

23 The microscopic theory of diffusion

23.1 Brownian Motion and Diffusion

Water molecules are very very small relative to the size of a typical imaging voxels, which might be $\approx 1 \text{ mm}^3$ and thus contain ?? water molecules. It is hopeless to describe the precise motion of this collection, or *ensemble*, of particles as this would require the simultaneous solution of ?? equations of motion. So we are forced to think in terms of the macroscopic descriptions of their microscopic motions that captures the essential features that will manifest in macroscopically measurable quantities. Whether or not our conclusions suffer from such a reduced description depends upon the relevance of the information we have ignored. As we know from classical thermodynamics, one does not need to exactly solve the equations of motion for classical gas molecules, for example, to describe a great deal of its behavior. The reason for this is rooted in the relevance of the *information* necessary to construct a predictive model (?).

Let us begin then with *Boltzmann's constant* k , which relates the microscopic quantity of the energy of a particle with the macroscopic property of the temperature: It is the ratio of the *gas constant* R to *Avogadro's number* N_A

$$k = \frac{R}{N_A} = 1.38 \times 10^{-23} \text{ J/K} \quad (23.1)$$

where J stands for *Joules* and K stands for *degrees Kelvin*. Boltzmann's constant relates the microscopic to the macroscopic through the *ideal gas law*:

$$pV = nRT \quad (23.2)$$

which says that the product of the pressure p and volume V is equal to the product of the quantity n of a substance, its absolute temperature T and the proportionality constant (the gas constant) $R = 8.314 \text{ J/(mol} \cdot \text{K)}$. Boltzmann's constant is $k = R/N_A$ so the ideal gas law can be written in the form

$$pV = NkT \quad (23.3)$$

where $N = n/N_A$ is the number of molecules of gas. Eqn 23.3 is now a statement about the microscopic properties of a gas and thus Boltzmann's constant can be viewed as relating the microscopic to the macroscopic.

A particle at absolute temperature T has a kinetic energy $kT/2$ along each axis, independent of the size of the particle (?), so for a particle with mass m and velocity v , this must be equal to the classical kinetic energy:

$$\frac{1}{2}mv^2 = \frac{1}{2}kT \quad (23.4)$$

The particle velocity fluctuates, but on average $\langle v^2 \rangle = kT/m$ so the *root-mean-squared* or *rms* velocity is

$$\langle v^2 \rangle^{1/2} = (kT/m)^{1/2} \quad (23.5)$$

From Exercise 23.1 we see that the predicted rms velocity of a molecule at can be quite fast ($\approx 50m/sec$ at room temp). However, if the molecule is immersed in a complex aqueous environment it will be constantly hitting and bouncing off other molecules, which are also moving, and will therefore be rapidly changing location in a complicated way. A collection of such particles initially confined to a small area will therefore eventually spread out in space. This is called *diffusion*, which we can define as *the random migration of molecules due to motion induced by thermal energy*. The dynamics of biological fluids that lead to Brownian motion are exceedingly complicated and if we tried to follow the equations of motion for each particle the problem would be intractable. So once again, as in the the determination of the macroscopic magnetism (Chapter 13), it is necessary to build the bridge between the microscopic dynamics and the macroscopic observables through plausible reasoning, i.e., probability theory.

Example 23.1 Calculate the rms velocity of a molecule of molecular weight 1 kg at room temperature ($300K^\circ$).

Solution

For a molecular weight of 1 kg, the molecule has mass

$$m = 1kg/mole = \frac{1000g}{6 \times 10^{23}molecules} = 1.67 \times 10^{-21}g \quad (23.6)$$

At $300K^\circ$ $kT = 4.14 \times 10^{-14}g - cm^2/sec^2$ thus

$$\langle v^2 \rangle^{1/2} = (kT/m)^{1/2} = \left(\frac{4.14 \times 10^{-14}g - cm^2/sec^2}{1.67 \times 10^{-21}g} \right)^{1/2} \approx 50m/sec \quad (23.7)$$

23.2 The random walk

MRI is all about the imaging of spatial distributions of spins and so we need a concise way to model the spatial locations of diffusing particles as a function of time. Although diffusion of water in the human body is an exceedingly complex process, it is most useful to have a simple conceptual model with which to describe, and perhaps to better understand, the process of diffusion. There is indeed such a model and, somewhat remarkably, its simplicity does not preclude its accuracy in the description of diffusion, and in fact facilitates its use as a reliable computational model. This model is called the *random walk*. (An excellent introductory text is which influenced this chapter is (?).) A 2D random walk is depicted in Figure 23.1, where the motion of a single entity we generically call a "particle" is considered.

The first thing that we do is simplify the *spatial* characteristics of the problem by assuming that particles can only be at predefined discrete points and that these points are arranged on a Cartesian grid, sometimes called a *lattice* (in which case the locations of the points are called

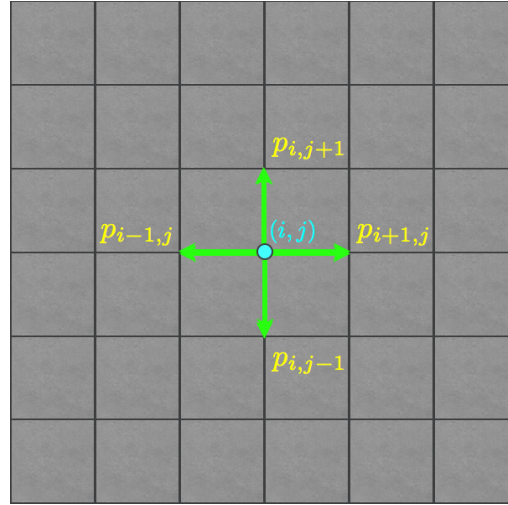


Figure 23.1 The random walk in 2D. A particle starting at location (i, j) at time t on a Cartesian grid of points can move to one of the four neighboring grid points with probability $p_{i\pm 1, j\pm 1}$ where $i \neq j$.

vertices). While this is certainly a constraint on the allowable locations of the particles, keep in mind that this grid can be defined at any scale. That is, we can arbitrarily choose the dimensions of the distance between the grid points. So as long as that dimensions is much smaller than the dimensions of the physical problem (e.g., much smaller than a voxel's side dimension), then this is not much of constraint. (Of course, computationally, as the dimensions of the grid are made smaller, the number of grid points in a volume grow rapidly, and increases the computational burden). Next we characterize the *temporal* characteristics of the problem by saying that at the next (discrete) time point $t + 1$, the particle at location (i, j) jumps to any one of neighboring grid points, say $(i, j + 1)$, with a probability $p_{i,j+1}$. In 1D, there are two grid points to jump to. In 2D, there are four, and in 3D there are 6 (so the number of available grid points is apparently $2d$ where d is the dimension of the problem.) Since the particle must jump to one of the neighboring points, the probability that it ends up at another point is 1 which we can state formally (for a particle starting at location $(0, 0)$) as $\sum_{i=0}^1 \sum_{j=0}^1 p_{i,j} = 1$.

In the simplest case, the probabilities of jumping between any two grid points are all identical. So in the 2D case shown in Figure 23.1 that means $p_{i,j+1} = p_{i,j-1} = p_{i+1,j} = p_{i-1,j}$. Since the sum over probabilities must be 1 it is clear that $p = 1/4$. What does this look like if we start a particle at $(0, 0)$ and let this process run for n discrete time steps? An example of three different realizations of this for $n = 10000$ time steps is shown in Eqn 23.2. The distribution of final points and the corresponding histogram along the x -direction is shown in Figure 23.3. It appears visually that this distribution is Gaussian. (We'll prove that momentarily). Note that we could have drawn the blue line in Figure 23.3a in *any* angle through the origin and gotten the same Gaussian distribution. This is called *isotropic* Gaussian distribution and so the process that generated it is called *Gaussian diffusion*. A Gaussian distribution is defined by two parameters - the mean and the variance. If the distributions along any line drawn through an arbitrary angle through the origin (e.g. Figure 23.3b) are the same, then it must be that their variances

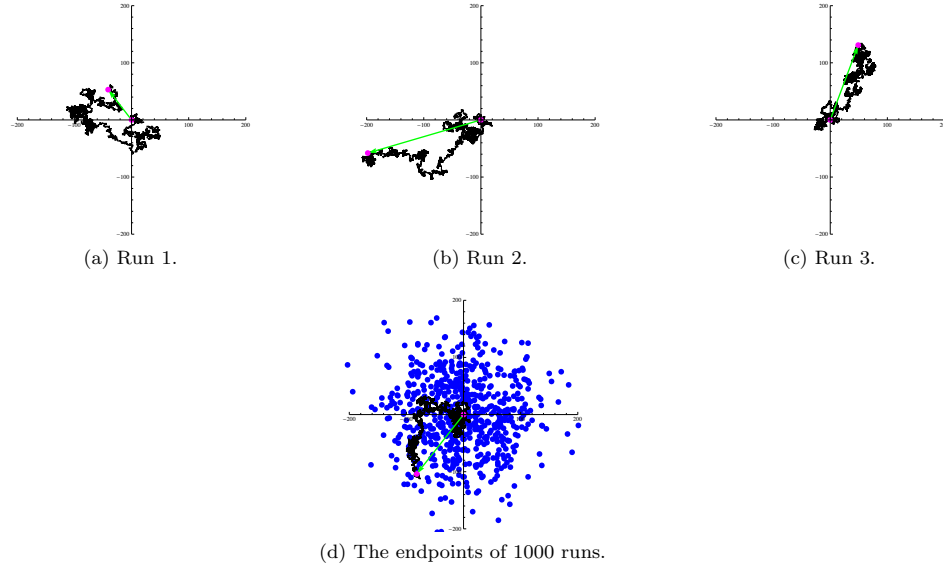


Figure 23.2 Two-dimensional random walk for $n = 10000$ time steps for equal probabilities of jumping between any two grid points. Three realizations are shown in (a-c). Repeating this many times results in the distribution of final particle locations (for one set of realizations) shown in (d).

are the same. (The means are the same - they all share the same origin where the peak of the distribution - its mean - is located). Having a variance that is independent of the direction is, in fact, the definition of isotropic diffusion. So now we've seen qualitatively that this simple random walk model appears to give a Gaussian distribution. Let's go ahead and put this on a more quantitative footing by proving it.

23.3 The random walk and the diffusion coefficient

Let's consider a group, or *ensemble*, of N non-interacting particles (i.e., they don't hit each other) that move with velocity v for a time τ (and thus a distance $\delta = v\tau$) in one-dimension (right or left) with equal probability $p(r) = p(l) = 1/2$. We'll also assume that whatever a particle does at the k 'th step is not influenced by what it did at the previous (i.e., $(k-1)$ 'st) step. That is, the probability p_k of moving left or right at the k 'th step is independent of p_{k-1} . The steps are then said to be *statistically independent* and thus the probability $p_{n,n-1,\dots,1}$ of a particle going through a particular sequence of n left/right steps is just the product of probabilities at each step: $p_{n,n-1,\dots,1} = \prod_{i=1}^n p_i$. What is the mean and variance of the final distribution of the N particles after n steps?

Let $x_{i,n}$ be the position of the i 'th particle after the k 'th step. Its position relative to its previous position $x_{i,k-1}$ is just

$$x_{i,k} = x_{i,k-1} \pm \delta \quad (23.8)$$

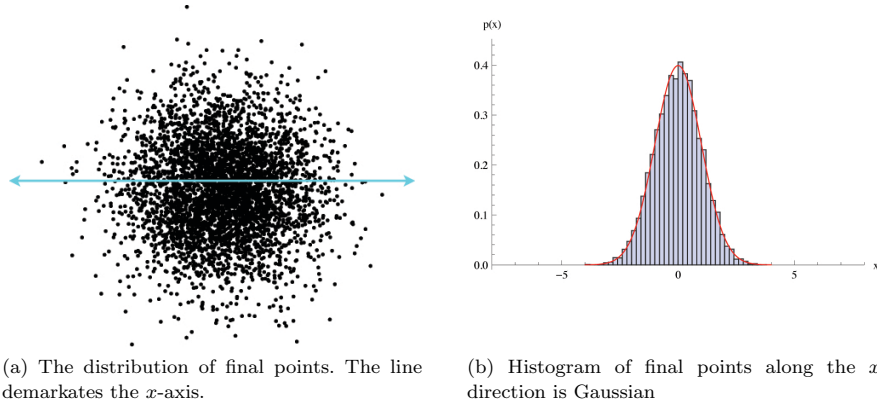


Figure 23.3 The distribution of final points (Figure 23.2 (d))

The average position of the N particles after one step is then, using Eqn 23.8,

$$\langle x \rangle_N = \frac{1}{N} \sum_{i=1}^N x_{i,k} = \underbrace{\frac{1}{N} \sum_{i=1}^N x_{i,k-1}}_{\langle x_{k-1} \rangle_N} + \underbrace{\frac{1}{N} \sum_{i=1}^N (\pm \delta)}_0 \quad (23.9)$$

where $\langle \rangle_N$ is used to denote the average of N . The second term is 0 because the sign is “+” for about 1/2 the particles and “-” for the other half. But this just says that $\langle x_k \rangle_N = \langle x_{k-1} \rangle_N$ - the average position does not change from step to step. So the average position never changes, and since the particles start at the origin, it is clear that

$$\langle x \rangle_N = 0 \quad (23.10)$$

and so the particles spread symmetrically about the origin. By how much do they spread, though? To answer this, we need to look at the variance $\langle x^2 \rangle_N - \langle x \rangle_N^2 = \langle x^2 \rangle_N$, the mean squared position after k steps:

$$\langle x_k^2 \rangle_N = \frac{1}{N} \sum_{i=1}^N x_{i,k}^2 \quad (23.11)$$

From Eqn 23.8

$$x_{i,k}^2 = x_{i,k-1}^2 \pm 2\delta x_{i,k-1} + \delta^2 \quad (23.12)$$

Putting Eqn 23.12 into Eqn 23.11 gives

$$\langle x_k^2 \rangle_N = \underbrace{\frac{1}{N} \sum_{i=1}^N x_{i,k-1}^2}_{\langle x_{k-1}^2 \rangle_N} + \underbrace{\frac{1}{N} \sum_{i=1}^N [\pm 2\delta x_{i,k-1}]}_0 + \underbrace{\frac{1}{N} \sum_{i=1}^N \delta^2}_{\delta^2} \quad (23.13)$$

where the second term vanishes because, as we just found, $\langle x_{k-1} \rangle_N = 0$. Therefore

$$\langle x_k^2 \rangle = \langle x_{k-1}^2 \rangle + \delta^2 \quad (23.14)$$

Since $x_i(0) = 0$ for all particles, for a total of n steps, this leads to

$$\langle x_n^2 \rangle = n\delta^2 = (\delta^2/\tau) t \quad (23.15)$$

since each step takes the same time period τ the total time t to take n steps is just $t = n\tau$. This can be written in the form

$$\langle x^2 \rangle = 2Dt \quad (23.16)$$

where we have defined the *diffusion coefficient*

$$D = \frac{\delta^2}{2\tau} \quad (23.17)$$

So we see that the mean square root distance $\langle x^2 \rangle^{1/2} = (2Dt)^{1/2}$, the measure of how far a particle moves in time t , i.e., the spreading, is *proportional to the square root of time*, rather than a linear function of time as it would be for a group of particles all moving in the same direction with velocity v , i.e., $x = vt$, such as in flow. So from this very simple model we are able to produce an expression for the diffusion coefficient consistent with Einstein's expression in Section 1.6. But we haven't yet shown that the distribution is a Gaussian and thus characterized by the mean and variance given in Eqn 23.10 and Eqn 23.16, respectively.

23.4 How the random walk becomes Gaussian

The situation in the previous section where the particle moves with equal probabilities to the right or the left and is a specific case of more general case in which a particles is allowed to move to the left with probability p and to the right with probability $q = 1 - p$. In this case the probability of a particle takes $n = r + l$ steps, moving r steps to the right and l steps to the left is given by the well-known *binomial*:

$$p(l; n, p) = \frac{n!}{l!r!} p^l q^r = \frac{n!}{l!(n-l)!} p^l q^{n-l} \quad (23.18)$$

Note that since the total number of steps n is given and the probabilities sum to 1, this expression has been written in terms of only l and p (the right most equation), and thus just in terms of the probability of the particle moving to the right. (We could just as well have looked at the left motion.) The binomial distribution which has mean and variance

$$\mu = \langle l \rangle = np \quad (23.19a)$$

$$\sigma^2 = \langle l^2 \rangle - \langle l \rangle^2 = npq \quad (23.19b)$$

For n and np large, the binomial distribution can be approximated by the Gaussian distribution

$$p(l) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-(l-\mu)^2/2\sigma^2} \quad (23.20)$$

We now need to convert to spatial and temporal coordinates to make the proper connection with diffusion. The distance the particle moves in n time steps of length τ is

$$x_n = (l - r)\delta = (2l - n)\delta \quad (23.21)$$

so the mean and variance of x_n are (using Eqn 23.19)

$$\mu_x = \langle x_n \rangle = (2 \langle l \rangle - n) \delta = 0 \quad (23.22a)$$

$$\sigma_x^2 = \langle x_n^2 \rangle = (4 \langle l^2 \rangle - 4 \langle l \rangle n + n^2) \delta^2 = n \delta^2 \quad (23.22b)$$

and from Eqn 23.16 $n \delta^2 = 2Dt$ with the diffusion coefficient being given by Eqn 23.17, thus

$$p(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-x^2/2\sigma^2} \quad (23.23)$$

where the variance is $\sigma^2 = 2Dt$. This is just a one-dimensional Gaussian distribution.

23.5 Isotropic Gaussian diffusion

We've shown how a random walk in one dimension results in the one-dimensional Gaussian distribution Eqn 23.23. It is easy to now extend this to a two-dimensional random walk where the particles move independently, with the same probability, in each direction. Because their motion is independent, the probability of moving in x is independent of the probability of moving in y , then $p(x, y) = p(x)p(y)$, each of the form Eqn 23.23, and the final distribution of particles is

$$p(x, y) = \frac{1}{2\pi\sigma^2} e^{-(x^2+y^2)/2\sigma^2} \quad (23.24)$$

where the variance is $\sigma^2 = 2Dt$. This is shown several useful graphical forms in Figure 23.4. Since the particles can jump with equal probability in each direction, the final distribution is circularly symmetric about the origin. This is called *isotropic diffusion*. This is easily extended to three dimensions isotropic Gaussian distribution where

$$p(x, y, z) = \frac{1}{(2\pi\sigma^2)^{3/2}} e^{-(x^2+y^2+z^2)/2\sigma^2} \quad (23.25)$$

where $\sigma^2 = 2Dt$. A single instantiation of a three-dimensional random walk is shown in Figure 23.5a. The final distribution of 10000 particles undergoing a random walk in three-dimensions is shown in Figure 23.5b.

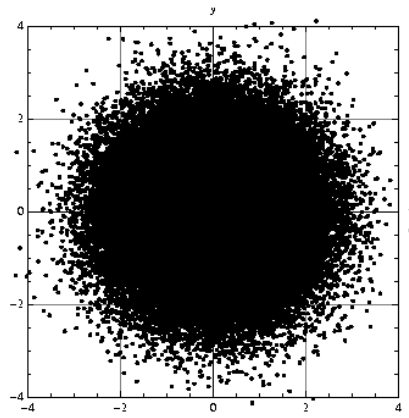
Problems

23.1 Using the fact that $p(x, y) = p(x)p(y)$ each of the form Eqn 23.23, show that $p(x, y)$ has the form Eqn 23.24. Do the same for Eqn 23.25.

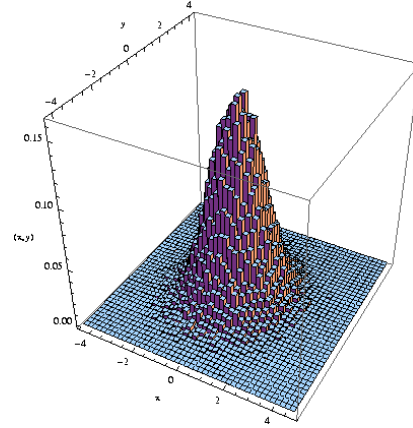
23.6 Anisotropic Gaussian diffusion

We've been considering only the situation in which the probability of moving in any direction is the same. This is equivalent to assuming that the variance or, equivalently, diffusion coefficient, is the same in each direction. In order to study situations in which this is not the case, we can generalize the previous analysis by using the general form of the expression for the Gaussian distribution of the final particle positions, the multivariate Gaussian distribution. For a general n -dimensional vector $\mathbf{x} = (x_1, \dots, x_n)$, this is

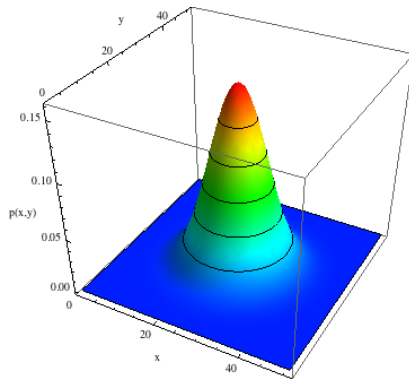
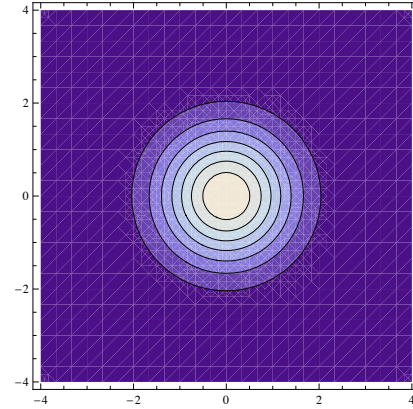
$$p(\mathbf{x}) = \frac{1}{\sqrt{(2\pi)^n |\boldsymbol{\Sigma}|}} \exp \left[-\frac{1}{2} (\mathbf{x} - \boldsymbol{\mu})^t \boldsymbol{\Sigma}^{-1} (\mathbf{x} - \boldsymbol{\mu}) \right] \quad (23.26)$$



(a) Final distribution of particles.



(b) 2D histogram of the points in (a), i.e., the number of particles in each small patch is plotted on the z-axis.

(c) Two-dimensional Gaussian pdf $p(x,y)$ representing (b).(d) Contour plot of $p(x,y)$ in (c).**Figure 23.4** Graphical representations of the 2D random walk.

where $\boldsymbol{\mu} = (\mu_1, \dots, \mu_n)$ is the vector of mean values, and $\boldsymbol{\Sigma}$ is the covariance matrix, and $|\boldsymbol{\Sigma}|$ is its determinant. For the moment we consider only the case of a diagonal covariance matrix:

$$\boldsymbol{\Sigma} = \begin{pmatrix} \sigma_1^2 & & 0 \\ & \ddots & \\ 0 & & \sigma_n^2 \end{pmatrix} \quad (23.27)$$

which results in Eqn 23.26 taking the form of the product of independent distributions:

$$p(\mathbf{x}) = \sum_{i=1}^n \frac{1}{\sqrt{2\pi\sigma_i^2}} \exp \left[-\frac{1}{2} \frac{(x_i - \mu_i)^2}{2\sigma_i^2} \right] \quad (23.28)$$

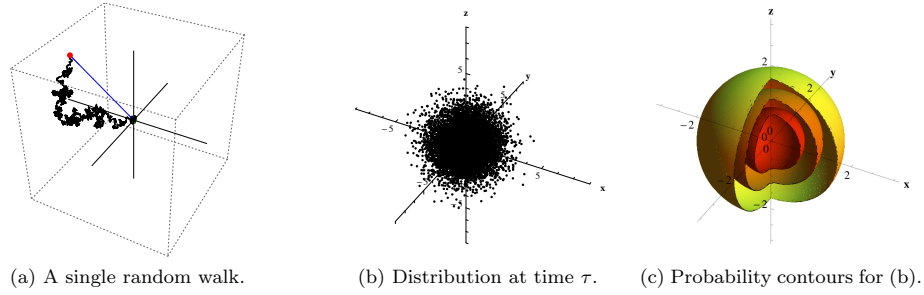


Figure 23.5 Random walk in three dimensions. A single random walk is shown in (a). In (b) is shown the distribution of final positions of an ensemble of particles initially at $\{x, y, z\} = \{0, 0, 0\}$ at $t = 0$. Three (arbitrary) density contours of (b) are shown in (d).

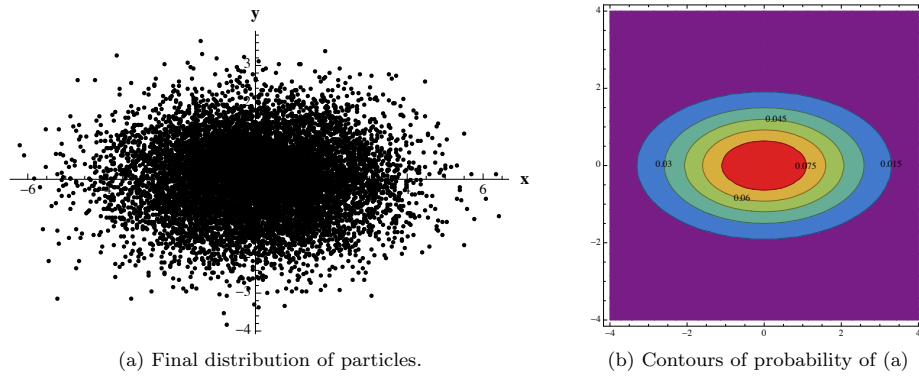


Figure 23.6 Anisotropic diffusion in 2 dimensions for $D_x = 3D_y$.

demonstrating that the existence of off-diagonal terms in the covariance matrix induce correlations in the probability distributions. We will consider this later, but for the present problem of the random walk where \mathbf{x} represents spatial coordinates, the expression Eqn 23.28 is enough to demonstrate the effect of different diffusion coefficients. The two dimensional distribution is

$$p(x, y) = \frac{1}{2\pi\sigma_x^2\sigma_y^2} \exp\left(-\frac{1}{2}\left[\frac{(x-\mu_x)^2}{2\sigma_x^2} + \frac{(y-\mu_y)^2}{2\sigma_y^2}\right]\right) \quad (23.29)$$

where $\sigma_i^2 = 2D_it$, $i = x, y$. Differences in the diffusion coefficients in the x and y directions thus result in different variances in the distributions in these directions, as shown in Figure 23.6. The three-dimensional case where $\sigma_i^2 = 2D_it$, $i = x, y, z$. Differences in the is shown in . These examples in which the diffusion is different along the different directions is called *anisotropic diffusion* and results, in two-dimensions, in probability contours that are ellipses (Figure 23.6b). In three dimensions the contours are ellipsoids (Figure 23.7b).

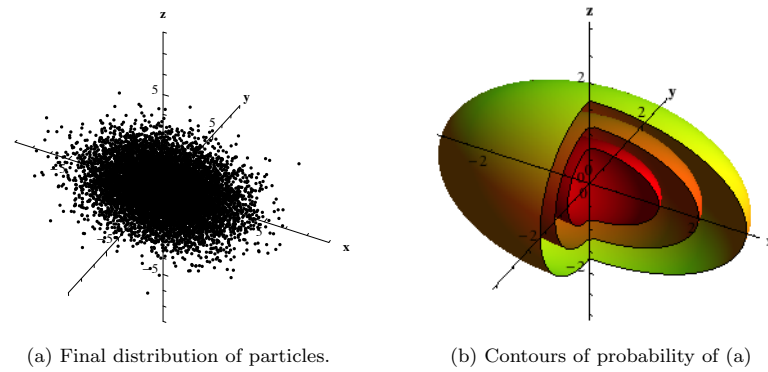


Figure 23.7 Anisotropic diffusion in 3 dimensions for $D_x = 3D_y = 3D_z$.

Problems

23.2 Verify that Eqn 23.26 reduces to Eqn 23.24 and Eqn 23.25 for $\mu_x = \mu_y = \mu_z = 0$ and $\sigma_x = \sigma_y = \sigma_z = \sigma$.

Suggested reading

1. *Random Walks in Biology* by Berg (Oxford, 1989) (?)
An excellent introductory text.