# Diffusion of Topical Glaucoma Treatment in the Cornea

BENG 221

Gabrielle Colvert
Mark Fleming
Julia Hardy

## I. Problem Statement

An existing treatment for lowering intraocular pressure (IOP) in Glaucoma patients is the topical application of the drug Brimonidine. However, administration of this drug in the form of eye drops has its limitations. We propose an alternative topical medication delivery method via contact lens. By mathematically modeling this situation we can study how the medication diffuses through the cornea of the eye to relieve symptoms of Glaucoma. Using this model and the dynamic data it produces we can propose the most effective treatment plan for patients with Closed-angle Glaucoma using the new delivery method.

## II. Introduction to Glaucoma

The human eye is a complex organ. Its function of gathering light is dependent on intricate processes. For our discussion of Glaucoma, we first delve into process of how the eye controls the fluid inside it.

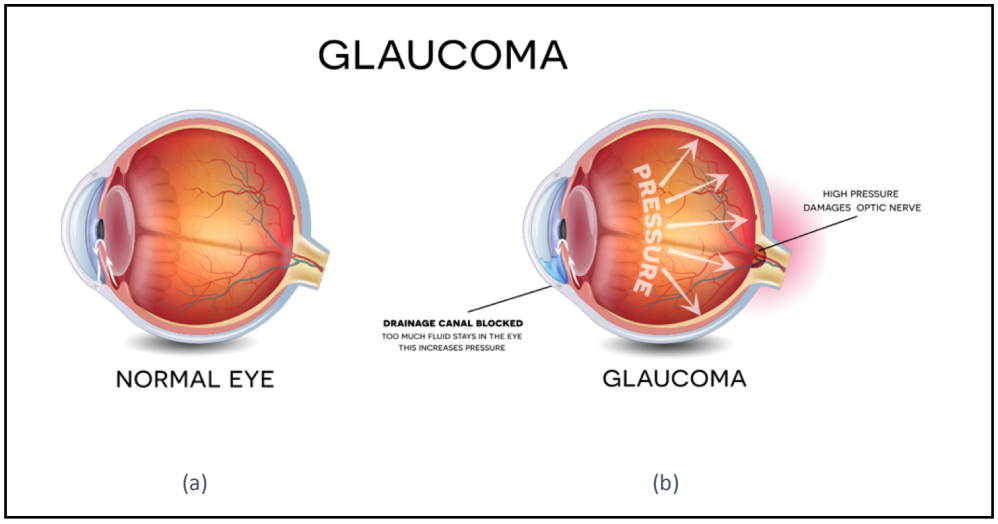


*Figure 1*: a.) Healthy, normal eye and b.) Eye suffering from Glaucoma [8].

Simply described, the eye is a sphere of fluid with a lens at the front and light detection at the back by the retina (see Figure 1(a)), The fluid is excreted by glands within the eye to support its shape and nourish the tissues within the eye. This fluid drains from the eye through canals near the cornea. Intra-ocular pressure (IOP) is controlled by the trabecular mesh, which stretches across the drainage canal openings. Glaucoma is caused by excessive fluid buildup, most often due to impaired drainage (see Figure 1(b)). Left untreated, this increase in IOP may eventually damage the optic nerve, which transmits visual information from the retina to the brain. Damage to the optic nerve can cause blindness. In fact, Glaucoma causes about 9 to 12 percent of blindness in the United States, and affects approximately 3 million people. [1].

Two types of fluid-drainage impairment can cause Glacoma. The most common form, Open-angle, is created when the fluid flows too slowly through the trabecular mesh [2] (see Figure 2).

Open-Angle Fluid Impairment

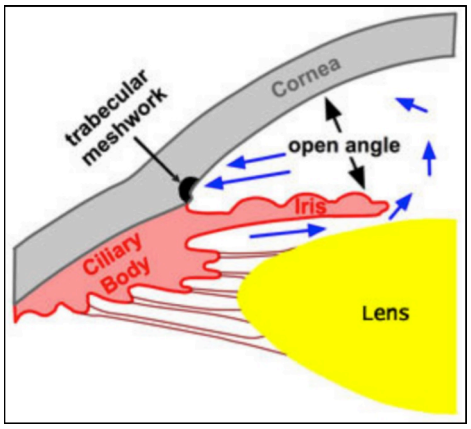


*Figure 2:* Fluid exits too slowly as the meshwork itself is dysfunctional [9].

Closed-angle Glaucoma (also known as Angle-Closure Glaucoma) results when iris tissues cover the trabecular mesh and completely block the fluid from exiting the eye [2] (see Figure 3). Though less common, Closed-angle Glaucoma presents acutely and requires immediate attention. Symptoms of Closed-angle Glaucoma often include excessive fluid pressure, pain, nausea, redness of the eye, and blurred vision [2]. Existing treatments for this type of Glaucoma include conventional surgery, laser trabeculoplasty, and oral and topical medication [2]. The focus of this paper is minimally invasive treatment with medication.

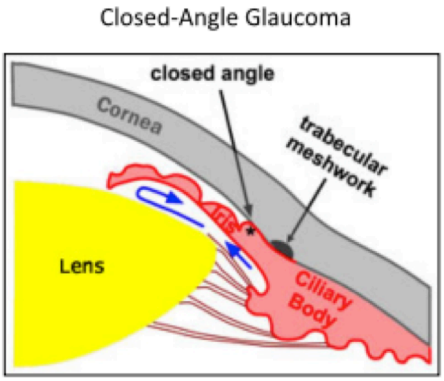


*Figure 3: Meshwork is blocked and fluid cannot flow out of the eye [9].*

For our project, we chose Brimonidine, a topically applied Glaucoma medication. This FDA-approved drug is an effective treatment for Closed-Angle Glaucoma [3]. Dosage is typically 1 or 2 drops of 1% or 2% solution into the eye up to three times per day [4]. The difficulty of adherence to the rigorous daily regimen associated with applying eye drops causes the treatment to be less effective for many patients [5] and much of the drug does not remain within the eye. An alternative delivery method for Brimonidine would ideally eliminate the traditional method of placing drops into the eye several times per day.

## III. Our Proposal

We propose the topical application of the IOP-lowering drug Brimonidine via a contact lens to create a more cost effective and easier to use delivery mechanism for Glaucoma patients. The contact lens contains only one drop of the drug and has the initial mass, $M_0$. In order to mathematically model this system, we made several key assumptions. First, the contact lens and liquid are infinitely long and infinitely thin. This eliminated the need to consider how the dimensions of these objects affected our model. Second, the trabecular meshwork acts like a sink. This allowed us to ignore the flow properties within and past the trabecular meshwork. Lastly, we assume that movement occurs in one dimension along the x-axis and that net diffusion along the y and z-axis is zero.

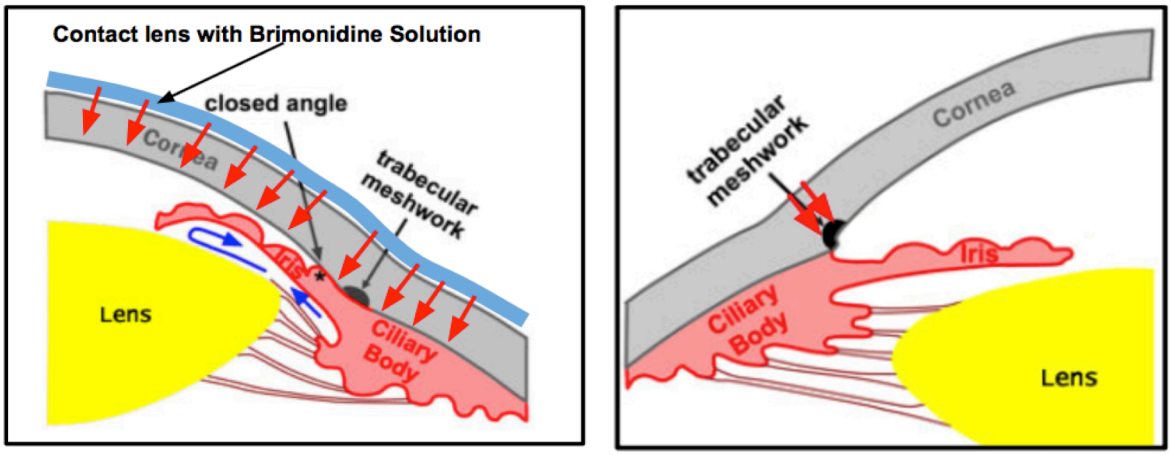


*Figure 4*: (left) *Brimonidine* diffuses through the cornea to interact with the target area to open the trabecular meshwork. (right) Once the trabecular meshwork is open *Brimonidine* will diffuse through the cornea to enter the trabecular meshwork, which acts like a sink. [9]

For the mathematical model, we divided the diffusion dynamics in the cornea into two separate time intervals. In Situation 1, we examined the initial diffusion of the drug across the entire length of the cornea, L, before the trabecular meshwork was unblocked. The initial mass of the drug is immediately present at outer end of the cornea at t=0. Therefore, there is no diffusion of the drug into or out of our system. In Situation 2, we modeled the drug diffusing from the cornea into the unblocked trabecular meshwork. We assume that since the contact lens has been removed there is no drug entering our system and that the meshwork at x=L acts like a sink as discussed earlier. Figure 4 is a visual representation of these dynamics within the cornea for Situations 1 and 2. Through these mathematical models, we observe the diffusion patterns as the drug first enters the eye and the outward diffusion after the medication has effectively opened the trabecular meshwork.

## IV. Analytical Methods

In this section, we will discuss the use of analytical methods to model the dynamics of our system. The model is divided in Situation 1 (the diffusion of the drug through the cornea) and Situation 2 (the diffusion of the drug into the trabecular mesh).

### A. Situation 1: *Diffusion Across the Cornea*

The diffusion across the cornea is modeled using the diffusion equation, as seen in Equation 1

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial t^2}, D = 5.5\times10^{-6}\ mm^2/s \tag{1}$$

where u is concentration, t is time, and D is diffusivity constant [6]. D accounts for diffusion through both the outer epithelial cells and the cornea [7]. The diffusion equation is evaluated using the boundary and initial conditions seen in Equations 2-4.

$$\frac{\partial u}{\partial x}(0,t) = 0 \tag{2}$$

$$\frac{\partial u}{\partial x}(L,t) = 0 \tag{3}$$

$$u(x,0) = \delta(x)M_0 \tag{4}$$

Equation 2 represents the boundary condition at the surface of the eye, x=0, of zero flux because until t=0 there is no diffusion into the eye. Equation 3 represents the boundary condition at the trabecular meshwork at the end of the cornea. At x=L, or 0.535 mm, the flux is zero because while the trabecular meshwork is blocked, the drug nor the ocular fluid can diffuse out of the cornea. Equation 4 represents the initial condition at t=0, when the drug is first introduced to the eye; the delta function creates an infinite pulse (just after t=0) of the initial mass, $M_0$=0.2 mg.

The diffusion equation is evaluated using separation variables, as seen in Equations 5a-g.

$$u(x,t) = T(t)X(x) \tag{5a}$$

$$X(x) = Bcos\left(\frac{n\pi}{L}x\right) \tag{5b}$$

$$T(t) = Ae^{-D\left(\frac{n\pi}{L}\right)^2 t} \tag{5c}$$

$$u(x,t) = A_0 + \sum_{n=1}^{\infty} A_n e^{-D\left(\frac{n\pi}{L}\right)^2 t} \cos\left(\frac{n\pi}{L}x\right) \tag{5d}$$

$$A_0 = \frac{1}{L}\int_{0^-}^{L} \delta(x) M_0 = \frac{M_0}{L} \tag{5e}$$

$$A_n = \frac{2}{L}\int_{0^-}^{L} \delta(x) M_0 \cos\left(\frac{n\pi}{L}x\right) = \frac{2M_0}{L} \tag{5f}$$

$$u(x,t) = \frac{M_o}{L} + \sum_{n=1}^{\infty} \frac{2M_o}{L} e^{-D\left(\frac{n\pi}{L}\right)^2 t} \cos\left(\frac{n\pi}{L}x\right) \tag{5g}$$

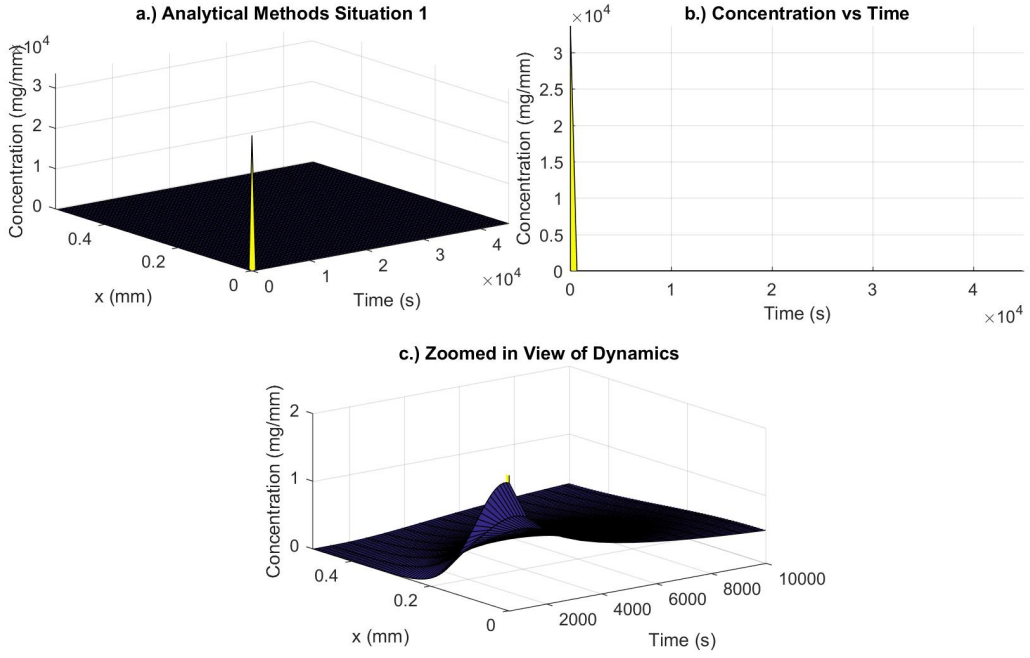


*Figure 5*: a.) Concentration profile in terms of time and distance, x, of Situation 1 results in a delta spike when time and distance are both just after 0. Theoretically the peak would inifitely tall, but due to the limitations of plotting, the height of spike related to the number of sumations. b.) The concentration reaches a steady state of 0.3738 mg/mL, which is equivalent to the initial mass distributed over L, at t=9.96E4. c.) The dynamics of the concentration profile just after the spike show an expoential decay along both Time and x for Situation 1.

Figures 5 shows the delta function right after zero and the steady state concentration value of 0.3736 mg/mm, or $M_0/L$, is reached by 28 hours. The delta pulse is approaching infinity, but the amplitude is limited by the number of finite terms in our series. We expected a steady state value because the trabecular meshwork is still blocked so the drug is unable to leave the cornea. Therefore, we are left with a linear density across the cornea.

**B. Situation 2:** *Diffusion into the Trabecular Meshwork After Steady State is Reached*

Assuming the trabecular meshwork opens like a switch after the concentration reaches steady state, the diffusion into the trabecular meshwork is modeled using the diffusion equation (see Equation 1), which begins a new time period. The diffusion equation is evaluated using the boundary and initial conditions seen in Equations 6-8.

$$\frac{\partial u}{\partial x}(0,t) = 0 \tag{6}$$

$$u(L,t) = 0 \tag{7}$$

$$u(x,0) = \frac{M_0}{L} \tag{8}$$

Equation 6 represents the boundary condition at the surface of the eye, x=0, of zero flux because until t=0 the concentration is at steady state so there is no diffusion into the eye. Equation 7 represents the boundary condition at the trabecular meshwork, x=L, of zero concentration because the trabecular meshwork acts as a sink. Equation 8 represents the initial condition at t=0, when the drug is at steady state, so it has an initial value of the initial mass over the length from the cornea to the trabecular meshwork.

The diffusion equation is evaluated using separation of variables. The solution is very similar to situation 1, however, a difference appears when the new boundary and initial conditions are applied to solve for λ. Equations 9a-e show the solution to Situation 2, where $A_n$ is calculated in the same manner as in situation 1.

$$u(x,t) = T(t)X(x) \tag{9a}$$

$$X(x) = Bcos\left(\frac{\pi(1+2n)}{2L}x\right) \tag{9b}$$

$$T(t) = Ae^{-D\left(\frac{\pi(1+2n)}{2L}\right)^2 t} \tag{9c}$$

$$u(x,t) = \sum_{n=0}^{\infty} A_n e^{-D\left(\frac{\pi(1+2n)}{2L}\right)^2 t} cos\left(\frac{\pi(1+2n)}{2L}x\right) \tag{9d}$$

$$u(x,t) = \sum_{n=0}^{\infty} \frac{4M_o}{L(\pi(1+2n))}(-1)^n e^{-D\left(\frac{\pi(1+2n)}{2L}\right)^2 t} cos\left(\frac{\pi(1+2n)}{2L}x\right) \tag{9e}$$

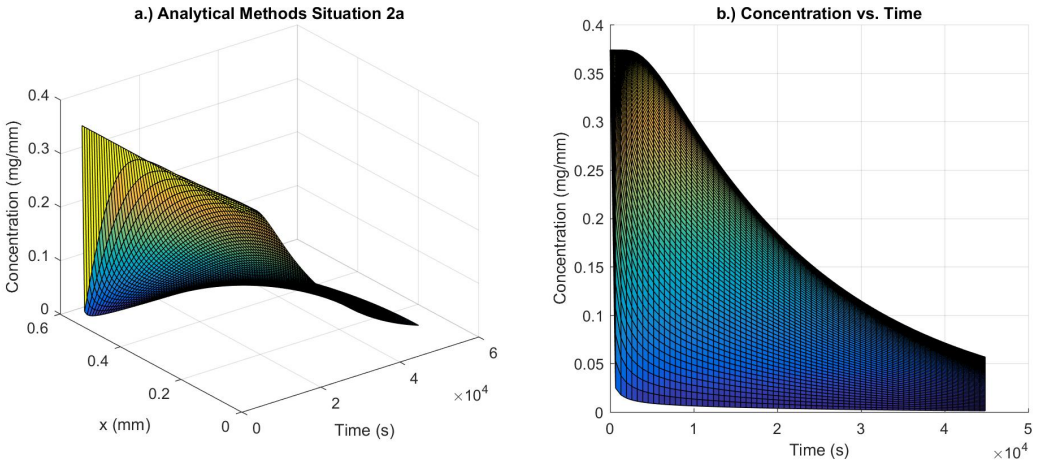


*Figure 6*: a.) Concentration profile in terms of time and distance, x, of Situation 2 results in an exponential decay with time and parabolic decay with distance. At time of 0, the magnitude along all of x, except L, is at the steady concentration of Situation 1, which satisfies our initial condition. b.) The concentration profile has zero flux along time of zero, which satisfies our boundary condition. The concentration returns to zero after a time of 1E5 seconds.

Figures 6 satisfies the boundary conditions of zero flux along the x-axis, a boundary concentration of zero at L, and an initial magnitude of 0.3739 along x (except L) at t=0. Also, there is an exponential decay with time and parabolic decay with distance. This is expected because before the trabecular meshwork is open there is no diffusion out of the cornea and after the trabecular meshwork is open the diffusion occurs until the concentration is approximately zero.

## V. Numerical Methods

In this section, we will discuss the use of numerical methods in MATLAB to verify our analytical solutions and more accurately model the dynamics of our system. The model is still divided into Situation 1 (the diffusion of the drug through the cornea) and Situation 2 (the diffusion of the drug into the trabecular mesh). For all the situations, we used MATLAB's built-in *pdepe* function to approximate the solution to our partial differential equation subject to our boundary conditions and the initial condition.

### A. Situation 1: *Diffusion Across the Cornea*

The first step was to verify that our analytical solution to Situation 1 was correct. We used the same differential equation, initial condition, boundary conditions, and parameters as in our analytical section (see Equations 1-4). Figure 7 shows the resulting plots of the numerical approximation. As in the analytical solution there is a delta pulse which represents our initial input of the drug at t=0. In our analytical method, the amplitude of this spike approaches infinity, but in the numerical method it is equal to the initial mass of the drug as shown in Figure 7(a). We get a finite value rather than an infinite number due to the numerical approximation methods used by MATLAB's *pdepe.* The drug then diffuses across the cornea and reaches a steady state value since we have no flux on either end of the model. As shown in Figure 7(b), the steady state is equal to 0.00303 mg/mm. Due to MATLAB's *pdepe* approximations it is not immediately clear that this is our expected value, or the linear density of $M_0/L$ = 0.374 mg/mm. If we take the steady state value from Figure 7(b) and multiply by the length of our *xmesh* vector as determined by our step size, dx, divided by the total length, L, we get our anticipated value for the steady state concentration, as seen in Equation 10. Therefore, from the results of this numerical analysis we can assume that our analytical solution is correct for Situation 1.

$$0.00303\,\frac{mg}{mL} \times \frac{length\ of\ xmesh}{L} = 0.374\,\frac{mg}{mm} = \frac{M_0}{L} \tag{10}$$

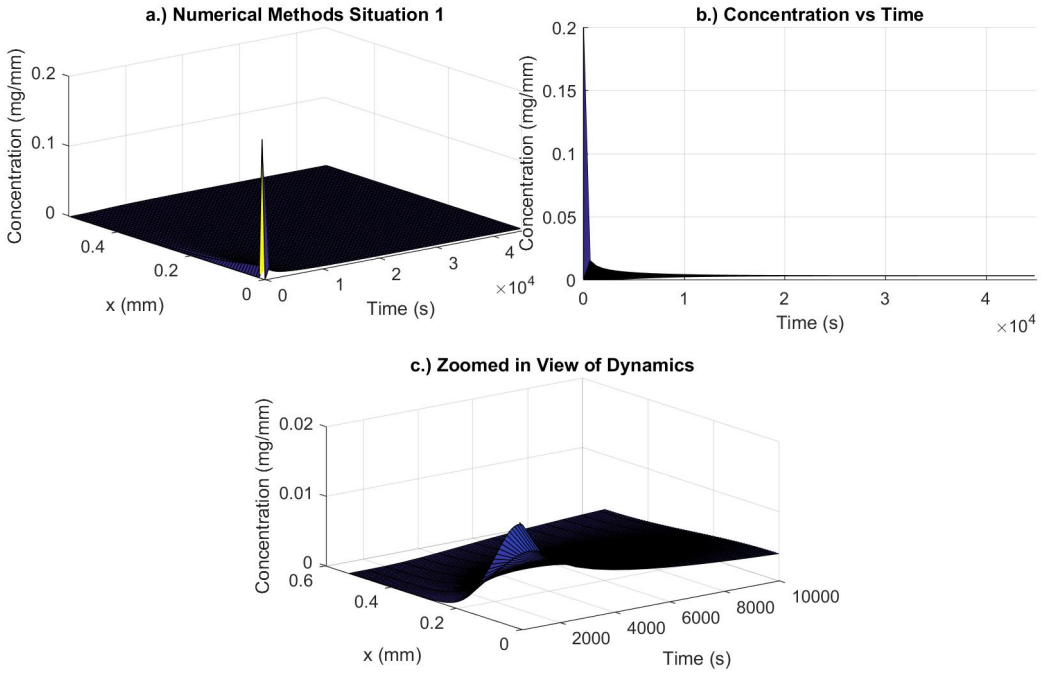


*Figure 7:* a.) This is the *pdepe* solution to Situation 1 where there is a delta peak at one time step after 0 with an amplitude of 0.2, or the initial mass of the drug, b.) The concentration profile over time of Situation 1. We see the graph reach a steady state value of 0.003 mg/mm which, after being multiplied by steps/length, is equal to $M_0/L$, c.) This is the zoomed in view of the dynamics of Situation 1. We can see that as time increases, the drug diffuses across the cornea and approaches a steady state across L.

**B. Situation 2a:** *Diffusion into the Trabecular Mesh After Steady State is Reached*

As in the section above, we wanted to verify that our analytical solution was correct for Situation 2. Using the same differential equation, parameters, initial condition, and boundary conditions (see Equations 1, 6-8) as in our analytical method section we solved for the solution numerically in MATLAB. Figure 8 shows the resulting plots for this approximation. As shown in Figure 8(a), at t=0 the graph starts at the constant concentration of $M_0/L$ for all values of x. This is expected because we assumed our system reached steady state in Situation 1 before the trabecular mesh was unblocked and the drug could diffuse into it. Therefore, we assumed our initial condition for this situation to be the final state of Situation 1. In addition, we see that at x=L for all time points, the concentration is at zero just as in our analytical methods. This is because we set the right-hand boundary condition to zero, or a sink, so that when the drug reaches L, it immediately leaves the cornea. Lastly, in Figure 8(b) the concentration of the drug in the cornea is essentially zero after approximately 47 hours. These dynamics achieved by a numerical approximation are very similar to what we saw in our analytical methods section. Therefore, we can verify that our analytical solution is correct.

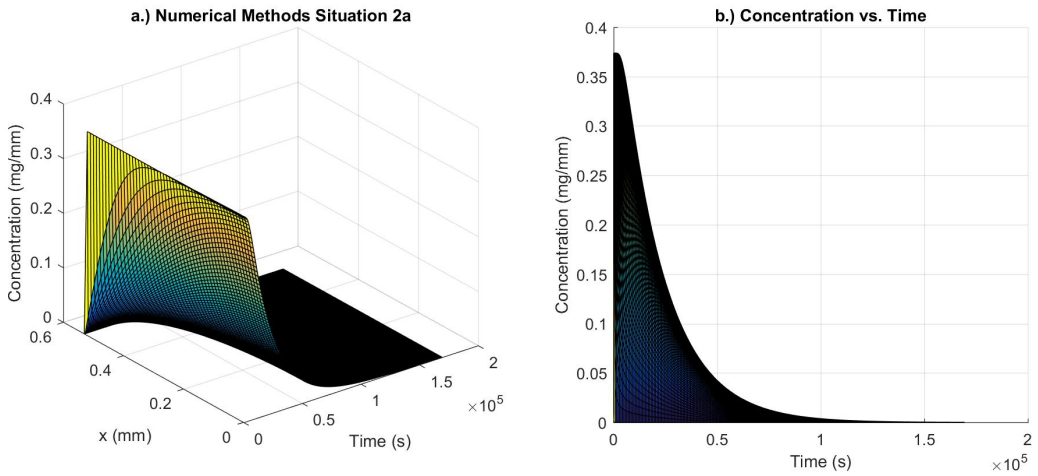


*Figure 8*: a.)This is the *pdepe* solution to Situation 2a. The value at t=0 across all x values is the final steady state value from Situation 1, or $M_0$/L. b.) This is the plot of concentration vs. time within the cornea after the meshwork is unblocked. At the end of the time period , the concentration of the drug in the cornea is approximately zero

**C. Situation 2b:** *Diffusion into the Trabecular Mesh after Critical Concentration is Reached*

In this section, we wanted to better represent the dynamics of the system to propose the most effective treatment plan for patients with Glaucoma. Instead of assuming the meshwork is unblocked after a steady state concentration is reached, we found that the drug is most effective after two hours of contact with the tissues [3]. Therefore, using our data from Situation 1, we found that around t=2 hours the mass of the drug is $M_c$= 0.00202 mg. The modified differential equation and initial condition are shown in Equations 11-13. We used the same boundary conditions as in Situation 2a. The differential equation now includes a source term to represent the rest of the drug that still needs to diffuse through the cornea from situation 1. The source term includes a decaying exponential that is dependent on time and multiplied by the difference between the initial mass of the drug and the critical mass. The initial condition is the critical mass at which the meshwork was unblocked multiplied by a decreasing exponential. We use the decaying exponential term because we assume the concentration is no longer constant across the cornea and varies depending on the distance x. With equations 11-13 of the diffusion equation, initial condition, and the boundary conditions as stated we get the following plots in Figures .

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{dt^2} + s \tag{11}$$

$$s = (M_0 - M_c)pe^{-kt}, \qquad with\ constants\ p\ and\ k \tag{12}$$

$$u(x,0) = Mc * e^{-kx} \tag{13}$$

As shown in Figures 9 and 10, the concentration at x=0, t=0 is the critical mass 0.00202 mg which then decays exponentially across the length of the cornea. This represents that the concentration across L is no longer uniform at the beginning of this time period because the mesh was unblocked before steady state was reached. The concentration then increases due to the source term in the differential equation to the maximum value as shown in Figure 16. This maximum value is approximately $M_0$-$M_c$ or the amount of drug that is left to diffuse through the cornea. After the peak, the drug diffuses out across L and into the mesh at x=L. Since we assumed that the mesh is a sink, the concentration is always zero at x=L. At the end of the time period, the concentration of the drug in the cornea is zero because the total amount diffused into the trabecular meshwork.

Now the model more accurately represents the expected dynamics and we can use it to propose an effective treatment plan for patients with Glaucoma. From Situation 1, we know that the drug has its maximum effect after 2 hours of being in contact with the tissues. After 2 hours we reach a critical drug mass at x=L of 0.00202 mg. The meshwork opens and acts like a sink and that .00202 mg immediately diffuses out of the cornea. The rest of the drug, or $M_0$-$M_c$, remains and will now diffuse out while still affecting the tissue around it. Since the meshwork is unblocked, the drug will remain effective and keep it open until about 75% of the initial 0.2 mg has diffused out of the cornea. Using the model, we see that only 25%, or 0.05 mg, remains at the trabecular meshwork after 16.67 hours. Therefore, we can assume at the drug remains effective for about 18.67 hours after application.

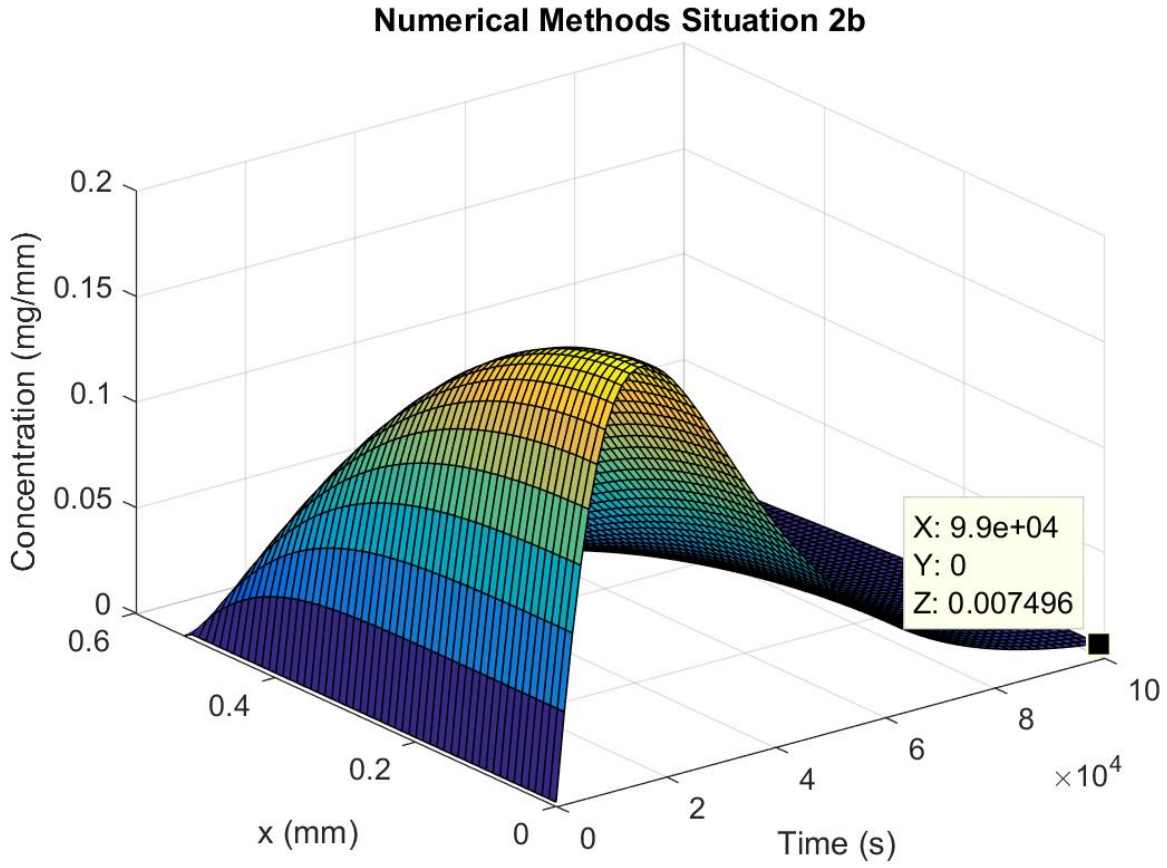


*Figure 9*: This is the *pdepe* solution to Situation 2b which now has the source term and the decaying exponential as the initial condition starting at $M_c$=0.00202 mg.

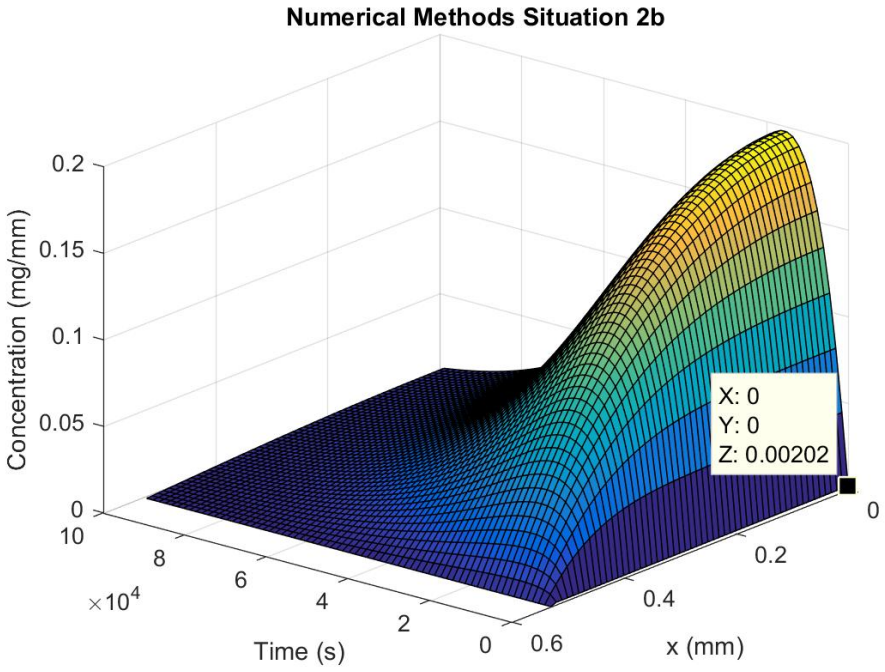


*Figure 10*: This is the *pdepe* solution to Situation 2b and shows the diffusion profile with the source term.

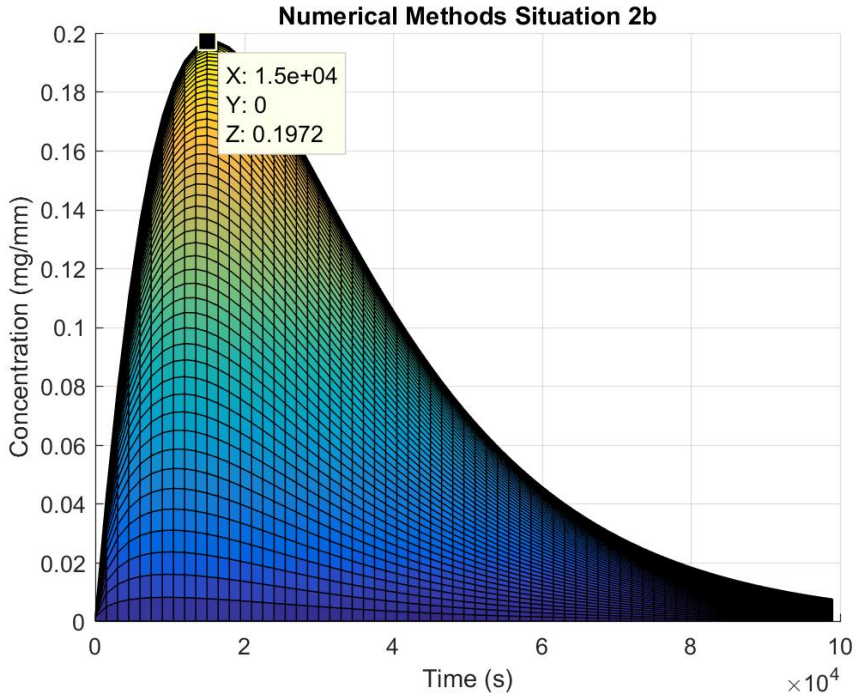


*Figure 11:* This is the *pdepe* solution to solution 2b where the maximum value is $M_0$-$M_c$ with the source term and exponentially decaying intital condition.

## VI. Conclusion

Overall, our analytical and numerical methods accurately represented the dynamics of our model for the diffusion of the IOP lowering drug, Brimonidine, across the cornea and into the trabecular meshwork. In situation one, both methods displayed the diffusion across the cornea after the initial delta impulse of the drug at t=0 and a steady state concentration. The analytical solution more accurately represented the delta pulse as approaching infinity whereas the numerical method had the amplitude of the pulse as a finite value due to MATLAB's *pdepe* approximation. In addition, our analytical method showed that the concentration in the cornea reached a steady state value of $M_0/L$, or the linear density. After a simple conversion, we also saw that the numerical method had the same result.

For Situation 2b, we changed our differential equation and initial condition to more accurately describe the dynamics of the system once the drug diffuses into the meshwork. Using the critical mass of the drug, $M_c$, we modeled a distance-dependent concentration at t=0 to show that the concentration after the meshwork became unblocked was not at equilibrium. The source term was added to account for the rest of the drug after $M_c$ that had not yet diffused through the cornea to site of interest.

Further studies should be done to model the exact behavior of the meshwork rather than assuming it acts as a sink. The right-hand flux boundary condition for Situation 2b can be changed to reflect this once it is well understood. In addition, we assumed that the source and the initial condition for this situation acted as a decaying exponential; however, research should be done to better characterize their dynamics. Lastly, because the eye is a 3D object, the system should ideally be modeled using all three axes to fully understand how diffusion occurs in the cornea and into the trabecular meshwork.

Although our model is based on several assumptions, it is still useful for studying the effects of our proposed topical drug delivery method for treating Closed-Angle Glaucoma. The drug initially reaches the meshwork within two hours of application and remains in the cornea for over 36 hours. Using our model in Situation 2b we found that the drug remains at an effective concentration for about 16.67 hours. This implies that the patient would only need to apply one drop of the drug via the contact lens once per day as it still affects the tissues for up to 18.67 hours. Typical IOP patterns show a spike during the night while patients sleep with it remaining higher in the early morning [10]. After further analysis of our model and studies into the mechanics of the meshwork, doctors will be able to recommend an application protocol for the patients. Due to the prolonged exposure of the medication to the eye, the patients will only need to apply the medication once before bed for18.67 hours of effectiveness during IOP spikes.

This procedure would be much simpler for the patient than using eye drops, which requires them to use 1-2 drops per application up to 3 times per day. The necessary adherence to a rigorous eye drop regimen often results in patient neglect to apply the eye drops thereby reducing effectiveness. In addition, when a patient applies eye drops, much of the liquid does not remain in the eye but is removed when he/she blinks. Lastly, for some patients the drug ceases to work after a period of time because of the large doses required for the eye drops [10]. However, our proposed delivery of the drug could prolong its effectiveness due to the smaller and less frequent dose required. Due to all these concerns, our contact lens delivery mechanism has the potential to be more cost effective and easier to use while still successfully lowering IOP in Glaucoma patients.

## VII. MATLAB Code

### A. Graphing of Analytical Solutions to Situations 1 and 2:

```
function situations1n2_analytical
% Homogeneous PDE: Linear (1-D) Diffusion
% BENG 221 project Situations 1 and 2
% Julia Hardy, Gabby Colvert, Mark Fleming

% constants
global D L M0 t_final
D = 5.5e-6;
L = 0.535;
M0= .2;
t_final= 4.5e4;

dx = 0.008; % step size in x dimension
dt = 650;  % step size in t dimension
xmesh = 0:dx:L; % domain in x
tmesh = 0:dt:t_final;  % domain in t
nx = length(xmesh); % number of points in x dimension
nt = length(tmesh); % number of points in t dimension


%situation 1: Diffusion through the Cornea
sol_sep = zeros(nt, nx);
for n = 1:1:t_final-1
    k = (pi*n)/(L);
    sol_sep = sol_sep +(((2*M0)/(L))*exp(-D*(k^2)*tmesh)' *
cos(k*xmesh));
end

figure(1)
subplot(2, 4, 1:2)
surf(tmesh,xmesh,(M0/L)+sol_sep')
title('a.) Analytical Methods Situation 1')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
axis([0 t_final 0 L 0 inf])

subplot(2, 4, 3:4)
surf(tmesh,xmesh,(M0/L)+sol_sep')
title('b.) Concentration vs Time')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
axis([0 t_final 0 L 0 inf])

subplot(2, 4, 6:7)
surf(tmesh,xmesh,(M0/L)+sol_sep')
```

```
title('c.) Zoomed in View of Dynamics')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
axis([dt 1E4 0 0.5 0 2])

%situation 2: Diffusion into the Meshwork
sol_sep_2 = zeros(nt, nx);
for n = 0:1:t_final-1
    k = (pi*(1+2*n))/(2*L);
    sol_sep_2 = sol_sep_2 + 4*M0/(L*pi*(1+2*n))*((-1)^n)*exp(-
D*k^2*tmesh)'*cos(k*xmesh);
end

figure(2)
subplot(1,2,1)
surf(tmesh,xmesh,sol_sep_2')
title('a.) Analytical Methods Situation 2a')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')

subplot(1,2,2)
surf(tmesh,xmesh,sol_sep_2')
title('b.) Concentration vs. Time')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
```

**B. Graphing of Numerical Solution to Situation 1:**

```
function situation1_num

% diffusion constant
global D L t_final
D = 5.5e-6;
L=0.535;
t_final=4.5e4;
% domain
dx = 0.008; % step size in x dimension
dt = 650;  % step size in t dimension
xmesh = 0:dx:L; % domain in x
tmesh = 0:dt:t_final;  % domain in t

length(xmesh)

sol_pdepe = pdepe(0,@pdefun,@ic,@bc,xmesh,tmesh);

subplot(2, 4, 1:2)
surf(tmesh,xmesh,sol_pdepe')
title('a.) Numerical Methods Situation 1')
```

```
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
axis([0 t_final 0 L 0 inf])

subplot(2, 4, 3:4)
surf(tmesh,xmesh,sol_pdepe')
title('b.) Concentration vs Time')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
axis([0 t_final 0 L 0 inf])

subplot(2, 4, 6 : 7)
surf(tmesh,xmesh,sol_pdepe')
title('c.) Zoomed in View of Dynamics')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')
axis([650 10000 0 .6 0 0.02])


% function definitions for pdepe:
% --------------------------------------------------------------

function [c, f, s] = pdefun(x, t, u, DuDx)
% PDE coefficients functions

global D
c = 1;
f = D * DuDx; % diffusion
s = 0; % homogeneous, no driving term

% --------------------------------------------------------------

function u0 = ic(x)
% Initial conditions function
M0=0.2; % initial mass of drug
u0 = (x==0.008)*M0; % delta impulse at center with weight M0

% --------------------------------------------------------------

function [pl, ql, pr, qr] = bc(xl, ul, xr, ur, t)
% Boundary conditions function

pl = 0; % N/A
ql = 1;  % zero flux left boundary condition
pr = 0; % N/A
qr = 1;  % zero flux right boundary condition
```

**C. Graphing of Numerical Solution to Situation 2a:**

```
function situation2a_num

% diffusion constant
global D L M0
D = 5.5e-6;
L=0.535;
M0=0.2;

% domain
dx = 0.01; % step size in x dimension
dt = 700;  % step size in t dimension
xmesh = 0:dx:L; % domain in x
length(xmesh)
tmesh = 0:dt:1.7e5;  % domain in t

sol_pdepe = pdepe(0,@pdefun,@ic,@bc,xmesh,tmesh);

subplot(1,2,1)
surf(tmesh,xmesh,sol_pdepe')
title('a.) Numerical Methods Situation 2a')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')

subplot(1,2,2)
surf(tmesh,xmesh,sol_pdepe')
title('b.) Concentration vs. Time')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')

% function definitions for pdepe:
% ------------------------------------------------------------

function [c, f, s] = pdefun(x, t, u, DuDx)
% PDE coefficients functions

global D
c = 1;
f = D * DuDx; % diffusion
s = 0; % homogeneous, no driving term

% ------------------------------------------------------------

function u0 = ic(x)
% Initial conditions function
%Mc=0.00202;
global L M0
u0=M0/L;
%u0 = Mc*exp(-x)/L;
```

```
% --------------------------------------------------------------

function [pl, ql, pr, qr] = bc(xl, ul, xr, ur, t)
% Boundary conditions function

pl = 0; % N/A
ql = 1;  % zero flux left boundary condition
pr = ur; % zero value right boundary condition, sink @ x=L
qr = 0;  % N/A
```

**D. Graphing of Numerical Solution to Situation 2b:**

```
functionsituation2b_num

% diffusion constant
global D L Mc M0 k p
D = 5.5e-6;
L=0.535;
Mc=0.00202;
M0=0.2;
k=0.00009; %constant 1
p=1.5e-4; %constant 2

% domain
dx = 0.01; % step size in x dimension
dt = 1500;  % step size in t dimension
xmesh = 0:dx:L; % domain in x
tmesh = 0:dt:1e5;  % domain in t
sol_pdepe = pdepe(0,@pdefun,@ic,@bc,xmesh,tmesh);

surf(tmesh,xmesh,sol_pdepe')
title('Numerical Methods Situation 2b')
xlabel('Time (s)')
ylabel('x (mm)')
zlabel('Concentration (mg/mm)')



% function definitions for pdepe:
% --------------------------------------------------------------

function [c, f, s] = pdefun(x, t, u, DuDx)
% PDE coefficients functions

global D M0 Mc L k p
c = 1;
f = D * DuDx; % diffusion
s = (M0-Mc)*p*exp(-k*t); % source from situation 1
```

```
% --------------------------------------------------------------------

function u0 = ic(x)
% Initial conditions function
%Mc=0.00202;
global Mc k
%u0=.2/L;
u0 = Mc*exp(-k*x); %intial condition -- not constant concentration at
t=0

% --------------------------------------------------------------------

function [pl, ql, pr, qr] = bc(xl, ul, xr, ur, t)
% Boundary conditions function
pl = 0; % N/A
ql = 1;  % zero flux left boundary condition
pr = ur; % zero value
qr = 0;  % N/A
```

## VIII. References


[1] Glaucoma Reserch Foundation, "Glaucoma Facts and Stats," [Online]. Available: http://www.Glaucoma.org/.

[2] "Facts About Glaucoma," National Eye Institute, [Online]. Available: https://nei.nih.gov/health/Glaucoma/Glaucoma_facts. [Accessed October 2016].

[3] "Brimonidine in the treatment of Glaucoma and ocular hypertension," [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1936355/. [Accessed October 2016].

[4] "Angle-Closure Glaucoma," [Online]. Available: http://www.aao.org/munnerlyn-laser-surgery-center/angleclosure-Glaucoma-19. [Accessed 2016].

[5] Y. K. A. D. H. G. S. S. M. P. b. B. Chianga, "Sustained reduction of intraocular pressure by supraciliary delivery of brimonidine-loaded poly(lactic acid) microspheres for the treatment of Glaucoma," *Journal of Controlled Release,* vol. 228, no. April 2016, pp. 48-57, 2016.

[6] B. C. X. W. a. M. R. P. Yoo-Chun Kim, "Ocular delivery of macromolecules," *J Control Release,* vol. Sep 28, no. 0, pp. 172-181, 2014.

[7] Z. M. Doughty MJ, "Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach," *Surv Ophthalmol,* vol. 44(5), no. Mar-Apr, pp. 367-408, 2000.

[8] "Brandon Eye Clinic," [Online]. Available: http://brandoneye.com/wp-content/uploads/2015/07/Glaucoma.png. [Accessed October 2016].

[9] "Optometrist Australia," [Online]. Available: http://optometrist.com.au/. [Accessed October 2016].

[10] A. Coleman, 'Glaucoma', *The Lancet*, vol. 354, no. 9192, pp. 1803-1810, 1999.