

# ASYMPTOTIC SAMPLING DISTRIBUTIONS MADE EASY: LOOSE LINKAGE IN THE ANCESTRAL RECOMBINATION GRAPH

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**ABSTRACT.** Understanding the interplay between recombination and resampling is a significant challenge in mathematical population genetics and of great practical relevance. Asymptotic results about the distribution of samples when recombination is strong compared to resampling are often based on the approximate solution of certain recursions, which is technically hard and offers little conceptual insight. This work generalises an elegant probabilistic argument, based on the coupling of ancestral processes but so far only available in the case of two sites, to the multilocus setting. This offers an alternative route to, and slightly generalises, a classical result of Bhaskar and Song.

## 1. INTRODUCTION

Recombination is a genetic mechanism that reshuffles genetic information between parent individuals in the context of sexual reproduction, and plays an important role in the creation and maintenance of genetic diversity. Due to their inherent nonlinearity, mathematical models for recombination have been a major challenge for mathematical population geneticists since their conception more than one hundred years ago [26, 32].

A powerful idea in modern mathematical population genetics is to understand the effect of evolution on the distribution of a sample by considering its evolutionary history backward in time by means of *ancestral processes*. In particular, the *ancestral recombination graph* (ARG) [19, 14, 15, 21] describes the coupled ancestries of multiple genetic sites under recombination.

In the deterministic setting, that is, when discarding the random fluctuations related to the loss of genetic diversity via resampling, the ARG simplifies considerably. This is because resampling corresponds to coalescence of lineages and its absence therefore implies their conditional independence. Indeed, it was shown that the ARG simplifies to a simple *partitioning process* [7] that describes the distribution of an individual's genetic heritage across its ancestors. This led to a linearisation of the nonlinear forward-time model and an explicit solution formula. Later, this approach was extended to include other evolutionary forces such as selection [3, 4], migration [5] as well as mutation and more [2]. See also [8] for a very readable survey.

In the majority of natural populations, however, resampling plays an important role. Therefore, it is critical for the practical inference of evolutionary parameters to understand the distribution of samples also in this case. Because the ARG is then no longer analytically

tractable, much effort has been put into the development of efficient computational methods [14, 13, 17, 25, 28, 30, 34, 31, 11, 29].

At the same time, *approximate* formulae and expansions for the sampling distribution are available when recombination is strong compared to resampling [22, 24, 9, 23, 21]. Much of this work is based on a recursive representation for the sampling distribution that goes back to Golding [18]; see also [12]. In particular, this includes the work [9] of Bhaskar and Song, which seems to be the only work to date that treats more than two sites. It is based on a generalisation of Golding’s recursion to more than two sites and its approximate solution. The technical effort is considerable and while some probabilistic interpretation in terms of noncentral hypergeometric distributions is given, the connection to the underlying ancestral structure is anything but obvious.

Therefore, it seems desirable to find an alternative approach that exploits the genealogical structure of the problem more efficiently. This was accomplished in [21] for the case of two sites. Based on the insight that for ‘infinitely’ strong recombination, the ARG reduces to a collection of independent Kingman coalescents, one for each site, the authors constructed a coupling between such a collection and the full ARG. Ultimately, this led to an approximation of the sampling distribution, with the first-order correction in the reciprocal of the recombination rate expressed in terms of single-site sampling distributions, in a way that does not depend on the mutation model used, a property called *universality* by the authors.

The main goal of this work is to provide an alternative proof of the general result of Bhaskar and Song [9] that yields deeper insight into the probabilistic structure of the problem. Incidentally, this allows us to generalise their result from single-crossover recombination to arbitrary recombination patterns without additional effort. Inspired by the argument in [21], based on an *untyped* version of the ARG, the main difference and major novelty of this work is the introduction of a *typed* version of the ARG which we encode as a Markov process taking values in the finite point measures on the type space.

The rest of the paper is organised as follows. To make the presentation as self-contained as possible, we start by recalling the ARG and the associated *sampling-distribution*. In Section 3, we describe the typed, measure-valued ARG, along with a version for infinitely strong recombination. In Section 4, we couple these two processes and derive the first-order correction in terms of the single-site sampling distributions and probabilities of certain events in this coupling. These probabilities are evaluated in Section 5 via an elementary inclusion-exclusion argument, which ultimately leads to the formula given in [9].

## 2. THE ANCESTRAL RECOMBINATION GRAPH AND THE DISTRIBUTION OF A SAMPLE

We are interested in the genotype composition of a finite random sample from a stationary population that has evolved under recombination, site-independent mutation and resampling. We assume that it consists of infinitely many haploid individuals, where *haploid* means that each individual carries a single set of genes only. In particular, genotypes are identified with

genetic sequences. We denote the set of genetic sites by

$$S = \{1, \dots, n\},$$

and the set of potential alleles at site  $i \in S$  by  $X_i$ . We will assume the  $X_i$  to be finite. Furthermore, we also assume the  $X_i$  to be mutually disjoint<sup>1</sup>.

With this,

$$X := \prod_{i \in S} X_i$$

is the set of *complete genotypes*. In order to describe samples in which individuals may be observed at different subsets of sites, we also define for any  $A \subseteq S$  the set

$$X_A := \prod_{i \in A} X_i$$

of *partial genotypes observed at A*; for  $A = \emptyset$ , we set  $X_\emptyset := \{\epsilon\}$ , where  $\epsilon$  is the empty sequence. The set of *partial genotypes* is then given by the disjoint union

$$\mathcal{X} := \bigcup_{A \subseteq S} X_A.$$

For simplicity, we will refer to the elements of  $\mathcal{X}$  as *types* and denote, for any  $x \in \mathcal{X}$ , by  $d(x)$  the unique  $A \subseteq S$  with  $x \in X_A$ . We say that an individual of type  $x$  is *observed at*  $d(x)$ .

Consequently, we represent the type frequencies within samples by finite counting measures on  $\mathcal{X}$ . Generally, we denote the set of finite counting measures on some set  $M$  by

$$\mathcal{N}(M) := \left\{ \sum_{x \in \mathcal{T}} \nu_x \delta_x : \mathcal{T} \subseteq M \text{ finite, } \nu_x \in \mathbb{N} \right\},$$

where  $\delta_x$  is the point mass (or Dirac-measure) in  $x$  and  $\mathbb{N}$  does not include 0. The set  $\mathcal{T} \subseteq M$  is called the *support* ( $\text{supp}(\nu)$ ) of  $\nu = \sum_{x \in \mathcal{T}} \nu_x \delta_x$ , and the total mass of  $\nu$  is denoted by  $\|\nu\| := \sum_{x \in \mathcal{T}} \nu_x$ . The unit point masses are also referred to as *particles*.

We need some additional notation regarding types and type compositions. Given  $x \in \mathcal{X}$  and  $B \subseteq S$ , we write  $x|_B$  for the *marginal of x with respect to B*, that is, the type  $y \in X_{d(x) \cap B}$  with  $y|_i = x|_i$  for all  $i \in d(x) \cap B$ , where  $x|_i := x|_{\{i\}}$  denotes the  $i$ -th component of  $x$ .

We call two types  $x, y \in \mathcal{X}$  *compatible*  $x|_{d(x) \cap d(y)} = y|_{d(x) \cap d(y)}$ , and *incompatible* otherwise. Note that  $x$  and  $y$  are always compatible if  $d(x) \cap d(y) = \emptyset$ . For compatible types, we define their *join*  $x \sqcup y$  via  $(x \sqcup y)|_i = x|_i$  for  $i \in d(x)$  and  $(x \sqcup y)|_i = y|_i$  for  $i \in d(y)$ .

For  $\nu \in \mathcal{N}(\mathcal{X})$ , we write  $\nu^{\supseteq A}$  for the restriction of  $\nu$  to  $\bigcup_{B \supseteq A} X_B$ , and  $\nu^B$  for the marginal w.r.t.  $B$ , defined for all  $E \subseteq X_B$  via

$$\nu^B(E) := \sum_{\substack{x \in \mathcal{X} \\ x|_B \in E}} \nu(x).$$

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<sup>1</sup>This is a purely technical assumption that allows us to keep track at which sites certain alleles are observed. If one wants to use the same alphabet (say, the set  $\{\mathbf{A}, \mathbf{C}, \mathbf{G}, \mathbf{T}\}$  of nucleotides or  $\{0, 1\}$  for biallelic sites, this may be realised by adding the different sites as additional indices, say  $X_i = \{\mathbf{A}^i, \mathbf{C}^i, \mathbf{G}^i, \mathbf{T}^i\}$  or  $X_i = \{0^i, 1^i\}$

Furthermore, we write  $\nu^{\supseteq A, B}$  for the marginal of  $\nu^{\supseteq A}$  with respect to  $B$ . In words,  $\nu^{\supseteq A}$  describes the subsample consisting of individuals that are observed at a superset of  $A$ , while  $\nu^B(x_B)$  for  $x_B \in X_B$  is the number of individuals that have the marginal type  $x_B$  with respect to  $B$ . Note that  $\nu^{\supseteq B, B} = \nu^B$ .

To describe the effect of recombination, we use partitions of  $S$  as in [7] to describe the fragmentation of genetic material of individuals across their parents. Recall that a *partition of a set  $M$*  is a collection of nonempty, mutually disjoint subsets of  $M$ , called *blocks*, that cover  $M$ . The set of all partitions of  $S$  is denoted by  $\mathbf{P}(S)$  and for any  $\mathcal{A} \in \mathbf{P}(S)$  and for any nonempty  $B \subseteq S$ , we call

$$\mathcal{A}|_B := \{A \cap B : A \in \mathcal{A}\} \setminus \{\emptyset\}$$

the partition *induced by  $\mathcal{A}$  on  $B$* .

We assume that mutation occurs independently at different sites and with rate  $u_i \geq 0$  at site  $i$ . Upon mutation at site  $i$ , we write  $M_i(x_i, y_i)$  for the probability that an allele  $x_i \in X_i$  is replaced by  $y_i \in X_i$ . We call  $M_i$  the *mutation kernel at site  $i$* ; as the  $X_i$  are finite,  $M_i$  can be interpreted as a Markov matrix and  $u_i(M_i - \text{Id})$  is a generator. We call the associated continuous-time Markov chain on  $X_i$  the *mutation chain at site  $i$* . In order to guarantee asymptotically stable allele frequencies, we will assume that the  $M_i$  are irreducible. This implies that the mutation chain at any site  $i$  converges to its unique stationary distribution  $\pi_i$ , given by the unique left eigenvector of  $M_i$  with respect to the eigenvalue 1.

To understand how the composition of a sample is affected by recombination and mutation together with resampling, we will consider its evolutionary history, which is captured by the *ancestral recombination graph* (ARG); see [19, 14, 15, 21]. We give a somewhat informal graphical description.

A sample from the population at present is represented by a finite set of leaves and their ancestral lines as vertical lines, emanating from the leaves and growing from bottom to top. We call the ancestral line associated with a leaf observed at  $A \subseteq S$  *ancestral to  $A$* . Recombination, mutation and resampling manifest themselves as follows.

- (1) Resampling is captured by the pairwise coalescence of lines, indicating that a pair of individuals has found a common ancestor. Any ordered pair of ancestral lines, say, ancestral to  $A$  and  $B$ , coalesces, independently of all the other pairs, at rate 1 into a single line ancestral to  $A \cup B$ .
- (2) Recombination results in the *fragmentation* of lineages. Independently for any partition  $\mathcal{A}$  of  $S$ , any line is independently of all the others and at rate  $\varrho_{\mathcal{A}} \geq 0$  hit by an  $\mathcal{A}$ -recombination event  $\boxed{\mathcal{A}}$ , indicating that the individual at the affected (*offspring*) line is the offspring of  $|\mathcal{A}|$  parents, corresponding to the blocks of  $\mathcal{A}$ ; the elements of each block are the sites that the offspring inherits from the corresponding parent. This leads to the fragmentation of the offspring line into multiple parental lines. If the offspring line is ancestral to  $B \subseteq S$ , the parental lines correspond to the blocks of the induced partition  $\mathcal{A}|_B$  rather than  $\mathcal{A}$ , because only the sites in  $B$  are relevant for the sample.

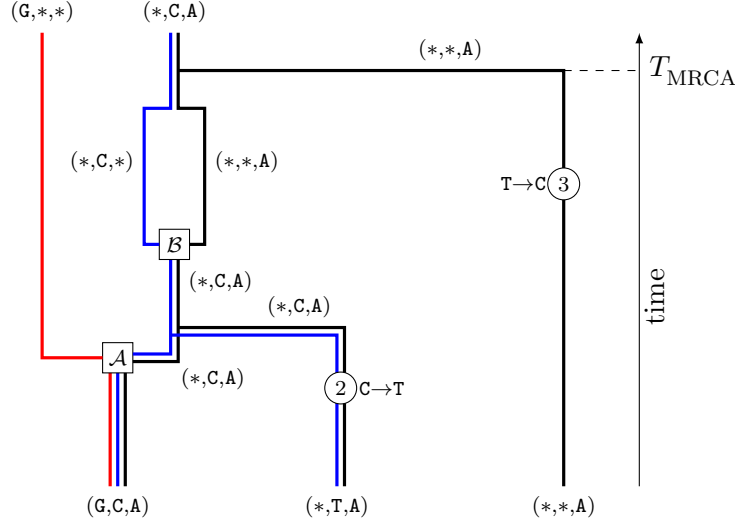


FIGURE 1. A realisation of the ARG, started from 3 leaves, observed at  $\{1, 2, 3\}$ ,  $\{2, 3\}$  and  $\{3\}$  (left to right). The first, second and third site are encoded red, blue and black and the sets of alleles are given by  $X_1 = X_2 = X_3 = \{A, C, G, T\}$ . Unobserved sites are denoted by  $*$ . The fragmentation events are governed by the partitions  $\mathcal{A} = \{\{1\}, \{2, 3\}\}$  and  $\mathcal{B} = \{\{1, 3\}, \{2\}\}$ . The letters  $G$ ,  $C$  and  $A$  in the ancestral sequences are the result of independent mutation beyond  $T_{\text{MRCA}}$  on the red, blue and black lines, respectively.

- (3) Mutations are represented by *mutation marks*  $\textcircled{i}x_i \rightarrow y_i$  which indicate mutation at site  $i$  from the allele  $x_i$  to the allele  $y_i$ . They appear on each line independently with respective rates  $u_i M_i(x_i, y_i)$ , independently for each  $i \in S$  and  $x_i, y_i \in X_i$ .

See Fig. 1 for an illustration.

**Remark 2.1.** As there is (at the type of its construction) no fixed initial type configuration in the ARG, we have to account in (3) for mutations starting from *all* possible alleles. Thus, many mutations will usually be silent, see Fig. 1.

The ARG enables us to relate the type configuration of a sample at present to that of their ancestors at any previous time. Given a realisation of the ARG with finite runtime, we call the top ends of the lines the *ancestors* of the sample. More specifically, the top end of a line ancestral to  $A$  corresponds to an ancestor observed at  $A$ . Given an assignment of types to the ancestors (where an ancestor observed at  $A$  is assigned a type in  $X_A$ ), we propagate the types along the lines, from top to bottom, until we arrive at the leaves. We proceed according to the following rules.

- (1) When encountering a recombination event, the types  $x_1, \dots, x_r$  at the parental lines are joined to form the type  $x_1 \sqcup \dots \sqcup x_r$  at the offspring line.

- (2) When encountering a coalescence event (say, between lines ancestral to  $A$  and  $B$ ), if  $x$  is the type of the common ancestor, then  $x|_C$  is the type at the line that participated in the coalescence that is ancestral to  $C \in \{A, B\}$ .
- (3) When a mutation  $\textcircled{i}x_i \rightarrow y_i$  is encountered while the allele at site  $i$  at that line is  $x_i$ , it is changed to  $y_i$ ; otherwise, the mutation is silent.

**Remark 2.2.** Note that rule (3) together with the rates at which mutation marks appear indeed makes it so that the alleles at different sites for each individual effectively evolve according to the independent mutation chains.

We want to use the ARG to understand the distribution of a sample drawn at *stationarity*. Recall that in order to guarantee asymptotically stable allele frequencies, we assumed that the mutation kernels  $M_i$  are irreducible. We will now see that this is indeed sufficient for the distribution of samples consisting of multiple individuals to have a unique stationary distribution as well.

Let  $T_{\text{MRCA}}$  be the *time of the most recent common ancestors*, that is, the first time at which there is at most one line ancestral to a superset of  $\{i\}$  for each  $i \in S$ . In an ARG of total runtime  $t$ , it is clear that  $\mathbb{P}(T_{\text{MRCA}} < t) \rightarrow 1$  as  $t \rightarrow \infty$ . The types of the ancestors at time  $T_{\text{MRCA}}$  are the result of independently evolving mutation chains, run for time  $t - T_{\text{MRCA}}$ ; this is because every mutation after  $T_{\text{MRCA}}$  affects only a single individual alive at time  $T_{\text{MRCA}}$ . In the limit  $t \rightarrow \infty$ , the type of an ancestor at time  $T_{\text{MRCA}}$  observed at  $A$  is distributed according to  $\bigotimes_{i \in A} \pi_i$ . To summarise, we can produce a random sample from the population at stationarity in three steps.

- (1) Run the ARG until (backward) time  $T_{\text{MRCA}}$ .
- (2) Assign to the top end of each ancestral line, observed at, say,  $A$ , an independent sample from  $\bigotimes_{i \in A} \pi_i$ .
- (3) Propagate these types from top to bottom, following the rules above.

For any  $\nu \in \mathcal{N}(\mathcal{X})$ , we write  $q(\nu)$  for the probability of obtaining an *ordered* sample configuration with frequencies  $\nu$ , i.e. in which each  $x \in \mathcal{X}$  appears  $\nu(x)$  times when the ARG in step (1) is started from  $\nu(X_A)$  leaves observed at  $A$  for all  $A \subseteq S$ ; we will see a more formal definition in Section 3. Note that due to exchangeability, that is, the invariance of the evolution of the ARG under permutation of lines, any sample configuration with the same frequencies is observed with the same probability.

To proceed, we assume that the recombination rates  $\varrho_{\mathcal{A}}$  are of the form  $\varrho \cdot r_{\mathcal{A}}$  where  $\varrho$  is a global scaling parameter that we will send to  $\infty$ , and  $r_{\mathcal{A}} \geq 0$  are constants. We will further assume without loss of generality that any two sites may be separated by recombination. This means that for any two  $i, j \in S$ ,  $i \neq j$ , there is an  $\mathcal{A} \in \mathbf{P}(S)$  with  $\varrho_{\mathcal{A}} > 0$  and  $\mathcal{A}|_{\{i, j\}} = \{\{i\}, \{j\}\}$ . Otherwise we can lump  $i$  and  $j$  together and treat them as a single site. Intuitively speaking,  $\varrho = \infty$  means that there will never be a line that is ancestral to  $A \subseteq S$  with  $|A| > 1$ , because such lines are immediately broken up into the lineages of the individual sites. We can then construct the random sample by running instead  $n$  independent coalescents, one for each site (or equivalently, start with leaves ancestral to singletons only and

forbid merging between lines ancestral to different sites). We denote the associated sampling distribution by  $q_\infty$ , which is given by the product

$$(1) \quad q_\infty(\nu) = \prod_{i=1}^n q(\nu^{\{i\}})$$

of distributions of one-dimensional marginal samples, which we take as given. Note that  $q_\infty(\nu)$  only depends on the individual allele frequencies, but not on how they are arranged into types.

In the case of parent-independent mutation, that is, for  $M_i(x_i, y_i) = M_i(y_i)$  independently of  $x_i$  for all  $i$ , an explicit formula is available; see [21, Remark 2.1]. Namely,

$$q(\nu^{\{i\}}) = \frac{1}{(u_i)_{\overline{n_i}}} \prod_{x_i \in X_i} (u_i M_i(y_i))_{\overline{\nu^{\{i\}}(x_i)}},$$

where  $(z)_{\overline{m}} := z(z+1) \dots (z+m-1)$  denotes the  $m$ -th ascending factorial of  $z$  and  $n_i := \|\nu^{\{i\}}\|$  is the number of individuals that are observed at a (possibly proper) superset of site  $\{i\}$ . For general finite allele models, approximate single-site sampling formulae are available in [10].

For  $\varrho$  large but *finite*, we consider the expansion

$$(2) \quad q(\nu) = q_\infty(\nu) + \varrho^{-1} q_1(\nu) + \mathcal{O}(\varrho^{-2})$$

of  $q$  in terms of the reciprocal of the recombination rate. Our goal is to generalise the expression for  $q_1$  in terms of  $q_\infty$ , which was given in [9] for the special case of single-crossover recombination, to arbitrary recombination schemes.

**Theorem 2.3.** *The first-order term in the expansion (2) is given by*

$$(3) \quad q_1(\nu) = \sum_{x \in \mathcal{X}} q_\infty(\sigma(\nu) - \sigma(\delta_x)) \sum_{\substack{d(x) \subseteq A \subseteq S \\ |A| \geq 2}} \frac{(-1)^{|A \setminus d(x)|}}{\bar{r}_A} \binom{\nu^{\supseteq A, d(x)}(x)}{2},$$

where

$$\bar{r}_A := \sum_{\substack{\mathcal{B} \in \mathcal{P}(S) \\ \mathcal{B}|_A \neq \{A\}}} r_{\mathcal{B}}$$

is the total fragmentation rate of  $A$  and  $\sigma$  is the linear fragmentation map defined via  $\sigma(\delta_x) := \sum_{i \in d(x)} \delta_{x|_i}$  on point masses and extended linearly.

For  $\nu \in \mathcal{N}(\mathcal{X})$ , the particles that make up  $\sigma(\nu)$  should be thought of as fragments of the particles that make up  $\nu$ . Theorem 2.3 will be proved in Section 5 by analysing a coupling between two ARGs, with finite and infinite recombination rate, respectively.

**Remark 2.4.** In this work, we consider a finite-alleles model of mutation. However, we stress that our arguments do not rely on the concrete form of the mutation model. In particular, the extension to the infinite alleles / infinite sites model would be straightforward.

It is important to note that the outer sum in (3) runs over *all* types, including the empty type  $\epsilon$  in which case the inner sum runs over all subsets  $A$  of  $S$ . To prove Theorem 2.3, we start by introducing a slightly different version of the ARG which, albeit slightly more involved than the graphical construction at a first glance, is better suited to our purposes.

### 3. A MEASURE-VALUED COALESCENT WITH RECOMBINATION

We have introduced the ARG as a random graphical construction and we have seen how it can be used to construct a random sample from a population that has evolved for a long time under recombination, mutation and resampling. Now, our goal is to approximate the probability that this leads to an arbitrary but fixed (ordered) sample with given frequencies  $\nu$ .

For this purpose, it is more convenient to work with a *typed* approach. The idea is to equip the leaves of the ARG with the types that we want to observe and keep track, as we look further and further into the past, of the type configurations at earlier times that lead to the desired sample. By exchangeability, it will be enough to keep track of the frequencies in these configurations, which justifies our measure-valued approach.

For instance, let us reconsider the example in Fig. 1. The type frequencies at the leaves are given by  $\nu = \delta_{(G,C,A)} + \delta_{(*,T,A)} + \delta_{(*,*,A)}$ , where  $*$  is used to mark unobserved sites. We see that the first event that is encountered on the ancestral line of the leaf with type  $(*,T,A)$  is the mutation  $(2)C \rightarrow T$ . Therefore, in order to observe the desired allele  $T$  in this individual, there are *two* possibilities for the allele just prior to (above) the mutation; it needs to be either  $T$  itself, or  $C$  because the  $C$  would have mutated to the desired  $T$ . If we stopped the ARG right after that first mutation we would need to observe an ordered sample with frequencies  $\nu'_1 = \delta_{(G,C,A)} + \delta_{(*,T,A)} + \delta_{(*,*,A)}$  or  $\nu'_2 = \delta_{(G,C,A)} + \delta_{(*,C,A)} + \delta_{(*,*,A)}$ .

In order to efficiently keep track of these multiple possibilities we need to allow for some ambiguity in the specification of alleles by working with *fuzzy* types. For  $i \in S$ , we denote by  $\tilde{X}_i$  the set of nonempty subsets of  $X_i$  and, in analogy to our earlier definitions, we define for  $A \subseteq S$

$$\tilde{X}_A := \prod_{i \in A} \tilde{X}_i$$

and

$$\tilde{\mathcal{X}} := \bigcup_{A \subseteq S} \tilde{X}_A.$$

As before,  $\tilde{X}_\emptyset = \{\epsilon\}$  where  $\epsilon$  is the empty sequence. We call  $\tilde{\mathcal{X}}$  the set of *fuzzy types*. For a fuzzy  $x \in \tilde{\mathcal{X}}$ , the marginalisations  $x|_B$  and the set  $d(x)$  of observed sites are defined in analogy with the definitions in Section 2. Moreover, we embed the set  $\mathcal{X}$  of (exact) types in  $\tilde{\mathcal{X}}$  by identifying any  $x \in \mathcal{X}$  with  $(\{x|_i\})_{i \in d(x)} \in \tilde{\mathcal{X}}$ . This also gives an embedding of  $\mathcal{N}(\mathcal{X})$  into  $\mathcal{N}(\tilde{\mathcal{X}})$  and is our justification for using the same notations for fuzzy and exact types.

The notions of compatibility and join need to be adapted slightly. We call  $x, y \in \tilde{\mathcal{X}}$  *compatible* if for all  $i \in d(x) \cap d(y)$ , we have  $x|_i \cap y|_i \neq \emptyset$  and *incompatible*, otherwise. Their



join  $x \sqcup y$  is then defined via

$$(4) \quad (x \sqcup y)|_i := \begin{cases} x|_i & \text{for } i \in d(x) \setminus d(y) \\ y|_i & \text{for } i \in d(y) \setminus d(x) \\ x|_i \cap y|_i & \text{for } i \in d(x) \cap d(y). \end{cases}$$

Note that this is consistent with our earlier definition for exact types. From now on, we will refer to fuzzy types simply as types until mentioned otherwise.

Let us talk more systematically about the effects of the transitions in the (graphical) ARG on (the type frequencies of) configurations that lead to the desired sample. We start with mutation. Assume that we encounter a mutation  $(\dot{i})y_i \rightarrow z_i$  and that, just below the mutation, we want to see  $x \in \tilde{\mathcal{X}}$ . Let  $m_i(x; y_i, z_i)$  be the (fuzzy) type that needs to be observed just before the mutation to make this happen. Clearly, as mutation only affects site  $i$ , we must have  $m_i(x; y_i, z_i)|_j = x_j$  for all  $j \in d(x) \setminus \{i\}$ . If  $z_i \in x_i$ , then observing  $y_i$  right before the mutation would work as well as observing any allele in  $x_i$ . On the other hand, if  $z_i \notin x_i$ , then  $y_i$  would not work, even if  $y_i \in x_i$ . Thus,

$$(5) \quad m_i(x; y_i, z_i)|_j = \begin{cases} x_j & \text{if } j \neq i \\ x_i \cup \{y_i\} & \text{if } j = i \text{ and } z_i \in x_i \\ x_i \setminus \{y_i\} & \text{if } j = i \text{ and } z_i \notin x_i. \end{cases}$$

Note that it might happen that  $m_i(x; y_i, z_i) = \emptyset$ . In this case, it is impossible to observe our desired sample, and it makes no sense to trace its genealogy further. For this purpose, we introduce a cemetery state  $\Delta$ .

The effect of coalescence is straightforward. If two lines with types  $x$  and  $y$  coalesce, we need to observe at the common ancestral line and at the sites in  $d(x) \cap d(y)$  alleles that shown up in both  $x$  and  $y$ . If  $x$  and  $y$  are incompatible, this is not possible and we end up in  $\Delta$ . Otherwise, the type of the ancestral line will have to be  $x \sqcup y$  as in Eq. (4).

The effect of recombination is also easy to understand. In order to observe a certain offspring type  $x$ , the fragments we need to observe at the parental lines are simply the marginals of  $x$  with respect to the blocks of  $\mathcal{A}|_{d(x)}$ , with  $\mathcal{A}$  being the partition defining the fragmentation event. More concisely, the type configuration of the parental lines must have frequencies

$$\sum_{\substack{A \in \mathcal{A} \\ A \cap d(x) \neq \emptyset}} \delta_{x|_A}.$$

To summarise:

**Definition 3.1.** The *measure-valued* ARG (mARG)  $\mathcal{R} = (\mathcal{R}_t)_{t \geq 0}$  is a continuous-time Markov chain on  $\mathcal{N}(\tilde{\mathcal{X}}) \cup \{\Delta\}$  with the following transitions starting from  $\nu \in \mathcal{N}(\tilde{\mathcal{X}})$ .

(1) **Coalescence:** Independently for any  $x, y \in \tilde{\mathcal{X}}$ ,

$$\nu \rightarrow \begin{cases} \nu - \delta_x - \delta_y + \delta_{x \sqcup y} & \text{if } x \text{ and } y \text{ are compatible} \\ \Delta & \text{if } x \text{ and } y \text{ are not compatible} \end{cases},$$

at rate  $\nu(x)\nu(y)$  if  $x \neq y$  and  $\nu(x)(\nu(x) - 1)$  if  $x = y$ . Alternatively, the rate can in both cases be written more concisely as  $\nu(x)(\nu - \delta_x)(y)$ .

- (2) **Recombination:** Independently for any  $x \in \tilde{\mathcal{X}}$  and any partition  $\mathcal{A}$  of  $S$ ,

$$\nu \rightarrow \nu - \delta_x + \sum_{\substack{A \in \mathcal{A} \\ A \cap d(x) \neq \emptyset}} \delta_{x|_A}$$

at rate  $\varrho_{\mathcal{A}}\nu(x)$ .

- (3) **Mutation:** Independently for each  $x \in \tilde{\mathcal{X}}$ , each  $i \in d(x)$  and each  $y_i, z_i \in X_i$ ,

$$\nu \rightarrow \begin{cases} \nu - \delta_x + \delta_{m_i(x; y_i, z_i)} & \text{if } m_i(x; y_i, z_i) \neq \emptyset \\ \Delta & \text{if } m_i(x; y_i, z_i) = \emptyset \end{cases}$$

at rate  $\nu(x)u_i M_i(y_i, z_i)$  and with  $m_i(x; y_i, z_i)$  as given in Eq. (5).

It is useful to think of  $\mathcal{R}$  (and of  $\mathcal{R}^\infty$ , see below) as a collection of evolving particles, corresponding to the unit Dirac measures; see Remark 4.2. We say that a particle  $\delta_x$  is observed at  $d(x)$ .

Recall that in Section 2 we constructed a sample at stationarity by running the ARG until the time of the most recent common ancestors and then assigning types to them, sampled independently according to the stationary distributions of the mutation chains. Here, this means that we let  $\mathcal{R}$  run until it is *simple* in the following sense.

**Definition 3.2.** We call  $\nu \in \mathcal{N}(\tilde{\mathcal{X}})$  *simple* if

- (1)  $A = B$  or  $A \cap B = \emptyset$  for all  $A, B \subseteq S$  with  $\nu(\tilde{X}_A) > 0$  and  $\nu(\tilde{X}_B) > 0$  and
- (2)  $\nu(\tilde{X}_A) \leq 1$  for all  $A \subseteq S$ .

This means that the sets of sites at which different individuals are observed are mutually disjoint, where (2) guarantees that each set is observed at most once.

We can now give a formal definition of the sampling distribution  $q$ , based on the mARG.

**Definition 3.3.** We define the stopping time

$$T := \min\{t \geq 0 : \mathcal{R}_t \text{ is simple or } \mathcal{R}_t = \Delta\}$$

and set

$$(6) \quad q(\nu) := \mathbb{E}[q(\mathcal{R}_T) \mid \mathcal{R}_0 = \nu],$$

where

$$(7) \quad q(\nu) := \begin{cases} \prod_{x \in \text{supp}(\nu)} \prod_{i \in d(x)} \pi_i(x|_i) & \text{if } \nu \text{ is simple} \\ 0 & \text{if } \nu = \Delta. \end{cases}$$

Note that  $q(\nu) = q(\sigma(\nu))$  if  $\nu$  is simple.

**Remark 3.4.** The definition of  $q$  in Eq. (6) very loosely resembles a duality relation for Markov processes; see [20] for a survey. It seems like an interesting problem to try and find a dual diffusion process, describing the evolution forward in time. For two sites, such a diffusion process was found in [21], although no formal duality relation was established. It was based on expressing type frequencies in terms of marginal frequencies and linkage disequilibrium (i.e, correlation between the two sites), which linearised the problem. For the case of more than two sites considered here, a possible starting point might be the linearisation discussed in [7] which works for an arbitrary number of sites and general patterns of recombination.

In line with our goal of deriving an approximation for  $q$  for large  $\varrho$ , we now define a version of  $\mathcal{R}$  “with infinite recombination rate”, denoted by  $\mathcal{R}^\infty = (\mathcal{R}_t^\infty)_{t \geq 0}$ . As we discussed already in Section 2 in the untyped setting, the effect of ‘infinite’ recombination is that any particle  $\delta_x$  with  $d(x) \geq 2$  is split immediately into the fragments  $\sum_{i \in d(x)} \delta_{x|_i}$ . This also means that we will neglect in  $\mathcal{R}^\infty$  coalescence between particles observed at different sites because they would be split again immediately.

**Definition 3.5.** The *split* measure-valued ARG (smARG) is a continuous-time Markov chain  $\mathcal{R}^\infty = (\mathcal{R}_t^\infty)_{t \geq 0}$  on  $\mathcal{N}(\tilde{\mathcal{X}}_1)$  where  $\tilde{\mathcal{X}}_1 := \tilde{X}_1 \dot{\cup} \dots \dot{\cup} \tilde{X}_n \subseteq \tilde{\mathcal{X}}$ , performing the following transitions starting from  $\nu$ .

- (1) **Coalescence:** Independently for any  $i \in S$  and  $x_i, y_i \in \tilde{X}_i$ ,

$$\nu \rightarrow \begin{cases} \nu - \delta_{x_i} - \delta_{y_i} + \delta_{x_i \sqcup y_i} & \text{if } x_i \text{ and } y_i \text{ are compatible} \\ \Delta & \text{if } x_i \text{ and } y_i \text{ are not compatible,} \end{cases}$$

at rate  $\nu(x_i)\nu(y_i)$  if  $x_i \neq y_i$  and  $\nu(x_i)(\nu(x_i) - 1)$  if  $x_i = y_i$ .

- (2) **Mutation:** Independently for each  $i \in S$  and  $x_i \in \tilde{X}_i$ , and  $y_i, z_i \in X_i$ ,

$$\nu \rightarrow \begin{cases} \nu - \delta_{x_i} + \delta_{m_i(x_i; y_i, z_i)} & \text{if } m_i(x_i; y_i, z_i) \neq \emptyset \\ \Delta & \text{if } m_i(x_i; y_i, z_i) = \emptyset, \end{cases}$$

at rate  $u_i M(y_i, z_i) \nu(x_i)$  with  $m_i(x_i; y_i, z_i)$  as in Eq. (5).

In perfect analogy with Definition 3.3, we now use  $\mathcal{R}^\infty$  to give a formal definition of  $q_\infty$ .

**Definition 3.6.** We define the stopping time

$$T^\infty := \min\{t \geq 0 : \mathcal{R}_t^\infty \text{ is simple or } \mathcal{R}_t^\infty = \Delta\}$$

and set, for any  $\nu \in \mathcal{N}(\mathcal{X})$ ,

$$q_\infty(\nu) := q_\infty(\sigma(\nu)) := \mathbb{E}[q_\infty(\mathcal{R}_{T^\infty}^\infty) \mid \mathcal{R}_0^\infty = \sigma(\nu)],$$

where we let

$$(8) \quad q_\infty(\nu) := \begin{cases} \prod_{x \in \text{supp}(\nu)} \prod_{i \in d(x)} \pi_i(x) & \text{if } \nu \text{ is simple} \\ 0 & \text{if } \nu = \Delta. \end{cases}$$

for any simple  $\nu \in \mathcal{N}(\tilde{\mathcal{X}}_1)$ , and  $q(\Delta) := 0$ .

**Remark 3.7.** By comparing Eqs. (7) and (8), we see that  $q(\nu) = q_\infty(\sigma(\nu))$  for all simple  $\nu$ . This will be important when we compare  $q_\infty$  and  $q$  in Section 4. Moreover, because particles observed at different loci behave independently in  $\nu$ , we have for all  $\nu \in \mathcal{N}(\tilde{\mathcal{X}})$  that  $q_\infty(\nu) = \prod_{i \in S} q_\infty(\nu^{\{i\}}) = \prod_{i \in S} q(\nu^{\{i\}})$ , in line with Eq. (1), as it must be.

We can think of  $\mathcal{R}^\infty$  as the limit of  $\mathcal{R}$  as  $\varrho \rightarrow \infty$ . In order to prove Thm. 2.3, we will need to understand how these two processes are related for large but finite  $\varrho$ . We will accomplish this by coupling these two processes. This coupling will play a role analogous to the coupling processes  $C^{(\varrho)}$  and  $D^{(\infty)}$  investigated in [21, Sect. 4], which are the line counting processes associated with the ARG and a collection of independent Kingman coalescents, respectively. In order to facilitate the coupling, the untyped process  $D^{(\infty)}$  had to be equipped with additional information, keeping track of the types of lines in the ARG (ancestral to a single or both sites) to which the lines that make up the independent Kingman coalescents correspond. This seems difficult to generalise to the case of more than two sites. Fortunately, this will not be necessary in our typed approach.

#### 4. THE COUPLING

The fundamental idea behind the coupling of  $\mathcal{R}$  and  $\mathcal{R}^\infty$  will be to think of the particles that make up  $\mathcal{R}^\infty$  as fragments of the particles that make up  $\mathcal{R}$ . We will therefore try and couple  $\mathcal{R}$  and  $\mathcal{R}^\infty$  in such a way that  $\sigma(\mathcal{R}_t) = \mathcal{R}_t^\infty$  as long as possible by matching transitions in  $\mathcal{R}$  with transitions in  $\mathcal{R}^\infty$ . Once a transition occurs in either  $\mathcal{R}$  or  $\mathcal{R}^\infty$  that cannot be matched, we give up and let the two process evolve independently according to Def. 3.1 and 3.5 from then on.

There are no issues matching recombinations, as allele frequencies are not affected by recombination; particles are merely broken up into smaller fragments and thus,  $\sigma(\mathcal{R}_t) = \sigma(\mathcal{R}_{t-})$  if a recombination event occurs at time  $t$  (Here,  $t-$  is the time immediately before the event). Matching mutations is no problem either because mutation occurs independently at different sites to begin with.

The matching of coalescence events is somewhat more tricky. Assume that a coalescence occurs in  $\mathcal{R}$  at time  $t$  between two particles with types  $x$  and  $y$ ; for the sake of simplicity, we assume them to be compatible. If  $d(x) \cap d(y) = \emptyset$ , then  $\sigma(\mathcal{R}_t) = \sigma(\mathcal{R}_{t-})$  and we simply let  $\mathcal{R}_t^\infty := \mathcal{R}_{t-}^\infty$ . If  $d(x) \cap d(y) = \{i\}$  for some  $i \in S$ , we have  $\sigma(\mathcal{R}_t) = \sigma(\mathcal{R}_{t-}) - \delta_{x|_i} - \delta_{y|_i} + \delta_{x|_i \sqcup y|_i}$ . To get the same effect in  $\mathcal{R}^\infty$ , we perform a coalescence between particles of type  $x|_i$  and  $y|_i$ . Because coalescences in  $\mathcal{R}$  with  $|d(x) \cap d(y)| \leq 1$  can be matched with coalescences in  $\mathcal{R}^\infty$ , we call such an event a *good coalescence*.

On the other hand, if  $|d(x) \cap d(y)| \geq 2$  with  $i \neq j$ , we would need to perform two *simultaneous* coalescences in  $\mathcal{R}^\infty$ , which is not a valid transition for  $\mathcal{R}^\infty$ . So if that happens, we just give up and call it a *bad coalescence of type 1*.

If we left it at that, the pairwise coalescence rates in  $\mathcal{R}^\infty$  would be too low. This is because in  $\sigma(\mathcal{R}_{t-})$ , for any  $i \in S$  and any  $x_i \in \tilde{X}_i$  and  $y_i \in \tilde{X}_i$ , particles of types  $x_i$  and  $y_i$  arise not only as fragments of types  $x$  and  $y$  with  $d(x) \cap d(y) = \{i\}$ , but also as fragments of particles

of types  $x'$  and  $y'$  with  $|d(x) \cap d(y)| \geq 2$ . Because such coalescences have no corresponding transition in  $\mathcal{R}$ , we call them *bad coalescences of type 2*. To summarise, bad coalescence of type 1 are present in  $\mathcal{R}$  but not in  $\mathcal{R}^\infty$ , while bad coalescences of type 2 are present in  $\mathcal{R}^\infty$ , but not in  $\mathcal{R}$ .

**Definition 4.1.** The *coupled* mARG (cmARG)  $(\tilde{\mathcal{R}}, \tilde{\mathcal{R}}^\infty) = ((\tilde{\mathcal{R}}_t, \tilde{\mathcal{R}}_t^\infty))_{t \geq 0}$  is a continuous-time Markov chain with state space  $(\mathcal{N}(\tilde{\mathcal{X}}) \cup \{\Delta\}) \times (\mathcal{N}(\tilde{\mathcal{X}}_1) \cup \{\Delta\})$  with  $\tilde{\mathcal{X}}_1$  as in Definition 3.5. When  $(\tilde{\mathcal{R}}, \tilde{\mathcal{R}}^\infty)$  is in state  $(\nu, \mu)$  with  $\mu \neq \sigma(\nu)$ ,  $\tilde{\mathcal{R}}$  and  $\tilde{\mathcal{R}}^\infty$  perform independent transitions according to Defs. 3.1 and 3.5. Whenever  $\mu = \sigma(\nu)$ , the following transitions are performed independently of each other, but jointly for  $\tilde{\mathcal{R}}$  and  $\tilde{\mathcal{R}}^\infty$ .

- (1) **Good coalescence:** Independently for all  $x, y \in \tilde{\mathcal{X}}$  with  $|d(x) \cap d(y)| \leq 1$ ,
 
$$(\nu, \sigma(\nu)) \rightarrow \begin{cases} (\nu - \delta_x - \delta_y + \delta_{x \sqcup y}, \sigma(\nu) + \sum_{i \in d(x) \cap d(y)} (\delta_{x|_i \sqcup y|_i} - \delta_{x|_i} - \delta_{y|_i})) & \text{if } x \text{ and } y \text{ are compatible} \\ (\Delta, \Delta) & \text{if } x \text{ and } y \text{ are not compatible,} \end{cases}$$
 at rate  $\nu(x)\nu(y)$  if  $x \neq y$  and at rate  $\nu(x)(\nu(x) - 1)$  if  $x = y$ .
- (2) **Bad coalescence (type 1):** Independently for all  $x, y \in \tilde{\mathcal{X}}$  with  $|d(x) \cap d(y)| \geq 2$ ,
 
$$(\nu, \sigma(\nu)) \rightarrow \begin{cases} (\nu - \delta_x - \delta_y + \delta_{x \sqcup y}, \sigma(\nu)) & \text{if } x \text{ and } y \text{ are compatible} \\ (\Delta, \sigma(\nu)) & \text{if } x \text{ and } y \text{ are not compatible,} \end{cases}$$
 at rate  $\nu(x)\nu(y)$  if  $x \neq y$  and at rate  $\nu(x)(\nu(x) - 1)$  if  $x = y$ .
- (3) **Bad coalescence (type 2):** Independently for all  $x, y \in \tilde{\mathcal{X}}$  with  $|d(x) \cap d(y)| \geq 2$  and each  $i \in d(x) \cap d(y)$ ,
 
$$(\nu, \sigma(\nu)) \rightarrow \begin{cases} (\nu - \delta_{x|_i} - \delta_{y|_i} + \delta_{x|_i \sqcup y|_i}, \sigma(\nu)) & \text{if } x|_i \text{ and } y|_i \text{ are compatible} \\ (\nu, \Delta) & \text{if } x|_i \text{ and } y|_i \text{ are not compatible,} \end{cases}$$
 at rate  $\nu(x)\nu(y)$  if  $x \neq y$  and at rate  $\nu(x)(\nu(x) - 1)$  if  $x = y$ .
- (4) **Recombination:** Independently for all  $\mathcal{A} \in \mathbf{P}(S)$  and all  $x \in \tilde{\mathcal{X}}$ ,
 
$$(\nu, \sigma(\nu)) \rightarrow \left( \nu - \delta_x + \sum_{\substack{A \in \mathcal{A} \\ A \cap d(x) \neq \emptyset}} \delta_{x|_A}, \sigma(\nu) \right)$$
 at rate  $\varrho_{\mathcal{A}}\nu(x)$ .
- (5) **Mutation:** Independently for each  $x \in \tilde{\mathcal{X}}$ ,  $i \in d(x)$  and  $y_i, z_i \in X_i$ ,
 
$$(\nu, \sigma(\nu)) \rightarrow \begin{cases} (\nu - \delta_x + \delta_{m(x; y_i, z_i)}, \sigma(\nu) - \delta_{x|_i} + \delta_{m(x; y_i, z_i)|_i}) & \text{if } m(x; y_i, z_i)|_i \neq \emptyset \\ (\Delta, \Delta) & \text{if } m(x; y_i, z_i)|_i = \emptyset \end{cases}$$
 at rate  $u_i M_i(y_i, z_i) \nu(x)$  with  $m(x; y_i, z_i)$  as in Eq. (5).

**Remark 4.2.** There is an obvious way to embed the measure-valued processes  $\tilde{\mathcal{R}}$  and  $\tilde{\mathcal{R}}^\infty$  within coupled, coalescing and fragmenting, typed particle systems. Starting  $\tilde{\mathcal{R}}$  from  $\nu$  and  $\tilde{\mathcal{R}}^\infty$  from  $\sigma(\nu)$ , we start the corresponding particle systems with  $\nu(x)$  particles of each type  $x \in \mathcal{X}$  and  $\sigma(\nu)(x_i) = \nu^{\{i\}}(x_i)$  particles of type  $x_i \in X_i$  for each  $i \in S$ , respectively.

Now, (1) and (2) in Definition 4.1 imply that each ordered pair of particles with types  $x$  and  $y$  in  $\tilde{\mathcal{R}}$  such that  $|d(x) \cap d(y)| = 1$  ( $\geq 2$ ) independently performs a good coalescence (bad coalescence of type 1) at rate 1, and hence such coalescences occur with total rate  $\nu(x)(\nu - \delta_x)(y)$ . Moreover, (3) implies that any ordered pair of particles in  $\tilde{\mathcal{R}}$  with types  $x$  and  $y$ , independently and independently for each  $i \in d(x) \cap d(y)$  triggers a bad coalescence of type 2 between a randomly chosen pair of particles in  $\tilde{\mathcal{R}}^\infty$  of type  $x_i \in X_i$  and  $y_i \in X_i$ . Furthermore, (4) implies that each particle  $\tilde{\mathcal{R}}$  with, say, type  $x$ , is, independently at rate  $\varrho_{\mathcal{A}}$ , fragmented into fragments of types  $x|_A$  for each  $A \in \mathcal{A}|_{d(x)}$ . Finally, (5) implies that mutation happens for each particle independently and at each site  $i$  at rate  $u_i$  and the allele change is governed by the mutation kernel  $M_i$ ; here, every particle in  $\tilde{\mathcal{R}}$  is matched to its single-site fragments in  $\tilde{\mathcal{R}}^\infty$ .

Because of permutation invariance, the concrete particles that are involved in each event can simply be chosen randomly and thus, the law of the particle system is uniquely determined by the evolution of the frequency process, which is the cmARG. This argument was also used in [21] who expressed the law of the untyped ARG (for two loci) in terms of its line counting process which they termed the *ancestral process*.

To make this formally rigorous, one could, for instance, assign a uniform (on  $[0, 1]$ ) label to each point mass, i.e. consider the cmARG as a process on subsets of  $\tilde{\mathcal{X}}$  and work with relations between particles at different times; we refer the curious reader to [16] where a similar construction has been carried out for the ancestral selection graph [27].

We hope that the fact that  $(\tilde{\mathcal{R}}, \tilde{\mathcal{R}}^\infty)$  is indeed a coupling of  $\mathcal{R}$  and  $\mathcal{R}^\infty$  is clear from our discussion at the beginning of this Section. For the sake of completeness, we also give a formal proof; this is essentially an exercise in marginalisation.

**Lemma 4.3.** *Let  $\nu \in \mathcal{N}(\tilde{\mathcal{X}})$  and let  $(\tilde{\mathcal{R}}, \tilde{\mathcal{R}}^\infty)$  be a cmARG, started in  $(\nu, \sigma(\nu))$ . Then,  $\tilde{\mathcal{R}} = \mathcal{R}$  and  $\tilde{\mathcal{R}}^\infty = \mathcal{R}^\infty$  in distribution, where  $\mathcal{R}$  and  $\mathcal{R}^\infty$  are started in  $\nu$  and  $\sigma(\nu)$ , respectively.*

*Proof.* We see that taking (1) and (2) from Def. 4.1 together and considering only the first component gives precisely the transitions in (1) from Def. 3.1. The left component of (4) in Def. 4.1 is precisely (2) in Def. 3.1. The left component of the transition (5) in Def. 4.1 is just (3) in Def. 3.1. This shows that  $\tilde{\mathcal{R}} = \mathcal{R}$  in distribution.

To see that also  $\tilde{\mathcal{R}}^\infty = \mathcal{R}^\infty$  in distribution, note that in (5) of Def. 4.1 transitions

$$\sigma(\nu) \rightarrow \begin{cases} \sigma(\nu) - \delta_{x_i} + \delta_{m(x_i; y_i, z_i)} & \text{if } m(x_i; y_i, z_i) \neq \emptyset \\ \Delta & \text{if } m(x_i; y_i, z_i) = \emptyset \end{cases}$$

occur independently for different  $x_i \in X_i$  (as well as different  $y_i, z_i$ ) because  $x \neq y$  when  $x|_i \neq y|_i$ . The total transition rate is given by

$$u_i M_i(y_i, z_i) \sum_{x \in \tilde{\mathcal{X}}} \nu(x) \mathbb{1}_{x|_i = x_i}(x) = u_i M_i(y_i, z_i) \sigma(\nu)(x_i) = u_i M_i(y_i, z_i) \sigma(\nu)(x_i),$$

in line with (2) in Def. 3.5. Similarly, taking (1) and (3) from Def. 4.1 together shows that for each  $i \in S$ ,  $x_i \in \tilde{X}_i$  and  $y_i \in \tilde{X}_i$ , transitions

$$\sigma(\nu) \rightarrow \begin{cases} \sigma(\nu) - \delta_{x_i} - \delta_{y_i} + \delta_{x_i \sqcup y_i} & \text{if } x_i \text{ and } y_i \text{ are compatible} \\ \Delta & \text{if } x_i \text{ and } y_i \text{ are incompatible} \end{cases}$$

occur independently. Summing over all  $x, y \in \tilde{\mathcal{X}}$  with the right marginals at site  $i$  and noting that the rates in Def. 4.1 (1) and (3) can be written concisely as  $\nu(x)(\nu - \delta_x)(y)$ , we obtain the total rate for such a transition. It is given by

$$\begin{aligned} & \sum_{x, y \in \tilde{\mathcal{X}}} 1_{x|_i = x_i}(x) 1_{y|_i = y_i}(y) \nu(x)(\nu - \delta_x)(y) \\ &= \left( \sum_{x \in \tilde{\mathcal{X}}} 1_{x|_i = x_i}(x) \nu(x) \right) \cdot \left( \sum_{y \in \tilde{\mathcal{X}}} 1_{y|_i = y_i}(y) \nu(y) \right) \\ &\quad - \sum_{x \in \mathcal{X}} 1_{x|_i = x_i}(x) 1_{x|_i = y_i}(x) \nu(x) \\ &= \sigma(\nu)(x_i) \sigma(\nu)(y_i) - \delta_{x_i}(y_i) \sigma(\nu)(x_i), \end{aligned}$$

in line with (1) in Def. 3.1.  $\square$

In what follows, we will write  $\mathbb{P}_\nu$  for the law of  $(\tilde{\mathcal{R}}, \tilde{\mathcal{R}}^\infty)$ , started from  $(\nu, \sigma(\nu))$ , and  $\mathbb{E}_\nu$  for the corresponding expectation. We will also drop the tilde and work throughout with versions of  $\mathcal{R}$  and  $\mathcal{R}^\infty$  that are coupled in this way.

In the case that a bad coalescence occurs, we say that the coupling has *failed*. The following Lemma shows that for large  $\varrho$ , the probability for failure is of order  $\varrho^{-1}$ . Moreover, if the coupling fails, we know that, with high probability, the bad coalescence that led to failure is the first event apart from recombination. In particular the absence of mutations prior to the bad coalescence will come in very handy when computing the sampling probability conditional on failure.

**Lemma 4.4.** *We define the events*

$$E := \{\text{No bad coalescence occurs until } \tilde{T}\},$$

where  $\tilde{T} := \min(T, T^\infty)$  is the smallest time  $t$  such that both  $\mathcal{R}_t$  and  $\mathcal{R}_t^\infty$  are either simple or in the cemetery and

$$F := \{\text{The first transition apart from recombination is a bad coalescence}\}.$$

Then, the following holds.

- (1) on  $E$ , we have  $\tilde{T} = T^\infty = T$  and  $\sigma(\mathcal{R}_t) = \mathcal{R}_t^\infty$  for all  $t \in [0, T]$
- (2)  $\mathbb{P}_\nu(E) = 1 - \mathcal{O}(\varrho^{-1})$ .
- (3)  $\mathbb{P}_\nu(E \cup F) = 1 - \mathcal{O}(\varrho^{-2})$ .

*Proof.* The statement (1) is easily shown by applying  $\sigma$  to the left component of the state after each transitions in Definition 4.1.

To show (2) and (3), we introduce two sequences of stopping times,  $\tau_1, \tau_2, \dots$ , and  $\sigma_1, \sigma_2, \dots$ . Let  $\sigma_1 := 0$ . We call a particle a *singleton* if its type is observed at a single site only and define inductively for all  $i \geq 1$

$$\tau_i := \inf\{s > \sigma_i : \text{all particles in } \mathcal{R}_s \text{ are singletons}\},$$

and

$$\sigma_{i+1} := \inf\{s > \tau_i : \mathcal{R}_s \text{ contains non-singletons}\}.$$

The claims (2) and (3) will follow from the following two observations.

- (a) For all  $i$ , the probability that at least  $k$  events occur in  $[\sigma_i, \tau_i]$  that are not recombinations is bounded by  $\mathcal{O}(\varrho^{-k})$ .
- (b) The total number of such intervals before the time of the most recent common ancestor(s) has a subexponential tail, i.e.  $G := \max\{i \in \mathbb{N} : \tau_i < T\}$  satisfies  $\mathbb{P}_\nu(G \geq t) \leq C\gamma^t$  for some constant  $C$  and  $\gamma \in (0, 1)$ .

Let's first see how (a) and (b) together imply the claims. For (2), note that bad coalescences (either of type 1 or 2) can only occur in some interval  $[\sigma_i, \tau_i]$ . But the probability that a bad coalescence (or any coalescence, or mutation, for that matter) occurs in any of these intervals is of order  $\varrho^{-1}$  by (a). And because of (b), a union bound implies that the total probability of observing a bad coalescence is bounded by  $\mathcal{O}(\varrho^{-1})$ .

To see (3), recall that the complement of  $E \cup F$  is the event that there is a bad coalescence that is *not* the first event apart from recombination. This leaves two possibilities. Either there is a bad coalescence in  $[\sigma_i, \tau_i]$  for some  $i \geq 2$ , or there are at least two non-recombination events in  $[\sigma_1, \tau_1] = [0, \tau_1]$ . But in both cases, there must be two non-recombination events in some  $[\sigma_i, \tau_i]$  (for  $i \geq 2$ , there is exactly one non-singleton particle in  $\mathcal{R}_{\sigma_i}$ , so one additional good coalescence has to occur for a bad one to be possible), and by (a) and (b), the probability that this happens is of order  $\varrho^{-2}$ .

To show (a) and (b), we compare the coalescent to a random walk. For (a), note that on  $[\sigma_i, \tau_i]$ , the total rate of *nonsilent* recombination is bounded from below by  $c\varrho$  where  $c := \min\{r_{\mathcal{A}} : \mathcal{A} \in \mathbf{P}(S), r_{\mathcal{A}} \neq 0\}$ . At the same time, the total rate of events that are not recombinations is bounded from above by a uniform constant  $C$ , because the total number of particles remains bounded at all times. Also note that any coalescence increases the possible number of consecutive nontrivial fragmentations by not more than  $n = |S|$ . Thus, the number of nonfragmentation events in  $[\sigma_i, \tau_i]$  events is stochastically dominated by the number of upward steps performed by a random walk on  $\mathbb{Z}$ , started from some  $M > 0$  and before hitting  $\mathbb{Z}_{\leq 0}$ , with homogeneous transition probabilities

$$p(z, z-1) = \frac{\varrho c}{\varrho c + C}, \quad p(z, z+n) = \frac{C}{\varrho c + C}.$$

Lemma 5.2 then yields the desired bound.

To (b): If  $\nu = \mathcal{R}_t$  is not simple, then either there are subsets  $A$  and  $B$  of  $S$  with  $\nu(\tilde{X}_A) > 0$ ,  $\nu(\tilde{X}_B) > 0$  and  $A \cap B \neq \emptyset$ . Or, there is an  $A \subseteq S$  with  $\nu(\tilde{X}_A) \geq 2$ . In the former case, a coalescence between particles of (compatible) types  $x_A \in \tilde{X}_A$  and  $x_B \in \tilde{X}_B$  leads to a



decrease of the total masses of  $\tilde{X}_A$  and  $\tilde{X}_B$  (while increasing that of  $\tilde{X}_{A \cup B}$ ). In the latter case, a coalescence between two compatible particles with types  $x, y \in \tilde{X}_A$  decreases the mass of  $\tilde{X}_A$ . In any case, we call such a coalescence *reducing*.

Now, if  $\mathcal{R}_{\tau_i}$  is not simple, there is at least one possible reducing coalescence. Also, the total coalescence rate can be bounded by the same constant  $C$  used earlier. Therefore, the coalescence at time  $\sigma_{i+1}$  is a reducing coalescence with probability at least  $1/C$ . And because  $\mathcal{R}$  can only perform a finite number of reducing coalescences before becoming simple or hitting  $\Delta$ , we see that  $G$  is stochastically dominated by a random variable with negative binomial distribution. In particular,  $G$  has a subexponential tail.  $\square$

**Remark 4.5.** The proof of Lemma 4.4 also shows that for any  $M > 0$ , the constant implied by the  $\mathcal{O}$  are uniform for all  $\nu$  with  $\|\nu\| \leq M$ .

Lemma 4.4 immediately yields the decomposition

$$\begin{aligned} q(\nu) &= \mathbb{E}_\nu[q(\mathcal{R}_T)] \\ &= \mathbb{E}_\nu[q(\mathcal{R}_T), E] + \mathbb{E}_\nu[q(\mathcal{R}_T), F] + \mathcal{O}(\varrho^{-2}) \\ &= \mathbb{E}_\nu[q(\mathcal{R}_T^\infty), E] + \mathbb{E}_\nu[q(\mathcal{R}_T), F] + \mathcal{O}(\varrho^{-2}) \\ &= \mathbb{E}_\nu[q(\mathcal{R}_T^\infty)] - \mathbb{E}_\nu[q(\mathcal{R}_T^\infty), F] + \mathbb{E}_\nu[q(\mathcal{R}_T), F] + \mathcal{O}(\varrho^{-2}) \\ &= q_\infty(\sigma(\nu)) + \mathbb{E}_\nu[q(\mathcal{R}_T), F] - \mathbb{E}_\nu[q(\mathcal{R}_T^\infty), F] + \mathcal{O}(\varrho^{-2}). \end{aligned}$$

Thus, we have identified  $\varrho^{-1}q_1(\nu)$  in Eq. (2) as

$$(9) \quad \mathbb{E}_\nu[q(\mathcal{R}_T), F] - \mathbb{E}_\nu[q(\mathcal{R}_T^\infty), F].$$

In particular, we have already shown that

$$(10) \quad q(\nu) = q_\infty(\sigma(\nu)) + \mathcal{O}(\varrho^{-1}),$$

because  $F \subseteq E$  and the probability of  $E$  is bounded by  $\mathcal{O}(\varrho^{-1})$  by Lemma 4.4. In order to evaluate Eq. (9), we subdivide the event  $F$  further, according to the type of *that first bad coalescence* (TFBC) and according to the types involved. Because we know that, with high probability, no mutation occurs before TFBC, so we may now return to working with exact ( $\mathcal{X}$ ) rather than fuzzy types ( $\tilde{\mathcal{X}}$ ).

**Definition 4.6.** We write  $F^i$  for the event that TFBC is a bad coalescence of type  $i$ . Furthermore, we denote, for all  $x \in \mathcal{X}_{\geq 2} := \mathcal{X} \setminus \mathcal{X}_1$ , by  $F_x^1$  the event that TFBC is of type 1 and between particles with compatible types  $y$  and  $z$  such that  $y|_{d(y) \cap d(x)} = z|_{d(y) \cap d(x)} = x$ . Likewise, for  $i \in S$  and  $x_i \in X_i$ , we write  $F_{x_i}^{2,i}$  for the event that TFBC is of type two and between two particles with type  $x_i$ .

Note that the events  $F^1$  and  $F^2$  also contain bad coalescence between incompatible particles. By restarting after TFBC, we obtain the behaviour of  $(\mathcal{R}, \mathcal{R}^\infty)$  conditional on the events in Definition 4.6.

**Lemma 4.7.** For all  $i \in S$ ,  $x_i \in X_i$ , and  $x \in \mathcal{X}_{\geq 2}$ ,

- (1)  $\mathbb{E}_\nu[q(\mathcal{R}_T) \mid F_x^1] = q_\infty(\sigma(\nu) - \sigma(\delta_x)) + \mathcal{O}(\varrho^{-1})$
- (2)  $\mathbb{E}_\nu[q(\mathcal{R}_{T^\infty}^\infty) \mid F_{x_i}^{2,i}] = q_\infty(\sigma(\nu) - \delta_{x_i}) + \mathcal{O}(\varrho^{-1})$
- (3)  $\mathbb{E}_\nu[q(\mathcal{R}_T) \mid F^2] = \mathbb{E}_\nu[q(\mathcal{R}_{T^\infty}^\infty) \mid F^1] = q_\infty(\sigma(\nu)) + \mathcal{O}(\varrho^{-1})$

*Proof.* We only show (1); the rest follows along the same lines. On  $F_x^1$ , we restart  $\mathcal{R}$  at the time of TFBC and denote by  $\nu'$  the type frequencies immediately after. In principle,  $\nu'$  is random due to the presence of recombinations prior to TFBC. However, we can be sure that  $\sigma(\nu') = \sigma(\nu) - \sigma(\delta_x)$  conditional on  $F_x^1$  due to TFBC between particles with common marginal  $x$ . Thus,

$$\mathbb{E}_\nu[q(\mathcal{R}_T) \mid F_x^1] = \mathbb{E}[\mathbb{E}_{\nu'}[q(\mathcal{R}_T)]] = \mathbb{E}[q(\nu')] = q_\infty(\sigma(\nu) - \delta_x) + \mathcal{O}(\varrho^{-1}),$$

where the outer expectation is with respect to  $\nu'$  and we used Eq. (10) in the last step.  $\square$

Decomposing  $F$  in (9) into the events from Definition 4.6 yields together with Lemma 4.7 the decomposition

$$\begin{aligned}
 & \varrho^{-1} q_1(\nu) \\
 &= \sum_{x \in \mathcal{X}_{\geq 2}} \mathbb{E}_\nu[q(\mathcal{R}_T), F_x^1] - \sum_{i \in S} \sum_{x_i \in X_i} \mathbb{E}_\nu[q(\mathcal{R}_{T^\infty}^\infty), F_{x_i}^{2,i}] \\
 &+ \mathbb{E}_\nu[q(\mathcal{R}_T), F^2] - \mathbb{E}_\nu[q(\mathcal{R}_{T^\infty}^\infty), F^1] \\
 (11) \quad &= \sum_{x \in \mathcal{X}_{\geq 2}} \mathbb{P}_\nu(F_x^1) q_\infty(\sigma(\nu) - \sigma(\delta_x)) - \sum_{i \in S} \sum_{x_i \in X_i} \mathbb{P}_\nu(F_{x_i}^{2,i}) q_\infty(\sigma(\nu) - \delta_{x_i}) \\
 &+ (\mathbb{P}_\nu(F_2) - \mathbb{P}_\nu(F_1)) q_\infty(\sigma(\nu)),
 \end{aligned}$$

and it remains to evaluate the probabilities.

## 5. TAMING BAD COALESCENCES

To compute the probabilities  $\mathbb{P}_\nu(F^1)$ ,  $\mathbb{P}_\nu(F^2)$ ,  $\mathbb{P}_\nu(F_x^1)$  and  $\mathbb{P}_\nu(F_{x_i}^{2,i})$ , we will make use of the following inclusion-exclusion principle; see [1, Chapter IV, 4.18].

**Lemma 5.1.** *Let  $M$  be a finite set and  $g : 2^M \rightarrow \mathbb{R}$ . Setting*

$$G(A) := \sum_{B \supseteq A} g(B),$$

*$g$  can be recovered from  $G$  via*

$$g(A) = \sum_{B \supseteq A} (-1)^{|B \setminus A|} G(B).$$

*Here the underdot marks the summation variable.*  $\square$

In what follows, we will apply this with  $M = S$ . For instance, to compute  $\mathbb{P}_\nu(F_x^1)$ , we set

$$\begin{aligned}
 g(A) &:= \mathbb{P}_\nu(\text{TFBC is between particles of type } y \text{ and } z \\
 &\text{such that } y|_{d(x)} = z|_{d(x)} = x \text{ and } d(x) \cap d(y) = A)
 \end{aligned}$$

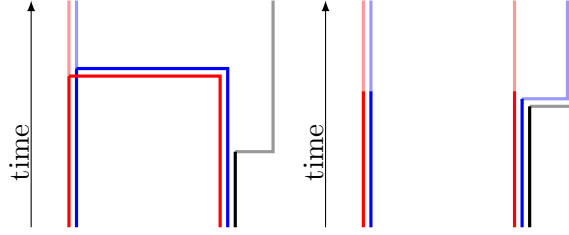


FIGURE 2. Left: a coalescence of a pair of particles initially observed at  $\{1, 2\}$  and  $\{1, 2, 3\}$ , both supersets of  $A = \{1, 2\}$ , triggering a bad coalescence of type 1. Right: the split of the particle initially observed at  $\{1, 2, 3\}$  makes this impossible. Sites 1, 2 and 3 are color coded red, blue and black. Observed particles are opaque, while non-observed particles are transparent.

for all  $A \subseteq S$ ; then  $\mathbb{P}_\nu(F_x^1) = g(d(x))$ . In order to apply Lemma 5.1, the first step is to compute

$$G(A) := \mathbb{P}_\nu(\text{TFBC is between particles of type } y \text{ and } z \\ \text{such that } y|_{d(x)} = z|_{d(x)} = x \text{ and } d(x) \cap d(y) \supseteq A).$$

To do this, we track the evolution (in  $\mathcal{R}$ ) of a fixed (ordered) pair of particles of types  $y$  and  $z$  as in the event defining  $G(A)$ ; see Remark 4.2. Note that this entails that both of them are observed at (some superset of)  $A$ . Each of the two particles suffers independent fragmentation due to recombination. Whenever possible, we keep tracking the unique particle that is still observed at a (now smaller) superset of  $A$ ; see Fig. 2. Otherwise, if any of the two particles is hit by a recombination event that splits  $A$ , which happens at rate  $2\varrho\bar{r}_A$  with

$$\bar{r}_A := \sum_{\substack{B \in \mathbf{P}(S) \\ B|_A \neq \{A\}}} r_B,$$

we terminate our observation. We also terminate the observation if any of the two particles is either hit by a mutation or coalesces with a third particle. Note that such events occur with bounded rate. Clearly, the observed pair triggers the event defining  $G(A)$  if and only if the termination is due to coalescence of the pair, which happens at rate 1 and hence with probability

$$\frac{1}{2\varrho\bar{r}_A + 1 + \mathcal{O}(1)} = \frac{1}{2\varrho\bar{r}_A} + \mathcal{O}(\varrho^{-1}).$$

Now all we need to do is count the total number of such pairs, which is  $2\binom{\nu^{\supseteq A, d(x)}(x)}{2}$ ; keep in mind that we consider *ordered* pairs. Therefore,

$$G(A) = \frac{1}{\varrho\bar{r}_A} \binom{\nu^{\supseteq A, d(x)}(x)}{2} + \mathcal{O}(\varrho^{-1})$$

and Lemma 5.1 yields

$$(12) \quad \mathbb{P}_\nu(F_x^1) = g(d(x)) = \sum_{A \supseteq d(x)} \frac{(-1)^{|A \setminus d(x)|}}{\varrho \cdot \bar{r}_A} \binom{\nu^{\supseteq A, d(x)}(x)}{2} + \mathcal{O}(\varrho^{-1}).$$

For  $F^1$ , we need to take into account *all* bad coalescences of type 1, including those that send us to the graveyard. Moreover, the types don't matter, so we have to count the number of all particles. So, in this case we have

$$G(A) := \frac{1}{\varrho \cdot \bar{r}_A} \binom{\|\nu^{\supseteq A}\|}{2} + \mathcal{O}(\varrho^{-1})$$

for the probability of triggering  $F^1$  by the coalescence of some pair of particles observed at a superset of  $A$  before being ripped apart, and thus

$$(13) \quad \mathbb{P}_\nu(F^1) = \sum_{\substack{A \subseteq S \\ |A| \geq 2}} g(A) = \sum_{\substack{A \subseteq S \\ |A| \geq 2}} \sum_{B \supseteq A} \frac{(-1)^{|B \setminus A|}}{\varrho \cdot \bar{r}_B} \binom{\|\nu^{\supseteq B}\|}{2} + \mathcal{O}(\varrho^{-1}).$$

Now, onto  $F_{x_i}^{2,i}$ . Here, we start with

$$G(A) := \frac{1}{\varrho \cdot \bar{r}_A} \binom{\nu^{\supseteq A, \{i\}}(x_i)}{2} \cdot 1_{i \in A} + \mathcal{O}(\varrho^{-1})$$

the probability of triggering  $F_{x_i}^{2,i}$  by a coalescence of some pair of particles observed at some common superset of  $A$  (which must now of course contain  $i$ , hence the indicator) and obtain

$$(14) \quad \begin{aligned} \mathbb{P}_\nu(F_{x_i}^{2,i}) &= \sum_{\substack{i \in A \subseteq S \\ |A| \geq 2}} g(A) = \sum_{\substack{i \in A \subseteq S \\ |A| \geq 2}} \sum_{B \supseteq A} \frac{(-1)^{|B \setminus A|}}{\varrho \cdot \bar{r}_B} \binom{\nu^{\supseteq B, \{i\}}(x_i)}{2} + \mathcal{O}(\varrho^{-1}) \\ &= - \sum_{\substack{A \supseteq \{i\} \\ |A| \geq 2}} \frac{(-1)^{|A \setminus \{i\}|}}{\varrho \cdot \bar{r}_A} \binom{\nu^{\supseteq A, \{i\}}(x_i)}{2} \end{aligned}$$

from Lemma 5.1, where we used the identity

$$\sum_{\substack{i \in A \subseteq B \\ |A| \geq 2}} (-1)^{|A \setminus \{i\}|} = -1.$$

Last not least, we consider  $F^2$ . Here, we again need to consider the total mass of the measures  $\nu^{\supseteq A}$  as in our computation of  $\mathbb{P}_\nu(F^1)$ . But we must keep in mind that each pair of particles with types  $x$  and  $y$  induces a different bad coalescence of type 2 for each site in  $d(x) \cap d(y)$ , leading to an additional factor  $|A|$ .

$$(15) \quad \mathbb{P}_\nu(F^2) = \sum_{\substack{A \subseteq S \\ |A| \geq 2}} |A| \sum_{B \supseteq A} \frac{(-1)^{|B \setminus A|}}{\varrho \cdot \bar{r}_B} \binom{\|\nu^{\supseteq B}\|}{2} + \mathcal{O}(\varrho^{-1}).$$

Combining Eq. (11), Lemma 4.7 and Eqs. (13) to (15) yields an explicit expression for  $\varrho^{-1}q_1$ . However, to make the result look more appealing, we first use the identity

$$\sum_{\substack{A \subseteq B \\ |A| \geq 2}} (|A| - 1)(-1)^{|A|} = 1 \quad \text{for all } B \subseteq S, \quad |B| \geq 2$$

to see that

$$\mathbb{P}_\nu(F_2) - \mathbb{P}_\nu(F_1) = \sum_{\substack{A \subseteq S \\ |A| \geq 2}} \frac{(-1)^{|A|}}{\varrho \cdot \bar{r}_A} \cdot \binom{\|\nu^{\supseteq A}\|}{2}.$$

With this, we obtain

$$q_1(\nu) = \sum_{x \in \mathcal{X}} q_\infty(\sigma(\nu) - \sigma(\delta_x)) \sum_{\substack{d(x) \subseteq A \subseteq S \\ |A| \geq 2}} \frac{(-1)^{|A \setminus d(x)|}}{\bar{r}_A} \binom{\nu^{\supseteq A, d(x)}(x)}{2},$$

which finishes the proof of Theorem 2.3; recall that the total mass can be identified with the marginal with respect to the empty set of sites, i.e.  $\nu^{\supseteq A, \emptyset}(\epsilon) = \|\nu^{\supseteq A}\|$ .  $\square$

## APPENDIX

In the main text, we used the following elementary result about excursions in random walks

**Lemma 5.2.** *Let  $(X_t)_{t \geq 0}$  be a (continuous-time) random walk on  $\mathbb{Z}$  with upward steps of bounded size and downward steps of size 1. Assuming that the rates for the upward transitions stay constant and that the rate for a downward step scales linearly with  $\varrho$ , we have that for any  $C > 0$*

$$\mathbb{P}(X \text{ makes at least } k \text{ upward steps before hitting } 0 \mid 0 < X_0 \leq C) = \mathcal{O}(\varrho^{-k}),$$

where the implicit constant may depend on  $C$ .

*Proof.* Let  $M$  be an upper bound for the size of the upward jumps. Assuming that  $X$  has not hit 0 immediately after the  $k$ -th upward step. Then, its maximal height at that time is (assuming that we *only* see upward steps until then)  $C + kM$ . This means that in between any of the  $k$  upward steps, there can not have been more than  $C + kM$  downward steps. Now, the distribution of the number  $Y_i$  of downward moves between the  $i-1$ th and the  $i$ th upward move is given by i.i.d. geometric random variables with success probability  $1 - \mathcal{O}(\varrho^{-1})$ . Therefore,

$$\begin{aligned} \mathbb{P}(X \text{ makes at least } k \text{ upward steps before hitting } 0 \mid 0 < X_0 \leq C) \\ \leq \mathbb{P}(\max_{1 \leq i \leq k} Y_i < C + kM) = (1 - (1 - \mathcal{O}(\varrho^{-1}))^{C+kM})^k = \mathcal{O}(\varrho^{-k}), \end{aligned}$$

keeping in mind that  $C, k$  and  $M$  are all constant.  $\square$

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