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CLONAL TURNOVER VERSUS CLONAL DECAY: A NULL MODEL FOR OBSERVED PATTERNS OF ASEXUAL LONGEVITY, DIVERSITY AND DISTRIBUTION

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Phylogenetic and phylogeographic studies suggest that a majority of asexual organisms are evolutionarily recent offshoots of extant sexual taxa and that old clonal lineages tend to be isolated from their sexual and younger asexual counterparts. These observations have often been interpreted as support for the long-term disadvantages of asexuality resulting from the mechanisms of clonal decay. Although clonal decay is likely to be an important mechanism that limits the temporal and spatial distribution of asexual lineages, we argue here that contemporary phylogenetic analyses, which are mostly restricted to simple comparisons of "recent" and "ancient" clones, need to be tested against an appropriate null model of neutrality. We use computer simulations to show that many empirical observations of the distribution of asexuality do not in fact reject a null model of the neutral turnover of clones spawned by sexual relatives. In particular, neutral clonal turnover results in qualitatively similar pattern of clonal spatial distribution and age structure, as does a process that includes clonal decay. Although there are important quantitative differences between predictions made by the two models, we show that published empirical data are still inadequate to distinguish between them. Further work on sexual-asexual complexes is therefore required before clonal turnover can be rejected as a parsimonious explanation of the spatial distribution and age structure of asexual lineages.

KEY WORDS: **Age of clones, ancient asexuals, asexual reproduction, clonal diversity, phylogeny.**

Asexual reproduction has evolved repeatedly, but its distribution in the tree of life tends to be very "twiggy" because lineages that have abandoned sex tend to be short-lived evolutionary dead-ends (see Vrijenhoek 1998 and Simon et al. 2003 for reviews). Notwithstanding the persistence of several well-known ancient asexuals (which have been viewed as evolutionary "scandals;" Judson and Normark 1996), there would thus appear to be broad phylogenetic evidence for a long-term disadvantage of asexual

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reproduction—whatever its short-term costs and benefits. Several processes have been hypothesized to account for this long-term disadvantage. These include: Muller's ratchet (the accumulation of mildly deleterious mutations through drift; Muller 1964; Leslie and Vrijenhoek 1980; Chao 1990; Lynch and Gabriel 1990; Storhas et al. 2000; Paland and Lynch 2006); evolution under the "Red Queen" (the adaptation of parasites to genetically identical clones; Bell 1982; Lively et al. 1990; Howard and Lively 1994; Dybdahl and Lively 1998), and the inability of clonal organisms to respond to environmental change in general (Weissman 1889, rev. in Vrijenhoek 1998). Indeed, these hypotheses are discussed almost routinely as possible reasons for the low observed ages of clonal lineages, however these are inferred. We might refer to such mechanisms responsible for the decrease of clonal fitness over time as the "clonal decay hypothesis" to distinguish them from other class of explanations for the persistence of sex, which do not necessarily assume a gradual decay in asexual fitness (see e.g., Kondrashov 1993; Doncaster et al. 2000).

A common idea is that clonal decay leads to the extinction of older asexual lineages through being displaced by their competitively superior sexual and younger asexual counterparts. For example, Law and Crespi (2002) found that the putative ancient asexual walking stick species *Timena genevieve* are geographically separated from its sexual progenitor *T. podura* in California by at least 250 km, suggesting "that *T. genevieve* has dispersed far enough to limit competition with its sexual counterpart" (p. 1716). In a similar study, Neiman et al. (2005) observed that both sexual populations and their recent clonal derivatives of the freshwater snail *Potamopyrgus* are widespread over the South Island of New Zealand, whereas two putative ancient asexual lineages are restricted to northern areas in which there is a virtual absence of sexual progenitors. These authors hypothesised that the ancient asexuals were able to persist only in lakes in which they did not face competition with the sexuals and "fresh" clones, or where there was a lower prevalence of parasitizing trematodes. Alternatively, they suggested that asexuality had perhaps been able to persist in lakes "with relatively stable [climatic] and geological history" (p. 1950), implying an absence of selection under environmental change (Neiman et al. 2005).

The focus on potential effects of competition, or its absence, between asexual clones and their sexual progenitors to explain the generally low age of clones and restriction of ancient asexual lineages to isolated areas would seem to be reasonable, given the central quest to understand the evolution and maintenance of sex versus asex. However, it overlooks an alternative, simpler, explanation for the observed patterns. Here, we suggest that much of the same patterns of clonal age and spatial distribution might be observed following the neutral turnover of successive clones spawned by a sexual progenitor species. In other words, we draw attention to the possibility that old asexual lineages might be displaced by younger asexual lineages spawned by the same sexual parents, potentially through a neutral process of clonal turnover. This neutral explanation is particularly relevant when taking into account ongoing discussion as to how long it takes the long-term disadvantages of asexuality to significantly affect the fate of an asexual lineage. This uncertainty comes from the fact that efficiency of clonal decay depends on many parameters, such as mutation rate or population size (Gordo and Charlesworth 2000), interaction among mildly deleterious mutations (Kondrashov 1994), and the diversity of clonal versus parasite assemblages (Hamilton et al. 1990).

We do not wish to suggest that the long-term failure of asexual lineages compared to their sexual counterparts is not ultimately the outcome of genome degeneration or a loss of evolvability (i.e., we have no argument with the clonal decay hypothesis). Rather, we propose that a simple model of clonal turnover might be used as a reasonable null model against which to test hypotheses that invoke selective differences between sexual and asexual lineages. We first expand on our idea in terms of a simple model comparing the clonal decay and clonal turnover hypotheses, and we illustrate the model with results of simple computer simulations. Importantly, we find that patterns predicted by the neutral model are much the same as those predicted for the clonal decay model under a broad range of parameters. Finally, we evaluate the neutral clonal turnover with respect to patterns observed in several studies of asexual species including the examples of *Timema* walking sticks and *Potamopyrgus* snails above. Based on phylogenetic data, the clonal-decay model would thus appear to have weaker support than has sometimes been claimed.

DESCRIPTION OF CLONAL TURNOVER MODEL AND SIMULATION

The idea of clonal turnover is not new. Indeed, clonal turnover has been advanced as a hypothesis to explain the long-term persistence of asexuality through the consecutive replacement of older asexual lineages by new ones (see e.g., Butlin et al. 1999, or Paland et al. 2005 for references). Although not always stated explicitly, the hypothesis seems to imply that new clones allow asexuality to persist in situations where, in their absence, it would succumb to the selective clonal decay of lineages as they age (e.g., Paland et al. 2005). Our hypothesis here is different, and it leads to different predictions. We suggest that, as a null hypothesis, the distribution of clonal ages might be determined through the neutral replacement of one clone by another through a process of drift. It would then seem reasonable to demand the rejection of this neutral process before turning to explanations that may invoke clonal decay.

The neutral clonal turnover model is in many respects similar to population genetic or macroecological models incorporating drift. Under the neutral theory of macroecology, for instance, abundance patterns are determined by the flux of species through

a system due to a neutral process of speciation (or migration) and extinctions (Hubbell 2001), just as the number and size of classes of neutral alleles segregating at a genetic locus is determined by the mutation rate to new alleles and their rate of loss through genetic drift (Kimura and Crow 1964). Similarly, a clonal turnover model would predict clonal abundance patterns in terms of the rate of their generation, either by mutation from established clones or through their repeated generation from sexual species. By analogy with the model of mutation–drift equilibrium (Kimura and Crow 1964), we expect that the neutral distribution of ages in a population of clones should be geometrically distributed, with its mean being the reciprocal of the rate of influx of new clones into the asexual community. Thus, individual clones will be prevented from becoming ancient by their neutral loss as newer clones become abundant, just as alleles are prevented from indefinite persistence by the process of genetic drift (see below). In geographically widespread sexual–asexual complexes, such as *Timena* walking sticks or *Potamopyrgus* snails, the clonal turnover model predicts that clones that coexist with sexual lineages that spawn new clones into the population should be shorter lived than those isolated from the sexual parents; by contrast, clones may become "ancient" if they are geographically removed from the source of newer clones that might replace them. This is of course just the pattern observed in the *Timena* and *Potamopyrgus* systems for which models of clonal decay were invoked.

To illustrate the relative correspondence of predictions made by the clonal turnover and the clonal decay models, we first conducted forward simulations of a single asexual population composed of N individuals. The model assumed that the asexual population receives an influx of new clones at rate c (e.g., as a result of dispersal from a sexual population). Clonal decay was modeled by invoking a Poisson-distributed number of new deleterious mutations per generation, with expectation U, reducing the fitness of each clonal individual by a fraction s. The fitness of clones carrying k mutations was thus given by $(1 - s)^k$. We assumed soft selection, such that N progeny per deme were sampled each generation from parents in proportion to parental fitness. For geographically subdivided clonal complexes, we conducted forward simulations of a one-dimensional stepping-stone model, with n asexual demes of N individuals per deme, and with demes connected by migration between neighbors at rate m. In this case, new clones, produced at rate c by sexual progenitor (see above), were introduced only to the first deme in the array. Other characteristics were identical to the single-population model. In all simulations, full pedigrees were recorded for populations that were allowed to evolve for at least 15,000 generations. We then calculated: the number of clonal lineages through time; their average age (defined as average time since their production from a mutation-free sexual progenitor); their geographic spread through the linear array of demes; and the pairwise divergences in time from a most recent common ancestor (MRCA) of every possible pair of individuals (c.f., Higgs and Woodcock 1995). The MRCA was either an asexual individual or the sexual ancestor of the clone.

There is an important simplification inherent to the present model because it assumes no interactions between sexual and clonal population other than through sexuals giving rise to new clones. Our model thus applies directly only to cases in which sexual and asexual lineages do not co-occur (see e.g., Lynch 1984 for some details), although it assumes that in other sexual–asexual systems both groups may not out compete each other. Because we are interested here only in evaluating the possibility of phylogeographic support for clonal decay models rather than mechanisms for the maintenance of sex versus asex, the simplified model assumptions would seem to be reasonable. In particular, our simple model allows us to focus solely on effects of clonal decay on the distribution of clonal age-classes without including many additional parameters describing complex interactions between sexual and asexual populations.

Results

In the absence of deleterious mutations ($s = 0$), the distribution of clone ages reached a steady-state equilibrium with the mean age related positively to population size and negatively to the rate of influx of new clones. For a neutral model with a single deme, the distribution of clone ages followed a geometric distribution with mean c^{-1} (where the c is the rate of the influx of new clones). As expected, the accumulation of deleterious mutations reduced the ages reached by clones before their extinction (Fig. 1). As noted by Gordo and Charlesworth (2000), this effect was strongest for intermediate values of s: with small s, mutations clearly affected

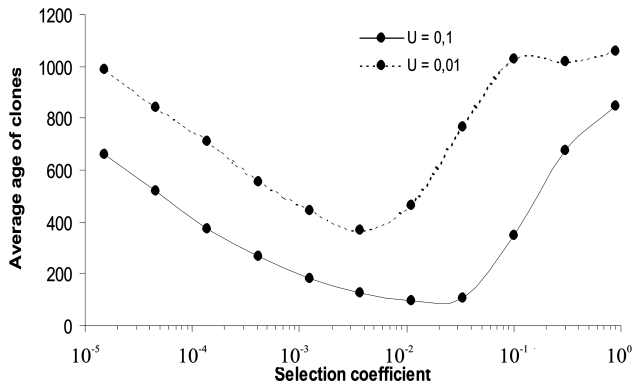

Figure 1. **The average age of clones in a population of an asexual complex fed by new clones at rate of 0.001 per generation. Each population comprised 1000 individuals. The selection coefficient, plotted on the abscissa, is the multiplicative deleterious effect of each new mutation acquired by the asexual lineage; mutations accumulated at rate of 0.1 or 0.01 per generation (indicated). The expected age for a neutral model is 1000 generations.**

fitness, and thus persistence times, relatively little; with high *s*, individuals affected by new mutations were substantially less likely to reproduce immediately, and this effectively slowed the mutation accumulation process (Fig. 1).

Geographical structure, as represented by the simple two-deme source–sink model (Fig. 2) slowed the process of clonal turnover in relatively isolated demes in much the same way as a reduced influx of clones through their generation from sexual progenitors. In particular, clones that became established further away from the source of new clones attained higher ages (Fig. 2A), and clonal diversity decreased with distance from the source of new clones, so that average clone age correlated negatively with local diversity (Fig. 2B). The interdeme differences in clonal ages and diversities correlated negatively with the migration rate (Fig. 2). Importantly, deleterious mutations did not affect these relative patterns qualitatively, although there were substantial quantitative differences in mean ages attained by clones (Figs. 1, 2) and in pairwise distances between individuals, as expected (cf, Higgs and Woodcock 1995; Fig. 3).

Discussion

The results of our simulations are intuitive. The influx of new asexual lineages into a "community" of related clones reduces the mean age reached by older clones as a result of neutral clonal turnover. This influx can be caused by the generation of new clonal lineages from a parental sexual species from which they are spawned locally, or it can be due to migrant lineages. In the first instance, the age distribution and the local diversity of clones is regulated by the balance between mutation to new clonal lineages and their extinction by drift, whereas in the second the balance is between migration and drift. As noted in the introduction, both processes have clear analogues in the generation and maintenance of neutral allelic variation in populations under mutation–drift or migration–drift equilibrium (Kimura and Crow 1964), or in the maintenance of macroecological diversity under models of ecological drift equilibria (Hubbell 2001). The lack of qualitative differences between neutral and clonal decay models suggests that simple comparisons of distributions and diversities

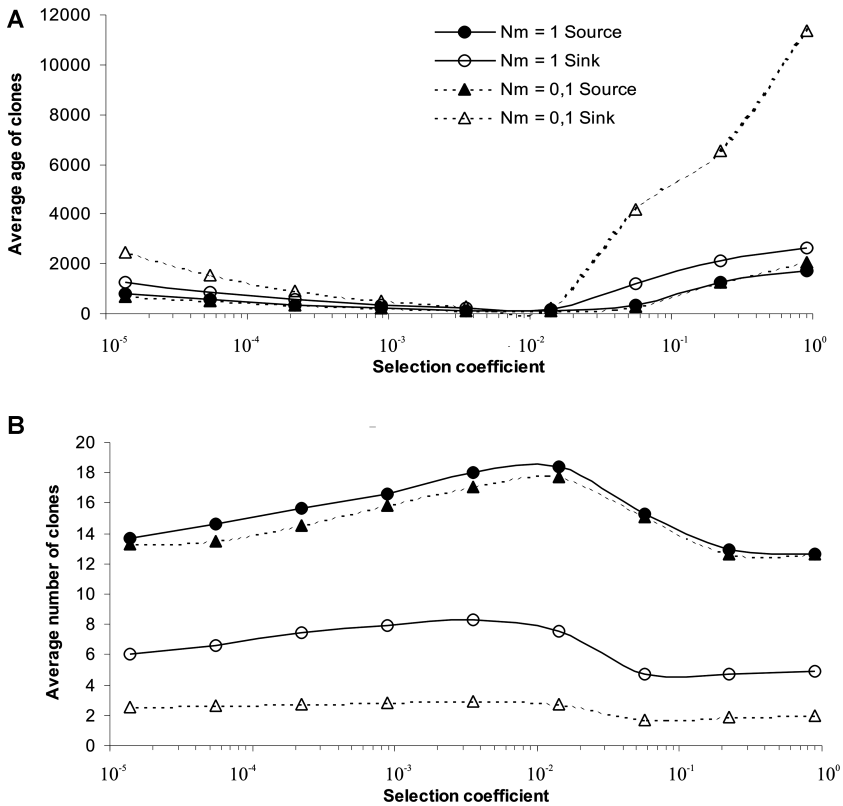

Figure 2. The average age (A) and the average number of clones (B) in source and sink populations (indicated) of an asexual complex fed by new clones into the source population at rate of 0.001 per generation. Each population comprised 1000 individuals, and the source and sink populations were linked through the migration of $Nm = 1.0$ and $Nm = 0.1$ individuals per generation, respectively. The selection coefficient, plotted on the abscissa, is the multiplicative deleterious effect of each new mutation acquired by the asexual lineage; mutations accumulated at rate 0.1 per generation. Under fully neutral simulation, $Nm = 1.0$ resulted in clonal ages of 2460 and 3890 generations in source and sink demes, respectively. Corresponding numbers of clones were 12.7 and 5, respectively. With $Nm = 0.1$, average clonal ages changed to 2370 and 21,730, respectively, and numbers of clones to 12.7 and 2.

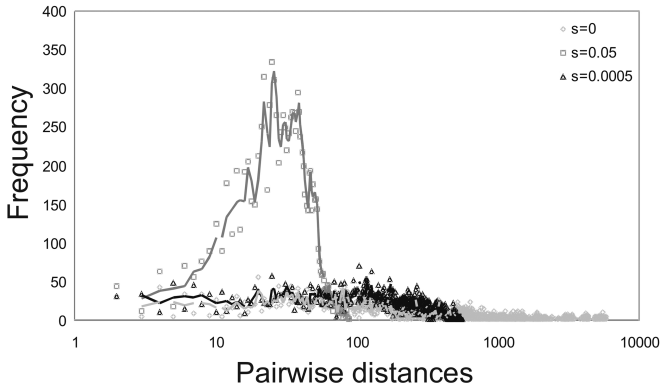

Figure 3. The distribution of pairwise distances (in generations) from a most recent common ancestor of asexual individuals averaged over 60 simulation runs. Simulated population consisted of $N = 300$ individuals, and the rate of recruitment of new clonal individual per generation was $c = 0.001$. The three overlaid datasets correspond to simulations under neutrality (light gray line with diamonds), and multiplicative deleterious effects of acquired mutations s set to 0.05 (dark gray line with squares) and 0.0005 (black line with triangles). Mutations accumulated at rate $U = 0.5$ per generation.

of "recent" and "ancient" clones do not necessarily provide strong evidence for the fitness decrease of clones as they get older, and that other types of evidence should be used to point toward clonal decay, such as experimental studies (see e.g., Leslie and Vrijenhoek 1980; Chao 1990; Lively et al. 1990; Dybdahl and Lively 1998; Storhas et al. 2000).

The clonal-turnover model, as illustrated by our simulations, makes several predictions. First, clonal lineages should, on average, be younger in natural systems with a high frequency of switches to asexuality than in complexes in which the recruitment of new clones is less frequent. Although testing this prediction quantitatively is made difficult by the need for data on rates of asexual lineage generation, by problems in proper assessment of clonal ages (see e.g., Little and Hebert 1996), and by errors associated with usage of molecular clocks in unrelated organisms, comparisons between extreme scenarios are possible. For instance, the diverse asexual lineages of the fish *Poeciliopsis monacha-lucida* have apparently been generated by multiple origins from a sexual progenitor through hybridization (Quattro et al. 1991). These multiple lineages would appear to be much younger than the related asexual lineage *P. monacha-occidentalis*, which likely originated from a single hybridization event as much as 10^5 years ago (Quattro et al. 1992). It is at least plausible that the *P. monacha-occidentalis* clone has persisted for so much longer than any of the *P. monacha-lucida* clones, because these latter have been subject to ongoing clonal turnover.

A second prediction is that asexual lineages should be younger in sympatry with their sexual progenitors than in allopatry. Although there are few suitable phylogeographic analyses for the determination of both the age and distribution of clonal lineages, it would seem that most reports corroborate this prediction: older clonal lineages tend to occur in the absence of sexual progenitor, or, in case of hybrid asexuals, in areas in which the reproductive contact between parental species is not possible, whereas recent lineages are frequently observed close to their sexual progenitors. For example, such a pattern is evident in *Squalius alburnoides* freshwater fish hybridogens (Cunha et al. 2004), parthenogenetic lineages of *Campleloma* snails of both hybrid and nonhybrid origin, (Johnson and Bragg 1999; Johnson 2006), asexual lineages of *Lasaea* clams (O′Foighil and Smith 1995), or gynogenetic *Cobitis* loaches (Janko et al. 2005). If we consider as ancient only those asexual lineages that are substantially diversified but monophyletic relative to sexual progenitors, this pattern is also apparent in the flatworm *Schmidtea polychroa* (Pongratz et al. 2003).

A third prediction is that the distributional range of particular clonal lineages should correlate positively with their age. This pattern appears to be implied by the data on *S. alburnoides* complex cited above (Cunha et al. 2004). It is also apparent in *P. monacha-lucida* lineages versus *P. monacha-occidentalis* asexuals (Quattro et al. 1991, 1992), as well as in *Campleloma* snails (Johnson 2006) and *Cobitis* loaches (Janko et al. 2005), although distribution data from *S. polychroa* flatworms run counter to the prediction (Pongratz et al. 2003). Interestingly, old and young lineages coexist in *S. alburnoides*, *Campleloma*, *Cobitis*, and *S. polychroa* asexual complexes, suggesting that clonal decay has been insufficient for competitive exclusion by "fresh" clones.

Finally, the clonal turnover model predicts that clonal diversity should decrease with geographic distance from the sexual progenitor. A similar prediction was discussed by Butlin et al. (1999). This expectation is met in both the examples cited in the introduction, i.e., in *Timema* walking sticks and *Potamopyrgus* snails. In these species, recent clones also occur in sympatry with sexual progenitors or adjacent to their range, whereas ancient lineages are isolated or occur in areas with low frequency of sexuals, implying a reduced possibility of new clonal recruitment. *Potamopyrgus* data further suggest that many recently originated clones are only locally distributed, whereas the most ancient lineage is geographically widespread (Neiman and Lively 2004; Neiman et al. 2005). It is perhaps significant that the ranges of both young and ancient *Timema* clones were shifted northward from their sexual progenitors to the same extent (Law and Crespi 2002), and coexistence of recent and ancient *Potamopyrgus* clones has been documented in four of the six lakes inhabited by ancient clones (in one of these lakes, the ancient clones even strongly outnumbered the young ones; see Table 1 in Neiman et al. 2005). Such patterns would seem to be inconsistent with the idea that ancient clones suffer reduced competitive ability or show greater vulnerability to

climatic changes (see also Law and Crespi 2002); they are more in keeping with a simpler model of clonal turnover.

Clearly, the patterns reviewed above may have been strongly influenced by selective differences between clones, and ultimately between clones and their sexual progenitors: if there were no disadvantages of asexuality, sex would be lost due to twofold cost of males. Currently, there is a diverse array of theories explaining the persistence of sex, only some of which assume or invoke a time-dependent fitness decrease of clones (Lynch 1984; rev. in Kondrashov 1993; rev. in Vrijenhoek 1998; Peck et al. 1998; Doncaster et al. 2000). It is not our aim here to test any of these hypotheses, nor to claim that our study yields support for explanations for the persistence of sex that do not invoke decay; to the contrary, there is increasing evidence for the genetic degeneration for nonrecombining genomic compartments through processes such as Muller's Ratchet, for example in the degeneration of Y chromosomes (Gordo et al. 2002; Bachtrog 2004; Charlesworth et al. 2005). Finally, we note that some organisms may be more vulnerable to clonal decay than others. For example, organisms with large population sizes are expected to be less affected by Muller's Ratchet (e.g., Kondrashov 1993), whereas high clonal recruitment rate may speed-up the turnover of clones and may prevent parasites from adapting to single predominant genotype (Lively and Howard 1994).

Our results simply suggest the need to evaluate these hypotheses against a neutral null hypothesis of clonal turnover. Unfortunately, it will not be easy to distinguish between the hypothesis of clonal decay with the more parsimonious model of clonal turnover (or generally the nondecay hypotheses) through the use of phylogeographic data. Our simulations further emphasize that clonal lineages can go extinct by chance alone even without the mechanisms of clonal decay. Importantly, given our uncertainty about the speed of such mechanisms (see the introduction), our model at least points to the possibility that clones may disappear before clonal decay could significantly affect their fitness. Spread of clonal lineages into geographically isolated areas may, therefore, allow their long-term persistence not only through limiting their competition with sexuals and "fresh" clones, as assumed by traditional hypotheses, but also by decreasing their probability of being lost by drift.

Although both clonal turnover and clonal decay models give the same qualitative predictions, it might be possible, in principle, to distinguish the two models in quantitative terms, because clone ages should be highest under the assumption of neutrality and the distribution of clone ages should have a long tail that is truncated by selection. However, we do not yet appear to be in a position to estimate the recruitment rate of new clones, effective sizes, and the geographical structure of asexual populations with sufficient accuracy for such comparisons to be made successfully and the analyses of clonal diversity and phylogeographic data presented in the studies cited in this article would seem to be insufficient for that end. Gordo et al. (2002) have shown that neutral and decay models lead to different predictions of genetic variability in monoclonal populations. From that point of view, different shapes of simulated interindividual relationships under both models in multiclonal populations (Fig. 3) are promising and may motivate further developments.

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