Moran Model

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1 The Moran Model

1.1 Formulation

The Moran model was introduced by P. A. P. Moran in a 1958 paper as an alternative to the Wright-Fisher model which allows for overlapping generations. It makes the following assumptions:

1. The population size is constant. To facilitate comparison with the Wright-Fisher model, we will assume that there are $2N$ haploid individuals.

2. Each individual reproduces at rate 1 and gives birth to a single offspring.

3. Whenever a birth occurs, one of the existing $2N$ individuals, including the parent, is chosen uniformly at random and replaced by the new offspring.

Because individuals die at the same rate that they reproduce, the lifespan of each individual is exponentially distributed with mean 1, which is also the generation time for the population. Like the Wright-Fisher model, the Moran model describes a neutrally-evolving population in which individual longevity and fecundity are independent of genotype. Several versions of this model can be found in the literature, including discrete-time versions in which birth-death events occur at regular intervals and versions that assume that the same individual cannot both give birth and die in any one birth-death event. When N is large, all of these versions are very similar to one another.

If we assume that the population initially contains two alleles, say A and a, and we let X_t denote the number of copies of A present at time t, then the process $X = (X_t : t \geq 0)$ is a continuous-time Markov chain with values in the set $\{0, 1, \cdots, 2N\}$ and transition rates

$$
\begin{aligned}
q_{i,i+1} &= i \cdot \frac{2N - i}{2N} \\
q_{i,i-1} &= (2N - i) \cdot \frac{i}{2N}.
\end{aligned}
$$

For example, for the number of copies of A to increase by 1, an individual carrying an A allele must reproduce and their offspring, which also carries an A allele, must replace an individual carrying an a allele. Since there are i copies of A in the population and each reproduces at rate 1, the total rate of reproduction of A alleles is just i. Likewise, since there are $2N - i$ copies of a, the probability that one of these is replaced by the new offspring is just $(2N - i)/2N$. Multiplying these two terms gives the desired rate. Notice that we can also write $q_{i,i+1} = q_{i,i-1} = 2N p_i (1 - p_i)$, where $p_i = i/2N$ is the frequency of A. This shows that the number of copies of A increases at the same rate that it decreases (another signature of neutrality) and also that the total rate of events affecting the frequency of A is of order $2N$ provided that neither allele is very rare. In particular, the diagonal entries of the rate matrix are $q_{ii} = -4N p_i (1 - p_i)$.

Because the number of copies of A changes by at most one in any birth-death event, X is said to be a **generalized birth-death process**. As we will see throughout these notes, this property will allow us to perform a number of calculations exactly that typically can only be done approximately in the Wright-Fisher model. It is primarily for this reason that the Moran model is so popular in the theoretical literature on population genetics. On the other hand, it is usually easier and more efficient to simulate the Wright-Fisher model using the Poisson and normal approximations to the binomial distribution than it is to simulate the Moran model exactly.

When we introduced the Wright-Fisher model, we saw that genetic drift leaves the expected frequency of each allele unchanged, but causes the expected heterozygosity to decline geometrically at rate $(1 - 1/2N)$. For comparison, we will examine how these expectations change under the Moran model. This will be done with the help of the following lemma.

Lemma 1. *Suppose that $X = (X_t : t \geq 0)$ is a Markov chain with values in a finite state space $E = \{1, \cdots, n\}$ and rate matrix Q. Let $f : E \to \mathbb{R}$ be a real-valued function and for each $i \in E$ and $t \geq 0$ define $u_i(t)$ to be the following expectation*

$$u_i(t) = \mathbb{E}[f(X_t)|X_0 = i].$$

Then the functions $u_1(t), \cdots, u_n(t)$ satisfy the following differential equations:

$$\frac{d}{dt}u_i(t) = \sum_k p_{ik}(t) \left(\sum_j q_{kj}(f(j) - f(k)) \right), \quad i \in E,$$

where $p_{ik}(t) = \mathbb{P}(X_t = k|X_0 = i)$ is the transition probability of X.

Proof. We first recall that the transition probabilities $p_{ij}(t)$ satisfy the Kolmogorov forward equations, which take the form

$$\frac{d}{dt}p_{ij}(t) = \sum_k p_{ik}(t)q_{kj}.$$

Consequently,

$$
\begin{aligned}
\frac{d}{dt}u_i(t) &= \frac{d}{dt}\sum_j p_{ij}(t)f(j) = \sum_j \frac{d}{dt}p_{ij}(t)f(j) \\
&= \sum_j \sum_k p_{ik}(t)q_{kj}f(j) \\
&= \sum_k p_{ik}(t)\sum_j q_{kj}f(j) \\
&= \sum_k p_{ik}(t)\left(\sum_{j \neq k} q_{kj}f(j) + q_{kk}f(k) \right) \\
&= \sum_k p_{ik}(t)\left(\sum_{j \neq k} q_{kj}(f(j) - f(k)) \right),
\end{aligned}
$$

where we have used the fact that $q_{kk} = -\sum_{j \neq k} q_{kj}$ to pass to the final line. $\square$

If $f(i) = i$ is the identity function, then $u_i(t) = \mathbb{E}[X_t|X_0 = i]$ is just the expected the number of copies of A at time t given that initially there were i copies. Using the transition rates of the Moran model, we find that for $1 \leq k \leq 2N - 1$

$$\sum_j q_{kj}(f(j) - f(k)) = 2Np_k(1 - p_k)[(k + 1) - k + (k - 1) - k] = 0.$$

Alternatively, if $k = 0$ or $k = 2N$, then this sum also vanishes since these are absorbing states and the transition rates are equal to 0. Thus, from the above lemma, we find that

$$\frac{d}{dt}\mathbb{E}[X_t|X_0 = i] = 0$$

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for every $i \in \{0, \cdots, 2N\}$, which shows that the expected number of copies of A is constant for all time and therefore $\mathbb{E}[X_t|X_0 = i] = \mathbb{E}[X_0|X_0 = i] = i$. In particular, if we let $p_t = X_t/2N$ denote the frequency of A at time t, then it follows that

$$\mathbb{E}[p_t|p_0 = p] = p$$

for all $t \geq 0$, which is analogous to the behavior of the Wright-Fisher model.

To calculate the expected heterozygosity under the Moran model, let $f(i) = 2\frac{i(2N-i)}{4N^2} = 2p_i(1-p_i)$ and note that

$$\bar{H}_i(t) = \mathbb{E}[f(X_t)|X_0 = i].$$

A little algebra shows that

$$\sum_j q_{kj}(f(j) - f(k))$$

$$= 2Np_k(1-p_k)\left[2\left(p_k + \frac{1}{2N}\right)\left(1 - p_k - \frac{1}{2N}\right) + 2\left(p_k - \frac{1}{2N}\right)\left(1 - p_k + \frac{1}{2N}\right) - 4p_k(1-p_k)\right]$$

$$= 2Np_k(1-p_k) \cdot \left(-\frac{1}{N^2}\right)$$

if $1 \leq k \leq 2N - 1$, while the corresponding expression vanishes if $k = 0$ or $k = 2N$. It then follows from the lemma that the expected heterozygosity satisfies the following equation

$$\frac{d}{dt}\bar{H}_i(t) = \sum_k p_{ik}(t) \cdot \left(-\frac{1}{N}2p_k(1-p_k)\right)$$

$$= -\frac{1}{N}\bar{H}_i(t),$$

which has solution

$$\bar{H}_i(t) = e^{-t/N}\bar{H}_i(0),$$

where $\bar{H}_i(0) = 2p_i(1 - p_i)$. Thus, as in the Wright-Fisher model, the expected heterozygosity decays exponentially in the Moran model at a rate that is inversely proportional to the population size. However, the two models do differ in one respect. Recall that for the Wright-Fisher model we have

$$\bar{H}_i(t) = \left(1 - \frac{1}{2N}\right)^t \bar{H}_i(0) \approx e^{-t/2N}\bar{H}_i(0),$$

where the approximation is quite accurate when N is large. Comparison of this expression with that derived above shows that a population of size $2N$ governed by the Moran model looses variation twice as rapidly as a population of size $2N$ governed by the Wright-Fisher model.

It is also of interest to compare the distribution of the genealogy of a sample of n individuals under the Moran and Wright-Fisher models for a population of size $2N$. In the latter case, we saw that if N is much larger than n and if time is measured in units of $2N$ generations, then the distribution of the genealogy can be approximated by Kingman's coalescent in which each pair of lineages coalesces at rate 1 and only pairwise coalescent events occur, i.e., there are no multiple or simultaneous mergers. The same is true of the Moran model, with one important difference.

Theorem 1. *Suppose that n individuals are sampled from a haploid population of size $2N$ governed by the Moran model. If time is measured in units of N generations, then the genealogy of the sample has the same distribution as Kingman's coalescent.*

Proof. Under the Moran model, individuals reproduce independently of one another, at rate 1, and give birth to only one offspring at a time. Consequently, if we look backwards in time, the genealogy of a random sample can only contain pairwise mergers (corresponding to birth-death events). Given a sample of n lineages, a coalescent event will occur whenever there is a birth-death event in which both the birth and the death involve two different individuals in the sample. Since birth events involving the sample occur at rate n, while the probability that their offspring is one of the remaining $n-1$ individuals is $(n-1)/2N$, it follows that the total rate of coalescence involving these n lineages is $n(n-1)/2N$ when time is measured in units of generations. If, instead, time is measured in units of N generations, then the coalescence rate is $\binom{n}{2}$, which is also the rate of coalescence under Kingman's coalescent. $\square$

Since Kingman's coalescent is obtained from the Moran model by rescaling time by a factor of N rather than $2N$, we see that when time is measured in units of generations coalescence events occur twice as rapidly in a population governed by the Moran model as in a population of the same size governed by the Wright-Fisher model. This is analogous to the difference that we saw in the rate at which variation is lost under these two models. However, in all other respects, the two models are very similar whenever N is sufficiently large. For this reason, we say that the **effective population size** of a population of size $2N$ governed by the Moran model is equal to N, meaning that such a population behaves like a population of size N governed by the Wright-Fisher model, at least as far as the statistics of genetic drift and coalescence are concerned.

1.2   Fixation

Notice that 0 and $2N$ are absorbing states for the Moran model and let

$$\tau = \min\left\{t \geq 0 : X_t \in \{0, 2N\}\right\}$$

be the time to fixation of one or the other allele. By examining the jump chain of the Moran model, it can be shown that τ is almost surely finite, i.e., $\mathbb{P}(\tau < \infty) = 1$, as was also true of the Wright-Fisher model. Thus, in the absence of both mutation and immigration, a population described by the Moran model will eventually lose all but one of the alleles initially present. Our next result shows that the fixation probability of A is the same under the Moran model and the Wright-Fisher model.

Theorem 2. *Let $u(i) = \mathbb{P}(X_\tau = 2N | X_0 = i)$ be the probability that A is eventually fixed in a population of size $2N$ that initially contains i copies of A. Under the Moran model, $u(i) = p_i = i/2N$ is equal to the initial frequency of A.*

Proof. Because τ is almost surely finite and X_t is bounded between 0 and $2N$ for all $t \geq 0$, the identity $\mathbb{E}[X_t|X_0 = i] = i$, which holds for all fixed times $t \geq 0$, also holds when we replace t by the random stopping time τ:

$$i = \mathbb{E}[X_\tau|X_0 = i] = 2N \cdot \mathbb{P}(X_\tau = 2N|X_0 = i) + 0 \cdot \mathbb{P}(X_\tau = 0|X_0 = i) = 2N \cdot u(i).$$

Then, dividing the first and the last terms by $2N$ gives $u(i) = i/2N$. $\square$

Our next objective is to determine how long it takes, on average, for A to be fixed conditional on that event occurring, i.e., we wish to calculate the following conditional expectation:

$$\bar{\mathbb{E}}_i[\tau] = \mathbb{E}[\tau|X_0 = i, X_\tau = 2N].$$

However, before tackling this, we will first state and prove a useful generalization of Theorem 2.

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Proposition 1. *Let $X = (X_t : t \geq 0)$ be the Moran model for a population of size $2N$ and for each $a \in \{0, \cdots, 2N\}$ let*

$$T_a = \min\{t \geq 0 : X_t = a\}$$

be the first hitting time of a. Here we define $T_a = \infty$ if X never visits a. Then, for each pair of integers a, b between 0 and $2N$ with $a < b$ and for each integer $i \in [a, b]$, the probability that X visits state b before it visits state a is

$$\mathbb{P}(T_b < T_a | X_0 = i) = \frac{i - a}{b - a}.$$

Proof. Once again, we can use the jump chain embedded in the Moran model to prove that the process will eventually visit one of the two states a or b whenever the initial state i is between a and b, i.e., the hitting time $T_{a,b} = \min\{T_a, T_b\}$ is almost surely finite under this condition. It follows that

$$i = \mathbb{E}[X_{T_{a,b}} | X_0 = i] = b \cdot \mathbb{P}(T_b < T_a | X_0 = i) + a \cdot \mathbb{P}(T_a < T_b | X_0 = i).$$

However, since $T_{a,b}$ is almost surely finite whenever i is between a and b, it follows that either $T_b < T_a$ is true or $T_a < T_b$ is true and so

$$\mathbb{P}(T_a < T_b | X_0 = i) = 1 - \mathbb{P}(T_b < T_a | X_0 = i).$$

The result then follows upon substituting this expression into the first identity and solving. $\square$

Theorem 3. *Under the Moran model with two alleles, A and a, the expected time to fixation of either allele is approximately*

$$\mathbb{E}_i[\tau] \approx -2N \left\{ p \log(p) + (1 - p) \log(1 - p) \right\},$$

where $p = i/2N$ is the initial frequency of A and time is measured in units of generations. Similarly, the expected time fixation conditional on eventual fixation of A is approximately

$$\bar{\mathbb{E}}_i[\tau] \approx \frac{-2N(1 - p)}{p} \log(1 - p).$$

Proof. If S_j is the amount of time that the process X spends in state j before time τ, then $\tau = S_1 + \cdots + S_{2N-1}$ and so the unconditioned expected time to fixation is equal to

$$\mathbb{E}_i[\tau] = \sum_{j=1}^{2N-1} \mathbb{E}_i[S_j].$$

Furthermore, if N_j is the number of times that X visits state j before time τ and we let $q_j = 2j(2N - j)/2N$ be the rate at which the process leaves state j, then because each visits lasts on average $1/q_j$ generations, we have

$$\mathbb{E}_i[S_j] = \frac{1}{q_j} \mathbb{E}_i[N_j].$$

To calculate the expected value of N_j, we can reason as follows. Let T_k be the hitting time of k as defined in Proposition 1 and notice that N_j will be greater than 0 if and only if the process hits state j before either allele is fixed in the population. If i is between 0 and j, then by Proposition 1 this probability is

$$\mathbb{P}_i(N_j \geq 1) = \mathbb{P}_i(T_j < T_0) = \frac{i}{j}.$$

Similarly, if i is between j and $2N$, then this probability is

$$\mathbb{P}_i(N_j \geq 1) = \mathbb{P}_i(T_j < T_{2N}) = 1 - \mathbb{P}_i(T_{2N} < T_j) = 1 - \frac{i - j}{2N - j} = \frac{2N - i}{2N - j}.$$

Suppose that $N_j \geq 1$. In this case, following the first visit from i to j, the process is at state j and its history prior to that time is independent of the number of subsequent visits to state j. In fact, if we let π_j denote the probability that the process never returns to state j when it starts in state j, then

$$\mathbb{P}_i(N_j \geq n + 1 | N_j \geq n) = 1 - \pi_j$$

for every $n \geq 1$. This shows that conditional on $N_j \geq 1$, N_j is geometrically-distributed with success parameter π_j and so

$$\mathbb{E}_i[N_j] = \mathbb{P}_i(N_j \geq 1) \cdot \frac{1}{\pi_j}.$$

To calculate π_j, observe that because the process is equally likely to move to state $j - 1$ or to state $j + 1$ when it leaves state j, we have

$$
\begin{aligned}
\pi_j &= \frac{1}{2} \cdot \mathbb{P}_{j-1}(T_0 < T_j) + \frac{1}{2} \cdot \mathbb{P}_{j+1}(T_{2N} < T_j) \\
&= \frac{1}{2} \cdot \frac{1}{j} + \frac{1}{2} \cdot \frac{1}{2N - j} \\
&= \frac{2N}{2j(2N - j)}.
\end{aligned}
$$

This shows that the expected number of visits to state j prior to fixation is

$$\mathbb{E}_i[N_j] = \begin{cases} \frac{i}{j} \cdot \frac{2j(2N-j)}{2N} & \text{if } i \leq j \\ \frac{2N-i}{2N-j} \cdot \frac{2j(2N-j)}{2N} & \text{if } i \geq j, \end{cases}$$

and therefore

$$\mathbb{E}_i[S_j] = \begin{cases} \frac{i}{j} & \text{if } i \leq j \\ \frac{2N-i}{2N-j} & \text{if } i \geq j, \end{cases}$$

since (fortuitously) $q_j = 1/\pi_j$. Summing then gives

$$
\begin{aligned}
\mathbb{E}_i[\tau] &= \sum_{j=1}^{i-1} \frac{2N - i}{2N - j} + \sum_{j=i}^{2N-1} \frac{i}{j} \\
&= 2N \cdot \left\{ \left(1 - \frac{i}{2N}\right) \cdot \frac{1}{2N} \sum_{j=1}^{i-1} \frac{1}{1 - j/2N} + \left(\frac{i}{2N}\right) \cdot \frac{1}{2N} \sum_{j=i}^{2N-1} \frac{1}{j/2N} \right\} \\
&\sim 2N \left\{ (1 - p) \int_0^p \frac{1}{1 - q} dq + p \int_p^1 \frac{1}{q} dq \right\} \\
&= -2N \left\{ p \log(p) + (1 - p) \log(1 - p) \right\},
\end{aligned}
$$

where $p = i/2N$ is the initial frequency.

To calculate the conditional mean fixation time, observe that the transition probabilities of the Moran model conditional on eventual fixation of A are

$$
\begin{aligned}
\bar{p}_t(i, j) &= \mathbb{P}(X_t = j | T_{2N} < T_0, X_0 = i) \\
&= \mathbb{P}(X_t = j | X_0 = i) \cdot \frac{\mathbb{P}(T_{2N} < T_0 | X_t = j, X_0 = i)}{\mathbb{P}(T_{2N} < T_0 | X_0 = i)} \\
&= p_t(i, j) \cdot \frac{\mathbb{P}(T_{2N} < T_0 | X_t = j)}{\mathbb{P}(T_{2N} < T_0 | X_0 = i)} \\
&= p_t(i, j) \cdot \frac{j/2N}{i/2N} \\
&= p_t(i, j) \cdot \frac{j}{i}.
\end{aligned}
$$

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In fact, it can be shown that the Moran model conditioned on eventual fixation of A is also a continuous-time Markov chain, with transition rates $\bar{q}_{ij} = q_{ij} \cdot (j/i)$. Since $\bar{q}_{ij} > q_{ij}$ whenever $j > i$, the frequency of A is disproportionately likely to increase in the conditioned process, as might be expected. In this case, we can express the conditional mean time to fixation as the sum

$$\bar{\mathbb{E}}_i[\tau] = \sum_{j=1}^{2N-1} \bar{\mathbb{E}}_i[S_j],$$

where $\bar{\mathbb{E}}_i[S_j]$ is the mean occupancy time in state j by the conditioned process. Since

$$S_j = \int_0^\infty 1_j(X_t)dt,$$

where $1_j(X_t)$ is equal to 1 if $X_t = j$ and 0 otherwise, the conditional expectation of this variable is

$$
\begin{aligned}
\bar{\mathbb{E}}_i[S_j] &= \bar{\mathbb{E}}\left[\int_0^\infty 1_j(X_t)dt\right] = \int_0^\infty \bar{\mathbb{E}}[1_j(X_t)]dt \\
&= \int_0^\infty \bar{p}_t(i,j)dt = \left(\frac{j}{i}\right)\int_0^\infty p_t(i,j)dt = \frac{j}{i}\cdot\mathbb{E}_i[S_j].
\end{aligned}
$$

Using the value of $\mathbb{E}_i[S_j]$ calculated above, we find

$$\bar{\mathbb{E}}_i[S_j] = \begin{cases} 1 & \text{if } i \le j \\ \frac{2N-i}{i}\cdot\frac{j}{2N-j} & \text{if } i \ge j. \end{cases}$$

Summing from 1 to $2N-1$ then gives

$$
\begin{aligned}
\bar{\mathbb{E}}_i[\tau] &= \sum_{j=1}^{i-1}\frac{2N-i}{i}\cdot\frac{j}{2N-j} + \sum_{j=i}^{2N-1} 1 \\
&= \left\{2N\cdot\left(\frac{1-i/2N}{i/2N}\right)\cdot\frac{1}{2N}\sum_{j=1}^{i-1}\frac{j/2N}{1-j/2N} + 2N-i\right\} \\
&= 2N\cdot\left\{\left(\frac{1-i/2N}{i/2N}\right)\cdot\frac{1}{2N}\sum_{j=1}^{i-1}\frac{j/2N}{1-j/2N} + (1-i/2N)\right\} \\
&\sim 2N\left\{\frac{(1-p)}{p}\int_0^p\frac{q}{1-q}dq + (1-p)\right\} \\
&= 2N\left\{\frac{(1-p)}{p}(-\log(1-p)-p) + (1-p)\right\} \\
&= -\frac{2N(1-p)}{p}\log(1-p).
\end{aligned}
$$

$\square$

If A is initially present in a single copy ($i = 1$ in the notation of Theorem 3), then the mean time to fixation of either allele is

$$\mathbb{E}_1[\tau] = \sum_{j=1}^{2N-1}\frac{1}{j} \sim \log(2N),$$

while the mean time to fixation conditional on eventual fixation of A is

$$\bar{\mathbb{E}}_1[\tau] = \sum_{j=1}^{2N-1} = 2N-1.$$