Backstory of: Genetic rescue of small inbred populations: meta-analysis reveals large and consistent benefits of gene flow

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The critical event that eventually led to the first of my meta-analysis papers on genetic rescue occurred in February 2007 at a book writing session on the second edition of "Introduction to Conservation Genetics" (Frankham et al., 2010) at Jonathan Ballou's house in the Washington, D.C. area. Upon reaching the topic of outbreeding depression (where the effects of crossing populations results in harmful fitness effects in the progeny), we both expressed serious disquiet that the risks of outbreeding depression were being overplayed, while the potential fitness benefits of crossing (genetic rescue) were largely being ignored. One of us said "we must be able to predict the risk of outbreeding depression". A few days later inspiration struck and we had the key to doing this: harmful effects on fitness of crossing populations typically arise when the crossed populations have fixed chromosomal differences, and/or are adapted to different environments. We subsequently recruited Katherine, Ralls, Mark Eldridge, Michele Dudash, Charles Fenster and Robert Lacy and jointly transformed this insight into a paper that was published in Conservation Biology (Frankham et al., 2011).

That work was critical to the ability to use genetic rescue (variously called outcrossing or augmentation of gene flow) as a tool to save small inbred population fragments from extinction, and thereby reduce population and species extinction risks. As genetic rescue had been attempted in very few cases, we decided to write a book on "Genetic Management of Fragmented Animals and Plant Populations" in an attempt to create a paradigm shift where the discovery of genetically differentiated populations was followed, not by the conclusion that separate management of fragments was required, but by asking if any of the populations were suffering genetic erosion (inbreeding, loss of genetic variation, reduced fitness, reduced ability to evolve and elevated extinction risk), and if so, was a genetic rescue attempt justified.

I drafted Chapter 6 on Genetic rescue for the book, and then decided that it needed some examples which were put into a Table. At this point, I finally recognized that a fully-fledged meta-analysis was required, as there was no overview of the effects of outcrossing in a conservation context, i.e. when an inbred population fragment with low genetic diversity was crossed to another population and where the risk of outbreeding depression in the resulting progeny was low. The meta-analysis was done without external research funding as I have been officially retired since 2002 (but am still scientifically active) and do not have grant money for any of the work described here. I am great fan of meta-analyses: not only can they be done without research funds, but they are typically highly cited, similar to reviews, and are superior scientifically to them.

By mining the literature, I found 156 relevant comparisons of inbred parents and their outcrossed progeny, and 145 had beneficial effects on fitness. Only one of the cases where crossing was harmful was a convincing case of outbreeding depression (in a selfing nematode), the others likely being chance observations due to low statistical power. The median fitness benefit from augmenting gene flow was 148% in wild/stressful conditions and 45% in benign/captive ones. Consequently, there are huge potential benefits from augmenting gene flow into population fragments suffering from genetic erosion, provided the risk of outbreeding depression in proposed crosses is low. Thus, the two main impediments to genetic rescue attempts have been removed.

This paper was published in Molecular Ecology (Frankham, 2015) (currently 123 citations in Google Scholar), and was accompanied by a commentary from Donald Waller (Waller, 2015). He praised the paper, but was not convinced about the persistence of the benefits over generations. Consequently, I did further analyses on my database to compare the effects of crossing on fitness in the F1, F2 and F3 generations and this confirmed that the benefits persisted to an extent that was, if anything, better than expected. This led to the publication of a second genetic rescue meta-analysis paper in Biological Conservations (Frankham, 2016).

Writing of our book continued (with Paul Sunnucks being added as another author) and it was submitted to Oxford University Press in December 2016. However, during the subsequent copy editing I realised that the second genetic rescue meta-analysis paper was incomplete, as the persistence of fitness benefits following crossing is expected to depend on the breeding system. Persistence of fitness benefits across generations is expected for outbreeders, but habitual selfing after crossing will lead to loss of benefits, while mixed mating species should experience only partial persistence of fitness benefits. I subsequently extended the analyses of my database from F3 to F13 and found no significant decline in fitness benefits for outbreeding species. Further, Bijlsma et al. (2010) found no significant change in fitness between F10 and F15 generations in outbreeding *Drosophila* flies. The updated findings were included in the published version of our "Genetic Management of Fragmented Animal and Plant Populations" book (Frankham et al., 2017). This was followed by a related paper calling for a paradigm shift in the genetic management of fragmented populations (Ralls et al., 2017).

References

R. Bijlsma, M. D. D. Westerhof, L. P. Roekx, and I. Pen. Dynamics of genetic rescue in inbred Drosophila melanogaster populations. *Conservation Genetics*, 11(2):449–462, feb 2010. doi: 10.1007/s10592-010-0058-z. URL https://doi.org/10.1007%2Fs10592-010-0058-z.

Richard Frankham. Genetic rescue of small inbred populations: meta-analysis reveals large and consistent benefits of gene flow. *Molecular Ecology*, 24(11):2610–2618, mar 2015. doi: 10.1111/mec.13139. URL https://doi.org/10.1111%2Fmec.13139.

Richard Frankham. Genetic rescue benefits persist to at least the F3 generation based on a meta-analysis. *Biological Conservation*, 195:33–36, mar 2016. doi: 10.1016/j.biocon.2015.12.038. URL https://doi.org/10.1016%2Fj.biocon.2015.12.038.

Richard Frankham, Jonathan D. Ballou, and David A. Briscoe. *Conservation Genetics, 2nd edition*. Cambridge University Press, 2010. doi: 10.1017/cbo9780511809002.003. URL https://doi.org/10.1017%2Fcbo9780511809002.003.

Richard Frankham, Jonathan D. Ballou, Mark D. B. Elridge, Robert C. Lacy, Katherine Ralls, Michelle R. Dudash, and Charles B. Fenster. Predicting the Probability of Outbreeding Depression. *Conservation Biology*, 25(3):465–475, apr 2011. doi: 10.1111/j.1523-1739.2011.01662.x. URL https://doi.org/10.1111%2Fj.1523-1739.2011.01662.x.

Richard Frankham, Jonathan D. Ballou, Katherine Ralls, Mark Eldridge, Michele R. Dudash, Charles B. Fenster, Robert C. Lacy, and Paul Sunnucks. *Genetic Management of Fragmented Animal and Plant Populations*. Oxford University Press, sep 2017. doi: 10.1093/oso/9780198783398.001.0001. URL https://doi.org/10.1093%2Foso%2F9780198783398.001.0001.

Katherine Ralls, Jonathan D. Ballou, Michele R. Dudash, Mark D. B. Eldridge, Charles B. Fenster, Robert C. Lacy, Paul Sunnucks, and Richard Frankham. Call for a Paradigm Shift in the Genetic Management of Fragmented Populations. *Conservation Letters*, oct 2017. doi: 10.1111/conl.12412. URL https://doi.org/10.1111%2Fconl.12412.

Donald M. Waller. Genetic rescue: a safe or risky bet? *Molecular Ecology*, 24(11):2595–2597, may 2015. doi: 10.1111/mec.13220. URL https://doi.org/10.1111%2Fmec.13220.