# Diffusion of Neurotransmitters

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**Abstract**

*In this project we will model the diffusion of neurotransmitters in the synaptic cleft. This is the dominant mechanism for transporting signals between neurons. Fick's second law of diffusion is used to predict how the concentration of neurotransmitters change over time, and we will solve this equation by three different methods. The implicit forward Euler method, the explicit backward Euler method, and the explicit Crank-Nicolson scheme. The source code for this project can be found at www.github.com/vegardbs/diffusion*

## I. Introduction

In this section we give some information about the biological system we are investigating, followed by a closed form solution to the diffusion equation in that system. Lastly we discuss the differences between explicit and implicit algorithms.

### I. The Synapse

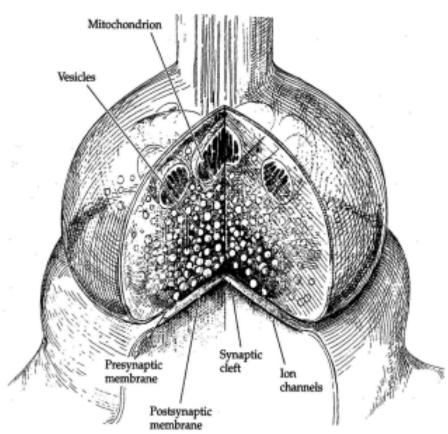


**Figure 1:** *A sketch of the internal components of a synapse. The top structure is the axon of a neuron and the bottom knob-like structure is the receiving neuron.*

A synapse is the junction through which neurons signal each other and to non-neuronal cells like muscles or glands. A sketch of a synapse is found in Fig. 1. Synapses allow neurons to form connected circuits within the body and are crucial biological components that form the basis of thought and perception.

An electrochemical wave (action potential) travels along the axon of a neuron. Once the action potential reaches the synaptic cleft, which separates the sending and receiving cells, neurotransmitters are released into it. The neurotransmitters diffuse across the synaptic cleft. Once they reach the other side of the cleft (the post-synaptic membrane) they bind to receptors and are transported across. In our model we assume the following:

- The influx of neurotransmitters from the presynaptic side is constant, thus the concentration is at a maximum there.
- Neurotransmitters reaching the receptors at the postsynaptic side is instantly absorbed through the membrane, thus the concentration there is zero.
- There are no neurotransmitters in the cleft for t<0.

## II. Closed Form Solution

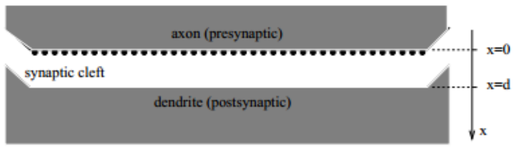


**Figure 2:** *A one-dimensional model of the synaptic cleft, shown here at t=0.*

In Fig.2 a 1D model of the synaptic cleft is shown. The distance between the pre and post-synaptic membrane is d. We now consider the diffusion of the neurotransmitters across this area. Fick's second law of diffusion in one dimension is mathematically described by

$$\frac{\partial u(x,t)}{\partial t} = D\frac{\partial^2 u(x,t)}{\partial x^2} \tag{1}$$

Here $u(x,t)$ is the concentration of particles at position x and time t, and D is the diffusion constant. The assumptions listed above is mathematically expressed as

- $u(0,t) = u_0 = 1$, for $t \geq 0$
- $u(d,t) = u(1,t) = 0$, for $t \geq 0$
- $u(x,0) = 0$, for $0 < x < 1$

Here we have set $d = 1$ (the length of the cleft) and $u_0 = 1$ (the maximum concentration). We begin by redefining the steady state solution. It can easily be found to be

$$u_s(x) = 1 - x$$

We define a new function, $v(x)$, with the properties

$$v(x) = u(x) - u_s(x)$$

and boundary conditions $v(0) = v(1) = 0$. To solve this we assume that the solution is separable and we can write.

$$v(x,t) = v(x)v(t)$$

Inserting this expression into Eq.1 and dividing by $v(x)v(t)$ on both sides we obtain

$$D\frac{v''(x)}{v(x)} = \frac{v'(t)}{v(t)}$$

Since the right side has to be equal to the left side we can define a constant of separation $\lambda$

$$D\frac{v''(x)}{v(x)} = \frac{v'(t)}{v(t)} = -\lambda^2$$

Thus we have two equations of two different variables.

$$v''(x) + \lambda^2 v(x) = 0$$

and

$$v'(t) + D\lambda^2 v(t) = 0$$

The solution of these equations are

$$v(x) = A\sin(\lambda x) + B\cos(\lambda x)$$

$$v(t) = Ce^{-\lambda^2 Dt}$$

With the boundary conditions previously mentioned we find that $B = 0$ and $\lambda = n\pi$ where $n = \pm 0, \pm 1, \pm 2...$ By connecting the two solutions again we obtain

$$v(x,t) = v(x)v(t) = A_n sin(n\pi x)e^{-D(n\pi)^2 t}$$

This solution is valid for any n. Since the diffusion equation is linear, a superposition of solutions for various n will also be a solution. Thus we write the solution as a sum

$$v(x,t) = \sum_{n=1}^{\infty} A_n \sin(n\pi x)e^{-D(n\pi)^2 t}$$

Invoking the last boundary condition $u(x,0) = 0$ or similarly $v(x,0) = x - 1$ we obtain the following equation

$$u(x,0) = x - 1 = \sum_{n=1}^{\infty} A_n \sin(n\pi x)$$

The constant $A_n$ can now be found from the theory of Fourier series, and it is defined as

$$A_n = 2\int_0^1 (x-1)sin(n\pi x)dx = -\frac{2}{n\pi}$$

Inserting this into the previous solution we have

$$v(x,t) = -\sum_{n=1}^{\infty} \frac{2}{n\pi}\sin(n\pi x)e^{-D(n\pi)^2 t} \tag{2}$$

or

$$u(x,t) = 1 - x - \frac{2}{n\pi}\sum_{n=1}^{\infty}\sin(n\pi x)e^{-D(n\pi)^2 t} \tag{3}$$

## III. Implicit and Explicit algorithms

Explicit and implicit methods are approaches used in numerical analysis for obtaining numerical solutions of time-dependent ordinary and partial differential equations.

Explicit methods calculate the state of a system at a later time from the state of the system at the current time, while implicit methods find a solution by solving an equation involving both the current state of the system and the later one.

## II. Methods

We want to use three different algorithms to solve the differential equation

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2}$$

using three different algorithms.

1. The explicit forward Euler algorithm
2. The implicit backward Euler algorithm
3. The implicit Crank-Nicolson algorithm

In the following section we use the short hand $u_{i,j} = u(x_i, t_j)$, $u_{i+1,j+1} = u(x_i + \Delta x, t_j + \Delta t)$, etc.

### I. Forward Euler

We use the standard approximation for the derivatives to obtain

$$u_t = \frac{u_{i,j+1} - u_{i,j}}{\Delta t}$$

with a truncation error that goes like $O(\Delta t)$, and

$$u_{xx} = \frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\Delta x^2}$$

with a truncation error that goes like $O(\Delta x^2)$. Setting $Du_{xx} = u_t$ and defining

$$\alpha = D\frac{\Delta t}{\Delta x^2}$$

we find the explicit scheme

$$u_{i,j+1} = \alpha u_{i-1,j} + (1-2\alpha)\,u_{i,j} + \alpha u_{i+1,j} \quad (4)$$

This is an explicit scheme since we can find any unknown quantity $u_{i,j}$ by using the previously calculated $u_{i,j-1}$. The truncation error for this scheme is $O(\Delta x^2)$ and $O(\Delta t)$.

### II. Backward Euler

In the backward Euler method we use the backward definition of the derivative and obtain

$$u_t = \frac{u_{i,j} - u_{i,j-1}}{\Delta t}$$

again with a truncation error $O(\Delta t)$, and

$$u_{xx} = \frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\Delta x^2}$$

with a truncation error of $O(\Delta x^2)$. We define the same $\alpha$ as in the forward Euler case, and setting these expression into Eq.1 we now obtain

$$u_{i,j-1} = -\alpha u_{i-1,j} + (1-2\alpha)u_{i,j} - \alpha u_{i+1,j} \quad (5)$$

This is an implicit algorithm since it relies on determining the vector $u_{i,j-1}$ instead of $u_{i,j+1}$. We can write this as a matrix-vector multiplication where the matrix is a tridiagonal matrix.

$$\hat{A} = \begin{bmatrix} 1+2\alpha & -\alpha & 0 & ... & 0 \\ -\alpha & 1+2\alpha & -\alpha & ... & 0 \\ 0 & -\alpha & 1+2\alpha & ... & 0 \\ 0 & ... & ... & ... & -\alpha \\ 0 & ... & ... & -\alpha & 1+2\alpha \end{bmatrix}$$

$$\vec{U}_j = \begin{bmatrix} u_1, j \\ u_2, j \\ u_3, j \\ \cdots \\ u_n, j \end{bmatrix}$$

Thus the algorthm can be expressed as

$$\hat{A}\vec{U}_j = \vec{U}_{j-1}$$

The truncation error for this scheme is $O(\Delta x^2)$ and $O(\Delta t)$.

## III. Crank-Nicolson

The Crank-Nicolson scheme is a combination of the implicit forward Euler and the explicit backward Euler. The scheme yields a truncation in time which goes like $O(\Delta t^2)$. By Taylor expanding the backward and forward Euler schemes, we obtain

$$-\alpha u_{i-1,j} + (2+2\alpha)u_{i,j} - \alpha u_{i+1,j} =$$

$$\alpha u_{i-1,j-1} + (2-2\alpha)u_{i,j} + \alpha u_{i+1,j+1}$$

We can also define this as a matrix-vector multiplication with $U_j$ as defined previously, and the matrix $\hat{B}$ defined as

$$\hat{B} = \begin{bmatrix} 2 & -1 & 0 & ... & 0 \\ -1 & 2 & -1 & ... & 0 \\ 0 & -1 & 2 & ... & 0 \\ 0 & ... & ... & ... & -1 \\ 0 & ... & ... & -1 & 2 \end{bmatrix}$$

Now the Crank-Nicolson scheme can be defined as

$$\left(2\hat{I} + \alpha\hat{B}\right)\vec{U}_j = \left(2\hat{I} - \alpha\hat{B}\right)\vec{U}_{j-1}$$

The truncation error for this scheme is $O(\Delta x^2)$ and $O(\Delta t^2)$.

## IV. Spectral Radius and Stability

To require that the solution of the different schemes approaches a definite value, we need to require that the spectral radius $\rho(\hat{A})$ satisfy

$$\rho(\hat{A}) = max\left\{|\lambda| : det(\hat{A} - \lambda\hat{I})\right\} < 1$$

A general tridiagonal matrix

$$\hat{A} = \begin{bmatrix} a & b & 0 & ... & 0 \\ c & a & b & ... & 0 \\ 0 & c & a & ... & 0 \\ 0 & ... & ... & ... & b \\ 0 & ... & ... & c & a \end{bmatrix}$$

has eigenvalues $\lambda_i = a + s\sqrt{bc}\cos(i\pi/n+1)$ where i=1:n. If all eigenvalues are lager than zero, stability is guaranteed, since the spectral radius is smaller than 1. For the three algorithms discussed, their stability is thus ensured with the following conditions:

**Forward Euler** $-1 < 1 - \alpha 2(1 - cos(\theta)) < 1$ which gives $\alpha = \Delta t/\Delta x^2 \leq 1/2$

**Backward Euler** $\lambda_i = 1 + \alpha(2 - 2cos(\theta))$ which is always larger than 1, thus the matrix is positive definite and the scheme is always stable.

**Crank-Nicolson** Here the spectral radius has to satisfy $|(2+\alpha\lambda_i)^{-1}(2-\alpha\lambda_i)| < 1$, and since $\lambda = 2 - 2cos(\theta)$, this scheme is table for all values of $\alpha$

## III. Results

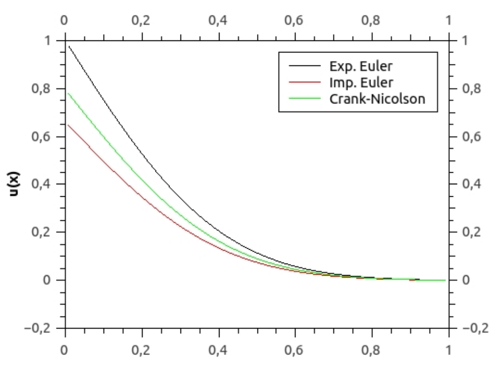


**Figure 3:** *Particle density over the synaptic cleft at t = 0.05 sec.*

In Figure 3. we have plotted $u(x,t)$ vs $x$ at $t = 0.05$ sec, for the three different schemes. We see that at this time the solution is still exponential and has not reached a stable state.

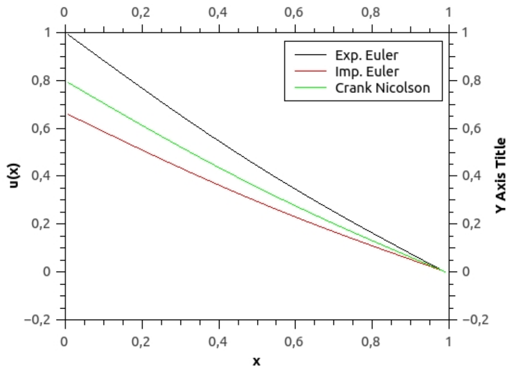


**Figure 4:** *Particle density over the synaptic cleft at t = 0.25 sec.*

In Figure 4. $u(x,t)$ is plotted again, but this time $t = 0.25$ sec. At this time the solution is close the stable linear decay at equilibrium.

The closed form solution was found previously to be

$$u(x,t) = 1 - x - \frac{2}{n\pi}\sum_{n=1}^{\infty}\sin(n\pi x)e^{-D(n\pi)^2 t}$$

The exponential term dominates the solution at low t, so the solution should approach 0 fast as a function of x. As t increases the solution converges towards $u(x,t) = 1 - x$, which is a linear solution. All three of our methods satisfy this behaviour.

In Table 1. we have listed all the properties of the different schemes. All of the solutions gave good results, however the Crank-Nicolson should be the preferred method of solution since it is stable for $\alpha$ and has the smallest truncation error for all the schemes.

**Table 1:** *Algorithm properties*

| Scheme | Truncation Error | Stability |
|---|---|---|
| Forward Euler | $O(\Delta x^2)$ and $O(\Delta t)$ | $\alpha \leq 1/2$ |
| Backward Euler | $O(\Delta x^2)$ and $O(\Delta t)$ | All $\alpha$ |
| Crank-Nicolson | $O(\Delta x^2)$ and $O(\Delta t^2)$ | All $\alpha$ |

## IV. Conclusion

In this project we have solved the diffusion equation for a system of neurotransmitters moving across the synaptic cleft. We solved the equation analytically, and with three different computational schemes. All the schemes gave good results, but the Crank-Nicolson is the most ideal since it is always stable and has the smallest truncation error. The forward Euler is the easiest to implement, but it is only stable for $\alpha \leq 1/2$ which limits its usefulness. In accordance with the analytical solution the numerical solutions were exponential decays at low t, and near linear decays at high t.