Success probability for selectively neutral invading species in the line model

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Abstract:
We consider a spatial (line) model for invasion of a population by a single mutant with a stochastically selectively neutral fitness landscape, independent from the fitness landscape for non-mutants. This model is similar to those considered in [FSDN+17, FSDKK19]. We show that the probability of mutant fixation in a population of size $N$ is greater than $1/N$, which would be the case if there were no variation in fitness whatsoever. In the small variation regime, we recover precise asymptotics for the success probability of the mutant. This demonstrates that the introduction of randomness provides an advantage to mutations in this model, and shows that the advantage increases with the system size.

Keywords: birth-death process, random environment, RWRE.

MSC Classification: 60J80, 92D15.
1 Introduction

Evolution in random environments has attracted attention of ecologists and mathematical biologists for a long time. Consider competition dynamics between two types of organisms whose reproduction and death rates may be different in different spatial locations. It is clear that organisms with larger reproduction rates and lower death rates are more likely to rise from low numbers and eventually replace their slow reproducing, rapidly dying counterparts. The situation becomes more complicated if the environment consists of different patches, where different types enjoy evolutionary advantage while others are suppressed. Depending on the properties of this patchy environment, the reproduction and death rates of the organisms, and the details of the evolutionary process, a number of outcomes can be observed, see e.g. [CW81, Pul88, HCM94, HG04], and also “modern coexistence theory” [ESAH19].

Two examples of biological systems where evolution takes place in the presence of spatial randomness, are biofilms and tumors. Biofilms are collectives of microorganisms, such as bacteria or fungi, that coexist on surfaces within a slimy extracellular matrix. Evolutionary dynamics of these microorganisms take place in an environment characterized by significant heterogeneities, both in physical and chemical parameters, such as heterogeneities in the interstitial fluid velocity, gradients in the distribution of nutrients and other metabolic substrates/products [SF08, JFM14]. It has been suggested [BTS04] that different organisms may respond differently to these diverse environmental stimuli, giving rise to evolutionary co-dynamics that can be modeled by using models similar to those studied here. The second example is evolution in cancerous populations, where the presence of highly heterogeneous environments has been documented, see e.g. [LCU+07, GML10]. Cancerous cells in different locations across a tumor are exposed to different concentrations of oxygen, nutrients, immune signaling molecules, inflammatory mediators, and other non-malignant cells that comprise the tumor microenvironment. Understanding tumor evolution under these spatially heterogeneous conditions is essential for understanding and combating long-standing challenges in oncology such as drug resistance in tumors. It also presents opportunities for creating new therapeutic strategies [Yua16].

An important focus of many theoretical studies of evolution in random environments is the probability and timing of mutant fixation. It is commonly assumed that the population of organisms (or agents) remains constant and birth/death updates are performed with rules governed by the organisms’ fitness parameters (birth and/or death rates). Interactions of replacing dead organisms by offspring of others happen along edges of a network that defines “neighborhoods”. For example, in a model characterized by agents on a complete graph, every agent is in the neighborhood of everyone else, and therefore a dead organism can be replaced by offspring of any other agent. On the other hand, on a circular graph, each agent has exactly two neighbors. These two types of graphs were studied in the recent papers [FSDN17, FSDKK19], in the context of the evolutionary co-dynamics of two types of agents, the “wild types” (or “normal”), and the “mutants”. It was assumed that, for each realization of the evolutionary competition process, for each of the $N$ sites, the birth and/or death rates of both types were assigned by randomly drawing from the same distributions of values. Then the probability of mutant fixation, starting from a given initial location of mutant agents among the $N$ spots, was calculated. Finally, this probability was averaged over all realizations of the fitness values. It was found that, somewhat surprisingly, the mutants showed an advantage compared to the normal types, as long as their initial number was smaller than a half. This result can be obtained for particular (relatively small) numbers of $N$, but no asymptotic results for large values of $N$ were obtained analytically.

In this paper, we obtain rigorous results for the probability of mutant fixation for a similar problem. We consider the following model. The spatial environment consists of $N$ sites, numbered $1, \ldots, N$ arranged in a
At each site there are two real parameters representing fitnesses: a mutant fitness and a normal fitness, each chosen IID $1 \pm \delta$. These fitnesses will remain fixed while the state of each site will change. Site 1 begins with state “mutant” and all other sites begin with the state “normal”. The evolution proceeds as follows: for each pair of neighbors $u$ and $v$, $u$ attempts to replace the type of $v$ with its own type at rate 1, with success probability equal to the fitness of $v$ corresponding to the state of $u$ divided by the total fitness of $v$. For instance, if $u$ is “mutant,” then at rate 1 $u$ will attempt to make $v$ mutant with success probability equal to the mutant fitness at $v$ divided by the sum of mutant and normal fitnesses at $v$. Since there are only finitely many sites and only two types, the process eventually fixates in one of two states: all mutants or all normal. We are interested in the probability of the event $G$ of fixating in the state where all sites are mutants, and in particular how the probability that $G$ occurs changes—after averaging over the random environment—as $\delta$ varies. More concretely: should more or less randomness help the mutant dominate?

If $\delta = 0$, there is no differential fitness and the fitness environment is deterministic. After $k$ replacements, the mutants will always either be extinct or occupy some interval $1, \ldots, X_k$. The process $\{X_k\}$ is a simple random walk stopped when it hits 0 or $N$, hence the probability that it stops at $N$ is precisely $1/N$.

When $\delta > 0$, the dynamics are more complicated. In fact they are the dynamics of a birth-death process in a random environment; equivalently, the dynamics may be thought of as a variant of the voter model where each site may be more or less susceptible to a given type. A very similar model, but with circular boundary conditions (1 and $N$ are neighbors), was analyzed in [FSDN+17]. There, it was proved for $4 \leq N \leq 8$ and empirically observed for much larger values of $N$ that the probability of a mutant takeover is strictly greater than $1/N$. The goal of this paper is to establish the analogous result rigorously for the line model and to give precise asymptotics for the annealed probability of a mutant takeover.

## 2 Notation and results

Let $(\Omega_N, \mathcal{F}_N, P_N)$ be a probability space on which are defined independent Rademacher random variables (that is $\pm 1$ fair coin flips) $B_1, \ldots, B_N$ and $B'_1, \ldots, B'_N$, as well as rate 1 Poisson processes $\xi_i^{(i,j)}$ for $1 \leq i, j \leq N$ and $|i-j| = 1$, independent of the Rademacher variables and of each other. For $\delta \in (0, 1)$, the normal fitness at site $k$ is the quantity $\mu_k := 1 + \delta B_k$ and the mutant fitness at site $k$ is the quantity $\nu_k := 1 + \delta B'_k$; in this way, the model is defined simultaneously for all $\delta$, although we will not do much to exploit this simultaneous coupling.

The states of the process are configurations where each site has a mutant (one) or normal cell (zero). Due to the geometry, the only possible configurations are mutant cells at some initial segment of sites $[1, k]$ and normal cells thereafter. Hence we can identify the state space with $\{0, 1, \ldots, N\}$, with 0 corresponding to mutant extinction. At times $\xi_i^{(i,j)}$, cell $i$ tries to reproduce at site $j$. This only matters if $i = k$ or $j = k$. Sampling only when the configuration changes yields a discrete time birth and death chain, absorbed at 0 and $N$, whose transition probabilities are easily characterized. Define the random quantities

$$\beta_k := \frac{\mu_k}{\nu_k + \mu_k}.$$  \hspace{1cm} (1)

From state $k$ the only relevant directed edges are $(k, k+1)$ and $(k, k-1)$ both attempted at rate 1 and succeeding with respective probabilities $\beta_{k+1}$ and $1 - \beta_k$. Hence, denoting $p(k, k+1)$ by $p_k$, we have

$$p_k = \frac{\beta_{k+1}}{\beta_{k+1} + (1 - \beta_k)}.$$  \hspace{1cm} (2)
Let $G = G(\delta)$ denote the event that the absorbing state $N$ is reached before the absorbing state 0, under dynamics for the given $\delta$. Our first result is an asymptotic expression for $P_N(G(\delta))$ in the regime where $N \to \infty$ and $\delta \sqrt{N} \to c$.

**Theorem 1** (asymptotics when $\delta \sqrt{N} \to c$). Fix $c > 0$ and suppose $N \to \infty$ and $\delta \sqrt{N} \to c$. Then

$$N P_N(G(\delta)) \to g(c) \quad (3)$$

where

$$g(c) = \mathbb{E} \left[ \frac{1}{\int_0^1 \exp(\sqrt{2} c B_s) \, ds} \right]$$

for a standard Brownian motion $\{B_s\}$. The function $g$ is continuous and strictly increasing on $(0, \infty)$. It satisfies

$$g(c) - 1 \sim \frac{c^2}{24} \quad \text{as } c \downarrow 0; \quad (4)$$

$$g(c) \sim \frac{c}{\sqrt{\pi}} \quad \text{as } c \to \infty. \quad (5)$$

In the regime where $\delta \gg N^{-1/2}$ but still $\delta \ll (\log N)^{-\epsilon}$, the asymptotic behavior of $P_N(G(\delta))$ is as follows.

**Theorem 2.** Assuming $\delta \sqrt{N} \to \infty$, suppose that there is an $\epsilon > 0$ such that $\delta (\log N)^{\epsilon} \to 0$. Then

$$P_N(G(\delta)) \sim \frac{\delta}{\sqrt{\pi N}}.$$  

We do not expect this to hold if $\delta = \Theta(1)$ as $N \to \infty$ because without scaling, the graininess of the random walk may lead to a different constant than would be obtained by a Brownian approximation. Nevertheless, we believe the condition $\delta = o(\log N)^{-\epsilon}$ to be unnecessary and we conjecture the following.

**Conjecture 3.** If $\delta \sqrt{N} \to \infty$ and $\delta \to 0$ then

$$\frac{\mathbb{P}_N(G(\delta))}{\delta N^{-1/2}} \to \frac{1}{\sqrt{\pi}}.$$

**Theorem 4.** Let $N = 2k$ be an even integer and let $Q_N$ denote $P_N$ conditioned on $\sum j B_j = \sum j B'_j$. Then $Q_N(G(\delta)) = 1$ for all $N$ and all $\delta$.

The outline of the remainder of the paper is as follows. In the next section we show how the computation of $P_N(G(\delta))$ reduces to computing an expectation of a functional of a random walk. We then verify in the
case $\delta \sim cN^{-1/2}$ that the expectation commutes with the Brownian scaling limit. Section 4 computes the corresponding expectations for Brownian motion, based on results of Matsumoto, Yor and others. Section 5 puts this together to prove Theorem 1. We also give the relatively brief proof of Theorem 4, which is a discretization of a similar result for the class of so-called Exchangeable Increment processes. Theorem 2 is proved in Section 6. This is proved in two stages, first when $\delta$ is required to decrease more rapidly than $(\log N)^{-1}$ and then when this is relaxed to $(\log N)^{-\epsilon}$. The final section presents some numerical simulations and further questions.

3 A scaling result

The following explicit formula for the probability of a birth and death process started at 1 to reach $N$ before 0 is well known.

**Proposition 5.** In a birth and death process, let $p_k$ be the probability of transition to $k+1$ from $k$ and let $q_k := 1 - p_k$ be the probability of transition to $k-1$. Let $Q_x$ denote the law of the process starting from $x$ and $\tau_a$ the hitting time at state $a$. Then

$$Q_1(\tau_N < \tau_0) = \frac{1}{\sum_{k=0}^{N-1} \prod_{j=1}^{k} \frac{q_j}{p_j}}.$$  \hfill (6)

*Here, the first term of the sum is the empty product, equal to 1 by convention.*

PROOF: The $k^{th}$ summand in the denominators is the resistances between $k$ and $k+1$ in a resistor network equivalent to the birth and death process. The expression for $Q_1$ is the ratio of the conductance from 1 to $N$ to that plus the conductance from 1 to 0. \hfill $\square$

We now show that the denominator is close to a functional of a random walk, which is close to a functional of a Brownian motion, and that these approximations are good enough to pass expectations to the limit.

For $1 \leq k \leq N-1$ denote

$$X_k := \log \frac{q_k}{p_k} = \log \frac{1 - \beta_k}{\beta_{k+1}}$$

$$\bar{X}_k := \log \frac{1 - \beta_{k+1}}{\beta_{k+1}} = \log \frac{\nu_{k+1}}{\mu_{k+1}}$$

with partial sums $S_k := \sum_{j=1}^{k} X_j$ and likewise for $\bar{S}$. The definition of $X_k$ is chosen so that Equation (6) becomes

$$\mathbb{P}_N(G(\delta)) = \mathbb{E} \frac{1}{\sum_{k=0}^{N-1} \exp(S_k)}.$$  \hfill (7)

On the other hand $\bar{X}_k$ are chosen so that $\{\bar{S}_k\}$ is precisely a simple random walk on the lattice $\delta' \mathbb{Z}$, with holding probability $1/2$, where

$$\delta' := \log \frac{1 + \delta}{1 - \delta} = 2\delta + O(\delta^2).$$

Because

$$|\bar{S}_k - S_k| = |\log(1 - \beta_{k+1}) - \log(1 - \beta_1)| \leq C\delta$$  \hfill (8)
as long as \( \delta \leq 1 - \varepsilon \), Donsker’s theorem gives

\[
(S_{\lfloor tN \rfloor})_{t \in (0,1)} \xrightarrow{N \to \infty} \sqrt{2} \cdot c \cdot B(t)
\]

in the càdlàg topology whenever \( \delta \sqrt{N} \to c \), where \( B(t) \) is Brownian motion.

In a moment we will show

**Lemma 6.** Suppose \( \delta \) and \( N \) vary so that \( \delta \sqrt{N} \) remains bounded away from zero and infinity. Then the random variables \( \{N \mathbb{P}_N(G(\delta))\} \) are uniformly integrable.

Together with (6) and (9) this lemma immediately implies the following result, which is the first part of Theorem 1.

**Theorem 7** (scaling limit). Fix \( c > 0 \) and suppose \( N \to \infty \) and \( \delta \sqrt{N} \to c \). Then

\[
N \mathbb{P}_N(G(\delta)) \to E \left[ \frac{1}{\int_0^1 \exp(\sqrt{2}cB_s) \, ds} \right]
\]

where \( (B_s) \) is standard Brownian motion.

**Proof of Lemma 6.** For a simple random walk, the reflection principle gives

\[
P[\min_{j \leq n} S_j \leq -r] = P[S_n = -r] + 2P[S_n < -r]
\leq 2P[S_n \leq -r]
\leq 2 \exp(-2r^2/n)
\]

where the last bound is by Hoeffding’s inequality. Because \( \{\tilde{S}_k\} \) is a simple random walk scaled by \( \delta' \) and holding with probability \( 1/2 \), for all \( k \in \mathbb{Z}^+ \) and \( t > 0 \),

\[
P[\min_{j \leq k} \tilde{S}_j < -t] \leq 2 \exp \left( -\frac{2t^2}{\log \left( \frac{4+\delta}{4-\delta} \right) k} \right).
\]

A consequence of (7) is that

\[
\left| \frac{\sum_{j=1}^N \exp(\tilde{S}_j)}{\sum_{j=1}^N \exp(S_j)} - 1 \right| = o(1).
\]

It therefore suffices to show that the variables

\[
N \to \infty \sum_{j=1}^N \exp(S_j)
\]

are uniformly integrable. Applying (10) shows that

\[
P[\min_{k \leq N\varepsilon} \tilde{S}_k \leq -1] \leq 2 \exp(-B/\varepsilon)
\]

for \( B \) depending continuously on \( \delta \sqrt{N} \). Thus from

\[
\sum_{j=1}^N \exp(S_j) \leq \varepsilon \exp \left( \min_{j \leq \varepsilon N} \tilde{S}_j \right).
\]
we have, for each $K > 0$,
\[
\mathbb{E}
\left[
\frac{N}{\sum_{j=1}^{N} \exp(S_j)} \mathbb{1}\left\{ \frac{N}{\sum_{j=1}^{N} \exp(S_j)} \geq K \right\}
\right]
= \int_{x \geq K} \mathbb{P}\left[ \sum_{j=1}^{N} \exp(S_j) \geq x \right] \, dx
\leq \int_{x \geq K} \mathbb{P}\left[ \min_{j \leq \langle eN/x \rangle} \bar{S}_j \leq -1 \right] \, dx
\leq \int_{x \geq K} 2 \exp(-Cx/e) \, dx.
\]

This inequality holds for all $N$ and converges to zero as $K \to \infty$, thereby showing uniform integrability. The convergence of means and Theorem 7 follow from uniform integrability together with convergence in distribution. \qed

4 Evaluation of the Brownian integral

\begin{align*}
A_\alpha(t) &:= \int_{0}^{t} e^{\alpha B_s} \, ds ; \\
m_\alpha(t) &:= \mathbb{E}[A_\alpha(t)]^{-1}.
\end{align*}

In this notation, Theorem 4 proves the first statement of Theorem 1 with
\[ g(c) := m_c \sqrt{\frac{1}{2}}. \]

To finish the proof of Theorem 1, it remains to evaluate (14). Expectations such as the one in (13) have been well studied.

**Proposition 8** ([MY05]). Let $\{B_t : t \geq 0\}$ be a standard Brownian motion and let $A(t) := \int_{0}^{t} e^{2B_s} \, ds$. Then,
\begin{align*}
\mathbb{E}[A_2(t)^{-1}|B_t = x] &= \frac{xe^{-x}}{t \sinh x} \quad \text{if } x \neq 0 ; \\
\mathbb{E}[A_2(t)^{-1}|B_t = 0] &= t^{-1} ; \\
m_2(t) &\sim \sqrt{\frac{2}{\pi t}} \text{ as } t \to \infty.
\end{align*}

**Proof:** The first two are proved as Matsumoto and Yor [MY05, Proposition 5.8]. The third is stated as (5.8) there, cited from [HY04], but there is a typo (a parameter $\alpha$ is introduced without a definition). A quick derivation is to integrate (15). Letting $y := x/\sqrt{t}$,
\begin{align*}
m_2(t) &= t^{-1} \int \frac{xe^{-x}}{\sinh(x)} \, dN(0,t)(x) \\
&= t^{-1/2} \int \frac{ye^{-\sqrt{ty}}}{\sinh(\sqrt{ty})} \, dN(0,1)(y).
\end{align*}

As $t \to \infty$, the quantity $ye^{-\sqrt{ty}}/\sinh(\sqrt{ty})$ converges pointwise to $2|y|1_{y<0}$. Truncating, integrating and taking limits gives
\[ t^{1/2}m_2(t) \to \int_{-\infty}^{0} 2|y| \, dN(0,1)(y) = \mathbb{E}[N(0,1)] = \sqrt{\frac{2}{\pi}}. \]
The next lemma uses Brownian scaling to transfer these results to the $-1$ moment of $\int_0^1 e^{\alpha B_s} \, ds$.

**Lemma 9.** For $\alpha, \nu, t > 0$,

$$m_\alpha(t) = \frac{\alpha^2}{\nu^2} m_\nu \left( \frac{\alpha^2}{\nu^2} t \right). \tag{18}$$

It follows that

$$m_\alpha(1) \sim \frac{\alpha}{\sqrt{2\pi}} \text{ as } \alpha \to \infty. \tag{19}$$

**Proof:** Let $f_\alpha(x, t)$ denote the density of $A_\alpha(t)^{-1}$ at $x$. Let $W_t := (\alpha/\nu) B_{\nu^2 t/\alpha^2}$. Then $\{W_t\}$ is also a standard Brownian motion and $\alpha B_t = 2W_t$. Hence,

$$f_\alpha(x, t) \, dx = \mathbb{P}\left( \left[ \int_0^t e^{\alpha B_s} \, ds \in [x, x + dx] \right] \right)$$

$$= \mathbb{P}\left( \frac{1}{(\nu/\alpha)^2} \int_0^t e^{2W_u} \, du \in [x, x + dx] \right)$$

$$= \mathbb{P}\left( \frac{1}{(\nu/\alpha)^2} \int_0^\infty e^{2W_u} \, du \in [(\nu/\alpha)^2 x, (\nu/\alpha)^2 x + (\nu/\alpha)^2 x + (\nu/\alpha)^2 dx] \right)$$

$$= \frac{\nu^2}{\alpha^2} f_\nu \left( \frac{\nu^2}{\alpha^2} x, \frac{\alpha^2}{\nu^2} t \right) \, dx. \tag{20}$$

Consequently, changing variables to $\theta = (\nu^2/\alpha^2)x$,

$$m_\alpha(t) = \int_{-\infty}^\infty x f_\alpha(x, t) \, dx$$

$$= \frac{\nu^2}{\alpha^2} \int_{-\infty}^\infty x f_\nu \left( \frac{\nu^2}{\alpha^2} x, \frac{\alpha^2}{\nu^2} t \right) \, dx$$

$$= \frac{\alpha^2}{\nu^2} \int_{-\infty}^\infty \theta f_\nu \left( \frac{\alpha^2}{\nu^2} t \right) \, d\theta$$

$$= \frac{\alpha^2}{\nu^2} m_\nu \left( \frac{\alpha^2}{\nu^2} t \right),$$

proving (18). Set $\nu = 2$ and $t = 1$, plug into (17) and send $\alpha$ to infinity to obtain

$$m_\alpha(1) = \frac{\alpha^2}{4} m_2 \left( \frac{\alpha^2}{4} \right) \sim \frac{\alpha^2}{4} \sqrt{\frac{2}{\pi \alpha^2/4}} = \frac{\alpha}{\sqrt{2\pi}},$$

proving (19).



**5 Proofs of Theorems 1 and 4**

**Proof of Theorem 1.** We have already evaluated $g$. Continuity and strict monotonicity will follow from Lemma 10 below. The estimate (4) follows immediately from (14) and (19). It remains to prove (3), that
is, to estimate \( g(c) = m_c \sqrt{2} (1) \) near \( c = 0 \). Integrating (14) gives

\[
t m^2(t) = \int \frac{xe^{-x}}{\sinh(x)} dN(0,t)(x) .
\]

Plugging in \( xe^{-x}/\sinh(x) = 1 - x + x^2/3 + O(x^3) \) gives

\[
t m^2(t) = 1 + \frac{t^3}{3} + O(t^{3/2})
\]
as \( t \downarrow 0 \). Using (18) with \( \alpha = c \sqrt{2} \) and \( \nu = 2 \) then gives

\[
g(c) = \frac{c^2}{2} m_2 \left( \frac{c^2}{2} \right) = 1 + \frac{c^2 + o(1)}{6},
\]

proving (4).

\[ \square \]

**Lemma 10.** The function \( \phi(x) := xe^{-x}/\sinh(x) \) is strictly convex. It follows that \( \int \phi(x) dN(0,t)(x) \) is strictly increasing in \( t \).

**Proof:** We show that \( \phi''(x) > 0 \) for \( x \neq 0 \). Computing, \( \phi''(x) = e^{-x}(\sinh(x))^{-3} h(x) \) where

\[
h(x) = x + 1 + (x - 1) e^{2x}.
\]

Because we have taken out a factor of the same sign as \( x \), we need to show that \( h \) is positive on \((0, \infty)\) and negative on \((-\infty, 0)\). Verifying first that \( h(0) = h'(0) = 0 \), the proof is concluded by observing that \( h''(x) = 4xe^{2x} \) has the same sign as \( x \). \[ \square \]

**Proof of Theorem 4** Extend the definition of \( X_k \) in the proof of Theorem 7 by reducing modulo \( N \), thus \( X_N := \log(1 - \beta_N) - \log \beta_1 \) and so forth. This makes the sequence \( \{X_k : k \geq 1\} \) periodic and shift invariant, that is, \( (X_1, \ldots, X_{N-1}, X_N) \overset{D}{=} (X_2, \ldots, X_N, X_1) \). Observe also that \( Q_N(S_N = 0) = 1 \) because \( S_N = \sum_{j=1}^{N} \log(1 - \beta_j) - \sum_{j=1}^{N} \log \beta_j \) and the multiset of \( N \) values of \( \beta_j \) is the same as the multiset of \( N \) values of \( 1 - \beta_j \). By shift invariance,

\[
\mathbb{E}f(X_1, \ldots, X_N) = N^{-1} \sum_{k=1}^{N} f(X_{k+1}, \ldots, X_{k+N}). \tag{21}
\]

Shifting the \( X \) sequence by \( k \) shifts the \( S \) sequence to \( (S_{k+1} - S_k, \ldots, S_{k+N} - S_k) \), in other words, \( S_k \) is subtracted from each terms and the terms are cyclically permuted. This turns \( 1/\sum_{j=0}^{N-1} \exp(S_j) \) into \( \exp(S_k)/\sum_{j=0}^{N-1} \exp(S_j) \). Plugging into (21) and summing gives

\[
\mathbb{E} \frac{1}{\sum_{j=0}^{N-1} \exp(S_j)} = N^{-1} \sum_{k=0}^{N-1} \frac{\exp(S_k)}{\sum_{k=0}^{N-1} \exp(S_k)} = N^{-1}
\]

proving Theorem 4. \[ \square \]

## 6 Proof of Theorem 2

### 6.1 KMT Coupling and Preliminaries

A key result for studying this larger regime \( \delta \) is coupling of random walk to Brownian motion.
Lemma 11 (KMT-Coupling). Let $X_k$ be a simple random walk with i.i.d. increments $\xi$ so that $E[\xi] = 0, E[\xi^2] = 1$ and $E[e^{t|\xi|}] < \infty$ for $t$ sufficiently small. Extend $X_k$ to continuous time by defining $X_t = X_{\lfloor t \rfloor}$. Then there exists a constant $C$ so that for all $T > e$ there is a coupling so that
\[
P \left[ \sup_{t \in [0,T]} |X_t - B_t| \geq C \log(T) \right] \leq \frac{1}{T^2}
\]
where $B_t$ is standard Brownian motion.

Proof. This is stated as equation (17) in [AD13]. In fact one can replace $T^{-2}$ by a stretched exponential; a slightly weaker result that may be quoted from [LL10, Theorem 7.1.1] is that for any $\alpha > 0$ there is a $C_\alpha$ such that
\[
P \left[ \sup_{t \in [0,T]} |X_t - B_t| \geq C_\alpha \log(T) \right] \leq T^{-\alpha}.
\]
(22)

Another basic lemma is the well known uniform estimate for random walk hitting probabilities.

Lemma 12. Let $\{S_n\}$ be a random walk whose IID increments $\{X_n\}$ satisfy the hypotheses of the KMT coupling. Then, if $u$ ranges over $[M^\varepsilon, M^{1/2-\varepsilon}]$ for some $\varepsilon \in (0,1/2)$,
\[
P(\max_{1 \leq j \leq M} S_j \leq u) \sim \sqrt{\frac{2}{\pi}} \frac{u}{M^{1/2}}
\]
as $M \to \infty$, uniformly in $u$ and the random walk.

Proof. For Brownian motion run to time $M$, the reflection principle gives
\[
P(\sup_{0 \leq t \leq M} B_t \leq u) = 1 - 2P_0(B_M \geq u)
\]
which is asymptotic to $(2/\pi)^{1/2}uM^{-1/2}$ uniformly as $u$ varies over the $(0,M^{1/2-\varepsilon})$ for any $\varepsilon \in (0,1/2)$. Pick $\alpha > 1/2$. By (22), one then has
\[
\sqrt{\frac{2}{\pi}} \frac{u - C_\alpha \log M}{M^{1/2}} - M^{-\alpha} \leq \P(\max_{1 \leq j \leq M} S_j \leq u) \leq \sqrt{\frac{2}{\pi}} \frac{u + C_\alpha \log M}{M^{1/2}} + M^{-\alpha}.
\]

We will prove Theorem 2 in two cases, both of which will make further use of the KMT coupling. Two relevant functionals of random walk will correspond to two functionals of Brownian motion, and we will need to show that the expectations in the random walk case are asymptotically equivalent to those in the Brownian motion case. For this, we require a few results to show that these functionals are sufficiently well-behaved.
6.2 Two Brownian functionals

The functionals of interested are

\[ X_M := \int_0^M \exp(B_s) \, ds \]
\[ Y_M := \frac{B_M^-}{\int_0^M \exp(2B_s) \, ds} \]

where we use the notation \( Z^- := \max\{-Z, 0\} \).

**Lemma 13.** The family of variables \( \left\{ \frac{X_M}{\mathbb{E}X_M} \right\}_{M \geq 1} \) is uniformly integrable.

**Proof.** First note that \( \mathbb{E}[X_M] = \Theta(M^{-1/2}) \) by Brownian scaling together with Proposition 8. We claim that there exists a universal \( C > 0 \) so that \( \mathbb{P}[X_M \geq t] \leq C t^{-2} M^{-1/2} \). For \( t \leq M^{1/3} \), note that \( \mathbb{P}[X_M \geq t] \) is at most the probability that both \( \min_{0 \leq s \leq 1} B_s \leq -\log(t) \) and that after first hitting \(-\log(t)\), \( B_s \) does not spend more than 1 unit of time above \(-\log(t)\). Let \( \tau = \inf\{s \in [0, 1] : B_s = -\log(t)\} \). The reflection principle gives

\[ \mathbb{P}\left[ \inf_{s \in [0, 1]} B_s \leq -\log(t) \right] = 2 \mathbb{P}[B_1 \leq -\log(t)] \leq C \exp\left(-\frac{1}{2}(\log(t))^2\right). \]

Conditioned on \( \tau < \infty \), note that the probability \( B_s \) does not go above \(-\log(t)\) for more than 1 unit of time is \( 2 \pi \text{arcsin}(\sqrt{1/(M-\tau)}) = \Theta(M^{-1/2}) \) by the strong Markov property together with Lévy’s arcsin law. Thus, for \( t \leq M^{1/3} \), we have

\[ \mathbb{P}[X_M \geq t] \leq C \exp\left(-\frac{1}{2}(\log(t))^2\right) \frac{1}{\sqrt{M}}. \]

For \( t > M^{1/3} \), note that we still must have

\[ \mathbb{P}\left[ \inf_{s \in [0, 1]} B_s \leq -\log(t) \right] \leq C \exp\left(-\frac{1}{2}(\log(t))^2\right) = O(t^{-2}M^{-1/2}) \]

because \( t \geq M^{1/3} \). With the bound \( \mathbb{P}[X_M \geq t] \leq C t^{-2} M^{-1/2} \) for all \( t, M \), we then compute

\[ \mathbb{E}\left[ \frac{X_M}{\mathbb{E}X_M} \mathbf{1}_{X_M/\mathbb{E}X_M \geq K} \right] \leq C \sqrt{M} \int_K^\infty t^{-2} M^{-1/2} \, dt \leq C/K \to 0 \]

as \( K \to \infty \). \( \Box \)

We find the asymptotics of the first two moments of the other functional:

**Lemma 14.** As \( M \to \infty \) we have \( \mathbb{E}Y_M \to 1 \) and \( \mathbb{E}Y_M^2 \sim 4\sqrt{2/\pi} \sqrt{M} \).

**Proof.** By (15), we compute

\[ \mathbb{E}\int_0^M \frac{B_M^-}{\exp(2B_s) \, ds} \]

\[ = \int_{\mathbb{R}} -x^2 e^{-x^2} \mathbf{1}_{x \leq 0} \frac{dN(0, M)(x)}{M \sinh(x)} \]

\[ = \int_{\mathbb{R}} -y^2 e^{-\sqrt{My}} \mathbf{1}_{y \leq 0} \frac{dN(0, 1)(y)}{\sinh(\sqrt{My})}. \]
As $M \to \infty$, $e^{-\sqrt{My}}/\sinh(\sqrt{My}) \to -2 \cdot 1_{y<0}$; truncating, integrating and taking limits then gives
\[ E \left[ \frac{B_M}{\int_0^M \exp(2B_s) \, ds} \right] \to \int_{-\infty}^0 2y^2 dN(0,1)(y) = 1. \]

By differentiating Equation (5.7) of [MY05] twice with respect to $\lambda$, we have that
\[ E \mathbb{E} \left[ \exp(2B_M) \right] = e^{-2x (x^2 \sinh(x) + Mx \cosh(x) - M \sinh(x)) / M^2 \sinh(x)^3}. \]

This implies that
\[ E\left[ \frac{Y_M^2}{\sqrt{M}} \right] = \int_\mathbb{R} \frac{e^{-2x} 1_{y<0} (x^4 \sinh(x) + Mx^3 \cosh(x) - Mx^2 \sinh(x))}{M^{5/2} \sinh(x)^3} \, dN(0,M)(x) \]
\[ = \int_\mathbb{R} \frac{e^{-2y\sqrt{M}} 1_{y<0} (M^2 y^4 \sinh(\sqrt{My}) + M^{5/2} y^3 \cosh(\sqrt{My}) - M^2 y^2 \sinh(\sqrt{My}))}{M^{5/2} \sinh(\sqrt{My})^3} \, dN(0,1)(y). \]

The integrand converges to $-4y^3 1_{y<0}$ as $M \to \infty$; truncating, integrating and taking limits shows
\[ \frac{E[Y_M^2]}{\sqrt{M}} \to \int_\mathbb{R} -4y^3 1_{y<0} \, dN(0,1)(y) = 4 \sqrt{\frac{2}{\pi}}. \]

Lastly, we show that the expectation of $Y_M$ is not dominated by the contribution when $Y_M$ is much larger than $\sqrt{M}$.

**Lemma 15.** Let $Y_M$ denote the random variable $\frac{B_M}{\int_0^M \exp(2B_s) \, ds}$. Then for all events $E$ with $P[E] \leq M^{-1/2-\varepsilon}$ for some $\varepsilon > 0$ we have $E[Y_M 1_E] = o(1)$ as $M \to \infty$.

**Proof.** Using Lemma [14] together with Chebyshev’s inequality, we see that
\[ P[Y_M \geq t] \leq C \sqrt{Mt}^{-2} \]
for some constant $C$. This implies that
\[ E[Y_M 1_{Y_M \geq M^{1/2+\varepsilon}/2}] = \int_{M^{1/2+\varepsilon}/2}^\infty P[Y_M \geq t] \, dt \leq CM^{-\varepsilon/2} = o(1). \]

We then may write
\[ E[Y_M 1_E] = E[Y_M 1_E 1_{Y_M \geq M^{1/2+\varepsilon}/2}] + E[Y_M 1_E 1_{Y_M < M^{1/2+\varepsilon}/2}] \leq o(1) + M^{1/2+\varepsilon/2} P[E] \to 0. \]
6.3 Medium-sized case: $N^{-1/2} \ll \delta \ll 1/\log N$.

**Lemma 16.** There exists a constant $C'$ so that for $\delta$ in $[\varepsilon, 1-\varepsilon]$ we have

$$e^{-C' \delta \log(N)} \cdot \int_0^1 \frac{1}{N} \exp \left( \sqrt{N} \delta' B_t / \sqrt{2} \right) dt \leq \mathbb{E} \left[ p(N) \right] \leq e^{C' \delta \log(N)} \cdot \int_0^1 \frac{1}{N} \exp \left( \sqrt{N} \delta' B_t / \sqrt{2} \right) dt + 1/N^2.$$  

where $E$ is an event with $\mathbb{P}(E) \leq N^{-2}$.

**Proof.** For $t \in [0, N]$, define $\tilde{S}_t = \tilde{S}_{\lceil t \rceil}$. Then note that

$$\sum_{j=1}^N \exp(\tilde{S}_j) = \int_0^N \exp(\tilde{S}_t) dt.$$  

By (7) and (8), we have

$$\exp(-C \varepsilon \delta) \leq p(N) \cdot \left( \int_0^N \exp(\tilde{S}_t) dt \right) \leq \exp(C \varepsilon \delta).$$  

Note that $\tilde{S}_k$ is a random walk whose increments have variance $(\delta')^2$. By Lemma 11 there exists a coupling so that

$$\mathbb{P} \left[ \sup_{t \in [0, N]} \left| \frac{\sqrt{2}}{\delta'} \tilde{S}_t - B_t \right| \geq C \log(N) \right] \leq \frac{1}{N^2}.$$  

Letting $E_N$ denote the event on the left-hand side, conditioned on the event $E_N$, we have

$$\exp \left( -C \varepsilon \delta - \frac{C \delta'}{\sqrt{2}} \log(N) \right) \leq p(N) \cdot \left( \int_0^N \exp(\delta' B_t / \sqrt{2}) dt \right) \leq \exp \left( C \varepsilon \delta + \frac{C \delta'}{\sqrt{2}} \log(N) \right).$$  

Since $\delta' \leq C_{\varepsilon} \delta$ for some constant $C_{\varepsilon}'$, we can find a new constant $C''$ so that

$$\exp \left( -C'' \delta \log(N) \right) \leq p(N) \cdot \left( \int_0^N \exp(\delta' B_t / \sqrt{2}) dt \right) \leq \exp \left( C'' \delta \log(N) \right)$$  

conditioned on $E_N$. Because $p(N) \leq 1$, and $\mathbb{P}[E_N] \leq \frac{1}{N^2}$, the lemma follows from taking expectations and Brownian scaling. \hfill \Box

**Proof of Theorem 2 for medium $\delta$.** Because $\delta \log(N) \to 0$, Lemmas 11 and 13 imply

$$\mathbb{E} [p(N)] \sim \frac{1}{N} \sqrt{\delta' \pi / \sqrt{2}} (1).$$  

Applying Lemma 9 completes the proof. \hfill \Box
6.4 Large case: \( \delta = o(1/(\log N)^c) \)

Let \( r > 6 \) be a real parameter, set \( T := \lfloor \delta^{-r} \rfloor \). Note that \( \exp(\delta^{-r}) \approx \exp(N^{r\varepsilon}) \) grows faster than any polynomial in \( N \) once \( r\varepsilon > 1 \). Also, we may assume that \( \delta^{-r} = o(N^{s}) \) for any positive \( s \) because the medium case already covers the regime \( \delta \leq (\log N)^{-2} \), say, and in the complement of this case, certainly any negative power of \( \delta \) grows more slowly than any power of \( N \).

Recalling the process \( \{\tilde{S}_k\} \) from Section 3.1 we denote \( Z := \tilde{S}_T \), \( A := \sum_{k=0}^{T-1} \exp(\tilde{S}_k) \), and let \( F \) denote \( \sigma(\tilde{S}_1, \ldots, \tilde{S}_k) \). For a real number or random variable \( X \), we use the notation \( X^+ := \max(X, 0) \) for the positive part of \( X \) and \( X^- := \min(X, 0) \) for the negative part of \( X \).

**Lemma 17.**

\[
P_N(G(\delta)) = (1 + o(1)) \frac{2}{\delta' \sqrt{\pi N}} \left( \frac{E Z^-}{A} + O \left( E \frac{\delta^{-s}}{A} \right) \right) + O(e^{-\delta^{-s}}).
\]

**Proof.** Recall from (8) that \( \{\tilde{S}_n\} \) is uniformly close to \( \{S_n\} \) as \( \delta \to 0 \), therefore \( \text{(11)} \) implies \( P_N(G(\delta)) \sim \mathbb{E}(A^{-1}) \) which we will use instead of \( \text{(11)} \).

We show the asymptotic equality in the statement of the theorem as two inequalities:

\[
P_N(G(\delta)) \geq (1 + o(1)) \frac{2}{\delta' \sqrt{\pi N}} \left( \frac{E Z^-}{A} + O \left( E \frac{\delta^{-s}}{A} \right) \right); \tag{23}
\]

\[
P_N(G(\delta)) \leq (1 + o(1)) \frac{2}{\delta' \sqrt{\pi N}} \left( \frac{E Z^-}{A} + O \left( E \frac{\delta^{-s}}{A} \right) \right) + e^{-\delta^{-s}}. \tag{24}
\]

Fix \( s \) and \( s' \) such that \( r/2 - 1 > s' > s > \varepsilon^{-1} \). Let \( G' \) denote the event \( \{\max_{T \leq m \leq N} \tilde{S}_m \leq -\delta^{-s}\} \). We condition on \( F_T \).

\[
P_N(G(\delta) | F_T) = P_N(G(\delta) | A, Z) \\
\geq P_N(G(\delta) \cap G' | A, Z) \\
\geq \frac{1}{A + Ne^{-\delta^{-s}}} P_N(G' | A, Z) \tag{25}
\]

Since \( \tilde{S}_m/(\delta' / 2) \) is a random walk with centered increments of variance 1, Lemma 12 gives

\[
P_N(G' | A, Z) \sim \sqrt{\frac{2}{\pi(N - T)}} \frac{(-Z - \delta^{-s})^+}{\delta' / \sqrt{2}} \sim \frac{2(Z + \delta^{-s})^-}{\delta' \sqrt{\pi N}}.
\]

Combining with (24) gives

\[
P_N(G(\delta) | F_T) \geq (1 + o(1)) \frac{2}{\delta' \sqrt{\pi N}} \frac{(Z + \delta^{-s})^-}{A + Ne^{-\delta^{-s}}}.
\]

The quantity \( A \) is at least 1, while \( Ne^{-\delta^{-s}} \to 0 \), therefore \( A + Ne^{-\delta^{-s}} \sim A \). Taking unconditional expectations now gives (23).

For the reverse inequality, let \( G'' \) denote the event \( \{\max_{T \leq m \leq N} \tilde{S}_m \leq \delta^{-s}\} \). On the complement of this event, at least one summand in the denominator of (7) is at least \( \exp(\delta^s) \). Because \( P_N(G(\delta) | A, Z) \) is always at most \( 1/A \), we see that

\[
P_N(G(\delta) | F_T) = P_N(G(\delta) | A, Z)
\]

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\[ \leq \frac{1}{A} \mathbb{P}_{N}((G(\delta) \cap C') | A, Z) + \exp(-\delta^{-s}) \]
\[ \leq (1 + o(1)) \sqrt{\frac{2}{\pi(N - T)}} \frac{(\delta - s - Z)^{+}}{A\delta' / \sqrt{2}} + e^{-\delta^{-s}}. \]

Again, taking unconditional expectations finishes, yielding (21).

We are now in a position to apply the KMT coupling to find the expectations that appear in Lemma 17.

**Lemma 18.**

\[ \mathbb{E} \frac{Z^{-}}{A} \sim \delta^{2}; \quad (26) \]
\[ \mathbb{E} \frac{1}{A} \sim \frac{2}{\delta' \sqrt{\pi T}}. \quad (27) \]

**Proof.** By Lemma 11, there exists a coupling of \( \{ \tilde{S}_{t} \}_{0 \leq t \leq T} \) and \( \{ B_{t} \}_{0 \leq t \leq T} \) so that

\[ \mathbb{P} \left[ \sup_{t \in [0, T]} \left| \frac{\tilde{S}_{t}}{\delta'/\sqrt{2}} - B_{t} \right| \geq C \log(T) \right] \leq \frac{1}{T^2}. \]

Let \( E \) denote the event in the above probability; conditioned on \( E^{c} \), we have

\[ A = \int_{0}^{T} \exp(\tilde{S}_{s}) \, ds = \int_{0}^{T} \exp(\delta' B_{s} / \sqrt{2} + O(\delta' \log(T))) \, ds \sim \int_{0}^{T} \exp(\delta' B_{s} / \sqrt{2}) \, ds \]

where the last asymptotic equality follows from \( \delta' \log(T) = O(\delta \log \delta) \rightarrow 0 \). This means that

\[ \mathbb{E}[A^{-1}] = \mathbb{E}[A^{-1} 1_{E}] + \mathbb{E}[A^{-1} 1_{E^{c}}] = O(T^{-2}) + (1 + o(1)) \mathbb{E} \int_{0}^{T} \exp(\delta' B_{s} / \sqrt{2}) \, ds . \quad (28) \]

By Brownian scaling,

\[ \int_{0}^{T} \exp \left( \delta' B_{s} / \sqrt{2} \right) \, ds = \int_{0}^{T} \exp \left( 2(B_{(\delta')^{2}s/2s}) \right) \, ds = 2^{T(\delta')^{2}/2^{3}} \left[ \int_{0}^{T(\delta')^{2}/2^{3}} \exp(2B_{s}) \, ds \right]. \]

By assumption, \( T(\delta')^{2} \rightarrow \infty \); further, the uniform integrability statement in Lemma 13 shows that

\[ \mathbb{E} \left[ \left( \int_{0}^{T(\delta')^{2}/2^{3}} \exp(2B_{s}) \, ds \right)^{-1} 1_{E^{c}} \right] \sim \mathbb{E} \left[ \left( \int_{0}^{T(\delta')^{2}/2^{3}} \exp(2B_{s}) \, ds \right)^{-1} \right] \]

since the variables \( 1_{E}X_{M}/\mathbb{E}[X_{M}] \) converge almost surely to 0 and are uniformly integrable. From here, (28) then gives

\[ \mathbb{E}[A^{-1}] = O(T^{-2}) + (1 + o(1)) \cdot \frac{2^{3}}{(\delta')^{2}} \cdot \sqrt{\frac{2}{\pi T}} \cdot \delta' \frac{1}{2^{3/2}} = O(T^{-2}) + (1 + o(1)) \frac{2^{2}}{\delta' \sqrt{\pi T}} \sim \frac{2}{\delta' \sqrt{\pi T}}. \]

Similarly,

\[ \mathbb{E}[Z^{-}/A] = \mathbb{E} \left[ \frac{Z^{-}}{A} \cdot 1_{E} \right] + \mathbb{E} \left[ \frac{Z^{-}}{A} \cdot 1_{E^{c}} \right] \]

15
\[
O(T^{-2}) + \frac{\delta'}{\sqrt{2}} E \left[ \frac{B_T 1_{E^c}}{\int_0^T \exp \left( \delta' B_s / \sqrt{2} \right) ds} \right] + O \left( \delta \log(T) E \left[ \left( \int_0^T \exp(\delta' B_s / \sqrt{2}) ds \right)^{-1} \right] \right)
\]

\[
= O \left( \frac{\log(T)}{\sqrt{T}} \right) + \frac{\delta'}{\sqrt{2}} E \left[ \frac{B_T 1_{E^c}}{\int_0^T \exp \left( \delta' B_s / \sqrt{2} \right) ds} \right].
\]

Using Brownian scaling, note

\[
\frac{B_T}{\int_0^T \exp(\delta' B_s / \sqrt{2}) ds} = \frac{\delta'}{2^{3/2}} \frac{B_{(2^{3/2}/\delta')}^T}{\int_0^{(2^{3/2}/\delta')} \exp(2B_s) ds} = \frac{\delta'}{2^{3/2}} Y_M
\]

where we set \( M = (2^{3/2}/\delta')^2 T \). By Lemma 15 together with Lemma 4, we have

\[
E[Y_M 1_{E^c}] = E[Y_M] + o(1) = 1 + o(1).
\]

Combining the above equalities provides

\[
E[Z^- / A] = O \left( \frac{\log(T)}{\sqrt{T}} \right) + (1 + o(1)) \cdot \frac{\delta'}{\sqrt{2}} \frac{\delta'}{2^{3/2}} \sim \delta^2.
\]

\[\square\]

**Proof of Theorem 2 for large \( \delta \):** Combining Lemma 17 with Lemma 18 gives

\[
P_N(G(\delta)) = (1 + o(1)) \frac{2}{\delta' \sqrt{\pi N}} \left( E \frac{Z^-}{A} + O \left( \frac{\delta^2}{A} \right) \right) + O(e^{-\delta^-})
\]

\[
= (1 + o(1)) \frac{1}{\delta \sqrt{\pi N}} \left( \delta^2 + O \left( \frac{1}{\delta \sqrt{T}} \right) \right) + O(e^{-\delta^-})
\]

\[
\sim \frac{\delta}{\sqrt{\pi N}}
\]

where we used that \( T = \Omega(\delta^r) = \Omega(\delta^{-6}) \) to show that \( \delta^2 + O(\delta^{-1} T^{-1/2}) \sim \delta^2 \). \[\square\]

### 7 Numerical simulations and further questions

To double check the results of Theorem 1 we simulated the process for \( N = 250 \) and \( c = 2 \). Thus, \( \delta = c / \sqrt{N} = 2 / \sqrt{250} \approx 0.126 \). Theorem 1 predicts that as \( N \to \infty \), \( N P_N(G(\delta)) \to g(2) \). Numerically evaluating the integral defining \( g(2) \) gives approximately 1.516. Our quick and dirty Monte Carlo simulation gives \( NP_N(G(\delta)) = 1.521 \pm 0.06 \). We could have done more simulations to lower the standard error, but in fact because we ran simulations for \( N = 10m \) for every \( m \leq 25 \), there is already greater accuracy. Figure 1 shows all of these data points, as well as similar data for \( c = 3 \) and \( 1 \leq m \leq 15 \) (here \( g(3) \approx 1.97 \)). The limits predicted by Theorem 1 are corroborated, or at least not contradicted, by the data.

Next we ran simulations to investigate Conjecture 3. Recall, the limit is known when \( \delta \to 0 \) as fast as any power \( (\log N)^{-\epsilon} \), whereas this should fail when \( \delta \) remains constant; the conjecture covers the ground in
Figure 1: The average mutant fixation probability, \( \langle P_N \rangle \) times \( N \) as a function of \( N \) for the line model. The fitness of both mutants and normals at different locations are drawn from the same two-valued distribution function, where values \( 1 - \delta \) and \( 1 + \delta \) are equally likely. Two different values of \( \delta \) are used: \( 2/\sqrt{N} \) (red points) and \( 3/\sqrt{N} \) (blue points). The points are based on stochastic simulations and each data point represents the average over \( 10^6 \) independent realizations.

between, which is clearly too slim to distinguish numerically. The best we could do was to hold \( \delta \) constant, thus allowing \( c := \delta \sqrt{N} \) to go to infinity. On one hand, we might expect

\[
\sqrt{\pi N} P_N(G(\delta)) \approx \delta
\]

because a constant \( \delta \) just barely violates the hypotheses of Theorem 2. On the other hand, one might expect \( g(c) \) that \( NP_N(G(\delta)) \) is well approximated by \( g(c) \), leading to

\[
\sqrt{\pi N} P_N(G(\delta)) \approx \frac{g(\delta \sqrt{N}) \sqrt{\pi}}{\sqrt{N}},
\]

which is asymptotic to \( \delta \) by 4. Indeed, the data (red points in Figure 2) is a very good match for (29) (the blue curve in Figure 2), which can be seen to be asymptotic to 0.2.

Among the open questions on this model, one that looms large is whether these results or something similar can be transferred to the circular model. Between the line and circle model, neither seems inherently more compelling; however the fact that the birth and death chain reasoning holds only for the line model has prevented us from understanding the situation on any other graphs or initial conditions. We enumerate some problems in what we expect to be increasing order of difficulty.

**Problem 1.** On a line segment graph, extend the model to the case where the initial configuration is something other than mutants in an interval containing an endpoint.

**Problem 2.** Extend the analysis to a circle.
Figure 2: Formula Eq. (29) \( g(\sqrt{\pi/N}) \sqrt{\pi/N}, \) blue curve) is compared with the stochastic simulation results for \( \sqrt{\pi \times N \langle P_N \rangle} \) (red points), plotted a functions of \( N \), with \( \delta = 0.2 \).

We were curious whether empirically, the circle appears to behave differently from the line. Figure 3 shows the comparison. It appears that the limiting value of \( N \mathbb{P}_N(G(\delta)) \) for the circle is just a shade less than for the line. But also, it appears that the value approaches the limit much faster for the circle, and perhaps with less sample variance. On a circle, starting with a single mutation, the interval set of mutant sites remains an interval, which can now grow and shrink at both ends rather than just on the right. These two growth processes are not independent, but may still be the reason we observe faster convergence and lesser variance.

**Problem 3.** Extend the analysis to any graph with a vertex of degree at least 3. The difficulty here is that the cluster of mutants can become disconnected.

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\[ \delta = c/\sqrt{N}, \ c = 2 \]

Figure 3: Comparison of the line and the circle model. The quantity \( N\langle P_N \rangle \) is plotted as a function of \( N \) for the circle model (blue dots) and line model (red dots) with \( \delta = 2/\sqrt{N} \). For each value of \( N \), the average of \( 10^6 \) random simulations is presented.

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