

# Notes 23 : Wright-Fisher diffusion

MATH 833 - Fall 2012

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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 23.1 (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  $\omega$ .
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  $\varepsilon > 0$ ,

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

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  $t \in \mathbb{R}_+$ ,

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

and

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

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

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

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

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

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

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

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

and

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

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

**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:

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

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

and

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

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

$$\sum_{n < [t/h_N]} \mathbb{E}|\varepsilon_{i,n}^N| \rightarrow 0, \quad (9)$$

where  $[z]$  is the integer part of  $z$ . Then, under further technical conditions ( $\mu$  and  $\sigma^2$  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 distributions of a diffusion  $\{X(t)\}_{t \in \mathbb{R}_+}$  with infinitesimal drift  $\mu$  and variance  $\sigma^2$ .

(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  $A \rightarrow a$  (respectively  $a \rightarrow A$ ) mutation occurs immediately after birth with probability  $\alpha$  (respectively  $\beta$ ). 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

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

Assume  $\alpha$ ,  $\beta$  and  $s$  scale with  $N$  as

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

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

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

so that

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

Similarly,

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

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

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

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.