Lecture 24 : Wright-Fisher diffusion

MATH285K - Spring 2010 *Lecturer: Sebastien Roch*

References: [Dur08, Chapter 7], [KT81, Chapter 15].

1 Diffusions: An Informal Overview

In this lecture, we consider a different scaling limit of the Wright-Fisher model—this time going forward in time. This limit involves diffusion processes. Because of the technical difficulties arising in the theory of diffusions, we only give a rather informal discussion of this topic.

Informal Definition. Formally:

> A real-valued, continuous-time stochastic process $\{X(t) : t \in \mathbb{R}_+\}$ which satisfies the strong Markov property and possesses (almost surely) continuous sample paths is called a *(one-dimensional) diffusion*.

Instead of explaining what this means, we give a canonical example which should be familiar:

EX 24.1 (Brownian motion) *A real-valued stochastic processes* $\{B_t : t \in \mathbb{R}_+\}$ *is a* Brownian motion *if it has the following properties:*

1. $B_0(\omega) = 0$, $\forall \omega$.
2. *The map* $t \mapsto B_t(\omega)$ *is a continuous function of* t *for all* ω.
3. *For every* $t, h \geq 0$, $B_{t+h} - B_t$ *is independent of* $\{B_u : 0 \leq u \leq t\}$ *and has a Gaussian distribution with mean* 0 *and variance* h.

Brownian motion arises naturally as the properly re-scaled limit of random walks.

For our purposes, it will be enough to consider diffusions defined on a closed interval $I = [l, r]$. Moreover, we only consider diffusions that satisfy the following properties:

- For every $\varepsilon > 0$,

$$\lim_{h\downarrow 0} \frac{1}{h}\mathbb{P}[|X(t+h) - x| > \varepsilon \,|\, X(t) = x] = 0, \tag{1}$$

  for all $x \in I$. (All diffusions satisfy this version of "continuity," unlike jump chains for instance.)

- Let $\Delta_h X(t) = X(t+h) - X(t)$. For all $l < x < r$ and $t \in \mathbb{R}_+$,

$$\lim_{h\downarrow 0} \frac{1}{h}\mathbb{E}[\Delta_h X(t) \,|\, X(t) = x] = \mu(x), \tag{2}$$

  and

$$\lim_{h\downarrow 0} \frac{1}{h}\mathbb{E}[(\Delta_h X(t))^2 \,|\, X(t) = x] = \sigma^2(x), \tag{3}$$

  where μ, the *infinitesimal drift* (not to be confused with genetic drift), and σ^2, the *infinitesimal variance*, are continuous functions of x. In particular, the process is *time-homogeneous*. Moreover for $r = 3, 4, \ldots$

$$\lim_{h\downarrow 0} \frac{1}{h}\mathbb{E}[|\Delta_h X(t)|^r \,|\, X(t) = x] = 0. \tag{4}$$

- The process is *regular*, that is, for all x, y in the interior of I

$$\mathbb{P}[T(y) < \infty \,|\, X(0) = x] > 0, \tag{5}$$

  where $T(y)$ is the hitting time of y, that is, the first time y is reached.

We illustrate the moment conditions in the case of Brownian motion.

EX 24.2 (Brownian motion: Infinitesimal moments) *By the Gaussian increments, we have immediately*

$$\mathbb{E}[\Delta_h X(t) \,|\, X(t) = x] = 0,$$

$$\mathbb{E}[(\Delta_h X(t))^2 \,|\, X(t) = x] = h,$$

and

$$\mathbb{E}[(\Delta_h X(t))^4 \,|\, X(t) = x] = 3h^2.$$

More generally, for Brownian motion with drift μ and variance σ^2, that is, $\mu t + \sigma B_t$, the first limit above is μ and the second, σ^2.

Convergence to diffusions. Let $\{X_n^N\}_{n\geq 0}$ be a sequence of Markov chains over I. Let $\Delta X_n^N = X_{n+1}^N - X_n^N$. Assume the following conditions are satisfied:

$$\mathbb{E}[\Delta X_n^N \mid X_n^N] = h_N \mu(X_n^N) + \varepsilon_{1,n}^N, \tag{6}$$

$$\mathbb{E}[(\Delta X_n^N)^2 \mid X_n^N] = h_N \sigma^2(X_n^N) + \varepsilon_{2,n}^N, \tag{7}$$

and

$$\mathbb{E}[(\Delta X_n^N)^4 \mid X_n^N] = \varepsilon_{4,n}^N, \tag{8}$$

where $h_N \downarrow 0$ and for all $t > 0$ and $i = 1, 2, 4$

$$\sum_{n<[t/h_N]} \mathbb{E}|\varepsilon_{i,n}^N| \to 0, \tag{9}$$

where $[z]$ is the integer part of z. Then, under further technical conditions (μ and σ^2 must correspond to a well-defined diffusion; see e.g. [Dur96, (2.2) or (3.3) in Chapter 5]), the finite-dimensional distributions of the process

$$X^N(t) = X_{[t/h_N]}^N$$

converge to the finite-dimensional ditributions of a diffusion $\{X(t)\}_{t\in\mathbb{R}_+}$ with infinitesimal drift μ and variance σ^2.

(For more general tightness and truncated moment conditions, see [Dur96, (7.1) or (8.2) in Chapter 8]. Moreover, the discrete-time process need not be Markov.)

2 Wright-Fisher diffusion

Consider a haploid population with N individuals and two alleles A and a. Denote by i the number of A-types. Assume that a $A \to a$ (respectively $a \to A$) mutation occurs immediately after birth with probability α (respectively β). Further suppose that A is positively selected so that the relative survival abilities of A and a in contributing to the next generation are in the ratio $1 + s$ to 1 where $s > 0$. (One way to think about this is to assume that all A-types survive to maturity, but only a fraction $\frac{1}{1+s}$ of a-types survive.) We still assume that the next generation has N individuals following a binomial sampling scheme where the probability of being A is

$$p_i = \frac{[i(1-\alpha) + (N-i)\beta]}{[i(1-\alpha) + (N-i)\beta] + \frac{1}{1+s}[i\alpha + (N-i)(1-\beta)]}. \tag{10}$$

Assume α, β and s scale with N as

$$\alpha = \frac{\gamma_1}{N}, \qquad \beta = \frac{\gamma_2}{N}, \qquad s = \frac{\phi}{N}.$$

Let Z_n^N be hte number of A-types in generation n (at birth). We are claiming that, in the limit $N \to \infty$, the process

$$\frac{Z_{[Nt]}^N}{N},$$

behaves like a diffusion. We apply the conditions above to $X_n^N = \frac{Z_n^N}{N}$.

Mutation only. Assume that $\gamma_1, \gamma_2 > 0$ and $s = 0$. We compute the limiting infinitesimal drift and variance. By (10),

$$\begin{aligned}
\mathbb{E}\left[\Delta X_n^N \,|\, X_n^N = \frac{i}{N}\right] &= p_i - \frac{i}{N} \\
&= \frac{i(1-\alpha) + (N-i)\beta}{N} - \frac{i}{N} \\
&= -\alpha \frac{i}{N} + \beta \left(1 - \frac{i}{N}\right) \\
&= \frac{1}{N}\left[-\gamma_1 \frac{i}{N} + \gamma_2 \left(1 - \frac{i}{N}\right)\right],
\end{aligned}$$

so that

$$\mu(x) = -\gamma_1 x + \gamma_2 (1-x).$$

Similarly,

$$\begin{aligned}
\mathbb{E}\left[(\Delta X_n^N)^2 \,|\, X_n^N = \frac{i}{N}\right] &= \frac{i^2}{N^2} - 2\frac{i}{N} p_i + \frac{N p_i (1-p_i) + N^2 p_i^2}{N^2} \\
&= \frac{1}{N}\left\{p_i(1-p_i) + \left(p_i - \frac{i}{N}\right)^2\right\} \\
&= \frac{1}{N}\left\{\frac{i}{N}\left(1 - \frac{i}{N}\right) + O\left(\frac{1}{N}\right)\right\},
\end{aligned}$$

so that

$$\sigma^2(x) = x(1-x).$$

See [KT81] for a computation of the fourth moment.

Selection only. Assume $\phi > 0$ and $\alpha = \beta = 0$. As above

$$\begin{aligned}
\mathbb{E}\left[\Delta X_n^N \mid X_n^N = \frac{i}{N}\right] &= p_i - \frac{i}{N} \\
&= \frac{(1+s)i}{(1+s)i + (N-i)} - \frac{i}{N} \\
&= \frac{1}{N}\left\{N\frac{(1+s)i}{N+si} - i\right\} \\
&= \frac{1}{N}\left\{s\frac{Ni - i^2}{N+si}\right\} \\
&= \frac{1}{N}\left\{\phi\frac{\frac{i}{N} - \frac{i^2}{N^2}}{1 + \frac{\phi}{N}\frac{i}{N}}\right\} \\
&= \frac{1}{N}\left\{\phi\frac{i}{N}\left(1 - \frac{i}{N}\right) + O\left(\frac{1}{N}\right)\right\}
\end{aligned}$$

so that

$$\mu(x) = \phi x(1-x).$$

The second moment calculation is essentially identical to the mutation only case.

Further reading

The material in this section was taken from Chapter 15 of [KT81].

References

[Dur96] Richard Durrett. *Stochastic calculus*. Probability and Stochastics Series. CRC Press, Boca Raton, FL, 1996.

[Dur08] Richard Durrett. *Probability models for DNA sequence evolution*. Probability and its Applications (New York). Springer, New York, second edition, 2008.

[KT81] Samuel Karlin and Howard M. Taylor. *A second course in stochastic processes*. Academic Press Inc. [Harcourt Brace Jovanovich Publishers], New York, 1981.