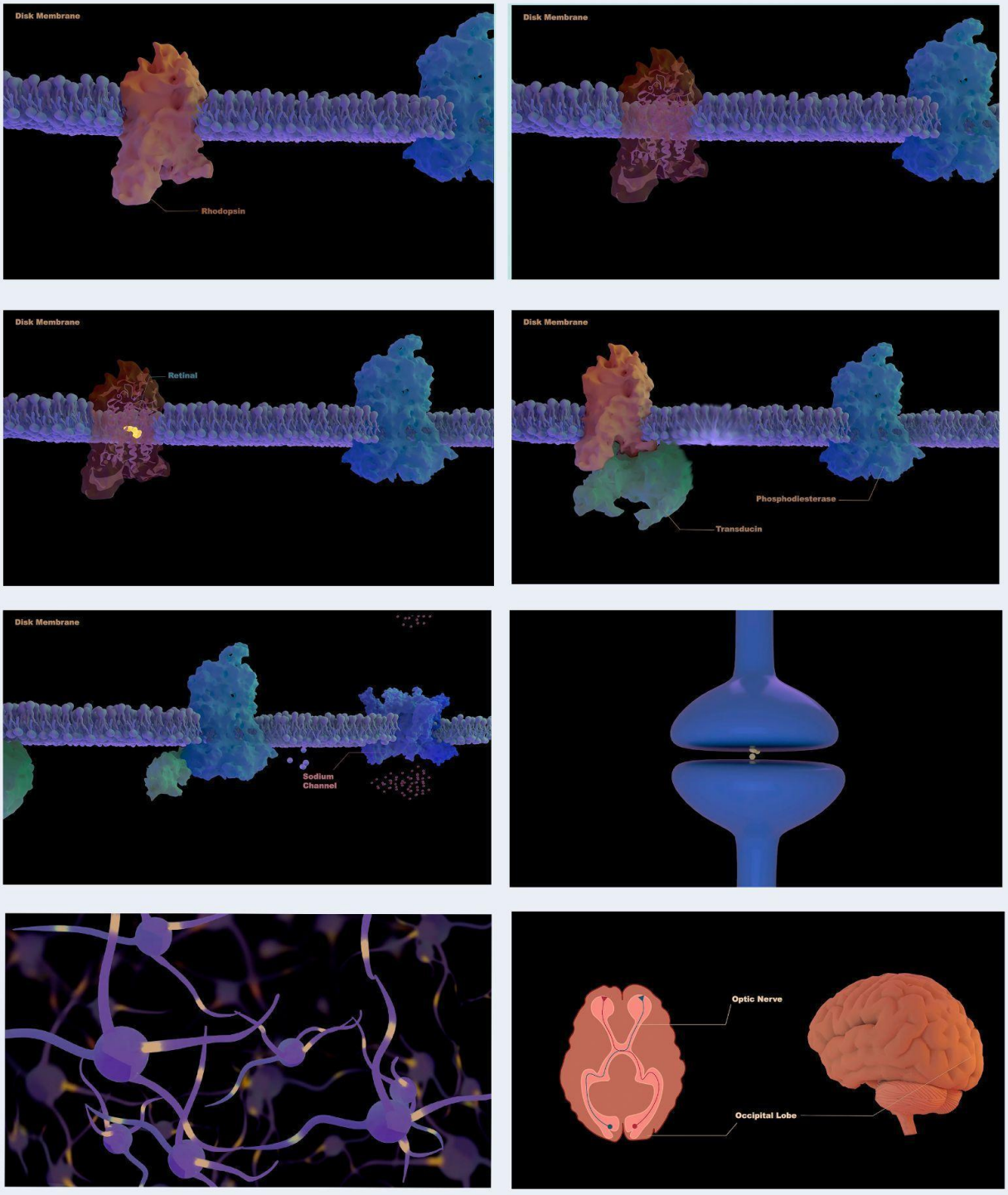








Final Animation



Conclusion

My goal was to create an animation for college students that tells the story of dynamic biomedical processes within the human eye and brain, such as cell interaction, ligand binding, and neuron transmission. It would be deemed successful if the animation can help students understand the relationship of each different biological structure in the visual system. In the future, I would like to continue creating a series of animations about the human visual system. The next 3D animation could tell the story of 3 different types of cone cells that allow humans to have color vision. I would like to further discuss mutations that lead to deficiencies in cone cell development, resulting in different forms of color blindness.

I would also like to explore more about realistic and real-time rendering that explains other dynamic biomedical processes within the human body such as tumor growth, blood flow, or angiogenesis. It has always been a challenge for medical illustrators to find accurate reference data for the actual structure of a tumor, blood vessels, and the actual time that takes them to grow and develop. Without first-hand research data, most medical illustrators would then choose to use a schematic model for a rough simulation. For instance, a 3D cylindrical shape can stand for the blood vessel and a sphere with a bubbly surface can stand for a tumor. The animations that are created using schematic models are considered “accurate” for the lay audience or undergraduate students. However, for audiences with profound medical knowledge such as surgeons or medical school students, this level of accuracy is considered insufficient.

To find accurate references to create animations and illustrations for professional audiences, as a medical illustrator; I have to dive into the field of biomedical imaging to do some background research for my projects. At RIT, Professor Perkins taught us to use 3D scientific visualization software such as OsiriX (http://homepage.mac.com/rossetantoine/osirix) and 3D Slicer (www.slicer.org) to find references for our illustrations and 3D modeling projects. After exploring this software with some DICOM files collected from MRI and CT scans, we learned how to create 3D models and illustrations based on the DICOM file to improve the accuracy of the information that we try to deliver. The question that still bothers me is that a lot of existing DICOM data available to us online is incomplete and none of the software we learned at school can refer to the dynamic nature of the human body. It’s still impossible to solve the problem of

how to simulate accurate tumor growth or angiogenesis to create accurate animations for more sophisticated audiences. To figure this out I need to do more research and collaborate with Biomedical imaging professionals who are researching real-time imaging techniques. Emerging technology like optical coherence tomography (OCT) for high-resolution imaging of soft tissue (Jeffrey, et al., 2017) and quantitative susceptibility mapping (QSM) (Cho, et al., 2020) at Cornell MRI research lab could offer new possible solutions to my questions. The QSM method enables a better understanding of disease progression including cancer, ischemic strokes, Parkinson's diseases, Multiple Sclerosis, liver malfunctions, by quantifying the endogenous contrast agents. Since the QSM method is voxel-based it allows me to see a huge potential in improving the data accuracy in 3D modeling of the biological forms.

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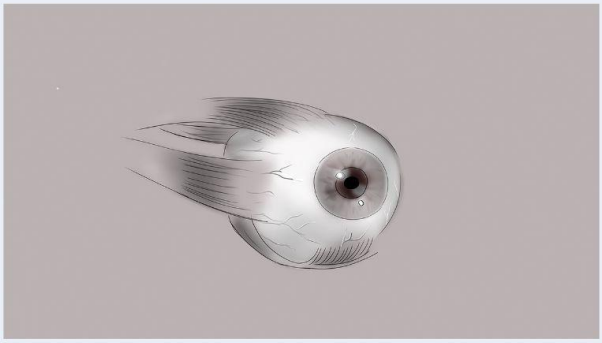
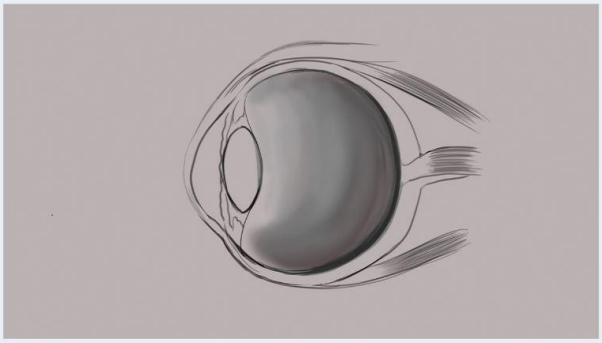
Script

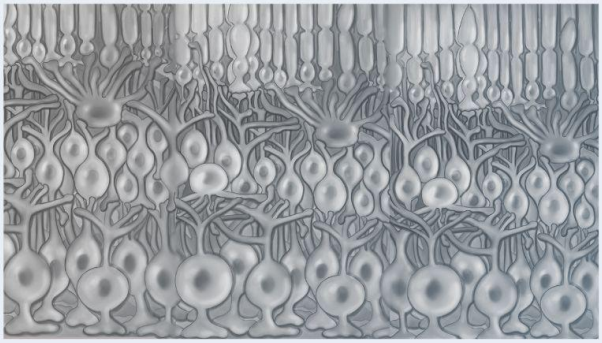
Script	Video Action
(1) For a human to see stimuli in their environment, light rays must be collected and focused on the retina.	1. A whole eyeball 3D model, with camera movement rotating around 2. when camera moving lateral, half of the eyeball fades away and a lateral view of cut eyeball
(1) The retina contains millions of light-sensitive cells like rods and cones and other nerve cells that receive and organize visual information. Your retina sends this information to your brain through your optic nerve, enabling you to see.	1. Camera zooming in and with a label appear on screen show the exact location of retina
(1) Rods and cones are two types of photoreceptors in the retina.	1. Camera zooms into what's inside the retina showing a multilayer cell model. These are 6 types of cell: Rod, Cone, Bipolar, Amacrine cell and Horizontal cells. Cells in different layers slightly moving and interacting with each other constantly
(1) Rods are responsible for vision at low light levels. In a dark environment, rods are depolarized and release glutamate which will then inhibit bipolar cells. On the other hand, in a light environment, rods are hyperpolarized and no longer release glutamate.	1. Zoom in to show one of the rod cells, with a label appear on the screen showing "rod" 2. Background changed to dark and release of glutamate (molecular model) to inhibit the bipolar cells is shown. When the background color turned light, glutamate stop releasing
(1) Cones are centralized in the fovea. Cones are responsible for daylight vision. A photoreceptor pigment, rhodopsin, is present in rod cells. It consists of a protein called opsin that is attached with the light-absorbing component, retinal	1. Zoom in to show one of the cone cells, with a label appear on the screen showing "rod" 2. Zoom into the disc region of rod cell (to the level of lipid bilayer), and show the structure of rhodopsin protein (molecular model)

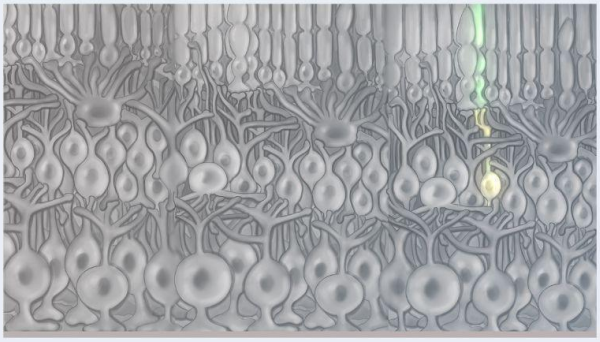
	3. zoom in a little bit more to see the photo absorbing structure of the retinal.
(1) The retinal component of rhodopsin absorbs light, the conformation of rhodopsin is changed, and then a G protein is activated. Activated G protein stimulates cGMP, hydrolysis of cGMP takes place, reducing its concentration, Na+ channels are closed, the influx of intracellular Na+ is reduced, and the photoreceptor cell is hyperpolarized.	1.Using molecular model to show the structural change of Rhodopsin protein and then show the cascade of G protein activation-----Na+ channel closing----influx of intracellular Na+-----and the hyperpolarization of membrane potential
(1) Thus, photoreceptors produce a hyperpolarizing generator potential instead of a depolarizing generator potential, which is observed in other receptors. Rods and cones do not fire action potentials.	1.Zoom out back to the layered cell view, with bipolar cell lighting up transducing signal form rod and cone to the gila cell.
(1) The rods and cones make synaptic contacts with the dendrites of bipolar and horizontal cells. The signals from rods and cones are transmitted to the bipolar and horizontal cells via chemical synapses.	1.keep the “light” transduction on all the time. Zooming into the synapse of bipolar cell, showing synapse releasing neurotransmitter via chemical synapses also showing the horizontal cell receiving the NTs.
(1) Visual signals are transduced and converted to neural signals. The brain integrates the visual information and provides a perception.	1. zoom out to the view of a brain with cortex region “lighted” up to simulate perception.

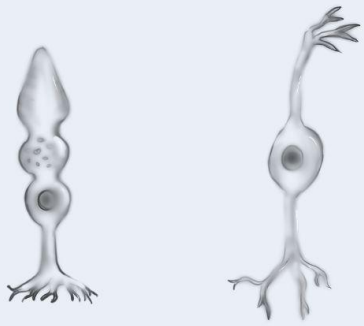
Storyboard

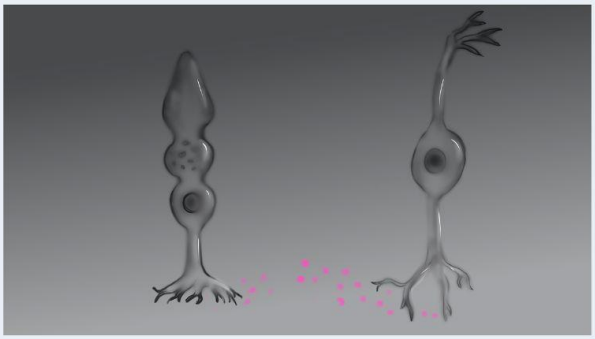




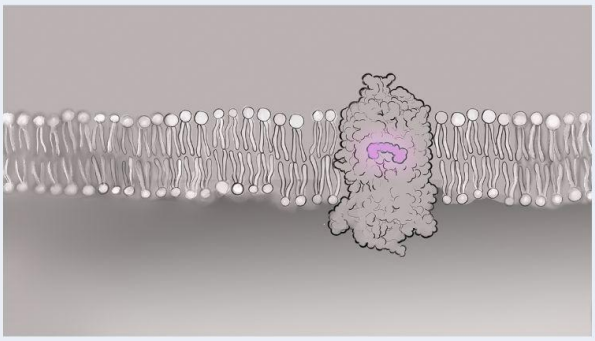


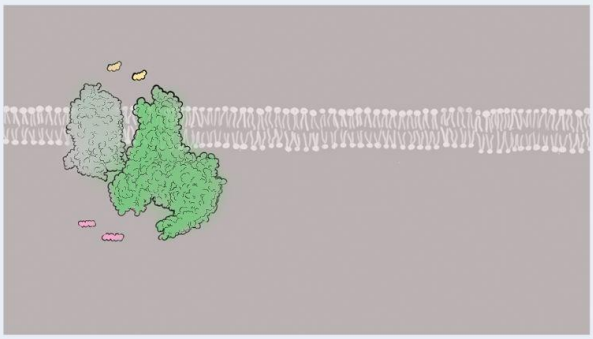


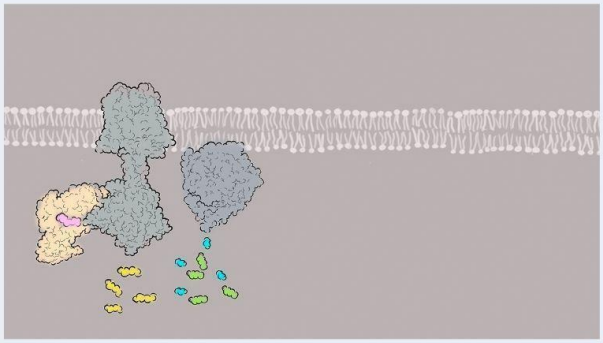


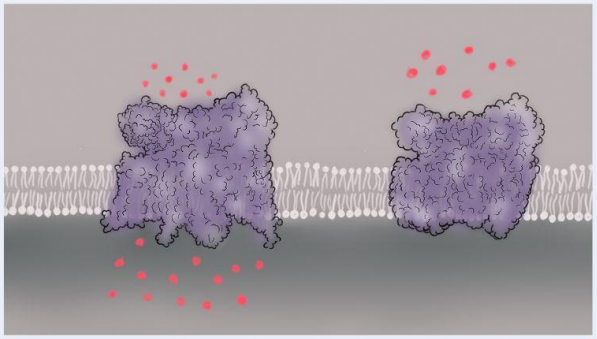


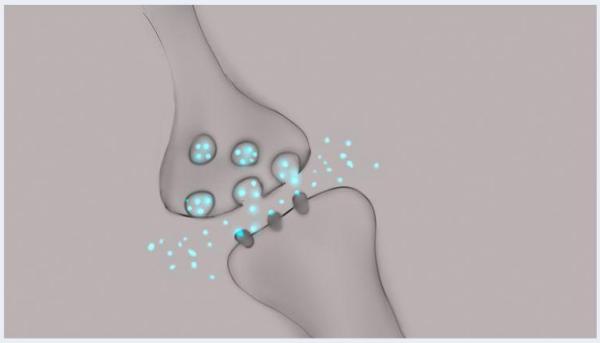
Storyboard

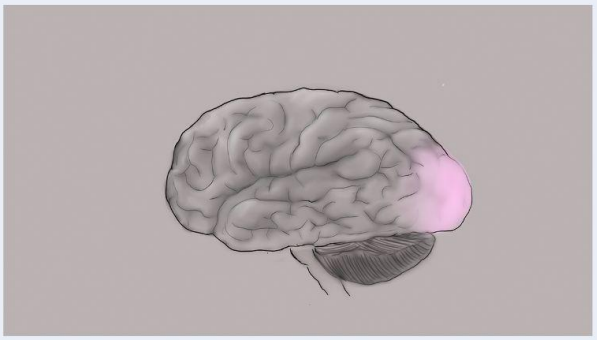












Video Link to YouTube:

https://youtu.be/cIklotwfMOM