# Stochastic Models for Genetic Evolution

*Teacher:* F. den Hollander
*Written examination:* Monday 28 January 2013, 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, 3; (2) 3, 5, 2, 5; (3) 5, 3, 5; (4) 7, 4, 3, 7; (5) 3, 5, 3, 6; (6) 3, 3, 3; (7) 4, 3, 5, 8. *Total:* 100. Pass: $\geq 55$; no pass: $\leq 54$.

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

(b) What are the five basic forces of genetic evolution?

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

(b) What are the state space and the transition matrix of the associated Markov chain?

(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 $H_0$, $n$ and $N$.

(3) (a) Describe the Wright-Fisher diffusion and explain how it arises from the Wright-Fisher model via space-time scaling.

(b) What process is dual to the Wright-Fisher diffusion?

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

(4) (a) Give the definition of the Kingman coalescent.

(b) Explain what it means that the Kingman coalescent comes down from infinity.

(c) Given the definition of the most recent common ancestor of the population in the WF-model in the scaling limit.

(d) How long ago did the most recent common ancestor live on average (in scaled time units).

(5) (a) In what way is mutation added to the standard Wright-Fisher model?

(b) What are the state space and the transition matrix of the associated Markov chain?

(c) What is the most important consequence of mutation?

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

(6) (a) In what way is selection added to the continuous-time variant of the standard Wright-Fisher model called the Moran model?

(b) What are the state space and the transition rates of the associated Markov process?

(c) What is the most important consequence of selection?

(7) (a) Give a description of the stepping stone model on $\mathbb{Z}^2$ (based on simple random walk) and its key parameters $N$, $\nu$, $\mu$.

(b) What is the definition of the probability that two individuals randomly drawn from two given colonies $x$ and $y$ are identical by descent?

(c) What are the two main regimes for the stepping stone model on the $L$-torus in $\mathbb{Z}^2$ as a function of $L$, $\nu$ and $\mu$? What is the intuition behind these regimes?

(d) Let $\tau$ be the time to coalescence of the lineages of two individuals randomly drawn from two randomly chosen colonies on the $L$-torus in $\mathbb{Z}^2$ in the absence of mutation. Let $N = N(L)$ and $\nu = \nu(L)$ be such that $\lim_{L\to\infty} 4\pi N\nu/\log L = \alpha \in (0,\infty)$. In this limit it is known that $w - \lim_{L\to\infty} \tau/C_L = \mathrm{EXP}(1)$ with $C_L = (1+\alpha)L^2 \log L/2\pi\nu$. Add mutation with probability $\mu$ per unit of time, and compute the probability that the two individuals are identical by descent. How can the result be interpreted for small $\mu$?