A diploid population model for copy number variation of genetic elements

Peter Pfaffelhuber \textsuperscript{1}  
Anton Wakolbinger \textsuperscript{2}

Abstract
We study the following model for a diploid population of constant size $N$: Every individual carries a random number of (genetic) elements. Upon a reproduction event each of the two parents passes each element independently with probability $\frac{1}{2}$ on to the offspring. We study the process $X^N = (X^N(1), X^N(2), \ldots)$, where $X^N_t(k)$ is the frequency of individuals at time $t$ that carry $k$ elements, and prove convergence (in some weak sense) of $X^N$ jointly with its empirical first moment $Z^N$ to the “slow-fast” system $(Z, X)$, where $X_t = \text{Poi}(Z_t)$ and $Z$ evolves according to a critical Feller branching process. We discuss heuristics explaining this finding and some extensions and limitations.

Keywords: Poisson approximation; Feller branching diffusion; transposable elements; slow-fast system.

MSC2020 subject classifications: Primary 92D15, Secondary 60J80; 60F17; 60G57.

1 Introduction and main result

The motivation of the present study is twofold. From a mathematical point of view it leads to a new large population limit of a system of particles performing a coordinated and spatially structured critical branching in a rapidly fluctuating random environment given by a bi-parental Moran graph; see also Remark \textsuperscript{2.1} for a more detailed description. The biological motivation is to model the evolution of transposable elements. These are repetitive sequences of 100 base pairs or longer, which are able to relocate within the genome of a host; see e.g. \textit{Bourque et al. (2018)} for a review on transposable elements.

We thus consider a population of size $N$ (the number of diploids) undergoing random reproduction events at rate $N^2/2$. Each individual has a type in $\mathbb{N}_0$, where type $k$ means that the individual carries $k$ genetic elements (GEs) in its genome. At a reproduction event a randomly chosen individual dies, and a randomly chosen pair of individuals produces some offspring. If the types of the parents are $k$ and $l$, then the type of
the offspring has a binomial distribution with parameters \( k + l \) and \( \frac{1}{2} \), i.e. it inherits each parental GE independently with probability \( \frac{1}{2} \). Thus, if \( x_k \) denotes the current fraction of individuals of type \( k \in \mathbb{N}_0 \), and \( x := (x_k)_{k \in \mathbb{N}_0} \), then the jump rate from \( x \) to \( x + (e_m - e_n)/N \) is

\[
\sum_{k,l} x_kx_l \binom{k + l}{m} 2^{-(k+l)},
\]

where \( e_m \) is the \( m \)th unit vector, \( m = 0, 1, 2, \ldots \). This gives rise to a Markovian jump process \( X^N := (X^N_t)_{t \geq 0} \) taking its values in \( \mathcal{P}(\mathbb{N}_0) \), the set of probability measures on \( \mathbb{N}_0 \) endowed with the topology of weak convergence. We write

\[
Z_t^N := \sum_{k=1}^{\infty} k X_t^N(k)
\]

for the average number of GEs per individual at time \( t \). Our main result concerns the convergence in distribution of the sequence of stochastic processes \( (Z^N, X^N) \) as \( N \to \infty \). The limiting process will turn out to be \((Z, X)\), where \( Z \) is a standard Feller branching diffusion obeying the SDE

\[
dZ_t = \sqrt{Z_t} dW_t, \quad Z_0 = z
\]

and

\[
X_t = \text{Poi}(Z_t), \quad t > 0,
\]

where \( \text{Poi}(\lambda) \) denotes the Poisson distribution on \( \mathbb{N}_0 \) with parameter \( \lambda > 0 \).

To specify a topology underlying this convergence we define the weighted occupation measure of \( \xi \in \mathcal{D}(\mathcal{P}(\mathbb{N}_0)) \), the set of càdlàg \( \mathcal{P}(\mathbb{N}_0) \)-valued paths indexed by \( t \in [0, \infty) \), as the probability measure

\[
\Gamma_\xi([0, t] \times A) := \int_0^t e^{-s}1_{\{\xi_s \in A\}} ds,
\]

where \( t \geq 0 \) and \( A \) is a measurable subset of \( \mathcal{P}(\mathbb{N}_0) \). Following Kurtz (1991) we say that a sequence \((\xi^N)\) in \( \mathcal{D}(\mathcal{P}(\mathbb{N}_0)) \) converges in measure to a \( \xi \in \mathcal{D}(\mathcal{P}(\mathbb{N}_0)) \) if the sequence of probability measures \( \Gamma_{\xi^N} \) converges weakly to \( \Gamma_\xi \). On \( \mathcal{D}(\mathbb{R}_+) \) we will use the Skorokhod topology, see e.g. Chapter 3 in Ethier and Kurtz (1986).

**Theorem 1.1.** Let \( X^N \) be the \( \mathcal{P}(\mathbb{N}_0) \)-valued Markov jump process with jump rates as in (1.1), starting in \( X^N_0 \) with atoms of size \( N^{-1} \). Assume that, for some \( z > 0 \), \( Z^N_0 \overset{N \to \infty}{\to} z \) in probability, and \( \sup_N \mathbb{E} \left[ \sum_{k=1}^{\infty} k^3 X^N_0(k) \right] \to 0 \). Then \((Z^N, X^N)\) converges in distribution to \((Z, X)\) obeying (1.2) and (1.3), where \( \mathcal{D}(\mathbb{R}_+) \times \mathcal{D}(\mathcal{P}(\mathbb{N}_0)) \) is equipped with the Skorokhod topology in the first, and with the topology of convergence in measure in the second coordinate.

In particular, Theorem 1.1 shows that the average number of GEs per individual becomes Markovian in the limit \( N \to \infty \). This average follows the dynamics of a Feller branching diffusion, and the distribution of the total number of GEs is Poisson at all points in time. The proof of Theorem 1.1 can be found in Section 3.

## 2 Perspectives and background

**Remark 2.1** (An individual-based graphical construction). The following individual-based construction of the process \( X^N \) gives a heuristic explanation of why Poisson limits and Feller’s branching diffusion appear in the situation of Theorem 1.1. Let \( \Pi_{hij}, \) \( h, i, j \in \{1, \ldots, N\} \), be a family of independent rate \( N^{-1} \) Poisson point processes on the
Copy number variation of genetic elements

time axis. At each time point \( t \) of \( \Pi_{hij} \) draw a pair of arrows, one from \((i, t)\) to \((h, t)\) and one from \((j, t)\) to \((h, t)\). This gives rise to the bi-parental Moran graph \( G_N \) with vertex set \( \{1, \ldots, N\} \times \mathbb{R}_+ \); see Figure 1.

![Figure 1: A detail of the bi-parental Moran graph \( G_N \), with a point of \( \Pi_{hij} \) at \( t_1 \). In this realisation the ancestry of the individual \((h, t_1)\) (drawn with bold lines) is a binary splitting tree \( T \) with root at \((h, t_1)\).](image)

The graph \( G_N \) serves as a random environment for a coordinated, structured branching process of the population of GEs. Specifically, for \( t_1 \in \Pi_{hij} \) (as in Figure 1), each GE arriving at \((i, t_1)\) tosses a fair coin. In case of “success” it puts one offspring at \((h, t_1)\), and in any case it continues to live at \((i, t_1)\) if \( h \neq i \). The same happens for the GEs arriving at \((j, t_1)\). The population at \((h, t_1)\) is replaced by the sum of the offspring of the populations at \((i, t_1)\) and \((j, t_1)\).

Now consider the genealogy of the GEs in an annealed picture, i.e. averaged over \( G_N \). Then the offspring of a single GE experiences a critical binary branching process with branching rate \( N \) and with “locally coordinated branching” in the sense that GEs living in the same host are affected by simultaneous reproduction events. This local coordination of the branching induces a dependence also between the offspring of different GEs that were present at time \( t = 0 \). It turns out, however, that the population of GEs is continuously spread quickly enough over the space \( \{1, \ldots, N\} \) of hosts so that the dependencies introduced by the local coordination become negligible as \( N \to \infty \).

More precisely, let the GE numbers at time \( t = 0 \) be given by a, say, i.i.d. family \( (\zeta^N_i(0))_{i \in \{1, \ldots, N\}} \) of \( \mathbb{N}_0 \)-valued random variables with finite third moment, and let \( (\zeta^N_i(t))_{i=1, \ldots, N} \) be the GE numbers at time \( t \) that arise through the reproduction dynamics along the random graph \( G_N \) as described above. Then already at time \( t_1 = \log \log N/N \) (and thus before an effective change of the total number of GEs has occurred) the numbers \( \zeta^N_h(t_1) \) of GEs in host \((h, t_1)\) are close to Poisson.

This can be seen by tracing the ancestry of \((h, t_1)\) in \( G_N \) back to time \( 0 \); see the bold lines giving rise to a binary tree in Figure 1. Thanks to the assumption \( t_1 = \log \log N/N \), the parental lineages of \((h, t_1)\) from time \( t_1 \) down to time \( 0 \) collide only with small probability; hence the ancestry of \((h, t_1)\) forms with high probability a binary splitting tree \( T \) with root at \((h, t_1)\), (order of) \( \log \log N \) generations and (order of) \( \log N \) leaves at time \( 0 \). In the situation of Figure 1 the random number \( \zeta^N_h(t_1) \) arises, conditional on \( \zeta^N_i(t_1) \) and \( \zeta^N_j(t_1) \), as the sum of two independent binomially distributed random variables with parameters \( \zeta^N_i(t_1), \frac{1}{2} \) and \( \zeta^N_j(t_1), \frac{1}{2} \), respectively. Playing this back to time.
Copy number variation of genetic elements

0 along the tree $T$, a reasoning similar as in the proof of Lemma 3.8 shows that the distribution of $\zeta_i^n(t)$ is close to Poisson for large $N$.

It is easily seen that the total number of GEs, $N Z^N = \sum_{i=1}^N \zeta_i^n(t)$, is a martingale. As time proceeds, the ongoing (quick) Poissonization of $(\zeta_i^n)_{i=1}^N$ happens conditional on the current value of $Z^N$. As it turns out (cf. Proposition 3.9), the near-Poissonicity of $(\zeta_i^n(t))_{i=1,...,N}$ helps to control the quadratic variation of $Z^N$ and to prove that $Z^N$ converges as $N \to \infty$ to a standard Feller branching diffusion.

Remark 2.2 (Stochastic slow/fast systems). As we will see, $(Z^N, X^N)$ is a slow/fast system, for which $POI$, the set of Poisson distributions on $\mathbb{N}_0$, forms a stable manifold. Such systems have been studied intensively, see e.g. Kurtz (1992), Pardoux and Veretennikov (2001), Berglund and Gentz (2006). We could not find a result in the general theory which covers the situation of our Theorem, but the method of Katzenberger (1991) comes pretty close. More precisely, as will become clear in the proof of Theorem 1.1, $Z^N$ is slow in the sense that there is an operator which describes the (asymptotically) fastest part of the dynamics of $X^N$ and which vanishes on functions depending only on the first moment of $x$; see Lemma 3.3 and (3.16). In other words, the fast dynamics has the property that $POI$ is invariant. The dynamics is therefore only governed by motions within $POI$; this as well as the convergence of $Z^N$ to $Z$ is guaranteed by Theorem 1.1.

The setting of a slow/fast dynamics giving rise to a dynamics on a lower dimensional manifold was given (for finite-dimensional semimartingales) in Katzenberger (1991). We failed to show the conditions of Katzenberger (1991) on the convergence towards the manifold, since we are lacking a general bound how the fast dynamics pushes the system to the manifold. Rather, we use martingale arguments for this convergence; see Proposition 3.7. These are not sufficient to show convergence in the Skorokhod sense (as in Katzenberger (1991)), but only in the sense of convergence of occupation measures. Thus, the question whether $X^N$ converges to $X$ in the Skorokhod sense on each time interval $[\varepsilon, \infty)$ remains open.

Remark 2.3 (Convergence in measure). Tightness criteria for càdlàg processes with respect to convergence in measure were given in Meyer and Zheng (1984), and refined in Kurtz (1991). In contrast to these approaches, we show convergence in measure of $X^N$ in two steps. First, we show tightness of $\Gamma_{X^N}$ (as random probability measures on $[0, \infty) \times P(\mathbb{N}_0)$). In a second step, we show that any limit $\Gamma$ must a.s. be concentrated on $[0, \infty) \times POI$. We then prove convergence of $Z^N$ to the Feller branching diffusion $Z$ and conclude that $\Gamma = \Gamma_X$ for $X = (\text{Poi}(Z_t))_{t \geq 0}$; see Section 3.5.

Remark 2.4 (Moment assumptions). The assumption of uniform boundedness of the expectation of the third moment of $X_t^N$ translates via Corollary 3.6 to $X_t^N$. This is used in the proof of the key Proposition 3.7 to obtain the uniform integrability of the second moment of $Y^N$, where $Y^N$ is distributed according to the weighted occupation measure of $X^N$. One may conjecture that the uniform integrability of the second moments of $X_0^N$ is enough to guarantee the uniform integrability of $\rho_2(Y^N)$. Proving this, however, seems to require considerable additional technical efforts.

Remark 2.5 (Transposable elements). Let us briefly explain the assumptions on the dynamics of $X^N$ as a model for the evolution of transposable (genetic) elements (GEs). In the model that underlies (1.1), we implicitly assume that each individual is diploid in the sense that it consists of two sets of chromosomes. The assumption that the GEs of

---

\footnote{We will see in the proof of Corollary 3.6 that the difference between the second factorial moment and the square of the first moment of $X_t^N$ converges exponentially fast to 0. With additional efforts, and under suitable assumptions on the initial condition, it might be possible to obtain by similar techniques an analogous result also for all the higher factorial moments. However, it remains unclear whether such a result would help to meet the conditions of Theorem 5.1 of Katzenberger (1991) (when extended to the infinite-dimensional setting).}
both parents are inherited independently is satisfied when GEs jump frequently within the genome, and GEs on each chromosome are not inherited together, which is the case in a high-recombination limit (also referred to as free recombination). Under these assumptions, whenever an individual carrying a total of $k$ GEs produces an offspring, it passes on one copy of its set of chromosomes, which carries a binomially distributed number of GEs with parameters $k, \frac{1}{2}$. Since the offspring has two parents with $k$ and $l$ GEs, it thus has a binomially distributed number of GEs with parameters $k + l, \frac{1}{2}$. From this explanation we find the two main assumption for the biological dynamics on diploids:

- GEs jump frequently;
- Recombination between GEs is free.

**Remark 2.6** (Context and novelty of the model). Bi-parental population models have been studied to some extent. Chang (1999) and Rohde et al. (2004) analyse the common ancestry of all living humans. Coron and Le Jan (2020) study the distribution of the genetic material which an ancestor contributes to today’s population. They consider a scaling limit of a biparental model in which first the number of generations and then the population size tends to infinity. Other population genetic models (e.g. Lambert et al., 2021) implicitly assume two parents by using an ancestral recombination graph (Griffiths and Marjoram, 1997). Wakeley and co-authors study the effect of the bi-parental pedigree on the evolution of allele frequencies (e.g. Wakeley et al., 2012, 2016). Additional related work has been done by Baird et al. (2003) (for a study of the amount of genetic material from a single individual which is present anywhere in the population after some time) and Foutel-Rodier and Schertzer (2022) (for a branching process approximation within the same model).

A novelty in our model lies in the study of a large population on the evolutionary timescale (i.e. one unit of time is $O(N)$ generations) together with a free recombination on the generation timescale, in the sense that the two parents of each individual are effectively involved at each reproduction event. Thus, in our setting we are able to combine the rescaling of time with a rapid and free recombination, and to prove convergence in the limit of large populations on the evolutionary timescale. In spirit, our model fits the framework of the Poisson Random Field approach taken by Sawyer and Hartl (1992); see also Sethupathy and Hannenhalli (2008) for a review. In such models, all loci evolve independently due to free recombination. We do not model genomic loci explicitly but consider the total number of GEs, which are distributed somewhere in the genome. Starting from an individual-based finite population model, we show that this total number is for large populations asymptotically Poisson in each individual genome, with a random intensity that follows Feller’s branching diffusion on the evolutionary timescale.

**Remark 2.7** (Extensions). The population model with jump rates given through (1.1) is neutral in the sense that (i) the number of GEs does not change on average in all individuals and (ii) the probability to be involved in a reproduction event does not depend on the number of GEs an individual carries. Both assumption can be relaxed. For (i), we might assume that an individual of type $k$ acquires new GEs at rate $\mu + k\nu$, and each GE is lost (or silenced) at rate $\beta$. For (ii), we might assume that an individual of type $k$ is chosen as a parent with probability proportional to $(1 - \alpha/N)^k \approx 1 - k\alpha/N$, for some $\alpha \in \mathbb{R}$. Under this selective model, we strongly conjecture that Theorem 1.1 still holds, but with (1.2) changed to

$$dZ = (\mu + (\nu - \beta - \alpha)Z)dt + \sqrt{Z}dW,$$

i.e. to a non-critical Feller branching diffusion with immigration.
3 Proof of Theorem 1.1

The arguments from the graphical construction in Remark 2.1 give some intuition why Theorem 1.1 holds. However, our proof proceeds via a different route. The main steps are as follows: After introducing some notation in Section 3.1, we analyse the generator of $X^N$ in Section 3.2 by collecting terms which are of order $N^1, N^0, N^{-1},...$, i.e. $G^N = NG_1 + G_0 + O(N^{-1})$; see Lemma 3.4. Moreover, we will see that $G_1 f = 0$ if $f$ only depends on $x$ via its first moment $\rho_1(x)$; see Lemma 3.3. For convergence to the manifold of Poisson distributions we require only the highest order term, $G_1$. In Section 3.3, we first give a characterization of random Poisson distribution in Lemma 3.8 and use this in order to show that the limit of occupation measures $\Gamma_{X^N}$ is concentrated on Poisson distributions using martingale arguments; see Proposition 3.7. Then, in Section 3.4, we use these results in order to show convergence of $Z^N$ as $N \to \infty$; see Proposition 3.9. Finally, in Section 3.5, we collect these insights to complete the proof of Theorem 1.1.

3.1 Notation and basics

Definition 3.1 (Moments, generating functions, state space). 1. We identify a probability measure $x$ on $\mathbb{N}_0$ with the sequence $(x_0, x_1, ...)$ of its weights. For $j = 1, 2, ...$, we denote by

$$\rho_j(x) := \sum_{k=j}^{\infty} k \cdots (k-j+1)x_k$$

the $j$th factorial moment of $x$. In particular, $\rho_1(x)$ is the mean of $x$. We put

$$\psi_s(x) := \sum_{k=0}^{\infty} x_k (1-s)^k, \quad s \in [0, 1]. \quad (3.1)$$

2. The state space of $X^N$ is

$$E_N := \left\{ x \in \mathcal{P}(\mathbb{N}_0) : Nx_k \in \mathbb{N}_0 \text{ for all } k \in \mathbb{N}_0 \right\}. \quad (3.2)$$

Remark 3.2. 1. For $x \in \mathcal{P}(\mathbb{N}_0)$ all of whose moments are finite we have

$$\rho_n(x) = \sum_{k=n}^{\infty} k(k-1) \cdots (k-n+1)x_k = (-1)^n \frac{\partial^n}{\partial s^n} \psi_s(x) \bigg|_{s=0}, \quad n = 1, 2, ...$$

$$\psi_s(x) = \sum_{k=0}^{\infty} (1-s)^k x_k = 1 + \sum_{n=1}^{\infty} \rho_n(x) \frac{(-s)^n}{n!}, \quad s \in [0, 1], \quad (3.3)$$

where the last equality holds provided the series converges (which is certainly true for $x \in E_N$ or $x \in \mathcal{P}O(I)$).

2. An $x \in \mathcal{P}(\mathbb{N}_0)$ equals Pois($\lambda$) if and only if either of the following conditions (i) or (ii) is satisfied:

(i) $\psi_s(x) = e^{-\lambda s}, \quad s \in [0, 1] \quad$ (ii) $\rho_n(x) = \lambda^n, \quad n = 1, 2, ...$

In particular we will make use of the fact that $\rho_2(x) - \rho_1^2(x) = 0$ for $x \in \mathcal{P}O(I)$.

3.2 Analysing the generator of $X^N$

We will now analyse the generator $G^N$ of $X^N$. Using the jump rates from (1.1), we find for $f : E_N \to \mathbb{R}$, and $e_m$ the $m$th unit vector,

\[ G^N f(x) = \frac{N^2}{2} \sum_{m,n} x_n \sum_{k,l} x_k x_l \left( \frac{k+l}{m} \right) 2^{-(k+l)} \left( f(x + (e_m - e_n)/N) - f(x) \right). \quad (3.4) \]
Copy number variation of genetic elements

First, we will analyse the action of the generator on functions only depending on \( \rho_1(x) \) (Lemma 3.3), and on generating functions (Lemma 3.4). Afterwards, we are dealing with control of second and third moments, which we achieve by taking derivatives of the generating functions (Corollary 3.6). In the next section, in Proposition 3.7, we will see that \( |\rho_2(X_t^N) - \rho_2^1(X_t^N)| \) becomes small (cf. (3.16)). Together with the following lemma, this points to the fact that \( G^N \) acts on functions of the form \( x \mapsto g(\rho_1(x)) \) asymptotically like the generator of Feller’s branching diffusion.

**Lemma 3.3.** Let \( G^N \) be as in (3.4) and \( f \) be of the form \( f(x) = g(\rho_1(x)) \) for some \( g \in C^4_\infty(\mathbb{R}_+) \). Then, \( f \) only depends on the first moment of \( x \). That is, \( G^N \mapsto g(\rho_1(x)) \) acts on functions of the form \( x \mapsto g(\rho_1(x)) \) asymptotically like the generator of Feller’s branching diffusion.

**Proof.** Since

\[
g(\rho_1(x + (e_m - e_n)/N)) = g(\rho_1(x)) + N^{-1}g'(\rho_1(x))(m-n) + \frac{1}{2}g''(\rho_1(x))N^{-2}(m-n)^2 + o(N^{-2}),
\]

we write

\[
G^N = NG_1 + G_0 + o(1),
\]

\[
(G_1(g \circ \rho_1))(x) = \frac{1}{2}g'(\rho_1(x)) \sum_{m,n} x_n \sum_{k,l} x_k x_l \binom{k + l}{m} 2^{-(k+l)} (m-n)
\]

\[
= \frac{1}{2}g'(\rho_1(x)) \left( \sum_{k,l} x_k x_l \frac{k + l}{2} \sum_m \binom{k + l - 1}{m - 1} 2^{-(k+l-1)} - \sum_n nx_n \right)
\]

\[
= \frac{1}{2}g'(\rho_1(x)) \left( \sum_k x_k^2 + \sum_l x_l^2 - \sum_n nx_n \right) = 0,
\]

\[
(G_0(g \circ \rho_1))(x) = \frac{1}{4}g''(\rho_1(x)) \sum_{m,n} x_n \sum_{k,l} x_k x_l \binom{k + l}{m} 2^{-(k+l)}
\]

\[
\cdot (m(m-1) + n(n-1) - 2mn + m + n)
\]

\[
= \frac{1}{4}g''(\rho_1(x)) \left( \sum_{k,l} \binom{k + l}{m} \frac{4}{(k(k+1)+l(l+1)+2kl)/4}
\]

\[
+ \sum_n n(n-1)x_n - 2\rho_1^2(x) + 2\rho_1(x) \right)
\]

\[
= \frac{1}{4}g''(\rho_1(x)) \left( \frac{1}{2}\rho_2(x) + \frac{1}{2}\rho_1^2(x) + 2\rho_1(x) - 2\rho_1^2(x) + 2\rho_1(x) \right)
\]

\[
= \frac{1}{2}g''(\rho_1(x)) (\rho_1(x) + 2\rho_2(x) - \frac{3}{4}\rho_1^2(x),
\]

and the result follows.

Now we analyse the structure of \( G^N \) by collecting terms for the same powers in \( N \), when using products of \( \psi_s \).

**Lemma 3.4.** Let \( G^N \) be as in (3.4). For \( \ell = 1, 2, ... \) and \( s := (s_1, ..., s_\ell) \in [0, 1]^\ell \), set

\[
f_s(x) := \prod_{i=1}^\ell \psi_{s_i}(x).
\]

(3.5)
Then there exist operators $G_1, G_0, G_{-1}, \ldots$ obeying

$$G^N f_s = \sum_{i=1}^{\ell} N^{2-i} G_{2-i} f_s,$$

(3.6)

$$G_{2-i} f_s = \frac{1}{2} \sum_{j \subseteq (J_{|j|=i}) \ j \notin J} \left( \prod_{j \notin J} \psi_{s_j} \right) \sum_{K \subseteq J} (-1)^{|J \setminus K|} \psi_s^{2(1-(1-s_K)/2)} \psi_1 - (1-s_{j \setminus K}),$$

where the family of subsets $K \subseteq J$ includes also the empty set and $(1-s_K) := \prod_{j \in K} (1-s_j)$ (and the empty product equals 1).

Remark 3.5 (Form of $G_1$ and $G_0$). Note that $G_{2-i}$ is of order $i$ in the sense that $G_{2-i} \psi_s$ is a sum over all possible subsets $J \subseteq \{1, \ldots, \ell\}$ of cardinality $i$, where it leaves all factors $(\psi_{s_j})_{j \notin J}$ untouched and only acts on the factors $(\psi_{s_j})_{j \in J}$. So, in order to compute $G_1 \psi_s$ and $G_0 \psi_s$, it suffices to give these terms for $\ell = 1$ and $\ell = 2$, respectively. For $r, s \in [0, 1]$, we find from (3.6)

$$2G_1 \psi_s = \psi_s^{2r/2} - \psi_s,$$

(3.7)

$$2G_0 \psi_r \psi_s = \psi_{1-(1-r)(1-s)} - \psi_r \psi_s^{2r/2} + \psi_s^{2(1-(1-r)(1-s))/2}.$$

Proof. We obtain, collecting terms proportional to $N^{2-i}$ for $i = 1, \ldots, \ell$,

$$G^N f_s(x) = \sum_{m,n} x_n \sum_{k,\ell} x_{k,\ell} \left( \frac{k + \ell}{m} \right) 2^{-(k+\ell)} \prod_{i=1}^{\ell} \left( \psi_s(x) + N^{-1}((1-s)^m - (1-s)^n) - f_s(x) \right)$$

$$= \frac{1}{2} \sum_{m,n} x_n \sum_{k,\ell} x_{k,\ell} \left( \frac{k + \ell}{m} \right) 2^{-(k+\ell)} \sum_{i=1}^{\ell} N^{2-i} \prod_{j \subseteq (J_{|j|=i}) \ j \notin J} ((1-s_j)^m - (1-s_j)^n) \prod_{j \in J} \psi_{s_j}(x)$$

$$= \sum_{i=1}^{\ell} N^{2-i} G_{2-i} f_s(x)$$

with

$$2G_{2-i} f_s(x) = \sum_{j \subseteq (J_{|j|=i}) \ j \notin J} \left( \prod_{j \notin J} \psi_{s_j}(x) \right) \sum_{m,n} x_n \sum_{k,\ell} x_{k,\ell} \left( \frac{k + \ell}{m} \right) 2^{-(k+\ell)} \prod_{j \in J} ((1-s_j)^m - (1-s_j)^n)$$

$$= \sum_{j \subseteq (J_{|j|=i}) \ j \notin J} \left( \prod_{j \notin J} \psi_{s_j}(x) \right) \sum_{K \subseteq J} (-1)^{|J \setminus K|} \sum_{k,\ell,m} x_{k,\ell} \left( \frac{k + \ell}{m} \right) 2^{-(k+\ell)} \left( \prod_{j \in K} (1-s_j) \right)^m$$

$$\cdot \sum_n x_n \left( \prod_{j \in J \setminus K} (1-s_j) \right)^n.$$  

(3.8)

Taking the sum over $m$, the right hand side of (3.8) turns into

$$\sum_{j \subseteq (J_{|j|=i}) \ j \notin J} \left( \prod_{j \notin J} \psi_{s_j}(x) \right) \sum_{K \subseteq J} (-1)^{|J \setminus K|} \sum_{k,\ell} x_{k,\ell} \left( \frac{1 + \prod_{j \in K} (1-s_j)}{2} \right)^{k+\ell} \psi_s - \prod_{j \in J \setminus K} (1-s_j)(x)$$
Copy number variation of genetic elements

\[
= \sum_{j \leq (|J| = i)} \left( \prod_{j \notin J} \psi_{s_j}(x) \right) \sum_{K \subseteq J} (-1)^{|J| - |K|} \psi^2_{(1-(1-s_K)/2)}(x)\psi_{1-(1-s_{J\setminus K})(x)}.
\]

We have thus obtained (3.6). From the form of \(G_{2-i}\) we see that \(G_{2-i}f_x = 0\) if \(i > \ell\) (since there is no \(J \subseteq \{1, \ldots, \ell\}\) with \(|J| = i\) and the outer sum is empty).

\[\Box\]

**Corollary 3.6** (Martingale property of \(Z^N\) and uniform bounds on 2nd and 3rd moments).

a) The process \(Z^N = r_1(X^N)\) is a martingale.

b) For all \(t\) and \(N\), and for some constants \(C, C' < \infty\), which do not depend on \(N\),

\[
E[r_2(X^N)] \leq E[r_1(X^N)](t + 1) + E[r_2(X^N)],
\]

(3.9)

\[
E[r_3(X^N)] \leq Ct + C'E[r_3(X^N)].
\]

(3.10)

**Proof.** Using (3.3) and (3.7) we obtain

\[
-G^N r_1(x) = \frac{d}{ds}G^N \psi_s(x)|_{s=0} = \frac{d}{ds} \frac{N}{2} (\psi^2_{s/2}(x) - \psi_s(x))|_{s=0} = 0,
\]

(3.11)

\[
G^N r_2^2(x) = r_1(x) + \frac{3}{4} (r_2 - r_2^2(x)),
\]

(3.12)

\[
G^N r_2(x) = \frac{d^2}{ds^2}G^N \psi_s(x)|_{s=0} = \frac{N}{2} \frac{d^2}{ds^2} (\psi^2_{s/2}(x) - \psi_s(x))|_{s=0}
\]

\[
= \frac{N}{2} \left( \frac{1}{2} r_1^2(x) + \frac{5}{4} r_2(x) - r_2(x) \right) = \frac{N}{4} (r_1^2(x) - r_2(x)),
\]

(3.13)

Assertion a) is immediate from (3.11). Combining (3.12) and (3.13) we see that

\[
\frac{d}{dt} E[r_2^2(X^N)] = -\frac{N+1}{4} E[r_2^2(X^N)] - r_2(X^N) + E[r_1(X^N)].
\]

(3.14)

Since \((r_1(X^N))_{t \geq 0}\) is a martingale, we have \(E[r_1(X^N)] \equiv \mu\), and we can solve (3.14) by

\[
E[r_2^2(X^N)] - r_2(X^N)] = e^{-(N+3)t/4} E[r_2^2(X^N)] - r_2(X^N)] + (1 - e^{-(N+3)t/4}) \frac{4}{N+3} \mu.
\]

As a consequence,

\[
E[r_2^2(X^N)] - E[r_2(X^N)] = \frac{N}{4} \int_0^t E[r_2^2(X^N)] - r_2(X^N)]ds
\]

\[
= \frac{N}{N+3} \left( 1 - e^{-(N+3)t/4} \right) E[r_2^2(X^N)] - r_2(X^N)] + \frac{N}{N+3} \mu (t - \frac{4}{N+3} (1 - e^{-(N+3)t/4}))
\]

\[
\leq E[r_2^2(X^N)] - r_2(X^N)] + \mu t,
\]

and (3.9) follows from \(r_2^2(X^N) - r_2(X^N) \leq r_1(X^N)\). For (3.10), we employ similar calculations as in (3.13) and obtain

\[
G^N r_3 = \frac{3N}{8} (r_2 r_1 - r_3),
\]

\[
G^N (r_2 r_1) = \frac{N}{4} r_1 (r_2 - r_2) + \frac{3}{2} r_2 + \frac{9}{4} r_2^2 + \frac{5}{8} r_3 - \frac{5}{8} r_2 r_1,
\]

\[
G^N r_1 = \frac{9}{4} r_2 r_1 - \frac{5}{4} r_3 + r_2 + \frac{3}{2} (\frac{7}{2} r_3 - \frac{1}{2} r_2 r_1 - \frac{3}{4} r_1 - \frac{7}{2} r_1).
\]

Thus for \(a, b, c \in \mathbb{R}\) we have

\[
G^N (a r_1 + b r_2 + c r_1)
\]

\[
= \left( -\frac{3N}{8} a + \frac{5}{8} b - c \frac{3}{8} \right) r_3 + \left( a \frac{3N}{8} - b \left( \frac{N}{4} - \frac{1}{2} \right) + c \left( \frac{9}{4} - \frac{9}{8} \right) \right) r_2 r_1
\]

\[
+ \left( \frac{b}{2} - c \frac{3}{8} \right) r_2 + \left( \frac{b}{2} + c \left( \frac{3}{8} \right) \right) r_2.
\]
From this we deduce the existence of numbers \( a_1 = 1, b_1 = -3 + o(1), c_1 = 2 + o(1), a_2 = o(1), b_2 = \frac{1}{2} + o(1), c_2 = -\frac{1}{2} + o(1) \) and \( \lambda_1 = \frac{3}{4} + o(1), \lambda_2 = \frac{1}{4} \) such that the function \( f_1^N(x) := a_1 \rho_3(x) + b_1 \rho_2(x) \rho_1(x) + c_1 \rho_1^2(x) \) obeys

\[
N f_1^N(x) = -\lambda_1 N f_1^N(x) + (b_1 \frac{3}{2} - c_1 \frac{9}{8}) \rho_2(x) + (b_1 \frac{1}{2} + c_1 (9 + \frac{1}{16})) \rho_1^2(x), \quad i = 1, 2.
\]

(Here, we do not display the exact form of the six \( o(1) \) terms which we found using the computer algebra system sageMath (The Sage Developers, 2020). The sagemath commands are given in the latex sourcefile of the arxiv version of our paper.) In particular, this shows that \( G N f_1^N(x) + \lambda_1 N f_1^N(x) \) is a bounded function of \( (\rho_2(x), \rho_1^2(x)) \). Thus, with the same calculation as for the second moments we obtain

\[
E[f_1^N(X_1^N)] = e^{-\lambda_1 N} E[f_1^N(X_0^N)] + O(N^{-1}), \quad i = 1, 2. \tag{3.15}
\]

Finally, we find \( y = 1 + o(1) \) and \( z = 10 + o(1) \) with \( g f_1^N(x) + z f_2^N(x) = \rho_3(x) - \rho_2(x) \rho_1(x) \) and therefore,

\[
E[\rho_3(X_1^N)] - E[\rho_3(X_0^N)] = -3 \int_0^1 E[g f_1(X_s^N) + z f_2(X_s^N)] ds.
\]

Plugging in (3.15), we obtain the assertion (3.10). \( \square \)

### 3.3 Random Poisson distributions

Recall from (1.4) the occupation measure \( \Gamma_X \) of \( X^n \) (which is a random probability measure on \( \mathbb{R}_+ \times \mathcal{P}(\mathbb{N}_0) \)). We will show in this section:

**Proposition 3.7.** Let the assumptions from Theorem 1.1 be satisfied. Then
(a) the sequence \( (\Gamma_{X^n})_{N=1,2,...} \) is tight,
(b) any limit point \( \Gamma \) is concentrated on the set of Poisson distributions, in the sense that \( \Gamma([0, \infty) \times \mathcal{P}(\mathcal{O})) = 1 \), and

\[
\int_0^\infty e^{-s} E[|\rho_2(X_s^N) - \rho_1^2(X_s^N)||ds = E\left[ \int |\rho_2(x) - \rho_1^2(x)||\Gamma_{X^n}(ds, dx) \right] \xrightarrow{N \to \infty} 0. \tag{3.16}
\]

We prepare the proof of this proposition by a characterization of random Poisson distributions on \( \mathbb{N}_0 \).

**Lemma 3.8** (Characterization of random Poisson distributions). Let \( \psi_n \) and \( \rho_n \) be as in Definition 3.1. Let \( \psi_s \) be a \( \mathcal{P}(\mathbb{N}_0) \)-valued random variable with \( \rho_1(Y) < \infty \) almost surely. Then the following are equivalent:

1. \( Y \) has the same distribution as \( \text{Poi}(\rho_1(Y)) \).
2. \( E[e^{-\lambda \psi_s(Y)}|\rho_1(Y)] = \exp\left(-\lambda e^{-s \rho_1(Y)}\right) \) almost surely, for all \( \lambda \geq 0 \).
3. For all \( n = 1, 2, ..., \) and \( s_1, ..., s_n \in [0, 1] \), we have almost surely

\[
E[\psi_{s_1}(Y) \cdots \psi_{s_n}(Y)|\rho_1(Y)] = \frac{1}{n} \sum_{j=1}^n E\left[ \psi_{s_j/2}^2(Y) \prod_{k \neq j} \psi_{s_k}(Y)|\rho_1(Y) \right].
\]

**Proof.** 1. \( \Rightarrow \) 3.: By assumption we have almost surely

\[
E[\psi_{s_1}(Y) \cdots \psi_{s_n}(Y)|\rho_1(Y)] = E[e^{-(s_1 + \cdots + s_n) \rho_1(Y)}|\rho_1(Y)] = e^{-(s_1 + \cdots + s_n) \rho_1(Y)}.
\]

Since the right hand side only depends on \( s_1 + \cdots + s_n \), the result follows from taking expectations and summing in

\[
E[\psi_{s_1}(Y) \cdots \psi_{s_n}(Y)|\rho_1(Y)] = E\left[ \psi_{s_j/2}^2(Y) \prod_{k \neq j} \psi_{s_k}(Y)|\rho_1(Y) \right].
\]
Copy number variation of genetic elements

3. ⇒ 2.: We start with the following observation: For \( s > 0 \) let \((s_{kj})_{k\in\mathbb{N}, j=1,...,k}\) be asymptotically negligible (in the sense that \( \sup_j |s_{kj}| \xrightarrow{k \to \infty} 0 \)) and \( \sum_j s_{kj} = s \). Then, since

\[
\psi_{s_{kj}}(Y) = \sum_{i=0}^{\infty} Y_i (1-s_{kj})^i = 1 - (s_{kj} + o(s_{kj})) \sum_i i Y_i,
\]

we have

\[
\log \left( \prod_{j=1}^{k} \psi_{s_{kj}}(Y) \right) = \sum_{j=1}^{k} \log(1 - (s_{kj} + o(s_{kj})) \rho_1(Y)) \xrightarrow{k \to \infty} -s \rho_1(Y). \tag{3.17}
\]

Now, we come to proving the assertion: Fix \( s \in [0, 1] \) and \( n = 1, 2, ..., \) and let \( \Pi_k \) be a random partition of \([0, ns]\) with \( k \) elements, which arises iteratively as follows: Starting with \( \Pi_n = \{[0, s), [s, 2s), \ldots, [(n-1)s, ns)\} \), let \( \Pi_{k+1} \) arise from \( \Pi_k \) by randomly taking one partition element \([a, b]\) from \( \Pi_k \), and adding the two elements \([a, (a+b)/2)\) and \([(a+b)/2, b)\) to \( \Pi_{k+1} \). (For \( n = 1 \), we can e.g. have \( \Pi_1 = \{[0, s)\}, \Pi_2 = \{[0, s/2), [s/2, s)\}, \Pi_3 = \{[0, s/4), [s/4, s/2), [s/2, s)\} \). \( \Pi_4 = \{[0, s/4), [s/4, 3s/8), [3s/8, s/2), [s/2, s)\}, \ldots \). From 3. we find almost surely

\[
E[\psi_{s}^n(Y)|\rho_1(Y)] = E\left[ \prod_{\pi \in \Pi_n} \psi_{|\pi|}(Y)|\rho_1(Y) \right] = E\left[ \prod_{\pi \in \Pi_{n+1}} \psi_{|\pi|}(Y)|\rho_1(Y) \right].
\]

since the expectation of the right hand side also runs over the \( n \) possible random partitions \( \Pi_{n+1} \), which arise by splitting one element of length \( s \) into two elements of length \( s/2 \). It is not hard to see that – almost surely – every partition element in \( \Pi_k \) eventually gets split in two, so \( \{\pi : \pi \in \Pi_k\} \) is asymptotically negligible as \( k \to \infty \).

Therefore, \( \prod_{\pi \in \Pi_k} \psi_{|\pi|}(Y) \xrightarrow{k \to \infty} e^{-ns \rho_1(Y)} \) almost surely as in (3.17), so we see using dominated convergence that almost surely

\[
E[\psi_{s}^n(Y)|\rho_1(Y)] = \lim_{k \to \infty} E\left[ \prod_{\pi \in \Pi_k} \psi_{|\pi|}(Y)|\rho_1(Y) \right] = e^{-ns \rho_1(Y)}.
\]

Therefore,

\[
E[e^{-\lambda \psi_{s}(Y)}|\rho_1(Y)] = \sum_{n=0}^{\infty} \frac{(-\lambda)^n}{n!} e^{-ns \rho_1(Y)} = e^{-\lambda e^{-s \rho_1(Y)}}.
\]

2.⇒1.: Conditional on \( \rho_1(Y) \), we see that almost surely \( \psi_{s}(Y) = e^{-s \rho_1(Y)} \) for all \( s \in [0, 1] \), which means that \( Y \sim \text{Poi}(\rho_1(Y)) \). \( \square \)

Proof of Proposition 3.7. The occupation measures \( \Gamma_{X_N} \), defined according to (1.4), are random elements of \( \mathcal{P}([0, \infty) \times \mathcal{P}(\mathbb{N}_0)) \). By Markov’s inequality and Prohorov’s criterion, for \( C > 0 \) the set

\[
K_C := \{ x \in \mathcal{P}(\mathbb{N}_0) : \rho_1(x) \leq C \}
\]

is relatively compact in \( \mathcal{P}(\mathbb{N}_0) \). Hence, again by Prohorov’s criterion, tightness of \( \{\Gamma_{X_N}\} \) follows if for all \( \varepsilon > 0 \) there exist \( T, C < \infty \) such that

\[
P(\Gamma_{X_N}([0, T] \times K_C) \geq 1 - \varepsilon) \geq 1 - \varepsilon \quad \text{for all } N. \tag{3.18}
\]

For given \( \varepsilon > 0 \) let \( T \) be such that \( \int_0^T e^{-t} dt \geq 1 - \varepsilon \). Because of Corollary 3.6, \( \rho_1(X_N^t) \) is a non-negative martingale, hence by Doob’s inequality and due to the assumptions of Theorem 1.1 there exists a finite constant \( C \) such that

\[
P( \sup_{0 \leq t \leq T} \rho_1(X_N^t) \leq C ) \geq 1 - \varepsilon. \tag{3.19}
\]
Copy number variation of genetic elements

The event in the l.h.s. of (3.19) equals \( \{ X_i^N \in K_C \text{ for all } t \in [0, T] \} \), and due to our assumption on \( T \) this implies the event in the l.h.s. of (3.18). Thus we infer the validity of (3.18), showing assertion (a) of the proposition.

In order to prove assertion (b), recall \( f_s \) from (3.5) and choose \( g \) bounded and smooth. We are going to argue using the martingale

\[
\left( N^{-1} g(\rho_1(X_i^N)) f_s(X_i^N) - \int_0^t N^{-1} G^N g(\rho_1(X_i^N)) f_s(X_i^N) dr \right)_{t \geq 0},
\]

(3.20)

As \( N \to \infty \), we find that \( N^{-1} g(\rho_1(X_i^N)) f_s(X_i^N) \xrightarrow{N \to \infty} 0 \) since \( g \) and \( f_s \) are bounded. Moreover, from Lemma 3.3 and Lemma 3.4,

\[
N^{-1} G^N g(\rho_1(x)) f_s(x) = g(\rho_1(x)) G_1 f_s(x) + O(N^{-1}),
\]

and \( G_1 f_s \) is given by (3.7). Therefore, multiplying (3.20) by \( 2/\ell \) and taking \( N \to \infty \), we find that for any weak limit \( \Gamma \) of \( \Gamma_{X^N} \) as \( N \to \infty \) that

\[
\frac{1}{\ell} \left( \int_0^1 e^{r} \left( g(\rho_1(x)) \sum_{j=1}^{\ell} \left( \psi_{s_j/2}(x) \prod_{k=1}^{\ell} \psi_{s_k}(x) - \prod_{k=1}^{\ell} \psi_{s_k}(x) \right) \right) \Gamma(dr, dx) \right)_{t \geq 0}
\]

is a martingale with continuous paths and vanishing quadratic variation, hence vanishes. Consequently, if \( Y \) is a \( P(\mathbb{N}_0) \)-valued random variable which, given \( \Gamma \), has distribution \( \Gamma(dx) := \Gamma([0, \infty) \times dx) \), we have

\[
\frac{1}{\ell} \mathbb{E} \left[ g(\rho_1(Y)) \sum_{j=1}^{\ell} \psi_{s_j/2}(Y) \prod_{k=1}^{\ell} \psi_{s_k}(Y) \right] = \mathbb{E} \left[ g(\rho_1(Y)) \prod_{k=1}^{\ell} \psi_{s_k}(Y) \right],
\]

which implies

\[
\frac{1}{\ell} \mathbb{E} \left[ \left( \sum_{j=1}^{\ell} \psi_{s_j/2}(Y) \prod_{k=1}^{\ell} \psi_{s_k}(Y) \right) \rho_1(Y) \right] = \mathbb{E} \left[ \prod_{k=1}^{\ell} \psi_{s_k}(Y) \rho_1(Y) \right]
\]

since \( g \) was arbitrary. From Lemma 3.8 we see that \( \Gamma \) must be concentrated on \( \mathcal{POI} \).

Finally, for proving (3.16), consider a probability space with \( Y^N \sim \Gamma_{X^N}, Y \sim \Gamma_X \) and \( Y^N \xrightarrow{N \to \infty} Y \) almost surely. From Corollary 3.6 we see, using Jensen’s inequality, that

\[
\sup_{N} \mathbb{E}[(\rho_2(Y^N)^{3/2}] = \sup_{N} \int_0^{\infty} e^{-t} \mathbb{E}[(\rho_2(X_i^N)^{3/2}]dt \leq \sup_{N} \int_0^{\infty} e^{-t} \mathbb{E} \left[ \sum_{k=2}^{\infty} k^3 X_i^N(k) \right] dt < \infty,
\]

which implies that \( (\rho_2(Y^N))_N \) and \( (\rho_2(Y^N))_N \) are uniformly integrable. Hence,

\[
\int_0^{\infty} e^{-t} |\rho_2(Y^N) - \rho_2^2(Y^N)|dt = |\rho_2(Y^N) - \rho_2^2(Y^N)| \xrightarrow{N \to \infty} |\rho_2(Y) - \rho_2^2(Y)| = 0
\]

in \( L^1 \), and (3.16) follows.

\[ \Box \]

3.4 Convergence of \( Z^N \) to Feller’s branching diffusion

**Proposition 3.9.** Let the assumptions of Theorem 1.1 be satisfied. Then \( Z^N \) converges as \( N \to \infty \) in distribution with respect to the Skorokhod topology on \( D(\mathbb{R}_+) \) to \( Z \), where \( Z \) solves (1.2).
Copy number variation of genetic elements

Proof. For the claimed limit of \( Z^N = \rho_1(X^N) \) as \( N \to \infty \), we need to show existence (i.e. tightness) and uniqueness. Recall from Corollary \[3.6\] and eq. \[3.12\] that \((\rho_1(X^N))_{N=1,2,...}\) are non-negative martingales and have quadratic variation processes \( M^1, M^2, ... \) with

\[
M_t^N = \int_0^t \rho_1(X_s^N) + \frac{3}{2} \left( \rho_2(X_s^N) - \rho_1^2(X_s^N) \right) ds.
\]

For tightness of \((\rho_1(X^N))_{N=1,2,...}\), we use the Aldous-Rebolledo criterion, see e.g. Theorem 1.17 in Etheridge (2001). So, we have to show that

1. for all \( t \geq 0 \), the family \((\rho_1(X^N_t))_{N=1,2,...}\) is tight;
2. for every sequence \( \tau_1, \tau_2, ... \) of stopping times, bounded by \( T < \infty \) and for every \( \varepsilon > 0 \), there exists \( \delta > 0 \) such that

\[
\lim_{N \to \infty} \sup_{0 \leq \theta \leq \delta} \mathbb{P}(M^N(\tau_N + \theta) - M^N(\tau_N) > \varepsilon) < \varepsilon.
\]

For 1., the Markov inequality implies that for \( \varepsilon > 0 \) there exists a finite constant \( C_\varepsilon \) independent of \( t \) and \( N \) such that

\[
\sup_N \mathbb{P}(\rho_1(X^N_1) > C_\varepsilon) \leq \varepsilon.
\]

In particular, this implies that \((\rho_1(X^N_t))_{N=1,2,...}\) is tight for all \( t \geq 0 \). For 2., we take \( \varepsilon, \tau_1, \tau_2, ... \), as above, and use \( \delta := \varepsilon/(2C_\varepsilon) \) and write

\[
\lim_{N \to \infty} \sup_{0 \leq \theta \leq \delta} \mathbb{P}\left( \int_{\tau_N}^{\tau_N+\theta} \rho_1(X^N_s) ds > \varepsilon/2 \right)
\leq \lim_{N \to \infty} \sup_{0 \leq \theta \leq \delta} \mathbb{P}\left( \int_{\tau_N}^{\tau_N+\delta} \rho_1(X^N_s) ds > \varepsilon/2 \right)
+ \mathbb{P}\left( \int_0^T |\rho_2(X^N_s) - \rho_1^2(X^N_s)| ds > \varepsilon/2 \right)
\leq \sup_N \mathbb{P}( \sup_{0 \leq t \leq T} \rho_1(X^N_t) > \varepsilon/(2\delta) ) \leq \varepsilon,
\]

where we have used Proposition \[3.7\] in the second to last, and the martingale property of \( \rho_1(X^N) \) (see Corollary \[3.6\]) together with Doob’s maximal inequality in the last step. For uniqueness, we use Theorem 8.2.b \( \Rightarrow \) a in Ethier and Kurtz (1986), and the fact that the generator of \( Z \) is \( Gf(z) = \frac{1}{2}zf''(z) \) for \( f \in C_0^2(\mathbb{R}_+) \). We write

\[
f(\rho_1(X^N_{t+s})) - f(\rho_1(X^N_t)) - \int_t^{t+s} Gf(\rho_1(X^N_u)) du
= f(\rho_1(X^N_{t+s})) - f(\rho_1(X^N_t)) - \int_t^{t+s} G^N f(\rho_1(X^N_u)) du
+ \frac{3}{2} \int_t^{t+s} f''(\rho_1(X^N_u)) (\rho_2(X^N_u) - \rho_1^2(X^N_u))
\]

by Lemma \[3.3\]. Hence, (8.7) in Ethier and Kurtz (1986) follows from Proposition \[3.7\].

3.5 Completion of the proof of Theorem 1.1

We know from Proposition \[3.7\] that the sequence \((\Gamma_{X^N})\) is tight. In addition, noting that the topology of convergence in measure on \( \mathcal{D}(\mathbb{R}_+) \) is weaker than the Skorokhod
Copy number variation of genetic elements

topology, we see from Proposition 3.7 that $\Gamma_{Z} \xrightarrow{N \to \infty} \Gamma_{Z}$. Hence, we see that the family of bi-variate random probability measures $(\Gamma_{(X_{N'}, Z_{N'})})$ is tight, and

$$\Gamma_{(X_{N'}, Z_{N'})}(A) = 1,$$

with $A := [0, \infty) \times \{(x, z) \in \mathcal{P}(\mathbb{N}_0) \times \mathbb{R}_+ : \rho_1(x) = z}\}$.

Let us define for $C > 0$ the set

$$B_C := [0, \infty) \times \{x \in \mathcal{P}(\mathbb{N}_0) : \rho_2(x) \leq C\} \times [0, \infty),$$

and note that $A \cap B_C$ is closed (since $x \mapsto \rho_1(x)$ is continuous on a set with bounded second moments). By Corollary 3.6 for all $\varepsilon > 0$ there is $C > 0$ such that for all $N$

$$\mathbb{P}(\Gamma_{(X_{N}, Z_{N})}(B_C) \geq 1 - \varepsilon) \geq 1 - \varepsilon.$$  \hfill (3.21)

Let us consider a weak limit $\Gamma$ of $\Gamma_{(X_{N'}, Z_{N'})}$ along a subsequence $N'$. We may choose a probability space where $\Gamma_{(X_{N'}, Z_{N'})} \xrightarrow{N' \to \infty} \Gamma$ almost surely. On this space, by the Portmanteau Theorem,

$$\Gamma(A) \geq \Gamma(A \cap B_C) \geq \limsup_{N' \to \infty} \Gamma_{(X_{N'}, Z_{N'})}(A \cap B_C) = \limsup_{N' \to \infty} \Gamma_{(X_{N'}, Z_{N'})}(B_C).$$

For every $\varepsilon > 0$, choosing $C > 0$ such that (3.21) holds, we therefore find

$$\mathbb{P}(\Gamma(A) \geq 1 - \varepsilon) \geq 1 - \varepsilon$$

which implies $\Gamma(A) = 1$ almost surely. From Proposition 3.7 we know that

$$\Gamma(D) = 1,$$

with $D := [0, \infty) \times \text{POI} \times [0, \infty)$

almost surely, and we can conclude that $\Gamma(A \cap D) = 1$ almost surely. Hence, we are done by noting that

$$A \cap D = [0, \infty) \times \{(x, z) : x = \text{Poi}(z)\}.$$ 

Acknowledgements

We thank Peter Czuppon, Jonathan Henshaw and Judith Korb for discussions concerning the dynamics of transposable elements. PP is partly supported by the Freiburg Center for data analysis and modeling (FDM). AW is partly supported by DFG SPP 1590.

References

Baird, S. J., N. H. Barton, and A. M. Etheridge (2003). The distribution of surviving blocks of an ancestral genome. *Theoretical population biology* 64(4), 451–471.

Berglund, N. and B. Gentz (2006). *Noise-induced phenomena in slow-fast dynamical systems: a sample-paths approach*. Springer Science & Business Media.

Bourque, G., K. H. Burns, M. Gehring, V. Gorbunova, A. Seluanov, M. Hammell, M. Imbeault, Z. Izsvák, H. L. Levin, T. S. Macfarlan, D. L. Mager, and C. Feschotte (2018, 11). Ten things you should know about transposable elements. *Genome Biol* 19(1), 199.

Chang, J. (1999). Recent common ancestors of all present-day individuals. *J. Appl. Probab.* 31, 1002–1026.

Coron, C. and Y. Le Jan (2020). Genetics of the biparental moran model. [https://arxiv.org/abs/2007.15479](https://arxiv.org/abs/2007.15479).

Etheridge, A. (2001). *An introduction to superprocesses*. American Mathematical Society.

Ether, S. N. and T. G. Kurtz (1986). *Markov Processes. Characterization and Convergence*. John Wiley, New York.
Copy number variation of genetic elements

Foutel-Rodier, F. and E. Schertzer (2022). Convergence of genealogies through spinal decomposition, with an application to population genetics. [https://arxiv.org/abs/2201.12412](https://arxiv.org/abs/2201.12412).

Griffiths, R. C. and P. Marjoram (1997). An ancestral recombination graph. In Progress in population genetics and human evolution (Minneapolis, MN, 1994), Volume 87 of IMA Vol. Math. Appl., pp. 257–270. Springer, New York.

Katzenberger, G. S. (1991). Solutions of a stochastic differential equation forced onto a manifold by a large drift. Ann. Probab. 19, 1587–1628.

Kurtz, T. G. (1991). Random time changes and convergence in distribution under the Meyer-Zheng conditions. Ann. Probab. 19, 1010–1034.

Kurtz, T. G. (1992). Averaging for martingale problems and stochastic approximation. In Applied stochastic analysis (New Brunswick, NJ, 1991), Volume 177 of Lecture Notes in Control and Inform. Sci., pp. 186–209. Berlin: Springer.

Lambert, A., V. M. Pina, and E. Schertzer (2021). Chromosome painting: how recombination mixes ancestral colors. Ann. Appl. Probab. 31(2), 826–864.

Meyer, P.-A. and W. A. Zheng (1984). Tightness criteria for laws of semimartingales. Ann. Inst. H. Poincaré Probab. Statist. 20, 353–372.

Pardoux, E. and A. Y. Veretennikov (2001). On Poisson equation and diffusion approximation 1. Ann. Probab. 29, 1061–1085.

Rohde, D. L., S. Olson, and J. T. Chang (2004, Sep). Modelling the recent common ancestry of all living humans. Nature 431(7008), 562–566.

Sawyer, S. A. and D. L. Hartl (1992, Dec). Population genetics of polymorphism and divergence. Genetics 132(4), 1161–1176.

Sethupathy, P. and S. Hannenhalli (2008). A tutorial of the poisson random field model in population genetics. Adv Bioinformatics 4, 257864.

Wakeley, J., L. King, B. S. Low, and S. Ramachandran (2012). Gene genealogies within a fixed pedigree, and the robustness of Kingman’s coalescent. Genetics 190(4), 1433–1445.

Wakeley, J., L. King, and P. R. Wilton (2016, 07). Effects of the population pedigree on genetic signatures of historical demographic events. Proc Natl Acad Sci 113(29), 7994–8001.