



Letter to the Editor

Accumulation of deleterious mutations in hybridogenetic organisms

European water frog hybrids *Rana esculenta* (*Rana ridibunda* × *Rana lessonae*) reproduce hemiclonally, transmitting only the *ridibunda* (R), and excluding the *lessonae* (L), genome through their gametes; hybridity is restored at each generation by matings of *esculenta* (RL) with coexisting *lessonae* (LL). This peculiar genetic system is called hybridogenesis and may be considered as an extreme form of meiotic drive, in which a whole genome is transmitted at the expenses of the other. In other words, *R. ridibunda* is a genetic parasite of *R. lessonae*.

Hybridogenesis is known for another amphibian species (a hybrid probably between *R. esculenta* and *Rana perezi*) and in other animal taxa, for example *Poeciliopsis* (Schultz, 1966), *Bacillus* (Mantovani and Scali, 1992), *Trophidophoxinellus* (Carmona et al., 1997). I will discuss the *R. esculenta* complex, but the following arguments are valid also for the other taxa.

Natural matings between two hybrids *esculenta* usually lead to inviable RR tadpoles. This inviability is thought to result from unmasked deleterious alleles on the clonally transmitted R genomes (Guex et al., 2002), as spontaneous deleterious mutations are expected to accumulate through Muller's ratchet in the R genome. The hybrid persists probably because of heterosis (Hotz et al., 1999). Therefore the advantage conferred by heterosis seems to be greater than the deleterious effects of hemiclonality.

Here I suggest that deleterious mutations accumulate in the *lessonae* genome too, but for a completely different reason, not previously noticed. Since the hybrid *R. esculenta* is a dead end for the *lessonae* (L) genome, mutations with deleterious effects acting *only* in *R. esculenta* (that is, deleterious only for the R genome) can accumulate in the L genome, simply because there is no selection against R-acting deleterious mutations, neither in *R. esculenta* (RL, but transmitting only the R genome) or in *R. lessonae* (LL).

The same logic applies to male-acting deleterious mutations in the mitochondrial genome: in species where mitochondria are transmitted only through females, mutations with deleterious effects restricted to males can accumulate because of the absence of natural

selection for these mutations in females (Frank and Hurst, 1996). In this case the equilibrium frequency of germline mitochondrial mutations is approximately $q = \mu/s_F$, where μ is the mitochondrial mutation rate in the female germ line and $1-s_F$ is the fitness of a female with the mutation relative to a female with fitness of one (Frank and Hurst, 1996).

In the case of hybridogenesis, diploidy alters these calculations, which are valid only for the haploid case. Let us assume a deleterious effect in both *R. lessonae* (LL) and *R. esculenta* (RL). If $1-s_R$ and $1-s_L$ are the fitness of, respectively, a *R. esculenta* and a *R. lessonae* with the mutant allele, relative to a fitness of one, and μ is the mutation rate in the *lessonae* germ line, then, if the mutant allele is completely recessive, its equilibrium frequency will be $q = \sqrt{(\mu/s_L)}$, no matter the value of s_R . However this case is not very interesting for us because completely recessive mutations will not be effective in the hybrid *R. esculenta*. Moreover the majority of deleterious mutations are partially recessive.

With partial or complete dominance, if fitness is multiplicative, that is fitness for an individual with the homozygous mutation is $(1-s_L)^2$ and fitness for an heterozygous individual is $(1-s_L)$, relative to a *R. lessonae* with fitness of one, then the equilibrium frequency of the deleterious allele is $q = \mu/s_L$ as in the haploid case. In the general case (not restricted to multiplicative fitness) we know from standard population genetics that the approximate equilibrium frequency is $q = \mu/hs_L$, where h is the dominance of the mutant allele. This solution is only an approximation of the exact equilibrium, but is it accurate enough if $\mu \ll hs_L$. Imagine that $\mu = 10^{-4}$ and that $s_L = 0.01$, that is the mutation has only mild effects on *R. lessonae* (LL): with complete dominance ($h = 1$) the equilibrium frequency q of the deleterious allele will be about 0.01. Therefore such a mutation will have a negligible effect on *R. lessonae* but fitness for *R. esculenta* with the deleterious allele will be reduced from 1 to $1-s_R$, no matter how strong is selection (that is, s_R may be up to 1) on *R. esculenta*.

This effect depends on how frequently mutations with $s_R > s_L$ arise. Frank and Hurst (1996) mention possible mutations of mitochondrial genes with different effects in males and females. In our case mutations must have different effects not between males and females, but

between the parental species and the hybrid. While I am not aware of any evidence that such mutations exist in hybridogenetic organisms, it is probably not unlikely that some genes in the whole (nuclear) genome may have different importance in the two species and that, therefore, mutations in these genes may affect one species and not (or scarcely) the other.

In certain circumstances, such R-acting deleterious alleles might accumulate not only because of recurrent mutations, but also because they will confer an advantage to the L genome, reducing the frequency of RL individuals and therefore reducing the frequency with which the L genome is eliminated from the population. In other words there will be selection, in *R. lessonae*, to maintain R-acting deleterious mutations, or even selection to enhance the deleterious effects of these mutations (selection for increasing s_R), but only if the two species hybridise. However, this argument requires a form of group selection, which is generally a very weak evolutionary force, unless the population structure is such that the advantage of the mutation for L is direct—for example because of reduced competition (the hybrid and the parental species are often found in the same ponds). This could be tested rather easily by crossing (i) RR with LL deriving from a zone where the two species form hybridogenetic hybrids and (ii) RR with LL deriving from a zone where RR is absent or where it is present but hybridogenetic hybrids are not formed (see Hotz et al., 1985): the F1 progeny of the first cross (i) should have lower fitness than the progeny of the second (ii) cross.

The simple accumulation of R-acting deleterious mutations in the L genome of the hybrid, on the other

hand, does not require specific assumptions of group selection, but is a consequence of the very genetic system of hybridogenesis. This effect might explain why hybridogenesis is so rare in nature and may contribute to understand the observed decline of *R. esculenta* populations in favour of *R. ridibunda* in Europe.

References

- Carmona, J.A., Sanjur, O.I., Doadrio, I., Machordom, A., Vrijenhoek, R.C., 1997. Hybridogenetic reproduction and maternal ancestry of polyploid Iberian fish: the *Throphidophoxinellus alburnoides* complex. *Genetics* 146, 983–993.
- Frank, S.A., Hurst, L.D., 1996. Mitochondria and male disease. *Nature* 383, 224.
- Guex, G.D., Hotz, H., Semlitsch, R.D., 2002. Deleterious alleles and differential viability in progeny of natural hemiclinal frogs. *Evolution* 56 (5), 1036–1044.
- Hotz, H., Mancino, G., Bucci Innocenti, S., Ragghianti, M., Berger, L., Uzzell, T., 1985. *Rana ridibunda* varies geographically in inducing clonal gametogenesis in interspecies hybrids. *J. Exp. Zool.* 236 (2), 199–210.
- Hotz, H., Semlitsch, R.D., Gutmann, E., Guex, G.D., Beerli, P., 1999. Spontaneous heterosis in larval life-history traits of hemiclinal frog hybrids. *Proc. Natl Acad. Sci. USA* 96 (5), 2171–2176.
- Mantovani, B., Scali, V., 1992. Hybridogenesis and androgenesis in the stick insect *Bacillus rossius-grandii benazzii* (Insecta, Phasmoidea). *Evolution* 46, 783–796.
- Schultz, R.J., 1966. Hybridization experiments with an all-femal fish of the genus *Poeciliopsis*. *Biol. Bull.* 130, 415–429.

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