Quantifying the probability of evolutionary rescue

Matthew M. Osmond* (ORCiD: 0000-0001-6170-8182), Department of Ecology and Evolutionary Biology, University of Toronto, Toronto, Canada
Hildegard Uecker* (ORCiD: 0000-0001-9435-2813), Research Group Stochastic Evolutionary Dynamics, Department of Theoretical Biology, Max Planck Institute for Evolutionary Biology, Plön, Germany
Carla Alejandre (ORCiD: 0000-0003-2141-618X), Centro de Astrobiología (CAB), CSIC-INTA, Carretera de Ajalvir km 4, Torrejón de Ardoz, 28850, Madrid, Spain
Ernesto Berríos-Caro (ORCiD: 0000-0002-2080-1273), Center for Advanced Biotechnology and Medicine, Rutgers University, Piscataway, NJ 08854 & Stochastic Evolutionary Dynamics Group, Max Planck Institute for Evolutionary Biology, Plön, Germany & Evolutionary Ecology and Genetics, Christian-Albrechts-University of Kiel, Kiel, Germany
Dale T. Clement (ORCiD: 0000-0001-7327-3323), Department of Biology, Wake Forest University, 834 Wake Forest Rd., Winston Salem, NC 27109 & School of Biological Sciences, Washington State University, Pullman, WA 99164
Peter Czuppon (ORCiD: 0000-0003-1462-7237), Aix Marseille Univ, CNRS, I2M, Marseille, France & Institute for Evolution and Biodiversity, University of Münster, Münster, Germany
Léonard Dekens, Theoretical Biology Lab, The Francis Crick Institute, London NW1 1AT, United Kingdom
Puneeth Deraje, (ORCiD: 0000-0001-6948-7089) Department of Ecology and Evolutionary Biology, University of Toronto, Ontario, Canada
Jeremy A. Draghi, Dept. of Biological Sciences, 4001 Derring Hall, Virginia Tech, Blacksburg, VA, 24060 USA
Asad Hasan, Department of Zoology, University of British Columbia, BC V6T 1Z4, Canada
Robert D. Holt (ORCiD: 0000-0002-6685-547X), Department of Biology, The University of Florida, Gainesville, Florida, USA 32611
Teemu Kuosmanen (ORCiD: 0000-0002-8724-5048), Department of Computer Science, Organismal and Evolutionary Biology Research Programme, University of Helsinki, Helsinki, Finland
Alexander Longcamp, Department of Biological Sciences, Mississippi State University, Mississippi State, MS 39762, USA
Loïc Marrec (ORCiD: 0000-0003-0941-6603), Département de Biologie Computationnelle, Université de Lausanne, Lausanne, Switzerland & Swiss Institute of Bioinformatics, Lausanne, Switzerland
Guillaume Martin, ISEM, Université de Montpellier, CNRS, IRD, Montpellier, France
Christin Nyhoegen (ORCiD: 0000-0002-8447-040X), Freie Universität Berlin, Institute of Pharmacy, Department of Clinical Pharmacy and Biochemistry, Berlin, Germany – Present address: Institute of Integrative Biology, ETH Zurich, Zurich, Switzerland
Maria E. Orive (ORCiD: 0000-0003-4825-0554), Department of Ecology & Evolutionary Biology, University of Kansas, 1200 Sunnyside Ave., Lawrence, KS 66045 USA
Vrinda Ravi Kumar (ORCiD: 0000-0001-6054-2694), Biology Centre, Czech Academy of Sciences, Branišovská, České Budějovice, Czech Republic 370 05
Remus Stana, UT Southwestern Medical Center, Dallas, 5323 Harry Hines Blvd., Dallas, Texas 75390
Lindi M. Wahl (ORCiD: 0000-0003-1163-0940), Mathematics, Western University, London, N6A 5B7, Canada
Masato Yamamichi (ORCiD: 0000-0003-2136-3399), Center for Frontier Research, National Institute of Genetics, 1111 Yata, Mishima, Shizuoka 411-8540, Japan

* *These two authors contributed equally. We had to pick an order.*
Co-corresponding authors: mm.osmond@utoronto.ca, uecker@evolbio.mpg.de

All authors except for the two co-first authors are listed alphabetically.

Abstract

While evolutionary rescue is now a well-established term, there are subtleties in precisely defining it and conceptual complications in quantifying its probability. In this Perspective, we pay special attention to three issues: 1) How do we know that a population would go extinct in the absence of evolution? 2) How do we determine the probability of rescue if persistence is possible in the absence of evolution? 3) How can we capture the time-varying effect of evolution on persistence? Through this, we gain a dynamic and nuanced view that goes beyond certain extinction and ultimate persistence and demonstrate how to quantify the time-varying effect of evolution on persistence from extinction times of ensembles of evolving and non-evolving populations.

Keywords: evolutionary rescue, modeling, resistance, conservation, counterfactual, extinction times

1 Introduction

Environmental change is a driving force of population extinction. Nonetheless, nature is resilient and populations that adapt sufficiently rapidly may survive. This process of escape from extinction through adaptive evolution, "evolutionary rescue" (Gomulkiewicz and Holt, 1995), is of wide interest both in conservation biology, where the goal is to promote rescue, and in medicine and agriculture, where the goal is to prevent pathogen or pest survival (Alexander et al., 2014; Kreiner et al., 2018).

Evolutionary rescue has been studied in models, the lab, the field, and – albeit not under this name – in the clinic (Carlson et al., 2014; Bell, 2017; Balstad et al., 2026; Uecker et al., 2026). Irrespective of context, by definition, population survival is considered as rescue only when adaptive evolution is the critical factor for survival. In practice, identifying rescue can be challenging because to infer that evolution was necessary for survival implies knowledge of the counterfactual: what would have happened in the absence of evolution?

In most situations of rescue we think of extinction as being certain in the absence of evolution, as in the modeling paper by Gomulkiewicz and Holt (1995) that defined rescue (Figure 1a). Then any population that survives is considered rescued, and the probability of rescue is equal to the probability of persistence and can – if replicates are available – be estimated by the fraction of surviving populations. But what about scenarios where extinction in the absence of evolution is not certain (Figure 1b)? For example, a novel parasite might drive a host population to low numbers, reducing its ability to infect and therefore allowing the host population to rebound (Golas et al., 2021). In the process, the host population may go extinct by demographic stochasticity but extinction is not certain, even in the absence of evolution. Nevertheless, by increasing resistance to the parasite, evolution may reduce the chances of extinction. Whether one defines rescue to include such scenarios or restricts the term to scenarios in which extinction is certain in the absence of evolution is perhaps a matter of taste. If we do include such scenarios, which has merit because they involve an effect of adaptive evolution on persistence following environmental change, how then do we determine the probability of rescue?

Another complication is that in the very short term every population persists and in the long run there will be further environmental changes (Figure 1c). When we determine the probability of rescue we are therefore implicitly choosing a timescale (as pointed out by Martin et al., 2013). Even if focused on a specific environmental challenge, the probabilities of survival with and without evolution change over time. How do we best capture this dynamic effect of evolution on survival?

Below we discuss each of these three questions: 1) What would happen in the absence of evolution? 2) How do we determine the probability of rescue if persistence is possible even in the absence of evolution? 3) How can we capture the dynamic effect of evolution on persistence? In addressing these questions, we generate a dynamic and nuanced view of the probability of rescue that goes beyond certain extinction and ultimate persistence and show how the effect of evolution on persistence can be quantified in practice.

2 Going beyond certain extinction and ultimate persistence: A dynamic and nuanced view of the probability of rescue

2.1 What would have happened in the absence of evolution?

Evolutionary rescue occurs when a population survives due to evolution (by natural selection), when it would have otherwise gone extinct. Many experiments use a stress strong enough that any population that does not evolve will go extinct (e.g., Gonzalez et al., 2013; Ramsayer et al., 2013; Hufbauer et al., 2015; Olazcuaga et al., 2026). Similarly, many models consider scenarios where extinction without evolution is the obvious outcome, e.g., the wild-type population size decays exponentially or geometrically (e.g. Gomulkiewicz and Holt, 1995; Orr and Unckless, 2008). However, the situation is not always so simple, as illustrated by the host-parasite example in the Introduction. To claim a population has been rescued we then need to determine what would have happened in the absence of evolution. We may be able to get some sense of what would have happened without evolution from characteristics of evolving populations, such as population size trajectories, rates of phenotypic

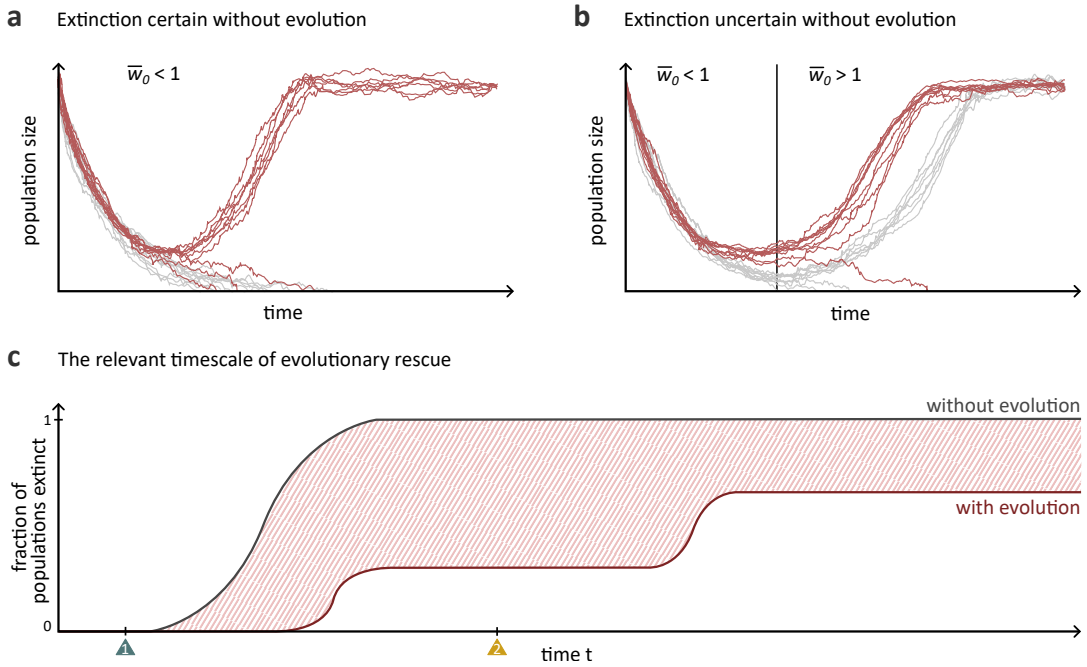

Figure 1: **Conceptual challenges in determining the probability of evolutionary rescue.** Panels a and b: Population size trajectories of replicate populations exposed to environmental change (red lines – with evolution: grey lines – without evolution). If the environment does not improve (i.e., the mean fitness of the non-evolving ancestral population, $\bar{w}_0$, remains below 1), all populations go extinct without evolution (panel a). By contrast, if the environment improves after some time, lifting $\bar{w}_0$ above 1, some populations may survive even without evolution (panel b). However, adaptive evolution increases the chance of survival, and more populations persist. Panel c: Fraction of populations extinct at time t with and without evolution over time. Following the first environmental change (blue triangle), all evolving and non-evolving populations persist initially but eventually all non-evolving populations inevitably go extinct, while some evolving populations survive the change. However, the environment does not stay constant indefinitely and at the next environmental change (yellow triangle), more of the evolving populations go extinct. The figure is purely illustrative and not based on an actual model.

evolution, and genetic information. Ideally, though, we would like to observe non-evolving populations for comparison. Evolution by natural selection requires heritable variation in fitness, which implies that there are two ways to turn evolution off, 1) removing heritability or 2) removing variation in fitness.

In experiments, removal of heritability can be mimicked – and thus no-evolution treatments be created – by re-sampling individuals each time-step from a stock population (Zhang and Buckling, 2011; Stewart et al., 2017; Olazcuaga et al., 2026), though this potentially introduces variation not present in the founders. While we will usually not be able to manipulate natural populations, we can model them to create no-evolution scenarios *in silico*. In models, heritability can be removed in a number of ways. For example, each offspring could be replaced by an individual from the population at the time of environmental change or all phenotypic variation converted to environmental variation. Alternatively, each offspring could be replaced by a random individual from the previous generation or phenotypes could be shuffled among offspring in a cohort to decouple genotype and phenotype (as has been done to assess the role of evolution in the response of coral reefs to climate change Matz et al., 2020). While all these approaches remove heritability, the latter (unlike the former) two allow for genetic drift and thus adaptive genotypes can potentially spread by chance. In models, one can also use the second possibility to stop evolution – removing variation in fitness – by giving everyone the mean fitness at the time of the environmental change. In quantitative genetics models this is sometimes done by giving every individual the mean trait value at the time of environmental change, as has been used to gauge

the effect of evolution in the response of prairie dogs and ground squirrels to plague (Golas et al., 2021) and coral reefs to warming waters (McManus et al., 2021). This approach could be extended to allow for plasticity by adding an environmentally-determined plastic effect on the phenotype. However, preventing evolution by removing phenotypic variation can substantially reduce the variance load (the decrease in population mean fitness due to the variation in individual phenotypes from the optimum phenotype), reducing population decline.

To know whether evolution was essential for survival of a population, we would ideally like to know how this specific population would have fared in the absence of evolution, i.e., a true counterfactual. Even in models – specifically, stochastic models – this can be hard. A simpler approach is to look at ensembles of non-evolving populations to determine the probability of survival in the absence of evolution.

2.2 When persistence in the absence of evolution is possible, how do we quantify the effect of evolution on persistence?

When extinction is certain without evolution, the probability of rescue equals the probability of population survival and can be estimated from the fraction of replicates (allowed to evolve) that persist. But what is the probability of rescue when extinction is not certain without evolution?

Let A be persistence with evolution and B be persistence without evolution, with the compliments, A^c and B^c, indicating extinction with or without evolution, respectively. If we can turn evolution off then we can calculate the probabilities of each, $P(A)$ and $P(B)$, as the fraction of replicates that survive. The probability of rescue is the probability that a population persists given it would have gone extinct without evolution, and can be written as the conditional probability

$$\begin{aligned} P_{\text{rescue}} &= P(A|B^c) \\ &= P(A \cap B^c)/P(B^c) \\ &= [P(A) - P(B) + P(A^c \cap B)]/P(B^c). \end{aligned} \tag{1}$$

The event $A^c \cap B$ is extinction with evolution but survival without, i.e. in these populations evolution has a negative effect on persistence. Note that even in (presumably rare) cases in which the net effect of evolution on persistence is negative ($P(A^c \cap B) > P(A \cap B^c)$), the rescue probability remains positive (as long as $P(A \cap B^c) > 0$) as it specifically measures the power of evolution to rescue those populations that would have been doomed otherwise. The term $P(A^c \cap B)$ is the only term in Eq. (1) for which we need true counterfactuals to calculate. Because of this, and because we think these events will generally be much less likely than the increased chance of persistence with evolution, $P(A) - P(B)$, we assume in the following that these events cannot occur, $P(A^c \cap B) = 0$, which is equivalent to assuming the probability of evolutionary suicide is zero, $P(A^c|B) = 0$ (Figure 2a). If evolutionary suicide is unjustifiably ignored, this would cause us to underestimate the probability of rescue.

Whether we are interested in the probability of rescue, as defined in Equation (1), or in another quantity depends on the question we are asking, potentially yielding quite different answers (Figure 2b). For rescue, we consider just those populations that would go extinct in the absence of evolution and ask what fraction of those survive due to evolution (Q1 in Figure 2b). We could also ask what fraction of all populations survive due to evolution, $P(A \cap B^c)$ (Q2 in Figure 2b) or more simply what the net effect of evolution on persistence, $\Delta P = P(A) - P(B)$, is. The key difference between $P(A \cap B^c)$ and rescue is that rescue is conditioned on extinction in the absence of evolution. This means that if extinction in the absence of evolution is rare (scenario 3 in Figure 2b), the probability of rescue can be quite high if evolution helps those few populations survive. In these cases we may not be so interested in rescue as extinction is rare anyways and may not even occur in a limited number of replicates. We could of course ask further questions, such as what fraction of surviving populations survived due to evolution, $P_{\text{evo-survival}} = P(A \cap B^c)/P(A \cup B)$ (Q3 in Figure 2b). Apart from answering these questions, we could use standard statistical concepts like odds ratio or relative risk to quantify evolution's effect on persistence / extinction risk.

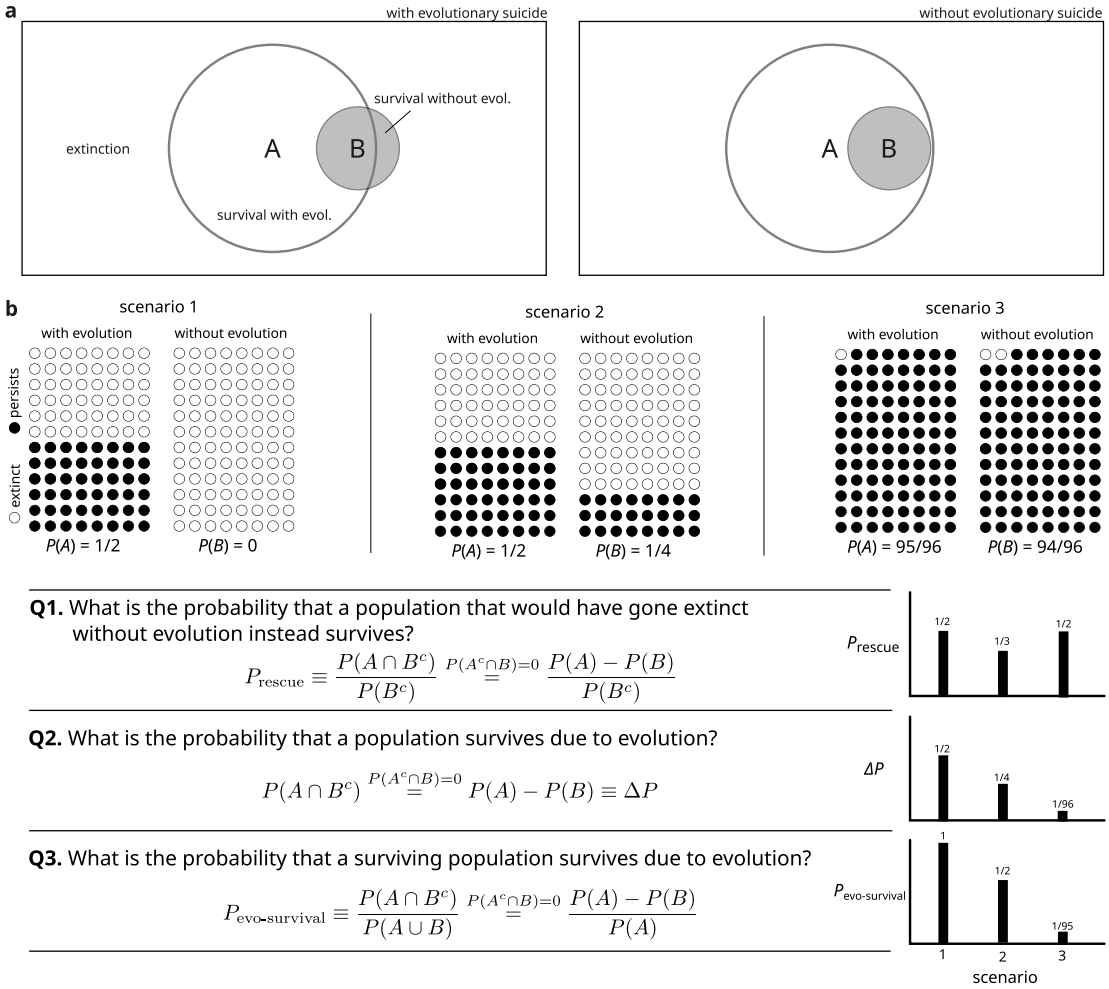

Figure 2: **Assessing the effect of evolution on persistence.** (a) Venn diagrams of persistence with, A, and without, B, evolution. On the left there are populations that would persist only if there is no evolution, $A^c \cap B$. On the right this does not occur, i.e., there is no possibility of evolutionary suicide, which is what we assume in panel (b). (b) Consider three scenarios, where 96 replicate populations are exposed to a stress with or without evolution. Scenario 1 is the simplest case where all non-evolving populations go extinct, which scenario 2 then relaxes, allowing some non-evolving populations to survive. In scenario 3, extinction is rare both with and without evolution. We estimate the probability of surviving with evolution, $P(A)$, by the fraction of populations that survive with evolution and the probability of surviving without evolution, $P(B)$, by the fraction that survive without evolution. The quantity we use to assess the effect of evolution on persistence depends on the question we are asking. Here we ask three questions, give the corresponding quantities as equations (and what they reduce to in the absence of evolutionary suicide), and their values under the three scenarios.

2.3 What is the timescale of rescue?

In Figure 2, we implicitly chose a time at which to determine whether a population survived or not. We can generalize each quantity and learn about the relevant timescale of rescue by considering persistence up to time t (A_t and B_t) and extinction by time t (A_t^c and B_t^c) with and without evolution. The respective probabilities can be obtained from the distributions of extinction times, T_{ext}, e.g. $P(A_t) = 1 - P(T_{\text{ext}} \leq t)$. In particular, the probability of rescue at time t is

$$\begin{aligned} P_{\text{rescue}}(t) &= P(A_t|B_t^c) \\ &= [P(A_t) - P(B_t) + P(A_t^c \cap B_t)]/P(B_t^c). \end{aligned} \tag{2}$$

Based on a one-locus two-alleles model and an abrupt-change scenario, Figure 3 illustrates the extinction time distributions and the time dependence of the three metrics considered in Figure 2. The model considers two mutants, one that has a growth rate larger than the wild type but less than zero such that it cannot persist long term ('subcritical mutant'; yellow) and one that has a positive growth rate and can thus persist long term ('supercritical mutant'; pink). The subcritical mutant may prolong persistence ($P(T_{\text{ext}} > t)$, panel a) but both the excess probability, $\Delta P(t) = P(A_t) - P(B_t)$, and the probability of rescue, $P_{\text{rescue}}(t)$, become zero eventually (panels b and c). With the supercritical mutant, both metrics converge to the same asymptote as extinction is certain in the absence of evolution. In contrast, $P_{\text{evo-survival}}(t) = P(A_t \cap B_t)/P(A_t \cup B_t)$ increases from 0 to 1, since at short time scales evolution is not necessary for persistence, while at large time scales virtually any population alive must have evolved.

Evolutionary rescue is defined by persistence with evolution and extinction in the absence of evolution. The timescale of rescue is therefore bounded between the times at which non-evolving populations begin to go extinct and the maximum time evolving populations persist. If non-evolving populations are expected to persist long enough that additional events (e.g., environmental amelioration, additional disturbances) likely occur before predicted extinction then rescue from the first environmental change may never be particularly relevant. If subcritical mutants delay extinction for a substantial time relative to non-evolving populations then rescue can become relevant at intermediate timescales even though it is predicted to fail eventually in the absence of additional events. This may in particular buy us time for conservation interventions that allow for long-term persistence. Finally, rescue from one environmental change might make populations more susceptible to the next one, depending on the pleiotropic effect of a rescue allele (Draghi, 2026).

3 Discussion

Here we have discussed how to quantify the time-varying effect of evolution on persistence when persistence in the absence of evolution is possible, which is often the case at least in the short term. We show in particular how to assess the probability of rescue over time (Equation 2). If evolutionary suicide is negligible (more precisely, $P(A^c \cap B) \ll P(A) - P(B)$), it is sufficient to turn off evolution and follow the fate of ensembles of evolving and non-evolving populations over time.

Above we have illustrated how to assess the effect of evolution on persistence in a simple two-allele model of rescue by standing genetic variation (Figure 3). An interesting future direction would be to extend this analysis to more models, which requires extinction time distributions with and without evolution. Extinction time distributions can always be determined by simulation, but there are also existing analytical approaches. For example, continuous branching diffusion has been applied to obtain extinction times with arbitrarily many asexually-reproducing genotypes (Gomulkiewicz et al., 2017), including the derivation of a convenient approximation used for asexual populations (Anciaux et al., 2019) that also provides qualitative insights for sexual populations (Xu et al., 2023). Results from the mathematical literature could be harnessed to include *de novo* mutations in the simple model from Figure 2 (Heinzmann, 2009). Branching process models allow indefinite persistence, approximating populations with large carrying capacities; following successful adaptation, longer-term extinction probabilities for populations with smaller carrying capacities may be derived with help from the ecological literature (Ovaskainen and Meerson, 2010). We can also consider extinction times in gradually changing environments, as in the quantitative genetics analysis by Bürger and Lynch (1995). In addition to

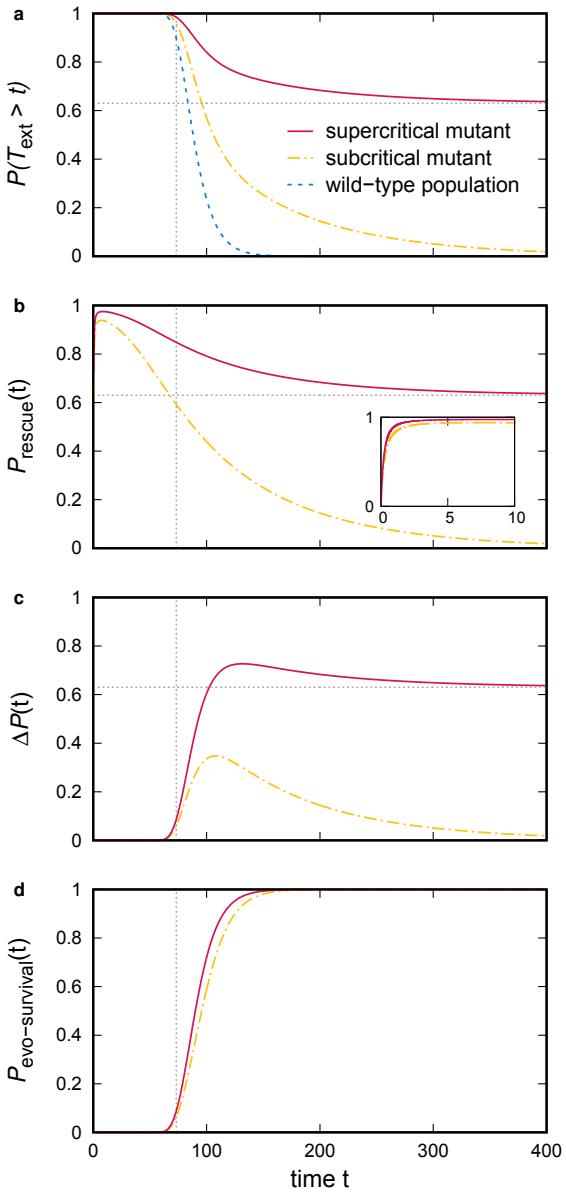

Figure 3: **Assessing the effect of evolution on persistence over time.** (a) Distribution of persistence times, (b) rescue probabilities, (c) excess probabilities, and (d) probabilities that a surviving population survives due to evolution. We consider two evolution scenarios: populations composed of mostly wild-type individuals with decline rate r and (i) a fraction p_0 of subcritical beneficial mutants with negative growth rate $-r+s_{\text{sub}}$ (dash-dotted yellow line) and (ii) a fraction p_0 of supercritical beneficial mutants with positive growth rate $-r+s_{\text{super}}$ (solid pink line), where s_{sub} and s_{super} are the selective advantages of the mutants. No new mutations occur during population decline. As a no-evolution scenario, we consider a population that is composed entirely of wild-type individuals (dashed blue line in panel a). For the calculation of $P_{\text{rescue}}(t)$ and $P_{\text{evo-survival}}(t)$, we set $P(A_t^c \cap B_t) = 0$. This is reasonable but confirming would require a rigorous mathematical treatment with the construction of a true counterfactual. The definition of $P_{\text{rescue}}(t)$, given in Eq. (2), is only practical if the risk of extinction without evolution is not vanishingly small. As visible in the inset of panel c, for small times, when extinction with and without evolution is very small (compare also to panel a), $P_{\text{rescue}}(0)$ is zero and then shoots up to values close to 1, which is due to a vanishingly small fraction of extinctions without evolution. For reference, we indicate in the graphs the time at which the extinction risk of a purely wild-type population is 10% (thin vertical line). Since in this example, all non-evolving populations go extinct in the absence of evolution, the excess probability ΔP and the probability of rescue P_{rescue} for the population with the supercritical mutant both converge to the ultimate probability of persistence, $\lim_{t\to\infty} P(T_{\text{ext}} > t)$ (horizontal grey line). The distributions of persistence times are analytically derived by jointly considering two single-type branching processes, as proposed by Holt and Gomulkiewicz (1997) and executed by Gomulkiewicz et al. (2017) based on branching diffusion. Details can be found in the Supplementary File S1. Parameters: $p_0 = 0.01$, $s_{\text{sub}} = 0.07$, $s_{\text{super}} = 0.09$, $N_0 = 10,000$, $r = 0.08$; all types have the same death rate $d = 1.0$.

determining the timescale that is relevant for evolutionary rescue, calculating extinction times may also help integrate with experiments where it is common to record extinction times (e.g. Lachapelle and Bell, 2012; Petkovic and Colegrave, 2023), sometimes even not only in the presence but also in the absence of evolution (Olazcuaga et al., 2026).

We have shown that we can calculate the probability of evolutionary rescue by monitoring ensembles of evolving and non-evolving populations (provided there is no possibility of evolutionary suicide, Equation 1). However, we will often want to know whether a *particular* population was rescued. For this we need the true counterfactual: would this specific population have gone extinct without evolution? In the absence of a true counterfactual, some information about a hypothetical non-evolving twin may be gained from population trajectories, genomic data etc. The issue of appropriate counterfactuals arises in other fields, such as comparing disease spread with and without interventions (Hudgens and Halloran, 2008; Kaminsky et al., 2019); we could learn from this both for the implementation of simulations and the interpretation of empirical data.

Data availability

Supplementary File S1 is included below. The code to generate Figure 3 (Supplementary File S2) is available at: `https://github.com/mmosmond/rescue-review-network`.

Author contributions

Conceptualization: Dale Clement, Peter Czuppon, Robert D. Holt, Guillaume Martin, Maria E. Orive, Matthew Osmond, Hildegard Uecker, Lindi Wahl, Masato Yamamichi

Formal analysis: Matthew Osmond, Hildegard Uecker

Project administration: Matthew Osmond, Hildegard Uecker

Visualization: Christin Nyhoegen, Matthew Osmond, Hildegard Uecker

Writing – original draft: Loïc Marrec, Matthew Osmond, Hildegard Uecker, Lindi Wahl

Writing – review & editing: everyone

Funding

The authors acknowledge funding from a large number of sources, specifically: Carla Alejandre: grants PID2021-122936NB-I00 and PID2024-159684NB-I00 funded by the Spanish Ministry of Science and Innovation/State Agency of Research MCIN AEI/10.13039/501100011033 and "ERDF A way of making Europe", and from the Consejería de Educación, Ciencia y Universidades de la Comunidad de Madrid through grant PIPF-2023/TEC29607; Ernesto Berríos-Caro: German Science Foundation (DFG) through a Walter Benjamin Position grant, GZ: BE 8013/1-1, Projektnummer: 512851323; Dale T. Clement: NSF DMS 2327799 (to N. K.), NSF DEB 2027446 (to A. S.); Léonard Dekens: Francis Crick Institute, which receives its core funding from Cancer Research UK (CC2240), the UK Medical Research Council (CC2240), and the Wellcome Trust, United Kingdom (CC2240); Asad Hasan: Natural Sciences and Engineering Research Council of Canada Doctoral Postgraduate Scholarship (PGS–D 601214); Robert D. Holt: National Science Foundation, DEB-1923513, and the joint NIFA-NSF-NIH Ecology and Evolution of Infectious Disease (EEID) award 2023-67015-40544, and the University of Florida Foundation; Guillaume Martin: project ANR-18-CE45-0019 RESISTE; Maria Orive: National Science Foundation DEB-1923495, joint NIFA-NSF-NIH Ecology and Evolution of Infectious Disease (EEID) award 2023-67015-4054, and the University of Kansas. Matthew Osmond: Natural Sciences and Engineering Research Council of Canada, grant RGPIN–2021-03207; Vrinda Ravi Kumar: Czech VEDA Fellowships (project number CZ.02.01.01/00/22_010/0008117); Lindi Wahl: Natural Sciences and Engineering Research Council of Canada, grant RGPIN-2019-06294; Masato Yamamichi: Japan Society for the Promotion of Science (JSPS) Grant-in-Aid for Scientific Research (KAKENHI) JP19K16223, JP20KK0169, JP21H02560, JP22H02688, JP22H04983, and JP25K02340, Australian Research Council (ARC) Discovery Project DP220102040, Japan Science and Technology Agency (JST) Core Research for Evolutional Science and Technology (CREST) JPMJCR23N5, Inamori Research Grant 2024, and Research Organization of Information and Systems (ROIS) Research Grant of Strategic Research Project 2024-SRP-10; Hildegard Uecker and Matthew Osmond: Workshop program of the Max Planck Institute for Evolutionary Biology.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We are grateful to Richard Gomulkiewicz and Helen Alexander for inspiring discussions at and after the SMBE satellite meeting on Evolutionary rescue at Kiel University in 2022. We hope that Richard

gives us his blessing for what we wrote. We also thank Ophélie Ronce for early discussions and Jitka Polechová, the Editors, and the Reviewers for many helpful comments. The article was initiated at the Workshop 'Mathematical models of evolutionary rescue', which took place in June 2023 at the Max Planck Institute for Evolutionary Biology in Plön. We would like to thank all workshop participants for their contributions and are furthermore grateful to the institute's Workshop program for funding the workshop and to Maren Lehmann and Corinna Plohmann for support with the organisation and logistics.

References

Alexander, H. K., Martin, G., Martin, O. Y., and Bonhoeffer, S. (2014). Evolutionary rescue: linking theory for conservation and medicine. *Evolutionary Applications*, 7(10):1161–1179.

Anciaux, Y., Lambert, A., Ronce, O., Roques, L., and Martin, G. (2019). Population persistence under high mutation rate: from evolutionary rescue to lethal mutagenesis. *Evolution*, 73(8):1517–1532.

Balstad, L. J., Baskett, M. L., Carlson, S. M., Cunningham, C. J., and Westley, P. A. (2026). Revisiting evolutionary rescue in the wild. *Trends in Ecology & Evolution*.

Bell, G. (2017). Evolutionary rescue. *Annual Review of Ecology, Evolution, and Systematics*, 48:605–627.

Bürger, R. and Lynch, M. (1995). Evolution and extinction in a changing environment: a quantitative-genetic analysis. *Evolution*, 49(1):151–163.

Carlson, S. M., Cunningham, C. J., and Westley, P. A. (2014). Evolutionary rescue in a changing world. *Trends in Ecology & Evolution*, 29(9):521–530.

Draghi, J. A. (2026). Evolutionary rescue by adaptive specialization in rapidly changing environments. *Journal of Evolutionary Biology*, 39(4):460–471.

Golas, B. D., Goodell, B., and Webb, C. T. (2021). Host adaptation to novel pathogen introduction: Predicting conditions that promote evolutionary rescue. *Ecology Letters*, 24(10):2238–2255.

Gomulkiewicz, R. and Holt, R. D. (1995). When does evolution by natural selection prevent extinction? *Evolution*, 49:201–207.

Gomulkiewicz, R., Krone, S. M., and Remien, C. H. (2017). Evolution and the duration of a doomed population. *Evolutionary Applications*, 10(5):471–484.

Gonzalez, A., Ronce, O., Ferriere, R., and Hochberg, M. E. (2013). Evolutionary rescue: an emerging focus at the intersection between ecology and evolution. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 368(1610):20120404.

Heinzmann, D. (2009). Extinction times in multitype Markov branching processes. *Journal of Applied Probability*, 46(1):296–307.

Holt, R. D. and Gomulkiewicz, R. (1997). The evolution of species' niches: a population dynamic perspective. In Othmer, H. G., Adler, F. R., Lewis, M. A., , and Dallon, J. C., editors, *Case Studies in Mathematical Modelling: Ecology, Physiology, and Cell Biology*, pages 25–50. Prentice Hall Englewood Cliffs, NJ.

Hudgens, M. G. and Halloran, M. E. (2008). Toward causal inference with interference. *Journal of the american statistical association*, 103(482):832–842.

Hufbauer, R. A., Szűcs, M., Kasyon, E., Youngberg, C., Koontz, M. J., Richards, C., Tuff, T., and Melbourne, B. A. (2015). Three types of rescue can avert extinction in a changing environment. *Proceedings of the National Academy of Sciences*, 112(33):10557–10562.

Kaminsky, J., Keegan, L. T., Metcalf, C. J. E., and Lessler, J. (2019). Perfect counterfactuals for epidemic simulations. *Philosophical Transactions of the Royal Society B*, 374(1776):20180279.

Kreiner, J. M., Stinchcombe, J. R., and Wright, S. I. (2018). Population genomics of herbicide resistance: Adaptation via evolutionary rescue. *Annual Review of Plant Biology*, 69:611–635.

Lachapelle, J. and Bell, G. (2012). Evolutionary rescue of sexual and asexual populations in a deteriorating environment. *Evolution*, 66(11):3508–3518.

Martin, G., Aguilée, R., Ramsayer, J., Kaltz, O., and Ronce, O. (2013). The probability of evolutionary rescue: towards a quantitative comparison between theory and evolution experiments. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 368(1610):20120088.

Matz, M. V., Treml, E. A., and Haller, B. C. (2020). Estimating the potential for coral adaptation to global warming across the Indo-West Pacific. *Global Change Biology*, 26(6):3473–3481.

McManus, L. C., Forrest, D. L., Tekwa, E. W., Schindler, D. E., Colton, M. A., Webster, M. M., Essington, T. E., Palumbi, S. R., Mumby, P. J., and Pinsky, M. L. (2021). Evolution and connectivity influence the persistence and recovery of coral reefs under climate change in the Caribbean, Southwest Pacific, and Coral Triangle. *Global Change Biology*, 27(18):4307–4321.

Olazcuaga, L., Melbourne, B. A., Nordstrom, S. W., and Hufbauer, R. A. (2026). Density dependence during evolutionary rescue increases extinction risk but does not prevent adaptation. *Ecology Letters*, 29(1):e70312.

Orr, H. A. and Unckless, R. L. (2008). Population extinction and the genetics of adaptation. *The American Naturalist*, 172(2):160–169.

Ovaskainen, O. and Meerson, B. (2010). Stochastic models of population extinction. *Trends in Ecology & Evolution*, 25(11):643–652.

Petkovic, N. and Colegrave, N. (2023). The effects of sex on extinction dynamics of *chlamydomonas reinhardtii* depend on the rate of environmental change. *Journal of Evolutionary Biology*, 36(12):1783–1795.

Ramsayer, J., Kaltz, O., and Hochberg, M. E. (2013). Evolutionary rescue in populations of *Pseudomonas fluorescens* across an antibiotic gradient. *Evolutionary Applications*, 6(4):608–616.

Stewart, G. S., Morris, M. R., Genis, A. B., Szűcs, M., Melbourne, B. A., Tavener, S. J., and Hufbauer, R. A. (2017). The power of evolutionary rescue is constrained by genetic load. *Evolutionary Applications*, 10(7):731–741.

Uecker, H., Osmond, M., Alejandre, C., Berríos-Caro, E., Clement, D., Czuppon, P., Dekens, L., Deraje, P., Draghi, J., Hasan, A., et al. (2026). Modeling evolutionary rescue. *EcoEvoRxiv*.

Xu, K., Vision, T. J., and Servedio, M. R. (2023). Evolutionary rescue under demographic and environmental stochasticity. *Journal of Evolutionary Biology*, 36(10):1525–1538.

Zhang, Q.-G. and Buckling, A. (2011). Antagonistic coevolution limits population persistence of a virus in a thermally deteriorating environment. *Ecology Letters*, 14(3):282–288.

Quantifying the probability of evolutionary rescue

Supplementary File S1

The distribution of persistence times and the excess and the rescue probability

We here provide the equations underlying Figure 3 in the main text. The calculations are equivalent to Holt and Gomulkiewicz (1997), just considering a continuous-time process here.

For a birth-death process with birth rate b and death rate d, the probability generating function for the number of individuals at time t, $n(t)$, given $n(0) = 1$, is given by

$$P(z,t) = \left(1 + \frac{1}{\frac{e^{-(b-d)t}}{z-1} - \frac{b}{b-d}\left(1 - e^{-(b-d)t}\right)}\right) \tag{S1}$$

(Allen, 2011), and for $n(0) = n_0$, we have

$$P_{n_0}(z,t) = P(z,t)^{n_0}. \tag{S2}$$

From this, we obtain the distribution of extinction times, T_{ext}, as

$$\begin{aligned} P(T_{\text{ext}} \leq t) = P_{n_0}(0,t) &= \left(1 + \frac{1}{-e^{-(b-d)t} - \frac{b}{b-d}\left(1 - e^{-(b-d)t}\right)}\right)^{n_0} \\ &= \left(\frac{e^{-(b-d)t} - 1}{e^{-(b-d)t} - \frac{b}{d}}\right)^{n_0}. \end{aligned} \tag{S3}$$

Let us now turn to a population that consists of m_0 mutant individuals with birth rates b_m and death rates d_m and $N_0 - m_0$ wild-type individuals with birth rates b_w and d_w. We ignore new mutations. From general branching process theory, we know that the probability generating function for the total number of individuals at time t is given by

$$P_{\text{total}}(z,t) = \left(P_{\text{mutant}}(z,t)\right)^{m_0} \times \left(P_{\text{wildtype}}(z,t)\right)^{N_0 - m_0}, \tag{S4}$$

where $P_{\text{mutant}}(z,t)$ and $P_{\text{wildtype}}(z,t)$ are given by Eq. (S1) with the appropriate birth and death rates.

The distribution of extinction times is thus given by

$$P(T_{\text{ext}} \leq t \,|\, \text{evolution}) = P_{\text{total}}(0,t) \\ = \left(\frac{e^{-(b_w-d_w)t}-1}{e^{-(b_w-d_w)t} - \frac{b_w}{d_w}} \right)^{N_0-m_0} \times \left(\frac{e^{-(b_m-d_m)t}-1}{e^{-(b_m-d_m)t} - \frac{b_m}{d_m}} \right)^{m_0}. \quad \text{(S5)}$$

For comparison, we consider a purely wild-type population, for which we have

$$P(T_{\text{ext}} \leq t \,|\, \text{no evolution}) = \left(\frac{e^{-(b_w-d_w)t}-1}{e^{-(b_w-d_w)t} - \frac{b_w}{d_w}} \right)^{N_0}. \quad \text{(S6)}$$

The probability of persistence up to at least time t with and without evolution (denoted by A_t and B_t) is given by

$$P(A_t) = P(T_{\text{ext}} > t \,|\, \text{evolution}) = 1 - P(T_{\text{ext}} \leq t \,|\, \text{evolution}) \quad \text{and} \quad \text{(S7)}$$
$$P(B_t) = P(T_{\text{ext}} > t \,|\, \text{no evolution}) = 1 - P(T_{\text{ext}} \leq t \,|\, \text{no evolution}), \quad \text{(S8)}$$

respectively.

Panel a of Figure 3 shows $P(A_t)$ (for two different values of b_m) and $P(B_t)$. The excess probability, generalized to time-dependent probability, shown in Panel b, is given by

$$P_{\text{excess}}(t) = P(A_t) - P(B_t) = 1 - P(T_{\text{ext}} \leq t|\text{evolution}) - (1 - P(T_{\text{ext}} \leq t|\text{no evolution}). \quad \text{(S9)}$$

Plugging both distributions into the generalization of Eq. (1) in the main text yields

$$\begin{aligned} P_{\text{cond}}(t) &= \frac{P(A_t) - P(B_t)}{1 - P(B_t)} \\ &= \frac{1 - P(T_{\text{ext}} \leq t|\text{evolution}) - (1 - P(T_{\text{ext}} \leq t|\text{no evolution}))}{P(T_{\text{ext}} \leq t|\text{no evolution})} \\ &= 1 - \frac{P(T_{\text{ext}} \leq t|\text{evolution})}{P(T_{\text{ext}} \leq t|\text{no evolution})} \\ &= 1 - \left(\frac{\left(e^{-(b_m-d_m)t}-1\right) \cdot \left(e^{-(b_w-d_w)t} - \frac{b_w}{d_w}\right)}{\left(e^{-(b_m-d_m)t} - \frac{b_m}{d_m}\right) \cdot \left(e^{-(b_w-d_w)t}-1\right)} \right)^{m_0}, \end{aligned} \quad \text{(S10)}$$

which is plotted in Panel c.

The probability of ultimate survival of the process, given $b_m > d_m$, denoted by P_{rescue} in the figure, is given by

$$P_{\text{rescue}} = \lim_{t\to\infty} P(A_t) = \left(\frac{d_m}{b_m} \right)^{m_0}. \quad \text{(S11)}$$

Since $\lim_{t\to\infty} P(B_t) = 0$, $P_{\text{excess}}(t)$ and $P_{\text{cond}}(t)$ both converge to this value.

References

Allen, L. J. (2011). *An introduction to stochastic processes with applications to biology* (2 ed.). Pearson Education.

Holt, R. D. and R. Gomulkiewicz (1997). The evolution of species' niches: a population dynamic perspective. In H. G. Othmer, F. R. Adler, M. A. Lewis, , and J. C. Dallon (Eds.), *Case Studies in Mathematical Modelling: Ecology, Physiology, and Cell Biology*, pp. 25–50. Prentice Hall Englewood Cliffs, NJ.