

Are Hybridogenetic Frogs Cyclical Parthenogens?

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SEXUAL AND ASEQUAL REPRODUCTION both have advantages and disadvantages¹⁻³. Most species reproduce either sexually or asexually, but cyclic parthenogenetic species alternate sexual and asexual reproduction with several asexual generations followed by a sexual generation³. Wright⁴ noted that 'the combination of pre- valuing uniparental reproduction with occasional cross breeding gives results with the favourable properties of both systems' (i.e. sexual and clonal reproduction). Recently, this prediction has been confirmed^{5,6}. It has been suggested that life cycles with occasional sex should be the norm, for they combine the advantages of sexual and asexual reproduction while incurring minimal costs of both systems⁵⁻⁸.

Despite its advantages, cyclic parthenogenesis is uncommon. It is observed in some invertebrates (e.g. aphids, cladocerans and rotifers⁹); but more species where sex has not yet been observed may be cyclical parthenogens⁹). Hitherto, cyclic parthenogenesis had not yet been described for vertebrates. Recent work by Hotz, Beerli and Spolsky¹⁰ on hybridogenetic frogs in the *Rana esculenta* complex suggests, however, that they have a reproductive system very similar to cyclic parthenogenesis.

Hybridogenesis¹¹ is a mode of reproduction in which one parental genome is not transmitted to the progeny. During gametogenesis, one genome is excluded while the other is transmitted clonally. Hybridogenesis has evolved at least three times: in the stick insect *Bacillus rossius-grandis benazzii*¹², in the teleost fish *Poeciliopsis*¹¹ and in the frog *Rana esculenta*¹³⁻¹⁵.

Rana esculenta (genotype RL, phenotype E) is not a conventional species: it originated from hybrid matings between *R. lessonae* (genotype LL, phenotype L) and *R. ridibunda* (genotype RR, phenotype R). During gametogenesis, *R. esculenta* excludes its parental (not necessarily paternal) *lessonae* genome before or during meiosis, duplicates the *ridibunda* genome and produces haploid gametes that contain only *ridibunda* genes. The *lessonae* genome is lost from the germ line¹⁶. Somatic hybridity is restored in the offspring through matings with *R. lessonae*. *Rana esculenta* is a perpetual F₁ hybrid (Table 1). This reproductive system has been called hemiclonal hybridogenesis¹⁵. Usually E × E mat-

ings lead to inviable offspring^{13,15}. They are thought to have high levels of homozygosity and an accumulation of deleterious mutations¹⁵.

Rana ridibunda is usually absent in mixed populations of *R. lessonae* and *R. esculenta* (the L-E system). But sometimes *R. ridibunda* occurs. Hotz, Beerli and Spolsky¹⁰ have recently shown that E × E matings at Trubeschloo, Switzerland (and other sites¹⁷), repeatedly led to viable offspring and fertile female *R. ridibunda*. Frogs have sex chromosomes (males XY) and *ridibunda* clones in *R. esculenta* always carry X (Refs 15,18). (Male *ridibunda* clones could arise by a L female × R male mating, but this type of mating does not occur for behavioural reasons^{14,18}.) Hence, offspring of E × E matings are always females. Their excess heterozygosity suggested that most successful E × E matings were between different clones¹⁰. The two *ridibunda* genomes are thought to recombine normally, producing recombinant clones freed from deleterious mutations¹⁰ (this has not yet been shown directly, but after genome duplication normal meiosis occurs¹⁵).

These findings bear on the evolutionary biology of sex, for *R. esculenta* can enjoy the advantages of asexual and sexual reproduction. Normally, E × L matings allow *R. esculenta* to reproduce hemiclonally. Its gametes contain only *ridibunda* genomes, its germ line is pure, and its genome is not diluted. This corre-

sponds to asexual reproduction in cyclic parthenogens. (The soma, however, is always hybrid.) Occasionally, *R. esculenta* may engage in E × E matings. When the offspring reproduce, recombination is likely to occur¹⁰, and mutations can be discarded in zygotes with reduced fitness. This corresponds to the sexual generation in cyclic parthenogens (Fig. 1).

Frogs cannot reproduce parthenogenetically, for the centrosome that forms the poles of the first mitotic spindle is contributed by the sperm¹⁹. Hence, *R. esculenta* cannot reproduce asexually and cannot have asexual generations in the sense of cyclic parthenogenesis. Instead, it uses the detour of hemiclonal reproduction. This detour, however, gives *R. esculenta* a newly mixed soma in every generation¹⁵; they have high somatic heterozygosity¹⁵. In the L-E system, females seem to choose mates. Female *R. esculenta* prefer *R. lessonae* males over *R. esculenta* males²⁰. Mate choice allows for behavioural control of sexual and hemiclonal generations, for assortative mating is possible. Thus, hybridogenetic frogs have overcome the constraints on parthenogenetic reproduction that rule out (cyclic) parthenogenesis in many taxa⁷ (e.g. genomic imprinting²¹).

How did such a complex reproductive system arise? The key may lie in an earlier male-female conflict. Although male *R. esculenta* arise from E female × L male matings,

Table 1. Mating table of the L-E system and offspring that would result if *R. ridibunda* were present^{a,b}

Species	Mating with		
	<i>lessonae</i> L	<i>esculenta</i> R	<i>ridibunda</i> R
<i>lessonae</i> L	<i>lessonae</i> LL ^c	<i>esculenta</i> LR ^c	<i>esculenta</i> LR ^d
<i>esculenta</i> R		<i>ridibunda</i> RR ^e	<i>ridibunda</i> RR ^e
<i>ridibunda</i> R			<i>ridibunda</i> RR ^e

^aSingle capital letters denote gametes, double capital letters denote genotypes.

^bThe gender of all individuals can be either male or female.

^cViable offspring.

^dOrigin of *R. esculenta*.

^eUsually inviable offspring.

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these males transmit only X sex chromosomes, for the Y is associated with the *lessoneae* genome that is excluded. All *ridibunda* clones in *R. esculenta* are female. Moreover, some *L-E* populations have an excess of female *R. esculenta*, and even XY females seem to exist¹⁸. A non-Y-linked gene that is expressed differently in hybrid and nonhybrid frogs may be responsible¹⁹. This suggests a male-female conflict that has previously been resolved in *R. ridibunda*. As soon as a female *ridibunda* clone is no longer associated with a male *ridibunda* clone, it kills the other part of the genome during meiosis. This may be the effect of a meiotic driver against Y in *R. ridibunda*. In the *L-E* system, male *R. ridibunda* do not even exist during the sexual generation, for the offspring of $E \times E$ matings are all female. This prevents the establishment of a bisexual *R. ridibunda* population in

which the advantages of hemiclinal reproduction for *ridibunda* clones would be lost. Hybridogenesis may have evolved out of such a male-female conflict: a drive against a paternal genome may have turned into a drive against a parental genome. Hence, one conflict created another^{21,22}: the former sexual conflict is now a conflict between *ridibunda* clones and *R. lessoneae* and other frog species; *R. ridibunda* forms hybridogenetic and normal hybrid systems with several frog species¹⁵.

Hybridogenesis is an example of how the advantages of sexual reproduction can be used while avoiding the costs (e.g. genome dilution). Such a strategy also occurs in other organisms: frogs are not the only species that 'rent a genome' for temporary use; pseudoarrhenotokous mites have, unlike arrhenotokous (haplodiploid) species, diploid males. But the paternal genome (not parental) is always excluded before spermatogenesis and is never transmitted to the progeny (paternal genome loss also occurs in some insects)²³.

The diversity in hybridogenetic and associated reproductive systems is amazing^{12,15}. Fascinating in themselves, these systems contain more information about evolution than might appear at first glance. Questions that now need answers include the following. How do *ridibunda* genomes exclude non-*ridibunda* genomes? What causes geographic variation in this ability¹⁵? What turns genetically male (XY) frogs into females? Male *R. esculenta* have a very low fertility¹⁴ and the exclusion of *lessoneae* genomes is probably the result of meiotic drive: does this provide a solution to the running debate about the causes of hybrid sterility and Haldane's rule? Is there recombination in *R. ridibunda* that arises through $E \times E$ matings or do these selfish haploid genomes try to exclude each other (i.e. there would be no recombination)? Do recombinant offspring show a release of hidden genetic variance²⁴, and how do they perform when faced with factors that are supposed to be important in the evolution and maintenance of sex, such as parasites²⁵?

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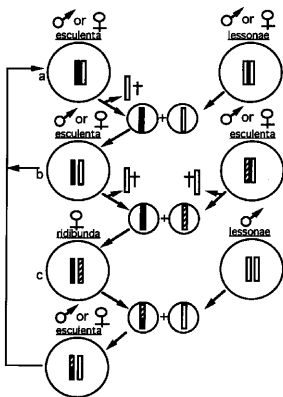


Fig. 1. Cyclical parthenogenesis in hybridogenetic frogs. Filled and hatched bars denote haploid *ridibunda* genomes, open bars haploid *lessoneae* genomes. Large circles are zygotes, small circles gametes. The gender of all individuals can be either male or female, except in (c) where *R. ridibunda* is always female, *R. lessoneae* male. (a) Hemiclinal generation: $E \times L$ mating. During gametogenesis the *lessoneae* genome is excluded. (b) Sexual generation: $E \times E$ mating, syngamy of two *ridibunda* clones. During gametogenesis the *lessoneae* genome is excluded. (c) The sexually produced offspring reproduces hemiclonally. During its gametogenesis, recombination is likely to occur.

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