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Exceptionally rare genomic combinations to skip sex: blending old ideas and new data

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Abstract

The unusual occurrence and developmental diversity of asexual eukaryotes still remain a puzzle. Despite asexual organisms have a theorized two-fold reproductive advantage over sexuals, asexual lineages are rare among multicellular eukaryotes. Justification of such disparity relies on the consequences of a lack of meiosis, which restricts genotype diversity and adaptation to novel conditions while accelerating the genetic degeneration that drives asexual lineages to an early demise. However, evidence indicates asexuals use different strategies to limit negative consequences of ameiosis, and age estimates show some asexual vertebrates and plants are much older than expected. If rapid extinction is not a factor influencing asexuals lifespan, then why asexuals are not more frequent? Here we review traditional ideas and new data and provide a novel unified evolutionary frame to understand the intriguing nature, developmental diversity and maintenance of asexual lineages. As a rule, *de novo* formation of a functioning asexual genome requires a unique assemblage combining particular sets of genes or gene states to disrupt cellular mechanisms of meiosis and gametogenesis, and affect discrete components of sexuality to produce clonal or hemiclonal offspring. We highlight two usually overlooked but essential conditions to understand the molecular nature of clonal organisms, i.e. a non-recombinant genomic assemblage retaining modifiers of the sexual program, and a complementation between altered reproductive components. These subtle conditions are the basis for physiologically viable and genetically balanced transitions between generations. Genomic and developmental evidence from asexual animals and plants indicates the lack of complementation of molecular changes in the sexual reproductive program is likely the main cause of asexuals´ rarity, and can provide an explanatory frame for the developmental diversity and lability of developmental patterns in some asexuals as well as for the discordant time to extinction estimations.

Keywords: amphimixis, apomixis, gynogenesis, hybridogenesis, parthenogenesis.

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Sexuality is ubiquitous to most eukaryotes, but approximately 1 in 10 000 species is asexual and have a patchy phylogenetic distribution (Bell 1982). The scarcity of obligate asexual lineages among multicellular taxa is at first sight counterintuitive if one considers their theorized two-fold reproductive advantage. Because they usually produce only one sex, every individual gives rise to offspring and with a lower investment in mating processes asexuality should be a much more successful and thus more widespread reproductive strategy. However, the absence of meiotic recombination is expected to hinder the creation of genotypic variation and/or adaptation to novel conditions (e.g. Red Queen, Tangled Bank, Lottery hypotheses), and is anticipated to accelerate the stochastic accumulation of slightly deleterious mutation and genetic degeneration (e.g. Muller´s ratchet, Hill-Robertson effect) leading to genomic decay and extinction of asexual lineages after a brief existence. This has been observed indeed in a few examples (Tucker et al. 2013) but this appears far from being the rule. Even with the prediction of an early demise, some well-known asexual lineages in vertebrates and plants for which age estimates exist had persisted much longer than expected from mathematical models derived from such theoretical considerations (Lampert and Schartl 2008; Pellino et al. 2013). Asexuals have developed a varied number of strategies to limit the negative consequences of ameiotic reproduction, e.g. by sporadic recombination, “mutation based” diversity and clonal competition (Avise 2015; Ferreira de Carvalho et al. 2016; Warren et al. 2018), and thus neither reduced genetic variability nor longevity are critical constrains (Williams 1975). If rapid extinction is not a factor influencing asexual lineages lifespan, then why asexuals are not more frequent? Why are they a rare phenomenon? Why do they display a variety of developmental strategies, as has been particularly noted in many studies on asexual species?

Stanley (1975) argued that asexual species are rare because speciation in asexuals (their origins) is exceedingly rare, and in the long-term species selection will eliminate most asexuals. However, as all asexuals arise from sexual forms, this doesn´t explain why the frequency of *de novo* formation or of successful establishment of asexuals in nature is not higher. According to Maynard Smith (1986) meiosis and sexuality is so entrenched in life that any shift away from it creates “sexual hang-ups” difficult to be overcome by selection. Sexual-to-asexual transitions might follow Dollo´s law of irreversibility (Dollo 1893), which states that once a complex feature is lost in evolution it cannot be regained with the same original state. In this context, the difficulties imposed to new asexuals by developmental constraints derived from its sexual ancestry are responsible for their observed low occurrence, a view connected to the “balance” and the “duplicate-gene asynchrony” hypotheses, the two more widely accepted views about the origin of asexuality in otherwise sexual organisms. The “balance” hypothesis, proposed by Moritz et al. (1989) to explain observations in animals, considered the divergence of parental genomes has to be the right one both to increase the rate of unreduced gametes and to maintain hybrid´s viability and fecundity. The “duplicate-gene asynchrony” hypothesis, proposed by Carman (1997) to explain observations in plants, considered that genes when originating from different genomes in polyploids respond differentially to temporal and spatial developmental signals causing the anomalies during meiosis and gametogenesis observed in apomicts (i.e. plants reproducing through asexual seeds) and polysporic species. Carman´s hypothesis also implies that not all plant families may express such asynchrony in the expression of female developmental genes.

In a study of embryogenic developments in aphids, Le Trionnaire et al. (2008) considered the switch between sexual and asexual developments to be a reproductive polyphenism, i.e. a phenotypic dichotomy triggered by photoperiodic cues. Even when this fits observations in organisms that cycle

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between sex and asexual states, it does not explain why some organisms are facultative asexuals (i.e. produce both sexual and asexual progeny under the same environmental conditions). Likewise, from a slightly different perspective, Carman et al. [(2011); see also Carman and Roche 2007] first suggested a similar conception for plants, recently reviewed by Albertini et al. [(2019); see also Carman et al. 2016] emphasizing the role of epigenetic regulations on reproductive transitions and suggesting that sex and apomixis in plants (and expectedly in asexuals from other kingdoms) might respond to an ancient polyphenism regulated by metabolic signalling.

In former years, different experimental crossings and setups preceded and gave support to the above ideas (e.g. Savidan 1982; Nogler 1984; Wetherington et al. 1987; Carman 2007) delineating most relevant developmental constraints associated to asexual origins (Vrijenhoek 1989; Asker and Jerling 1992). However, testing at molecular level such theoretical hypotheses based on empirical observations was not possible. More recently, new omics approaches provided the possibility of collecting massive sequence-level data and brought new tools of analysis that delivered new hints for testing and contrasting previous ideas. Even though these hypotheses have a clear theoretical frame and a conceivable causal basis, they lack a simple mechanistic explanation for the diversity and frequencies of intraspecific and interspecific developmental strategies observed in asexuals (e.g. Asker and Jerling 1992; Avise 2015).

In a recent study on the Amazon molly, Warren et al. 2018 concluded that its rarity is likely driven by the chance of occurrence of genomic combinations required to elude meiosis and create a functioning hybrid genome, and provided molecular evidence to the “rare formation” hypothesis (whose original idea can be tracked back to Stöck et al. 2010). In plants, agreeing with the “duplicate-gene asynchrony”, studies on several apomictic systems have shown global heterochronic gene expression and developmental asynchronies in apomeiotic ovules compared to sexual ones (e.g. Grimanelli et al. 2003; Sharbel et al. 2010; Polegri et al. 2010; Carman et al. 2011, 2019; Sahu et al. 2012; Hojsgaard et al. 2014; Schmidt et al. 2014, Rabiger et al. 2016; Shah et al. 2016; Ortiz et al. 2017). Despite this, those studies had also identified specific genes apparently needed for the emergence of apomixis which contradict Carman´s view and place the question about the existence of master genes shifting genetic developmental programs in plant ovules.

Yet, as we present below, framed appropriately, the recent “rare formation” and older hypotheses can respond to a single molecular basis of asexuality which might apply to all asexual taxa and be the foundation to explain the developmental diversity observed among them. Here we integrate old ideas with recent molecular and genomic data to provide a comprehensive sight on asexual origins. We highlight commonalities which benefit a causal explanation for both the developmental lability observed among and within asexuals, and the sporadic occurrence of asexual taxa. This new perspective offers a joining road for future research on phylogenetically divergent asexuals.

The molecular context and initial conditions toward asexuality

In vertebrates and plants, the groups for which molecular and developmental mechanisms are best characterized, the known asexual lineages are all of hybrid and/or polyploid origin. Even though some asexuals may not have a hybrid or polyploid origin, the presented concepts well apply to all asexuals, including invertebrates, displaying a wide developmental complexity which in different cases blurs definitions of sex (e.g. in parthenogenetic automixis, whereby two cell products of the

same meiosis fuse and start developing a new organism; reviewed in Suomalainen et al. 1987) and therefore are vaguely considered here.

Hybridization, i.e., the process of breeding individuals from the same or different populations or species, is a significant evolutionary force during speciation acting as an isolating reproductive barrier. Hybrid individuals combine from different genomes alleles having variable degrees of divergence, holding short- or long-term separate evolutionary histories and likely having deviating regulatory controls and spatiotemporal patterns of development. Therefore, hybridization results in intergenomic conflicts (genomic shock) where alleles at different loci do not interact well and exhibit altered expression patterns (transcriptomic shock) and a variety of abnormal developments leading to hybrid incompatibility (Johnson 2008). Similarly, polyploidy, i.e. the concurrence of more than two genome sets in a cell, can display the same irregularities owing not only to the interaction of divergent genomes (e.g. when polyploid formation involved hybridization of species) but also due to dosage effects and changes in the molecular stoichiometry of molecules and macromolecular complexes (e.g. when polyploid formation involved individuals from the same or different populations with similar or slightly similar genomes) (Birchler and Veitia, 2012). Another condition which may drive to comparable modifications at molecular level is inbreeding, an important factor in invertebrates with low vagility (e.g. acari, insects), wherein several asexual lineages are known.

Even viable hybrids or polyploids display highly reduced fertility or sterility owing to malfunction of cellular and molecular components of sexual reproduction, e.g., meiotic recombination and fertilization. On the contrary, combinations of parental genomes can be generated, which result in heterotic traits (hybrid vigor) and may, for instance, allow a hybrid lineage to occupy new ecological niches. Whenever reproduction can proceed, hybrid and/or polyploid lineages will gradually ameliorate gene expression and developmental patterns post-hybridization and post-polyploidization to recover sexual functions and fertility (Bomblies et al. 2015).

Alternatively, new hybrids and/or polyploids might produce offspring under a paucity or lack of sexual recombination. However, in such a case, since sexual reproduction is a complex, highly regulated mechanism involving multiple developmental steps and cell types, these organisms require a unique combination of changes in particular sets of genes able to disrupt the cellular mechanisms of meiosis and gametogenesis, and affect discrete components that loose sexual restrictions and simplify the formation of clonal or hemiclonal offspring (Figure 1). Mating independence may well be an example of loose sexual restrictions in animals. In plants, for instance, the two maternal-to-one paternal genome dosage (2m:1p) deterrent in sexuals for normal endosperm development is relaxed in asexuals (allowing a variety of ploidy states during seed formation; discussed in Hojsgaard 2018).

The genetic and epigenetic composition of such new asexual offspring will depend upon the components of sexual reproduction modified. However, in order to maintain an asexual condition, all new lineages must share a common fact, *id est* the particular set of genes states for asexuality have to remain unchanged at least in one genome (Figure 1). Having a non-recombinant genomic assemblage is a *condicio sine qua non* to retain that particular gene combination and epigenetic states needed to modify the sexual program and to transmit it unaltered to the offspring. Hence, in this frame the “sexual hang-ups” of Maynard-Smith can be pictured not as difficult to overcome by selection but rather as a consequence of recombination most likely segregating such particular genetic setting and disassembling the molecular basis for asexuality. A second condition linked to

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the emergence of an asexual lineage is the one of "complementation" between altered components of the sexual reproductive program, which is needed to maintain physiologically and genetically balanced intergenerational transitions. As an example, a new asexual in which meiotic chromosomal reduction is skipped during gametogenesis to produce unreduced gametes shall also avoid incorporating extra chromosomes during fertilization to assure the proper development of offspring.

Consequently, and opposed to sexual organisms, asexuals momentarily avoid genetic shuffling and character segregation, weakening amelioration and purging mechanisms by natural selection. As a result, asexuals are expected to retain post-hybridization genomic and transcriptomic shock states for more extended periods than under sexual reproduction (Hojsgaard 2018), likely a reason why asexuals often exhibit lower fitness compared to sexual relatives (Meirmans et al. 2012) even when they can display superior abilities populating diverse habitats (Kearney 2005; Hörandl 2006). The fact that reproductive tissues of long-existing clonal animals and plants display divergent patterns of gene expression and massive gene dis-regulation compared to sexual ancestors (e.g. Sharbel et al. 2010; Schedina et al. 2018) support this interpretation.

An integrated view

Under this view, the puzzling occurrence of multiple types of asexual developmental strategies sporadically observed in single lineages of animals and plants (see details below) can be explained as a consequence of the genomic state and the challenges derived from the first generations to the establishment of an asexual lineage. Getting the right non-recombinant genomic assemblage and complementation on reproductive changes in an individual may require more than a single attempt. Whenever a new asexual individual fulfilling the two above conditions arises, it may carry the genomic combinations required for one or more than one gametogenetic mechanism and show a variable incidence of different reproductive modes, including sexuality (i.e., facultative parthenogenesis). During first stages post-(intra- or inter-specific) hybridization, associated to the cytogenetic and molecular stabilization of the asexual lineage (Carman 2007; Avise 2015; Hojsgaard 2018), the new hybrid and/or polyploid will likely exhibit low coordination of gene expression and altered reproductive developments causing low reproductive efficiency (fitness). Such patterns have been observed in different recently established organisms exhibiting asexual reproduction or tendencies to asexuality (e.g. Landry et al. 2007; Hojsgaard et al. 2014a). Later, occasional recombination and sex in these individuals will play a pivotal role fine-tuning the efficiency of any reproductive mode and contributing to alleviate a reversal to the sexual program or to establish a persistent asexual lineage (Hojsgaard 2018). The occurrence in nature of different animal and plant groups displaying a variable incidence of diverse reproductive modes and patterns of clonal diversity may well represent a consequence of different developmental outcomes derived from merging particular genomes combining specific genes variants and genetic backgrounds, denoting distinct stages in the evolution of such asexual lineages. This implies that, once the parental species with the right genomic combinations met the appropriate ecological setups in nature, the chances for the emergence of lineages with tendencies toward asexuality will be high. Thus, on a short-time scale asexual lineages might arise on multiple times and show developmental variations on reproductive modes (as observed in many asexuals, see below). Sooner or later, and mainly driven by fertility, surviving aptitudes and –in specific cases- occasional gene flow (introgression), selection will sift the

more reproductively effective lineages and those carrying complemented mechanisms for asexuality will likely become established and persist.

A good example of such variation is the Iberian fish *Squalius alburnoides*. In this species, a wide range of parallel reproductive strategies from syngamy to gynogenesis and altered patterns of hybridogenesis -including paternal leakage- are combined to create a complex of diploid, triploid and tetraploid populations interacting with closely related sexual species. The production of gametes with or without meiosis is strictly depending on the combination of haplomes (Collares-Pereira et al. 2013) – showing the importance of the right genomic conditions to warrant an asexual mode of reproduction and pinpoint the potential to switch between reproductive modes if the genomic background and ecological conditions are met.

In the fish genus *Poeciliopsis*, diploid hybridogens of different genomic combinations exist. Hybridogens can accommodate various sexual haplomes transiently, but it is only the *P. monacha* haplome, common to all asexual lineages that can dominantly impose the reproduction mechanism of hemiclonality (Quattro et al. 1992a). Occasional failure of the meiotic mechanism responsible for the elimination of paternal chromosomes in diploid hybridogenetic biotypes had given rise to triploid gynogenetic biotypes where the sperm is only needed to induce embryogenesis (Quattro et al. 1992b).

In salamanders, gynogenesis is not complete, and the female genome routinely incorporates genetic information from sympatric sexual male donor DNA into their diploid or polyploid genomes (Avise 2008), a mechanism named kleptogenesis (Bogart et al. 2007). This might benefit the lineage with an exceptional longevity (Denton et al. 2018) because it can counteract the genomic decay and low genetic diversity by bringing in new genetic information. Like kleptogenesis, tychoparthenogenesis - the occurrence of sporadic parthenogenesis in sexual species- is unusual among asexual lineages (Avise 2015), and both represent weird cases in which selection driven “complementation” is achieved through incomplete or temporal functional alteration of components of the sexual reproductive program. So-called “facultative parthenogenesis” became well known from enigmatic cases where single females of sharks, snakes and Komodo dragons sired offspring after being deprived from males for extended periods may represent SOS mechanisms rather than natural reproductive strategies. Producing diploid eggs, e.g. through apomixis in those cases could be due to stochastic gene expression variation or epigenetic changes. Whether there is an adaptive mechanism behind these accidental cases, and if those lineages would be more prone to provide the genomic pre-condition for asexuality are interesting questions.

The importance of the right genomic combinations is supported by crossing experiments between the parental species that once gave rise to the gynogenetic *P. formosa*. In the interspecific hybrid females the majority of the oocytes have meiosis problems and are diploid (Lampert et al. 2007). While in the experimental situation these oocytes are fertilized to give rise to triploid offspring, the missing step to fully established gynogenesis is then just the suppression of karyogamy. Similarly, while finding the right genome combination to synthesize hybridogenetic fish of *Poeciliopsis* and *Pelophylax* frogs in the laboratory was after many attempts finally successful, in almost all other cases the many efforts to produce unisexual lineages from crossing the known parental species failed (see Choleva et al. 2012). In nature, however, long-term attempts have recurrently delivered in some species the right genome combinations transitioning to asexuality, as diverse assemblages of asexual lineages have arisen on multiple separate occasions (e.g. Vrijenhoek 1998; Simon et al.

2003; Neiman et al. 2009; Adolfsson et al. 2010; Paczesniak et al. 2013, 2014; Gibs and Denton 2016).

In plants, the embryological, molecular, and genetic evidence suggest that apomixis is induced in diploids by genomic and transcriptomic shocks initiated after inter- or intra-specific hybridization and is stabilized by a rise of ploidy, thus creating allo- and auto-polyploids (for a detailed discussion see Carman 2007, Hojsgaard 2018 and Hojsgaard and Hoerandl 2019). The observed hemizygosity of the genomic region for apomixis in autopolyploids (Ozias-Akins and van Dijk 2007) implies that a single haplome might be sufficient to cope with the mentioned conditions to establish an asexual lineage. However, modifier factors and gene dosage compensation are likely needed to stabilize apomixis functionally as most apomicts are polyploids, and so far the only documented diploid apomict belongs to the *Boechera holboellii* complex, a relative of *Arabidopsis thaliana* showing diploid sexuals, and diploid and triploid apomictic populations (Sharbel et al. 2010). Non-recombinant genomes in apomicts must combine a particular genomic setting and gene states to restrain the sexual pathway bypassing meiosis (i.e., apomeiosis) and initiating embryogenesis (parthenogenesis) and at the same time developing the seed nourishing tissue (endosperm).

As in animals, plants exhibit variations in the incidence of developmental pathways. Some asexual species show sporadically more than one type of apomixis (i.e. diplospory, apospory, adventitious embryony) (Bonilla and Quarin 1997; Hojsgaard et al. 2014b; Carman et al. 2019) and/or occasional non-complementarity between reproductive components causing, e.g. a decrease or an increase of ploidy in the progeny of apomicts after developing seeds from haploid gametes (i.e. haploid parthenogenesis) or from fertilized unreduced gametes (i.e. BIII hybrids) (Asker and Jerling 1992; Ozias Atkins and van Dijk 2007). All natural apomicts studied so far show major shifts in gene expression, the extent and patterning of which require further investigation. Such regulatory changes in gene expression -many related to germ cell specification and gametogenesis- are associated to temporal and spatial developmental asynchronies subject to environmental modulation (e.g. in *Boechera*, Sharbel et al. 2010, Schmidt et al. 2014, Shah et al. 2016; in *Brachiaria*, Rodriguez et al., 2003; in *Eragrostis*, Cervigni et al. 2008; in *Hieracium*, Okada et al. 2013, Rabiger et al. 2016; in *Panicum*, Yamada-Akiyama et al. 2009; in *Paspalum*, Quarin 1986, Polegri et al. 2010, Hojsgaard et al. 2013, Ortiz et al. 2017; in *Pennisetum*, Singh et al. 2007, Sahu et al. 2012; in *Poa*, Albertini et al. 2004; in *Tripsacum*, Grimanelli et al. 2003; in *Ranunculus*, Pellino et al. 2013, Hojsgaard et al. 2014a, Klatt et al. 2016, 2018; Barke et al. 2018).

Asexual plant lineages had also been resynthesized experimentally in rare cases (Quarin 2001) and multiple independent origins had been identified in natural populations (e.g. Sharbel and Mitchel-Olds 2001; Paun et al. 2006; Siena et al. 2008). Occasionally, these apomictic polyploids retain a low level of functional sexuality (i.e. facultative parthenogenesis) which might depend upon the genetic background and the ecological environment (Quarin 1986; Mateo de Arias, 2015; Klatt et al. 2016; Rodrigo et al. 2017) as well as the evolutionary age of the asexual lineage. Recently formed asexuals exhibit more dramatic changes in gene expression, developmental alterations, and reduced fertility, including non-complementarity in the alteration of sexual components and comparatively lower levels of apomixis than older natural lineages (Pellino et al. 2013; Hojsgaard et al. 2014a; Barke et al. 2018). The older the asexual lineage, the higher the efficiency of apomixis and the harsher the depletion of sex. Except for those regions within the genome associated to apomixis which do not recombine and provide stability for the asexual state, the haplomes of old apomicts are expected to display signatures of sporadic sex and chromosome repatterning. Therefore, functional shifts in

components of sexual reproduction can be linked to genomic regions behaving as supergenes (in which even individual genes can be identified) rather than complete haplomes (e.g., Ozias-Akins and van Dijk 2007; van Dijk et al. 2009; Conner et al. 2015).

The above stated conditions and the developmental and molecular evidence present in asexuals do not neglect the different hypotheses on asexual origins. In fact, they all agreed with the different standpoints and theoretical frames of each hypothesis and suggest a common molecular basis for asexuality. The “sexual hang-ups” from Maynard-Smith emphasize the consequences of shifting out of sex and indirectly, about the implications of having recombination between genetic sequences responsible for altering reproductive components. The “balance” hypothesis from Moritz and co-workers points indirectly toward the need of complementation of reproductive components to have a functional asexual organism, while the “rare formation” hypothesis from Warren and co-workers, the “duplicate-gene asynchrony” and “polyphenism” hypotheses from Carman and co-workers put more weight on a probable molecular basis, giving different relevance to genetic and epigenetic contributions.

A modular developmental frame and its evolutionary perspective

In all cases, the emergence of an asexual lineage requires non-recombination on specific genetic and genomic attributes, and a rarely met complementation on altered reproductive components to stabilize the lineage.

On the one hand, this explains why -once established- asexuality behaves as a dominant trait, whether in genetic inheritance studies (mainly in plants; Ozias-Atkins and van Dijk 2007), or because asexuals do not give birth to sexuals (mainly in animals; Avise 2015). This is not necessarily due to any individual component of the asexual machinery being dominant over the sexual counterpart but rather because meeting the conditions for asexuality implies unchanged transgenerational transmission, and any recombination between reproductive factors might modify regulatory mechanisms (e.g. epigenetic signals, *cis*- or *trans*- molecular interactions) and disassemble the molecular basis for asexuality.

On the other hand, in practical terms this means that we should observe parallelisms in functional reproductive changes among asexuals from taxonomically and phylogenetically diverse groups. Even though establishing an asexual lineage in plants may require different molecular and cellular interactions compared to animals as well as overcoming diverse ecological constraints (e.g. crowding, starvation, day length), the known asexual animals and plants show in fact intriguing parallelisms in functional aspects and modified components of sexual reproduction (Figure 1), unlikely to be a consequence of chance.

Molecular modifications of centromere proteins (CENH3) can induce paternal chromosomal elimination (Ravi and Chan, 2010). In plants, centromere-mediated genome elimination is used to produce maternal haploids (Kelliher et al. 2016), and case studies of rapid preferential uniparental chromosome elimination in wide-cross hybrids (e.g., *Avena sativa* × *Zea mays*) show changes on reproductive components alike those in hybridogenic animals (Figure 1). However, this mechanism is neither recurrent nor stable in nature and so far a system fully equivalent to that of hybridogenetic animals has not yet been discovered in plants. The majority of polyploid apomictic plants are pseudogamous (e.g., *Hypericum* sp.; *Paspalum* sp.; *Ranunculus* sp.), often tetraploids, and display

functional changes in the sexual reproductive program equivalent to those of gynogenetic animals (Figure 1). The combination of specific genomic modifications in pseudogamous apomicts allows them to annul the consequences of meiotic recombination and chromosomal reduction, while sperms are used to initiate the endosperm and thus stimulate embryogenesis and completion of the development of a functional seed. Finally, autogamous apomictic plants (e.g., *Antennaria* sp.; *Hieracium* sp.; *Erigeron* sp.) alike parthenogenetic animals (e.g., *Darevskia* sp.; *Aspidoscelis* sp.) had become free of the requirement of sperm fertilization, and the offspring is produced without the male contribution (Figure 1). These asexuals are highly associated with polyploidy (mainly triploids but also tetraploids) and represent the most extreme cases of asexuality. Particularly in animals, polyploids are likely by-side products of the process of stabilization of reproductive modes and the transition between sexual and asexual strategies in newly formed hybrid lineages. In plants, however, polyploidy is frequent and most polyploids are sexual though a potential role for transitional apomixis in the establishment of sexual polyploids shall not be discarded (Hojsgaard 2018).

This model of non-recombinant genomic assemblages and complemented reproductive components can also help us explain the occurrence of asexuals of very dissimilar ages. As the initial stage of establishment of a new asexual is the most critical one, the model anticipates that many asexual lineages will have an ephemeral lifespan and be short-lived. However, the likelihood of asexuals being much older than expected is also anticipated and hang upon the quality of the reproductive complementation and developmental lability (or its flexibility to incorporate variability and fine-tune reproductive fitness) of the asexual lineage.

We reason that the number of reproductive components and complexity of their molecular interactions needed during formation of an asexual organism increase from hybridogens to gynogens/pseudogamous apomicts and to parthenogens/autogamous apomicts (from left to right in Figure 1). This increasing complexity also reflects a conceivable evolutionary direction for asexuals and thus places the possibility of transient reproductive states displaying more than one reproductive mode (as discussed above). The increase in complexity implies a rise in the rarity of complementation between reproductive components, and thus a progressive decrease in the proportions of asexuals observed for each category is expected. In nature, such a rare complementation might have the additional challenge of meeting the right ecological setup, a concurrence not easy to replicate instantaneously under experimental conditions. This may explain why obtaining a first generation clonal hybrid is much harsher than crossing extant clonal hybrids (Vrijenhoek 1989; Mallet 2005). Anyhow, as anticipated, hybridogens are more frequent in nature and “more easy” to replicate under experimental conditions than gynogens or parthenogens (Choleva et al. 2012; Avise 2015). Similarly, in plants pseudogamous apomicts are much more frequent than autogamous apomicts. In nature, a reproductive system analogous to that of hybridogens is unmet in plants. Plausible reasons are likely connected to differences in their reproductive biology (e.g. frequent hermaphroditism, development of a gametophyte, double fertilization and parallel development of embryo and endosperm tissues), timing of germline specification and epigenetic resetting of maternal and paternal chromosomes (genomes) compared to animals (Feng et al. 2010; MacDonald 2012).

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411 *Conclusion*

412 Genomic and developmental restrictions imposed both by gene interactions, physiological
413 responses, and ontogeny of sexual processes hamper the evolution of asexuality in all living groups.
414 In both plants and animals, the first generations after hybridization and/or polyploidization have
415 drastic consequences on retaining specific genomic combinations needed to stabilize reproductive
416 modes and assure the lineage´s subsistence. The higher the complexity of cytological mechanisms
417 inducing asexuality, the lower the chances of putting together in a new individual the genomic
418 combinations required. While genomic decay is a long-term force acting upon asexuals, their rare
419 occurrence may well be determined by the stochastic chance of converging and maintaining the
420 appropriate genomic combinations and reproductive complementation rather than by a short-lived
421 fate. As implicitly exposed in many previous works, discussions of asexual lineages in the future
422 should emphasize the likelihood of their formation based on biochemical and molecular mechanisms
423 rather than on speculative discussions concerning shorter lifespans or degenerating fitness benefits.

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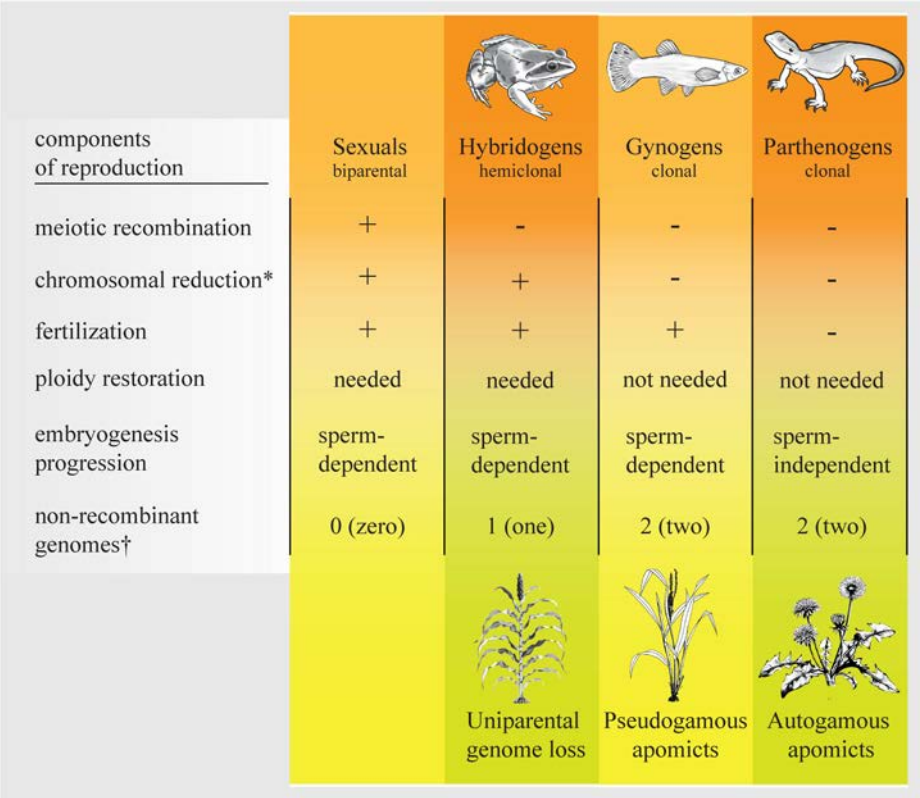

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426 **Figure 1.** Recurrent modification of components of sexual reproduction observed in asexual
427 organisms. The graph show the increase in the number and complexity of developmental changes
428 required in each reproductive category (occasional occurrence of deviations on reproductive
429 components in each category is expected but not included here; e.g. kleptogenesis). In
430 hybridogenetic species, the paternal chromosomes are eliminated during the formation of gametes,
431 and the offspring inherit only the maternal chromosomes. Fertilization by a male donor restores
432 ploidy and enables embryo development. Gynogenetic and pseudogamous apomict species are also
433 sperm-dependent because they still require fertilization to trigger the parthenogenetic development
434 of the diploid egg physiologically but need to skip meiosis to retain the ploidy of the genome. Sperm-

independent embryogenesis of unreduced eggs occurs in parthenogenetic and autogamous apomict species.

*: refers to the formation of gametes carrying half the number of chromosomes of the mother.
†: based on a potential parental contribution of up to two genome sets (2*n*; *n*=1x, 2x…*i*x) to the offspring.

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Competing interest

The authors declare there are no competing interests concerning this study.

Author Contributions

DH conceptualized and designed the study, collected data and drafted the manuscript; MS collected data and helped draft the manuscript. Both authors gave final approval for publication and agree to be held accountable for the work performed therein.

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