ENTROPY IN BIOLOGY

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Charles S. Peskin

Lecture 7 — continued

The diffusion equation corresponding to Brownian dynamics.

The generalized Einstein relation.

The Diffusion Equation Corresponding to Brownian Dynamics and the Generalized Einstein Relation

Consider the discrete-time stochastic process that implements Brownian dynamics for a system with n degrees of freedom:

(1) $$X^{m+1} = X^m + \Delta t \, \mathcal{S}^{-1} f(X^m) + (\Delta t)^{1/2} (2kT)^{1/2} \mathcal{S}^{-1/2} W^m$$

where $X \in \mathbb{R}^n$, $W \in \mathbb{R}^n$, $f : \mathbb{R}^n \to \mathbb{R}^n$

and where $\mathcal{S}$ is a positive-definite $n \times n$ symmetric matrix.

The random variables W^m are <u>independent</u> for different m, and for each m they satisfy

(2) $$E[W^m] = 0$$

(3) $$E[W^m (W^m)^T] = I$$

Let $\rho^m(x)$ be the probability density function for the random variable X^m.

A key observation is that X^m and W^m are independent, since X^m is determined by

$$W^{m-1}, W^{m-2}, \dots$$

and W^m is independent of all of those random variables.

Now consider an arbitrary smooth function $\phi : \mathbb{R}^n \to \mathbb{R}$ with sufficiently rapid decay at ∞ that we do not need to worry about any contributions from ∞ when we integrate by parts.

By Taylor series,

$$\phi(X^{m+1}) = \phi(X^m) + (\Delta t)^{1/2}(2kT)^{1/2}\, \rho^{-1/2} W^m \cdot \phi'(X^m) + (\Delta t)\left(\rho^{-1} f(X^m)\right)\cdot \phi'(X^m) + \frac{1}{2}(\Delta t)\, 2kT \left(\rho^{-1/2} W^m\right)^T \phi''(X^m)\, \rho^{-1/2} W^m + O\left((\Delta t)^{3/2}\right) \tag{4}$$

where ϕ' denotes the gradient of ϕ and ϕ'' denotes the Hessian (i.e., the matrix of second derivatives) of ϕ

Now we take the expected value on both sides of (4). Since W^m and X^m are independent and $E[W^m]=0$, the term with coefficient $(\Delta t)^{1/2}$ is zero.

In the term involving $\phi''(X^m)$, we have

(5) $$E\left[(W^m)^T \rho^{-1/2} \phi''(X^m) \rho^{-1/2} W^m\right] =$$

$$E\left[\operatorname{trace}\left((W^m)^T \rho^{-1/2} \phi''(X^m) \rho^{-1/2} W^{(m)}\right)\right] =$$

$$E\left[\operatorname{trace}\left(\rho^{-1/2} \phi''(X^m) \rho^{-1/2} W^m (W^m)^T\right)\right] =$$

$$\operatorname{trace}\left(E\left[\rho^{-1/2} \phi''(X^m) \rho^{-1/2}\right] \cancel{E\left[W^m (W^m)^T\right]}\right) =$$

$$E\left[\operatorname{trace}\left(\rho^{-1/2} \phi''(X^m) \rho^{-1/2}\right)\right] =$$

$$E\left[\operatorname{trace}\left(\rho^{-1} \phi''(X^m)\right)\right]$$

Thus, equation (4) becomes

(6) $$E[\phi(X^{m+1})] = E[\phi(X^m)]$$

$$+ \Delta t\, E[(\mathcal{f}^{-1} f(X^m)) \cdot \phi'(X^m)]$$

$$+ \Delta t\, kT\, E[\mathrm{trace}(\mathcal{f}^{-1} \phi''(X^m))]$$
$$+ O((\Delta t)^{3/2})$$

Making use of the definition of expected value, we can write out equation (6) as follows (with the summation convention in effect):

(7) $$\int_{\mathbb{R}^n} \rho^{m+1}(x)\phi(x)\,dx = \int_{\mathbb{R}^n} \rho^m(x)\phi(x)\,dx$$

$$+ \Delta t \int_{\mathbb{R}^n} \rho^m(x) (\mathcal{f}^{-1})_{ij}\, f_j(x)\, \frac{\partial \phi}{\partial x_i}(x)\,dx$$

$$+ (\Delta t)\, kT \int_{\mathbb{R}^n} \rho^m(x) (\mathcal{f}^{-1})_{ij} \frac{\partial^2 \phi}{\partial x_i \partial x_j}(x)\,dx$$

$$+ O((\Delta t)^{3/2})$$

Now we integrate by parts as needed to move all of the derivatives off of ϕ. Also, we divide by Δt and put all of the integrals together to get the following

(8)
$$\int_{\mathbb{R}^n} \left(\frac{\rho^{m+1}(x) - \rho^m(x)}{\Delta t} + \mathcal{J}^{-1}_{ij} \frac{\partial}{\partial x_i}\left(f_j(x)\rho^m(x)\right) - kT\,\mathcal{J}^{-1}_{ij} \frac{\partial^2 \rho^m}{\partial x_i \partial x_j}(x) \right) \phi(x)\, dx$$

$$= O\left((\Delta t)^{1/2}\right)$$

In equation (8), we let $\Delta t \to 0$, make use of the arbitrariness of ϕ, and make the assumption that there is a smooth function $\rho(x,t)$ such that

(9) $$\rho^m_{\Delta t}(x) \longrightarrow \rho(x,t)$$

as $m \to \infty$ with $\Delta t = t/m$. (Here we make it explicit that $\rho^m(x)$ depends on Δt, which has been understood up to now.) It then follows from (8) that $\rho(x,t)$ satisfies

(10) $$\frac{\partial \rho}{\partial t} + (\mathcal{J}^{-1})_{ij} \frac{\partial}{\partial x_i}\left(f_j(x)\rho(x,t)\right)$$

$$- kT(\mathcal{J}^{-1})_{ij} \frac{\partial^2 \rho}{\partial x_i \partial x_j}(x,t) = 0$$

Equation (10) can be rewritten as a multivariate drift-diffusion equation

(11) $$\frac{\partial \rho}{\partial t} + \frac{\partial F_i}{\partial x_i} = 0$$

(12) $$F_i = -D_{ij}\left(\frac{\partial \rho}{\partial x_j} - \frac{f_j}{kT}\rho\right)$$

where

(13) $$D_{ij} = kT\left(\mathcal{J}^{-1}\right)_{ij}$$

and equation (13) is the generalized Einstein relation, since $\mathcal{J}^{-1}$ is the mobility matrix. Note that D, like $\mathcal{J}^{-1}$, is symmetric and positive definite.

Notice, too, that if f is conservative, so that

$$f_j = -\frac{\partial U}{\partial x_j} \tag{14}$$

for some energy function $U(x)$, then

$$F_i = -D_{ij}\left(\frac{\partial \rho}{\partial x_j} + \frac{1}{kT}\frac{\partial U}{\partial x_j}\rho\right) \tag{15}$$

From this it is easy to see that any steady state with $F_i \equiv 0$ satisfies

$$\rho(x) = \frac{e^{-\frac{U(x)}{kT}}}{\int_{\mathbb{R}^n} e^{-\frac{U(\xi)}{kT}}\, d\xi} \tag{16}$$

In the derivation of Brownian dynamics, we only required that the mean potential energy of the system should be in agreement with thermodynamics, and moreover, we only required this for linear systems of forces, i.e., for quadratic energy functions. Here, we have the much more general result that the equilibrium distribution of configurations is in agreement with thermodynamics, and that this is true for any system of conservative forces. This is much more satisfying!

Also, as a byproduct, we now know how the Einstein relation generalizes for systems, see equation (13).

Although it was nice to see the time-dependent multivariable diffusion equation emerge from the foregoing discussion, it would have been simpler to assume that the process described by equation (1) has been running long enough to become stationary.

In that case, $\rho^m_{\Delta t}(x)$ does not depend on m, and equation (8) becomes

$$\int_{\mathbb{R}^n} \gamma_{ij}^{-1}\left(\frac{\partial}{\partial x_i}\left(f_j(x)\rho_{\Delta t}(x)\right) - kT\frac{\partial^2 \rho_{\Delta t}}{\partial x_i \partial x_j}(x)\right)\phi(x)\,dx \tag{17}$$

$$= O\left((\Delta t)^{1/2}\right)$$

Now, instead of the more complicated hypothesis (9), we need only assume that there is some function $\rho_0(x)$ such that

(18) $$\lim_{\Delta t \to 0} \rho_{\Delta t}(x) = \rho_0(x)$$

and then we can conclude from (17) by taking the limit $\Delta t \to 0$ that $\rho_0(x)$ satisfies the time-independent version of (10), or equivalently, the time-independent version of (11-12). Our main conclusions, which are the Einstein relation (13) and the Boltzmann distribution (16), follow just as well from this time-independent point of view.