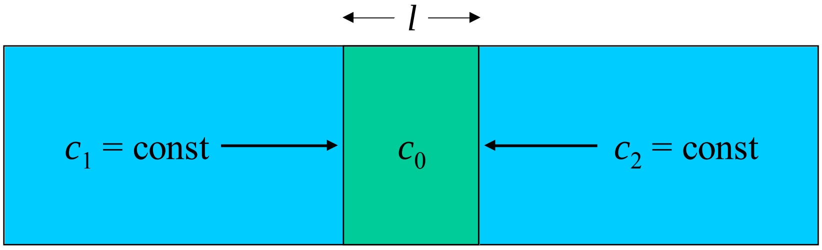
Diffusion through a plane sheet

- Diffusion through a plane sheet models flow through a membrane



- At the start: concentration in the membrane c_0
- Concentration c_0 changes until steady-state is established
- Common experimental setting: $c_0 = c_2 = 0$

Diffusion through a plane sheet

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- Boundary conditions: $c_0 = c_2 = 0$
- Solution:

$$\frac{q(t)}{lKc_1} = \frac{Dt}{l^2} - \frac{1}{6} - \frac{2}{\pi^2} \sum_{1}^{\infty} \frac{(-1)^n}{n^2} \exp\left(-Dn^2\pi^2 t / l^2\right)$$

- With $t \longrightarrow \infty$:

$$q(t) = \frac{DKc_1}{l}\left(t - \frac{l^2}{6D}\right)$$

- Intercept (lag time):

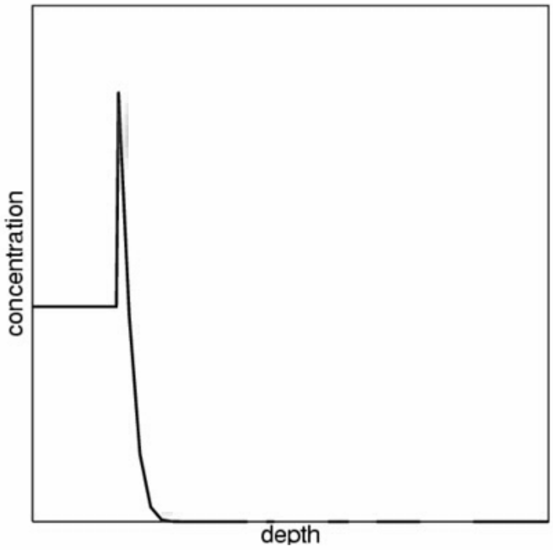
$$L = \frac{l^2}{6D}$$

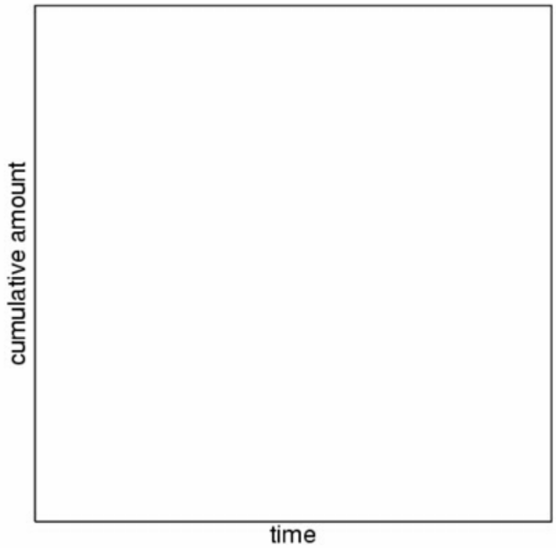
Diffusion through a plane sheet

Concentration-depth profile

Cumulated drug

Donor Barrier Akzeptor



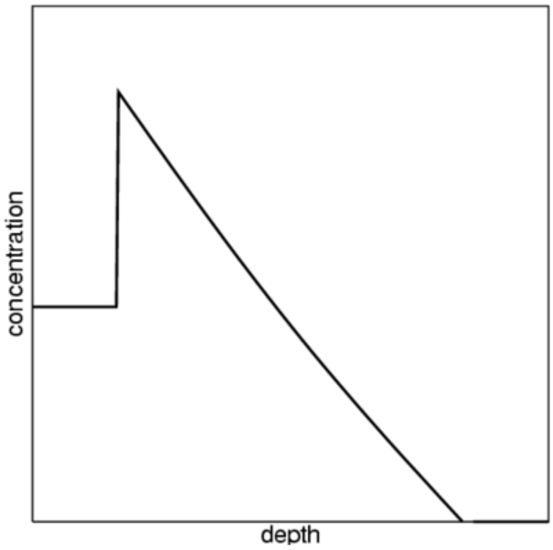


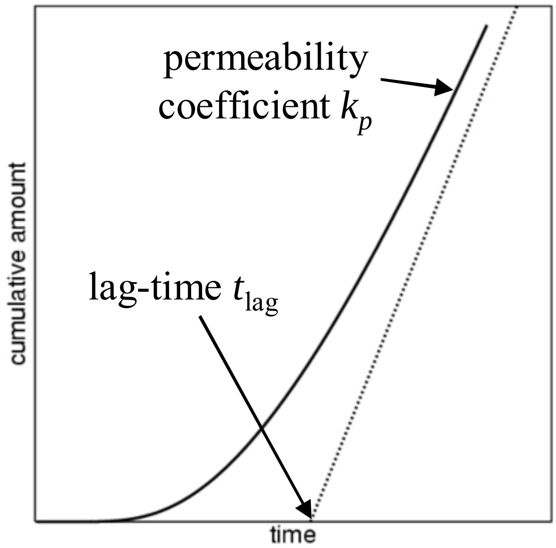
Permeability and lag-time

Concentration-depth profile

Cumulated drug

Donor Barrier Akzeptor





Time dependent solutions for Fick‘s second law: Diffusion from a single spot

- Point source of particles (*e.g.*, injection, small crystal)
- $t = 0$, all n_0 molecules at $r = 0$
- Concentration is finite at all points
- Number of particles is constant

- Flux is radial $$J_r = -D\frac{\partial c}{\partial r}$$

- Remember: $$\frac{\partial c}{\partial t} = -\frac{\partial J_r}{\partial r}$$

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

Time dependent solutions for Fick‘s second law: Diffusion from a single spot

- Point source of particles (*e.g.*, injection, small crystal)
- Diffusion is spherically symmetric
- $t = 0$, all n_0 molecules at $r = 0$
- Concentration is finite at all points
- Number of particles is constant

- The solution is:

$$c(r,t) = \frac{n_0}{(4\pi Dt)^{3/2}}\mathrm{e}^{-\frac{r^2}{4Dt}}$$

Steady-state solutions

- Sources
  - create particles
- Adsorbers
  - destroy particles

- Non-uniform distribution of particles
- Steady-state:

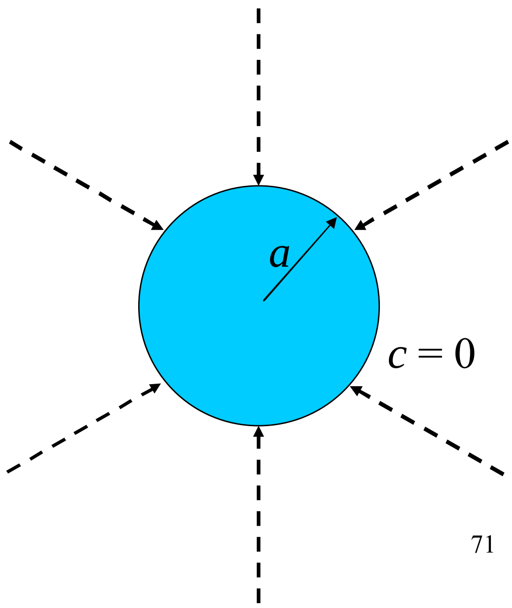
$$\frac{\partial c}{\partial t} = \nabla^2 c = 0$$

- Solution for spherically symmetric diffusion processes:

$$D \frac{1}{r^2} \frac{\partial}{\partial r}\left(r^2 \frac{\partial c}{\partial r} \right) = 0$$

Spherical adsorber

- Spherical adsorber of radius *a*
- Boundary conditions:
  - concentration at surface is 0, *i.e.*, $c(a,t) = 0$
  - concentration at infinite distance is c_0 = const



Spherical adsorber

- Spherical adsorber of radius *a*
- Boundary conditions:
  - concentration at surface is 0, *i.e.*, $c(a,t) = 0$
  - concentration at infinite distance is c_0 = const
- Solution:

$$c(r) = c_0\left(1 - \frac{a}{r}\right)$$

$$J_r(r) = -D\frac{\partial c}{\partial r} = -Dc_0\frac{a}{r^2}$$

Diffusion current

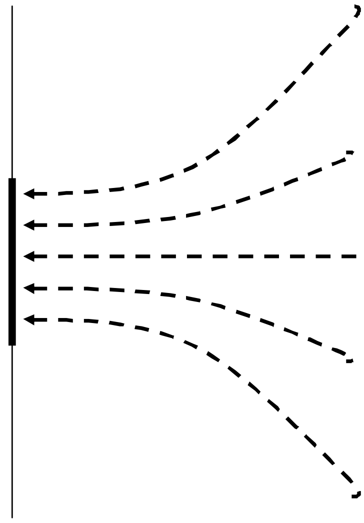
- Remember:
  - Flux $J_r(a)$ = number of particles entering the sphere per unit area in time τ
- Particles are adsorbed by the sphere at the rate flux * surface area:

$$I = -J_r(a) * 4\pi a^2$$
$$= 4\pi D a c_0$$

- I is called **diffusion current**

Disk-like adsorber

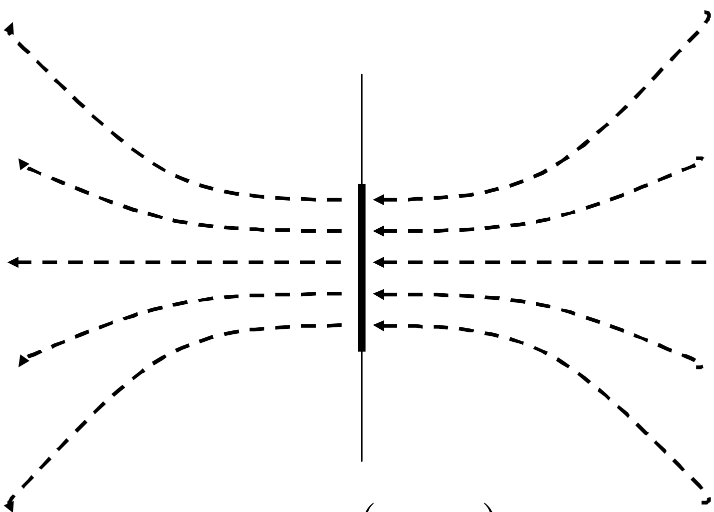
- Cylindrically symmetric problem
- Boundary conditions:
  - concentration at surface is 0
  - concentration at infinite distance is c_0 = const



$$I = 4Dsc_0$$

Disk-like aperture

- Cylindrically symmetric problem
- Boundary conditions:
  - concentration at surface is 0
  - concentration at distance x = -∞ is c_1 = const
  - concentration at distance $x = \infty$ is c_2 = const



$$I = 2Ds(c_2 - c_1)$$

Disk-like adsorbers on a sphere

- Nonadsorbing sphere of radius a
- N disk-like adsorbers of radius $s << a$
- Concentration at $r = \infty$ is c_0
- For small N: $I \propto N\, 4Dsc_0$
- For large N: $I = 4\pi Dac_0$

Disk-like adsorbers on a sphere

- In analogy to electricity: V c_0

$$I = V / R \qquad I = c_0 / R$$

- Diffusion resistance for sphere: $R_a = 1/4\pi Da$
- Diffusion resistance for each disk: $R_s = 1/4Ds$
- Total resistance: $R = R_a + R_s/N = 1/4\pi Da + 1/4DNs$

$$\begin{aligned} R &= R_a + R_s / N \\ &= \frac{1}{4\pi Da} + \frac{1}{4DNs} \\ &= \frac{1}{4\pi Da}\left(1 + \frac{\pi a}{Ns}\right) \\ &= R_a\left(1 + \frac{\pi a}{Ns}\right) \end{aligned}$$

Disk-like adsorbers on a sphere

- Solution:

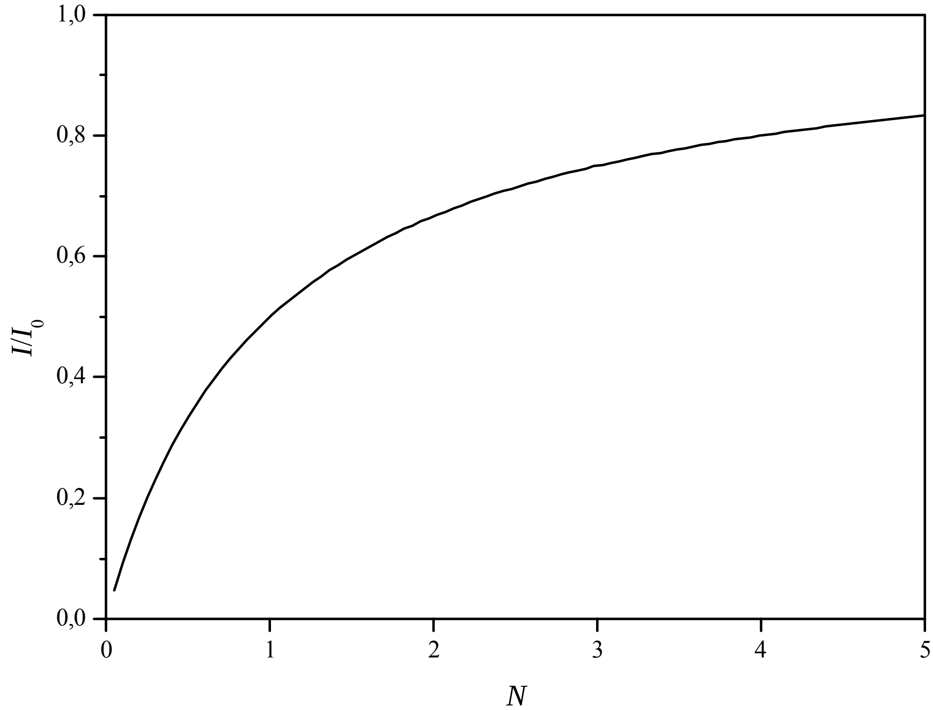
$$I = \frac{4\pi D a c_0}{1 + (\pi a / Ns)}$$

$$\frac{I}{I_0} = \frac{1}{1 + (\pi a / Ns)}$$

- The half maximum of I/I_0 is at:

$$N = \frac{\pi a}{s}$$

Disk-like adsorbers on a sphere



Disk-like adsorbers on a sphere

- Example:

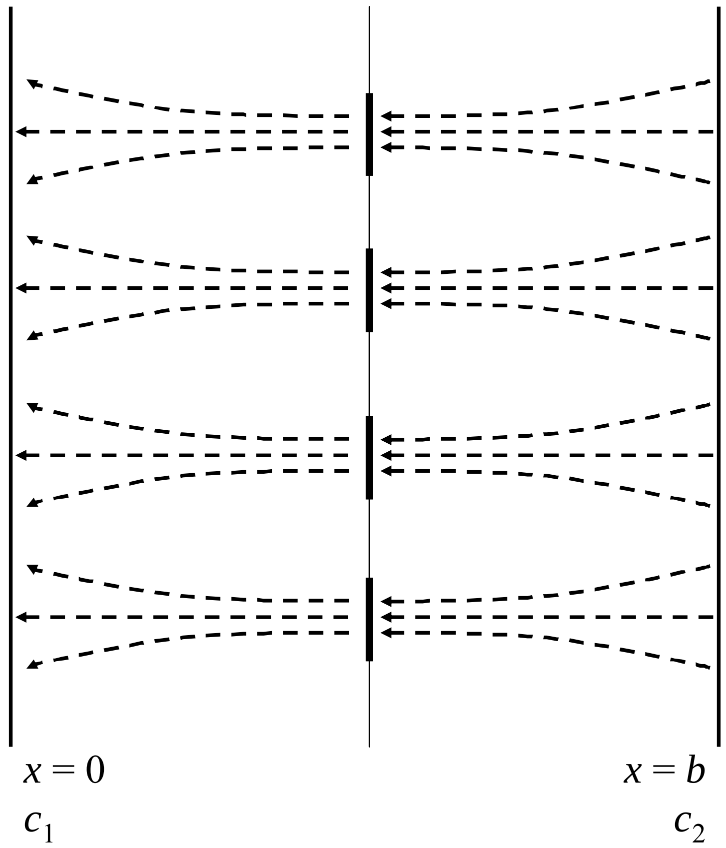
  $a = 5\ \mu m$
  $s = 10$ Å

  $N_{1/2} = \pi a/s = 15{,}700$

  Surface fraction covered by adsorbers:
  $N_{1/2}\pi s^2/4\pi a^2 = 1.6 \times 10^{-4}$

  Distance between neighboring adsorbers:
  $(4\pi a^2/N_{1/2})^{1/2} = 0.14\ \mu m = 1400$ Å

Diffusion through apertures in a planar barrier



Diffusion through apertures in a planar barrier

- $I_{2,1} = DA(c_2 - c_1)/b$
- $R_s = \frac{1}{2} Ds$
- $R_{\text{total}} = R_{2,1} + \dfrac{R_s}{N}$

$$= \frac{b}{DA} + \frac{1}{2DNs}$$

$$= \frac{b}{DA}\left(1 + \frac{A}{2Nsb}\right)$$

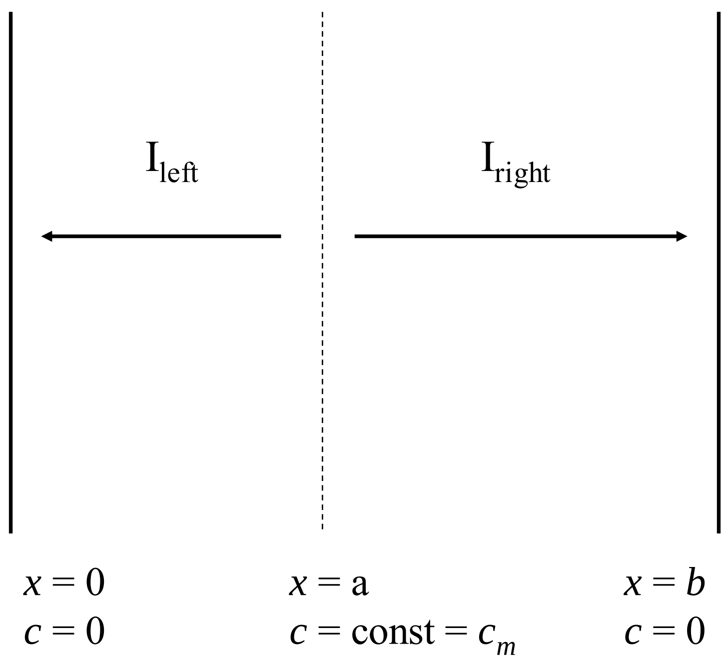
$$= \frac{b}{DA}\left(1 + \frac{1}{2nsb}\right)$$

with n = number of apertures per unit area

$$\frac{I}{I_{2,1}} = \frac{1}{1 + 1/2nsb}$$

Diffusion to capture: two adsorbing boundaries

- Particle released at $x = a$
- What is the probability of being adsorbed at $x = 0$?



Diffusion to capture: two adsorbing boundaries

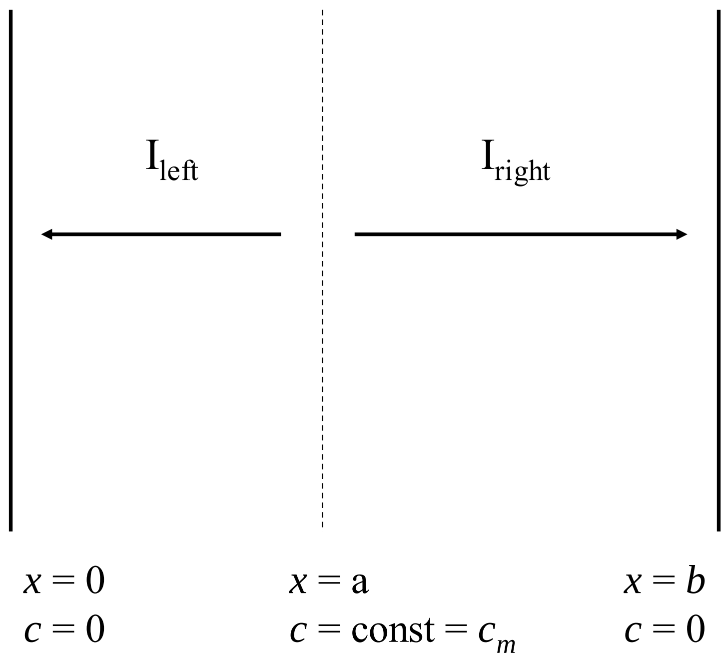
- $I_{left} = DAc_m/a$
- $I_{right} = DAc_m/(b\text{-}a)$

- Probability of being adsorbed at $x = 0$:

$$\frac{I_{left}}{I_{left} + I_{right}} = \frac{b-a}{b}$$

Mean time to capture: two adsorbing boundaries

- Particle released at $x = a$
- What is the mean time $W(a)$ for particles to be captured at $x = 0$ and $x = b$?



Mean time to capture: two adsorbing boundaries

- Particle may step left or right, so

$$W(x) = \tau + \frac{1}{2}\left[W(x+\delta) + W(x-\delta)\right]$$

$$2\tau + W(x+\delta) - W(x) + W(x-\delta) - W(x) = 0$$

$$\frac{2\tau}{\delta} + \frac{1}{\delta}\left[W(x+\delta) - W(x)\right] - \frac{1}{\delta}\left[W(x) - W(x-\delta)\right] = 0$$

$$\left.\frac{dW(x)}{dx}\right|_{x} - \left.\frac{dW(x)}{dx}\right|_{x-\delta} + \frac{2\tau}{\delta} = 0$$

$$\frac{d^2W}{dx^2} + \frac{2\tau}{\delta^2} = 0$$

$$\frac{d^2W}{dx^2} + \frac{1}{D} = 0$$

Mean time to capture: two adsorbing boundaries

- Boundary conditions:
  - adsorbing boundary

    $W = 0$
  - adsorbing boundary

    $dW/dx = 0$

- In the above example:
  - adsorbing boundaries:

    $W(0) = W(b) = 0$
  - solution: $$W(x) = \frac{1}{2D}\left(bx - x^2\right)$$
  - mean time to capture particle released at random position x:

$$\frac{1}{b}\int_0^b W(x)dx = \frac{b^2}{12D}$$

Mean time to capture: adsorbing and reflecting boundary

- Boundary conditions:
  - adsorbing boundary at $x = 0$
  - reflecting boundary at $x = b$

- With

  $W(0) = 0$
  $dW/dx = 0$ at $x = b$

  the solution is

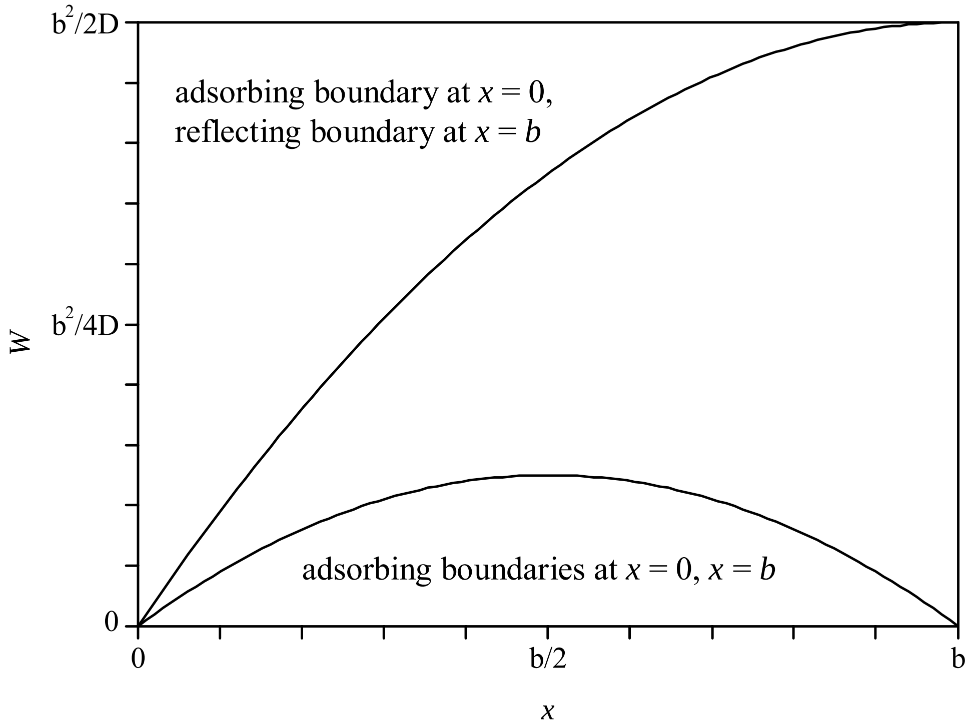
$$W(x) = \frac{1}{2D}\left(2bx - x^2\right)$$

Mean time to capture: adsorbing and reflecting boundary

Mean time to capture particle released at random position x:

$$\frac{1}{b}\int_0^b W(x)dx = \frac{b^2}{3D}$$

Mean time to capture



Mean time to capture

- In one dimension:

$$\frac{d^2W}{dx^2} + \frac{1}{D} = 0$$

- In two or three dimensions:

$$\nabla^2 W + \frac{1}{D} = 0$$

Junior Research Group

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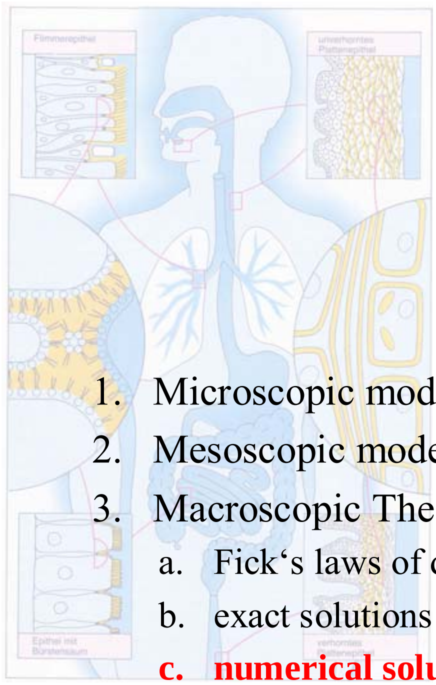

Diffusion

1. Microscopic modelling: Molecular dynamics
2. Mesoscopic modelling: Random walk
3. Macroscopic Theory
   a. Fick‘s laws of diffusion
   b. exact solutions
   c. **numerical solutions**

H.C. Berg: Random walks in biology - Princeton University Press

J. Crank: The mathematics of diffusion – Oxford University Press

Physical derivation

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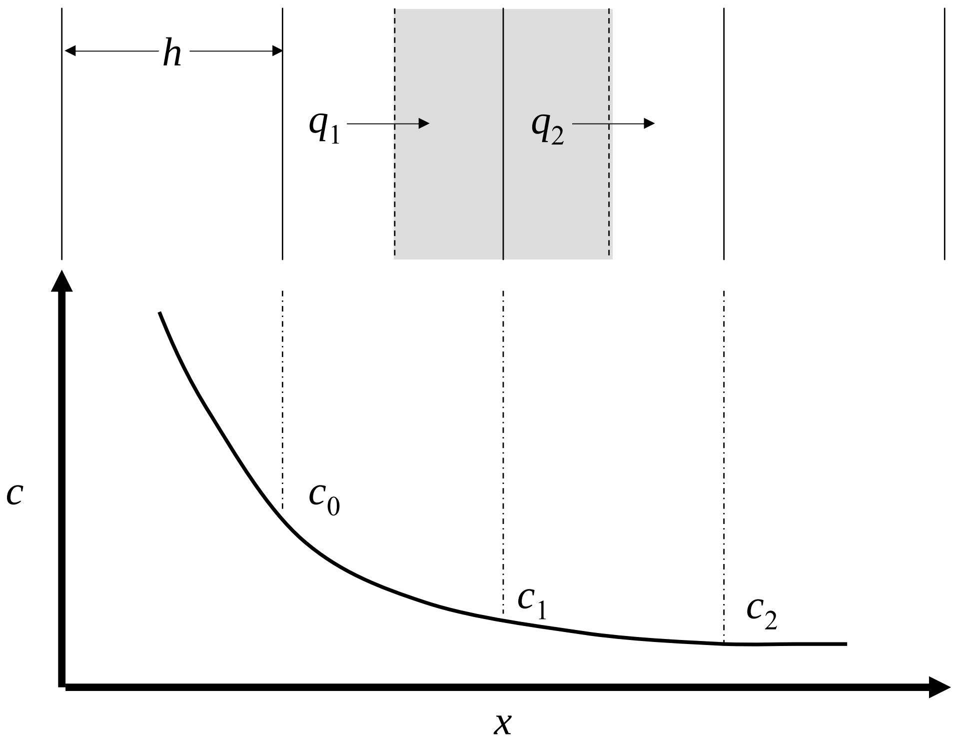


Physical derivation

- Amount diffusant entering through unit area in time τ:

$$q_1 = -\frac{D\tau}{h}(c_1 - c_0)$$

- Amount diffusant leaving through unit area in time τ:

$$q_2 = -\frac{D\tau}{h}(c_2 - c_1)$$

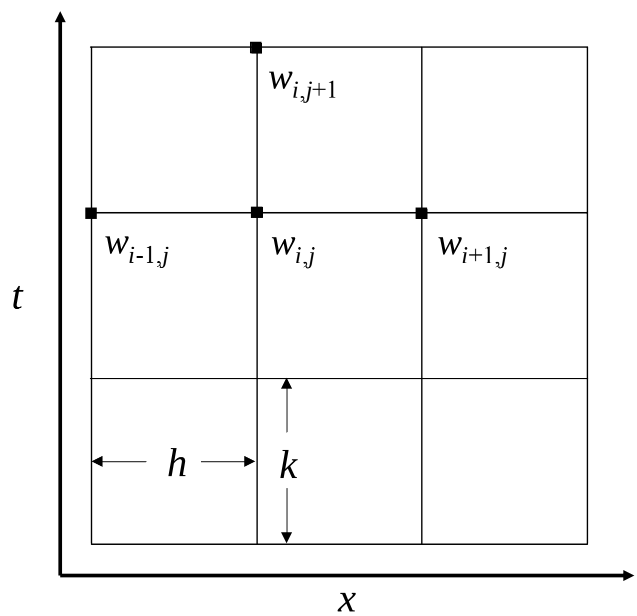
- Net gain of diffusant:

$$q_1 - q_2 = \frac{D\tau}{h}(c_0 - 2c_1 + c_2)$$
$$= h(c_1' - c_1)$$

$$\Delta c = c_1' - c_1 = \frac{D\tau}{h^2}(c_0 - 2c_1 + c_2)$$

Numerical solutions (one-dimensional)

- Select two grid constants h (space) and k (time)
- Grid points are (x_i, t_j) with $x_i = ih$ for $i = 0, 1, \ldots, m$ and $t_j = jk$ for $j = 0, 1, \ldots, n$.



Numerical solutions (one-dimensional): Forward scheme

- Explicit finite-difference formula:

$$w_{i,j+1} = \left(1 - \frac{2Dk}{h^2}\right) w_{i,j} + D\frac{k}{h^2}\left(w_{i+1,j} + w_{i-1,j}\right)$$

- Error: $\mathcal{O}(k+h^2)$
- Conditionally stable: $D\frac{k}{h^2} \leq \frac{1}{2}$
- Number of multiplications: $Z \cong 2n$

Forward scheme

With

$$\lambda = D\left(k/h^2\right)$$

and

$$\mathbf{A} = \begin{bmatrix} (1-2\lambda) & \lambda & 0 & \cdots & 0 \\ \lambda & (1-2\lambda) & \lambda & \ddots & \vdots \\ 0 & \lambda & \ddots & \ddots & 0 \\ \vdots & \ddots & \ddots & \ddots & \lambda \\ 0 & \cdots & 0 & \lambda & (1-2\lambda) \end{bmatrix}$$

this can be written as

$$\mathbf{w}^{(j)} = \mathbf{A}\mathbf{w}^{(j-1)}$$

Numerical solutions (one-dimensional): Backward scheme

- Implicit method

$$\frac{w_{i,j} - w_{i,j-1}}{k} - D\frac{w_{i+1,j} - 2w_{i,j} + w_{i-1,j}}{h^2} = 0$$

- Error: $\mathcal{O}(k+h^2)$
- Unconditionally stable
- Needs boundary conditions
- Values may be negative

Backward scheme

With

$$\lambda = D\left(k / h^2\right)$$

and

$$\mathbf{A} = \begin{bmatrix} (1+2\lambda) & -\lambda & 0 & \cdots & 0 \\ -\lambda & (1+2\lambda) & -\lambda & \ddots & \vdots \\ 0 & -\lambda & \ddots & \ddots & 0 \\ \vdots & \ddots & \ddots & \ddots & -\lambda \\ 0 & \cdots & 0 & -\lambda & (1+2\lambda) \end{bmatrix}$$

this can be written as

$$\mathbf{A}\mathbf{w}^{(j)} = \mathbf{w}^{(j-1)}$$

Numerical solutions (one-dimensional)

- Implicit: Crank-Nicholson method

$$\frac{w_{i,j+1}-w_{i.j}}{k}-\frac{D}{2}\left[\frac{w_{i+1,j}-2w_{i,j}+w_{i-1,j}}{h^2}+\frac{w_{i+1,j+1}-2w_{i,j+1}+w_{i-1,j+1}}{h^2}\right]=0$$

- Error: $\mathcal{O}(k^2+h^2)$
- Unconditionally stable
- Number of operations (inluding solving the tridigonal system):

$$Z \cong 5n$$

- Needs boundary conditions
- Values may be negative

J. Crank, P. Nicolson. A practical method for numerical evaluation of solutions of partial differential equations of the heat-conduction type. *Proc. Camb. Phil. Soc.* **43**:50-67 (1947)

Crank-Nicholson method

With

$$\lambda = D\left(k / h^2\right)$$

and

$$\mathbf{A} = \begin{bmatrix} (1+\lambda) & -\frac{\lambda}{2} & 0 & \cdots & 0 \\ -\frac{\lambda}{2} & (1+\lambda) & -\frac{\lambda}{2} & \ddots & \vdots \\ 0 & -\frac{\lambda}{2} & \ddots & \ddots & 0 \\ \vdots & \ddots & \ddots & \ddots & -\frac{\lambda}{2} \\ 0 & \cdots & 0 & -\frac{\lambda}{2} & (1+\lambda) \end{bmatrix}$$

Crank-Nicholson method

and

$$\mathbf{B} = \begin{bmatrix} (1-\lambda) & \frac{\lambda}{2} & 0 & \cdots & 0 \\ \frac{\lambda}{2} & (1-\lambda) & \frac{\lambda}{2} & \ddots & \vdots \\ 0 & \frac{\lambda}{2} & \ddots & \ddots & 0 \\ \vdots & \ddots & \ddots & \ddots & \frac{\lambda}{2} \\ 0 & \cdots & 0 & \frac{\lambda}{2} & (1-\lambda) \end{bmatrix}$$

this can be written as

$$\mathbf{A}\mathbf{w}^{(j+1)} = \mathbf{B}\mathbf{w}^{(j)}$$

unknown concentrations

known concentrations

The tridiagonal linear system

- The equation

$$\mathbf{A}\mathbf{w}^{(j+1)} = \mathbf{B}\mathbf{w}^{(j)}$$

can be written as

$$\mathbf{A}\mathbf{x} = \mathbf{b}$$

which is basically a tridiagonal linear system:

$$b_1 x_1 + c_1 x_2 = d_1; i = 1$$
$$a_i x_{i-1} + b_i x_i + c_i x_{i+1} = d_i; i = 2, \ldots, n-1$$
$$a_n x_{n-1} + b_n x_n = d_n; i = n$$

Solving the tridiagonal linear system

- Direct methods
  - Gauss‘s elimination method without pivoting
  - LU decomposition / Thomas algorithm
  - Crout reduction
- Iterative methods
  - Jacobi method
  - Gauss-Seidel method
  - Successive over-relaxation method

LU decomposition

$b_1' = b_1$

$d_1' = d_1$

for k $= 2 \dots n$ do

$$a_k' = \frac{a_k}{b_{k-1}'}, \quad b_k' = b_k - a_k' c_{k-1}, \quad d_k' = d_k - a_k' d_{k-1}'$$

end

$$x_n = \frac{d_n'}{b_n'}$$

for k $= n-1 \dots 1$ do

$$x_k = \frac{d_k' - c_k x_{k+1}}{b_k'}$$

end

H.R. Schwarz: Numerische Mathematik – Teubner Verlag Stuttgart

G.D. Smith: Numerical solution of partial differential equations – Oxford University Press

Crank-Nicolson method w/ Crout reduction

```
Let nx = the number of data points + 1
Let c[x] be the concentration for x = 0,...,nx with
  c[0] = c[nx] = 0.

Step 1
  INPUT c[x] = input data for x = 1,...,nx-1
  Set c[0] = c[nx] = 0
  Set lambda = Dk/h²
  Set u[0] = 0

Step 2 (Initialization of C-N tridiagonal matrix)
  For x = 1 to nx-1
    Set l[x] = 1 + lambda + lambda/2 * u[x-1]
    Set u[x] = -lambda/(2*l[x])
```


Crank-Nicolson method w/ Crout reduction

```
Step 3  (Iteration of C-N algorithm for nt time steps)
  For t from 1 to nt
    Set z[0] = 0
    (Solution of tridiagonal system by Crout
  reduction)
    For x from 1 to nx-1
      Set z[x] = ( ( 1 – lambda ) c[x] +
              lambda/2 * ( c[x+1] + c[x-1] +
              z[x-1] ) ) / l[x]
    (Back substitution)
    For x from nx-1 to 1
      Set psi[x] = z[x] - u[x]*psi[x+1]

Step 4
  OUTPUT c[1] through c[nx-1]
```

Boundary conditions

- Dirichlet conditions:
  value at the boundary is function of time, *e.g.*, $w(0,t) = b(\mathrm{t})$
- Neumann conditions:
  specify flux at the boundary
- Mixed boundary conditions
- Periodic or wraparound boundary conditions

Numerical solutions: Two dimensional forward scheme

- Basic equation:

$$\frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right)$$

- Grid:
  - x, y space divided in elements of length h, k with indices a, b
  - timestep of length τ, index n
- Concentration at all points is known for $t = 0$
- Solution:

$$\frac{w_{a,b,n+1} - w_{a,b,n}}{\tau} = \frac{D}{h^2}\left(w_{a-1,b,n} - 2w_{a,b,n} + w_{a+1,b,n}\right) + \frac{D}{k^2}\left(w_{a,b-1,n} - 2w_{a,b,n} + w_{a,b+1,n}\right)$$

- Stable for:

$$D\left(\frac{1}{h^2} + \frac{1}{k^2}\right)\tau \le \frac{1}{2}$$

Mathematical derivation of solutions

- Approximate $$\left(\frac{\partial c}{\partial t}\right)_x = D\left(\frac{\partial^2 c}{\partial x^2}\right)$$

  by Taylor series

$$u(x+h) = u(x) + h\frac{\partial u(x)}{\partial x} + \frac{1}{2}h^2\frac{\partial^2 u(x)}{\partial x^2} + \frac{1}{6}h^2\frac{\partial^3 u(x)}{\partial x^3}\ldots$$

$$u(x-h) = u(x) - h\frac{\partial u(x)}{\partial x} + \frac{1}{2}h^2\frac{\partial^2 u(x)}{\partial x^2} - \frac{1}{6}h^2\frac{\partial^3 u(x)}{\partial x^3}\ldots$$

  e.g.: addition

$$u(x+h) + u(x-h) = 2u(x) + h^2\frac{\partial^2 u(x)}{\partial x^2} + O(h^4)$$

$$\Rightarrow \frac{\partial^2 c(x)}{\partial x^2} \cong \frac{c(x+h) - 2c(x) + c(x-h)}{h^2}$$

Miscellaneous equations

- Douglas equation
  - implicit $$(1-6\lambda)w_{i-1,j+1} + (10+12\lambda)w_{i,j+1} + (1-6\lambda)w_{i+1,j+1} = (1+6\lambda)w_{i-1,j} + (10-12\lambda)w_{i,j} + (1+6\lambda)w_{i+1.j}$$

    error: $\mathcal{O}(k^2+h^4)$
    unconditionally stable

  - explicit $$w_{i,j+1} = \frac{1}{2}(2-5\lambda+6\lambda^2)w_{i,j} + \frac{2}{3}\lambda(2\text{-}3\lambda)(w_{i+1,j} + w_{i-1,j}) - \frac{1}{12}\lambda(1\text{-}6\lambda)(w_{i+2,j} + w_{i-2,j})$$

    error: $\mathcal{O}(k^2+h^4)$
    conditionally stable: $\lambda \leq 2/3$

Miscellaneous equations

- Du Fort and Frankel
  - explicit

$$(1+2\lambda)w_{i,j+1} = 2\lambda(\mathrm{w}_{\mathrm{i-1,j}} + \mathrm{w}_{\mathrm{i+1,j}}) + (1-2\lambda)w_{i,j-1}$$

  - unconditionally stable
  - error: $\mathcal{O}(k^2+h^2)$

- Implicit three-time level difference equation

$$\frac{3}{2}\frac{w_{i,j+1}-w_{i,j}}{Dk} - \frac{1}{2}\frac{w_{i,j}-w_{i,j-1}}{Dk} = \frac{w_{i+1,j+1}-2_{wi,j+1}+w_{i-1,j+1}}{h^2}$$

  - unconditionally stable
  - error: $\mathcal{O}(k^2+h^2)$