Stochastic Models for Genetic Evolution

Teacher: L. Avena
Written examination: Wednesday 10 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) 8, 3, 3, 8; (4) 3, 3, 8, 2; (5) 3, 3, 9, 7; (6) 5, 8, 3, 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 *fixation* time τ. What is the interpretation of this quantity?

    (d) Compute $\mathbb{P}(X_\tau = 2N \mid X_0 = i)$ as a function of i and N.

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

    (b) The Markov chain X associated to the standard Wright-Fisher model evolves in discrete time. Assume instead that the transitions of X occur at exponential times of parameter 1. Does this change affect the space-time scaling limit?

(c) Give the definition of the standard Moran model and its generalized h-version.

(d) Describe (as much as possible) differences and similarities between the Wright-Fisher and the Moran model.

(4) (a) In what way is selection added to the standard Moran model?

(b) What are the state space and the transition rates of the associated Markov process with selection parameter $s \in (0,1)$?

(c) Let τ be the fixation time for the standard Moran model with selection parameter $s \in (0,1)$. Compute $\mathbb{P}(X_\tau = 2N \mid X_0 = i)$ as a function of i, N and s.

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

(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 with mutation parameters $u, v \in (0,1)$?

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

(d) Show that at equilibrium, as the population size N goes to infinity, the fraction of individuals of one type, say A, converge in probability to a deterministic value.

(6) (a) Give a description of the stepping stone model on a general connected graph G (based on simple random walk) and its key parameters N, ν, μ.

(b) Denote by $\mathbb{T}_{2,L}$ the L-torus in $\mathbb{Z}^2$. Consider the stepping stone model on $\mathbb{T}_{2,L}$ and let T be the time to coalescence of the lineages of two individuals randomly drawn from two uniformly chosen colonies on $\mathbb{T}_{2,L}$ 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 $w - \lim_{L\to\infty} T/C_L = \text{EXP}(1)$ with $C_L := 2NL^2$ if $\alpha = \infty$ and $C_L := (1+\alpha)L^2 \log L / 2\pi\nu$ otherwise. Add mutation with probability μ per unit of time, and derive an asymptotic estimate for the probability that the two individuals are identical by descent when L is big and μ is small.

(c) Describe the concept of *panmictic* behavior for general models with migration.

(d) Consider the stepping stone model on $\mathbb{T}_{2,L}$ in the regime described in point 6.b above. In which sense this model shows panmictic behavior? (*Hint*: Compare the estimate in point 6.b and the probability in point 5.c for small mutation parameter.)