MTH 428/528

Lectures 16-20

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Topics:

- Martingales
- Moran model with mutation
- Stationary distribution
Martingales.

**Definition.** A homogeneous Markov chain \( \{X_t\} \) is a martingale if

- \( E[|X_t|] < \infty \) for all \( t \geq 0 \), and
- \( E[X_{t+1} \mid X_t = x] = x \).

**Definition.** For a homogeneous Markov chain \( \{X_t\} \), a random variable \( \tau \) is a stopping time if for any \( t \geq 0 \), knowing \( X_0, X_1, \ldots, X_t \) (i.e. the trajectory of the process up to time \( t \)) is sufficient for determining whether the event \( \{\tau \leq t\} \) occurred or not.

**Optional Stopping Theorem.** Suppose a homogeneous Markov chain \( \{X_t\} \) is a martingale, and \( T \) is a stopping time with respect to \( X_t \). If \( P(T < \infty) = 1 \) and there is \( K > 0 \) such that \( |X_t| \leq K \) when \( t < T \), then

\[
E[X_T \mid X_0] = X_0.
\]
Martingales.

If Markov chain \( \{X_t\} \) is a martingale, then
\[
E[X_1 \mid X_0 = x] = x \quad \text{and} \quad E[X_2 \mid X_1 = y] = y.
\]
Then,
\[
E[X_2 \mid X_0 = x] = \sum_{y \in S} E[X_2 \mid X_1 = y, X_0 = x] P(X_1 = y \mid X_0 = x)
\]
\[
= \sum_{y \in S} E[X_2 \mid X_1 = y] P(X_1 = y \mid X_0 = x)
\]
\[
= \sum_{y \in S} y P(X_1 = y \mid X_0 = x) = E[X_1 \mid X_0 = x] = x
\]

So, \( E[X_2 \mid X_0 = x] = x \), and iterating the argument, we obtain
\[
E[X_t \mid X_0 = x] = x \quad \text{for all } t \geq 0.
\]
Moran model via martingales.

First, we observe that the Moran process is a martingale: there

\[ p_j = q_j = \frac{j(n - j)}{n^2}, \quad r_j = 1 - 2\frac{j(n - j)}{n^2} \]

and

\[ E[X_{t+1} \mid X_t = j] = (j + 1) \cdot p_j + j \cdot r_j + (j - 1) \cdot q_j = j. \]

Moreover, the Optional Stopping Theorem will allow us to answer the question of finding the probability of fixation with all \( n \) alleles being \( A \),

\[ \alpha = P(X_{T_f} = n \mid X_0 = j). \]

Indeed, by the Optional Stopping Theorem,

\[ 0 \cdot (1 - \alpha) + n \cdot \alpha = E[X_{T_f} \mid X_0 = j] = j. \]

Thus,

\[ P(X_{T_f} = n \mid X_0 = j) = \alpha = \frac{j}{n}. \]
Wright-Fisher Model via martingales.

Given that we know $X_t$, variable $X_{t+1}$ is a Binomial random variable with $n = 2N$ trials and $p = \frac{X_t}{n}$, i.e.

$$P(X_{t+1} = k \mid X_t = j) = \binom{n}{k} p^k (1 - p)^{n-k}, \quad \text{where } p = \frac{j}{n}.$$  

Then, $X_t$ is a martingale:

$$E[X_{t+1} \mid X_t = j] = np = j.$$  

Here too, by the Optional Stopping Theorem,

$$0 \cdot (1 - \alpha) + n \cdot \alpha = E[X_{T_f} \mid X_0 = j] = j$$

and therefore

$$\alpha : = P(X_{T_f} = n \mid X_0 = j) = \frac{j}{n}.$$
Martingales.

Definition. A sequence of random variables \( \{M_t\} \) is a martingale with respect to a homogeneous Markov chain \( \{X_t\} \) if

- \( M_t \) is a function of \( X_t, X_{t-1}, \ldots, X_0 \),
- \( E[|M_t|] < \infty \) for all \( t \geq 0 \), and
- 

\[
E[M_{t+1} \mid X_t, X_{t-1}, \ldots, X_0] = M_t.
\]

Optional Stopping Theorem. Suppose \( \{M_t\} \) is a martingale with respect to \( \{X_t\} \), and \( T \) is a stopping time with respect to \( X_t \). If \( P(T < \infty) = 1 \) and there is \( K > 0 \) such that \( |M_t| \leq K \) when \( t < T \), then

\[
E[M_T \mid X_0] = M_0.
\]
Martingales and harmonic functions.

Suppose \( \{X_t\} \) is a time homogeneous Markov chain (HMC).

We say that \( h(\cdot) \) is a harmonic function with respect to the transition probabilities \( \{p(x, y)\} \) if \( h \) satisfies the averaging property

\[
\sum_y p(x, y)h(y) = h(x).
\]

There, \( h(X_t) \) is a martingale with respect to \( \{X_t\} \):

\[
E[h(X_{t+1}) \mid X_t = x] = \sum_y p(x, y)h(y) = h(x)
\]

and

\[
E[h(X_{t+1}) \mid X_t] = h(X_t).
\]
Martingales and harmonic functions.

For a birth-and-death chain $X_t$, the probability harmonic function $h$ is the one satisfying the averaging property

$$h(k) = q_k h(k - 1) + (1 - q_k - p_k) h(k) + p_k h(k + 1)$$

The above recurrence relation, after being simplified as

$$q_k \left( h(k) - h(k - 1) \right) = p_k \left( h(k + 1) - h(k) \right)$$

yields $h(0) = A$, $h(1) = A + B$, and

$$h(k) = A + B \left( 1 + \sum_{j=2}^{k} \frac{q_1 \cdots q_{j-1}}{p_1 \cdots p_{j-1}} \right) \quad \text{for } k = 2, 3, \ldots$$

Thus $M_t = h(X_t)$ is a martingale with respect to $\{X_t\}$. 
Martingales and harmonic functions.

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$$h(k) = q_k h(k - 1) + (1 - q_k - p_k) h(k) + p_k h(k + 1)$$

The above recurrence relation yields $h(0) = A$, $h(1) = A + B$, and $h(k) = A + B \left( 1 + \sum_{j=2}^{k} \frac{q_1 \cdots q_{j-1}}{p_1 \cdots p_{j-1}} \right)$ for $k = 2, 3, \ldots$

Thus $M_t = h(X_t)$ is a martingale with respect to $\{X_t\}$. Define the following stopping time with respect to $X_t$,

$$T = \min\{t \geq 0 : X_t = 0 \text{ or } m\}.$$  

Then, given that $X_0 = j$ for $0 \leq j \leq m$,

$$P(X_T = m \mid X_0 = j) = \frac{h(j) - h(0)}{h(m) - h(0)}.$$
Martingales and harmonic functions.

Example. For a birth-and-death chain $X_t$ with $p_k = p$ and $q_k = q$ for all $k$, and $p \neq q$,

$$h(k) = qh(k - 1) + (1 - q - p)h(k) + ph(k + 1)$$

yielding

$$h(k) = A + B \left( \frac{q}{p} \right)^k$$

for $k = 0, 1, 2, 3, \ldots$

Define the following stopping time with respect to $X_t$,

$$T = \min\{t \geq 0 : X_t = 0 \text{ or } m\}.$$

Then, given that $X_0 = j$ for $0 \leq j \leq m$,

$$P(X_T = m \mid X_0 = j) = \frac{h(j) - h(0)}{h(m) - h(0)} = \frac{\left( \frac{q}{p} \right)^j - 1}{\left( \frac{q}{p} \right)^m - 1}.$$
**Moran model with mutation.**

Consider Moran model with mutation. We think of \( n = 2N \) haploid individuals (who have one copy of their genetic material in each cell), and a genetic locus with two alleles \( A \) and \( a \) that have the same fitness. This model evolves as following:

(i) At each time step, an individual chosen uniformly at random out of \( n \) individuals is being “replaced”.

(ii) To replace individual \( x \), we choose at random from the set of individuals, including \( x \) itself.

(iii) An allele \( A \) that is chosen mutates to allele \( a \) with probability \( \alpha > 0 \), while \( a \) mutates to allele \( A \) with probability \( \beta > 0 \).
Moran model with mutation.

(i) At each time step, an individual chosen uniformly at random out of $n$ individuals is being “replaced”.

(ii) To replace individual $x$, we choose at random from the set of individuals, including $x$ itself.

(iii) An allele $A$ that is chosen mutates to allele $a$ with probability $\alpha > 0$, while $a$ mutates to allele $A$ with probability $\beta > 0$.

\[
p(i, i + 1) = \frac{n - i}{n} \cdot \left( \frac{i}{n} \cdot (1 - \alpha) + \frac{n - i}{n} \cdot \beta \right)
\]

and

\[
p(i, i - 1) = \frac{i}{n} \cdot \left( \frac{i}{n} \cdot \alpha + \frac{n - i}{n} \cdot (1 - \beta) \right)
\]
Stationary distribution and reversibility.

For a homogeneous Markov chain with the transition probability matrix \( P = \left( p(i, j) \right)_{i, j \in S} \), the stationary distribution (aka ‘equilibrium distribution’) \( \pi \) is defined as follows:

\[
\pi P = \pi \iff \sum_{i \in S} \pi(i)p(i, j) = \pi(j).
\]

Thus \( \sum_{i} \pi(i)p(i, j) = \pi(j)\sum_{i} p(j, i) \), and for any state \( j \in S \),

\[
\sum_{i: i \neq j} \pi(i)p(i, j) = \sum_{i: i \neq j} \pi(j)p(j, i).
\]

Thus when restated in terms of traffic flow, the influx to the state \( j \) is equal to outflow from \( j \), for each \( j \). Thus the distribution stays unchanged.
Stationary distribution and reversibility.

The following are the detailed balance conditions (d.b.c.) also called time reversibility:

$$\pi(i)p(i, j) = \pi(j)p(j, i).$$

Restated in terms of traffic flow: for every pair of states $i$ and $j$ the traffic in between them is balanced (equalized), i.e. the traffic flow from $i$ to $j$ equals to the traffic flow from $j$ to $i$.

Observe that if d.b.c. are satisfied, the distribution will not change with time, i.e. $\pi$ is stationary;

$$\sum_{i: i \neq j} \pi(i)p(i, j) = \sum_{i: i \neq j} \pi(j)p(j, i).$$
Stationary distribution and reversibility.

Observe that in the case of a birth-and-death chain, the definition of a stationary distribution

\[ \pi P = \pi \iff \sum_{i \in S} \pi(i) p(i, j) = \pi(j). \]

can be rewritten as

\[ \pi_k = p_{k-1}\pi_{k-1} + (1-q_k-p_k)\pi_k + q_{k+1}\pi_{k+1} \quad \text{for } k = 1, 2, \ldots \]

The above equations can be shown to be equivalent to the detailed balance conditions (d.b.c.)

\[ \pi_{k-1}p_{k-1} = q_k\pi_k. \]

Hence, \( \pi_k = \frac{p_{k-1}}{q_k}\pi_{k-1} \) for \( k = 1, 2, \ldots \).
**Stationary distribution and reversibility.**

In the case of a birth-and-death chain, \( \pi_k = \frac{p_{k-1}}{q_k} \pi_{k-1} \)

and

\[
\pi_k = \frac{p_0 \cdots p_{k-1}}{q_1 \cdots q_k} \pi_0 \quad \text{for } k = 1, 2, \ldots.
\]

Next, if \( S = \{0, 1, \ldots, n\} \) is the state space,

\[
\pi_0 + \pi_1 + \ldots + \pi_n = 1
\]

implying

\[
\pi_0 + \frac{p_0}{q_1} \pi_0 + \ldots + \frac{p_0 \cdots p_{n-1}}{q_1 \cdots q_n} \pi_0 = 1.
\]

Hence,

\[
\pi_0 = \left(1 + \sum_{j=1}^{n} \frac{p_0 \cdots p_{j-1}}{q_1 \cdots q_j}\right)^{-1}
\]

and

\[
\pi_k = \frac{p_0 \cdots p_{k-1}}{q_1 \cdots q_k} \left(1 + \sum_{j=1}^{n} \frac{p_0 \cdots p_{j-1}}{q_1 \cdots q_j}\right)^{-1} \quad \text{for } k = 1, 2, \ldots.
\]
The gamma function.

The gamma function $\Gamma(\alpha)$ is defined as

$$\Gamma(\alpha) = \int_0^\infty e^{-x} x^{\alpha-1} dx$$

for all $\alpha > 0$. Integration by parts provides

$$\Gamma(\alpha + 1) = \alpha \Gamma(\alpha).$$

In particular, $\Gamma(k) = (k - 1)!$ for all integer $k > 0$.

Also, for $A > 0$,

$$A \cdot (A + 1) \cdot (A + 2) \cdot \ldots \cdot (A + k - 1) = \frac{\Gamma(A + k)}{\Gamma(A)}.$$
Stationary distribution for Moran process.

\[ A \cdot (A + 1) \cdot (A + 2) \cdot \ldots \cdot (A + k - 1) = \frac{\Gamma(A + k)}{\Gamma(A)}. \]

For the Moran model with mutation,

\[ p_i = \frac{n - i}{n} \cdot \left( \frac{i}{n} \cdot (1 - \alpha) + \frac{n - i}{n} \cdot \beta \right) = \frac{n - i}{n^2} \left( n \cdot \beta + i \cdot (1 - \alpha - \beta) \right) \]

Thus, if \( \alpha + \beta < 1 \),

\[ p_0 \ldots p_{k-1} = \frac{n! (1 - \alpha - \beta)^k}{(n - k)! n^{2k}} \cdot \frac{\Gamma \left( n \cdot \frac{\beta}{1 - \alpha - \beta} + k \right)}{\Gamma \left( n \cdot \frac{\beta}{1 - \alpha - \beta} \right)}. \]
Stationary distribution for Moran process.
If $\alpha + \beta < 1$,
\[ p_0 \cdots p_{k-1} = \frac{n!(1 - \alpha - \beta)^k}{(n - k)!n^{2k}} \cdot \frac{\Gamma\left(n \cdot \frac{\beta}{1-\alpha-\beta} + k\right)}{\Gamma\left(n \cdot \frac{\beta}{1-\alpha-\beta}\right)}. \]

Also,
\[ q_i = \frac{i}{n} \left(\frac{i}{n} \cdot \alpha + \frac{n - i}{n} \cdot (1 - \beta)\right) = \frac{i}{n^2} \left(n \cdot \alpha + (n-i) \cdot (1 - \alpha - \beta)\right) \]
and
\[ q_1 \cdots q_k = \frac{k!(1 - \alpha - \beta)^k}{n^{2k}} \cdot \frac{\Gamma\left(n \cdot \frac{\alpha}{1-\alpha-\beta} + n\right)}{\Gamma\left(n \cdot \frac{\alpha}{1-\alpha-\beta} + (n - k)\right)}. \]
Stationary distribution for Moran process.
If $\alpha + \beta < 1$,

$$p_0 \cdots p_{k-1} = \frac{n!(1 - \alpha - \beta)^k}{(n-k)!n^{2k}} \cdot \frac{\Gamma \left( n \cdot \frac{\beta}{1-\alpha-\beta} + k \right)}{\Gamma \left( n \cdot \frac{\beta}{1-\alpha-\beta} \right)}.$$ 

and

$$q_1 \cdots q_k = \frac{k!(1 - \alpha - \beta)^k}{n^{2k}} \cdot \frac{\Gamma \left( n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)}{\Gamma \left( n \cdot \frac{\alpha}{1-\alpha-\beta} + (n-k) \right)}.$$ 

Hence,

$$\pi_k = \frac{p_0 \cdots p_{k-1}}{q_1 \cdots q_k} \pi_0 = C(n,k) \frac{\Gamma \left( n \cdot \frac{\beta}{1-\alpha-\beta} + k \right) \Gamma \left( n \cdot \frac{\alpha}{1-\alpha-\beta} + (n-k) \right)}{\Gamma \left( n \cdot \frac{\beta}{1-\alpha-\beta} \right) \Gamma \left( n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)} \pi_0.$$
The beta function.

The beta function $B(a, b)$ is defined as

$$B(a, b) = \frac{\Gamma(a) \Gamma(b)}{\Gamma(a + b)} = \int_0^1 x^{a-1} (1 - x)^{b-1} dx$$

for all $a > 0$ and $b > 0$.

Then,

$$\pi_k = C(n, k) \frac{\Gamma \left( n \cdot \frac{\beta}{1 - \alpha - \beta} + k \right) \Gamma \left( n \cdot \frac{\alpha}{1 - \alpha - \beta} + (n - k) \right)}{\Gamma \left( n \cdot \frac{\beta}{1 - \alpha - \beta} \right) \Gamma \left( n \cdot \frac{\alpha}{1 - \alpha - \beta} + n \right)} \pi_0$$

$$= C(n, k) \frac{B \left( n \cdot \frac{\beta}{1 - \alpha - \beta} + k, n \cdot \frac{\alpha}{1 - \alpha - \beta} + (n - k) \right)}{B \left( n \cdot \frac{\beta}{1 - \alpha - \beta}, n \cdot \frac{\alpha}{1 - \alpha - \beta} + n \right)} \pi_0.$$
\[ B(a, b) = \int_0^1 x^{a-1} (1 - x)^{b-1} \, dx, \]

\[ \pi_k = C(n, k) \frac{B \left( n \cdot \frac{\beta}{1-\alpha-\beta} + k, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + (n - k) \right)}{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)} \pi_0, \]

and by the Binomial Theorem,

\[ 1 = \sum_{k=0}^{n} \pi_k = \frac{\sum_{k=0}^{n} C(n, k) B \left( n \cdot \frac{\beta}{1-\alpha-\beta} + k, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + (n - k) \right)}{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)} \pi_0 \]

\[ = \frac{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} \right)}{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)} \pi_0. \]
Stationary distribution for Moran process. Recall:

\[ \pi_k = C(n, k) \frac{B \left( n \cdot \frac{\beta}{1-\alpha-\beta} + k, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + (n - k) \right)}{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)} \pi_0 \]

and

\[ 1 = \frac{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} \right)}{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + n \right)} \pi_0. \]

Hence, we have exact solution:

\[ \pi_k = C(n, k) \frac{B \left( n \cdot \frac{\beta}{1-\alpha-\beta} + k, \ n \cdot \frac{\alpha}{1-\alpha-\beta} + (n - k) \right)}{B \left( n \cdot \frac{\beta}{1-\alpha-\beta}, \ n \cdot \frac{\alpha}{1-\alpha-\beta} \right)}. \]
Stationary distribution for Moran process. Recall:

\[ B(a, b) = \frac{\Gamma(a) \Gamma(b)}{\Gamma(a + b)} = \int_0^1 x^{a-1}(1 - x)^{b-1} \, dx \]

and

\[
\pi_k = C(n, k) \frac{B\left( n \cdot \frac{\beta}{1-\alpha-\beta} + k, n \cdot \frac{\alpha}{1-\alpha-\beta} + (n - k) \right)}{B\left( n \cdot \frac{\beta}{1-\alpha-\beta}, n \cdot \frac{\alpha}{1-\alpha-\beta} \right)}.
\]

We use Stirling’s approximation

\[
\Gamma(z) = \sqrt{2\pi} e^{-z} z^{z-\frac{1}{2}} \left(1 + O\left(\frac{1}{z}\right)\right) \quad \text{and} \quad m! = \sqrt{2\pi} e^{-m} m^{m+\frac{1}{2}} \left(1 + O\left(\frac{1}{m}\right)\right)
\]

and obtain for \( \rho := \frac{k}{n} \in [\epsilon, 1 - \epsilon], \quad \alpha = \frac{a}{n} \quad \text{and} \quad \beta = \frac{b}{n}, \)

\[
\pi_k = \frac{1}{n} \cdot \frac{\rho^{a-1}(1 - \rho)^{b-1}}{B(a, b)} \left(1 + o(1)\right).
\]
Stationary distribution for Moran process.
For $\rho := \frac{k}{n} \in [\epsilon, 1 - \epsilon]$, $\alpha = \frac{a}{n}$ and $\beta = \frac{b}{n}$,

$$\pi_k = \frac{1}{n} \cdot \frac{\rho^{a-1} (1 - \rho)^{b-1}}{B(a, b)} (1 + o(1)).$$