BENG 221

Modeling of Intrathecal Drug Delivery

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Introduction

Chronic pain syndrome is the persistence of severe pain that could result virtually any source and cause "marked changes in behavior, self-imposed restriction of daily activities, and heavy, largely ineffective use of the healthcare system" [1]. According to a National Health Interview Survey in 2012, it is estimated that about 25.3 million (11.2%) adults in the United States experience chronic pain, which is defined as any pain that last for more than three months [2]. Chronic pain can affect many aspects of the patient's life, including sleep, cognitive processes and brain function, mental health, cardiovascular health, sexual function, and the overall quality of life. The pathophysiology of the chronic pain syndrome shows that when the pain is left unattended, it will often become more and more serious, as well as more and more difficult to treat [3]. As shown in Figure 1, physically, chronic pain can cause activity avoidance, which will further lead to progressive deconditioning, and increased level of pain; psychologically, the pain will first lead to stress, anxiety, depression and these will further increase the perception of the pain.

Figure 1. Pathophysiology of Chronic Pain Syndrome [4]

Conventional methods for treating the chronic pain is through orally administered analgesics. Orally administered analgesics primarily rely on blood circulation to deliver the drugs to the central nervous system (CNS) to become effective. In this way, the amount of drug that eventually reach the CNS is quite low because of the low permeable blood-brain barrier and blood-cerebrospinal fluid barrier. Therefore, high dosage of drug is required to be administered so as to remain at an effective amount after reaching the CNS. But high dosage often companies more side effects, such as dizziness, drowsiness, constipation, etc. To circumvent the blood-brain barrier and blood-cerebrospinal fluid barrier, intrathecal administration has been developed to inject the drug directly into the cerebrospinal fluid, which is infused in both the brain and the spinal cord. It has been proven as useful in spinal anesthesia, chemotherapy, and pain management. Intrathecal administration bypasses the barriers and allows for targeted delivery of drug, thus it can significantly lower the drug needed.

Problem Statement

Though the intrathecal administration has been widely used, it is remained unclear about the diffusion profile of a drug inside the spinal cord and how much concentration will arrive at the brain. Since the brain is more sensitive to chemical than the spinal cord, the concentration of the drug at brain matters. In some cases, little drug is expected to reach the brain so as to reduce side effects, in other cases where area around the brain is affected, appropriate amount of drug is expected to reach the brain so as to be effective. Therefore, we model the intrathecal delivery of drug to investigate how the concentration profile of drug changes according to different injection location, injection concentration and among different age groups. The model can be further used in drug testing to measure the minimum effective dosage or the maximum nontoxic dosage.

Assumptions

There are several assumptions for our model. First, the shape of the cerebrospinal fluid is assumed to be a perfect cylinder, having the same radius and length as the spinal cord. As shown in Figure 2, the cerebrospinal fluid not only surrounds the spinal cord in a thin layer (the blue are), but also exists in the spinal canal (dark grey area) inside the spinal cord [5].

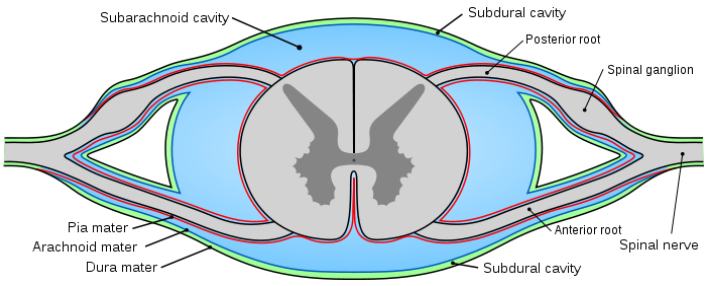

Figure 2. Anatomy of the Spinal Cord [6]

Second, the diffusivity of substances in the cerebrospinal fluid is the same as that in the water, because the cerebrospinal fluid is composed of predominantly water (99%) [7]. Third, the peripheral of the spinal fluid is assumed to be insulated. According to previous literature, it is shown that fresh cerebrospinal fluid is produced at a rate of 0.2mL to 0.7mL per minute while the total volume of 150mL [8]. Therefore, the circulation of cerebrospinal fluid is relatively slow compared to the diffusion rate of drugs. Fourth, the injection of the drug is assumed to be at the center of the cerebrospinal fluid, where r=0, to simplify calculations.

Mathematical Equation and General Solution

Based on the assumptions , the model can be described as a diffusion equation:

$$\frac{\partial C}{\partial t} = D\left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r} + \frac{1}{r^2}\frac{\partial^2 C}{\partial \theta^2} + \frac{\partial^2 C}{\partial z^2}\right)$$

Because the injection is at the center where r=0, by symmetry the equation can be reduced to:

$$\frac{\partial C}{\partial t} = D\left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial z^2}\right)$$

with initial condition:

$$C(r, z, 0) = C_0\delta(r, z)$$

and boundary conditions:

$$\frac{\partial}{\partial \mathrm{r}} C(R, z, t) = 0, \frac{\partial}{\partial \mathrm{r}} C(0, z, t) = 0$$

$$C(r, \infty, t) = 0, C(r, -\infty, t) = 0$$

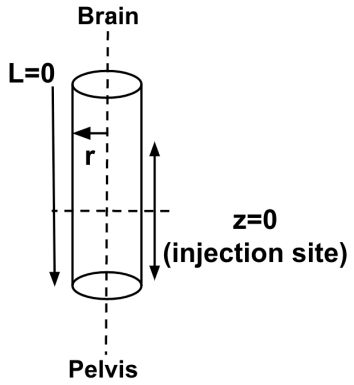

Figure 3. Model of the Cerebrospinal Fluid

It is worth notice that the injection site is set as z=0, and the drug diffuses into both directions.

By separation of variables, we have:

$$C(r, z, t) = g(r)h(z, t)I(t)$$

$$gh\frac{\partial I}{\partial t} + gI\frac{\partial h}{\partial t} = D\left(hI\frac{\partial^2 g}{\partial r^2} + \frac{1}{r}hI\frac{\partial g}{\partial r} + gI\frac{\partial^2 h}{\partial z^2}\right)$$

$$\frac{1}{D}\frac{1}{I}\frac{\partial I}{\partial t} + \frac{1}{D}\frac{1}{h}\frac{\partial h}{\partial t} = \frac{1}{g}\frac{\partial^2 g}{\partial r^2} + \frac{1}{g}\frac{1}{r}\frac{\partial g}{\partial r} + \frac{1}{h}\frac{\partial^2 h}{\partial z^2} = \eta$$

Diffusion along z direction can be regarded as a separate problem, which we have:

$$\frac{\partial C}{\partial \mathrm{t}} = \mathrm{D}\frac{\partial^2 C}{\partial \mathrm{z}^2}$$

With initial condition:

$$C(z, 0) = C_0\delta(z)$$

and boundary Condition

$$C(-\infty,t)=0.C(\infty,t)=0$$

Let $C(\xi,t)=F_z\big(C(z,t)\big)=\int_{-\infty}^{+\infty}C(z,t)e^{j\xi z}dz$

$$F_z\left(\frac{\partial}{\partial z}C(z,t)\right)=j\xi C(\xi,t)$$

$$F_z\left(\frac{\partial^2}{\partial z^2}C(z,t)\right)=(j\xi)^2C(\xi,t)=-\xi^2C(\xi,t)$$

Solution in time domain is:

$$C(\xi,t)=C(\xi,0)e^{-D\xi^2t}$$

By inverse Fourier Transform, we can have:

$$C(z,t)=F_z^{-1}\big(C(\xi,t)\big)=\frac{1}{2\pi}\int_{-\infty}^{+\infty}C(\xi,t)e^{-j\xi z}d\xi$$

$$C(z,t)=\frac{1}{2\pi}\int_{-\infty}^{+\infty}C(\xi,0)e^{-D\xi^2t}e^{-j\xi z}d\xi$$

$$C(z,t)=M(z)*N(z)=\int_{-\infty}^{+\infty}M(z_0)N(z-z_0)dz_0=\int_{-\infty}^{+\infty}\delta(z)N(z-z_0)dz_0$$

$$N(z)=F_z^{-1}\big(e^{-D\xi^2t}\big)=\frac{1}{2\pi}\int_{-\infty}^{+\infty}e^{-D\xi^2t}e^{-j\xi z}d\xi=\frac{1}{2\pi}\frac{1}{\sqrt{Dt}}e^{-\frac{z^2}{4Dt}}\int_{-\infty}^{+\infty}e^{-y^2}dy=\frac{1}{\sqrt{4\pi Dt}}e^{-\frac{z^2}{4Dt}}$$

$$h(z,t)=\frac{1}{\sqrt{4\pi Dt}}e^{-\frac{z^2}{4Dt}}$$

Also,

$$\frac{1}{D}\frac{1}{h}\frac{\partial h}{\partial t}=\frac{1}{h}\frac{\partial^2 h}{\partial z^2}$$

So,

$$\frac{1}{D}\frac{1}{I}\frac{\partial I}{\partial t}=\frac{1}{g}\frac{\partial^2 g}{\partial r^2}+\frac{1}{g}\frac{1}{r}\frac{\partial g}{\partial r}=-\lambda$$

$$\frac{\partial I}{\partial t}=-\lambda DI$$

So, $I(t)=e^{-\lambda Dt}$

$$\frac{1}{g}\frac{\partial^2 g}{\partial r^2}+\frac{1}{g}\frac{1}{r}\frac{\partial g}{\partial r}=-\lambda$$

Therefore, $g(r)=J_0(\sqrt{\lambda}r)$

So,

$$C(r,z,t) = g(r)h(z,t)I(t) = \sum_1^\infty A_n J_0\left(\sqrt{\lambda_n}r\right)\frac{1}{\sqrt{4\pi Dt}}e^{-\frac{z^2}{4Dt}}e^{-\lambda Dt}$$

From initial condition,

$$C(r,z,0) = C_0\delta(r,z) = C_0\delta(r)\delta(z) = \sum_1^\infty A_n J_0\left(\sqrt{\lambda_n}r\right)$$

$$\int_0^R C_0 J_0\left(\sqrt{\lambda_m}r\right)rdr = \int_0^R A_n J_0\left(\sqrt{\lambda_n}r\right)J_0\left(\sqrt{\lambda_m}r\right)rdr$$

$$A_n = \frac{C_0 J_1^2(\sqrt{\lambda_n}R)}{\frac{R^2}{\sqrt{\lambda_n}}J_1^2(\sqrt{\lambda_n}R)} = \frac{C_0}{\frac{R^2}{\sqrt{\lambda_n}}}$$

Therefore, the general solution is:

$$C(r,z,t) = \sum_n \frac{C_0}{\frac{R^2}{\sqrt{\lambda_n}}}J_0\left(\sqrt{\lambda_n}r\right)\frac{1}{\sqrt{4\pi Dt}}e^{-\frac{z^2}{4Dt}}e^{-\lambda Dt}$$

Parameters

Since morphine is the most commonly used analgesic in intrathecal injection, we will look at the diffusion profiles of morphine under different conditions. The following parameters n Table 1 were obtained from previous literatures [9,10,11,12]. The radius of spinal cord is taken from the average radius of spinal cord in people around 40 years old.

Radius of Spinal Cord (R)	0.79cm
Length of Spinal Cord (L)	45 cm
Diffusivity of Morphine (D)	$3x10^{-6}$ cm^2/s
Morphine Concentration at Injection (C_0)	1 mg/ml

Table 1. Parameters for Modeling

Diffusion Profiles

Concentration Profiles at Different Distances from Injection Site

By using the general solution above, the concentration profiles at different locations along the spinal cord can be investigated. Figure 4 shows concentration profile for radius vs. time at z=10, 20, 40 cm respectively. From these figures, it can be concluded that as z distance is increasing, the time needed to reach the peak value is increasing, meaning the response at these locations are more and more delayed. This phenomenon fits the real data because in real

life, any drug takes some time to be diffused for a certain distance. Moreover, it was noticed that as z position was increasing, the peak values at these positions are decreasing. This observation can also be proved by the fact that as the drug is diffusing to multiple locations, and its total amount is fixed, its concentration will keep decreasing by the time it reaches a certain distance.

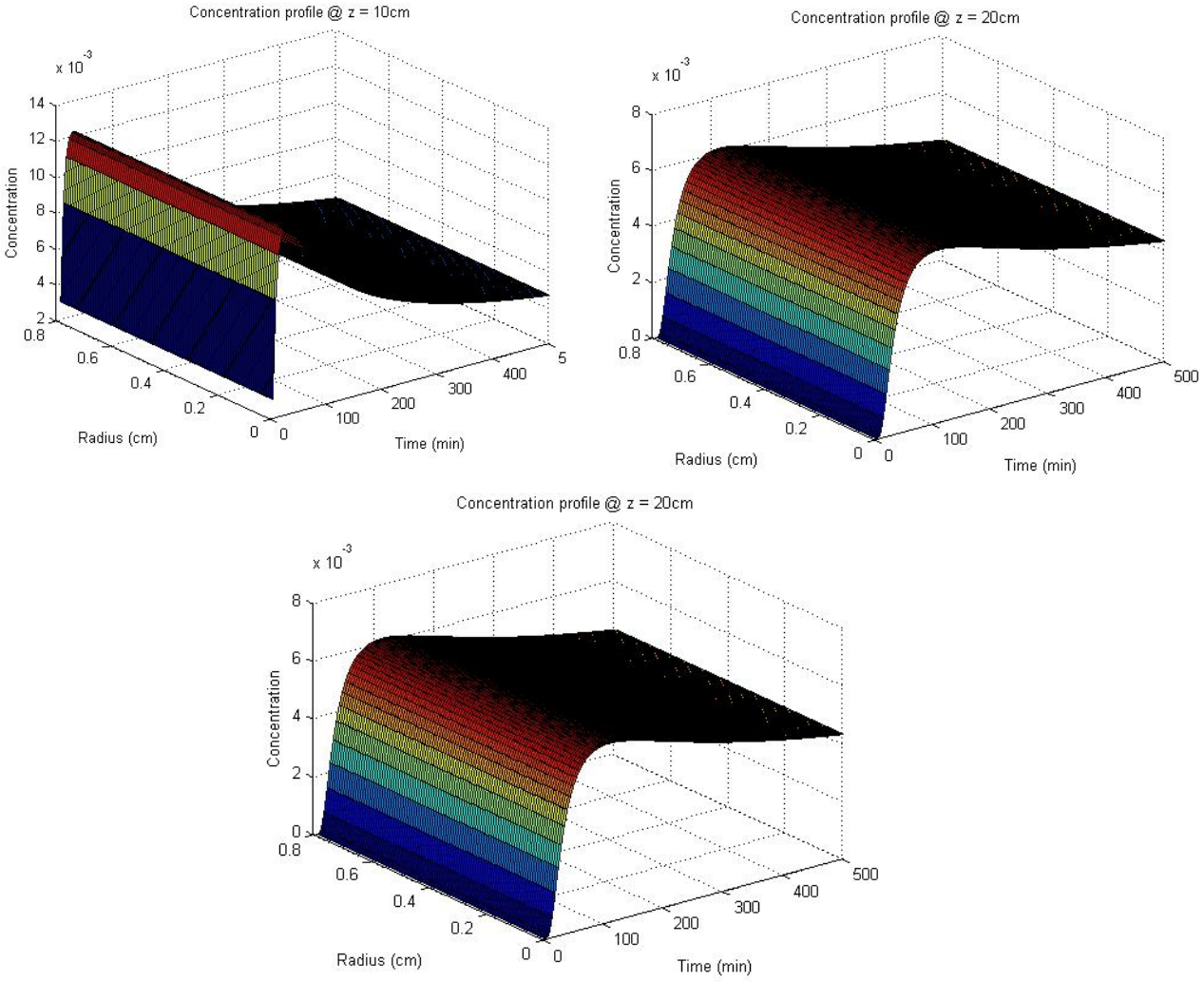

Figure 4. Concentration profiles at 10cm, 20cm, and 40cm from the injection site.

Concentration Profiles at Different Injection Locations From The Brain

Moreover, Figure 5 shows the concentration profile for z-position vs. time with a fixed radius r=0.4cm. From the figure, the concentration profile shows an exponential decrease with both z-position and time, which is also shown in the general solution. Also, the figure demonstrates that as time increases, the concentration at all locations will start decaying together before they achieve the equal concentration.

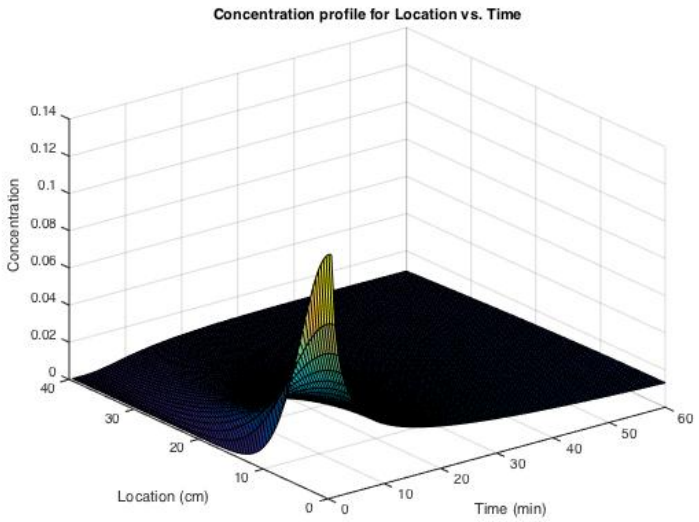

Fig 5. Concentration profiles at different injection locations away from the brain.

Brain Concentration Profiles Among Different Age Groups

In reality, several parameters in the general solution of the model can all be changed to influence the diffuse of the drug. While the spinal cord radius varies among patients of different ages, the doctors can directly control the other parameters. The change in the spinal cord radius needs to be modeled more closely to reality. According to Figure 6 [13], the radius of the spinal cord can be expressed as a linear function of age as follows:

$$R = 0.0602a + 14.593$$

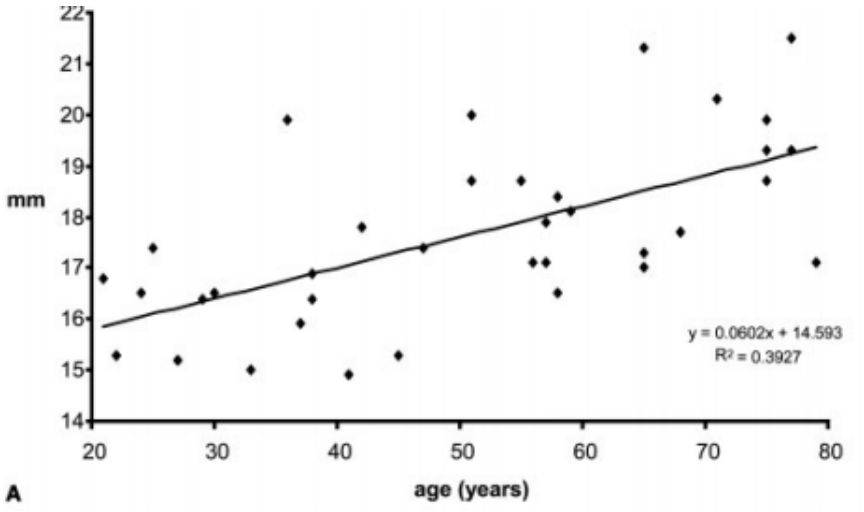

Figure 6. Radius of spinal cord as a function of age

Then, by replacing the spinal cord radius with patients' age in the general solution, the following equation can be reached:

$$C = \sum_n \frac{C_0\sqrt{\lambda_n}}{(0.0602a + 14.593)^2} J_0\left(\sqrt{\lambda_n} r\right) \frac{1}{\sqrt{4\pi Dt}} e^{-\frac{z^2}{4Dt}} e^{-\lambda Dt}$$

After the drug is injected into the spinal cord, it will diffuse to the brain. The concentration of the drug that diffuses to the brain needs to be controlled to prevent overdosing the brain. As a result, we will focus on the maximum concentration of the drug diffusing to the brain across time. In order to further explore the properties of the equation above, the sensitivity of this maximum concentration to different parameters, including patients' age, the injection concentration of the drug as well as the injection distance away from the brain, is investigated.

First, the maximum concentration (C_{max}) is plotted against patients' age and injection distance while fixing the injection concentration at 1mg/ml. The diffusivity coefficient is set to be $3x10^{-6}$ cm^2/s, which is typical for morphine as the most commonly used drug for spinal cord injection. We look at an injection distance starting from 10cm away from the brain because injecting at a too close position is considered unsafe [14]. The result is presented as Figure 7. From Figure 7, it can be seen that C_{max} is far more sensitive to the change in injection distance than to the change in age. C_{max} experiences significant drop with in the first several centimeters of injection distance. On the other hand, it keeps at a relatively stable level across different ages.

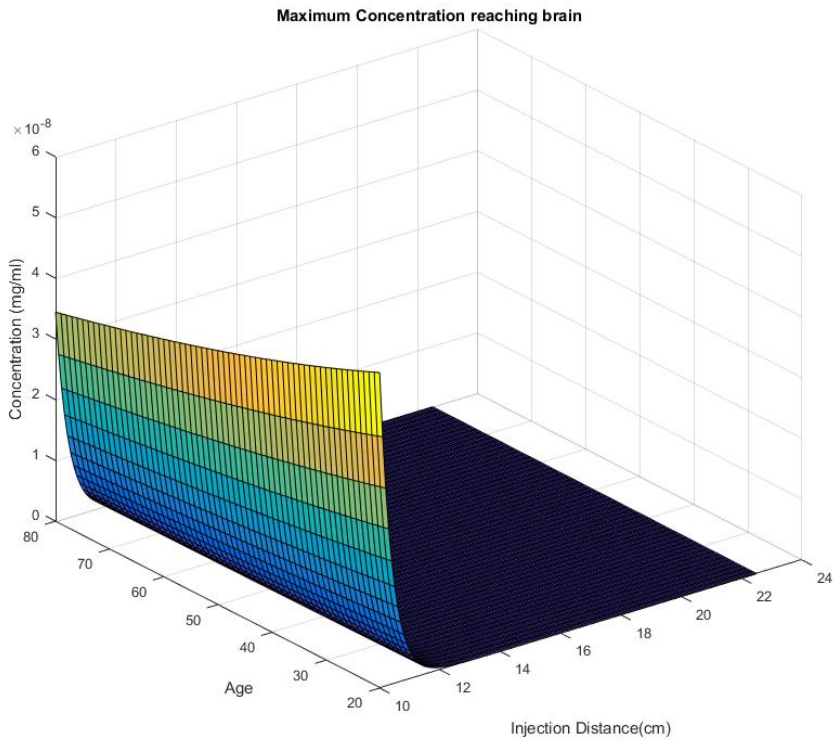

Figure 7. Maximum concentration as a function of age and injection distance

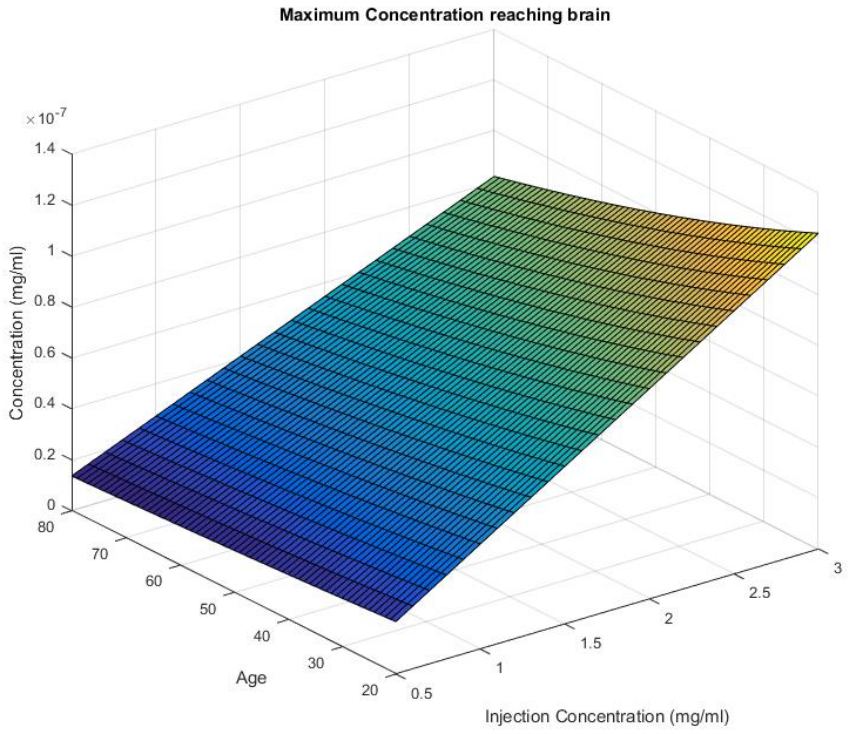

Figure 8. Maximum concentration as a function of injection concentration and age.

Next, fixing the injection distance at 10 cm away from the brain, C_{max} is plotted against patients' age and initial injection concentration of morphine. The resulting Figure 7 shows that though C_{max} increases almost linearly as the injection concentration increases, it remains relatively stable across ages. In other words, C_{max} is much more sensitive to the injection concentration change than to patients' age change.

Figure 7 and Figure 8 show that change in age barely influences the maximum concentration of drug that can diffuse to the brain. This is probably due to that the change in spinal cord radius caused by age difference is too small to significantly affect C_{max}. As a result, the influence age of can be neglected and how C_{max} changes with injection concentration and injection distance is investigated. Figure 9 shows the result. While injection distance turns to have a larger influence on C_{max}, C_{max} expresses significant sensitivity to both parameters. Therefore, in reality, these two parameters will be the primary concerns for the doctors to prevent overdosing the patients' brains.

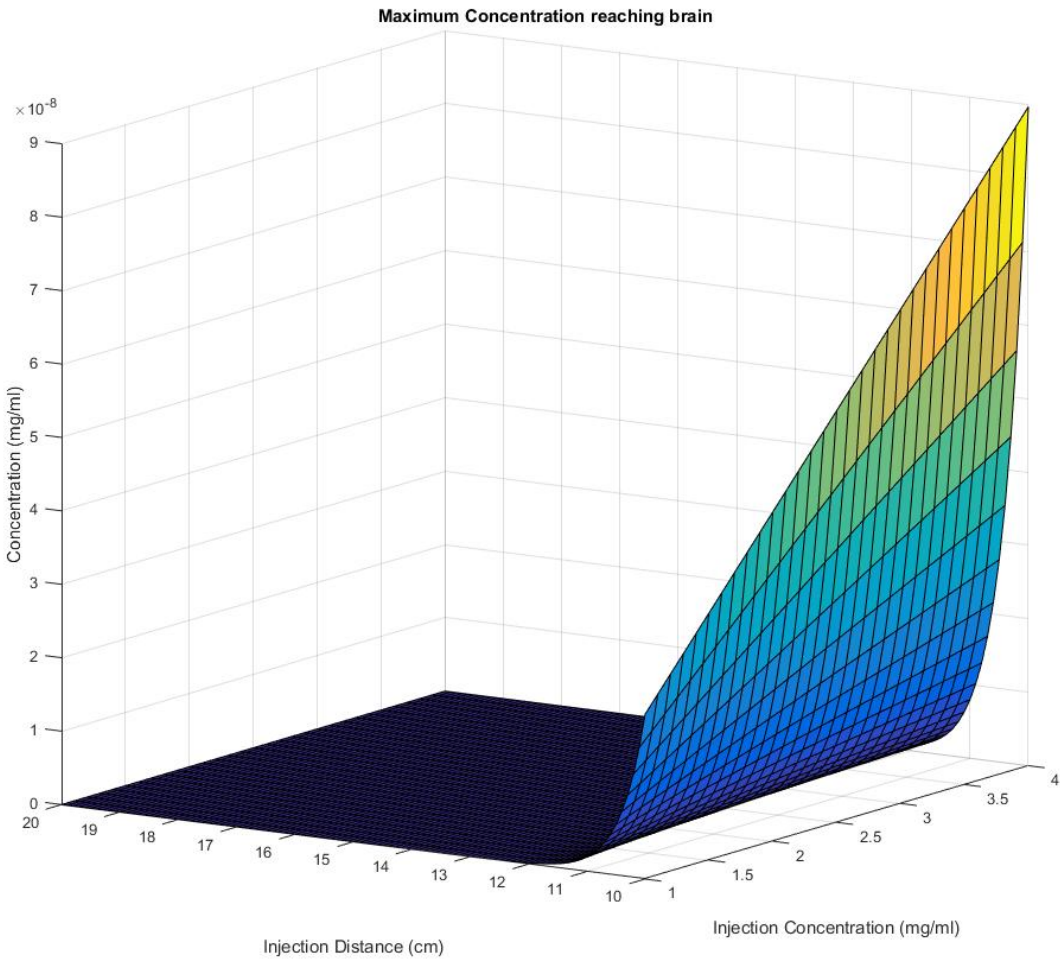

Figure 9. Maximum concentration as a function of injection concentration and injection distance

In order to apply the model more closely into reality, the equation is further manipulated. In reality, the drug like morphine is usually provided at several fixed concentrations. So for convenience consideration, the injection distance (Z) is expressed as a function of injection concentration (C_0) as followed:

$$Z = \sqrt{4Dtln\frac{\sum e^{-\lambda_n Dt}\frac{C_0\sqrt{\lambda_n}}{R^2}}{C_{max}}J_0(\sqrt{\lambda_n}R)}$$

To not overdose the brain, the maximum concentration of morphine that diffuses to the brain needs to be kept under 10^{-9}mg/ml [15]. Instead of diluting the morphine, the doctors can simply use this equation to compute a distance away from the brain to inject morphine into patients' spinal cord safely. Figure 10 shows a relationship between morphine's concentration and safe injection distance using equation. It makes sense in that as the injection concentration increases, the safe injection distance gets further away from the brain but with a decreasing growing rate. The decreasing growing rate is probably due to that as the injection distance

increases, more of the drug will diffuse towards the radial direction of the spinal cord and thus the concentration diffusing to the brain is decreased.

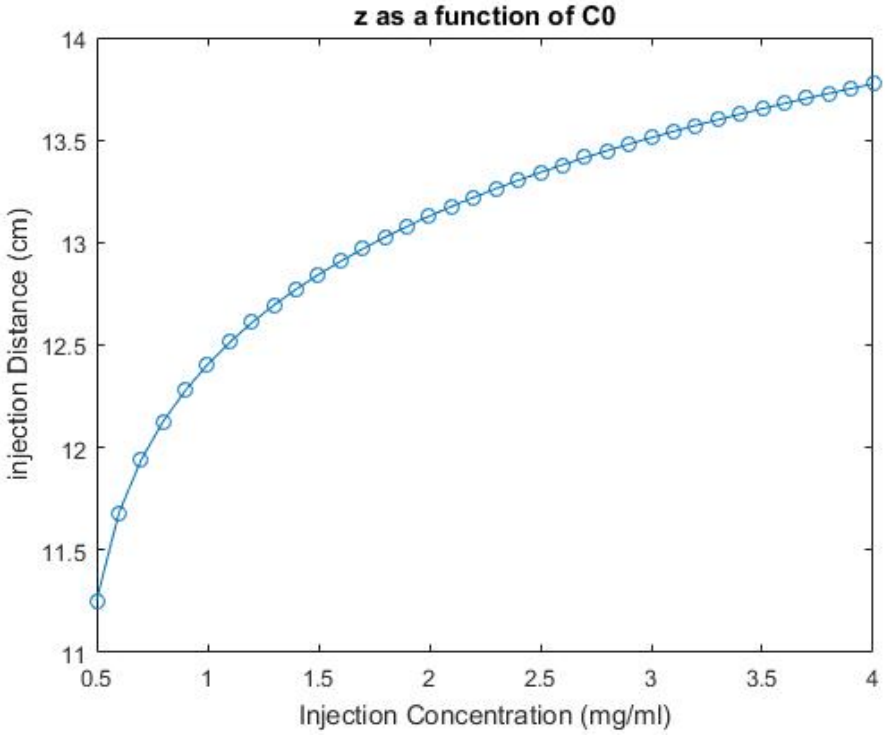

Figure 10. Injection distance as a function of injection concentration for morphine

Conclusion

From the results, it can be demonstrated that our model can well simulate the diffusion profile of real-world intrathecal drug injection. This model was also proved to be able to predict maximum injection concentration and the ideal injection location for any patients in a specific age group. However, there are still some limitations. For example, the overall shape of the cerebrospinal fluid is assumed to be a perfect cylinder with same radius everywhere. However, in real life, its structure is irregular as its radius varies at different locations, and the overall shape is s-shaped. Such assumption may lead to a small error with our final results, but we cannot build a more accurate model without clinical data. Also, zero-flux boundary condition was assumed at r=R, meaning CSF is isolated from external environment. However, in real life, CSF keeps circulating with external environment. This assumption is used to simplify the calculation. Also, Bessel function can hardly be used to solve the problem without such assumption. Moreover, the injection is assumed to be an impulse. However, in real life, injection usually takes several seconds. The reason why we used this assumption above is to simplify the initial condition. This limitation could hugely affect our results since concentration at some specific locations can easily be altered by several folds. Nonetheless, we amplified the signal in order to limit the effects of this limitation.

In the future, more clinical datasets are needed in order to well estimate the shape, or the structure of cerebrospinal fluid. Also, finite element method could be an ideal method to analyze diffusion profiles parts by parts.

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Code

```
%Bessel_roots = [2.4048 5.5201 8.6537 11.7915 14.9309];
Bessel_roots = [0, 3.8317, 7.0156,10.1735,13.3237];


R = 0.79; %cm
D = 3e-2;% mm/s
C_0 = 1;
z = 40; %cm
simt = 500;% min
simt = simt*60;
num_points = 100;
sqt_lambda= Bessel_roots/R;
lambda = sqt_lambda.^2;
A_n = @(i) (C_0)/((R^2*pi));
r_range = linspace(0,R,num_points);
t_range = linspace(0,simt,num_points);
[r_mesh,t_mesh] = meshgrid(r_range,t_range);

u_analytical= zeros(size(r_mesh));

for i = 1:5
    u_analytical = u_analytical +
A_n(i).*besselj(0,sqt_lambda(i)*r_mesh).*...
        (1./sqrt(4*pi*D*t_mesh)).*exp(-(z^2)/4/D./t_mesh).*exp(-
lambda(i)*D.*t_mesh);
end
rotate3d
surf(t_mesh./60, r_mesh,u_analytical)
xlabel('Time (min)')
ylabel('Radius (cm)')
zlabel('Concentration')
title(['Concentration profile @ z = ',num2str(z),'cm'])


bessj0 = inline('besselj(0,x)');

for n = 1:10
   z(n) = fzero(bessj0,[(n-1) n]*pi);
   %compute eigenvalue
   eVec(n)=z(n)*z(n);
end

tmesh=0:300;
C0=4.46*10^(-1);
D=3.1*10^(-1);
z=2;
ageVec=20:80;
RVec=(0.0602*ageVec+14.593)/2/10;
A=@(lumN,R) C0*sqrt(lumN)/(R^2*besselj(1,sqrt(lumN)*R));
n=10;

maxVec=zeros(1,length(RVec));
for i=1:length(RVec)
   rmesh=linspace(0,RVec(i));
```

```
    cMesh=zeros(length(rmesh),length(tmesh));
    for j=1:n
        cMesh=cMesh+A(eVec(j),RVec(i)).* besselj(0,sqrt(eVec(j)).*rmesh)'...
            *(1./sqrt(4*pi*D*tmesh).*exp(-z^2./(4*D*tmesh)).*exp(-
eVec(j)*D*tmesh));

    end
    maxVec(i)=max(max(cMesh));


end

plot(ageVec,maxVec);

% C=@(n,C0,lumN,R,D,r,t) A(n,C0,lumN,R)*besselj(0,sqrt(lumN)*r)...
%     *1/sqrt(4*pi*D*t);

bessj0 = inline('besselj(0,x)');

for n = 1:10
    z(n) = fzero(bessj0,[(n-1) n]*pi);
    %compute eigenvalue
    eVec(n)=z(n)*z(n);
end

tmesh=0:300;
C0=2000;
D=3.1*10^(-1);
zVec=10:0.1:22.5;
ageVec=20:80;
RVec=(0.0602*ageVec+14.593)/2/10;
% A=@(lumN,R) C0*sqrt(lumN)/(R^2*besselj(1,sqrt(lumN)*R));
A=@(lumN,R) C0*sqrt(lumN)/(R^2);

n=10;

cFinalMesh=zeros(length(ageVec),length(zVec));
for k=1:length(zVec)
    z=zVec(k);
    maxVec=zeros(1,length(RVec));
    for i=1:length(RVec)
        rmesh=linspace(0,RVec(i));
        cMesh=zeros(length(rmesh),length(tmesh));
        for j=1:n
            cMesh=cMesh+A(eVec(j),RVec(i)).*
besselj(0,sqrt(eVec(j)).*rmesh)'...
            *(1./sqrt(4*pi*D*tmesh).*exp(-z^2./(4*D*tmesh)).*exp(-
eVec(j)*D*tmesh));

        end
        maxVec(i)=max(max(cMesh));


    end
```

```
   cFinalMesh(:,k)=maxVec;
end

surf(zVec,ageVec,cFinalMesh)
xlabel('Injection Distance(cm)')
ylabel('Age')
title('Maximum Concentration reaching brain')
zlabel('Concentration (mg/ml)')

bessj0 = inline('besselj(0,x)');

for n = 1:10
   z(n) = fzero(bessj0,[(n-1) n]*pi);
   %compute eigenvalue
   eVec(n)=z(n)*z(n);
end

tmesh=0:300;
C0Vec=0.5:0.1:3;

D=3.1*10^(-1);
z=7;
ageVec=20:80;
RVec=(0.0602*ageVec+14.593)/2/10;
A=@(C0,lumN,R) C0*sqrt(lumN)/(R^2);
n=10;

cFinalMesh=zeros(length(ageVec),length(C0Vec));
for k=1:length(C0Vec)
   C0=C0Vec(k);
   maxVec=zeros(1,length(RVec));
   for i=1:length(RVec)
       rmesh=linspace(0,RVec(i));
       cMesh=zeros(length(rmesh),length(tmesh));
       for j=1:n
           cMesh=cMesh+A(C0,eVec(j),RVec(i)).*
besselj(0,sqrt(eVec(j)).*rmesh)'...
           *(1./sqrt(4*pi*D*tmesh).*exp(-z^2./(4*D*tmesh)).*exp(-
eVec(j)*D*tmesh));

       end
       maxVec(i)=max(max(cMesh));


   end
   cFinalMesh(:,k)=maxVec;
end

surf(C0Vec,ageVec,cFinalMesh)
xlabel('Injection Concentration (mg/ml)')
ylabel('Age')
title('Maximum Concentration reaching brain')
zlabel('Concentration (mg/ml)')

bessj0 = inline('besselj(0,x)');
```

```
for n = 1:10
   z(n) = fzero(bessj0,[(n-1) n]*pi);
   %compute eigenvalue
   eVec(n)=z(n)*z(n);
end

tmesh=0:300;
C0Vec=1000:100:4000;

D=3.1*10^(-1);
zVec=10:0.1:20;
age=40;
R=(0.0602*age+14.593)/2/10;
%A=@(C0,lumN,R) C0*sqrt(lumN)/(R^2*besselj(1,sqrt(lumN)*R));
A=@(C0,lumN,R) C0*sqrt(lumN)/(R^2);
n=10;

cFinalMesh=zeros(length(zVec),length(C0Vec));
for k=1:length(C0Vec)
   C0=C0Vec(k);
   maxVec=zeros(1,length(zVec));
   for i=1:length(zVec)
       z=zVec(i);
       rmesh=linspace(0,R);
       cMesh=zeros(length(rmesh),length(tmesh));
       for j=1:n
           cMesh=cMesh+A(C0,eVec(j),R).* besselj(0,sqrt(eVec(j)).*rmesh)'...
           *(1./sqrt(4*pi*D*tmesh).*exp(-z^2./(4*D*tmesh)).*exp(-
eVec(j)*D*tmesh));

       end
       maxVec(i)=max(max(cMesh));


   end
   cFinalMesh(:,k)=maxVec;
end
figure()
surf(C0Vec./1000,zVec,cFinalMesh)
xlabel('Injection Concentration (mg/ml)')
ylabel('Injection Distance (cm)')
title('Maximum Concentration reaching brain')
zlabel('Concentration (mg/ml)')

bessj0 = inline('besselj(0,x)');

for n = 1:10
   z(n) = fzero(bessj0,[(n-1) n]*pi);
   %compute eigenvalue
   eVec(n)=z(n)*z(n);
end

Cmax=1.0e-12;
%C0Vec=2*10^(-2):0.005:0.1;
```

```
C0Vec=0.5:0.1:4;
D=3.1*10^(-1);
zVec=zeros(1,length(C0Vec));
t=10;
age=40;
R=(0.0602*age+14.593)/2/10;
%A=@(lumN,R,C0) C0*sqrt(lumN)/(R^2*besselj(1,sqrt(lumN)*R));
A=@(lumN,R,C0) C0*sqrt(lumN)/(R^2);
sumFac=0;



for j=1:length(C0Vec)
   C0=C0Vec(j);
   for i=1:10
       sumFac=sumFac+A(eVec(i),R,C0)*exp(-eVec(i)*D*t);
   end

   zVec(j)=sqrt(4*D*t*log(sumFac/Cmax));


end
figure()
%f = fit(C0Vec',zVec','poly2')
plot(C0Vec,zVec,'-o')
xlabel('Injection Concentration (mg/ml)')
ylabel('injection Distance (cm)')
title('z as a function of C0')
```