

File S2: No recombination

For complete linkage, approximations have been derived in Iwasa *et al.* (2003, 2004). These approximations model all allele frequencies in the standing genetic variation deterministically. We extend these results by a stochastic treatment of the number of double mutants in the standing genetic variation.

The distribution of genotypes in the standing genetic variation. In principle, the number of single and double mutants in the population can be modeled as a two-type branching process with immigration. However, analytical solutions for the p.g.f. are not easily derived. We therefore propose two simpler approximations to estimate the contribution of the standing genetic variation for rescue. (1) If the population size is small, double mutants in the standing genetic variation can often be neglected; the number of single mutants is subject to stochasticity. The probability generating functions F_{Ab} and F_{aB} are given by Eq. (S1.13). (2) If the population size is large, the number of single mutant types is well approximated by their expected value (Eq. (S1.14)). The probability generating function for the number of double mutants F_{AB} is then given by Eq. (S1.17).

Establishment probability of the rescue mutant. After the change in the environment, a lineage initiated by one individual of type AB survives with probability $p_{\text{est}}^{(AB)}$ as given by Eq. (S1.20). A lineage that is founded by a single individual of type Ab (or aB) survives with probability $p_{\text{est}}^{(Ab)}$ as given by Eq. (S1.21). These results do not depend on the dynamics of the wildtype when $r = 0$ because of our assumption of a hard carrying capacity (no density dependence until $N \geq N_0$).

The probability of evolutionary rescue. We first consider the case that the number of double mutants before the change in the environment can be ignored. Rescue can now either pass via single mutants from the standing genetic variation or via newly generated single mutants. The number of successful offspring of a single type Ab individual is Poisson distributed with parameter $(1 + s_{Ab})p_{\text{est}}^{(Ab)}$. If n_{Ab} individuals of type Ab are present at the time of environmental change, they hence do not establish a permanent lineage with probability $\exp[-n_{Ab}(1 + s_{Ab})p_{\text{est}}^{(Ab)}]$. It remains to average over the distribution of n_{Ab} , for which one can conveniently use the p.g.f. F_{Ab} , Eq. (S1.13) (analogous for type aB). In order to determine the number of single mutants that get generated after the environmental change, we assume that the decay of the wildtype population size can be well described deterministically by $n_{ab}(t) \approx N_0(1 + s_{ab})^t$ (cf. Orr and Unckless, 2008; Uecker *et al.*, 2014). The number of de-novo generated single mutants is then given by $\sum_{t=0}^{\infty} u n_{ab}(t)(1 + s_{Ab}) \approx \frac{uN_0}{-s_{ab}}(1 + s_{Ab})$. With this, we obtain:

$$P_{\text{rescue}} = 1 - F_{Ab}(e^{-(1+s_{Ab})p_{\text{est}}^{(Ab)}})F_{aB}(e^{-(1+s_{aB})p_{\text{est}}^{(aB)}})e^{-\frac{uN_0}{-s_{ab}}(1+s_{Ab})p_{\text{est}}^{(Ab)} - \frac{uN_0}{-s_{ab}}(1+s_{aB})p_{\text{est}}^{(aB)}}. \quad (\text{S2.1})$$

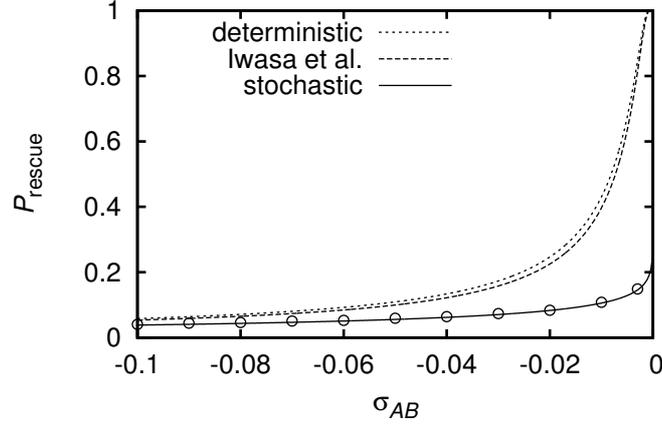


Fig. S2.1: Probability of evolutionary rescue as a function of σ_{AB} . The theoretical predictions are based on Eq. (S2.2) (solid line), Iwasa *et al.* (2003, 2004) (long-dashed line), and Eq. (S2.3) (short-dashed line). Parameter values: $\sigma_{Ab} = \sigma_{aB} = -0.01$, $s_{Ab} = s_{aB} = s_{ab} = -0.5$, $s_{AB} = 0.15$, $u = 10^{-5}$, $N_0 = 10^6$. Symbols denote simulation results. Each simulation point is the average of 10^5 replicates.

If single mutants are frequent and we describe double mutants stochastically, using the expected values \bar{n}_{Ab} and \bar{n}_{aB} , we have:

$$P_{\text{rescue}} = 1 - F_{AB} \left(e^{-(1+s_{AB})p_{\text{est}}^{(AB)}} \right) e^{-u(\bar{n}_{Ab} + \bar{n}_{aB})(1+s_{AB})p_{\text{est}}^{(AB)}} e^{-\bar{n}_{Ab}(1+s_{Ab})p_{\text{est}}^{(Ab)} - \bar{n}_{aB}(1+s_{aB})p_{\text{est}}^{(aB)}} \times e^{-\frac{uN_0}{-s_{ab}}(1+s_{Ab})p_{\text{est}}^{(Ab)} - \frac{uN_0}{-s_{ab}}(1+s_{aB})p_{\text{est}}^{(aB)}}. \quad (\text{S2.2})$$

If we can treat the number of double mutants deterministically, we obtain:

$$P_{\text{rescue}} = 1 - e^{-(1+s_{AB})\bar{n}_{AB}p_{\text{est}}^{(AB)}} e^{-u(\bar{n}_{Ab} + \bar{n}_{aB})(1+s_{AB})p_{\text{est}}^{(AB)}} e^{-\bar{n}_{Ab}(1+s_{Ab})p_{\text{est}}^{(Ab)} - \bar{n}_{aB}(1+s_{aB})p_{\text{est}}^{(aB)}} \times e^{-\frac{uN_0}{-s_{ab}}(1+s_{Ab})p_{\text{est}}^{(Ab)} - \frac{uN_0}{-s_{ab}}(1+s_{aB})p_{\text{est}}^{(aB)}}. \quad (\text{S2.3})$$

with

$$\bar{n}_{AB} = \frac{u(\bar{n}_{Ab} + \bar{n}_{aB})}{-\sigma_{AB}} (1 + \sigma_{AB}). \quad (\text{S2.4})$$

Comparison to Iwasa *et al.* (2003, 2004). We can compare our approximations to the approximation derived in Iwasa *et al.* (2003, p. 2574) and Iwasa *et al.* (2004, Eq. 9), who describe all allele frequencies prior to the environmental change deterministically (derived as the stationary solution of a system of differential equations). Consequently, as can be seen from Fig. S2.1, the approximation is in good agreement with Eq. (S2.3) (up to minor deviations due to details in the model and the analysis). Both strongly overestimate the real rescue probability in Fig. S2.1. The reason is that the number of double mutants in the standing genetic variation

– from which rescue mainly occurs in the parameter regime shown in the figure – is subject to strong fluctuations. This matters mainly for weakly deleterious double mutants: Then, the average number of double mutants is high enough to provide a population with a decent chance to survive, and the deterministic approximation assumes that each replicate population contains this average number of double mutants. Stochastically, however, some replicate populations have a very high chance to survive (but a single population can only get rescued once; the very high number of double mutants is hence redundant), while most of them contain no double mutants at all and go extinct.