Stochastic Models for Genetic Evolution

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Written examination: Tuesday 23 June 2015, 10:00–13:00.

- Write your name and student identification number on each piece of paper you hand in.
- All answers must come with a full explanation. Formulas alone are not enough. Formulate your answers clearly and carefully.
- The use of textbooks, lecture notes or handwritten notes is not allowed.
- The questions below are weighted as follows: (1) 2, 2; (2) 3, 2, 3, 8; (3) 6, 8, 5; (4) 2, 5, 2, 3, 8; (5) 3, 8, 8, 4; (6) 2, 4, 8, 4. *Total:* 100. Pass: ≥ 55; no pass: ≤ 54.

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(1) (a) How is the DNA-molecule organized and what role does it play for genetic evolution?

(b) Describe the five basic forces of genetic evolution.

(2) (a) Give the definition of the standard Wright–Fisher model with population size $2N$.

(b) Describe the state space and the transition matrix of the associated Markov chain $X = (X_n)_{n\geq 0}$.

(c) Give the definition of the *genetic variability* H_n at time n. What is the interpretation of this quantity?

(d) Compute $\mathbb{E}(H_n \mid H_0)$ as a function of n and N.

(3) (a) Describe the Wright–Fisher diffusion and its connection to the standard Wright–Fisher model.

(b) Let $D = (D_t)_{t\geq 0}$ be the death process on $\mathbb{N}$ where transions from n to $n-1$ occur at rate $\binom{n}{2}$. Denote by $Y = (Y_t)_{t\geq 0}$ the Wright–Fisher diffusion. In which sense D is the dual of the process Y.

(c) Use this dual process D to compute $\mathbb{E}(H_t \mid H_0)$ as a function of t, where $H_t := Y_t(1 - Y_t)$ is the genetic variability of the Wright–Fisher diffusion at time t.

(4) (a) Give the definition of the standard Moran model with fixed population size $2N$.

(b) Describe differences and similarities between the Wright–Fisher and the standard Moran model.

(c) In what way is *selection* added to the standard Moran model?

(d) What are the state space and the transition rates of the associated Markov process $(X_t^{(s)})_{t\geq 0}$ with selection parameter $s \in [0,1)$?

(e) Consider the Markov process $(X_t^{(s)})_{t\geq 0}$ in point (4.d) with *weak selection*, that is, with $s := \sigma/4N$ for some constant $\sigma > 0$. Describe under what type of space–time scaling it converges weakly to a diffusion process, and describe the resulting diffusion and its interpretation?

(5) (a) Define the Wright-Fisher model with *mutation* with parameters $u, v \in (0,1)$?

(b) Derive a formula for the probability that two randomly chosen individuals are identical by descent when the system is in equilibrium.

(c) Consider the case of *weak mutation*, that is, when $u := q/4N$ and $v := r/4N$ for some given constants $q, r > 0$. Let $Y^{(N)}$ be the fraction of individuals of one type, say A, in the Wright-Fisher model with weak mutation at equilibrium. As N goes to infinity, $Y^{(N)}$ converges weakly to a random variable Y with law given by a Beta distribution of parameter q and r, that is, the distribution identified by the density function $f_{q,r}(x) := C_{q,r}^{-1} x^{q-1}(1-x)^{r-1}\mathbb{1}_{x\in[0,1]}$, with $C_{q,r} := \Gamma(q)\Gamma(r)/\Gamma(q+r)$ and Γ being the Gamma–function. Sketch a proof of this convergence statement.

(d) Knowing the distribution of the random variable Y in point (5.c) above, describe in which sense the Wright-Fisher with weak mutation interpolates between the model with constant mutation and the one without mutation. (*Hint*: Describe the qualitative behaviour of the density function $f_{q,r}(x)$ for $q, r < 1$ and for $q, r > 1$.)

(6) (a) Define the hierarchical lattice Ω_M of order M.

(b) On Ω_M, describe the hierarchical model of coupled Wright–Fisher diffusions with migration.

(c) Define the k-block averages and explain as much as possible their local mean–field limit.

(d) In which sense the standard Wright–Fisher diffusion is a global attractor for this hierarchical model?