Applied Probability Trust (9 June 2004)

SOLVING THE FISHER-WRIGHT AND COALESCENCE PROBLEMS WITH A DISCRETE MARKOV CHAIN ANALYSIS

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Abstract

We develop a new, self-contained proof that the expected number of generations required for gene allele fixation or extinction in a population of size n is $O(n)$ under general assumptions. The proof relies on a discrete Markov chain analysis. We further develop an algorithm to compute expected fixation/extinction time to any desired precision.

Our proofs establish $O(nH(p))$ as the expected time for gene allele fixation or extinction for the Fisher-Wright problem where the gene occurs with initial frequency p, and $H(p)$ is the entropy function. Under a weaker hypothesis on the variance, the expected time is $O(n\sqrt{p(1-p)})$ for fixation or extinction. Thus, the expected time bound of $O(n)$ for fixation or extinction holds in a wide range of situations.

In the multi-allele case, the expected time for allele fixation or extinction in a population of size n with n distinct alleles is shown to be $O(n)$. From this, a new proof is given of a coalescence theorem about mean time to most recent common ancestor (MRCA) that applies to a broad range of reproduction models satisfying our mean and weak variation conditions.

Keywords: Fisher-Wright model, diffusion equation, population genetics, mitochondrial Eve, Markov chain, mean stopping time, coalescence, martingale

AMS 2000 Subject Classification: Primary 60J05

Secondary 60J20,60J22,60J70

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1. Introduction

R.M. Fisher [10] and S. Wright [27, 28] considered the following problem in population genetics. In a fixed size population of n haploid individuals carrying only gene alleles A and a, what is the expected number of generations before all n individuals carry only allele A, or all n individuals carry only allele a?

Formally, we assume neutral selection and that the successive generations are discrete, non-overlapping, and of fixed size n. If one generation contains i haploid members with allele A and $n-i$ with allele a, then the conditional probability that the next generation has exactly j members with allele A equals

$$p_{i,j} \;=\; \binom{n}{j}\left(\frac{i}{n}\right)^{j}\left(1-\frac{i}{n}\right)^{n-j}. \tag{1}$$

Modelling this as a Markov chain $\mathcal{M}$ having states $0,\ldots,n$, where state i represents the situation that exactly i alleles are of type A, it is clear that

$$\lim_{t\to\infty} Pr[\ \mathcal{M} \text{ is in either state 0 or } n \text{ at time } t] = 1$$

or, in other words, that eventually only one allele will be present in a population. The first time t where $\mathcal{M}$ is in state 0 or n is called the *absorption time* or the *stopping time*, where time is measured in terms of number of generations.

A series of contributions by R.A. Fisher [10], S. Wright [27, 28], M. Kimura [12, 13, 14], S. Karlin and J. McGregor [11], G.A. Watterson [25] and W.J. Ewens [5] solved the Fisher-Wright problem via the diffusion equation, a differential equation giving a continuous approximation to the Fisher-Wright process. (See [7, 22, 26] for a comprehensive overview of the diffusion equation approach and the rigorous justification of its applicability to the discrete Fisher-Wright problem.) Kimura [12], Watterson [25] and Ewens [5] established the mean stopping time for the diffusion equation associated with the Fisher-Wright process as [1]

$$-2n\,(p\ln p + (1-p)\ln(1-p)) \;=\; 2nH(p)$$

[1] The Fisher-Wright problem is generally stated for n diploid individuals, whereas we are working with n haploid individuals. Thus, for our setting, the quantity n replaces the quantity $2n$ in the usual formulation of the Fisher-Wright problem.

many generations, when starting from initial allele frequency of $p = i/N$, where $H(p)$ is the base e entropy function. W. Ewens has shown that this is an upper bound for the mean stopping time for the discrete Fisher-Wright problem and, in [6], estimated the error in the diffusion equation approximation with a logarithmic additive term.

This article presents a new self-contained proof that the expected number of generations required for gene allele fixation/extinction is $O(nH(p))$. Of course, this result is a weakening of the just-discussed approximation by the diffusion equation. However, the diffusion approximation proofs are long and arduous. In contrast, our proofs avoid the diffusion equation approach altogether and work solely with discrete Markov chains.

Our proof methods apply to a wide range of Markov models: our only assumptions are a *mean condition* and a *variation condition* as defined in Section 2. For instance, Cook and Rackoff suggested to us the following hypergeometric model for reproduction. (Schensted [21] earlier studied the hypergeometric model. A generalized hypergeometric model has been suggested by Möhle [20].) Assume that a population consists of discrete, non-overlapping generations of fixed size n. The $(i+1)$st generation is obtained from the i-th generation as follows: Each parent individual in the i-th generation has two offspring, yielding $2n$ potential offspring; a randomly chosen set of n of these potential offsprings survives to be the $(i+1)$st generation. Thus, each parent individual will have zero, one or two offspring survive in the succeeding generation. The hypergeometric model is based on sampling from a set of size $2n$ without replacement, whereas the Fisher-Wright model uses sampling with replacement. For the hypergeometric model, if a generation contains i individuals with allele A, then the probability that the next generation contains j individuals with allele A is equal to

$$q_{i,j} \;=\; \frac{\binom{2i}{j}\binom{2n-2i}{n-j}}{\binom{2n}{n}}. \tag{2}$$

The hypergeometric process satisfies the mean and variation conditions, and thus our theorems imply that it has expected absorption time $O(nH(p))$.

Since our approach is different from the traditional approach, it is likely our results cover some cases which cannot be covered by the diffusion equation approach. In fact, we prove similar stopping time results of the form $O(n\sqrt{p(1-p)})$ for Markov chains satisfying a weaker assumption on the variance of the number of individuals with a given allele. This weaker assumption is defined in Section 2 as the *weak variation* *condition*. The intuitive difference between the "weak variation condition" and the "variation condition" is that the weak variation condition allows for less variance in the sizes of sub-populations which have density close to zero or one, i.e., alleles which are carried by nearly all or nearly none of the population may have less variance. These theorems need no assumptions about exchangeability.

As part of our Markov chain analysis, Section 4 develops an algorithm to compute to any desired precision the expected absorption time as a function of i and n.

Our work was originally motivated by a question of Cook and Rackoff concerning the expected time for mitochondrial monomorphism to occur in a fixed-size population. Their question was motivated by Cann, Stoneking and Wilson [2], who used branching process simulation studies of Avise et al. [1] as corroborating mathematical justification for the "Mitochondrial Eve Hypothesis" that there is a 200,000 year old mitochondrial ancestor of all of current humanity. Avise et al. showed by computer simulation that if expected population size remains constant, then with probability one all members of some future generation will be mitochondrially monomorphic. Simulating n independent branching processes, each involving a Poisson random variable with mean 1, [1] cited $4n$ as an upper bound on the expected number of generations to absorption.

The Mitochondrial Eve question is a special case of the coalescence problem. The coalescent was introduced by Kingman [17, 15, 16] as a method for estimating the most recent common ancestor (MRCA) for a population. (See [23, 24] for an overview of applications of the coalescent.) The fundamental result for the coalescent is that if a population evolves with discrete non-overlapping generations of fixed size n with neutral selection, each child having only one parent, then it is expected that the $2n$-th generation before the present contains a common ancestor for the entire present generation. There are a number of proofs of the coalescent theorem in the literature, e.g., Donnelly [4] and Möhle [18, 20]. Many of these are based on approximating an evolutionary discrete death process with a continuous Markov process, but Möhle [20] proves some tight bounds using a discrete Markov analysis giving tight bounds of the form $2N_e(1-1/n)$ in many cases, including the binomial and hypergeometric processes. Here N_e is the *effective population size* and equals the inverse of the coalescent probability. N_e equals n in the binomial case and $2n-1$ in the hypergeometric case.

In Section 3, we use the combinatorial Markov chain analysis to give a new proof of the $O(n)$ coalescent theorem, based on the mean and weak variation conditions plus an additional assumption that lets us define the time-reversal of an evolutionary process. For instance, the binomial and hypergeometric processes, as well the generalized binomial and hypergeometric processes of Möhle [20], are proved to have $O(n)$ expected number of generations before a MRCA is reached. Unlike earlier proofs, our proof is based on the forward absorption times of the Fisher-Wright problem, rather than on an analysis of the death process.

2. Preliminaries and definitions

We restrict attention to haploid individuals, who carry a single set of genetic material and receive their genes from a single parent. However, our results can apply to diploid genes as well, as long as the genes are not sex- or reproduction-linked. We assume there is no mutation and that the evolutionary process is time-homogeneous.

The populations are assumed to consist of discrete, non-overlapping generations, each of size n. Each individual carries one of two alleles, A or a. If i individuals of a generation have allele A, then $n-i$ have allele a and the generation is in "state i." The population is modeled by a Markov chain (Q, M), where $Q = \{0, 1, 2, \ldots, n\}$ is the set of states and $M = (m_{i,j})$ is a a stochastic transition matrix. The *transition probability* $m_{i,j}$ is the probability that state i is followed immediately by state j. We often drop the Q from the notation and refer to M as a Markov chain.

We have $m_{0,0} = 1$ and $m_{n,n} = 1$ since the states 0 and n are *absorbing* states where all the individuals carrying the same allele. The Markov chain can be viewed as stopping once it enters one of these two states. The *mean stopping time* or the *expected absorption time* is the expected number of generations until an absorbing state is reached. The mean stopping time is a function of the initial state.

The Fisher-Wright problem concerns bounding the mean stopping time. For the traditional Fisher-Wright problem, the transition probabilities are defined by $m_{i,j} = p_{i,j}$ where the $p_{i,j}$'s are defined in (1). Sometimes, the probabilities $q_{i,j}$ from equation (2) are used instead. To generalize to a wider range of transition probabilities, we define a mean condition and two conditions on the variance of the probabilities.

Definition 1. A Markov chain satisfies the *mean condition* if, for all $n \geq 3$ and for all

$0 \leq i < n/2$,

$$\sum\nolimits_{j=0}^{n} jm_{i,j} \;\leq\; i$$

and, symmetrically, for all $n \geq i > n/2$,

$$\sum\nolimits_{j=0}^{n} jm_{i,j} \;\geq\; i.$$

If i individuals have allele A, then the quantity $\sum_j jm_{i,j}$ is the expected number of individuals with allele A in the next generation. The intuition of the mean condition is that the Markov chain does not have a tendency to drift towards the state $n/2$.

In the case of neutral selection, $\sum_j jm_{i,j} = i$ for all i, and the Markov chain is called a *martingale.*

Theorem 1. *The Markov chain with transition probabilities (1) or (2) satisfies the mean condition and is a martingale.*

This theorem is well-known, and its proof is omitted.

In addition to the mean condition, we need conditions that lower bound the variance in the population state. Recall that the standard deviation of the binomial distribution (1) is equal to $\sigma_{i,n} = \sqrt{\frac{i(n-i)}{n}}$.

Definition 2. Define $\sigma_{i,n} = \sqrt{\frac{i(n-i)}{n}}$. A family of Markov chains M_n satisfies the *variation condition* provided there are constants $\delta, \epsilon > 0$ such that for all $n \geq 2$ and $0 < i < n$,

$$\sum_{|j-i|>\delta\sigma_{i,n}} m_{i,j} \;>\; \epsilon. \tag{3}$$

The intuition is that the variation condition forces the state of the population to vary noticeably between generations; this plus the mean condition is enough to ensure that an absorbing state is reached in a finite amount of time.

The condition (3) can equivalently be stated as

$$Prob\big[|C_i - i| > \delta\sigma_{i,n}\big] \;>\; \epsilon,$$

where C_i is a random variable distributed according to the i-th row of M; note C_i can be interpreted as the number of children of i individuals. This means that there is non-negligible probability that the number of individuals with allele A changes by at least $\delta\sigma_{i,n}$. Since $\sigma_{i,n}$ is the standard deviation of the binomial process, we expect the binomial process to fulfill the variation condition. The intuition is that a process satisfies the variation condition provided its standard deviation is proportional to $\sigma_{i,n}$ or larger. (However, this is not a mathematically equivalent condition.)

The definition of the mean condition is stated in terms of families of Markov chains to allow us to prove results that hold asymptotically in n. For example, the transition probabilities given in (1), and in (2), specify families of Markov chains, one for each value of $n \geq 1$. It is important for the definition that δ, ϵ are fixed constants, independent of i and n.

Theorem 2. *The binomial distribution (1) satisfies the variation condition.*

Theorem 3. *The hypergeometric distribution (2) satisfies the variation condition.*

These theorems are presumably not new; however, we have not been able to find any place where they are proved in this strong form. The usual proofs of DeMoivre-Laplace theorem for the binomial and hypergeometric distributions (c.f. Feller [9]) prove the theorems only for fixed values of $p = i/n$, whereas, we need the theorems to hold for all values of i and n. We thus include the proofs of these theorems, but relegate them to the appendix.

Our main theorems will hold also under a weak form of the variation condition:

Definition 3. Let

$$\sigma'_{i,n} \;=\; \left(\frac{i}{n}\right)^{3/4} \left(\frac{n-i}{n}\right)^{3/4} n^{1/2}.$$

The *weak variation condition* holds for a family of Markov chains M_n, provided there are constants $\delta, \epsilon > 0$ such that for all $n \geq 2$ and $0 < i < n$,

$$\sum_{|j-i|>\delta\sigma'_{i,n}} m_{i,j} \;>\; \epsilon.$$

Since $\sigma'_{i,n} \leq \sigma_{i,n}$, the weak variation condition is less restrictive than the variation condition. Thus the variation condition implies the weak variation condition.

The bound $\sigma'_{i,n}$ for the weak variation condition differs most from the bound $\sigma_{i,n}$ when i is close to 0 or close to n. For these values of i, a Markov chain that satisfies the weak variation condition (but not the variation condition) is allowed to have variance substantially less than the variance of the the binomial distribution. Hypothetically speaking, such a Markov chain could arise in situations where alleles that occur rarely have some reproductive advantage. For example, this can occur with human intervention, where efforts are made to preserve a rare subspecies; or it might occur if scarcity of the allele conveys some reproductive advantage.

The mean condition implies that 0 and n are absorbing states. The weak variation condition implies that no other state is absorbing.

We can now state our main theorems for populations with two alleles. Let D_i denote the expected stopping time for a Markov chain started in state i. (D_i depends on both i and n, but we suppress the "n" in the notation.)

Theorem 4. *Suppose the Markov chain $M = (m_{i,j})$ satisfies the mean condition and the variation condition. Then the expected stopping time D_i is bounded by*

$$D_i \;=\; O(nH(i/n)),$$

where $H(p) = -p\ln p - (1-p)\ln(1-p)$ is the entropy function.

Theorem 5. *Suppose the Markov chain $M = (m_{i,j})$ satisfies the mean condition and the weak variation condition. Then the expected stopping time D_i is bounded by*

$$D_i \;=\; O(\sqrt{i(n-i)}).$$

We prove these theorems below, in Sections 4-6. First, however, Section 3 proves a corollary about the n allele situation and the MRCA.

3. The multi-allele case

This section extends the expected stopping time theorems to the case where there are n distinct alleles in the population. From this it proves upper bounds for expected time to coalescence under fairly general conditions.

The Markov chain model generalizes straightforwardly to multiple alleles; namely, in the multi-allele setting, a *state* consists of the numbers of individuals with each allele. The mean condition and the weak variation condition need to be redefined to apply multi-allelle evolution. For this, let $\mathcal{A}$ be any set of alleles. Let $n_{\mathcal{A}}(t)$ equal the number of individuals in generation t that carry an allele from $\mathcal{A}$. Define $p^{\mathcal{A}}_{i,j}$ to be the conditional probability

$$p^{\mathcal{A}}_{i,j} \;=\; Pr[n_{\mathcal{A}}(t+1) = j \,|\, n_{\mathcal{A}}(t) = i].$$

The mean condition is satisfied by the multi-allele Markov chain provided that, for every set $\mathcal{A}$ of alleles, the transition probabilities $p^{\mathcal{A}}_{i,j}$ satisfy the mean condition. The multi-allele Markov chain satisfies the (weak) variation condition provided there are fixed constants δ, ϵ such that, for every $\mathcal{A}$, the probabilities $p^{\mathcal{A}}_{i,j}$ satisfy the (weak) variation condition with those values of δ, ϵ.

The binomial and hypergeometric processes were earlier defined for populations with two alleles, but the definitions extend naturally to the multi-allele setting. In the multi-allele setting, the binomial process is as follows: each individual in generation $i+1$ receives its allele from an independently randomly chosen individual in generation i. The hypergeometic process is now defined by letting each individual in generation i have two offspring and then selecting a randomly chosen set of n of the offpring to survive as the next generation. Clearly the multi-allele binomial and hypergeometric processes both satisfy the (multi-allele) mean and variation conditions; indeed, for any set $\mathcal{A}$, the probability $p^{\mathcal{A}}_{i,j}$ for the multi-allele binomial, resp. hypergeometric, process is exactly equal the probability of (1), resp. of (2).

To better understand the generality of the mean and weak variation conditions, we define some processes which satisfy these conditions but are not martingales. The intuition will be that frequently occurring alleles confer a reproductive advantage. Let $\alpha(i)$ be a nondecreasing, positive function which is intended to represent the relative reproductive advantage when there are i individuals with a given allele. Let $\lambda(i) = i\alpha(i)$. The *binomial α-advantage* process is defined as follows: if there are i individuals with allele a, then each individual in the next generation has allele a with probability proportional to $\lambda(i)$. If there are just two alleles, this means the probabilities for the binomial α-advantage process are defined by

$$r_{i,j} \;=\; \binom{n}{j}\left(\frac{\lambda(i)}{\lambda(i)+\lambda(n-i)}\right)^{j}\left(\frac{\lambda(n-i)}{\lambda(i)+\lambda(n-i)}\right)^{n-j}.$$

For two alleles, these processes satisfy the mean and variation conditions.

The binomial α-advantage process generalizes in the obvious way to multi-alleles. However, this does not necessarily satisfy the multi-allele mean condition; for example, when $\alpha(1) = 1$ and $\alpha(n/3) = 2$ and there are $n/3$ individuals with a common allele a

It is also possible to define hypergeometric versions of the α-advantage process.

and the remaining individuals have distinct alleles and $\mathcal{A} = \{a\}$. Consider instead a thresholded version α-advantage process where the reproductive advantage applies only to alleles that form a majority of the population. For this, we require $\alpha(i) = 1$ for $i < n/2$ and $\alpha(i) > 1$ for $i \geq n/2$. The multi-allele process defined with such an α can be shown to satisfy the mean and variation conditions, but is not a martingale.

Theorem 6. *Suppose a population begins with n individuals with distinct alleles, and evolves according to a Markov chain that satisfies the multi-allele mean and weak variation conditions. Then the expected stopping time is $O(n)$.*

Proof. Consider any set $\mathcal{A}$ of alleles. Let $\overline{\mathcal{A}}$ be the complement of $\mathcal{A}$, thus $\{\mathcal{A}, \overline{\mathcal{A}}\}$ forms a partition of the alleles. We say $\mathcal{A}$ has *stopped* when either all individuals carry an allele from $\mathcal{A}$ or all individuals carry an allele from $\overline{\mathcal{A}}$. By Theorem 5, the expected stopping time for $\mathcal{A}$ is $< cn$ for some constant c. It follows that the probability that $\mathcal{A}$ stops in less than $4cn$ generations is greater than $3/4$.

There are 2^n sets $\mathcal{A}$. We wish to find the expected time at which more than one half of the sets $\mathcal{A}$ have stopped. We claim that the considerations in the last paragraph imply that with probability at least $1/2$, more than half of the sets $\mathcal{A}$ have stopped by time $4cn$. To prove this claim, note that if α is the probability that at least fraction β of the sets $\mathcal{A}$ have stopped by time $4cn$, then, for some $\mathcal{A}$,

$$Pr[\ \mathcal{A} \text{ has not stopped by time } 4cn] \ \geq \ (1-\alpha)(1-\beta).$$

The claim is proved by using $\alpha = 1/2 = \beta$.

Repeating this argument shows that, with probability at least $3/4$, more than half of the sets $\mathcal{A}$ are stopped by time $8cn$. More generally, with probability at least $1 - 1/2^i$, more than half of the sets $\mathcal{A}$ are stopped by time $4icn$. Therefore the expected time before more than half of the sets $\mathcal{A}$ are stopped is bounded by

$$\sum_{i=1}^{\infty} \frac{4icn}{2^i} \ = \ 8cn.$$

To complete the proof of the theorem, we claim that once a generation is reached where more than half of the sets $\mathcal{A}$ are stopped, then all the individuals carry the same allele. To prove this claim, let A_1 and A_2 be two alleles. We say that a set $\mathcal{A}$ separates A_1 from A_2 if $A_1 \in \mathcal{A}$ and $A_2 \in \overline{\mathcal{A}}$ or if, vice-versa, $A_1 \in \overline{\mathcal{A}}$ and $A_2 \in \mathcal{A}$. If we choose a random set $\mathcal{A}$, the probability it separates A_1 from A_2 is exactly 50%. Since more than one half of the sets $\mathcal{A}$ are stopped, there must therefore be some stopped $\mathcal{A}$ that separates A_1 from A_2. Thus, at least one of A_1 or A_2 has disappeared from the population. Since this argument applies to any pair of alleles A_1, A_2, it follows that there is only one allele left in the population.

Note that the above proof depends only on the fact that, for any subpopulation, the expected time for it to either become the entire population or to be eliminated is $O(n)$ generations. Thus the property of Theorem 6 is a robust phenomenon.

Theorem 6 is similar to a coalescence theorem. The viewpoint of coalescence is that the current generation is the end of an evolutionary process, and one considers which evolutionary sequences could have led to the current generation. That is, unlike Fisher-Wright, where one considers the evolution of future generations, the coalescence viewpoint considers the possible past evolutionary processes. The *expected coalescence time* is defined to be the expected number of generations elapsed since all individuals in the present generation had a common ancestor.

The usual assumption for coalescence is that the individuals in a generation choose their parents at random from the previous generation, and as Kingman [17] notes, this is mathematically equivalent to the binomial probabilities (1), To generalize this to other evolutionary processes, such as the hypergeometric process, it is necessary to define the time-reversals of the processes. We do this only for processes of the following type.

Definition 4. A Markov process $\mathcal{M}$ on n individuals is *controlled by function probabilities* provided there is a probability distribution $P(f)$ on the functions $f : [n] \to [n]$, where $[n] = \{1, 2, \ldots, n\}$, such that the process $\mathcal{M}$ evolves as follows. Given generation t containing individuals numbered $1, 2, \ldots, n$, choose a random function f according to the distribution P and, for each i, let the i-th individual of generation $t + 1$ inherit the allele of the $f(i)$-th individual of generation t.

As defined, these Markov processes differ from our previous notion of Markov process since the individuals are numbered or indexed. To revert to the previous kind of Markov process, the individuals could be randomly permuted in every evolutionary step. Equivalently, the probability distribution on functions could be required to be invariant under permutations of the domain and range of the function, that is, it could be required that $P(\pi \circ f) = P(f) = P(f \circ \pi)$ for all $f : [n] \to [n]$ and all one-to-one $\pi : [n] \to [n]$.

The binomial process can be defined as a Markov process controlled by function probabilities by letting $P(f)$ be equal to $1/n^n$, i.e., each function is equally likely. The hypergeometric process can likewise be defined as controlled by function probabilities: namely, to choose a random f, choose uniformly at random a one-to-one function $m : [n] \to [2n]$, and then choose f so that $f(x) = \lfloor m(x)/2 \rfloor$. In the hypergeometric case, the functions f do not all have equal probabilities.

Theorem 7. *Let a multi-allele Markov process be controlled by function probabilities and satisfy the multi-allele mean and weak variation conditions. Then the expected coalescence time is $O(n)$.*

Proof. This is an immediate corollary of Theorem 6. Note that the evolution through a series of k generations can be represented by a sequence of k functions, $f_1, \ldots, f_k$. The probability of this evolutionary sequence is the product $\Pi_i P(f_i)$. By Theorem 6, the expected value of k such that $f_1, \ldots, f_k$ causes coalescence is $O(n)$.

The function probability model for Markov processes is quite general; for instance, it includes the examples of processes for which Möhle [20, §5] has proved coalescence theorems (with the exception of the more-slowly evolving Moran model). However, as formulated above, the function probability model applies mainly to martingales, especially if the functions are required to be invariant under permutations of the range and domain. This is somewhat unexpected since, if the mean condition holds, the failure of the martingale property would be expected to only decrease the mean stopping time. It would be worthwhile to have more general techniques for formulating the time-reversal of an evolutionary process.

The method of duality, used by Möhle [19], is another technique for relating forward and backward evolutionary processes.

4. Calculating stopping times

We now discuss an algorithm to calculate the exact stopping times for a Markov chain for particular values of n. In addition, we develop some properties of the stopping time that are needed later for the proofs of the stopping time theorems.

One might think to try running random trials to try to determine stopping times experimentally. This turns out to be difficult since the stopping times have a fairly large standard deviation and a large number of trials are needed to accurately measure the stopping time. Instead, we describe an iterative algorithm that converges to the values D_i, the stopping times for a population of size n that starts with i individuals with allele A and the rest with a.

Let M^k be the k-th power of the Markov chain matrix M. The entries of M^k are denoted by $m_{i,j}^{(k)}$ and are transition probabilities for k-generation steps. We let M^∞ equal the limit of M^k as $k \to \infty$; its entries are $m_{i,j}^\infty = \lim_k m_{i,j}^{(k)}$. M^k and M^∞ are also stochastic matrices. A state $i_0 \in Q$ is said to be *absorbing* if $m_{i_0,i_0} = 1$. State j is said to be *accessible* from state i, or equivalently i can *reach* j, if there exists t for which $m_{i,j}^{(t)} > 0$. The mean condition and (weak) variation condition imply that 0 and n are the only absorbing states.

It is common to analyze Markov chains using eigenvalues and eigenvectors of the transition matrix M. Indeed, this has been done by Feller [8] for the binomial probabilities and by Cannings [3] for more general transition matrices under the assumption of exchangeability. We will not use eigenvectors or eigenvalues however.

For a Markov chain $\mathcal{M}$ with state set $Q = \{0, \ldots, n\}$, define the *mean stopping time vector* $\boldsymbol{D} = (D_0, \ldots, D_n)$ so that D_i is the expected number of transitions before $\mathcal{M}$, starting in state i, enters an absorbing state. Since 0 and n will be the only absorbing states, $D_0 = 0 = D_n$. From state i, in one step the Markov chain makes a transition to state j with probability $m_{i,j}$, hence

$$D_i = \begin{cases} 0 & \text{if } i \in \{0, n\} \\ 1 + \sum_{j=0}^n m_{i,j} D_j & \text{if } 0 < i < n. \end{cases} \tag{4}$$

Proposition 8. *If $M = (m_{i,j})$ satisfies the mean condition and 0 and n are the only absorbing states, then there is at most one vector $\boldsymbol{D}$ which satisfies (4).*

Before proving Proposition 8, we establish the following three lemmas. (Results similar to Lemmas 9 and 10 can be found in Möhle [19].)

Lemma 9. *Suppose that M satisfies the mean condition and that 0 and n are the only absorbing states.*

(a) *If* $0 < i < n/2$*, then there is a* $j < i$ *such that* $m_{i,j} \neq 0$*.*

(b) *If* $n > i > n/2$*, then there is a* $j > i$ *such that* $m_{i,j} \neq 0$*.*

(c) *If* $i = n/2$*, then there is a* $j \neq i$ *such that* $m_{i,j} \neq 0$*.*

Proof. (of Lemma 9). Part (c) is obvious from the fact that $n/2$ is not absorbing. To prove (a), suppose that $0 < i < n/2$. Since state i is not absorbing, $m_{i,i} \neq 1$. By the stochastic property, there are values $j \neq i$ such that $m_{i,j} > 0$. By the mean property, not all of these values of j are $\geq i$. This proves (a). Part (b) is proved similarly.

Lemma 10. *Suppose that* M *satisfies the mean condition and that* 0 *and* n *are the only absorbing states. Then there is a value* r*,* $1 \leq r \leq n/2$*, such that* $m_{i,0}^{(r)} + m_{i,n}^{(r)} \neq 0$ *for all* i*. That is, from any starting state* i*, there is non-zero probability of reaching an absorbing state within* $\lfloor n/2 \rfloor$ *steps.*

Proof. (of Lemma 10). This is a simple consequence of Lemma 9. For $i = i_0 < n/2$, let $i_0 > i_1 \geq i_2 \geq \cdots$ be chosen so that, for all k, if $i_k > 0$, then $m_{i_k,i_{k+1}} \neq 0$ and $i_{k+1} < i_k$. Then, clearly, $m_{i,i_k}^{(k)} \neq 0$ for all $k > 0$. Since the values i_k are decreasing down to zero, the sequence reaches zero in at most i steps. Thus, for $i < n/2$, $m_{i,0}^{(i)} \neq 0$. A symmetric argument shows that, for $i > n/2$, $m_{i,n}^{(n-i)} \neq 0$. Similarly, when n is even, at least one of $m_{n/2,0}^{(n/2)}$ or $m_{n/2,n}^{(n/2)}$ is non-zero.

Lemma 11. *Let* M *satisfy the mean condition and* 0 *and* n *be the only absorbing states. Then the entries of* M^∞ *are zero except in the first and last columns.*

Lemma 11 implies that an absorbing state is eventually reached with probability one.

Proof. (of Lemma 11). This follows from Lemma 10. Choose $r \leq n/2$ and

$$\epsilon = \min\{m_{i,0}^{(r)} + m_{i,n}^{(r)} : 0 \leq i \leq n\},$$

so that $\epsilon > 0$. Then, $(M^r)^k = M^{kr}$ has the property that all its entries outside the first and last columns are bounded above by $(1-\epsilon)^k$. More precisely, for each row i, $\sum_{j=1}^{n-1} m_{i,j} \leq (1-\epsilon)^k$. From this, it is immediate that the limit of these matrices exists and has zero entries everywhere except in the first and last columns.

We are now ready to prove Proposition 8.

Proof. (of Proposition 8). Suppose that $\boldsymbol{A} = (A_0, \ldots, A_n)$, $\boldsymbol{A} \neq \boldsymbol{D}$ also satisfies the equation (4), hence, $A_0 = 0 = A_n$, so $A_0 = D_0$, $A_n = D_n$. Define $\boldsymbol{C} = (C_0, \ldots, C_n)$ by $C_i = A_i - D_i$. It follows that $C_0 = 0 = C_n$ and for $0 < i < n$,

$$C_i = \sum_{j=0}^{n} m_{i,j} \cdot (A_j - D_j) = \sum_{j=0}^{n} m_{i,j} C_j.$$

In other words, $\boldsymbol{C} = M\boldsymbol{C}$. By induction on k, $\boldsymbol{C} = M^k \boldsymbol{C}$. By taking the limit as $k \to \infty$, $\boldsymbol{C} = M^{\infty}\boldsymbol{C}$. Then, by Lemma 11, $\boldsymbol{C}$ is the zero vector; i.e., $\boldsymbol{A} = \boldsymbol{D}$.

Proposition 8 established the uniqueness of a solution to equation (4). The next proposition establishes the existence of a solution and will form the basis of our algorithm for computing mean stopping times for particular values of n.

Define $\boldsymbol{E}^{(s)} = (E_0^{(s)}, \ldots, E_n^{(s)})$ by setting $E_i^{(0)} = 0$ for $0 \leq i \leq n$, and

$$E_i^{(s+1)} = \begin{cases} 0 & \text{if } i \in \{0, n\} \\ 1 + \sum_{j=0}^{n} m_{i,j} E_j^{(s)} & \text{if } 0 < i < n. \end{cases} \tag{5}$$

This is more succinctly expressed by letting $\textsc{ones} = (0, 1, 1, \ldots, 1, 1, 0)$ be the column vector of length $n+1$, consisting of 1's, with the exception of the first and last coordinates, and defining

$$\begin{aligned} \boldsymbol{E}^{(0)} &= (0, 0, \ldots, 0, 0) \\ \boldsymbol{E}^{(s+1)} &= \textsc{ones} + M\boldsymbol{E}^{(s)}. \end{aligned} \tag{6}$$

Proposition 12. *If M satisfies the mean condition and 0 and n are the only absorbing states, then the sequence $(\boldsymbol{E}^{(s)})_s$ is, in each component, nondecreasing and bounded. The limit $\boldsymbol{E}^{(\infty)}$ satisfies (4) and hence equals the vector $\boldsymbol{D}$ of mean stopping times.*

Proof. We prove $\boldsymbol{E}_i^{(s+1)} \geq \boldsymbol{E}_i^{(s)}$ for all i, by induction on s. For the base case, $E_0^{(0)} = E_0^{(1)} = 0 = E_n^{(0)} = E_n^{(1)}$ and $E_i^{(0)} = 0 < 1 = E_i^{(1)}$ for $0 < i < n$. For the inductive case, $E_i^{(s+1)} - E_i^{(s)} = \sum_{j=1}^{n-1} m_{i,j}(E_j^{(s)} - E_j^{(s-1)})$, where by the induction hypothesis, $E_j^{(s)} - E_j^{(s-1)} \geq 0$. Since $0 \leq m_{i,j} \leq 1$, the claim follows.

We now show the existence of an upper bound L such that $E_i^{(s)} \leq L$ for $0 \leq i \leq n$ and $s \geq 0$. By Lemma 10, for $r = \lfloor \frac{n}{2} \rfloor$, there is an $\epsilon > 0$, so that

$$m_{i,0}^{(r)} + m_{i,n}^{(r)} \geq \epsilon,$$

for all $0 \le i \le n$. From the proof of Lemma 11, $M^{rk} \cdot \textsc{ones} \le (1-\epsilon)^k \textsc{ones}$. It follows that for $t = rm + s$, where $0 \le s < r$,

$$\begin{aligned}
\boldsymbol{E}^{(t)} &= \sum_{i=0}^{t-1} M^i \cdot \textsc{ones} \;\le\; \left(\sum_{i<mr} M^i + M^{mr} \cdot \sum_{i<s} M^i \right) \cdot \textsc{ones} \\
&\le (\sum_{i<r} M^i) \cdot (\sum_{j<m} M^{rj}) \cdot \textsc{ones} + \sum_{i<s} M^i \cdot M^{mr} \cdot \textsc{ones} \\
&\le (\sum_{i<r} M^i) \cdot (\sum_{j<m} (1-\epsilon)^j) \cdot \textsc{ones} + \sum_{i<s} M^i \cdot (1-\epsilon)^m \cdot \textsc{ones} \\
&\le \frac{1}{\epsilon} \cdot (\sum_{i<r} M^i) \cdot \textsc{ones}
\end{aligned}$$

This provides an explicit upper bound.

For each i, the values $E_i^{(s)}$ form an nondecreasing sequence bounded above, so the limit $E_i^{(\infty)} = \lim_{s\to\infty} E_i^{(s)}$ exists. Applying limits to both sides of equation (6), it follows that $\boldsymbol{E}^{(\infty)}$ satisfies (4), hence by Proposition 8, it must be equal to $\boldsymbol{D}$.

Proposition 13. *Let $M = (m_{i,j})$ satisfy the mean condition and let 0 and n be the only absorbing states. Suppose that $F_0 = 0 = F_n$ and that, for $0 < i < n$, $F_i \ge 0$ and*

$$F_i \;\ge\; 1 + \sum\nolimits_{j=0}^{n} m_{i,j} F_j, \tag{7}$$

Then $F_i \ge D_i$ for all $0 \le i \le n$.

Proof. By induction on $s \ge 0$, we show that $\boldsymbol{F} \ge \boldsymbol{E}^{(s)}$. This is clear for $\boldsymbol{E}^{(0)}$, and in the inductive case, by (7) we have $\boldsymbol{F} - \boldsymbol{E}^{(s+1)} \ge M \cdot (\boldsymbol{F} - \boldsymbol{E}^{(s)})$. The entries of M are non-negative, so applying the induction hypothesis, the proof is complete.

From Lemmas 12 and 13, the following algorithm is guaranteed to correctly compute the mean stopping time to any precision ϵ.

Algorithm 14. (Mean Stopping Time.) *Let $M = (m_{i,j})$ be the transition matrix of a Markov chain which satisfies the mean condition and for which 0 and n are the only absorbing states.*

$\epsilon = 0.001$; $s = 0$; $\boldsymbol{E} = (0, 0, \ldots, 0, 0)$; `finished = false`

`while ( not finished ) {`

  $\boldsymbol{E}' = \textsc{ones} + M\boldsymbol{E}$; $\max = \max_{0 \le i \le n}(E'_i - E_i)$

  `if` $(\max < \epsilon)$ `{`   `// if appear to have accuracy` ϵ

```
        F = E + ε;  F′ = ONES + MF
        min = min_{0≤i≤n}(F_i − F′_i)
        if (min ≥ 0 ) finished = true
      }
    }
    return E
```

The algorithm admits an obvious extension to multiple alleles; however the algorithm's space requirement for ℓ alleles is $O(n^{\ell-1})$ plus the space, if any, needed to store the transition matrix.

By Proposition 13, Theorem 4 can be proved by showing there is a fixed constant $c > 0$ (with c independent of n) such that for $0 < i < n$,

$$cnH(i/n) \;\geq\; 1 + \sum_{j=0}^{n} m_{i,j} cnH(j/n).$$

Letting $\alpha = 1/c$, this means that Theorem 4 follows from the following lemma.

Lemma 15. *Suppose the transition probabilities satisfy the mean condition and the variation condition. Then there is a constant $\alpha > 0$ (independent of n), such that for $0 < i < n$,*

$$nH(i/n) \;\geq\; \alpha + \sum_{j=0}^{n} m_{i,j} nH(j/n). \tag{8}$$

Similarly, to prove Theorem 5, it suffices to prove the next lemma.

Lemma 16. *Suppose the transition probabilities satisfy the mean condition and the weak variation condition. Then there is a constant $\alpha > 0$ (independent of n), such that, for $0 < i < n$,*

$$\sqrt{i(n-i)} \;\geq\; \alpha + \sum_{j=0}^{n} m_{i,j} \sqrt{j(n-j)}. \tag{9}$$

These lemmas are proved in Section 6.

5. Some lemmas on secants and tangents

5.1. On vertical distance from a secant

Consider a function $f(x)$, let $h > 0$, and consider the secant to $f(x)$ at the points $x = a \pm h$, as shown in Figure 1. The next theorem gives a lower bound on the difference Δ

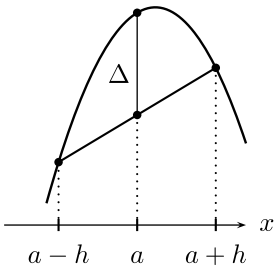

FIGURE 1: The function $f(x)$ and a secant line. The left-hand side of inequality (10) is equal to Δ, the vertical distance between $f(x)$ and the secant line at $x = a$.

between the value of $f(a)$ and the y-coordinate of the secant line at $x = a$ (see Figure 1). We will state the theorem only for the situation where f's second derivative is concave down, but of course it could be generalized somewhat.

Theorem 17. *Let $f : \mathbb{R} \to \mathbb{R}$ have continuous second derivatives, and assume its second derivative is concave down. Let $a, h \in \mathbb{R}$ with $h > 0$. Then*

$$f(a) - \frac{f(a+h) + f(a-h)}{2} \quad > \quad -\frac{h^2}{2} f''(a). \tag{10}$$

Proof. Fix a and let $g(h)$ be equal to the left-hand side of the inequality (10). Clearly $g(0) = 0$. In addition, its first derivative satisfies

$$\begin{aligned} g'(h) \quad &= \quad -\tfrac{1}{2}\left(f'(a+h) - f'(a-h)\right) \quad = \quad -\tfrac{1}{2}\int_{-h}^{h} f''(a+x)dx \\ &= \quad -\tfrac{1}{2}\int_0^h (f''(a+x) + f''(a-x))dx \\ &\geq \quad -\tfrac{1}{2}\int_0^h 2f''(a)dx \qquad\qquad \text{by the concavity of } f'' \\ &= \quad -hf''(a). \end{aligned}$$

Therefore,

$$g(h) \quad = \quad \int_0^h g'(y)dy \quad \geq \quad \int_0^h -yf''(a)dy \quad \geq \quad -\tfrac{h^2}{2} f''(a),$$

and the theorem is proved.

5.2. On secants parallel to tangents of $\sqrt{p(1-p)}$

Let $f(p)$ henceforth be the function $f(p) = \sqrt{p(1-p)}$ defined on the interval $[0, 1]$. We would like to establish the following theorem about parallel secant lines and tangent

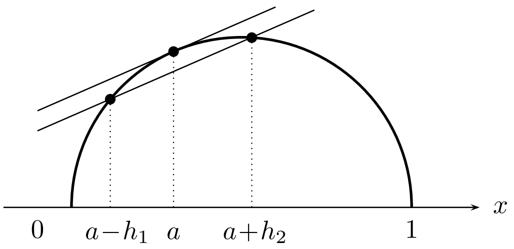

FIGURE 2: Illustration of Theorem 18.

lines to f. For future reference, we compute the first and second derivatives of f:

$$f'(x) \;=\; \frac{1-2x}{2\sqrt{x(1-x)}} \qquad \text{and} \qquad f''(x) \;=\; \frac{-1}{4(x(1-x))^{3/2}}.$$

It is easy to verify that the second derivative is concave down.

Theorem 18. *Suppose* $0 \le a - h_1 < a < a + h_2 \le 1$. *Further suppose that*

$$f'(a) \;=\; \frac{f(a+h_2) - f(a-h_1)}{h_2 + h_1}. \tag{11}$$

Then $h_1 \le 3h_2$ *and* $h_2 \le 3h_1$.

The situation of Theorem 18 is sketched in Figure 2. Equation (11) says that the slope of the secant line containing the points $(a-h_1, f(a-h_1))$ and $(a+h_2, f(a+h_2))$ is equal to the slope of the line tangent to f at $f(a)$. There are several simple observations to make. First, by the concavity of f, if the values of a and h_2 are fixed (respectively, the values of a and h_1 are fixed), then there is at most one value for $h_1 \in [0,1]$ (respectively, $h_2 \in [0,1]$) such that equation (11) holds. Second, since f' is a strictly decreasing function, the value of a is uniquely determined by the values of $a - h_1$ and $a + h_2$. Third, the theorem is easily seen to be true for $a = 1/2$, since in that case, $h_1 = h_2$. Fourth, since f is symmetric around $a = 1/2$ with $f(x) = f(1-x)$, it suffices to prove that $h_2 \le 3h_1$ as $h_1 \le 3h_2$ will then follow by symmetry.

Before starting the proof of Theorem 18, it is useful to note that the graph of the function $f(x) = \sqrt{x(1-x)}$ forms the upper half of the circle of radius 1/2 with center at the point $(\frac{1}{2}, 0)$. To prove this, just note that

$$\sqrt{x(1-x)} \;=\; \sqrt{(1/2)^2 - (x - 1/2)^2}.$$

Therefore, the situation of Theorem 18 is as illustrated in Figure 3. In the figure, the center of the semicircle is labeled P and the three points on the graph of $f(x)$ at $x =$

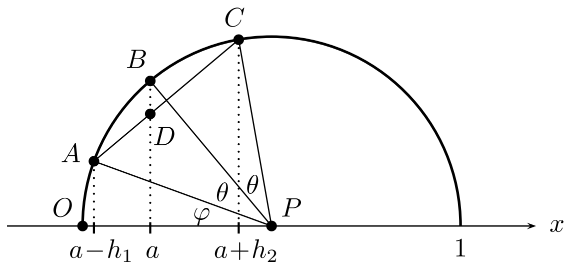

Figure 3: The situation in the proof of Theorem 18.

$a-h_1$, a and $a+h_2$ are labeled A, B and C. In order for the secant $\overline{AC}$ to be parallel to the tangent at B, it is necessary and sufficient that the angles $\angle APB$ and $\angle BPC$ are equal to the same value θ. We also let φ be the angle $\angle OPA$ where O is the point $(0,0)$.

We first prove $h_2 < 3h_1$ under the assumption that $\varphi = 0$: this is the same as the assumption that $a - h_1 = 0$. Clearly, it is sufficient to prove that

$$\frac{h_1+h_2}{h_1} \;<\; 4.$$

Since $\varphi = 0$, we have $h_1 = a = \frac{1-\cos\theta}{2}$, and $h_1 + h_2 = \frac{1-\cos(2\theta)}{2}$. So,

$$\frac{h_1+h_2}{h_1} \;=\; \frac{1-\cos(2\theta)}{1-\cos\theta} \;=\; \frac{2(1-\cos^2\theta)}{1-\cos\theta} \;=\; 2(1+\cos\theta),$$

which is clearly bounded by 4 since $\theta < \pi/2$.

It remains to prove the theorem for non-zero values of φ. However, we claim that the $\varphi = 0$ case is actually the worst case. To see this, consider Figure 3 again. Suppose we keep the angle θ fixed and let φ vary: then the values a, h_1 and h_2 and the points A, B, C and D are all functions of φ. We use $||AD||$ to denote the distance from A to D. Then by similar triangles,

$$\frac{||DC||}{||AD||} \;=\; \frac{h_2}{h_1}.$$

Clearly, $||DC||$ is a decreasing function of φ and $||AD||$ is an increasing function of φ, so the value of the fraction h_2/h_1 decreases as φ increases. We already proved $h_2/h_1 < 3$ for $\varphi = 0$, so therefore this holds for all values of φ. This completes the proof of Theorem 18.

As a corollary of Theorems 17 and 18 and the fact that f'' is concave down, we have:

Corollary 19. *Let f, a, h_1 and h_2 be as in the hypothesis to Theorem 18. Then,*

$$f(a) - \frac{h_2 f(a-h_1) + h_1 f(a+h_2)}{h_1+h_2} \;\geq\; -\frac{h_i^2}{18} f''(a)$$

for both $i = 1, 2$.

Proof. Let $h_{min} = \min\{h_1, h_2\}$. Consider the two secant lines S_1 and S_2 where S_1 is secant to the graph of f at $x = a - h_1$ and $x = a + h_2$, and S_2 is the secant line at $x = a - h_{min}$ and $x = a + h_{min}$. The value $(h_2 f(a - h_1) + h_1 f(a + h_2))/(h_1 + h_2)$ is the y-coordinate of the secant line S_1 at $x = a$. By the fact that f is concave down, the secant line S_2 is above the line S_1 for $a - h_{min} < x < a + h_{min}$, and, in particular, S_2 is above S_1 at $x = a$. By Theorem 17,

$$f(a) - \frac{h_2 f(a - h_1) + h_1 f(a + h_2)}{h_1 + h_2} \quad \geq \quad -\frac{h_{min}^2}{2} f''(a).$$

And by Theorem 18, for $i = 1, 2$, we have $h_i \leq 3h_{min}$, and this proves the corollary.

5.3. On secants parallel to tangents of the entropy function

The entropy function $H(p) = -p\ln(p) - (1-p)\ln(1-p)$ is defined on the interval $[0, 1]$. Its first and second derivatives are

$$\begin{aligned} H'(p) &= -\ln(p) + \ln(1-p) = \ln((1-p)/p) = \ln(\tfrac{1}{p} - 1) \\ H''(p) &= \frac{-1}{1-p} - \frac{1}{p} = \frac{-1}{(1-p)p}. \end{aligned}$$

It is easy to check that $H'(p)$ is strictly decreasing and is concave up for $p \leq 1/2$ and concave down for $p \geq 1/2$. Also, $H''(p)$ is concave down.

The next theorem states that $H(p)$ satisfies the same kind of property that Theorem 18 established for $\sqrt{p(1-p)}$.

Theorem 20. *Suppose* $0 \leq a - h_1 < a < a + h_2 \leq 1$. *Further suppose that*

$$H'(a) = \frac{H(a + h_2) - H(a - h_1)}{h_2 + h_1}. \tag{12}$$

Then $h_1 \leq (e-1)h_2$ *and* $h_2 \leq (e-1)h_1$, *where* e *is the base of the natural logarithm.*

We shall prove a weaker form of this theorem, namely, that there is a constant c such that $h_1 \leq ch_2$ and $h_2 \leq ch_1$, and then appeal to experimental results obtained by graphing functions in *Mathematica* to conclude that $c = (e-1)$ works.

The entropy function $H(p)$ is qualitatively similar to the function $f(p) = \sqrt{p(1-p)}$ in that it is concave down, is zero at $p = 0$ and $p = 1$, and attains its maximum at $p = 1/2$. So, Figure 2 can also serve as a qualitative illustration of Theorem 20. We introduce new variables, and let $r = a - h_1$ and $s = a + h_2$. Suppose the values r, a, s satisfy equation (12), that is, they satisfy

$$H'(a) \;=\; \frac{H(s) - H(r)}{s - r}. \tag{13}$$

Then, the values r, a, s are dependent in that any two of them determine the third. To prove the theorem, we must give upper and lower bounds on the ratio $h_2/h_1 = (s-a)/(a-r)$. The values of r, s come from the set $0 \le r < s \le 1$. The problem is that this set is not compact by virtue of having an open boundary along the line $r = s$. Even worse, the ratio is essentially discontinuous at $r = s = 0$ and at $r = s = 1$. For our proof, we will examine the values of the ratio along the line $r = s$ and at $r = 0$ (the case of $s = 1$ is symmetric), and argue by compactness of the remaining values of r, s that the ratio attains a finite maximum value and a positive minimum value.

We assume w.l.o.g. that $a < 1/2$. When also $s < 1/2$, then we have $h_1 < h_2$ by the fact that $H'(p)$ is concave up for $p \le 1/2$ and the fact that $H'(a)$ is the average slope of $H(p)$ for $p \in [r, s]$. Thus, for $s < 1/2$, it suffices to prove that $h_1/(h_1 + h_2) \ge 1/e$ and thereby obtain $h_2 \le (e-1)h_1$.

We start by proving the theorem in the case that $r = 0$. In this case,

$$\begin{aligned} \frac{H(s) - H(0)}{s - 0} \;&=\; \frac{H(s)}{s} \;=\; \frac{-s\ln(s) - (1-s)\ln(1-s)}{s} \\ &=\; \ln(s^{-1}(1-s)^{-(1-s)/s}). \end{aligned}$$

To find the value of a such that $H'(a)$ equals this last value, we need to solve

$$\frac{1}{a} - 1 = s^{-1}(1-s)^{-(1-s)/s}.$$

We are really interested in the value of a/s, since with $r = 0$, we have $a = h_1$ and $s = h_1 + h_2$, and we need to establish $a/s \ge 1/e$. Solving for a/s gives

$$\frac{a}{s} \;=\; \frac{(1-s)^{(1-s)/s}}{s(1-s)^{(1-s)/s} + 1}. \tag{14}$$

It is easy to check that $\lim_{s\to 0^+}(1-s)^{1/s} = 1/e$. Therefore, as $s \to 0^+$ the quantity (14) approaches the limit $1/e$.

Now consider the case $r = 0$ and $0 < s \le 1$ (so $a_1 \le 1/2$). Let $R(s) = a/s = Y/(sY + 1)$, where $Y(s) = (1-s)^{(1-s)/s}$. The first derivative of R is

$$R' \;=\; \frac{Y' - Y^2}{(sY + 1)^2} \tag{15}$$

with

$$Y' \;=\; Y\left(-\frac{1}{s^2}\ln(1-s) - \frac{1}{s}\right).$$

Note the numerator of (15) is equal to

$$Y \cdot \left[-\frac{1}{s^2}\ln(1-s) - \frac{1}{s} - (1-s)^{(1-s)/s}\right]. \tag{16}$$

The power series expansion for $\ln(1-s)$ shows that $\ln(1-s) < -s - s^2$ for $0 < s < 1$. Thus, (16) is positive and hence $R(s)$ is increasing and $1/e < R(s) \le 1$ for $0 < s \le 1$.

We have proved the $r = 0$ case of the theorem (and by symmetry, the $s = 1$ case). Now we consider the case where $r \approx s$. First, if $a = 1/2$, then of course, $s - a = a - r$, so $h_1 = h_2$ and the theorem is satisfied. More generally, compactness and continuity considerations imply that there is a $\delta > 0$ such that if $|a - 1/2| < \delta$, then $1/(e-1) < (s-a)/(a-r) < e-1$. (If $\delta = 1/2$ works, we are done, but for now we just know there is some such $\delta > 0$.) Now, fix a value of $a < 1/2 - \delta$. We consider values of r, s that correspond to this value for a. Again, $h_2 = s - a$ and $h_1 = a - r$. We are thinking of h_1 and h_2 increasing in such way that a stays fixed.

We claim that as h_1 and h_2 increase, the ratio h_2/h_1 is increasing, at least for h_2 and h_1 not too large. In order to prove this, it is equivalent to prove that

$$\frac{dh_2/dh_1}{h_2/h_1} \;>\; 1.$$

With a fixed, taking the first derivative of equation (12) gives

$$0 \;=\; -\frac{dh_1 + dh_2}{(h_1+h_2)^2}(H(a+h_2) - H(a-h_1)) + \frac{H'(a+h_2)dh_2 + H'(a-h_1)dh_1}{h_1+h_2}.$$

So, using (12) again and multiplying by $h_1 + h_2$,

$$0 \;=\; -(dh_1 + dh_2)H'(a) + H'(a+h_2)dh_2 + H'(a-h_1)dh_1.$$

Algebraic manipulation transforms this to

$$\frac{dh_2/dh_1}{h_2/h_1} \;=\; \frac{h_1(H'(a-h_1) - H'(a))}{h_2(H'(a) - H'(a+h_2))}. \tag{17}$$

H' is concave up and decreasing on $[0, 1/2]$, thus for $a - h_1 \ge 0$ and $a + h_2 < 1/2$,

$$h_1(H'(a-h_1) - H'(a)) \;>\; 2\int_{a-h_1}^{a}(H'(x) - H'(a))dx \tag{18}$$

$$h_2(H'(a) - H'(a+h_2)) \;<\; 2\int_{a}^{a+h_2}(H'(a) - H'(x))dx. \tag{19}$$

By $\int_{a-h_1}^{a} H'(x)dx = H(a) - H(a-h_1)$ and $\int_{a}^{a+h_2} H'(x)dx = H(a+h_2) - H(a)$ and using equation (12), the right-hand sides of (18) and (19) are equal. Therefore, (17) is greater than 1. This shows that the ratio h_1/h_2 is decreasing as long as $a+h_2 \le 1/2$ and $a-h_1 \ge 0$. If the Markov chain reaches $a-h_1 = 0$ with $a+h_2 \le 1/2$, then since we already have proved that $h_1/h_2 > 1/e$ at $a-h_1 = 0$ it follows that $h_1/h_2 > 1/e$ for all values of h_1 and h_2 for this a.

On the other hand, if the Markov chain stops with $a+h_2 = 1/2$ and $a-h_1 > 0$, it is sufficient to prove the following fact: For all r, a, s with $r \le s-\delta$, we have $h_1/h_2 > 1/e$. Now the set of points r, s with $0 \le r \le s-\delta$ and $s \le 1$ is compact, and the ratio h_1/h_2 is a continuous positive function of r, s. Thus it attains a minimum on this set. By graphing the function with *Mathematica* it is seen that h_1/h_2 is bounded below by $1/e$ by a fair margin. Thus we have proved the theorem. (If the reader dislikes the use of *Mathematica* here, then she can take this as a proof that there exists some constant $c > 0$, rather than as a proof that $c = e-1$ works.)

Corollary 21. *Let H, a, h_1 and h_2 be as in the hypothesis to Theorem 20. Then,*

$$H(a) - \frac{h_2 H(a-h_1) + h_1 H(a+h_2)}{h_1+h_2} \quad \ge \quad -\frac{h_i^2}{2(e-1)^2} H''(a)$$

for both $i = 1, 2$.

The proof of this corollary is identical to the proof of Corollary 19.

6. Proofs of the main theorems

This section presents the proofs of Lemmas 15 and 16, thus completing the proofs of the main theorems.

6.1. The weak variation condition lemma

We present the proof of Lemma 16. Let $f(x) = \sqrt{x(1-x)}$. Dividing equation (9) by n, we need to prove that, for some $\alpha > 0$,

$$f(\tfrac{i}{n}) \;\ge\; \tfrac{\alpha}{n} + \sum\nolimits_{j=0}^{n} m_{i,j} f(\tfrac{j}{n}), \qquad \text{for all } 0 < i < n. \tag{20}$$

Fix i and assume w.l.o.g. that $i \le n/2$; a symmetric argument will work for $i \ge n/2$. It will help to work with vectors in $\mathbb{R}^2$, and we define $\mathbf{P}_j$ to equal the following point (or vector) in $\mathbb{R}^2$:

$$\mathbf{P}_j \;=\; \big(j, f(\tfrac{j}{n})\big)\,.$$

Consider the summation

$$\mathbf{P} \;=\; \sum\nolimits_{j=0}^{n} m_{i,j}\mathbf{P}_j.$$

($\mathbf{P}$ depends on i, but we suppress any mention of i in the notation.) We want to establish an upper bound on the second coordinate of $\mathbf{P}$. First, however, consider the first component of $\mathbf{P}$. The mean condition implies that $\sum_{j=0}^{n} j m_{i,j} \;\le\; i$ since $i \le n/2$ (except that if this condition fails for $i = n/2$, then $i = n/2$ has to be handled in the symmetric argument for the case $i \ge n/2$). Therefore, $\mathbf{P}$'s first coordinate is $\le i$.

To bound the second coordinate, let $\mathcal{J}$ be the set of values j such that $|j-i| > \delta\sigma'_{i,n}$, where δ is the value from the weak variation condition. Then,

$$\mathbf{P} \;=\; \sum\nolimits_{j\notin\mathcal{J}} m_{i,j}\mathbf{P}_j + \sum\nolimits_{j\in\mathcal{J}} m_{i,j}\mathbf{P}_j.$$

Let $a = i/n$, and let T be the line tangent to the graph of $f(x)$ at $x = a$. Set $h_2 = \delta\sigma'_{i,n}/n$ and then choose h_1 so that the secant line S which is secant to f at $x = a - h_1$ and $x = a + h_2$ is parallel to T. That is to say, we are in the situation of Theorem 18. Thus, since $a \le 1/2$, we have $h_1 < h_2 \le 3h_1$.

As $f(x)$ is concave down, geometric considerations imply that each point $\mathbf{P}_j$ is on or below the tangent line T. Also, for every $j \in \mathcal{J}$, either $j/n < a - h_1$ or $j/n > a + h_2$. Therefore, again since f is concave down, for every $j \in \mathcal{J}$, the point $\mathbf{P}_j$ is on or below the secant line S. By the weak variation condition,

$$\sum_{j\in\mathcal{J}} m_{i,j} \;\ge\; \epsilon,$$

so in particular, the total weight of the points $\mathbf{P}_j$ which lie below the secant line S is $\ge \epsilon$. Define R to be the line parallel to T and S, lying between those lines, so that the distance from T to R is equal to ϵ times the distance from T to S. Since all the points $\mathbf{P}_j$ are on or below T, and the sum of the coefficients of $\mathbf{P}_j$ below the line S is $\ge \epsilon$, the point $\mathbf{P}$ lies on or below the line R.

Let $\pi_2(\mathbf{P})$ denote the y-component of $\mathbf{P}$, i.e., the value of the summation in (20). Since the slope of R is non-negative and the first coordinate of $\mathbf{P}$ is $\le i$, the value

$f(\frac{i}{n}) - \pi_2(\mathbf{P})$ is greater than or equal to ϵ times the vertical distance between $f(x)$ and the secant line S at $x = a = i/n$. Thus, by Corollary 19,

$$\begin{aligned} f(\tfrac{i}{n}) - \pi_2(\mathbf{P}) &\geq -\epsilon\frac{(h_2)^2}{18}f''(a) \;=\; -\,\epsilon\frac{(\delta\sigma'_{i,n}/n)^2}{18}f''(a) \\ &= -\epsilon\frac{\delta^2 i^{3/2}(n-i)^{3/2}}{18n^4}\cdot\frac{-1}{4(\frac{i(n-i)}{n^2})^{3/2}} \;=\; \frac{\epsilon\delta^2}{72}n^{-1}. \end{aligned}$$

To establish (20) and finish the proof of Lemma 16, choose $\alpha = \epsilon\delta^2/72$.

6.2. The variation condition lemma

The proof of Lemma 15 is similar to the proof of Lemma 16, but uses $H(p)$ in place of $f(p)$. We indicate only the changes in the proof. This includes defining $\mathcal{J}$ to be the set of values j such that $|j-i| > \delta\sigma_{i,n}$, and letting $h_2 = \delta\sigma_{i,n}/n$. At the end of the proof, the calculations change. Using Corollary 21, we have

$$\begin{aligned} H(\tfrac{i}{n}) - \pi_2(\mathbf{P}) &\geq -\epsilon\frac{(h_2)^2}{2(e-1)^2}H''(a) \;=\; -\,\epsilon\frac{(\delta\sigma_{i,n}/n)^2}{2(e-1)^2}H''(a) \\ &= -\epsilon\frac{\delta^2 i(n-i)}{2(e-1)^2n^3}\cdot\frac{-1}{(1-\frac{i}{n})\frac{i}{n}} \;=\; \frac{\epsilon\delta^2}{2(e-1)^2}n^{-1}. \end{aligned}$$

To finish the proof of Lemma 15, set $\alpha = e\delta^2/(2(e-1)^2)$.

Acknowledgements. We thank W.J. Ewens, I. Abramson, and an anonymous referee for helpful comments.

Appendix A. Proofs of variation conditions

We prove the variation condition holds for both the binomial and the hypergeometric distributions. Fix a Markov chain with transition matrix M on states $0,\ldots,n$, and fix i with $1 \leq i \leq n-1$. Define

$$a_k \;=\; m_{i,i+k},$$

for all k such that $0 \leq i+k \leq n$. We say that the *unimodal property* holds provided that $a_k \geq a_{k+1}$ for all $k \geq 0$ and that $a_k \geq a_{k-1}$ for all $k \leq 0$.

Lemma 22. *Suppose M is a transition matrix satisfying the unimodal property. For each i, let $k_0 = \lceil\sigma_{i,n}\rceil$ (we suppress in the notation the dependence of k_0 on i). Suppose* *that there is a constant $\alpha > 0$ such that, for all i,*

$$a_{k_0} > \alpha \cdot a_0 \qquad \text{and} \qquad a_{-k_0} > \alpha \cdot a_0.$$

Then the variation condition holds with any $\delta < \frac{1}{2}$ and $\epsilon = \alpha/(1+\alpha)$.

Proof. Fix i, $1 \le i \le n-1$. We need to show that

$$\frac{\sum_{k:|k|>\delta\sigma_{i,n}} a_k}{\sum_k a_k} \;>\; \frac{\alpha}{1+\alpha}. \tag{21}$$

First consider a_k's for non-negative values of k. By the unimodal property,

$$\sum_{0\le k\le\delta\sigma_{i,n}} a_k \;\le\; \sum_{0\le k\le\delta\sigma_{i,n}} a_0 \;\le\; \frac{k_0}{2}a_0.$$

Similarly,

$$\sum_{k>\delta\sigma_{i,n}} a_k \;\ge\; \sum_{\delta\sigma_{i,n}<k\le k_0} a_{k_0} \;\ge\; \frac{k_0}{2}a_{k_0} \;>\; \alpha\frac{k_0}{2}a_0.$$

Therefore,

$$\frac{\sum_{k>\delta\sigma_{i,n}} a_k}{\sum_{k\ge 0} a_k} \;>\; \frac{\alpha(k_0/2)a_0}{(k_0/2)a_0 + \alpha(k_0/2)a_0} \;=\; \frac{\alpha}{1+\alpha}.$$

A similar argument shows that

$$\frac{\sum_{(-k)>\delta\sigma_{i,n}} a_k}{\sum_{(-k)\ge 0} a_k} \;>\; \frac{\alpha}{1+\alpha}.$$

The previous two equations imply the desired condition (21).

Proof. (of Theorem 3). Let $q_{i,j}$ be the hypergeometric probabilities given in (2). Fix n. Also fix some $i \in \{1,\dots n-1\}$. Let $\sigma = \sqrt{i(n-i)/n}$, and let $k_0 = \lceil\sigma\rceil$. Let $a_{i,k} = q_{i,i+k}$. By Lemma 22, it will suffice to show that $a_{k_0}/a_0 > \alpha$ and $a_{-k_0}/a_0 > \alpha$, for some constant α. By the symmetry of the hypergeometric probabilities, $a_k = a_{-k}$, so we may assume w.l.o.g. that $i \le n/2$, and prove only $a_{k_0}/a_0 > \alpha$. An easy calculation shows that

$$\frac{a_k}{a_{k-1}} \;=\; \frac{(i-k+1)(n-i-k+1)}{(i+k)(n-i+k)}. \tag{22}$$

With $k = 1, 2$, this is

$$\frac{a_1}{a_0} \;=\; \frac{i(n-i)}{(i+1)(n-i+1)} \quad \text{and} \quad \frac{a_2}{a_1} \;=\; \frac{(i-1)(n-i-1)}{(i+2)(n-i+2)}.$$

For $k \le k_0$, we have

$$\begin{aligned}
\frac{a_k}{a_0} &= \frac{a_1}{a_0}\frac{a_2}{a_1}\cdots\frac{a_k}{a_{k-1}} \\
&= \frac{i(i-1)(i-2)\cdots(i-k+1)\cdot(n-i)(n-i-1)\cdots(n-i-k+1)}{(i+1)(i+2)(i+3)\cdots(i+k)\cdot(n-i+1)(n-i+2)\cdots(n-i+k)} \\
&= \frac{i}{i+k}\cdot\frac{i-1}{i+k-1}\cdots\frac{i-k+1}{i+1}\cdot\frac{n-i}{n-i+k}\cdot\frac{n-i-1}{n-i+k-1}\cdots\frac{n-i-k+1}{n-i+1} \\
&= \prod_{j=0}^{k-1}\frac{i-j}{i-j+k}\ \cdot\ \prod_{j=0}^{k-1}\frac{n-i-j}{n-i-j+k} \\
&> \left(\frac{i+1-k}{i+1}\right)^k\left(\frac{n-i-k+1}{n-i+1}\right)^k \ = \ \left(1-\frac{k}{i+1}\right)^k\left(1-\frac{k}{n-i+1}\right)^k \\
&> \exp\left(-\frac{\beta k^2}{i+1}\right)\cdot\exp\left(-\frac{\beta k^2}{n-i+1}\right) \qquad \text{where } \beta = 2\ln 2 \\
&> \exp\left(-\frac{\beta k^2}{i}\right)\cdot\exp\left(-\frac{\beta k^2}{n-i}\right) \ = \ \exp\left(-\frac{\beta n k^2}{i(n-i)}\right).
\end{aligned}$$

The inequality introducing the β factor deserves justification. Note $k/(i+1) \le k_0/(i+1) \le 1/2$ for all i and n. Likewise, $k/(n-i+1) \le 1/2$. The inequality follows from the the fact that $(1-c)^c \ < \ e^{-\beta c}$ for $0 < c \le 1/2$.

Consider the case of $k = k_0$. Note $k_0 \le i$ since $k_0 = \left\lceil\sqrt{i(n-i)/n}\right\rceil \le \left\lceil\sqrt{i}\right\rceil$. Also, $nk_0^2/(i(n-i)) \le 1$, since $k_0 \ge \sigma = \sqrt{i(n-i)/n}$. Thus,

$$\frac{a_{k_0}}{a_0} \ > \ e^{-\beta} \ = \ \frac{1}{4}.$$

This completes the proof of the theorem.

Proof. (of Theorem 2). Consider the binomial probabilities $p_{i,j}$ as defined by (1). Fixing i, and letting $a_k = p_{i,i+k}$, we have

$$\frac{a_k}{a_{k-1}} \ = \ \frac{(n-i-k+1)i}{(i+k)(n-i)} \quad \text{and} \quad \frac{a_{-k}}{a_{-(k-1)}} \ = \ \frac{(i-k+1)(n-i)}{(n-i+k)i}.$$

Both the quantities are clearly less than the corresponding ratio (22) obtained for the hypergeometric probabilities. Hence, by the previous proof,

$$\frac{a_{k_0}}{a_0} \ > \ \frac{1}{4} \quad \text{and} \quad \frac{a_{-k_0}}{a_0} \ > \ \frac{1}{4},$$

and, by Lemma 22, the proof is completed.

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