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Understanding the Evolution and Genomic Consequences of an Atypical Sexual System Through Population Genetic Simulations

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I. INTRODUCTION

In eukaryotes, most species reproduce sexually, while asexual reproduction is rare (GOODENOUGH and HEITMAN 2014; VRIJENHOEK 1998). Sexuality has indeed non-negligible short-term and long-term advantages that are for a great part explained by recombination (ENGELSTÄDTER 2008). In the short-term, recombination makes possible genetic shuffling allowing beneficial alleles to be brought together on the same chromosome and then selected together (an effect known as the HILL-ROBERTSON effect ; HILL and ROBERTSON 1966). In the long-term, it promotes variability and thus adaptation (FELSENSTEIN 1974), and reduces the effects of MULLER's ratchet (MULLER 1964) by purging deleterious alleles (KONDRASHOV 1993; MAYNARD SMITH 1989; HURST and PECK 1996). Nevertheless, it is admitted that sexual reproduction is much less efficient compared to asexuality in many ways (WILLIAMS 1975; MAYNARD 1978; STEARNS 2013; OTTO 2009; DONCASTER *et al.* 2000) and has costs that are absent from asexuality, making the prevalence of sexual reproduction the so-called paradox of sex (OTTO and LENORMAND 2002). Cost of sex is defined as "*the magnitude of the minimum compensatory benefits that enable sexual individuals to avoid being outcompeted by asexual individuals*" (STEARNS 2013; LEHTONEN *et al.* 2012). It must indeed be at the most of the same magnitude as its benefits to explain preeminence of sexual reproduction. This cost is mostly associated with the cost of males (MAYNARD 1978; WILLIAMS 1975, reviewed in HARTFIELD and KEIGHTLEY 2012 and LEHTONEN *et al.* 2012). If half of the offspring of a female are males that invest few resources in their own offspring, asexuality is exactly twice as beneficial as sexuality (LEHTONEN *et al.* 2012). However, many aspects of the life cycles of species lead to a rethinking of this simple analysis. There is for example an effect of the number of females impregnated by a single male (polygamy *vs.* monogamy), of the resource effectively invested in the production of males compared to the production of females, of the difficulty of finding partners, *etc.* (LEHTONEN *et al.* 2012). It thus seems difficult to define a general cause for the cost of sex, and so a general cause to the rarity of the asexuality among species.

I.a How to better understand sex-asex transitions?

Sexuality corresponds to dimeiotic reproduction, *i.e.* two different meiosis lead to the production of two gametes that contribute genetically together to the formation of the offspring's genome (Fig. 1). There is thus alternation between meiosis and syngamy, haploid phase then return to diploidy. Conversely, asexuality is a form of uniparental reproduction. It results from a single cell division process: mitosis (known as apomixis, *i.e.* clonality) or modified meiosis (known as automixis or monomeiotic reproduction). Asexuality always involve the punctual passage to a unicellular stage of the offspring,

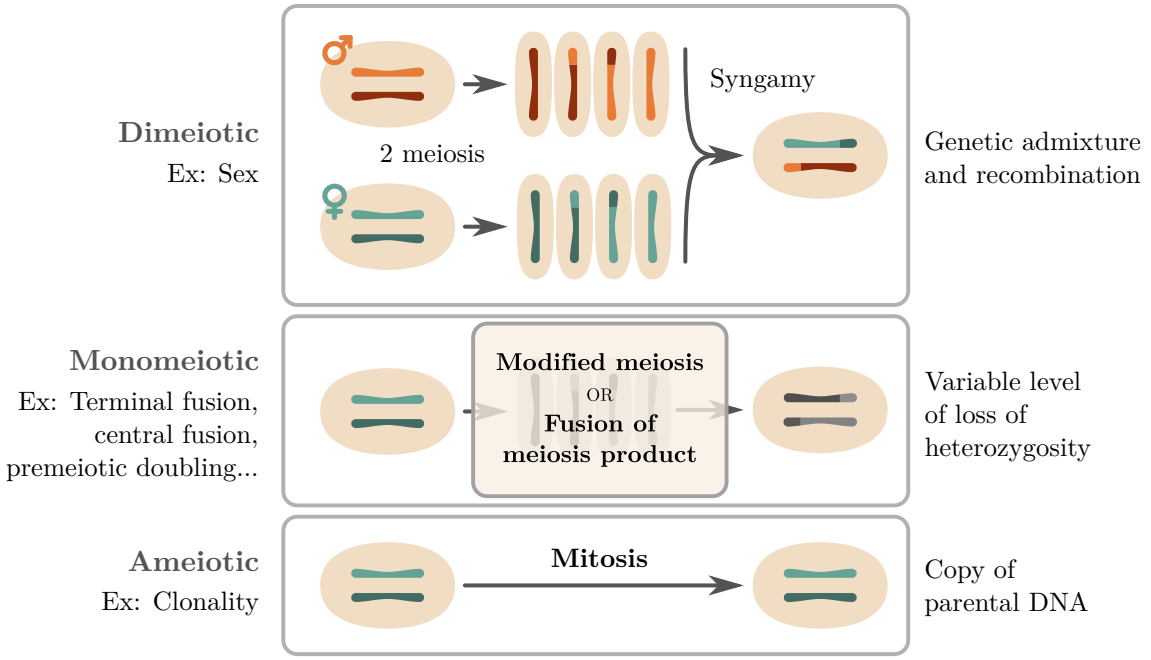


Figure 1: Several categorisations are possible in the way in which the genomes of offspring are arranged from the parental genomes. If we consider the cellular mechanisms capable of producing offspring we can distinguish three main categories (BOYER, MOLINIER, *et al.* n.d.): ameiotic, dimeiotic and monomeiotic reproduction. Ameiotic reproduction is what we call clonality, *i.e.* the production of offspring directly by mitosis. Dimeiotic reproduction involves two different germ cells producing haploid gametes which when fused together produce the offspring. These gametes may come from the same individual (self-fertilisation) or from two different individuals (allo-fertilisation). Sex is the usual equivalent of dimeiotic reproduction. Finally, there is monomeotic reproduction where a single germ cell allows the production of an offspring via modified meiosis or fusion of meiosis products. Thus "asexual" reproduction covers both ameiotic and monomeiotic reproduction.

which differentiates it from vegetative reproduction. This distinction is important, these two modes of reproduction having quite different physiological functioning (VAN DIJK 2009). In plants, for example, a distinction is made between asexual seed production (HAND and KOLTUNOW 2014, *e.g.* in the common dandelion *Taraxacum officinale*) and propagation by vegetative organs (LEI 2010, *e.g.* in the strawberry *Fragaria* sp.).

Asexuality is often supposed to lead to clonal reproduction, which suffers from the absence of recombination and genetic admixture. However, asexuality is not necessary synonymous of clonality and asexual reproduction often involves modified meiosis mechanisms that don't lead to clonal reproduction (LENORMAND *et al.* 2016; DE MEEÛS *et al.* 2007; MOGIE 1986). These would mainly be recent asexual lineages (BOYER, JABBOUR-ZAHAB, *et al.* 2021), making them likely intermediate stages in the evolution towards fully clonal asexuality. In these lineages the zygote is not formed by an equivalent of mitosis as in clonality, but by a modified meiosis that allows a single individual to produce a zygote with ploidy conservation.

Automictic reproduction (Fig. 1) sheds light on the over-simplicity of sex-asex transition models (BOYER, JABBOUR-ZAHAB, *et al.* 2021). Standard models often consider the transition to asexuality as a transition to mandatory clonality, without intermediate

stages. However, it is very likely that the evolution of asexuality is gradual. A neo-formed asexual system derived from a sexual system should thus emerge from the modification of the physiological mechanisms of sex. Therefore, the transition from sexuality to asexuality can occur through monomeiotic reproduction. For example, SIMION *et al.* (2021) recently showed that the emblematic case of Bdelloid rotifers, supposed to be an "ancient asexual scandal", are not clonal but reproduce asexually through a modified meiosis. Studying biological systems with non clonal asexual reproduction is thus likely key to better understand the paradox of sex.

I.b The case of an atypically asexual species

In this thesis I study the case of *Mesorhabditis belari* (Fig. 2), a nematode with a astonishing and atypical reproductive system, partly sexual and partly automictic (GROSMAIRE *et al.* 2019). It is a gonochoric species with ten pairs of chromosomes (NIGON 1949) whose sex is determined by an X/Y system (NIGON 1949; GROSMAIRE *et al.* 2019). Reproduction in *M. belari* always involves a spermatozoon fertilising an egg. In all cases, the egg cells are arrested in prophase I (MILLER *et al.* 2001) and the spermatozoa are 50% X and 50% Y (GROSMAIRE *et al.* 2019). After reproduction, two zygotic production pathways can be distinguished (GROSMAIRE *et al.* 2019, see Fig. 3). The first is a standard sexual way with the only difference that only males are produced. The entry of the male pronucleus and sperm centrosome triggers the completion of female meiosis with two polar globules being generated. The male and female genetic materials then form the first mitotic spindle. The second pathway is an asexual pathway, corresponding to gynogenetic automixis (GROSMAIRE *et al.* 2019). Gynogenesis (also called pseudogamy) corresponds to the formation of a zygote by the transmission of female genetic material alone, but with the need for the egg cell to be fertilised to trigger embryogenesis. The precise mechanism that allow the production of a gynogenetic zygote is not yet known. However, it is known that the first division of meiosis is aborted (GROSMAIRE *et al.* 2019; GROSMAIRE 2019). It is therefore a case of modified meiosis. This abortion gives a valuable clue to the mechanism, which is therefore probably the central fusion. Central fusion can manifest itself in two ways. Either meiosis is normal and the products of the first division of meiosis fuse, or the first division is aborted and the second division restores ploidy by separating the sister chromatids.

In central fusion many characteristics of the sexual syngamy are maintained. Since it is derived from meiosis, the need for physical contact between the chromosomes for their segregation is still relevant (KLECKNER 1996). Crossing over and recombination are therefore maintained in central fusion. This is in the case in *M. belari* as chiasmata are always observed at meiosis in cytological studies. If one crossover is systematically observed for a chromosome, there may be loss of heterozygosity (LOH) on the entire

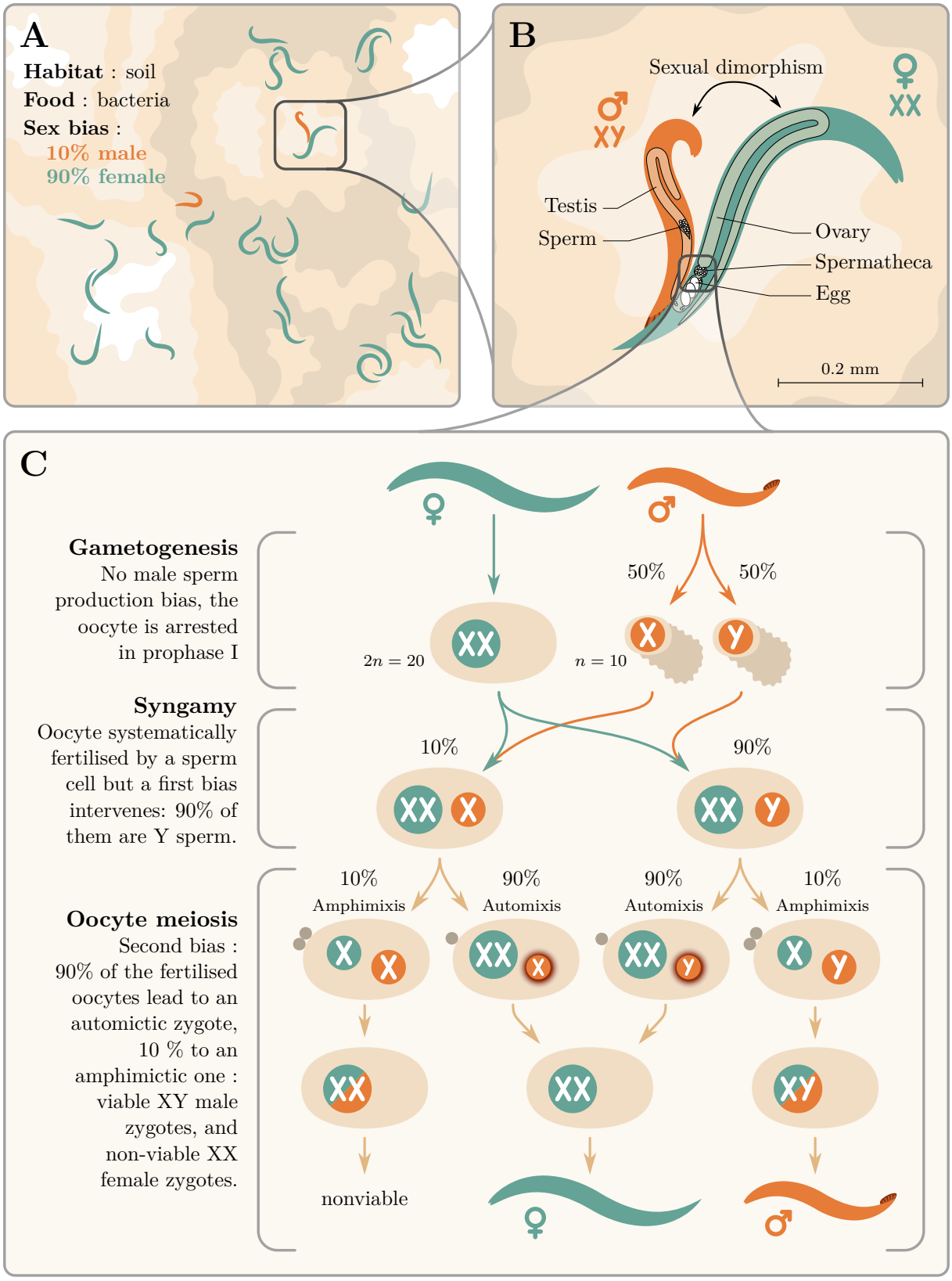


Figure 2: Biology of *Mesorhabditis belari*. (**A**) It is a bacterial-feeding free-living (not parasitic) species of anisogamous and gonochoric nematode with a strong female-biased sex ratio (90%). (**B**) The male (XY), smaller than the female (XX), provides the female with sperm through copulation, which she stores in her spermatheca. (**C**) This sperm is necessary to trigger further meiosis of the oocyte stuck in prophase I. The male genetic material is then either eliminated in autimixis or fused to the female genetic material in amphimixis. This determination of sex by an XY-type system thus depends on the type of fusion of the genetic material at the origin of the zygote formation.

recombined portion. In central fusion there is no LOH if there is segregation together of: (i) the two chromatids that did not recombine or (ii) the two chromatids that recombined together (Fig. 3). Recombinant chromosome portions always run from the chiasma to the tip of the chromosome. Thus LOH is more common at the tips than in the centre of the chromosomes but concerns the entire length of the chromosome (ENGELSTÄDTER 2017).

The increase in homozygosity should result in an increase in linkage disequilibrium. Linkage disequilibrium (LD) is a pairwise measure of whether two alleles that segregate in a population (*i.e.* have a frequency greater than 0 and less than 1) are: (i) randomly associated in the genomes of the individuals in the population (zero LD), (ii) more frequently associated than randomly (positive LD), or (iii) less frequently associated than randomly (negative LD). A "strong linkage disequilibrium" between two alleles corresponds to a very positive or very negative LD. When homozygosity is very high, the recombining chromosomes are very similar. Thus, recombination changes the allele combinations along the chromosomes very little. It leads to a mechanical increase in LD since recombination, the mechanism capable of breaking down allele associations, no longer does so (FLINT-GARCIA *et al.* 2003).

All things considered, the reproductive system of *M. belari* which involves 90% of females produced by central fusion automixis and 10% of males produced sexually should result in: (i) a high linkage disequilibrium compared to a comparable fully sexual population and (ii) a pattern of heterozygosity levels along the chromosome: highly homozygous ends and more heterozygous middle.

I.c Atypical reproduction, but a normal genome!

Despite these predictions, the genome of *M. belari* surprisingly has (i) no linkage disequilibrium, and (ii) a level of heterozygosity corresponding to that of a sufficiently large panmictic (sexual with random mating) population (no departure from HARDY-WEINBERG expectations), without a pattern along the genome.

The reason for no LD is probably closely related to the reason for the unexpected level of heterozygosity, the absence of many LOH as expected being potentially the reason for the weak linkages between loci.

The level of heterozygosity is measured by a statistic called F_{IS} which ranges from -1 when heterozygosity is complete to 1 when homozygosity is complete. A null F_{IS} corresponds to the HARDY-WEINBERG equilibrium found in panmictic populations. It is known that fully clonal populations have very negative F_{IS} (very high heterozygosity) due to an total absence of LOH and that population doing central fusion have a rather positive F_{IS} with a pattern along the genome as explained above. It is therefore surprising that a species in which all females are produced asexually has such a null F_{IS}. In addition,

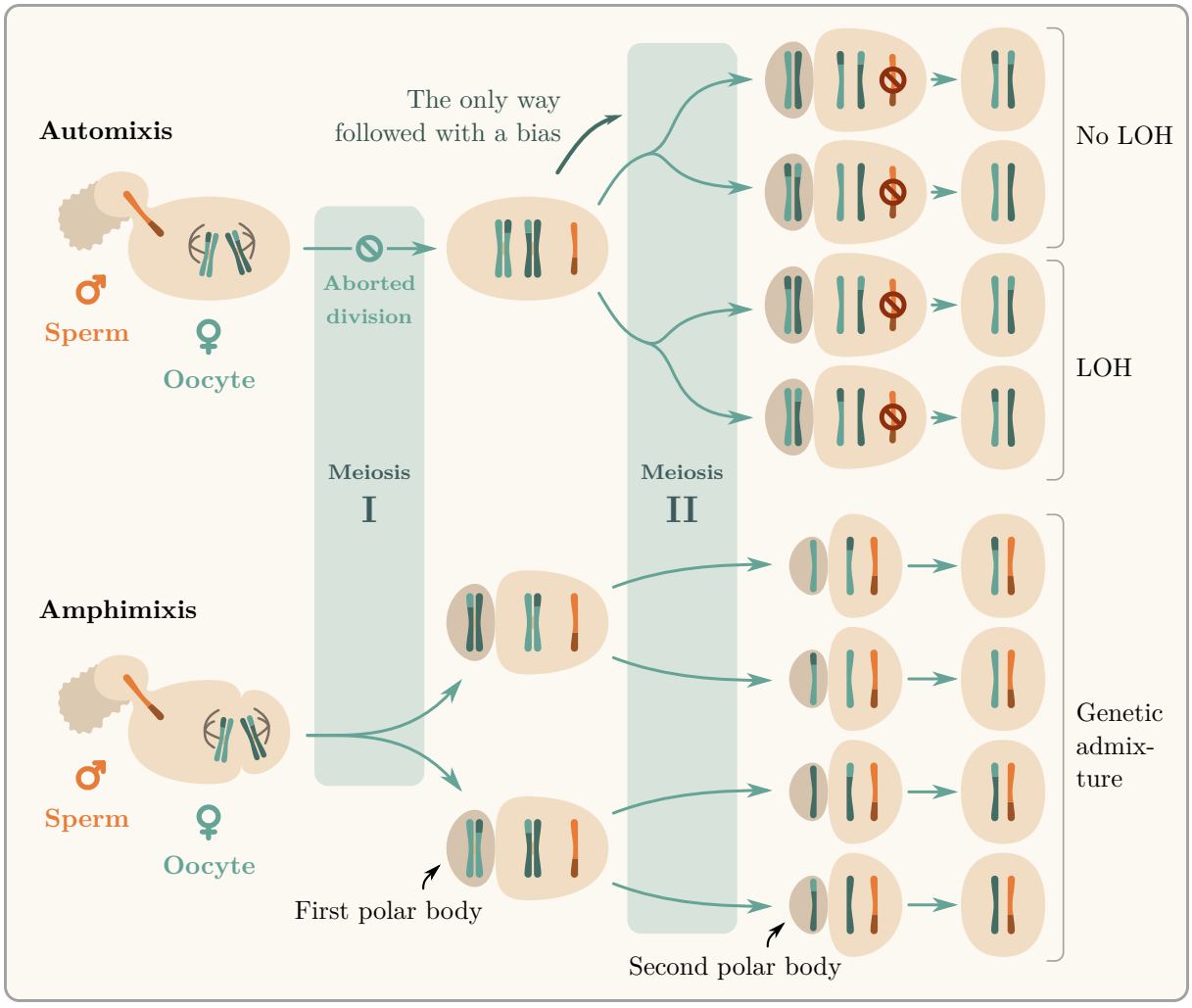


Figure 3: Reproductive pathways in *Mesorhabditis belari*. The form of automixis here is central fusion with abortion of the first meiosis division. Usually central fusion leads to a high loss of heterozygosity (LOH) due to recombination (lower pathway of automixis meiosis II). A chromosome segregation bias as hypothesised here, only the upper pathway occurs, without LOH.

the absence of LD shows that crossing-over does occur and should thus lead to LOH hence positive F_{IS}, at least in some genomic regions. Several hypotheses can explain this paradox.

First, a small proportion of females may be sexually produced. In a population without inbreeding, a small proportion of sexually produced females could push the F_{IS} towards zero and could also breakdown LD. Unpublished analytical results confirm this hypothesis but with a serious drawback: it takes a lot of sexually produced females (which should have been noticed experimentally) in a large random mating population, which is unlikely. In the case of a small population with high inbreeding, a small proportion of sexually produced females could push the F_{IS} towards 1 (high homozygosity over the whole genome). Analysis shows that a fairly precise combination of inbreeding level and sexually produced females is needed to obtain such a null F_{IS}. Thus although a proportion of sexually produced females is possible, it is unlikely that this parameter is sufficient to

explain the level of heterozygosity in *M. belari*.

A second hypothesis can be put forward to justify a null F_{IS}: taking into account deleterious mutations. Generally, a large proportion of mutations are deleterious and recessive (even if there is no consensual estimate of DFE in *Caenorhabditis elegans* yet (GILBERT *et al.* 2022), which is a species relatively close to *M. belari*). They therefore lead to a decrease in fitness, particularly for individuals that are homozygous. This is the case for offspring resulting from automixis where chromosomal segregation has led to a LOH (Fig. 3). If these individuals were eliminated from the population, the only remaining individuals who did not undergo LOH could explain the lack of LOH at the population level. This assumption is undermined by the low embryonic mortality observed in *M. belari* (GROSMAIRE *et al.* 2019). Nevertheless, it cannot be excluded that deleterious mutations, which advantage heterozygous genotypes by their recessiveness, may play a role here.

My third hypothesis implies the emergence of a mechanism never before observed. It is possible that the central fusion in *M. belari* is accompanied by a chromosome segregation bias. As mentioned before, in central fusion recombination is maintained. For there to be no LOH in the zygote, each of the 10 chromosome pairs must segregate in such a way as to achieve one of the two modes of segregation that maintain heterozygosity instead of segregating randomly (Fig. 3). It is possible that such a bias achieving this lack of LOH is the explanation for the characteristics of the *M. belari* genome. Recent cytological observations suggest that it may occur in *M. belari* (Delattre 2022, unpublished results). It is also possible that this bias is not total, and that a small frequency of LOH is possible.

A fourth and final hypothesis is that of strong inbreeding. It is based on the observation that the fertility of reproduction between brothers and sisters is higher than average (GROSMAIRE 2019). With a biased central fusion that equates to clonality (no LOH) with recombination, the F_{IS} should be very negative. Inbreeding could allow an increase in F_{IS} through loss of heterozygosity and thus allow a null F_{IS}.

Of course all four hypotheses are not mutually exclusive and it is possible that they interact in such a way that all four are necessary to explain the level of heterozygosity in *M. belari*. It is also difficult to predict the effects of their potential interactions on the genome dynamics of the species.

In order to explain this apparent incongruence between the reproductive system of *M. belari* and its level of heterozygosity and to test these hypothesis, I have built a population genetics model that allows to simulate the reproductive system of *M. belari* and to understand the effect of this system and of the different parameters mentioned above on the level of heterozygosity. This allows to understand what assumptions are insufficient and to what extent combinations of these parameters could explain a null F_{IS} throughout the genome and no LD.

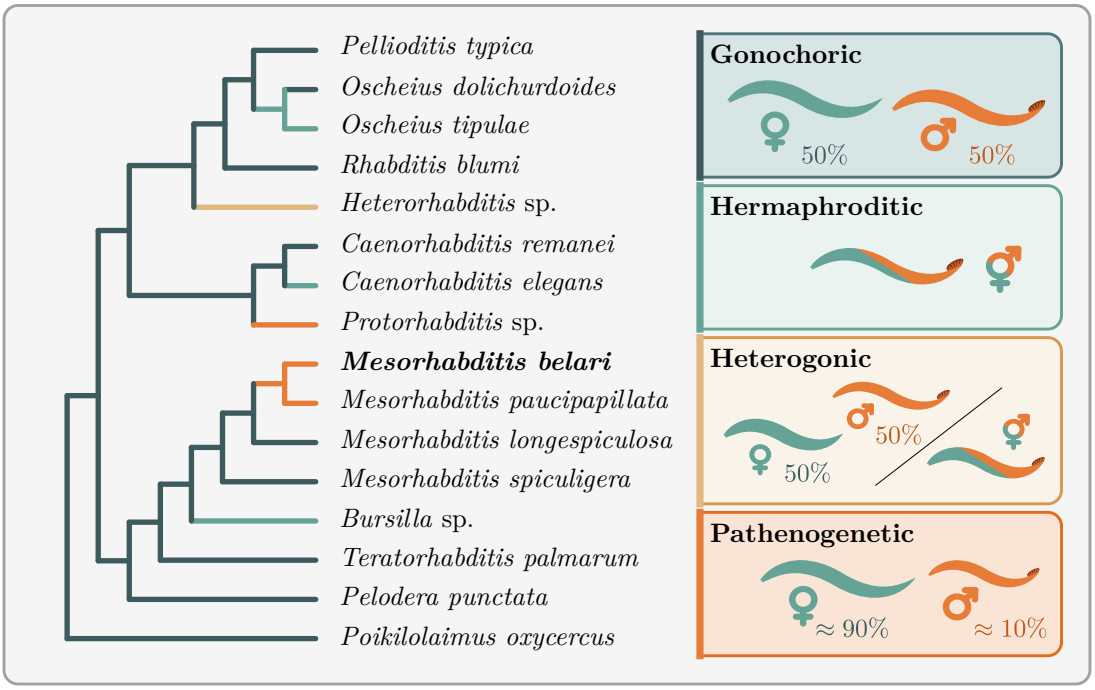


Figure 4: Phylogeny and reproduction modes in a sample of Rhabditidae species, a family of nematodes (adapted from LAUNAY *et al.* 2020 and KIONTKE and FITCH 2005). In this family, gonochoric sexual reproduction (separate males and females) is the ancestral state, but many species have diverged in this respect (KIONTKE and FITCH 2005). Some have lost this individual separated sexes (which is still maintained at the gamete level) and have become hermaphroditic, such as the well-studied *Caenorhabditis elegans*. Others have a form of alternation between hermaphodism and gonochorism, called heterogony, such as the species of the genus *Heterorhabditis*. Others, such as *M. belari*, have adopted an asexual system of reproduction (called parthenogenesis in animals).

I.d A reproductive system as a "missing link" in the evolution of clonality

The reproductive system of *M. belari* is still poorly understood. In any case, it is likely to be a system that is intermediate between sexual reproduction and clonal asexual reproduction. Thus, understanding the reproductive system of the species goes hand in hand with the study of the conditions of its evolution with the aim, in the longer term, of understanding the evolution of clonality. *M. belari* belongs to the Rhabditidae, a particularly diverse nematode family in terms of reproductive systems (Fig. 4). It is possible that in this family there is a greater potential for evolution of reproductive systems, in contrast to other clades potentially restricted by greater genetic and developmental constraints.

Several critical barriers to the evolution of asexuality exist (ENGELSTÄDTER 2008). Some of these barriers are still present in the *M. belari* breeding system. For example, the species still requires the activation of the egg cell by the entry of a sperm cell which probably also allows the supply of the male gamete centriole, that allows the formation of the meiotic spindle. However, at least two barriers have been overcome: the maintenance of ploidy through automixis and the biasing of the sex ratio of sexually produced individuals in order to avoid the lack of males. In addition, in *M. belari*, asexually produced females lose little or no maternal heterozygosity, thus avoiding a form of inbreeding depression

(ID) by the exposure of recessive deleterious mutations. It is indeed a barrier to the evolution of asexuality in that many types of automixis lead to a LOH (ENGELSTÄDTER 2008; ENGELSTÄDTER *et al.* 2011; SVENDSEN *et al.* 2015; ASHER 1970; PEARCY *et al.* 2006). This LOH leads to exposure of recessive deleterious alleles and thus to greater mortality of asexually produced individuals compared to sexually produced ones.

Assuming that *M. belari* reproduces by central fusion automixis, three parameters therefore distinguish the species from a standard sexual species: (i) the sex ratio of sexually produced individuals, (ii) the proportion of asexually produced females, and hypothetically (ii) the potential for biased chromosome segregation during central fusion.

We can imagine a scenario for the evolution of the reproductive system of *M. belari* through these three parameters. Let's consider a sexual population in which a mutant female does some central fusion automixis. The inbreeding depression of her automictic female offspring is low enough for them to reproduce and replace the resident fully sexual population. This pattern is repeated a few more times and a situation arises where many females are produced by automixis. The sexually produced individuals are always 50% female and 50% male. The chromosome segregation bias of the central fusion can evolve from this situation as females whose offspring have less LOH have a higher fitness due to a lower exposure of recessive deleterious mutations. It is more difficult to predict how the sex ratio bias of the sexually produced individuals would evolve. It is possible that if the population is subdivided and within subpopulations the lack of males (which are still required to trigger reproduction) may jeopardise its survival, the subpopulations that maximise the number of sexually produced males will be favoured.

To better understand the evolution of this atypical reprodutive system and to test the proposed scenario, I have developed a second model where the three parameters controlling the reproductive system can evolve.

II. MATERIAL AND METHODS

An individual-based, multi-locus model is chosen to approximate the genomic dynamics of *Mesorhabditis belari*. This model is implemented using the SLiM software (HALLER and MESSER 2019), where each individual's genome is explicitly defined.

II.a Genomic consequences of *Mesorhabditis belari*'s atypical reproductive system

I considered K subpopulations of size N, forming a total population of KN individuals. For all simulations the product KN is kept constant. I tested the effect of subpopulation size (increase in K, decrease in N) as a proxy for inbreeding to mimic reproduction

within small familial groups: the smaller the subpopulation, the higher the inbreeding rate within it compared to the whole population. There are separate sexes and a sex ratio $\rho = 0.9$ (female/total). The sex ratio is constant and imposed to each subpopulation. The generations are discrete and non-overlapping. Each individual is represented by a unique pair of autosome. This chromosome consist of $L = 10^5$ loci, with a rate of recombination per locus r equal to $1/L = 10^{-5}$, so that on average one recombination event is observed per gametogenesis (as is often empirically observed KLECKNER 1996). Since *M. belari* has holocentric chromosomes (there is no specific centromere ; REY *et al.* 2022), the location of the chiasma is randomly drawn according to a uniform distribution along the chromosome. The life cycle is shown on figure 5. First, mutations are imposed on the individuals. Then there is migration between populations. This is followed by the selection of breeders and finally a new generation is produced in each population independently by the reproduction of selected individuals.

Mutations

Two types of mutations are introduced. Their occurrence at a locus replaces the mutation that preceded them at the same locus. The first type of mutation is a neutral type, which has no effect on fitness of the inviduals that carry it. These mutations are introduced to model neutral genetic diversity and to consider the effect of the reproductive system and of the genome dynamics imposed by the second type of mutation on this diversity.

The other mutations are slightly deleterious ones, which impose a decrease in fitness on their carrier. They are characterized by a selection coefficient s equal to 0.01, and a dominance coefficient h (ranging from 0 for a fully recessive mutation to 1 for a fully dominant mutation). h is set to 0.25.

I ran simulations with only neutral mutations or with neutral and deleterious mutations to see the consequences of selection on genome characteristics.

Migration

Each subpopulation is linked to others by a migration rate m. At each generation, a number X_f of females are swapped among subpopulations, knowing that X_f follows a binomial distribution of parameter $n = \rho KN$ and $p = m$. The same procedure is carried out for males, with the variable X_m following a binomial distribution of parameter $n = (1 - \rho)KN$ and $p = m$. This separation of male and female migration treatments ensures that the sex ratio remains constant in each subpopulation, but it does not prevent a migrant from returning to its initial subpopulation (so the effective migration rate is $m(1 - 1/K)$). For the simulations, in order to isolate the populations and allow for inbreeding within them, the migration rate m is set to 0.0005.

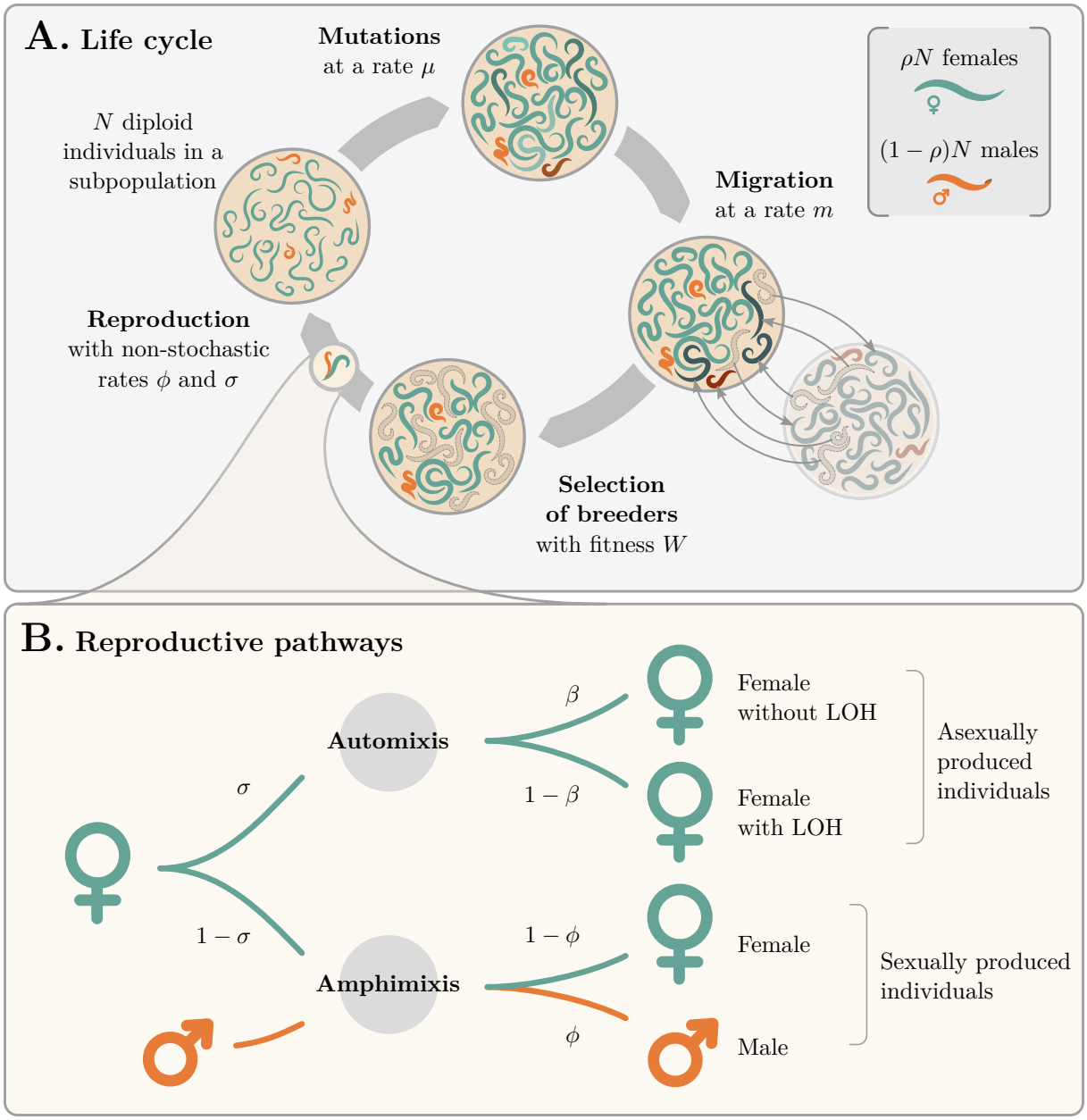


Figure 5: Life cycle of a subpopulation (**A**) with, in this case, two sub-populations exchanging individuals during migration, and (**B**) reproductive pathways considered.

Selection

Fitness is a probability of reproducing. Selection of breeders is independent in each of the populations (for a given individual only the fitness of the individuals in the same population has an effect on its probability of being sampled). The fitness of an individual corresponds to the product of the fitness effects of mutations it contains. It depends on the effect on fitness s, dominance h and the heterozygous or homozygous situation in which mutations are found. The fitness W_i of an individual i is thus :

$$W_i = (1-hs)^{n_1}(1-s)^{n_2} \quad (1)$$

with n_1 the number of heterozygous deleterious mutations, and n_2 the number of homozygous mutations. The selection is based on this fitness. The probability p_i of reproduction of a female i is calculated as

$$p_i = \frac{W_i}{\hat{W}} \tag{2}$$

where $\hat{W} = \sum_i W_i$ is the sum of fitness of females. The same procedure is followed for the drawing of the males.

In each generation and in each subpopulation, N females are drawn with replacement. The males are also drawn with replacement, but for reasons of efficiency of the simulations they are only drawn in the case of sexual reproduction.

Reproduction

The two ways of producing offspring are distinguished as in *M. belari* : a proportion σ of offspring are produced asexually by automixis (Fig. 5), mandatorily leading to the production of females. The rest of the reproduction events are standard sexual events, with mating with a randomly drawn males from the same subpopulation. The mating is completely random, hence there is no sibling-sibling preferential mating, contrary to what has been observed empirically. A proportion ϕ of those amphimictic events produce females. Thus we have a female sex ratio ρ which is such that

$$\rho = \sigma + (1 - \sigma)\phi \tag{3}$$

The rates σ and ϕ are non-stochastic, *i.e.* the number of offspring from each reproductive pathway is fixed *a priori* for each simulation's generation in order to have an asymptotically exact rate.

In order to test the effect of the sexual production of females, I test several ϕ values. Thus to keep the same sex ratio ρ over the whole set of simulations, it is the σ that decreases a little bit when ϕ increases.

Central fusion automixis is associated with a chromosome segregation bias β that leads to the non-random association of chromosomes in the genotypes of offspring when $\beta \neq 0.5$ (Fig. 5). I tested several values of this bias will in order to understand to what extent the central fusion must be biased to retrieve the observations on the *M. belari* genome.

For comparison purposes I also ran simulations replacing the central fusion with clonality and sex, preserving each time that only females are produced.

Burn-in

Each simulation of the *M. belari* system is preceded by a burn-in. This consists of running the model with sames parameters but a standard sexual reproduction and a sex ratio of 50:50. This burn-in period allows the simulation of the biology of the species

to be started on the basis of a population that already has *a priori* a non-virgin genetic background.

II.b Simulating the evolution of the reproductive system of *Mesorhabditis belari*

In the second model, I study the evolution of the atypical reproductive system of *M. belari* from a standard sexual population. Compared to the previous model controlling reproduction, the parameters σ (proportion of asexually produced offspring), ϕ (proportion of females among sexually produced individuals) and β (segregation bias) are no longer fixed but under the control of three independent evolving loci. At the end of the burn-in, instead of going directly to a reproductive system of the *M. belari* type, this triggers the beginning of the phase where the three loci defining this reproductive system can evolve. An important point to note is that this second model assumes that central fusion is not directly biased. Its bias is controlled by an independent locus. As biased central fusion has never been described in contrast to classic central fusion, it seems a conservative assumption.

Evolutionary dynamics of loci

Each evolving locus is independent of any other locus. Transmission from parents to children of an evolving locus follows the same rules as transmission of loci on the focal chromosome, taking into account the potential loss of heterozygosity through chromosome segregation during gynogenesis. It can take two different values, a resident value or a mutant value. At the beginning of the simulations, all individuals are homozygous for the resident allele and a mutant allele is randomly introduced in one individual of the population. If this mutant becomes fixed in the population, this mutant allele becomes the resident allele. If the mutant disappears, another mutant is directly reintroduced into the population at random (Fig. 6).

Genotype to phenotype map

The resident and mutant alleles are associated with G_r, G_m, their respective genotypic values, linked by the relation

$$G_m = G_r \pm \Delta \tag{4}$$

For σ only, G_σ cannot go below 0. The genotypic values are therefore all real multiples of Δ. I have choosen $\Delta = 0.1$ This is a relatively high value, but it allows the evolution of the parameters to be not too slow so that the simulations are not too long. The genotypic value of an individual corresponds to one of the two values of its alleles, drawn equiprobally.

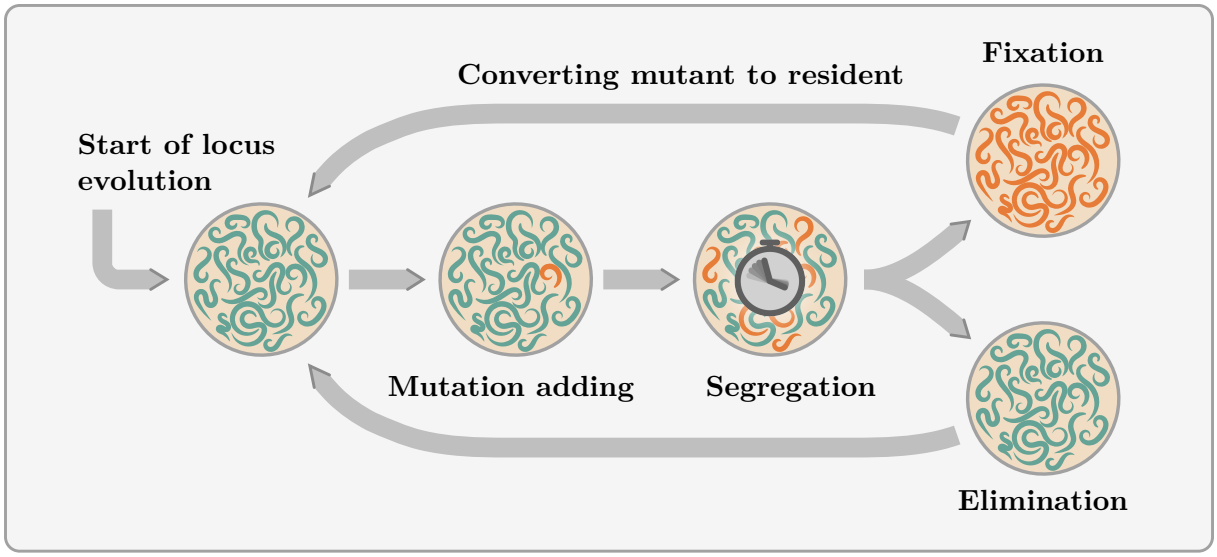


Figure 6: Evolutionary dynamics of the three evolving locus.

In order to reduce the infinite range of genotype values G and to take into account the starting value of each of the traits and their possible evolution, we define three functions for the three traits that convert genotypic values G into phenotypic values P. The gynogenesis rate starts at 0 and can theoretically go up to 1, the segregation bias and the segregation bias start at 0.5 and can reach 0 or 1:

$$P_\sigma = f(G_\sigma) \quad ; \quad P_\phi = \frac{1}{2}\left(1 + f(G_\phi)\right) \quad ; \quad P_\beta = \frac{1}{2}\left(1 - f(G_\beta)\right) \tag{5}$$

knowning that

$$f(x) = \begin{cases} 1 - \left(1 - \frac{2}{\pi}\tan^{-1}(ax)\right)^b, & \text{if } g > 0 \\ \left(1 - \frac{2}{\pi}\tan^{-1}(-ax)\right)^b - 1, & \text{otherwise} \end{cases} \tag{6}$$

The parameters a and b being form parameters that define whether the function tends more or less quickly to 1 as x increases. Here I use $a = 0.1$ and $b = 15$. A graphical representation of this function is given in Figure 7. Apart from causing the selection to slow down when the difference between the resident and mutant values if small, the use of such a function also asymptotically allows an accurate equilibrium value to be obtained (note that other functions with similar shape could be used).

The expression of the traits takes place during reproduction. It is then the value of the female traits that are used for the gynogenesis rate and the segregation bias and the male trait that controls the sex ratio of sexually produced offspring. In order to test the effect of the three evolving loci and their potential interactions, they will be made neutral (no effect on reproduction).

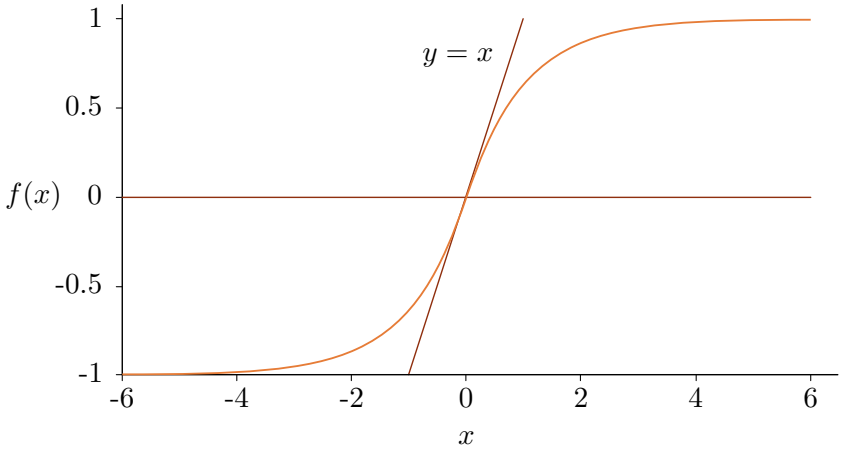


Figure 7: Representation of the function f that is used to convert the genotypic value to the phenotype values of traits. This is the upper loop which by multiple substitution leads to the evolution of the value of the loci at the population level.

Impose an additional inbreeding depression

The supposedly strong barrier to the evolution of asexuality (assuming that automixis mechanisms can emerge) is inbreeding depression (ID). ID corresponds to the decrease in fitness induced by a strong decrease in heterozygosity which leads to the exposure of recessive deleterious alleles (this decrease being caused by inbreeding or automixis for example). It is calculated as $1-w_1/w_0$ with w_0 the fitness of sexually produced individuals and w_1 the fitness of individuals undergoing a strong LOH. ID is usually expressed as a percentage: 10% ID means that individuals undergoing LOH have 10% less fitness than sexually produced individuals.

A strong ID should hold back the evolution of automixis if the chromosome segregation bias is not strong, preventing LOH. Since I am only modelling a single chromosome and the central fusion leads to a LOH in only half of the individuals produced, the maximum ID is 50% (the fitness of asexually produced females is on average 2 times smaller than that of sexually produced individuals). It is however very likely that in each automictic zygote, at least one chromosome experiences LOH, so they all undergo ID. In order to increase the reach of ID and to test its effect on the evolution of asexuality, I correct the fitness W of asexually produced individuals to $W_{corr} = CW$ such that

$$C = (1 - c)^{\beta(n-1)}; \tag{7}$$

With c the effect on the fitness of a chromosome and n the number of chromosome pairs (assumed constant, equals to 10). Thus when chromosome segregation bias β is equal to 1 (no LOH), there is no additional inbreeding depression imposed on asexually produced individuals.

I will test the effect of c on the evolution of automixis.

Extinction-recolonisation cycle of subpopulations

In this model, a higher migration rate is set, allowing the evolving loci to be transmitted not too slowly from one population to another. It should also be noted that here the parameters controlling reproduction are no longer fixed rates which ensure that all subpopulations have both males and females and can therefore reproduce. It is possible that populations may stochastically run out of males, especially if gynogenesis evolves and the percentage of males decreases. If a population has no more males, it becomes extinct. An extinct population is recolonised in the generation following its extinction by a male and at least one female randomly selected from the other population. This pair reproduces and together they form the next generation of the subpopulation.

II.c Statistics measured

The calculation of the statistics used is based on neutral mutations only. They are are performed at the scale of the whole population, not within each subpopulation. This way of calculating them is consistent with the way they were measured empirically, which makes the comparison meaningful.

Level of heterozygosity

I computed the F_{IS}, which is a measure of the deviation of the heterozygoty from what would be expected in random mating:

$$F_{IS} = 1 - \frac{H_o}{H_e} \tag{8}$$

with H_o the observed heterozygosity (percentage of heterozygous sites) and H_e the expected heterozygosity :

$$H_e = \frac{2}{L} \sum_{i=1}^{n} f_i(1 - f_i) \tag{9}$$

a sum over all the n mutations present in the population with f_i their respective frequencies. Watterson's θ and F_{IS} can be calculated on the whole genome or along it by dividing it into windows, allowing to distinguish if these measures have uneven values along the genome.

Linkage disequilibrium

Among the measures of LD that exist (DEVLIN and RISCH 1995), I have chosen r^2 (FLINT-GARCIA *et al.* 2003), one of the most common. It is a pairwise measurement that is done by pair of segregating mutations in a population. Let's consider two loci with two mutations each: one with mutations A and a with respective frequencies π_A and π_a

and a second with mutations B and b with respective frequencies π_B and π_b. The LD between these two loci is calculated as the difference between the frequency of the AB haplotype expected if there were a purely random arrangement between the two loci and that observed:

$$D = \pi_{AB} - \pi_A \pi_B \tag{10}$$

As the value of D is dependant on marginal mutation frequencies (GAUT and LONG 2003), only mutations that are present at more than 5% in the population are considered for the calculation. The standardized coefficient is then obtained as

$$r^2 = \frac{D^2}{\pi_A \pi_a \pi_B \pi_b} \tag{11}$$

(FLINT-GARCIA *et al.* 2003). The r^2 can range from 0 (for two unlinked alleles) to 1 (for two tightly linked alleles). Plotting r^2 as a function of the distance between positions of the mutation pairs for which it was measured helps to understand the pattern of linkage disequilibrium. Generally there is at least some positive linkage disequilibrium between nearby loci, and this decreases rapidly with distance.

III. RESULTS

III.a Genomic consequences of *Mesorhabditis belari*'s atypical reproductive system

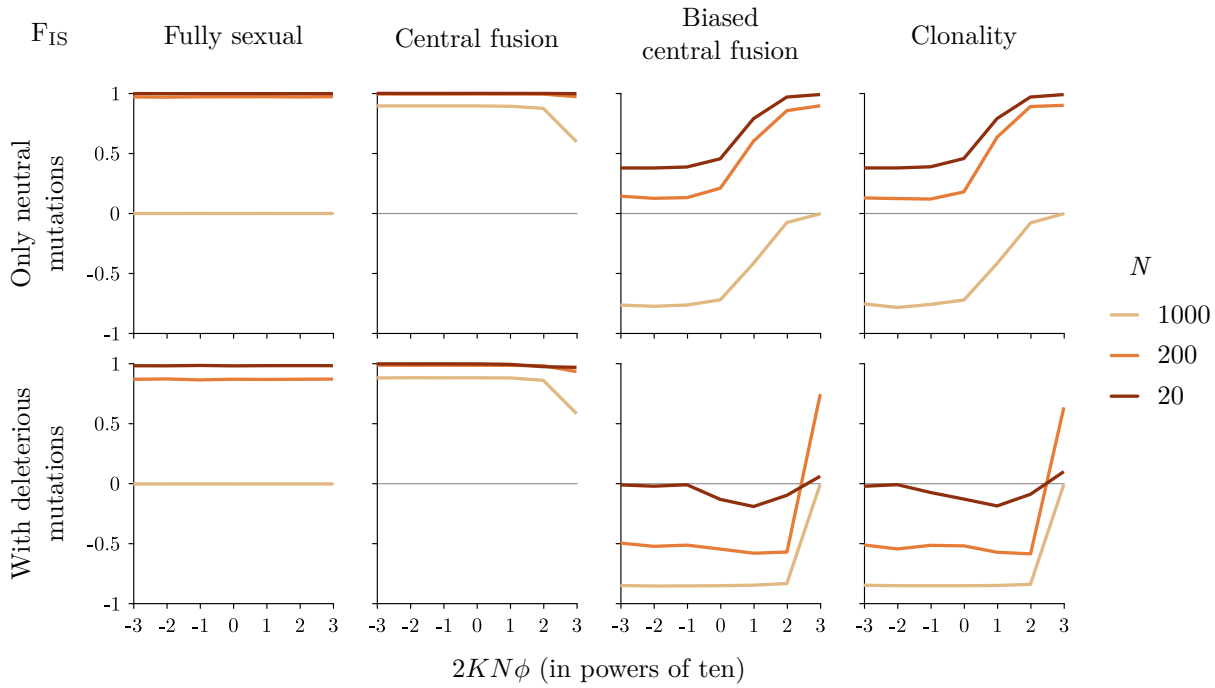
The aim is to explain why F_{IS} in *M. belari* is zero over the whole genome length and why there is no linkage disequilibrium through simulations testing different modes of reproduction. I will present the plotted results but a summary of these is available in Tab 1.

Level of heterozygosity

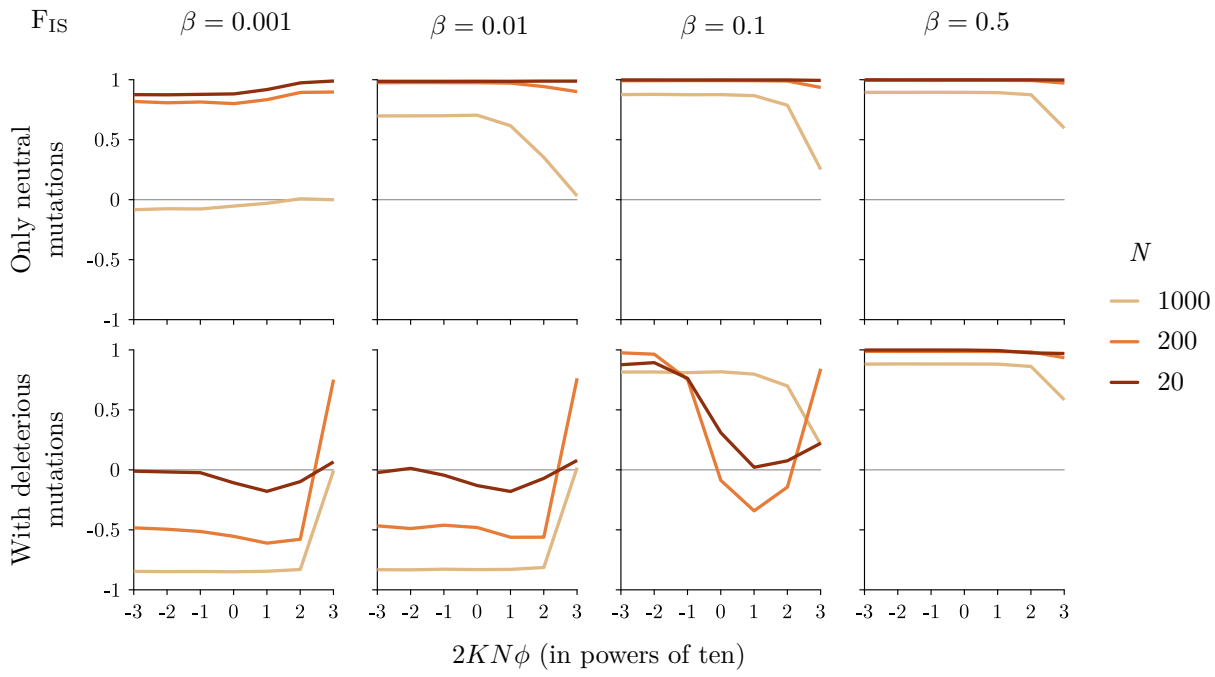
I first studied the genomic pattern of F_{IS} depending on the type of central fusion: classic central fusion, fully biased central fusion (without LOH) and different intermediate biased central fusion. Fully sexual and fully clonal reproduction were used for comparison. As expected, when reproduction is completely sexual, F_{IS} is zero in the case of a single large population and very positive when it is subdivided, regardless of the mutations considered (Fig. 8a). This confirms that this subdivision into populations generates a high rate of inbreeding.

In classic central fusion (50% of descendants undergoing LOH on part of their chromosome) the F_{IS} is highly positive whatever the size of the population, meaning that individuals become highly homozygotes (Fig. 8a). There is also an slight effect of inbreeding which increases the F_{IS} and a marginal effect of the proportion of sexually produced females. Here again there is little effect of the type of mutation considered. So globally, in central fusion, the loss of heterozygosity is so strong that the F_{IS} is close to one whatever the values of the other parameters.

In biased central fusion the results are very different. Given that the consequences on F_{IS} of biased central fusion (without any LOH) and clonality are similar (Fig. 8a), I will therefore describe here the consequences of these two modes of reproduction at once. Inbreeding increases F_{IS} in a very similar way whatever the rate of sexually produced females. The rate of sexually produced females also has the effect of increasing F_{IS}. It can be seen that this rate has little or no effect when it is low, between $2KN\phi = 10^{-3}$ and 10^{-1}. Considering deleterious mutations has the effect of globally reducing the F_{IS} for all parameter combinations. As deleterious mutations are recessive, the more heterozygous genotypes have an advantage, thus decreasing the homozygosity rate at the population level and thus the F_{IS}. Deleterious mutations allow to obtain a zero F_{IS} for low values of $2KN\phi$ and high inbreeding rate. There is therefore a balance here between the bias of central fusion which makes the F_{IS} negative as in clonality, and the inbreeding



(a) Different ways of producing females



(b) Different values of chromosome segregation bias β in central fusion

Figure 8: F_{IS} value after 10,000 generations (in addition to the 6,000 burn-in generations) as a function of the population rate of sexually produced females ($2KN\phi$), the level of inbreeding (imposed by N, the size of the subpopulation, knowing that KN is always equal to 1,000), the type of mutations (for deleterious mutations, $h = 0.25$ and $s = 0.01$), and finally the mode of reproduction. The values displayed are the averages over 100 simulations performed for each parameter combination. β is the central fusion bias (Fig. 5). Central fusion results shown in the upper graphs corresponds to a β bias of 0.5 (non-biased central fusion), equivalent to the lower right graph, and the biased central fusion to $\beta = 0$.

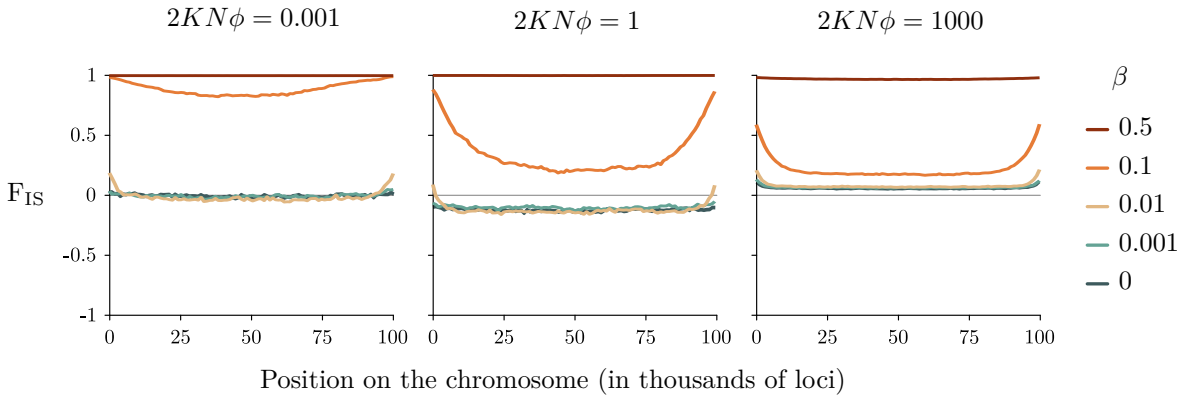


Figure 9: Chromosomal mapping of F_{IS} calculated by windows of 100 loci along the chromosome of 100,000 loci length, after 10,000 generations (in addition to the 6,000 burn-in generations), in 50 populations of 20 individuals, in central fusion and considering deleterious mutations, as a function of the population rate of sexually produced females ($2KN\phi$) and the different values of chromosome segregation bias β.

which increases it. It ultimately resulted in a zero score, especially when few females are produced sexually. As the difference between biased central fusion and clonality is only recombination, it has no significant effect on F_{IS} results.

For different bias values in central fusion (note that the results where $\beta = 0.5$ in Fig. 8b and central fusion in Fig. 8a correspond to identical reproductive systems), I have represented the F_{IS} along the genome (Fig. 9) in addition to the global F_{IS} (Fig. 8b). When only neutral mutations are considered, the F_{IS} of central fusion is globally very positive, whether for $\beta = 0.001$, 0.01, 0.1 or 0.5. When considering deleterious mutations, the F_{IS} obtained when $\beta = 0$ (biased centrale fusion Fig. 8a) is the same when $\beta = 0.001$ or $\beta = 0.01$ (Fig. 8b). Thus, deleterious mutations allow to obtain a zero F_{IS} for low values of $2KN\phi$ and high inbreeding rate when $\beta = 0.001$ or $\beta = 0.01$.

In addition, when β is between 0 and 0.5, regardless of the rate of sexually produced females, a pattern can be observed along the chromosome. The tips have a higher F_{IS} than the middle of the chromosome (Fig. 9). This was expected, as recombination causes homozygosity to be lost especially at the tips of chromosomes: the closer a locus is to a tip, the greater the probability that a recombination event will affect it. This pattern is most apparent when β is not too low ($\beta > 0.001$) and not too high ($\beta < 0.5$). When β is too low, the loss of heterozygosity is not high enough for such a pattern to emerge and conversely when β is high the loss of homozygosity is so high that it is maximal over the whole length of the chromosome.

Linkage disequilibrium

Secondly, I studied the linkage disequilibrium (LD, i.e. the tendency for mutations at different loci to be transmitted together) depending on reproduction modes. LD is low regardless of the reproductive mode considered when deleterious mutations are considered

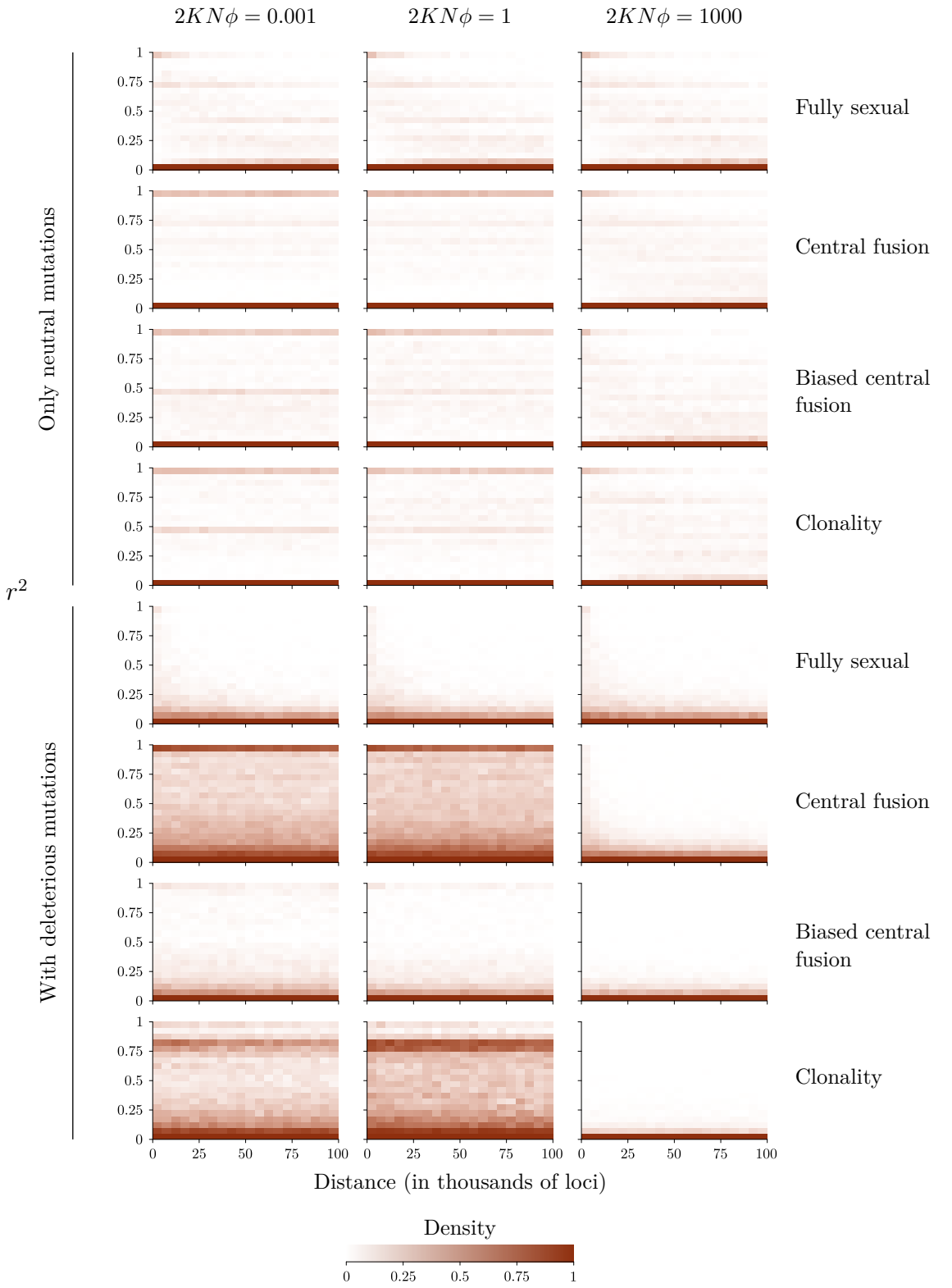


Figure 10: Density of linkage disequilibrium r^2 values as a function of the distance between the loci on which this pairwise statistic was measured, computed after 10,000 generations (in addition to the 6,000 burn-in generations) and as a function of the population rate of sexually produced females ($2KN\phi$), the type of mutations (for deleterious mutations, $h = 0.25$ and $s = 0.01$) and the different ways of producing females. Here we have $N = 20$ ($K = 50$), central fusion corresponds to $\beta = 0.5$ and the biased central fusion to $\beta = 0$.

Table 1: Summary of results. Only three scenarios that succeed in reproducing the empirical observations in *M. belari*.. Among them, only the one that considers deleterious mutations and a high inbreeding rate is realistic according to what is known empirically about *M. belari*.

Chromosome segregation bias	Rate of sexually produced females	Deleterious mutations	Inbreeding	F_{IS}	Linkage disequilibrium
Without	Low	Without	Low	≈ 0.9	High
			High	≈ 1	Low
		With	Low	≈ 0.9	High
			High	≈ 1	High
	High	Without	Low	≈ 0.5	Low
			High	≈ 1	Low
		With	Low	≈ 0.5	Low
			High	≈ 1	Low
With	Low	Without	Low	≈ -0.75	Low
			High	≈ 0.4	Low
		With	Low	≈ -0.75	Low
			High	≈ 0	Low
	High	Without	Low	≈ 0	Low
			High	≈ 1	Low
		With	Low	≈ 0	Low
			High	≈ 0.1	Low
Empirical observation in *M. belari*				0	Low

(Fig. 10). When deleterious mutations are considered, it seems that the LD is low in sex and in biased central fusion, but not in classic central fusion or in clonality. In classic central fusion, in spite of recombination, the large LOH has a large decrease in the effective recombination rate. Thus recombination no longer has the effect of breaking the links between loci, resulting in a large LD. In clonality the reason is quite different: there is no recombination so the links between the alleles are never broken, resulting in a large LD. Finally, there is globally no LD when a significant number of females are produced sexually ($2KN\phi = 1000$), sex having the effect of breaking the links between the loci through recombination.

III.b Simulating the evolution of the reproductive system of *Mesorhabditis belari*

The aim is to understand under what conditions the central fusion, its bias and the sex ratio bias of sexually produced individuals can evolve in a sexual population. As specified in section II.a and Figure 5, we will refer in the following to the automixis rate as σ, to the chromosome segregation bias of central fusion as β and to the sex ratio bias of sexually produced individuals as ϕ. The parameter C corresponds to the supplementary inbreeding depression (ID) level imposed on offspring produced through automixis.

When the three evolving loci are neutral, their evolution is driven only by genetic drift

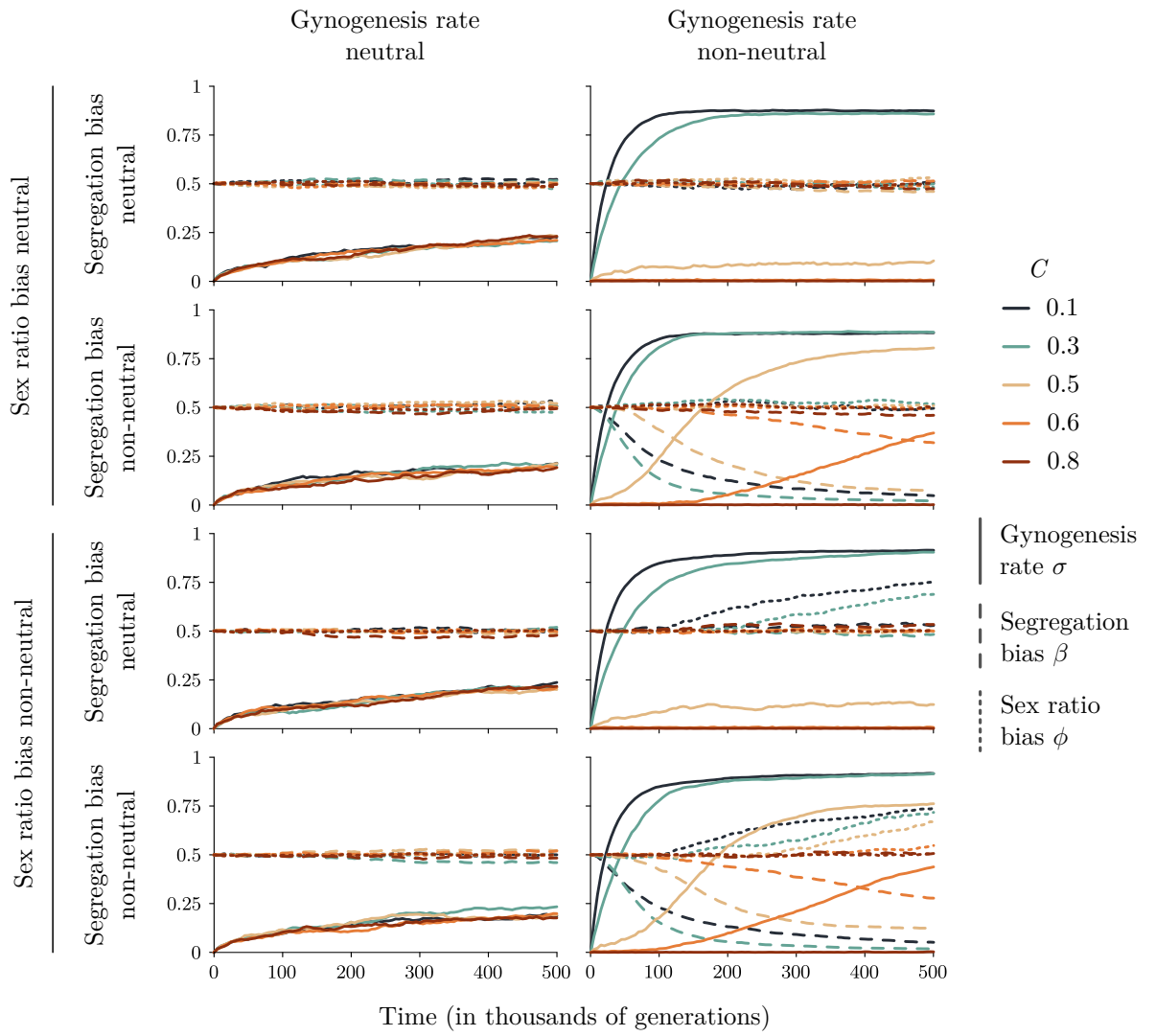


Figure 11: Phenotype values for the three evolving loci as a function of time, loci neutrality, and inbreeding depression C imposed in addition to that induced by the modelled chromosome. Time 0 corresponds to the end of the 6,000 generation burn-in. The other parameters are $K = 5$, $N = 100$.

(Fig. 11). On average the chromosome segregation bias β is equal to 0.5 and the sex ratio bias ϕ is equal to 0.5 throughout the simulations since they can evolve towards both 0 and 1. The gynogenesis rate σ cannot be negative and has a first value of 0, so it tends to increase with time by drift. When σ is neutral but one of the other two is not, the results are the same as when all three are neutral.

When only σ is not neutral, gynogenesis evolves to about 0.85 but only when $C < 0.5$. In the case where $C = 0.5$, the evolution is towards values lower than when it is neutral, meaning that gynogenesis is counter selected. In the case where $C > 0.5$, σ is on average about 0 over the duration of the simulations.

When both σ and β are non-neutral, the asymptotic value of σ when $C < 0.5$ is higher, of the order of 0.9. Notably, we also notice that the segregation bias allows for

an evolution of gynogenesis when $C = 0.5$ and $C = 0.6$. In general, the chromosome segregation bias evolves very quickly when $C \leq 0.5$. It is slower when $C = 0.6$. When $C = 0.8$, there is a counter-selection of σ since it remains at 0 whereas neutrally its value should increase a little.

When only σ and ϕ are non-neutral, the situation is close to when only σ is non-neutral. However, for values of C where gynogenesis is selected ($C < 0.5$), there is selection for an increase in the ϕ proportion of males in the sexually produced individuals. The increase in ϕ allows in parallel a slight increase in sigma.

When the three loci are non-neutral, there are: (i) fast selection of σ and β when $C < 0.5$, (ii) slower selection of σ and β when $0.5 \leq C < 0.8$ and (iii) counter selection of σ when $C = 0.8$. Once the sex ratio is biased in favour of females, ϕ is selected at relatively similar rates for the different values of C, taking into account the time lags in the selection of σ.

Thus, to summarise, when it cannot be biased, central fusion is only selected when the inbreeding depression is less than about 50% (i.e. the offspring produced by central fusion have a fitness at least equal to 50% of the fitness of the sexually produced offspring). When a second locus can bias the central fusion and reduce the loss of heterozygosity of the resulting offspring, central fusion can be selected for inbreeding depression values up to at least 60%. Finally, the sex ratio bias is only selected when the number of males in the population is low, i.e. when many females are produced asexually, thus biasing the overall sex ratio of the population.

IV. DISCUSSION

The reproductive system of the parthenogenetic nematode *Mesorhabditis belari* is not yet fully understood although it is likely to involve some form of central fusion. It has a genome-wide null F_{IS} and no linkage disequilibrium, despite a largely asexual reproductive system. The simulations whose results are presented here show : (i) that classic central fusion is not able to explain the genome characteristics of *M. belari*, (ii) that biased central fusion with high inbreeding and in simulations where deleterious mutations is able to explain the genome characteristics of *M. belari*, and (iii) that the evolution of central fusion automixis is favoured by the possibility to select a chromosome segregation bias allowing the avoidance of inbreeding depression cost.

IV.a Model predictions help to characterize the atypical reproductive system of *Mesorhabditis belari*

The classic central fusion fails to explain the genomic characteristics of *M. belari*. It appears that the loss of heterozygosity is too great to explain a null F_{IS}. The pattern of LD in this reproductive regime is also inconsistent with observations. The decay of the LD with distance is well known as a function of the effective recombination rate (HUDSON 2004). In classic central fusion there is recombination but so much LOH that the effective recombination is very reduced and so the LD is high.

Considering the effect of revessive deleterious mutations in classic central fusion showed no effect here. This is contrary to the hypothesis that their effect should have favoured heterozygous genotypes, tending to decrease F_{IS}. It is possible that imposing a higher mutation rate could indeed have had this effect, but it would require very high mutation rates. It would be neither realistic nor in agreement with empirical observations about embryo abortions. It is therefore unlikely that *M. belari* will carry out classical central fusion.

The biased central fusion is much more convincing to explain the genomic characteristics of *M. belari*, all the more so when deleterious mutations are considered. First, the null F_{IS} is obtained only when considering the biased central fusion or clonality, a low proportion of sexually produced females and a high inbreeding. Second, the low linkage disequilibrium is obtained only in biased central fusion and sex. Thus only the biased central fusion is able to explain both. In addition, there is a certain tolerance for some segregation events inducing LOH during central fusion (of the order of one percent), these do not affect the global F_{IS}. On the other hand, a pattern along the chromosome is observable from 1% of automixis events inducing LOH. The chromosome segregation bias of central fusion in *M. belari* is therefore probably very strong.

Central fusion is a particularly frequent form of automixis (LENORMAND *et al.* 2016).

However, to our knowledge, such a bias in chromosome segregation during central fusion has never been observed, nor even suggested. Experimental results not yet published confirm the existence of this bias. It is not yet possible to follow each pair of chromosomes individually, but it is possible to count the number of recombined and non-recombined chromosomes in an automictic zygote by staining. It turns out that an even number of recombinant and non-recombinant chromosomes is systematically observed, which is very unlikely if segregation were random.

IV.b How *Mesorhabditis belari*'s reproductive system may have evolved?

My modelling results and the experimental results of GROSMAIRE *et al.* (2019) (in addition to the unpublished results) fully agree in depicting a reproductive system of *M. belari* that has three main characteristics: (i) a gynogenesis rate of about 90%, (ii) a chromosome segregation bias during central fusion and (iii) a sex ratio bias of the sexually produced individuals, which are only males. It raises the question of how it may have evolved.

Like many other automixis mechanisms (ENGELSTÄDTER 2008; ARCHETTI 2010; ARCHETTI 2004) and contrary to clonality, central fusion leads to a loss of homozygosity through recombination, thus exposing recessive deleterious alleles and leading to inbreeding depression. So in what situation should gynogenesis evolve? According to which sequence of events? Is it necessary to have a very strong segregation bias for it to evolve, and according to what level of inbreeding depression? Is it possible that a male bias in sex determination leads to an increased production of males sexually, which would lead to the selection of an asexual production of females? This second model gives an first idea of the answers to these questions.

The model confirms that at too high levels of inbreeding depression, the evolution of classic central fusion automixis is prevented. This threshold being around 50%. It also shows that the possibility to select a chromosomal segregation bias allows an evolution of automixis for larger values of inbreeding depression, to at least 60%.

Once gynogenesis is selected, there is a trade-off that tends to stabilize its rate. It is indeed necessary for females to be fertilized to produce zygotes and it is therefore necessary that the females produce enough males. There are two strategies that allow pseudogamy to be viable (BEUKEBOOM and VRIJENHOEK 1998) considering this need for egg activation. The first, found in species in which there is only females, is the fertilisation of the female of the gynogenetic species by the sperm of males of other closely related species and is called sperm parasitism (ex : JANKO *et al.* 2007, reviewed in SCHLUPP 2005). The second is fertilisation by a conspecific that has a male function (a male or hermaphrodite). These two strategies do not imply the same conditions for maintaining the system. In the case of *M. belari*, the presence of a male places the species in the

second category, as do many species of parthenogenetic *Mesorhabditis* species (LAUNAY *et al.* 2020). This situation is stable if the males mostly fertilise female kin, so that the investment in males is not made to the benefit of the other females. In this framework, a sex ratio of 90% females is evolutionarily stable (GROSMAIRE *et al.* 2019). My model confirms this value of an evolutionarily stable strategy. It would be interesting to identify the reasons for this non-adoption of sperm parasitism in *Mesorhabditis*. This could be explained by the absence of a sufficiently large quantity of available sperm of a related species (by a lack of compatibility, or a refusal of copulation by males of the other species due to non-conspecificity).

It is also notable that the selection of a sex ratio bias in sexually produced individuals is more difficult to implement in the model. A sex ratio bias is indeed difficult to obtain according to FISHER's principle (FISHER 1930). This principle is a relatively simple verbal reasoning that explains the persistence of a 50:50 sex ratio. It explains that if a population produces more males than females for example, the females, who are less numerous, will have a better chance of reproducing than the males. Thus, females that produce more females have a favoured transmission, and their genotype spreads in the population. The same reasoning applies in the case of a higher production of males, so the population tends asymptotically to a 50:50 sex ratio, the proportion where there is no longer any advantage to produce more of one sex or the other. Since males do not pass on their genes to automictic females in *M. belari*, this reasoning only concerns the sex ratio of sexually produced individuals.

Here the reason for the sex ratio bias selection obtain here is population-wide selection. If a population goes extinct because of a lack of males, other populations that hypothetically produce more males will be more perennial and replace it. It should be noted, however, that the FISHER's principle is constantly applied within them, tending to reduce the sex ratio to 0.5. Without other conditions not explored here that would favour male production, it seems that a male production bias is not the cause of an evolutionary response through the production of asexual females, but rather a response to the lack of males due to the production of a large quantity of asexual females.

The models presented here have shown that deleterious mutations should not be neglected in population genetic models when they are likely to influence genome dynamics. Mutations are one of the major forces of evolution, the main source of genetic diversity, but they are also the source of many costs. Mutations imposed on species in a constant flow (CHINTALAPATI and MOORJANI 2020; HODGKINSON and EYRE-WALKER 2011) are mostly neutral or deleterious (EYRE-WALKER and KEIGHTLEY 2007). Deleterious mutations that evolution tends to purge therefore have a non-negligible effect on the genomes shaping. They cause background selection (CHARLESWORTH 2012; HUDSON and KAPLAN 1995), and linked selection (SLOTTE 2014) and thus affect neutral diversity. Since

the purging of deleterious mutations is greatly reduced in modes of reproduction where recombination and heterozygosity are altered, their consequences can no longer be considered negligible. The example of the evolution of *M. belari*'s system illustrates this. Indeed, a strong barrier to central fusion selection is LOH which induces a strong inbreeding depression by exposure of recessive deleterious alleles (ENGELSTÄDTER 2008; ARCHETTI 2010; ARCHETTI 2004). Chromosome segregation bias in *M. belari*'s automixis seems to be an inovation allowing the crossing of this barrier. In addition to this, the consideration of mutations has led to a better understanding of *M. belari*'s system, making it possible to better mimic the empirically measured species genome characteristics.

IV.c Conclusion

I have shown here by means of population genetic simulations that the reproductive system of the pseudogamic species *Mesorhabditis belari* most likely involves a never before observed type of automixis: biased central fusion. This innovation avoids the inbreeding depression that is inevitably imposed on the offspring when heterozygosity is lost in classic central fusion. In addition, I have shown that this central fusion bias may have facilitated the selection for pseudogamy in this species.

My work revealing the details of asexuality in a long-known species highlights that the study of asexuality is still in its infancy. Automixis has been known for a long time (MOGIE 1986), but has long been neglected by theoretical models. Recent research that have uncovered previously unrevealed automixis systems of well known species (NOUGUÉ *et al.* 2015; SIMION *et al.* 2021; GROSMAIRE *et al.* 2019) can initiate a new interest in these systems of transition to clonality. Thus, one advance in the understanding of the evolution of asexuality will be to abandon the idea that it is relevant to consider it as similar to the direct evolution of clonality, without considering the intermediate stages. In this respect, it is interesting to note that automictic systems have consequences much closer to those of self-fertilisation than to those of clonality: maintained recombination, loss of heterozygosity and therefore importance of deleterious mutations and the inbreeding depression they cause, etc. Obviously self-fertilisation is only possible when individuals are hermaphroditic, but in a way the somatic investment of *Mesorhabditis belari* females in males can be seen as an externalisation of the sperm production that they cannot produce themselves. This is comparatively close to the reduced investment of hermaphodites in male organs that, like males in *Mesorhabditis belari*, are degenerate (the so-called "selfing syndrome", which is characterised notably by a reduced pollen/ovule ratio ; SICARD and LENHARD 2011). It might therefore be useful to understand how the results of work on the evolution of selfing can be extended to those on automixis.

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Understanding the Evolution and Genomic Consequences of an Atypical Sexual System through Population Genetic Simulations

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Résumé. Les conditions de la transition de la sexualité à l'asexualité sont mal comprises. Cette transition est sans doute graduelle - les systèmes sexués (méiose) peuvent évoluer vers la clonalité (mitose) par le passage à un système intermédiaire (méiose modifiée). *Mesorhabditis belari* est un nématode parthénogénétique - avec seulement 10% de mâles, produits sexuellement, tandis que les femelles sont produites par autopseudogamie, une reproduction génétiquement asexuée où la fécondation est néanmoins nécessaire. La forme probable d'autopseudogamie implique une méiose modifiée appelée automixie par fusion centrale. En fusion centrale, la moitié des chromosomes présentent une perte d'hétérozygotie due à la recombinaison. Étonnamment, *M. belari* ne présente aucune perte d'hétérozygotie (LOH), comme s'il était à l'équilibre d'Hardy-Weinberg, et aucun déséquilibre de liaison. Ici, je teste l'hypothèse que cela puisse s'expliquer par un biais de ségrégation chromosomique qui empêche la LOH. Pour tester cette hypothèse, j'ai développé un modèle multi-locus centré sur l'individu. J'ai testé l'influence des mutations délétères, du niveau de consanguinité, de la proportion de femelles produites sexuellement et du taux de LOH en automixie. Les caractéristiques du génome de *M. belari* sont retrouvées en considérant des mutations délétères et une forte consanguinité, en cohérence avec ce que nous savons de l'espèce. Le modèle confirme également qu'un biais de ségrégation est nécessaire. Un second modèle montre que ce biais est rapidement sélectionné, même avec un niveau intermédiaire de dépression de consanguinité (jusqu'à 60 %).

Mots clefs. Génétique des populations - Système de reproduction - Pseudogamie - *Mesorhabditis belari* - Fusion centrale - Evolution de l'asexualité

Abstract. The conditions for the transition from sexuality to asexuality remain poorly understood. This transition is thought to be gradual – meiosis-based sexual systems can evolve towards mitosis-based clonality through a modified meiosis intermediate system. *Mesorhabditis belari* is a parthenogenetic nematode – with only 10% of males, produced sexually, while females are produced by autopseudogamy, a genetically asexual reproduction in which fertilisation is nonetheless required. The probable form of autopseudogamy involves modified meiosis call central fusion automixis. In central fusion, half of the chromosomes have a loss of heterozygosity due to recombination. Surprisingly, *M. belari* shows no loss of heterozygosity (LOH), as if it were at Hardy-Weinberg equilibrium, and no linkage disequilibrium. Here, I test the hypothesis that it may be explained by a chromosome segregation bias that prevents LOH – a mechanism that has never been described before. To test this hypothesis, I developed a multi-locus individual-based model. I tested the influence of deleterious mutations, the level of inbreeding, the proportion of sexually produced females and of the rate of LOH during automixis. *M. belari* genome's caracteristics are are found when considering deleterious mutations and with a high level of inbreeding, which is consistent with what we know about the species. The model also confirms that segregation bias during meiosis II is required to explain the observed genomic patterns. A second model shows that this bias is rapidly selected in a sexual population even with an intermediate level of inbreeding depression (up to 60%).

Key words. Population genetics - Reproductive system - Pseudogamy - *Mesorhabditis belari* - Central fusion - Evolution of asexuality