• Consider again

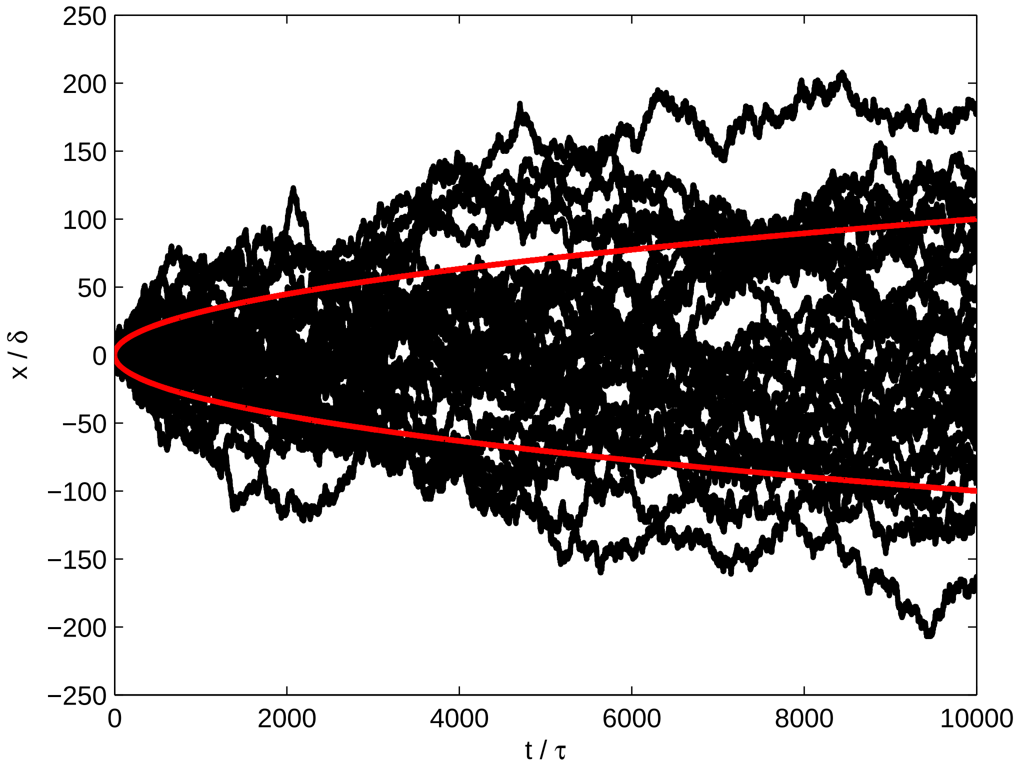
$$P(m, N) = \left(\tfrac{1}{2}\right)^N \frac{N!}{(\frac{N+m}{2})!(\frac{N-m}{2})!} \, .$$

Using **Stirling's approximation** for $K!$ when K is large, we can show that when N and $|m|$ are large, with m^2/N not too large, then

$$P(m, N) \approx \sqrt{\frac{2}{\pi N}}\, e^{-m^2/2N} \, .$$

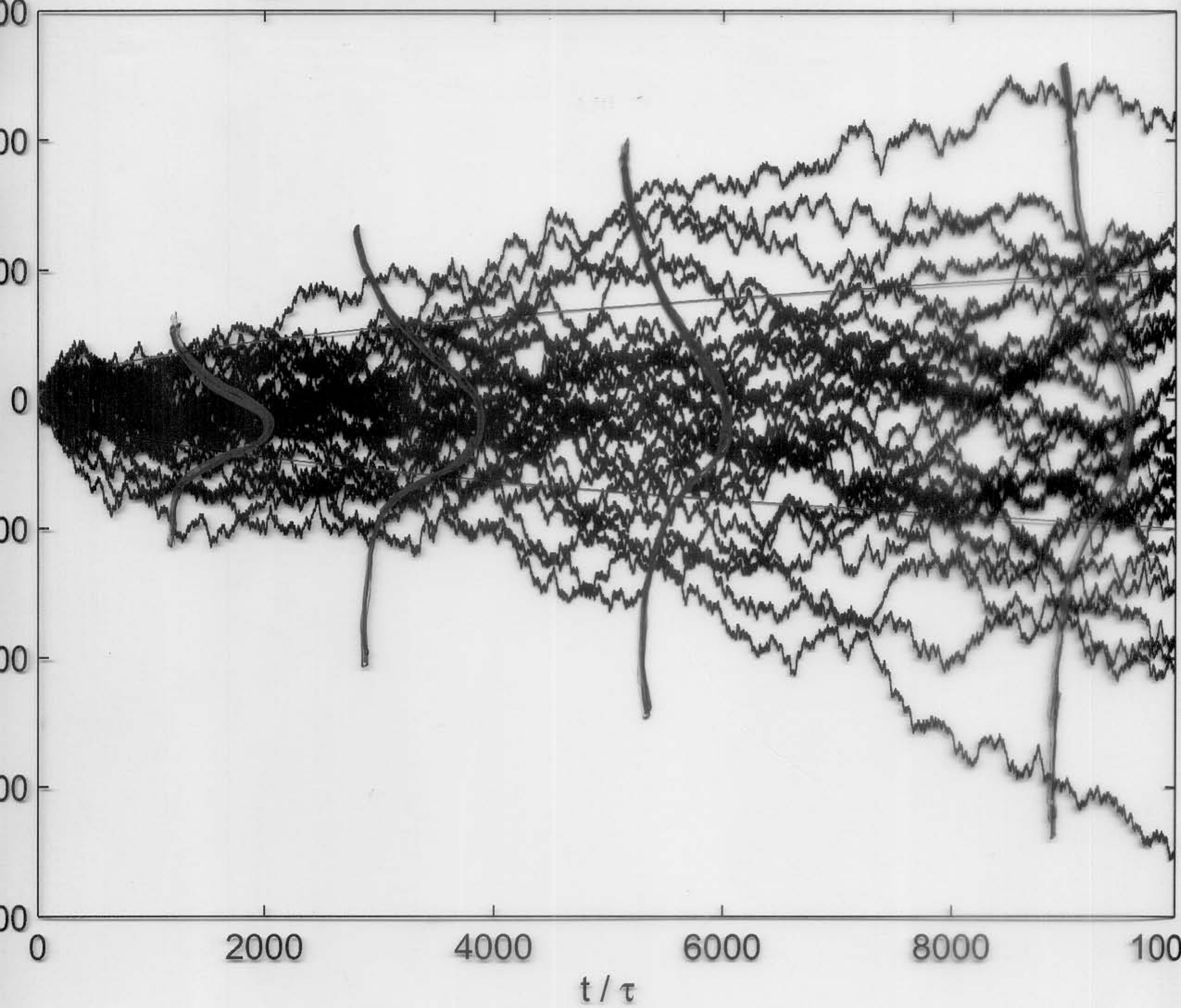
This is a good approximation even for quite small values of $|m|$ and N:–

(m, N)	$P(m, N)$	$\sqrt{\frac{2}{\pi N}}\, e^{-m^2/2N}$	Relative Error
$(\pm 2, 10)$	0.2051	0.2066	0.73%
$(\pm 5, 27)$	0.09714	0.09668	0.5%
$(\pm 200, 10000)$	0.0010799	0.0010798	0.01%



250
200
150
100
50
0
−50
−100
−150
−200
−250
x / δ
0
2000
4000
6000
8000
10000
t / τ

31 realizations



• We had

$$P(m,N) = \left(\tfrac{1}{2}\right)^N \frac{N!}{(\frac{N+m}{2})!(\frac{N-m}{2})!}) \approx \sqrt{\frac{2}{\pi N}}\, e^{-m^2/2N}$$

as $N \longrightarrow \infty$ and $|m| \longrightarrow \infty$ with m^2/N fixed and finite.

• We now set $x = m\delta$ and $t = N\tau$, and let $\delta \longrightarrow 0$ and $\tau \longrightarrow 0$ while $N \longrightarrow \infty$ and $|m| \longrightarrow \infty$, in such a way that x and t, as well as m^2/N, stay fixed and finite at values of our choosing. Make sure you can see that this is possible!

•Because

$$m^2/N = \left(\frac{x}{\delta}\right)^2 \left(\frac{\tau}{t}\right) = \frac{(x^2/t)}{(\delta^2/\tau)}\,,$$

this requires that

$$\frac{\delta^2}{2\tau} \quad (= D\,, \mathrm{say})$$

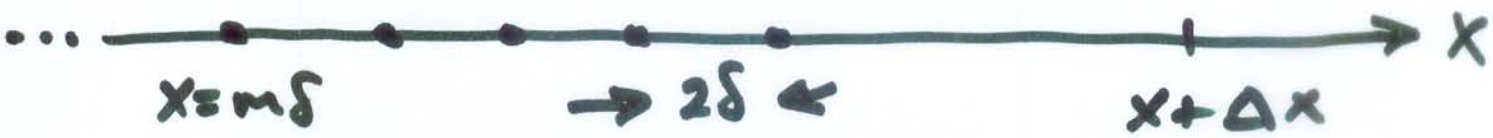
also remains fixed at some (positive) finite value.

•Now consider Δx such that $\delta \ll \Delta x \ll |x|\,.$

What is the probability $P(x,t)\Delta x$ that the particle is in $(x, x+\Delta x)$ at time t?

Ans:

$$P(x,t)\,\Delta x \approx \underbrace{\frac{\Delta x}{2\delta}}_{\text{no. of possible locations in } (x,\, x+\Delta x)} \; \underbrace{P(m,N)}_{\text{probability of such a location}}$$



Thus we arrive at

$$P(x,t) \approx \frac{P(m,N)}{2\delta} \approx \frac{1}{\sqrt{2\pi N \delta^2}}\, e^{-m^2/2N}$$

$$= \frac{e^{-x^2/4Dt}}{\sqrt{4\pi D t}}$$

where $x = m\delta$, $t = N\tau$, $D = \delta^2/2\tau$

as before.

•The formula

$$P(x,t) = \frac{e^{-x^2/4Dt}}{\sqrt{4\pi Dt}}$$

is exact in the limit

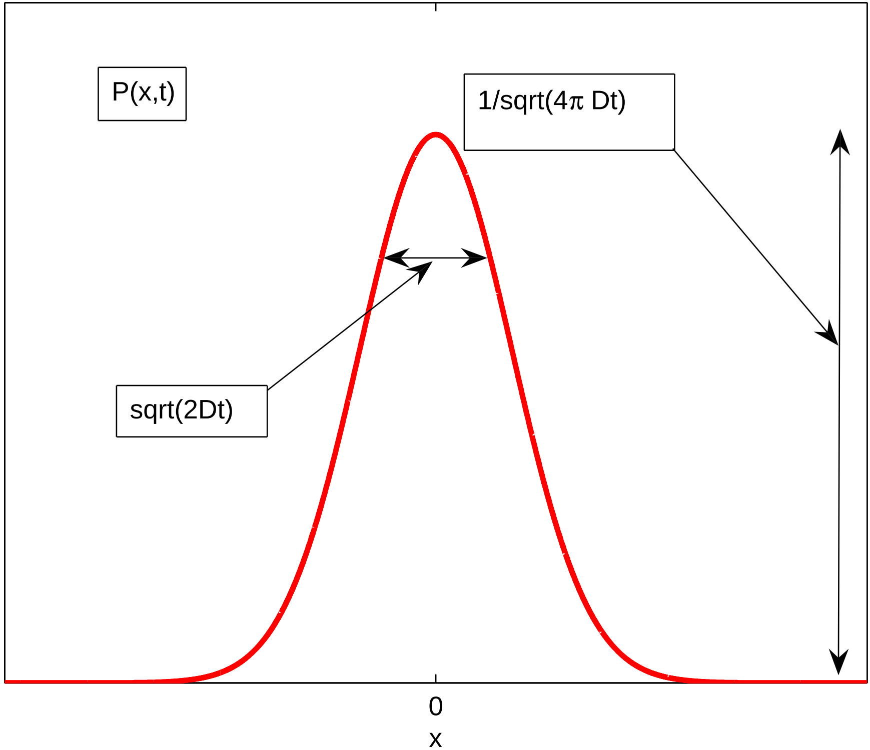
$$N \to \infty\,, \quad |m| \to \infty\,, \quad \delta \to 0\,, \quad \tau \to 0\,,$$

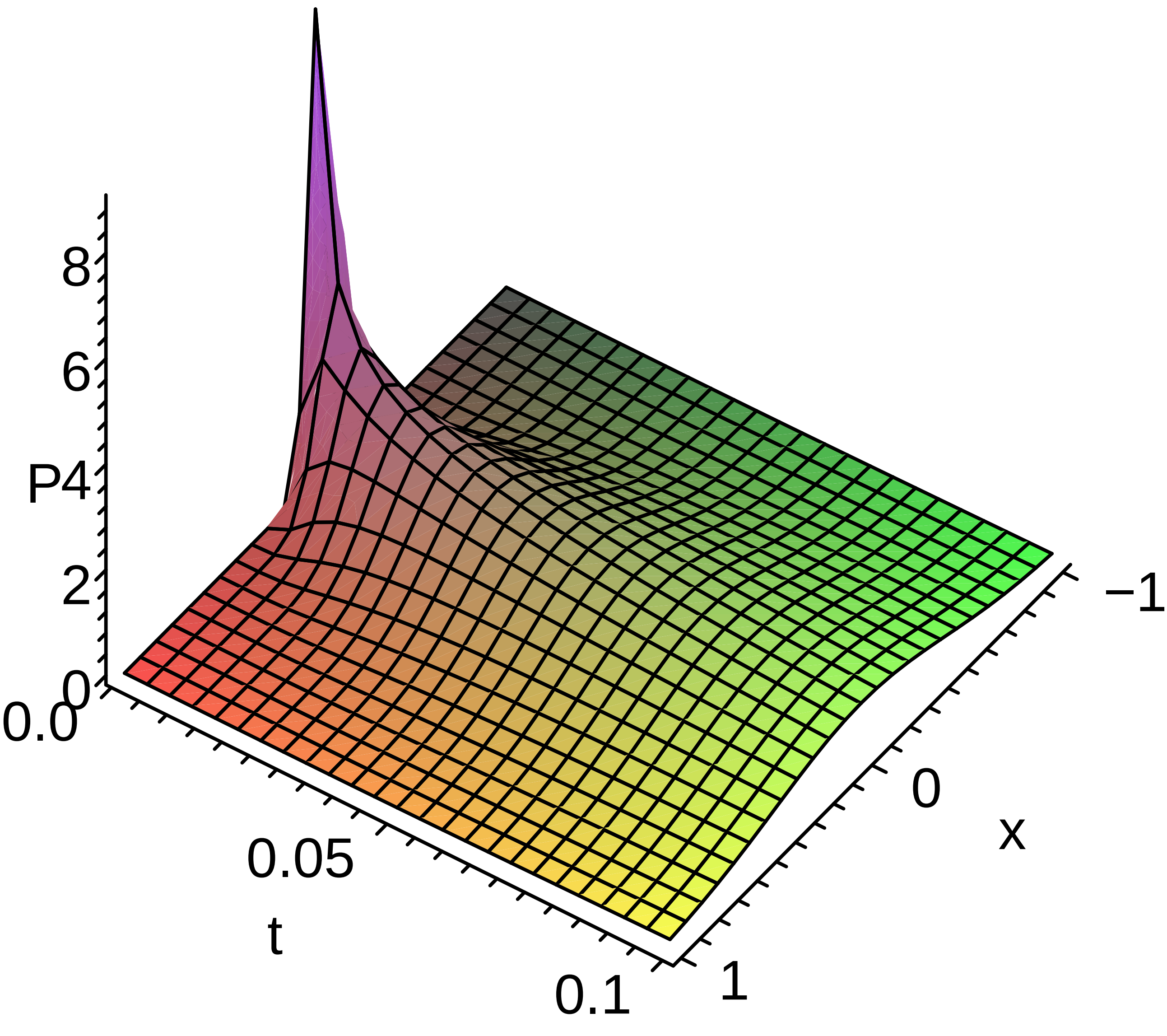
with

$$m\delta = x\,, \quad N\tau = t\,, \quad \frac{\delta^2}{2\tau} = D\,, \quad \frac{m^2}{N}$$

all fixed and finite.

At any time we have a Gaussian (or normal) distribution of probability along the X-axis — the graph is a bell-shaped curve:-


P(x,t)
1/sqrt(4π Dt)
sqrt(2Dt)
0
x



8
6
P4
2
0
0.0
0.05
t
0.1
1
0
x
−1

•The area under the curve is always 1 (conservation of probability):–

$$\int_{-\infty}^{\infty} \frac{e^{-x^2/4Dt}}{\sqrt{4\pi Dt}}\, dx = \frac{1}{\sqrt{\pi}} \int_{-\infty}^{\infty} e^{-y^2}\, dy = 1$$

•As $t \longrightarrow 0_+$, we have $P(x,t) \longrightarrow \delta(x)$ (infinite spike). This corresponds to a "bolus injection" of a finite quantity of diffusate at $x = 0$ at $t = 0$.

•Note that the distribution spreads over a distance L in a time determined by $L \approx \sqrt{2Dt}$, or $t \approx L^2/2D$. To go twice as far takes four times as long! To go ten times as far takes a hundred times as long, and so on.
This is the characteristic behaviour of the random walk that we saw before.
(See p. 1.13)

•The constant D is called the **diffusion coefficient**. The bigger is D, the faster is the diffusion (spreading). Particles with D twice the size, spread in half the time.

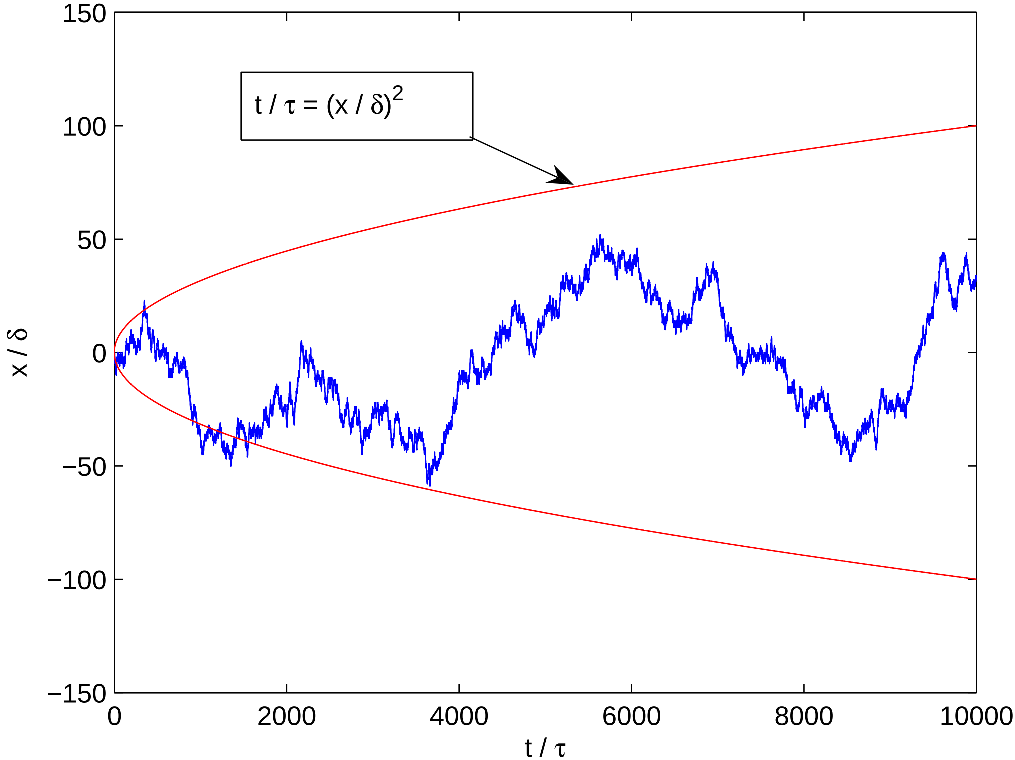
•For a big molecule like lysozyme in water, $D \approx 10^{-6} cm^2/sec$. To get across a swimming pool of width $L \approx 10m \approx 1000cm$ would take about 5×10^{11} sec, or $15,000$ years. (Contrast with p. 1.3)

•But to get across the width of a bacterium, $\approx 10^{-4} cm$, takes only 5×10^{-3}sec.

This is why diffusion is such an important transport mechanism on microscopic biological scales.

•**Aside:** While $P(x,t)$ is a nice smooth function (infinitely differentiable), the path $x(t)$ in the limit is typically continuous but nowhere differentiable. Such a path is said to describe (a realisation of) **Brownian motion.** (Look again at the figure on p. 1.15)

•Suppose now that there is a very large number $\mathcal{N}$ of particles, all performing 1-D random walks (independently), parallel to the X-axis:–



150
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−100
−150
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2000
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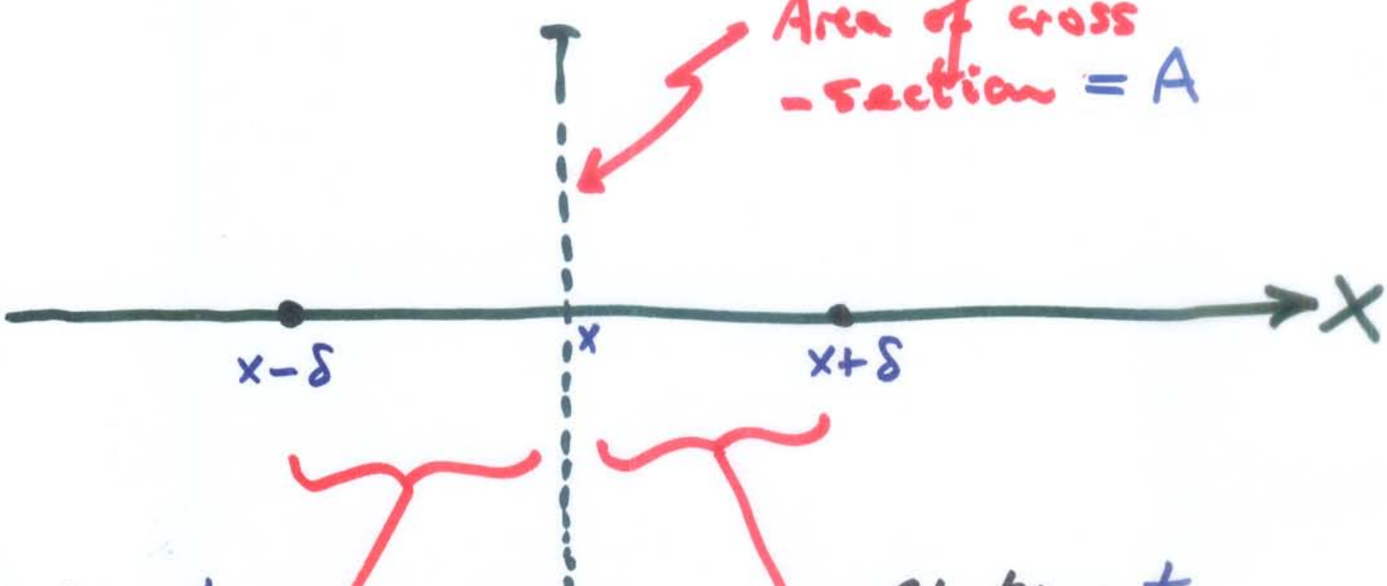
6000
8000
10000
x / δ
t / τ
t / τ = (x / δ)^2



At time t,
particles here $\approx \mathcal{N} P(x-\frac{\delta}{2},t)\delta$

– about $\frac{1}{2}$ go L, and about $\frac{1}{2}$ go R, across plane at x, in next time-interval of length τ.

At time t,
particles here $\approx \mathcal{N} P(x+\frac{\delta}{2},t)\delta$

– about $\frac{1}{2}$ go R, and about $\frac{1}{2}$ go L, across plane at x, in next time-interval of length τ.

•The net number crossing L to R across a plane of cross-sectional area A at x, in the time interval $[t, t+\tau]$ is

$$\approx \tfrac{1}{2}\mathcal{N}P(x-\tfrac{\delta}{2},t)\delta - \tfrac{1}{2}\mathcal{N}P(x+\tfrac{\delta}{2},t)\delta$$

The net **flux** L to R per unit area per unit time, at position x at time t, is therefore

$$J_1(x,t) \approx -\tfrac{1}{2}\mathcal{N}\left[P(x+\tfrac{\delta}{2},t) - P(x-\tfrac{\delta}{2},t)\right]\delta/A\tau$$

$$= -\frac{\delta^2}{2\tau}\left[\frac{\mathcal{N}P(x+\frac{\delta}{2},t)-\mathcal{N}P(x-\frac{\delta}{2},t)}{A\delta}\right]$$

$$= -D\left[\frac{\mathcal{N}P(x+\frac{\delta}{2},t)-\mathcal{N}P(x-\frac{\delta}{2},t)}{A\delta}\right]$$

•Now the number of particles per unit volume at x, t is the **concentration of diffusate**

$$c(x,t) \approx \frac{\mathcal{N} P(x,t)\delta}{A\delta}\,.$$

Then we have

$$J_1(x,t) \approx -D\left[\frac{c(x+\frac{\delta}{2},t) - c(x-\frac{\delta}{2},t)}{\delta}\right]\,.$$

As $\delta \longrightarrow 0$, we get

$$J_1(x,t) = -D\frac{\partial c(x,t)}{\partial x}$$

— **Fick's first equation**.

• **Aside: partial differentiation**:–

Given a function of several (independent) variables

$$F(x, y, \theta, t, \ldots),$$

then $\frac{\partial F}{\partial x}$ means: differentiate with respect to x, treating y , θ , t , $\ldots$ like constants.

Similarly $\frac{\partial F}{\partial \theta}$ means: differentiate with respect to θ, treating x , y , t , $\ldots$ like constants. And so on.

EX: $$F(x,y,\theta) = 3x^2 y\cos(\theta) + e^{6y}$$

$$\Rightarrow \frac{\partial F}{\partial x} = 6xy\cos(\theta), \quad \frac{\partial F}{\partial y} = 3x^2\cos(\theta) + 6e^{6y},$$

$$\frac{\partial F}{\partial \theta} = -3x^2 y\sin(\theta).$$

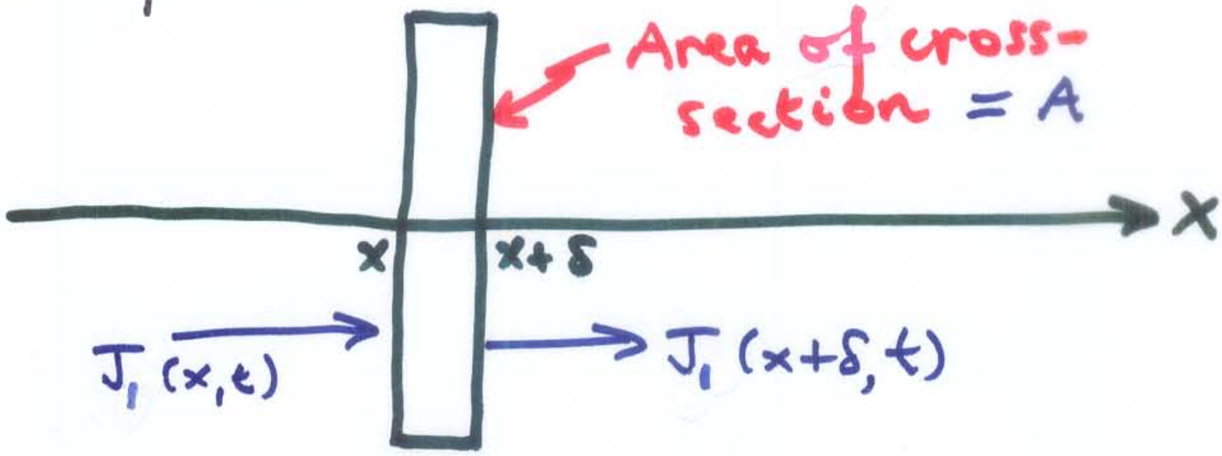
Then (order of differentiation doesn't matter!)

$$\frac{\partial^2 F}{\partial\theta\partial x} = -6xy\sin(\theta) = \frac{\partial^2 F}{\partial x\partial\theta}$$

and

$$\frac{\partial^3 F}{\partial\theta\partial x\partial y} = -6x\sin(\theta), \qquad \text{etc.}$$

• Going back to flux of particles, consider the changing concentration in the box of volume $A\delta$:—



\# particles in box at time t

$$\approx c(x,t)A\delta$$

\# particles in box at time $t+\tau$

$$\approx c(x,t+\tau)A\delta$$

Net flux of particles into box

$$\approx J_1(x,t)A\tau - J_1(x+\delta,t)A\tau$$

Therefore (conservation of particles!)

$$[c(x,t+\tau) - c(x,t)]A\delta \approx [J_1(x,t) - J_1(x+\delta,t)]A\tau$$

or

$$\frac{c(x,t+\tau) - c(x,\tau)}{\tau} \approx -\frac{[J_1(x+\delta,t) - J_1(x,t)]}{\delta}$$

As $\tau \longrightarrow 0$, $\delta \longrightarrow 0$, we get

$$\frac{\partial c(x,t)}{\partial t} = -\frac{\partial J_1(x,t)}{\partial x}$$

— **Fick's second equation**.

Subsituting in from Fick's first equation, we get

$$\frac{\partial c(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left[-D\frac{\partial c(x,t)}{\partial x}\right]$$

$$\Rightarrow \quad \frac{\partial c(x,t)}{\partial t} = D\frac{\partial^2 c(x,t)}{\partial x^2}$$

— **1-dimensional diffusion equation**.

•This is a partial differential equation (PDE) with

1 dependent variable c

2 independent variables x, t.

The PDE expresses conservation of number of particles during their random walks.

•It is important to see that this PDE must hold whenever we have a very large number of 'random walkers,' no matter how we distribute their starting positions on the X-axis.

•In the special case that we start them all at $x = 0$ at $t = 0$, we know that

$$c(x,t) \left(\approx \frac{\mathcal{N} P(x,t)}{A} \right) \approx \frac{\mathcal{N}}{A} \frac{1}{\sqrt{4\pi D t}} e^{-x^2/4Dt} .$$

It follows that the function

$$P(x,t) = \frac{1}{\sqrt{4\pi D t}} e^{-x^2/4Dt}$$

must satisfy the 1-D diffusion equation:–

Check:

$$\frac{\partial P(x,t)}{\partial t} = \frac{1}{\sqrt{4\pi D}} \frac{\partial}{\partial t} \left\{ t^{-\frac{1}{2}} e^{-x^2/4Dt} \right\}$$

$$= \frac{1}{\sqrt{4\pi D}} \left\{ -\frac{1}{2} t^{-3/2} e^{-x^2/4Dt} + t^{-\frac{1}{2}} \left(\frac{x^2}{4Dt^2} \right) e^{-x^2/4Dt} \right\}$$

$$= \frac{1}{\sqrt{4\pi D}} e^{-x^2/4Dt} \left\{ -\frac{1}{2} t^{-3/2} + \frac{x^2}{4D} t^{-\frac{5}{2}} \right\}$$

$$\frac{\partial P(x,t)}{\partial x} = \frac{1}{\sqrt{4\pi D}} \left\{ t^{-1/2} \left(\frac{-2x}{4Dt} \right) e^{-x^2/4Dt} \right\}$$

$$= \frac{1}{\sqrt{4\pi D}} \left\{ -\frac{x}{2D} t^{-\frac{3}{2}} e^{-x^2/4Dt} \right\}$$

$$\frac{\partial^2 P(x,t)}{\partial x^2} = \frac{1}{\sqrt{4\pi D}} \left\{ -\frac{1}{2D} t^{-3/2} e^{-x^2/4Dt} - \frac{x}{2D} t^{-\frac{3}{2}} \left(\frac{-2x}{4Dt} \right) e^{-x^2/4Dt} \right\}$$

$$\Rightarrow D \frac{\partial^2 P(x,t)}{\partial x^2} = \frac{1}{\sqrt{4\pi D}} \left\{ -\frac{1}{2} t^{-3/2} + t^{-5/2} \frac{x^2}{4D} \right\} e^{-x^2/4Dt}$$

$$= \frac{\partial P(x,t)}{\partial t}$$

•Many other simple functions satisfy the 1-D diffusion equation, for example

(1) $c(x,t) = e^{-\alpha^2 Dt} \sin(\alpha x), \quad \alpha = \text{const.}$

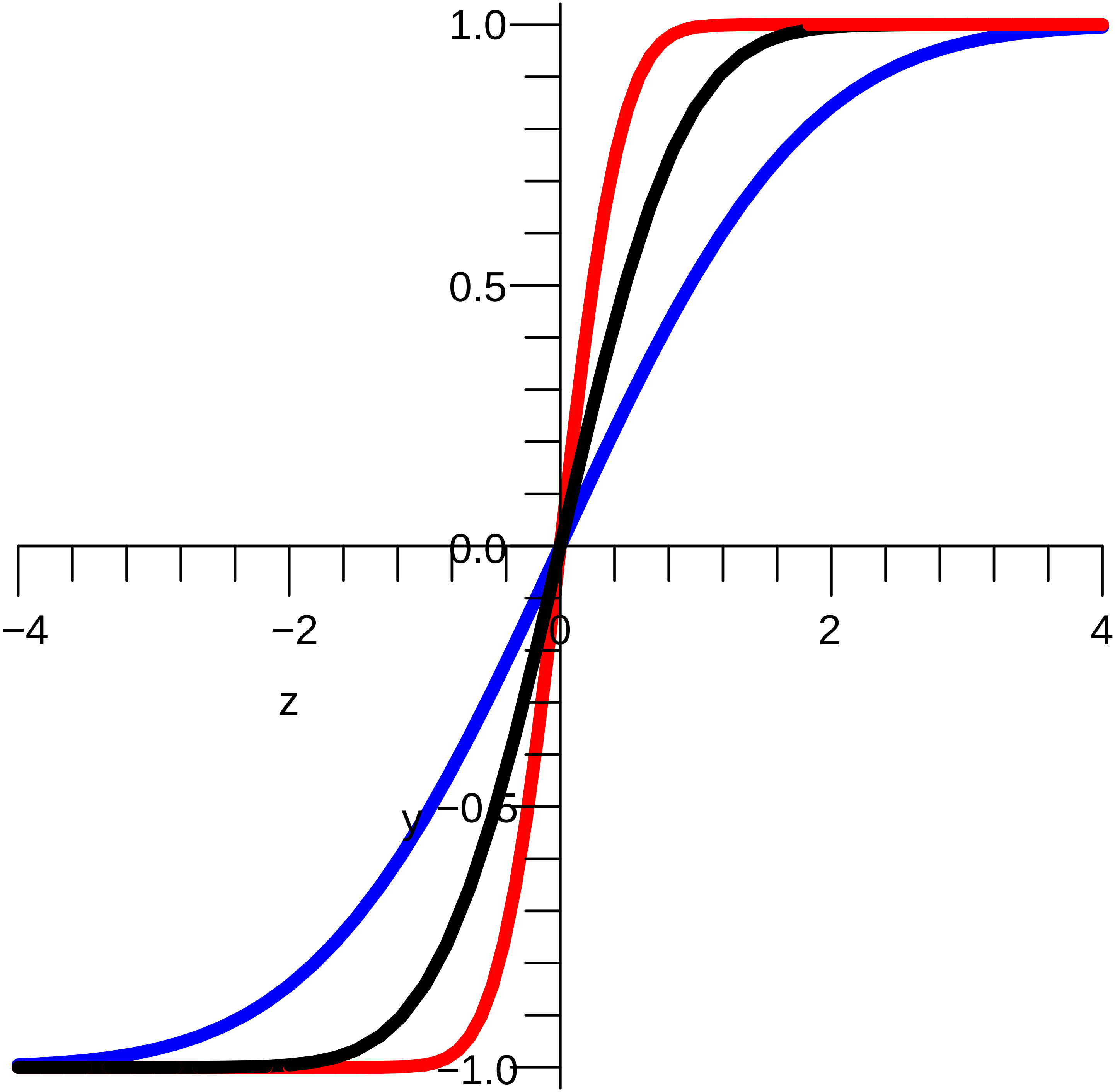
(2) $c(x,t) = Ax + B, \quad A,\ B = \text{consts.}$

(3) $c(x,t) = A \, \mathrm{erf}\left(\frac{x-a}{\sqrt{4Dt}}\right), \quad A,\ a = \text{const.},$

where

$$\mathrm{erf}(z) = \frac{2}{\sqrt{\pi}} \int_0^z e^{-y^2} \, dy$$

— the error function. See the graphs of $y = \mathrm{erf}(2z)$, $y = \mathrm{erf}(z)$, and $y = \mathrm{erf}(z/2)$ in the next figure:–



1.0
0.5
0.0
−4
−2
0
2
4
z
y
−0.5
−1.0

•A typical mathematical problem in diffusion is to find $c(x,t)$ in some region of interest, for times $t>0$, given some information about the initial state, at $t=0$, and about what is happening at the boundaries of the region. This is called an initial and boundary value problem for the diffusion equation (IVP & BVP).

•A great many problems of this type have been solved, by various methods. [See for example,
H.S. Carslaw and J.C. Jaeger, *Conduction of Heat in Solids* (Oxford UP, 1959),
and
J. Crank, *The Mathematics of Diffusion* (Oxford UP, 1975).]