Evolution, 2023, **77(10)**, 2186–2199
https://doi.org/10.1093/evolut/qpad129
Advance access publication July 17, 2023
Original Article

Why do hybrids turn down sex?

Frédéric Fyon[1], Waldir Miron Berbel-Filho[2], Ingo Schlupp[2], Geoff Wild[3], Francisco Úbeda[1]

[1]Department of Biology, Royal Holloway University of London, Egham, United Kingdom
[2]Department of Biology, University of Oklahoma, Norman, OK, United States
[3]Department of Applied Mathematics, University of Western Ontario, London, ON, Canada

Corresponding author: Frédéric Fyon, Department of Biology, Royal Holloway University of London, Egham TW20 0EX, United Kingdom.
Email: frederic.fyon@rhul.ac.uk

G.W. and F.U. have contributed equally to this work.

Abstract

Asexual reproduction is ancestral in prokaryotes; the switch to sexuality in eukaryotes is one of the major transitions in the history of life. The study of the maintenance of sex in eukaryotes has raised considerable interest for decades and is still one of evolutionary biology's most prominent question. The observation that many asexual species are of hybrid origin has led some to propose that asexuality in hybrids results from sexual processes being disturbed because of incompatibilities between the two parental species' genomes. However, in some cases, failure to produce asexual F1s in the lab may indicate that this mechanism is not the only road to asexuality in hybrid species. Here, we present a mathematical model and propose an alternative, adaptive route for the evolution of asexuality from previously sexual hybrids. Under some reproductive alterations, we show that asexuality can evolve to rescue hybrids' reproduction. Importantly, we highlight that when incompatibilities only affect the fusion of sperm and egg's genomes, the two traits that characterize asexuality, namely unreduced meiosis and the initiation of embryogenesis without the incorporation of the sperm's pronucleus, can evolve separately, greatly facilitating the overall evolutionary route. Taken together, our results provide an alternative, potentially complementary explanation for the link between asexuality and hybridization.

Keywords: asexual reproduction, maintenance of sex, evolution of asexuality, hybridization, reproductive assurance

Introduction

Sexual reproduction whereby diploid individuals produce haploid gametes that combine with other gametes to produce a new diploid individual—carrying two copies of each gene, one from each parent—is the dominant form of reproduction in organisms formed by cells with a nucleus (Eukaryotes). Sexual reproduction evolved from asexual reproduction in what has been considered a major transition in evolution Smith & Szathmary (1997). Although sexual reproduction in eukaryotes is stable over long periods of evolutionary time, certain forms of asexual reproduction have in turn evolved from sexual reproduction multiple times Avise (2015); Bell (1982); Simon et al. (2003). Some of the taxonomic groups where asexual reproduction has evolved independently include anemons, nematods, mollusks, arthropods, and vertebrates (see Figure 1 and references therein).

It is not clear how asexuality has evolved so many times in such diverse taxa. On the one hand, the evolutionary advantages that drove sexuality to outcompete asexuality originally are expected to still apply in these taxa. On the other hand, empirical evidence shows that asexual species evolving from sexual ancestors have to overcome many cytological and physiological obstacles Engelstädter (2008); Meirmans et al. (2012). In spite of the abundant scientific interest on what factors may drive the transition from sexuality to asexuality, these drivers remain elusive Simon et al. (2003).

One intriguing observation is that many of the asexual species evolving from sexual ancestors originated from the cross of two different species, that is, are of hybrid origin Beukeboom & Vrijenhoek (1998); Schlupp (2005); Simon et al. (2003). Most notably, all but one asexual species in vertebrates studied to this day have been shown to be of hybrid origin Simon et al. (2003); Sinclair et al. (2010). Why does hybridization favor the evolution of asexuality? Understanding the drivers of this transition will help us understand the evolutionary stability of sexual reproduction, a fundamental feature of multicellular organisms' physiology, behavior, diversity, and evolution.

It has been argued that asexuality can appear as the direct outcome of crossing two different sexual species. Incompatibilities between genes of different species (*genomic incompatibilities*) are thought to be able to disrupt key processes in sexual reproduction, such as meiosis and/or gamete recognition, leading to the spontaneous production of fully functional asexual progeny Janko et al. (2018); Mogie (1992); Moritz et al. (1989). This is supported by experimental crosses that obtain asexual progeny spontaneously Choleva et al. (2012); Drosopoulos (1978); Janko et al. (2018); Vrijenhoek (1993). In some species however, experimental crosses do not obtain asexual F1 hybrids Dries (2003); Lampert et al. (2007); Ptacek (2002); Stöck et al. (2010); Turner et al. (1980). Here we explore the conditions for natural selection to favor the evolution of asexuality from sexuality in those cases where asexuality does not appear spontaneously as a direct result of genomic incompatibilities. In doing so, we will explore whether a progressive evolution of asexuality is possible and

Received May 18, 2022; revisions received May 19, 2023; accepted July 05, 2023
Associate Editor: Maria E. Orive; Handling Editor: Tracey Chapman

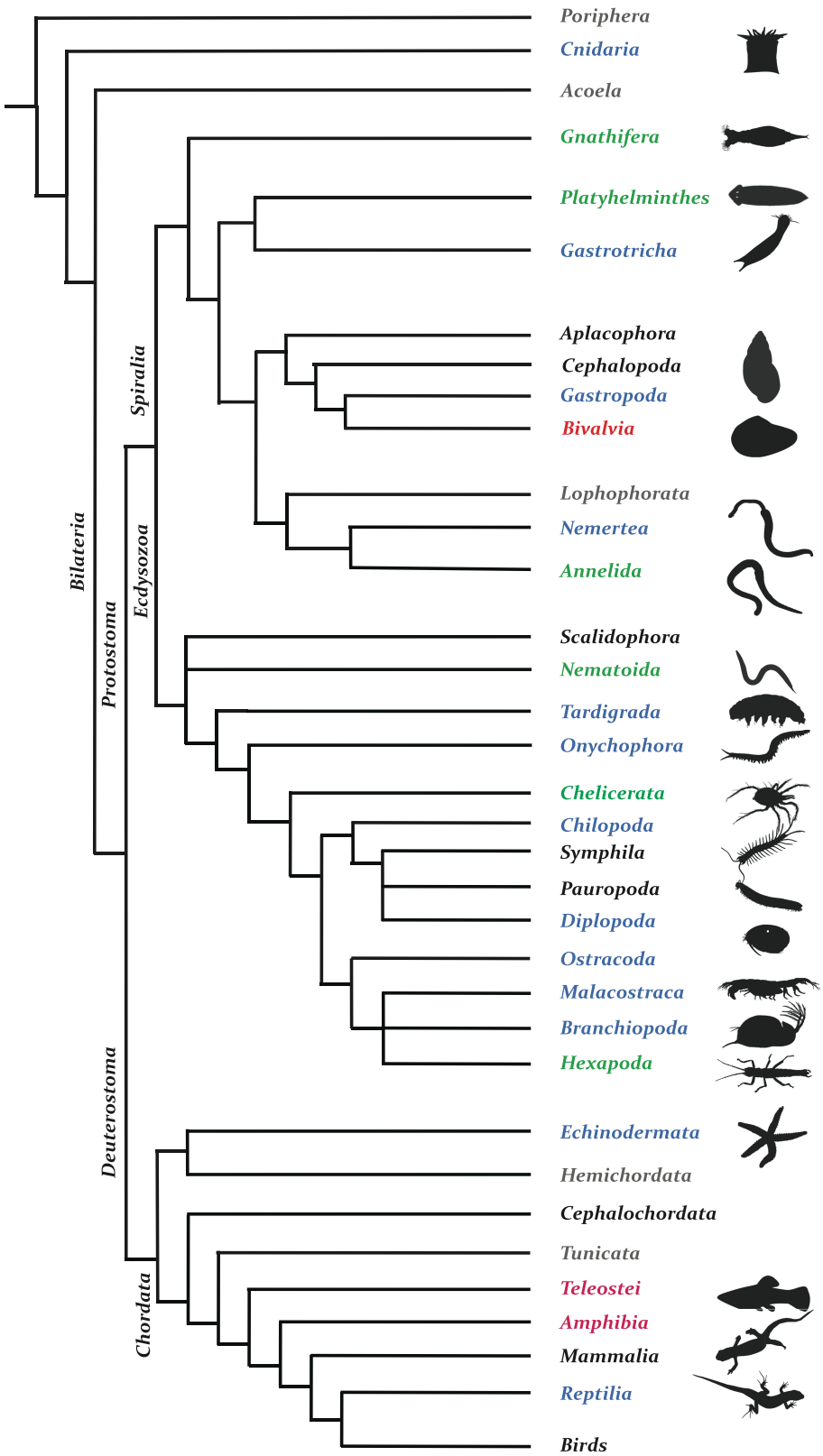

Figure 1. Distribution of reproductive modes within a simplified phylogeny of metazoans (adapted from GIGA Community of Scientists (2013); Giribet (2016); Laumer et al. (2019)). We are aware that some of the phylogenetic relationships represented here are debated and that we are comparing taxa at different levels; this phylogeny is presented merely for the purpose of illustrating the broad distribution of the different sexual and asexual reproductive modes among metazoans. Taxonomic groups for which there have been reports of true parthenogenetic species or races appear in blue, of gynogenetic (sperm-dependent parthenogenetic) species or races appear in red, and of both types of species or races appear in green. Gray taxa correspond to groups where vegetative reproduction (budding, fission) has been reported, while all species in black taxa exclusively reproduce sexually.

whether hybridization may act as a catalyst of the transition to asexuality.

For the spontaneous appearance of asexual hybrids, two reproductive processes need to be disrupted. First, the reduction in ploidy of germ cells—from diploid to haploid—needs to be prevented to generate diploid gametes (*unreduced gametic division*). Second, the fusion of maternal and paternal pronuclei in eggs needs to be averted to impede the transmission of the paternal genome (*no fusion*). In nature, this can take two forms. In truly parthenogenetic species, this fusion is prevented by the egg spontaneously entering embryogenesis, before any sperm has had any chance of fertilizing it Neaves & Baumann (2011). In gynogenetic species, this is achieved by a process commonly referred to as paternal genome elimination, whose actual cytological mechanism remains mostly unknown. In these species, the paternal pronucleus enters the egg following fertilization from a sperm cell. However, it is not decondensed and is rapidly removed from the egg, impeding it from fusing with the egg´s pronucleus Dedukh & Krasikova (2022). Here, we will refer as *no fusion* to any of these two alternatives. It has been argued that it may be difficult for genetic incompatibilities to result in the modification of these two traits of the reproductive systems at once to produce a viable and fertile asexual progeny Schlupp (2005). Instead, it has been suggested that the evolution of a progressive modification of the reproduction of the hybrids could be a potential route for the transition from sexuality to asexuality Schlupp (2005). However, this verbal argument has not been backed by any formal model. Here we formulate a mathematical model for the evolution of asexuality from sexual reproduction one trait at a time. We model the ecological conditions and the sequence of intermediate steps that may lead to asexual hybrids.

Here, we show that natural selection can favor the progressive (one trait at a time) evolution of asexuality: We propose an evolutionary route that decouples the evolution of unreduced meiosis and absence of fusion between parental pronuclei. The reason why each of the incremental steps is favored by natural selection is that each of them increases the reproductive opportunities of hybrids with otherwise limited reproductive output (i.e., increase *reproductive assurance*). We thus provide progressive routes that complement the spontaneous route that currently prevails as an explanation. Furthermore, we argue that these progressive routes are only available to hybrids, thus providing further support to the idea that hybrid species are hotspots for the transition from sexuality to asexuality.

Methods

Here we model the interactions between two sexual species and the hybrid resulting from crosses between them. Parental species and hybrids are assumed to coexist within the same environment. There have been different theories proposed to explain how an asexual hybrid can coexist with its parental species while being a resource and potentially a mate competitor (Heubel et al. (2009); Kokko et al. (2008); Leung & Angers (2018); Schley et al. (2004)). In this work, we use the simplest of this assumption and extend it to sexual hybrids: We assume that parental and hybrid populations do not compete for resources (but see Discussion and Supplementary Material for a relaxation of this hypothesis). That is, the three populations coexist in a given environment with death rates Ψ_i that depend only on the total number of individuals of that species i: $\Psi_i = 2N_i/K$ (N_i representing half the number of individuals from species i present in the environment, see Supplementary Material for further justification). Henceforth, we use subscripts 1 and 2 for the parental species and h for the hybrid species. Because we assume perfect symmetry between the parental species, we will generally use subscript p to refer to any of the two parental species. To simplify equations, we will use n_i to refer to the population sizes relative to the carrying capacity of the environment ($n_i = N_i/K$).

Birth rates are influenced by the mating preferences of the different populations (illustrated in Figure 2). We note c_p the preference of a parental female (1 or 2) for males from its own population, and c_h the preference of hybrid females for hybrid males.

As a result of birth by intraspecific matings and death by intraspecific competition for resources, the parental populations reach a stable equilibrium population size $n_p = \frac{1-c_p}{4}$ (see Supplementary Material for a demonstration). Henceforth, we will always assume that the parental population size is equal to this stable equilibrium.

Wild-type hybrid females mate with hybrid males with probability Φ. Φ is an increasing function of n_h and c_h whose expression is given in the Supplementary Material: Φ increases when hybrids female preference for hybrid males increases, or if there are relatively more hybrid males around. Note that hybrid and parental species do compete for mates; thus, Φ also depends on the amounts of parental males around, which in turn depends on c_p (see above; Φ decreases if there are relatively more parental males around). Alternatively, wild-type hybrids can mate with parental males (back-crossing) with probability $1 - \Phi$. Both kinds of matings, when productive, produce wild-type hybrids (see Figure 2).

The size of the population of wild-type hybrid females changes as a result of the birth and death mechanisms described above following:

$$\dot{n}_h = \theta + \left(\nu\frac{1-\Phi}{2} - 2n_h\right)n_h \qquad (1)$$

with ν denoting the viability of offspring produced by sexual hybrid females when backcrossing with parental males. We assume that this value is either 0 or 1, depending on the model of genomic incompatibilities we consider. θ refers to the birth of wild-type hybrids by hybridization between the parental species: $\theta = n_p(1-c_p) = c_p(1-c_p)/4$.

We can show that the dynamics in Equation 1 lead to a stable equilibrium size of the wild-type hybrid female population $\hat{n}_h$ (see Supplementary Material for a demonstration). Depending on the model of genomic incompatibilities we consider (see below), we can in some cases find an analytical closed-form expression of $\hat{n}_h$. In all cases, we can find $\hat{n}_h$ at least numerically.

We generally assume that both parental species and the wild-type hybrid population are fully sexual. Once the wild-type hybrid has reached its equilibrium, we introduce in the environment a *mutant hybrid* that can potentially display any mode of reproduction between fully sexual and fully asexual. In particular, the phenotype of the mutant hybrid species is characterized by three evolutionarily labile traits: production of diploid clonal eggs with probability $\alpha \in [0,1]$; absence of fusion of maternal and paternal pronuclei $\beta \in [0,1]$, and production of female progeny in proportion $\sigma \in [-1,1]$ (the proportion of females relative to males in the

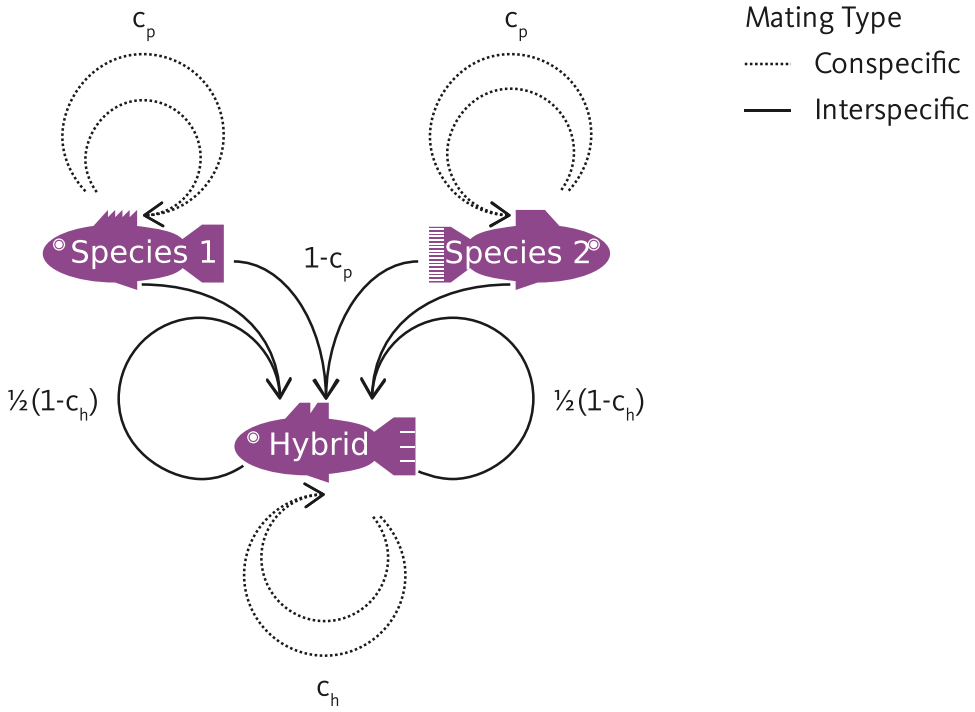

Figure 2. Reproduction and mating choices. Females from each parental species mate with males from the same species with preference c_p (Conspecific Matings), which gives birth to individuals of the same species. Alternatively, they can choose to mate with a male from the other parental species with preference $1-c_p$ (Interspecific Matings); in this case, they give birth to hybrid individuals. Females from the hybrid species can choose to mate with hybrid males with preference c_h (Conspecific Matings) or with males from the parental species with preference $1-c_h$ (Interspecific Matings). In both cases, they give birth to hybrid individuals. Conspecific Matings are shown in dashed lines, while Interspecific Matings are shown in plain lines.

progeny (sex ratio)is $\frac{1}{2}+\frac{1}{2}\sigma$). The three traits are female-only phenotypes: Mutant hybrid males do not express α, β, or σ though they do carry the genes for each. Notice that the phenotype corresponding to the hybrid wild-type population is ($\alpha=\beta=\sigma=0$) and that of a fully asexual population is ($\alpha=\beta=\sigma=1$).

There are two ways an organism can produce diploid clonal eggs (trait α) Engelstädter (2008); Galis & van Alphen (2020). First, they can be produced by circumventing meiosis to produce gametes via mitotic (unreduced) division, a process referred to as *apomixis*. Alternatively, they can be produced by duplicating the genome prior to meiosis to produce gametes via meiotic (reduced) division, a process referred to as *endoduplication*. In the latter case, meiotic products are identical to the germ-cell they originated from because recombination occurs between identical sister chromatids and therefore does not produce new combinations of genes. This latter mechanism is considered to be the mechanism used by many asexual vertebrates Neaves & Baumann (2011). Henceforth, we will just use the term *clonal eggs* to refer to the production of diploid, clonal eggs by any type of unreduced gametic division (apomixis or endoduplication).

The absence of fusion between egg and sperm pronuclei can also be realized in two ways, depending on whether we consider true parthenogenesis or gynogenesis. In the latter case, fusion is impeded as the sperm pronucleus is prevented from decondensing, and later on is discarded Dedukh & Krasikova (2022). In true parthenogenesis, this trait corresponds to spontaneous embryogenesis: The egg enters mitosis and embryogenesis before the fusion with a sperm cell Neaves & Baumann (2011). These two mechanisms can be modeled in the exact same way. For example, when a female has mated with a viable and fertile sperm, its meiotic egg could produce a viable offspring if and only if it does not spontaneously enter embryogenesis, or does not discard the sperm pronucleus. Alternatively, its clonal egg could produce a viable offspring if and only if it enters embryogenesis spontaneously—so that a sperm does not have time to fuse and transmit its genome—or if it discards the sperm's pronucleus.

Concerning the last trait, offsprings' sex ratios, it should arguably be modeled as a direct consequence of the first two: Clonal females should be expected to produce only females. However, the production of more females, as we show hereafter, provides a benefit per se. In order to decouple the selection for asexuality as a way to provide more females, and the selection for asexuality as for other benefits, we decided to formally consider sex ratios as an independent trait. This is the most conservative hypothesis; selection for asexuality should be easier when this assumption is relaxed.

Our model assumes that incompatibilities between parental species lead to some form of egg or sperm dysfunction in hybrids, which in turn affects the reproductive prospects of female hybrids. In the following, we will talk about sperm decondensation as a concrete example of what kind of incompatibilities the different scenarios correspond to. However, any kind of incompatibility that allows for embryogenesis triggering but produces unviable offspring would be valid. For example, we could have considered that the sperm pronucleus does decondense, but then fails to fuse with the egg's pronucleus due to incompatibilities in some maternal and paternal factors.

We first consider the case where hybrid sperm is viable but unable to decondense its own pronucleus following fertilization (henceforth the *sperm-fails-to-decondense scenario*).

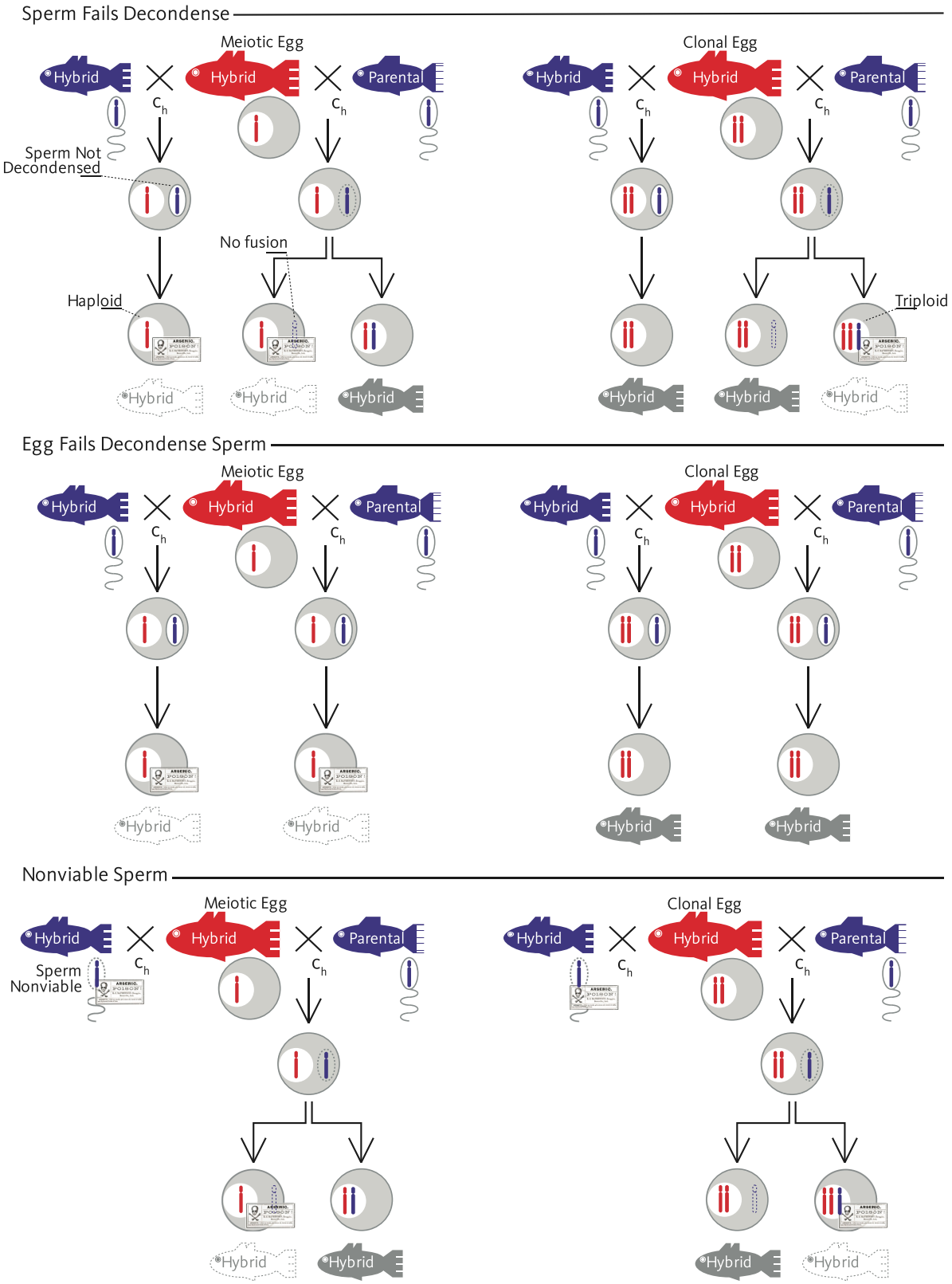

Figure 3. Hybrid female reproduction depending on the model considered, on the type of mate (hybrid or parental), on the type of egg (meiotic or clonal, the latter occurring with probability α) considered, and on the absence of fusion between maternal and paternal pronuclei (with probability β). Unviable offsprings are indicated with crossbones and white, dashed-bordered fishes. This happens whenever the embryo is haploid or triploid. The mother genetic material is indicated in red, while the father genetic material is shown in blue. Gray-filled fishes indicate viable offspring.

Thus, while all sperm is able to trigger embryogenesis by fusing with the egg, hybrid sperm is not able to contribute genetic material to the embryo while parental sperm is (see Figure 3, top panel). In this case, meiotic eggs can produce viable diploid offspring if the female mates with a parental male and if the pronuclei fuse (with probability $1 - \beta$). Note

that this means that in this model $\upsilon = 1$. Clonal eggs, however, can produce viable diploid offspring either if the female mate with a parental male and if there is no fusion between egg and sperm pronuclei (with probability β) or if the female mates with a hybrid male (see Figure 3, top panel, right-hand side). Notice that throughout this research we assume that haploid and triploid offsprings are lethal for simplicity. Empirical work shows that triploids often have reduced fitness Lamatsch et al. (2009). Notice also that, when mating with hybrid males, mutant hybrid females can achieve greater success through unreduced than reduced meiosis.

Second, we consider the alternative case when hybrid eggs are unable to decondense the pronucleus of the sperm fusing with the egg (henceforth *egg-fails-to-decondense-sperm scenario*). Thus, all sperm is able to trigger embryogenesis but unable to contribute genetic material to the embryo (see Figure 3, middle panel). In this case, meiotic eggs can never produce viable diploid offspring (not even in back-crosses with parental males: $\upsilon = 0$). Clonal eggs, however, can always produce viable diploid offsprings, independently from with which type of males the female has mated (see Figure 3, middle panel, right-hand side). This time, mutant hybrid females can achieve greater success through unreduced than reduced meiosis when mating with any kind of males.

Finally, we consider the case when hybrid sperm is nonviable (henceforth *nonviable-sperm scenario*). Now, hybrid sperm is unable to trigger embryogenesis and unable to contribute genetic material to the embryo while parental sperm is able to perform both functions (see Figure 3, bottom panel). In this case, hybrid eggs (both meiotic and clonal) can only produce viable offspring if they mate with parental males ($\upsilon = 1$). That said, mutant hybrid females employing reduced meiosis produce viable offspring only if pronuclei fuse ($1-\beta$), whereas those employing unreduced meiosis must avoid that fusion (β) to produce viable offspring.

Once a rare mutant hybrid female has been introduced in the environment, it should spread and invade if and only if it is able to produce more than one mutant hybrid daughter during its lifetime. Mathematically, this means that their growth rate, that we can also call fitness w, is strictly greater than 0. We can find a general equation for w that works for the three models:

$$w(\alpha,\beta,\sigma;\hat{n}_h) = \frac{1+\sigma}{2}\Big[\alpha(s\hat{\Phi} + (1-\hat{\Phi})\beta^x) + (1-\alpha)\upsilon\frac{1}{2}(1-\hat{\Phi})(1-\beta)\Big] - 2\hat{n}_h \qquad (2)$$

where υ (already mentioned), s, and x allow to take into account the differences induced by the assumptions of the three scenarios on the growth rate of mutant hybrids. In the *sperm-fails-to-decondense scenario*, we have $\upsilon = 1$, $s = 1$, and $x = 1$. In the *egg-fails-to-decondense-sperm-scenario*, we have $\upsilon = 0$, $s = 1$, and $x = 0$. Finally, in the *nonviable-sperm-scenario*, we have $\upsilon = 1$, $s = 0$ and $x = 1$. See Supplementary Material for the corresponding equations with υ, s, and x replaced by their values in each scenario.

If a mutant hybrid invades, then it coexists at a stable equilibrium with the parental species and wild-type hybrids, until such time as a new mutant hybrid arises. If this new mutant has a selective advantage (resp. disadvantage) relative to the established one, the new mutant will eliminate (resp. be eliminated by) its predecessor and establish itself (resp. be absent) in the equilibrium ecosystem. Ultimately, hybrid traits evolve in the long term through a succession of mutant invasion and displacement events. Because the equilibrium size of the mixed population of wild-type and established mutant hybrids is independent of the traits expressed by any new mutant that may arise, in the long-term selection will act to maximize w. Thus, by considering where w is positive and how it can be maximized, we seek to capture the transition from an ancestral sexual hybrid to a hybrid with a different reproductive phenotype.

Finally, we carry out simulations to establish the order in which this transition may have occurred over evolutionary time. We assume that evolution begins with the invasion of a mutant with the lowest values of α, β, and σ such that $w(\alpha,\beta,\sigma;\hat{n}_h) > 0$. We numerically calculate the resulting wild-type—mutant equilibrium. Then, we calculate selection gradients by taking the partial derivatives of $w(\alpha,\beta,\sigma;\hat{n}_h)$ with respect to α', β', and σ'. Here, α, β, and σ refer to the established mutant's phenotype, while α', β', and σ' refer to a new, rare mutant. Note that here $\hat{n}_h$ refers to the total number of hybrid females at the wild type—mutant equilibrium. By comparing these and finding the highest derivative, we find the direction toward which selection is pointing at the current wild type—mutant equilibrium. We assume that a mutant with a phenotype marginally different in that direction then spreads, invades, replaces the older mutant and we calculate the new wild type—mutant equilibrium. We repeat this process until no new mutant can spread. The algorithm used for these numerical simulations is available in the Mathematica file provided as Supplementary Material.

Results

Sperm-fails-to-decondense scenario

We start by considering whether a rare mutant that deviates from the wild-type reproductive phenotype, that is $\alpha = \beta = \sigma = 0$, can invade the hybrid population. That is, we set to find out the conditions for $w(\alpha,\beta,\sigma;\hat{n}_h) > 0$. In the case of this first model ($\upsilon = 1$, $s = 1$, and $x = 1$), this means:

$$\frac{1+\sigma}{2}\left[\alpha(\hat{\Phi} + (1-\hat{\Phi})\beta) + (1-\alpha)\frac{1}{2}(1-\hat{\Phi})(1-\beta)\right] > 2\hat{n}_h \qquad (3)$$

Using the fact that $\hat{n}_h$ and $\hat{\Phi}$ are by definition such that $\dot{n}_h = 0$, Equation 1 allows us to show that a necessary condition for $w(\alpha,\beta,\sigma;\hat{n}_h) > 0$ is $\alpha > 0$ (see Supplementary Material for a more detailed demonstration). Importantly, however, neither $\beta = 0$ nor $\sigma = 0$ preclude mutant invasion. Thus, in this scenario, a mutant must necessarily display some strictly positive rate of production of clonal eggs to have a chance to invade.

If a mutation can only modify one phenotypic trait, we understand that the first mutant to invade must necessarily produce clonal eggs at a certain rate. To obtain the invasion condition of such a mutant, we can assume $\beta = \sigma = 0$ to simplify the equations. Replacing $\hat{n}_h$ by its expression in the function of θ and $\hat{\Phi}$ obtained by solving $\dot{n}_h = 0$, this leads to:

$$\alpha > \alpha^* = \frac{\sqrt{32\theta + (1-\hat{\Phi})^2}}{3\hat{\Phi} - 1} \qquad (4)$$

with α^* being the lower bound of α such that a mutant with phenotype $(\alpha, 0, 0)$ can invade.

We plot on Figure 4A α^* in function of c_h and c_p (recalling that θ is a function of c_p), calculating $\hat{\Phi}$ numerically.

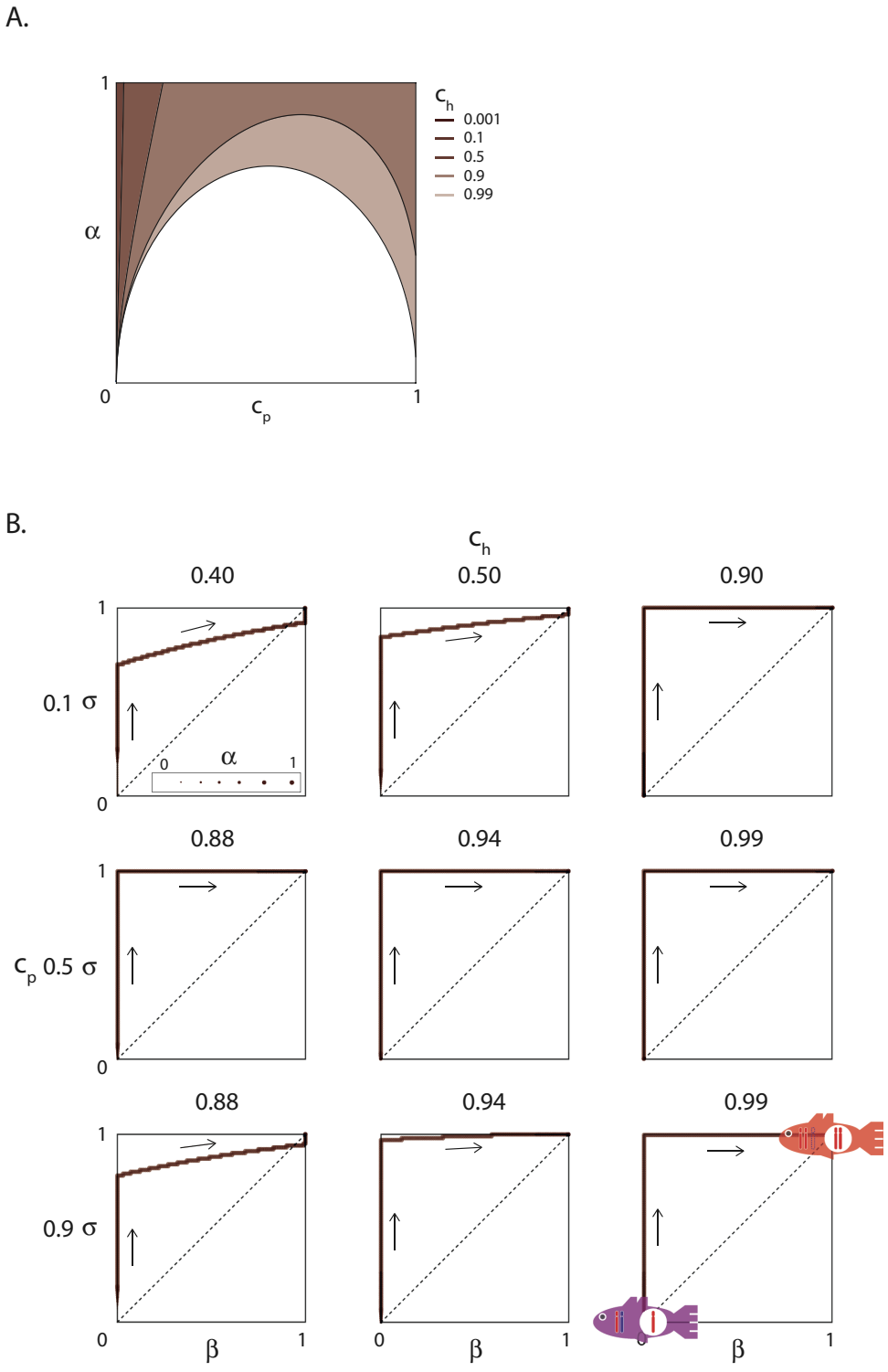

Figure 4. Evolution of asexuality in the sperm-fails-to-decondense scenario. (A) Values of $\alpha > \alpha^*$ (y-axis) where a mutant can invade are indicated in function of c_p (x-axis) and c_h as shaded areas. (B) Predicted evolutionary route to asexuality for nine combinations of c_p and c_h values. The size of the dot represents α, while x- and y-axes represent β and σ, respectively. These routes show the transition from sexual hybrids (bottom-left fish), which are diploid, produce haploid eggs and have maternally and paternally inherited chromosomes, to asexual hybrids (top-right fish), which are diploid, produce diploid eggs and have only maternally inherited chromosomes. The bottom limit α^* of α for the first mutant to spread varies in each case, and approximately equals respectively from left to right and top to bottom: ($c_p = 0.1$) 0.89, 0.72, 0.62; ($c_p = 0.5$) 0.91, 0.80, 0.72; ($c_p = 0.9$) 0.45, 0.59, 0.80.

α^* decreases with the preference for hybrids to mate with other hybrids c_h. When *no fusion* has not evolved ($\beta = 0$), hybrid females producing diploid clonal eggs gain reproductive opportunities with hybrid males, but lose reproductive opportunities with parental males (see Figure 3, top panel, right-hand side). Thus, mutant females producing clonal eggs gain a reproductive advantage over wild-type meiotic females only when the probability of hybrid females mating with

hybrid males $\hat{\Phi}$ is large enough; this probability increases with the preference of hybrid females for hybrid males c_h.

α^* reaches a maximum at intermediate values of the preference of each parental species to mate within itself c_p. This is because θ, the influx of wild-type hybrids by direct hybridization, is proportional to $c_p(1-c_p)$. θ is maximal at intermediate values of c_p, which increases α^* as can be seen from Equation 4. Larger values of θ means larger values of n_h. The invasion of a mutant is compromised by large values of θ (and thus intermediate values of c_p) as it tends to increase the death rate of mutant hybrids due to competition for resources with increased numbers of wild-type hybrids.

As explained in the Methods section, we can find the long-term evolutionary route of this system by derivating $w(\alpha, \beta, \sigma; \hat{n}_h)$, that is by looking at fitness gradients. We plot on Figure 4B these evolutionary routes. It stands out from these numerical computations that if the conditions are such that a first, partially apomictic mutant can invade ($\alpha > \alpha^*$), then complete asexuality ($\alpha = \beta = \sigma = 1$) ends up evolving always. We show in the Supplementary Material that indeed complete asexuality ultimately maximizes the mutant fitness function. Also, we see in Figure 4B that most of the time the evolution of asexuality happens in a stepwise process, with first the evolution of females producing exclusively clonal eggs ($\alpha = 1$), then the evolution of fully female-biased sex ratios within the offspring ($\sigma = 1$), and finally the evolution of females always preventing the fusion of maternal and paternal pronuclei ($\beta = 1$). Most importantly, these evolutionary routes show that the evolution of apomixis occurs before and independently from the evolution of pronuclei fusion impediment. In restricted parameter spaces, there may be some limited overlap between these steps, but this does not affect the qualitative prediction that in this model the evolution of clonal egg production does not require the evolution of a mechanism to prevent fusion between parental pronuclei in parallel.

In the following, we perform the same analysis for the other two models.

Eggs-fails-to-decondense-sperm scenario

From a modeling perspective a failure of hybrid eggs to decondense any sperm is equivalent to assuming that trait β, the prevention of pronuclei fusion is a direct result of hybridization. Therefore in this scenario, the wild-type hybrid has a reproductive phenotype characterized by ($\alpha = 0, \beta = 1, \sigma = 0$). Again, we start by considering whether a rare mutant that deviates from the wild-type reproductive phenotype can invade the hybrid population.

In this scenario ($\nu = 0$, $s = 1$ and $x = 0$), the mutant invasion condition ($w(\alpha, 1, \sigma; \hat{n}_h) > 0$) is:

$$\frac{1+\sigma}{2}\alpha > 2\hat{n}_h \tag{5}$$

Because $\hat{n}_h$ is necessarily positive, we realize that again invasion can only happen for values of α strictly positive. Because this is not the case for σ, in this scenario the first mutant to possibly invade must again be a mutant that produces clonal eggs at a certain rate. Assuming $\sigma = 0$, we can find the lower-bound α^* such that the mutant invades:

$$\alpha > \alpha^* = \sqrt{8\theta} \tag{6}$$

We plot in Figure 5A α^* in function of c_p. As can be seen from Equation 6, α^* here does not depend on c_h. This is because in this scenario, since pronuclei never fuse, mutant hybrid females producing clonal eggs can reproduce with both parental and hybrid males while meiotic females cannot reproduce with any of them (see Figure 3). Therefore, such mutant females gain a reproductive advantage over wild-type meiotic females with independence of the type of mating partner, and thus with independence of hybrid female mating preferences (c_h).

In this scenario, the invasion of a mutant only depends on θ, as made clear by Equation 6. As for the previous scenario, α^* increases with intermediate values of c_p because these lead to larger values of θ, of $\hat{n}_h$, and thus larger mutant death rates by competition for resources with wild-type hybrids.

Once the first mutant with phenotype ($\alpha^*, \beta = 1, \sigma = 0$) has spread and reached its equilibrium population size, we assume that new mutants with any phenotype may appear. We find that the mutant fitness function is again maximized by the asexual phenotype ($\alpha = 1, \beta = 1, \sigma = 1$) (see Supplementary Material for a demonstration).

Noticeably, the partial derivative of the fitness function with respect to α is always greater than the partial derivative with respect to σ (see Supplementary Material for a demonstration): The selection gradient is always greater in the direction of clonal egg production than in the direction of female-biased sex ratios. As such, we expect again in this model evolution to proceed in a stepwise process. Here, clonal egg production is expected to evolve first, and sex ratios afterwards, while prevention of pronuclei fusion is a direct result of genomic incompatibilities in the hybrid. This is illustrated by numerical simulations for different values of c_p shown on Figure 5B.

Nonviable-sperm scenario

In this scenario, $\nu = 1$, $s = 0$, and $x = 1$, such that the invasion condition for a mutant female hybrids ($w(\alpha, \beta, \sigma; \hat{n}_h) > 0$) is:

$$\frac{1+\sigma}{2}(1-\hat{\Phi})\left[\alpha\beta + \frac{(1-\alpha)(1-\beta)}{2}\right] > 2\hat{n}_h \tag{7}$$

As in the *sperm-fails-to-decondense* scenario, we can use the fact that $\hat{n}_h$ verifies $\dot{n}_h = 0$. This time, however, this allows us to show that in this model there can be no invasion of a mutant if $\alpha = 0$ or $\beta = 0$ (see Supplementary Material for a demonstration). Contrarily to the two previous scenarios, here a mutation affecting only clonal egg production can never spread; it must also affect spontaneous embryogenesis/paternal genome elimination. For the mutant to invade, α must verify:

$$\alpha > \alpha^* = \frac{\frac{1-\hat{\Phi}+\sqrt{32\theta+(1-\hat{\Phi})^2}-(1-\beta^*)}{(1-\hat{\Phi})(1+\sigma^*)}}{3\beta^*-1} \tag{8}$$

When resolving the inequation $\alpha^* \leq 1$, we realize that the invasion of a mutant can never happen for $\alpha \leq 1/3$ and $\beta \leq 1/2$. It thus appears that a mutation, in this scenario, must always very significantly alter the reproductive phenotype to be able to invade. This is confirmed by Figure 6A, where we plot α^* as a function of c_p for different values of c_h, β, and σ : α^* is actually always greater than 1/2, and rapidly increases for decreasing values of σ and β.

Figure 6A also shows that again, and for the same reason as before, α^* increases with intermediate values of c_p, since, as shown by Equation 8, α^* increases with θ. Contrarily to the first scenario, α^* now increases with c_h (we can see in Equation 8 that α^* increases with $\hat{\Phi}$). The particularity of this

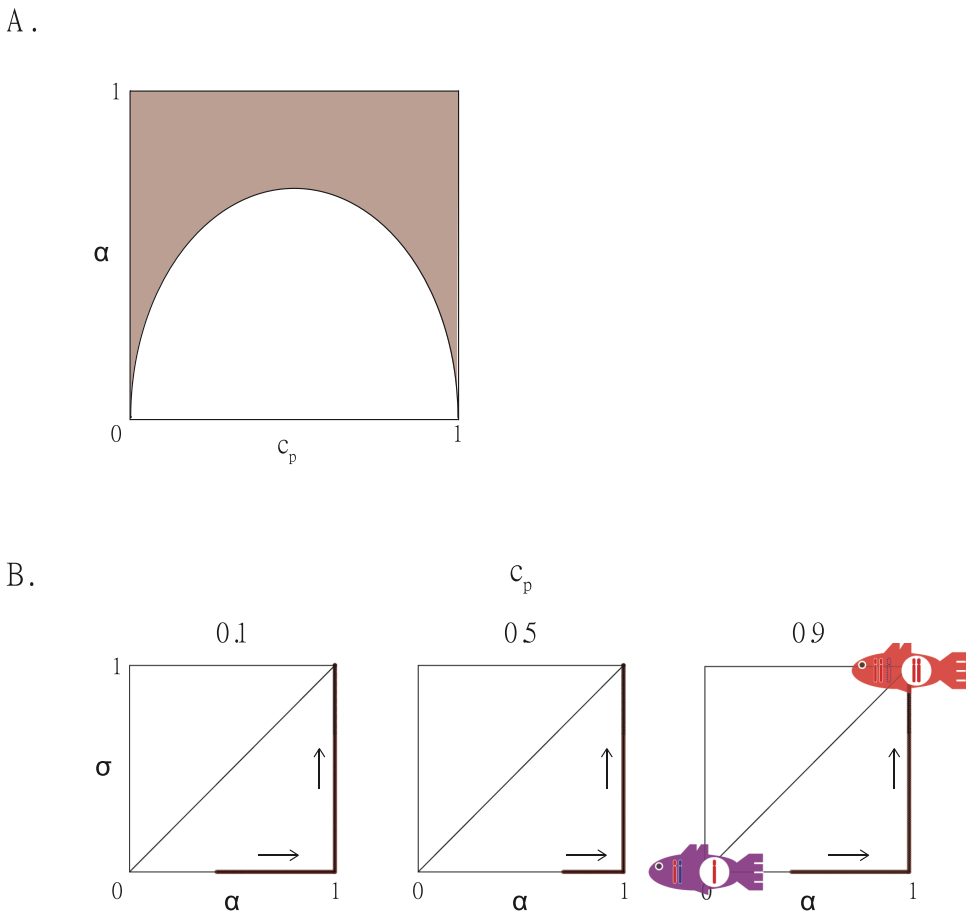

Figure 5. Evolution of asexuality in the egg-fails-to-decondense-sperm scenario. (A) Values of $\alpha > \alpha^*$ (y-axis) where a mutant can invade are indicated in function of c_p (x-axis) as shaded areas. These do not depend on c_h. (B) Predicted evolutionary route to asexuality for three values of c_p. This time, α appears on the x-axis, while σ is represented on the y-axis. These routes show the transition from sexual hybrids (bottom-left fish) to asexual hybrids (top-right fish). The bottom limit α^* of α for the first mutant to spread varies in each case, and approximately equal respectively from left to right: ($c_p = 0.1$) 0.42; ($c_p = 0.5$) 0.71; ($c_p = 0.9$) 0.42.

scenario is that a hybrid female, independently of whether it produces reduced or unreduced eggs, can never produce viable offspring when mating with a hybrid male (the sperm is unviable and thus unable to trigger embryogenesis). Thus, a mutant can gain a reproductive advantage over wild types only when mating with parental males, which happens with a probability $1-\hat{\Phi}$ that decreases with c_h. The mutant will gain a reproductive advantage only if it produces clonal eggs and prevents pronuclei fusion, which is why the mutation must affect both α and β at the same time.

Again, the mutant fitness function is maximized by a fully asexual mutant ($\alpha = 1, \beta = 1, \sigma = 1$). Once a first mutant has been able to invade, we thus expect the eventual evolution of complete asexuality by the spreads of new mutants displacing older ones. That is, even though the first step appears difficult in this scenario, if it happens we still predict the eventual spread of asexuality via an evolutionary process. We plot in Figure 6B the expected evolutionary routes to asexuality based on fitness gradients for different values of c_p and c_h. We confirm that in this scenario the first mutant must bring in important alterations of the three traits. Afterwards, we see that clonal egg production and pronuclei fusion prevention evolve jointly to $\alpha = 1$ and $\beta = 1$. Once this is reached, sex ratio evolves in turn to $\sigma = 1$.

Discussion

A number of transitions from sexuality to asexuality have taken place in hybrid species; this number is particularly large and disproportionate in vertebrates Beukeboom & Vrijenhoek (1998); Schlupp (2005). The prevailing explanation is that genomic incompatibilities between parental genomes result in the spontaneous birth of fully asexual hybrids from sexual parents Janko et al. (2018); Mogie (1992); Moritz et al. (1989). This explanation however does not account for all cases of asexual hybrids. For example, crosses between *Poecilia latipinna* and *Poecilia mexicana*, parental species of the asexual Amazon Molly, have repeatedly failed to produce asexual hybrids Dries (2003); Lampert et al. (2007); Ptacek (2002); Stöck et al. (2010); Turner et al. (1980). Similarly, crossings of *Daphnia pulex* and *Daphnia pulicaria* have failed in producing obligate parthenogenetic hybrids, though those are observed in the wild Heier & Dudycha (2009); Xu et al. (2015). In another line of evidence, a history of back-crossing has been suggested for the parthenogenetic stick insect *Timema shepardi* Schwande & Crespi (2009), as its genome disproportionately seems to display sequences inherited from one of its parental species, *Timema californicum*. A similar history of backcrossing has been argued in asexual hybrids of *D. pulex* and *D. pulicaria* to explain the complex

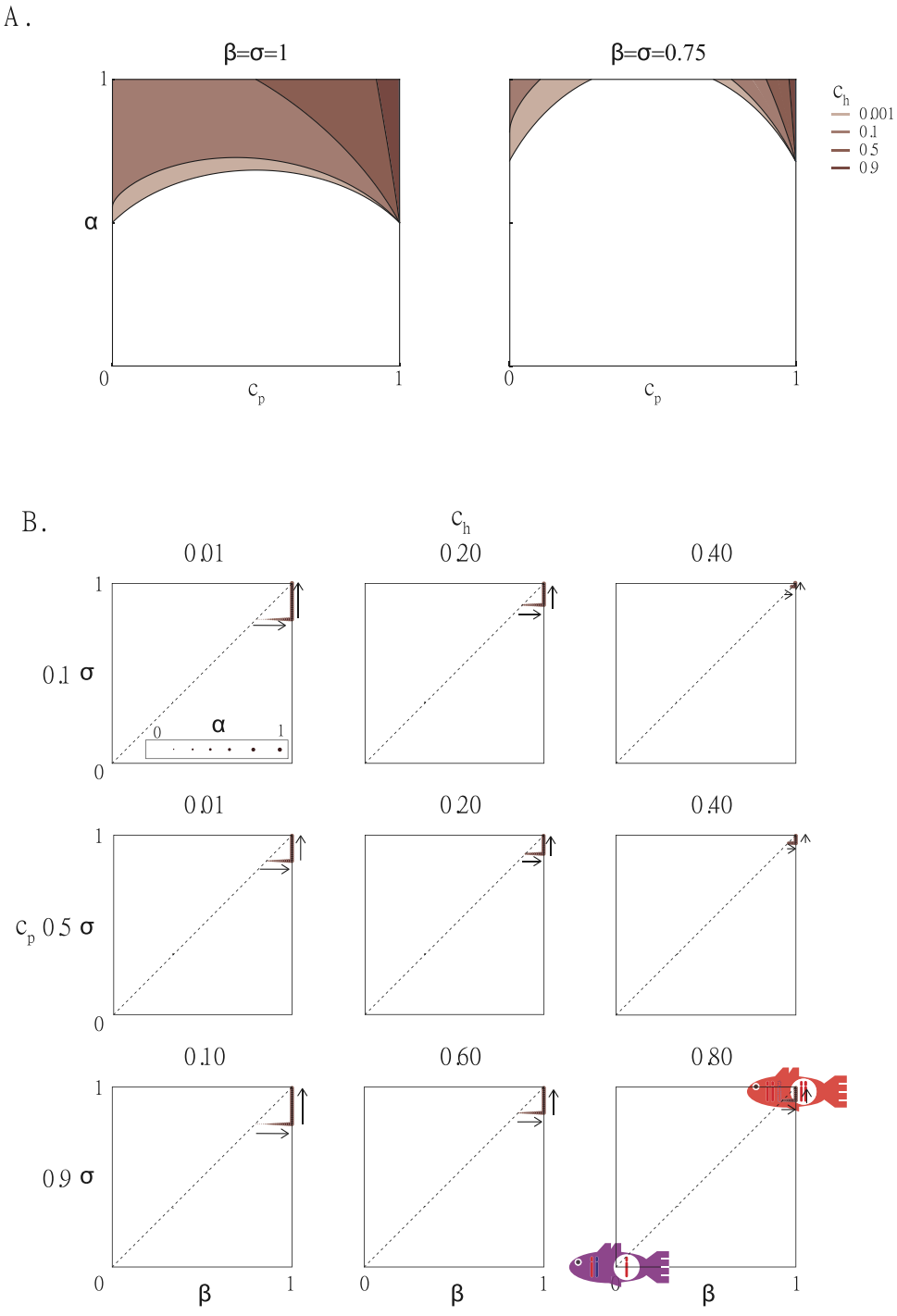

Figure 6. Evolution of asexuality in the nonviable-sperm scenario. (A) Values of $\alpha > \alpha^*$ (y-axis) where a mutant can invade are indicated in function of c_p (x-axis) and c_h as shaded areas for different values of β and σ. (B) Predicted evolutionary route to asexuality for nine combinations of c_p and c_h values. The size of the dot represents α, while x- and y-axes represent β and σ, respectively. These routes show the transition from sexual hybrids (bottom-left fish) to asexual hybrids (top-right fish). The first mutant to spread is assumed to have a mutation such that $\alpha = \beta = \sigma$ for simplicity. The bottom limit α^*, β^*, and σ^* for the first mutant to spread approximately equals respectively from left to right and top to bottom: ($c_p = 0.1$) 0.79, 0.88, 0.98; ($c_p = 0.5$) 0.85, 0.90, 0.96; ($c_p = 0.9$) 0.80, 0.85, 0.93.

and variable introgression patterns observed in these lineages Xu et al. (2015). Backcrosses imply that the original hybrids were at least partly sexual for a number of generations before obligate asexuality took hold. Here, we explore an alternative scenario where incompatibilities that disrupt limited parts of the reproductive process lead to the progressive evolution of asexuality by natural selection. Such evolutionary mechanism allows to explain cases mentioned above, as in this case (a) F1 are not yet asexual and (b) a number of sexual reproduction events happen before the spread of asexuality, potentially including backcrossing, and leading to a diversity of introgression patterns.

Our model allows for the different reproductive traits that characterize asexuality to evolve independently. We decouple the two components of amphimixis, that is, the fusion of the egg and sperm that triggers embryogenesis from the union of maternal and paternal genomes that traditionally restores ploidy. The three models we have analyzed in this manuscript represent two very different forms of fertilization disruption as a result of hybridization. In the first two scenarios, hybrid egg and sperm can fuse and embryogenesis can be triggered, but the union of maternal and paternal genome fails. In the first model, it fails because hybrid sperm is unable to provide the necessary machinery (e.g., it is unable to do its part in the decondensation of the sperm's pronucleus). In the second scenario, it fails because hybrid eggs are unable to provide the necessary machinery (again, e.g., they are unable to participate to sperm pronucleus decondensation). In contrast, in the third scenario, hybrid egg and sperm cannot even fuse, and thus hybrid embryogenesis cannot be triggered by hybrid sperm, for example, because hybrid males are unable to produce viable sperm. We show under which conditions asexuality can evolve from any of these disruptions. We propose a new link between hybridization and asexuality: that hybridization disrupts one of the two aspects of amphimixis, which in turns triggers the evolution of asexuality as a way to rescue hybrid reproduction. This is not a completely new idea. Previous studies have suggested that asexuality in hybrid females sometimes arises at the same time as male sterility, and allows to rescue them from extinction Dedukh et al. (2020); Kuroda et al. (2018). Here, we argue that asexuality could in fact evolve after male sterility; that male sterility provides a selective force that favors the evolution of asexuality.

This selective force can be seen as a form of reproductive assurance. Reproductive assurance theory contends that true parthenogenetic females gain a reproductive advantage over sexual ones because they do not need mating and fertilization (which may fail for a diversity of reasons) Eckert et al. (2006). Here, we show that this idea of reproductive assurance can actually apply to the evolution of both parthenogenesis and gynogenesis. Even though gynogens do need mates and fertilization (egg and sperm fusion), we show that they can still benefit from reproductive assurance if male gametes are not always able to transmit their genomes (in which case sexual females have limited reproductive outputs). Moreover, reproductive assurance has traditionally been associated with mate scarcity because of reduced population sizes or biased sex ratios Burke & Bonduriansky (2019); Gerritsen (1980); Markow (2013); Mraz & Mrazova (2021). Here, we argue that mates may not be lacking, but mates able to transfer their genetic material may be because of disruptions to the fusion of maternal and paternal pronuclei. Whenever this happens, we expect asexuality to receive a selective advantage.

Our work shows that this selection process may allow for a progressive (one phenotypic trait at a time) evolution of asexuality. We predict that when hybrid sperm can trigger embryogenesis but fails to have its pronucleus fusing with the egg's (first scenario), unreduced meiosis can evolve independently of other traits because females producing clonal eggs can have viable diploid progeny when mating with hybrid males even without preventing the incorporation of any paternal genome. We show that production of more females than males follows. Mechanisms to actively prevent fusion with sperm pronuclei, such as spontaneous embryogenesis (parthenogenesis) or paternal genome elimination (gynogenesis) are not required for any of these features to evolve and can evolve subsequently to allow clonal females to produce viable offspring when mating with parental males too, which becomes increasingly necessary as hybrid sex ratio gets more and more female-biased. Similarly, we predict that when hybrid sperm can trigger embryogenesis but hybrid eggs fail to incorporate sperm pronuclei (second scenario), unreduced meiosis evolves independently because it restores hybrid female fertility. A female bias sex ratio evolves afterwards. Spontaneous embryogenesis or paternal genome elimination does not evolve as the paternal genome is never incorporated by hybrid females anyway. Finally, we predict that when hybrids produce nonviable sperm (third scenario), unreduced meiosis cannot evolve independently, but require the concurrent evolution of spontaneous embryogenesis/paternal genome elimination. In this model, the conditions for asexuality to evolve are very restrictive. In particular, a fully, or almost fully asexual hybrid has to appear as a result of a mutation, which has been claimed to be difficult Neiman et al. (2014). In the first two scenarios, we propose an evolutionary path where unreduced meiosis and spontaneous embryogenesis/paternal genome elimination do not necessarily need to evolve together, which significantly simplify the underlying evolutionary processes. As such, we expect these scenarios to be particularly prone to the evolution of asexuality. Whichever scenario we consider, such genomic failures are arguably much more susceptible to appear in hybrid species that combine diverged parental genomes than in nonhybrid species, which would explain why so many asexual species are of hybrid origin. That is, we propose that many asexual species are hybrid species because hybrid species are a fertile ground for the evolution of asexuality by natural selection: Hybrid species have more chances to have limited reproductive capabilities, which may more or less easily be rescued by the evolution of asexuality.

To the best of our knowledge, there exists no conclusive evidence that shows how failure in the fusion of maternal and paternal pronuclei may happen as a result of genomic incompatibilities in hybrid species. This is because it is a complex cytological mechanism and until now there was no reason to specifically look for the mechanics of such disruption in hybrids; we hope our work will raise a stronger interest in investigating this. Although there are no specific examples of fusion failure in hybrids due to paternal or maternal factors, there are various indirect evidence that support that it is possible. On one hand, a diversity of cases where progeny of interspecific crosses did not incorporate paternal genetic material have been recorded Gibeaux et al. (2018); Lamelza et al. (2019); Sanei et al. (2011). On the other hand, there is evidence that egg products can prevent sperm pronucleus decondensation. For example, sperm pronuclei of the sexual common carp (*Cyprinus carpio*) are unable to decondense in egg extracts of the gynogenetic Gibel carp (*Carassius auratus gibelio*) Li & Gui (2003). Also, there is evidence that changes in the paternal genome can be responsible for maternal and paternal promucleus fusion failure. For example, nonfunctional mutations in Drosophila males (*Drosophila melanogaster*) lead to sperm pronucleus decondensation failure Fitch & Wakimoto (1998); Ohsako et al. (2003). Overall, several lines of evidence support the plausibility of the assumptions underlying the scenarios that involve a failure of the union of maternal and paternal pronuclei. The assumption of the third model, that hybrid sperm is nonviable, has been

frequently observed and relates to Haldane's rule Haldane (1922); Schilthuizen et al. (2011).

Our research underscores the importance of the mating structure on the evolution of asexuality in hybrids. We showed that random mating between parental species, that is intermediate values of c_p, makes the evolution of asexuality most difficult in the three scenarios (see Figures 4–6). However, we emphasized that this effect is really about asexual mutants having a harder time invading whenever there is a greater production of sexual hybrids by direct hybridization between the parental species. Thus, we predict that the evolution of asexuality in hybrids should rather be expected in cases of rare hybridization, whether it is because of mating choices (for example, large c_p), or because of the geographical distributions of the parental species. In the *sperm-fails-to-decondense scenario*, assortative mating within hybrids, that is $c_h \approx 1$, most favors the evolution of asexuality (see Figure 4) because hybrid male gametes unable to transmit their genomes allow females bearing clonal eggs to gain a reproductive advantage over meiotic females. In the *egg-fails-to-decondense-sperm scenario*, the likeliness that asexuality will evolve does not depend on hybrid matings (see Figure 5) because unreduced meiosis provides a reproductive advantage independently of with whom the females are mating. Finally, in the *nonviable-sperm scenario*, asexuality is most likely to evolve in cases of disassortative mating within hybrids ($c_h \approx 0$, see Figure 6) because matings with hybrid males are always fruitless. Again, frequencies of matings can be the result of behavior as well as population structure or environmental factors.

In our model, we made the assumption that there was no interspecific competition of any sort. This is unlikely to be true in real life. Hybrids tend to share phenotypic traits with their parental species, such that they usually partially or totally share resources and ecological niche. This assumption was used as it was the easiest way to ensure constant coexistence of the three species—here, we are not interested in the problem of the coexistence between asexual hybrids and their sexual ancestors; this question has been treated elsewhere Heubel et al. (2009); Kokko et al. (2008); Leung & Angers (2018); Schley et al. (2004). To make sure that this hypothesis was not biaising the results, we analyzed the model relaxing it. We describe in Supplementary Material the condition for coexistence of the three species and show that this alteration of the model does not qualitatively influence the results: If the species coexist in the long term, asexual mutants are selectively favored under the conditions and modes described here. Quantitatively, we see that interspecific competition for resources makes it more difficult for a first partially asexual mutant to spread. This is because an arising mutant now faces an increased number of competitors, namely individuals from all three populations, which increases its death rate. If the first mutant has been able to spread, then our prediction that evolution of full asexuality ensues is maintained.

By assuming that all hybrids compete equally with each other, we are also supposing that the hybrid species is phenotypically homogeneous. Again, this does not necessarily correspond to real-life situations. Hybrid zones generally display a wide diversity of intermediary, more or less admixed phenotypes (including phenotypes that may be extremely similar to the parental species) Barton & Hewitt (1985). Hybrid species can often be seen as a mosaic of classes that compete very differently with each other and with each of the parental species. A mutation may thus suffer from different competitive environments and thus have different evolutionary fates depending on the class of hybrids bearing it. However, we showed that assuming some interspecific competition is not providing any qualitatively different result. We predict that similarly, assuming different hybrid classes would greatly complicate the model, without bringing in any novelty. Most likely, the most favorable genetic background for a mutation to invade would be the one where competition is most limited. This, in turn, would depend on population dynamics and competition parameters and is hard to predict. This would not change the expectation that a partially asexual mutation is expected to invade when the benefits of producing clonal eggs overcome the costs of competition, and that afterwards asexuality is expected to fully evolve in a stepwise process.

Overall, we proposed here a theory for the evolution of asexuality in general, providing an evolutionary link between asexuality and hybridization, and showing that in certain cases unreduced meiosis can evolve independently of spontaneous embryogenesis or paternal genome elimination, significantly easing the evolutionary process. The main difference with previous theory is that here F1 hybrids are not readily asexual and that asexuality evolves as the result of a selective process. We illustrated our results assuming that F1 hybrids are completely sexual. This assumption tends to imply that ancestors of modern asexuals have gone through sexual reproduction events.

One caveat is that a majority of studies have reported fixed heterozygosity in asexual hybrid lineages—these often appear to be "frozen F1." Frozen F1s have been found in the three major branches of asexual vertebrates, namely fishes Janko et al. (2012); Warren et al. (2018); Yamada et al. (2015), amphibians Graf & Polls-Pelaz (1989), and reptiles Freitas et al. (2019). To be compatible with frozen F1 our model would require that asexual hybrids descend from F1 ancestors through a continuous lineage of clonal eggs, precluding any sexual reproduction event that would significantly reduce heterozygosity. That could happen for example under the restrictive assumption that F1 ancestors exhibit high rates of clonal egg production, either as the result of a strong mutation or as the result of genomic incompatibilities that make all F1 individuals produce many clonal eggs. While, for illustrative purposes, we used the case of wild-type hybrids (including F1) being completely sexual, our model works for the entire range between sexual and asexual F1 hybrids. When we assume that genomic incompatibilities give wild-type hybrids strictly positive rates of clonal egg production, numerical simulations (see Supplementary Material) show that results are qualitatively maintained. Invasion of a first mutation is slightly more difficult, as the birth rate of wild-type hybrids is increased, intensifying competition for newly arising mutants. Notably, the mutant rate of clonal egg production must be greater than the wild-type rate for a mutation to spread, which suggests that selection should not favor a return toward sexuality. Our model can in theory result in any number of sexual reproduction events before fixation of asexuality, thus in any degree of heterozygosity in the asexual hybrids.

We mentioned above that this could explain admixed ancestry found in some asexual lineages. However, it is true that a majority of studies have reported fixed heterozygosity in asexual hybrid lineages—these often appear to be "frozen F1." This has been found in the three major branches of asexual vertebrates, namely fishes Janko et al. (2012); Warren et al.

(2018); Yamada et al. (2015), amphibians Graf & Polls-Pelaz (1989), and reptiles Freitas et al. (2019). Such patterns are incompatible with sexual reproduction history, as a single event of sex would considerably reduce heterozygosity in the descendance.

High rates of clonal egg production spontaneously appearing in the F1 as a result of genomic incompatibilities do not necessarily mean that hybrids are entirely asexual (as assumed in the prevailing explanation of hybrids' asexuality). For example, F1 hybrids have been obtained in the lab that produce exclusively clonal eggs, but exhibit varying degrees of ability to discard paternal genomes Choleva et al. (2012). In this study, no F1 hybrid female were able to discard paternal genome for more than half of their eggs; thus, even though selection on standard deviation should play a role here thanks to pre-existent variability, selection on de novo mutations appears necessary to reach complete gynogenesis. Our model explains how partially asexual F1 hybrids, for example that produce clonal eggs but are not always able to discard paternal genome, should evolve toward an optimization of asexuality (which is compatible with hybrids of this system being fully asexual in the wild) rather than toward a regression back to sexuality.

Fine-tuning of partially asexual hybrid traits, instead of evolving back to sexuality, is not a trivial evolutionary outcome; here, we provide a solid basis to explain why in hybrid species such a path might indeed be favored. In that sense, we build here a general framework to think about how asexual hybrids may appear and thrive. Under the scenario of the prevailing explanation, asexuality appears in the F1 generation as a result of genomic incompatibilities—then, our model allows to understand how such asexuality is maintained against possible mutations that would take hybrid reproduction back toward sexuality. In addition, our work introduces an alternative scenario: Asexuality evolves as a result of selection for de novo mutations. In that case, our model describes the condition on selection and mutations for asexuality to progressively evolve, as well as the modalities of this evolution.

Supplementary material

Supplementary material is available online at *Evolution*.

Data availability

All the codes used to produce the results and figures present in this manuscript can be found in a Wolfram's Mathematica notebook stored in the GitHub public depository: https://github.com/FredericFyon/WhyHybridsTurnDownSex.

Author contributions

F.F., W.B., I.S., and F.U. conceived the research; F.F., G.W., and F.U. formulated the model; F.F., G.W., and F.U. analyzed the model; and F.F., G.W., and F.U. wrote the manuscript with input from W.B. and I.S.

Funding

This work was supported by the National Science Foundation (Division of Environmental Biology)/Natural Environment Research Council (NSFDEB-NERC) Research Grant NE/T009322/1.

Conflict of interest: The authors declare no conflict of interest.

Acknowledgments

F.U. thanks Diane Tran for invaluable advice and support.

References

Avise, J. C. (2015). Evolutionary perspectives on clonal reproduction in vertebrate animals. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(29), 8867.

Barton, N. H. & Hewitt, G. M. (1985). Analysis of hybrid zones. *Annual Review of Ecology and Systematics*, *16*(1), 113–148.

Bell, G. (1982). *The masterpiece of nature: The evolution and genetics of sexuality*. Croom Helm.

Beukeboom, L. W., & Vrijenhoek, R. C. (1998). Evolutionary genetics and ecology of sperm-dependent parthenogenesis. *Journal of Evolutionary Biology*, 11(6), 755–782.

Burke, N. W., & Bonduriansky, R. (2019). The paradox of obligate sex: The roles of sexual conflict and mate scarcity in transitions to facultative and obligate asexuality. *Journal of Evolutionary Biology*, *32*(11), 1230–1241.

Choleva, L., Janko, K., De Gelas, K., Bohlen, J., Šlechtová, V., Rábová, M., & Ráb, P. (2012). Synthesis of clonality and polyploidy in vertebrate animals by hybridization between two sexual species. *Evolution*, *66*(7), 2191–2203.

Dedukh, D., & Krasikova, A. (2022). Delete and survive: Strategies of programmed genetic material elimination in eukaryotes. *Biological Reviews*, *97*(1), 195–216.

Dedukh, D., Majtánová, Z., Marta, A., Pšenička, M., Kotusz, J., Klíma, J., Juchno, D., Boron, K., & Janko, A. (2020). Parthenogenesis as a solution to hybrid sterility: The mechanistic basis of meiotic distortions in clonal and sterile hybrids. *Genetics*, *215*(4), 975.

Dries, L. A. (2003). Peering through the looking glass at a sexual parasite: Are amazon mollies red queens? *Evolution*, *57*(6), 1387–1396.

Drosopoulos, S. (1978). Laboratory synthesis of a pseudogamous triploid 'species' of the genus *Muellerianella* (Homoptera, Delphacidae). *Evolution*, *32*(4), 916–920.

Eckert, C. G., Samis, K. E., & Dart, S. (2006). Reproductive assurance and the evolution of uniparental reproduction in flowering plants. In L. D. Harder, & S. C. H. Barrett (Eds.), *Ecology and evolution of flowers*. Oxford University Press.

Engelstädter, J. (2008). Constraints on the evolution of asexual reproduction. *BioEssays*, *30*(11–12), 1138–1150.

Fitch, K. R., & Wakimoto, B. T. (1998). The paternal effect gene ms(3)sneaky is required for sperm activation and the initiation of embryogenesis in *Drosophila melanogaster*. *Developmental Biology*, *197*(2), 270–282.

Freitas, S. N., Harris, D. J., Sillero, N., Arakelyan, M., Butlin, R. K., & Carretero, M. A. (2019). The role of hybridisation in the origin and evolutionary persistence of vertebrate parthenogens: A case study of *Darevskia* lizards. *Heredity*, *123*(6), 795–808.

Galis, F., & van Alphen, J. J. M. (2020). Parthenogenesis and developmental constraints. *Evolution & Development*, *22*(1–2), 205–217.

Gerritsen, J. (1980). Sex and parthenogenesis in sparse populations. *The American Naturalist*, *115*(5), 718–742.

Gibeaux, R., Acker, R., Kitaoka, M., Georgiou, G., van Kruijsbergen, I., Ford, B., Marcotte, E. M., Nomura, D. K., Kwon, T., Veenstra, G. J. C., & Heald, R. (2018). Paternal chromosome loss and metabolic crisis contribute to hybrid inviability in *Xenopus*. *Nature*, *553*(7688), 337–341.

GIGA Community of Scientists. (2013). The Global Invertebrate Genomics Alliance (GIGA): Developing community resources to study diverse invertebrate genomes. *Journal of Heredity*, *105*(1), 1–18.

Giribet, G. (2016). New animal phylogeny: Future challenges for animal phylogeny in the age of phylogenomics. *Organisms Diversity & Evolution*, *16*(2), 419–426.

Graf, J. D., & Polls-Pelaz, M. (1989). *Evolutionary genetics of the Rana esculenta complex* (pp. 289–301). New York State Museum.

Haldane, J. B. S. (1922). Sex ratio and unisexual sterility in hybrid animals. *Journal of Genetics*, *12*(2), 101–109.

Heier, C. R., & Dudycha, J. L. (2009). Ecological speciation in a cyclic parthenogen: Sexual capability of experimental hybrids between *Daphnia pulex* and *Daphnia pulicaria*. *Limnology and Oceanography*, *54*(2), 492–502.

Heubel, K. U., Rankin, D. J., & Kokko, H. (2009). How to go extinct by mating too much: Population consequences of male mate choice and efficiency in a sexual–asexual species complex. *Oikos*, *118*(4), 513–520.

Janko, K., Pačes, J., Wilkinson-Herbots, H., Costa, R. J., Roslein, J., Drozd, P., Iakovenko, N., Rídl, J., Hroudová, M., Kočí, J., Reifová, R., Šlechtová, V., & Choleva, L. (2018). Hybrid asexuality as a primary postzygotic barrier between nascent species: On the interconnection between asexuality, hybridization and speciation. *Molecular Ecology*, *27*(1), 248–263.

Janko, K., Kotusz, J., De Gelas, K., Šlechtová, V., Opoldusová, Z., Drozd, P., Choleva, L., Popiołek, M., & Baláž, M. (2012). Dynamic formation of asexual diploid and polyploid lineages: Multilocus analysis of cobitis reveals the mechanisms maintaining the diversity of clones. *PLoS ONE*, *7*(9), e45384.

Kokko, H., Heubel, K. U., & Rankin, D. J. (2008). How populations persist when asexuality requires sex: The spatial dynamics of coping with sperm parasites. *Proceedings of the Royal Science B: Biological Sciences*, *275*(1636), 817–825.

Kuroda, M., Fujimoto, T., Murakami, M., Yamaha, E., & Arai, K. (2018). Clonal reproduction assured by sister chromosome pairing in dojo loach, a teleost fish. *Chromosome Research*, *26*(4), 243–253.

Lamatsch, D. K., Lampert, K. P., Fischer, P., Geiger, M., Schlupp, I., & Schartl, M. (2009). Diploid Amazon mollies (*Poecilia formosa*) show a higher fitness than triploids in clonal competition experiments. *Evolutionary Ecology*, *23*(5), 687–697.

Lamelza, P., Young, J. M., Noble, L. M., Caro, L., Isakharov, A., Palanisamy, M., Rockman, M. V., Malik, H. S., & Ailion, M. (2019). Hybridization promotes asexual reproduction in Caenorhabditis nematodes. *PLOS Genetics*, *15*(12), e1008520.

Lampert, K. P., Lamatsch, D. K., Fischer, P., Epplen, J. T., Nanda, I., Schmid, M., & Schartl, M. (2007). Automictic reproduction in interspecific hybrids of poeciliid fish. *Current Biology*, *17*(22), 1948–1953.

Laumer, C. E., Fernández, R., Lemer, S., Combosch, D., Kocot, K. M., Riesgo, A., Andrade, S. C. S., Sterrer, W., Sørensen, M. V., & Giribet, G. (2019). Revisiting metazoan phylogeny with genomic sampling of all phyla. *Proceedings of the Royal Society B: Biological Sciences*, *286*(1906), 20190831.

Leung, C., & Angers, B. (2018). Imitating the cost of males: A hypothesis for coexistence of all-female sperm-dependent species and their sexual host. *Ecology and Evolution*, *8*(1), 266–272.

Li, C. J., & Gui, J. F. (2003). Comparative studies on in vitro sperm decondensation and pronucleus formation in egg extracts between gynogenetic and bisexual fish. *Cell Research*, *13*(3), 159–169.

Markow, T. A. (2013). Parents without partners: *Drosophila* as a model for understanding the mechanisms and evolution of parthenogenesis. *G3 Genes|Genomes|Genetics*, *3*(4), 757–762.

Meirmans, S., Meirmans, P. G., & Kirkendall, L. R. (2012). The costs of sex: Facing real-world complexities. *The Quarterly Review of Biology*, 87(1), 19–40.

Mogie, M. (1992). *Evolution of asexual reproduction in plants*. Springer.

Moritz, C., Brown, W. M., Densmore, L. D., Wright, J. W., Vyas, D., Donnellan, S., Adams, M., & Baverstock, P. (1989). Genetic diversity and the dynamics of hybrid parthenogenesis in *Cnemidophorus* (Teiidae) and *Heteronotia* (Gekkonidae). In R. M. Dawley & J. P. Bogart (Eds.), *Evolution and ecology of unisexual vertebrates*. New York State Museum.

Mraz, P., & Mrazova, V. (2021). Greater reproductive assurance of asexual plant compared with sexual relative in a low-density sympatric population: Experimental evidence for pollen limitation. *Journal of Evolutionary Biology*, *34*(9), 1503–1509.

Neaves, W. B., & Baumann, P. (2011). Unisexual reproduction among vertebrates. *Trends in Genetics*, *27*(3), 81–88.

Neiman, M., Sharbel, T. F., & Schwander, T. (2014). Genetic causes of transitions from sexual reproduction to asexuality in plants and animals. *Journal of Evolutionary Biology*, *27*(7), 1346–1359.

Ohsako, T., Hirai, K., & Yamamoto, M.-T. (2003). The *Drosophila misfire* gene has an essential role in sperm activation during fertilization. *Genes & Genetic Systems*, *78*(3), 253–266.

Ptacek, M. B. (2002). *Patterns of inheritance of mating signals in interspecific hybrids between sailfin and shortfin mollies (Poeciliidae: Poecilia: Mollienesia)* (pp. 329–342). Springer.

Sanei, M., Pickering, R., Kumke, K., Nasuda, S., & Houben, A. (2011). Loss of centromeric histone h3 (cenh3) from centromeres precedes uniparental chromosome elimination in interspecific barley hybrids. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(33), E498–E505.

Schilthuizen, M., Giesbers, M. C. W. G., & Beukeboom, L. W. (2011). Haldane's rule in the 21st century. *Heredity*, *107*(2), 95–102.

Schley, D., Doncaster, C. P., & Sluckin, T. (2004). Population models of sperm-dependent parthenogenesis. *Journal of Theoretical Biology*, *229*(4), 559–572.

Schlupp, I. (2005). The evolutionary ecology of gynogenesis. *Annual Review of Ecology, Evolution, and Systematics*, *36*(1), 399–417.

Schwander, T., & Crespi, B. J. (2009). Multiple direct transitions from sexual reproduction to apomictic parthenogenesis in timema stick insects. *Evolution*, *63*(1), 84–103.

Simon, J.-C., Delmotte, F., Rispe, C., & Crease, T. (2003). Phylogenetic relationships between parthenogens and their sexual relatives: The possible routes to parthenogenesis in animals. *Biological Journal of the Linnean Society*, *79*, 151–163.

Sinclair, E. A., Pramuk, J. B., Bezy, R. L., Crandall, K. A., & Sites, J. W., Jr. (2010). Dna evidence for nonhybrid origins of parthenogenesis in natural populations of vertebrates. *Evolution*, *64*(5), 1346–1357.

Smith, J. M., & Szathmary, E. (1997). *The Major transitions in evolution*. Oxford University Press.

Stöck, M., Lampert, K. P., Möller, D., Schlupp, I., & Schartl, M. (2010). Monophyletic origin of multiple clonal lineages in an asexual fish (*Poecilia formosa*). *Molecular Ecology*, *19*(23), 5204–5215.

Turner, B. J., Brett, B.-L. H., & Miller, R. R. (1980). Interspecific hybridization and the evolutionary origin of a gynogenetic fish, *Poecilia formosa*. *Evolution*, *34*(5), 917–922.

Vrijenhoek. R. C. (1993). The origin and evolution of clones versus the maintenance of sex in poeciliopsis. *Journal of Heredity*, *84*(5), 388–395.

Warren, W. C., García-Pérez, R., Xu, S., Lampert, K. P., Chalopin, D., Stöck, M., Loewe, L., Lu, Y., Kuderna, L., Minx, P., Montague, M. J., Tomlinson, C., Hillier, L. W., Murphy, D. N., Wang, J., Wang, Z., Garcia, C. M., Thomas, G. C. W., Volff, J.-N., ... Schartl, M. (2018). Clonal polymorphism and high heterozygosity in the celibate genome of the Amazon molly. *Nature Ecology & Evolution*, *2*(4), 669–679.

Xu, S., Spitze, K., Ackerman, M. S., Ye, Z., Bright, L., Keith, N., Jackson, C. E., Shaw, J. R., & Lynch, M. (2015). Hybridization and the origin of contagious asexuality in *Daphnia pulex*. *Molecular Biology and Evolution*, *32*(12), 3215–3225.

Yamada, A., Kodo, Y., Murakami, M., Kuroda, M., Aoki, T., Fujimoto, T., & Arai, K. (2015). Hybrid origin of gynogenetic clones and the introgression of their mitochondrial genome into sexual diploids through meiotic hybridogenesis in the loach, *Misgurnus anguillicuadatus*. *Journal of Experimental Zoology Part A: Ecological Genetics and Physiology*, *323*(9), 593–606.