



HAL
open science

Early-warning signals of impending speciation

Maïdie Sinitambirivoutin, Patrik Nosil, Samuel Flaxman, Jeffrey Feder,
Zachariah Gompert, Vasilis Dakos

► **To cite this version:**

Maïdie Sinitambirivoutin, Patrik Nosil, Samuel Flaxman, Jeffrey Feder, Zachariah Gompert, et al.. Early-warning signals of impending speciation. *Evolution - International Journal of Organic Evolution*, 2023, 77, pp.1444 - 1457. 10.1093/evolut/qpad054 . hal-04286033

HAL Id: hal-04286033

<https://hal.science/hal-04286033v1>

Submitted on 14 Nov 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Early-warning signals of impending speciation

Maidie Sinitambirivoutin¹, Patrik Nosil², Samuel Flaxman³, Jeffrey Feder⁴, Zachariah Gompert⁵, and Vasilis Dakos^{1,6}

¹Institute of Ecology and Environmental Sciences, Sorbonne University/CNRS/INRA/IRD/UPEC/Paris-Diderot University, Paris, France

²CEFE, Univ Montpellier, CNRS, EPHE, IRD, Univ Paul Valéry Montpellier 3, Montpellier, France

³Department of Ecology and Evolutionary Biology, University of Colorado, Boulder, CO, United States

⁴Department of Biological Sciences, University of Notre Dame, Notre Dame, IN, United States

⁵Department of Biology, Utah State University, Logan, UT, United States

⁶Institut des Sciences de l'Evolution Montpellier, Univ Montpellier/CNRS/EPHE/IRD, Montpellier, France

Corresponding authors: Institut des Sciences de l'Evolution de Montpellier, Univ Montpellier/CNRS/EPHE/IRD, Montpellier, France. Email: vasilis.dakos@umontpellier.fr; CEFE, Univ Montpellier, CNRS, EPHE, IRD, Univ Paul Valéry Montpellier 3, Montpellier 34293, France. Email: patrik.nosil@cefe.cnrs.fr

Abstract

Species formation is a central topic in biology, and a large body of theoretical work has explored the conditions under which speciation occurs, including whether speciation dynamics are gradual or abrupt. In some cases of abrupt speciation, differentiation slowly builds up until it reaches a threshold, at which point linkage disequilibrium (LD) and divergent selection enter a positive feedback loop that triggers accelerated change. Notably, such abrupt transitions powered by a positive feedback have also been observed in a range of other systems. Efforts to anticipate abrupt transitions have led to the development of “early warning signals” (EWS), that is, specific statistical patterns preceding abrupt transitions. Examples of EWS are rising autocorrelation and variance in time-series data due to the reduction of the ability of the system to recover from disturbances. Here, we investigate whether speciation dynamics in theoretical models also exhibit EWS. Using a model of genetic divergence between two populations, we search for EWS before gradual and abrupt speciation events. We do so using six different metrics of differentiation: the effective migration rate, the number of selected loci, the mean fitness of our studied population, LD , F_{ST} , and D_{abs} , a metric analogous to D_{XY} . We find evidence for EWS, with a heterogeneity in their strength among differentiation metrics. We specifically identify F_{ST} and the effective migration rate as the most reliable EWS of upcoming abrupt speciation events. Our results provide initial insights into potential EWS of impending speciation and contribute to efforts to generalize the mechanisms underlying EWS.

Keywords: abrupt speciation, adaptation, tipping point, linkage disequilibrium, genome wide congealing, stochastic model

Introduction

Speciation, defined as the emergence of new species, is often a complex phenomenon driven by multiple factors and processes. Cases of gradual divergence over time between geographically isolated populations are generally regarded as the most common, but not only, mode of speciation (Coyne & Orr, 2004; Mayr, 1942; Price, 2007). In such situations, divergence can build up in a fairly linear fashion (i.e., at a consistent rate over time), via the combination of selection and drift, and unimpeded by the homogenizing process of gene flow. However, geographic isolation is not always complete during the divergence process. In such cases, the dynamics of and progress toward speciation can be shaped by a complex interplay of environmental conditions (i.e., sources and strength of selection), the extent of migration between populations, and genetic architecture. For example, environmental differences can create divergent selection favoring different phenotypes in different populations, promoting speciation (Gavrilets, 2004). Migrants between populations will on the contrary often lead to gene flow that homogenizes populations or at least constrains divergence (Endler, 1977; Hendry et al., 2001).

In addition, theoretical work has explored the conditions under which gradual versus abrupt speciation arises (Flaxman

et al., 2013; Gavrilets, 2004; Nosil et al., 2017). In some models, this has uncovered the particular role of linkage disequilibrium (LD) in the speciation process. LD refers to statistical associations between genetic regions, which are often facilitated by, but are not synonymous with, physical linkage on the same chromosome. Specifically, LD corresponds to non-random associations between alleles at different loci (Hill & Robertson, 1968). LD can thus allow strongly favored alleles to increase the frequency of other associated alleles. In other words, direct selection on one locus can be transmitted to other loci in the genome, via LD with the selected locus. This process by which selection is transmitted from directly selected loci to other loci is termed “indirect selection” (following Gompert et al., 2017; Gompert et al., 2022; Kimura, 1971 and Lande & Arnold, 1983) and results in genetic hitchhiking (Charlesworth & Jensen, 2022; Smith & Haigh, 1974).

An interesting consequence of LD is that it can promote abrupt (i.e., sudden in time) rather than gradual speciation events (Flaxman et al., 2014; Nosil et al., 2017). This is because LD participates in a positive feedback loop with divergent selection (i.e., each amplifies the other) that can increase indirect selection and trigger accelerated change. This process prevents alleles affected by divergent selection

Received April 1, 2022; revisions received February 9, 2023; accepted April 13, 2023

© The Author(s) 2023. Published by Oxford University Press on behalf of The Society for the Study of Evolution (SSE).

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

from being lost by gene flow (which acts against selection's effect on increasing the frequencies of favored alleles in a population) and drift, and instead, it increases differentiation (Dent et al., 2003; Flaxman et al., 2014) (Figure 1). In essence, loci under divergent selection transition from evolving independently to exhibiting coupled dynamics (e.g., similar to multilocus coupling in hybrid zone theory, where the coupling is in space rather than time (Barton, 1983, and see Box 1 in Nosil et al. 2017 for explicit consideration of dynamics in time vs. space).

Although the exact dynamics of abrupt speciation events are yet to be fully uncovered, one observation is that it shares similarities with the behavior of a range of other systems exhibiting marked, abrupt changes triggered by positive feedbacks (Angeli et al., 2004). Typically, this type of abrupt changes occurs in systems that tend to exhibit two (or more) alternative stable states (but not necessarily so Hastings et al., 2018). When conditions are slowly changing, systems with alternative states often show small changes up to a point where a self-reinforcing positive feedback loop triggers accelerated and system-wide change. In the complex-systems literature, this bifurcation point where the positive feedback loop drives a sudden transition has generally been called a “tipping point” (Lenton, 2013; van Nes et al., 2016). In the case of speciation, simple models have suggested that two stable states might exist as a function of selection and migration rate (Flaxman et al., 2014; Nosil et al., 2017): one a state where all individuals belong to the same species versus a state of two distinct species. Depending on the initial conditions in these models, as adaptive evolutionary divergence occurs, the changing

LD acts as a driving force that pushes the system to cross the unstable threshold that divides the basins of attraction of the two states. Once that threshold is crossed, a sudden speciation event can unfold due to the positive feedback generated by the LD .

The existence of tipping points has been notably reported in the dynamics of climatic transitions (Alley et al., 2003), ecosystem shifts (like dryland desertification, or coral reef degradation Hughes, 1994; Scheffer et al., 2001), financial meltdowns (May et al., 2008), or even asthma attacks (Venegas et al., 2005). Perhaps the best-documented case of a tipping point is the one reported for shallow lakes shifting from a clear-water state to a turbid-water state (Scheffer et al., 1993). Clear lakes are characterized by the dominance of aquatic macrophytes, whereas in turbid lakes algae are dominant. The transition from a clear to a turbid-water state is caused by a positive feedback where algal growth increases turbidity that prevents macrophytes from growing, which leads to further increased turbidity, further reducing macrophyte growth and so on. Thus, as macrophytes disappear, the lake becomes dominated by algae and shifts abruptly and permanently to a turbid state.

A challenge in terms of understanding and predicting tipping point responses is that they occur suddenly (Figure 1A). Moreover, transitions induced by tipping points are difficult to stop because once the system arrives at such a state, the positive feedback that ensues propagates the system into a new state that is often associated with undesirable and irreversible effects. This has led to a search for statistical signals that precede tipping points, such that tipping points might be anticipated or even prevented before they occur (Scheffer

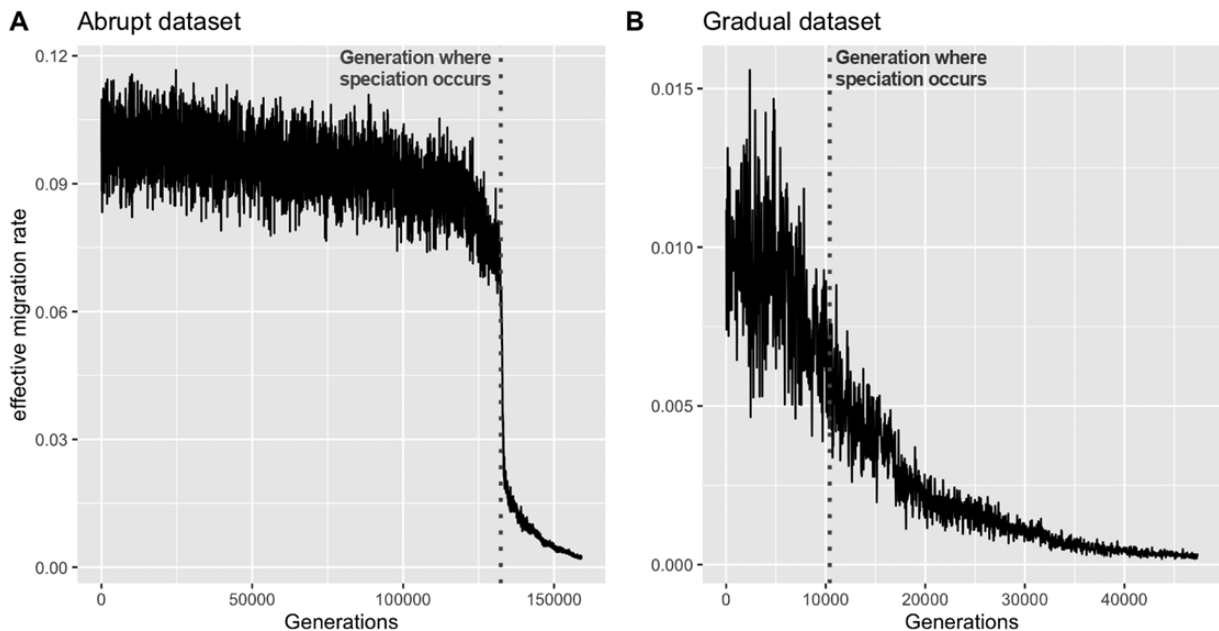


Figure 1. Examples of the dynamics of abrupt and gradual speciation. (B) Gradual speciation is characterized by a smooth decrease in m_e , the effective migration rate (i.e., the fraction of immigrants from the most recent migration step that produced offspring). (A) Abrupt speciation is characterized by a nonlinear drop in m_e at the time of speciation (such a time is shown here by the gray dotted vertical line). The figure was obtained from the *BU2S* model (see Methods for details), under a model simulating the genetic evolution of two populations of initially the same species placed in two different environments experiencing divergent selection, with migration allowed. The effective migration rate m_e represents the fraction of immigrants that contributed to reproduction in a given generation. As the two populations diverge, the residents become more adapted to their environment, and the immigrants relatively more unfit, leading to decreasing m_e . Abrupt speciation is characterized by initially slow and small changes in m_e , eventually leading to a sudden decrease in m_e at the time of speciation. During gradual speciation events, on the other hand, m_e decreases at a fairly constant rate. The following values of the selection strength (s) and migration probability (m) were used for this figure: (A) $m = 0.1$, $s = 0.01$; (B) $m = 0.01$, $s = 0.01$.

et al., 2009). The detection of such signals, so-called early-warning signals (EWS), has been an active field of research in ecology and other fields (Scheffer et al., 2012), but has yet to permeate evolutionary biology. Here, we apply it for the first time—to our knowledge—to speciation.

In principle, tipping points can be anticipated because close to them a system loses resilience and thus takes longer to recover from small perturbations, a phenomenon called critical slowing down (CSD) (van Nes & Scheffer, 2007) (Supplementary Figure S1). CSD is expected to create specific statistical patterns (EWS) in the system dynamics as the system approaches a tipping point (Dakos et al., 2012). Here we focus on the two core patterns characterizing CSD. First, CSD makes the system's current state more likely to resemble its past state (which can be measured by increasing autocorrelation through time) (Held & Kleinen, 2004). Second, CSD makes the system accumulate more extreme values due to fluctuations that do not dissipate quickly, thus resulting in increased variability (which can be measured by increasing standard deviation through time) (Carpenter & Brock, 2006).

Given that abrupt speciation can be driven by a positive feedback loop analogous to those seen in other systems, it is reasonable to ask if abrupt speciation is also forewarned by the same EWS. In other words, even if metrics we typically use to measure differentiation itself (such as F_{ST} and D_{XY}) hint that potentially speciation is taking place, they do not provide information on whether the dynamics of speciation will be gradual or abrupt (Figure 1). Instead it is the CSD-related EWS that could signal the imminence of an abrupt speciation event. Testing for such EWS is our objective here, in hopes that it will contribute to a better understanding of speciation (Nosil et al., 2020).

Importantly, our expectations are derived from past work (Flaxman et al., 2014; Nosil et al., 2017), which suggests that populations under divergent selection might exhibit two alternative stable states—weakly differentiated populations with low LD among adaptive alleles versus strongly differentiated species with high LD among adaptive alleles. Bistability implies the presence of an unstable point that divides the state space in trajectories leading to either undifferentiated populations or speciation. Close to this unstable point, slowing down is expected to enhance LD , thus pushing autocorrelation and variance toward a runaway (Dakos et al., 2013).

Building on previous work on speciation (Flaxman et al., 2014), we consider here a theoretical model that includes a system of two populations of the same species living in different environments and exchanging migrants between them. Over time, the two populations undergo genetic differentiation and eventually become two different species. We simulate a stochastic model of populations evolving under migration and selection (with drift and mutations) that generates speciation events over time; this can occur either gradually or abruptly, depending on the strength of the positive feedback loop between LD and the strength of total selection (i.e., direct selection plus indirect selection induced by LD). We measure statistical signals typically associated with critical slowing down for simulations exhibiting abrupt speciation events and we compare them to simulations where speciation occurs gradually. In addition, we compare patterns for selected loci to those expected in the absence of selection. Our results provide initial insights into potential EWS of impending speciation and generate clear avenues for further research.

Methods

The build-up-to-speciation model

Using the build-up-to-speciation (*BU2S*) model (Flaxman et al., 2014), we simulated the adaptation and genetic differentiation of a species to two different habitats, considering multiple loci that are either (a) causally related to adaptation (i.e., functional adaptive variants) or (b) neutral (i.e., no effect on fitness). The model involves two populations (hereafter referred to as population 1 and 2) of the same diploid species, in which there is initially zero genetic variation. At every generation, individuals migrate between populations with a probability m per individual (this is the gross migration rate). Individuals are assumed to have a diploid genome composed of four chromosomes of 50 cM each. Genetic variation arises through time via mutations. At each generation, 10 mutations are introduced at random loci in randomly chosen individuals. Each mutation is associated with a selection coefficient drawn from an exponential distribution with mean s . All individuals were initially homozygous at all loci, and ancestral alleles are favored in population 1. Newly arising mutations happen in a random individual in either population and introduce alleles favored in population 2. Note that this is an “infinite-alleles” or “infinite-loci” model. No two mutations will occur at exactly the same location, and each locus can harbor at most two alleles (where only the segregating loci are tracked during the simulation).

The fitness of an individual is determined multiplicatively as the product of contributions of all selected loci in its genome (neutral loci do not contribute to fitness). As this is a soft selection model (constant population size in every generation), fitness values are always relative (not absolute). The emergence of new alleles creates more variation in possible relative fitness values. Selection is symmetrical between the two populations, meaning that an allele favored in one population will be equally deleterious in the other one. The selection coefficient associated with the alleles of a selected locus is drawn from an exponential distribution of mean s , as in Flaxman et al. (2014). Let $w_{j1}(g_{ij})$ represent the contribution locus j makes to an individual's fitness in population 1, A_j the ancestral allele, B_j the mutated one, and S_j the selection coefficient at the j th locus. Let H_j be the dominance coefficient of B_j . We assumed codominance here ($H_j = 0.5$). We thus obtained $w_{j1}(A_jA_j) = 1 + S_j$, $w_{j1}(A_jB_j) = 1 + (1 - H_j)S_j = 1 + 0.5S_j$, and $w_{j1}(B_jB_j) = 1$. As selection was symmetrical across populations, in population 2 we had $w_{j2}(A_jA_j) = 1$, $w_{j2}(A_jB_j) = 1 + H_jS_j = 1 + 0.5S_j$, and $w_{j2}(B_jB_j) = 1 + S_j$.

The overall sequence of these events is as follows. At every generation, individuals first migrate. One at a time, offspring are then produced through the following sequence: for each offspring, parents are chosen stochastically (no assortative mating), with a probability of selection directly proportional to their fitness, and meiosis is then performed to obtain one gamete from each parent. The total number of offspring produced is the same as the number of parents in a population and generations are nonoverlapping (i.e., offspring replace parents). Thus, the total population size across both populations is held constant at 5,000 individuals (i.e., “soft selection”). The number of recombination events per meiosis was drawn from a Poisson distribution with mean equal to the total genome length (expressed in centi-Morgans) divided by 100. Thus, in a 200 cM genome, we expected a total of 2 recombination events per meiosis. The locations of the

recombination events were chosen at random (uniformly on the genome) after the number of events was drawn.

In line with previous work with the *BU2S* model (Flaxman et al., 2014), the time of speciation is defined as the last generation where the fitness of residents w_{res} is closer to the fitness of immigrants w_{imm} than to the maximum possible fitness in the resident's population w_{max} . Specifically, the time of speciation is the last generation where $\frac{w_{res}}{w_{imm}} > \frac{w_{max}}{w_{res}}$. The maximum possible fitness is calculated based on the alleles that are currently in the population at a given time. This definition of the “time of speciation” is somewhat arbitrary, but it is measurable and standardized such that it serves our goal here of representing a heuristic and operational way to objectively compare different simulation runs with different parameter values. To ensure the simulations reached the defined time of speciation, they were run until nearly complete reproductive isolation was attained. Near reproductive isolation was considered reached when the effective migration rate m_e decreased below a fixed threshold ($m_e = 1/(10,000N)$ with N the population size, here 5,000), m_e being the fraction of immigrants from the most recent migration step (i.e., that just arrived in the population) that produced offspring. In the event that this threshold was not attained, the simulation continued until the maximum number of generations (a parameter set at the beginning of the simulation, here 49,990 generations) was reached.

Previous work on the *BU2S* model (Flaxman et al., 2014) highlighted the ability of the model to result in either abrupt or gradual speciation events, dependent on the evolutionary parameters used. Specifically, different outcomes were observed by varying the migration probability m and the mean selection strength s (while holding all other parameters constant). With a higher $m:s$ ratio, gradual gene-by-gene divergence is prevented or constrained by the homogenizing effects of high gene flow resulting from migration. Speciation in these cases is more difficult to reach but when it does occur it is abrupt, triggered when the system reaches a tipping point where LD and divergent selection enter a positive feedback process that drives rapid divergence. Prior to this tipping point, neither component of this feedback loop is strong enough to prevent extensive gene flow from disrupting the differentiation. Thus, the feedback loop is not initiated until fit combinations of alleles arise by the combination of selection and chance, which at first is difficult, but becomes increasingly likely as new selected mutations arise. In contrast, under more similar strengths of selection and migration, speciation can take place progressively over time in a gradual gene-by-gene manner. This is because individual mutations experience sufficiently strong direct selection to overcome migration, even without strong feedback among selected loci due to LD . We thus here specifically focus on variation in the $m:s$ ratio to test for and compare EWS of gradual versus abrupt speciation.

Simulated data sets of abrupt and gradual speciation

We simulated data sets using the *BU2S* model that represented cases of abrupt and gradual speciation, as well as cases without speciation events (i.e., where the simulation goes on until the maximum number of generations) (Supplementary Table S1). Abrupt speciation data sets, where a sudden change of dynamics is visible at the time of speciation (Figure 1A), were generated by setting $m = 0.1$ and $s = 0.01$ (i.e., $m \gg s$). Gradual speciation data sets, where no marked change of

dynamics occurs at the time of speciation (Figure 1B), were generated by setting $m = s = 0.01$. We also generated neutral data sets to act as a control ($m = 0.1, s = 0$). In these data sets, the absence of selection prevented differentiation and thus speciation from occurring.

In our analysis, neutral data sets served as a control to assess the significance of our results. In the typical EWS literature, significance testing is performed by generating a surrogate (null) time series from a random process (Dakos et al., 2012). Here, instead of generating artificially such surrogates, we took advantage of the model itself to generate them and produced neutral data sets.

As our focus was on EWS that precede speciation events, we included only data from the beginning of the simulation to the time of speciation and focused downstream analyses on these time windows. Yet, the absolute elapsed time until speciation varied between abrupt, gradual, and neutral data sets. That is, speciation took longer for abrupt than gradual data sets (due to higher levels of homogenizing migration), while neutral data sets continued until the maximum number of generations. To be able to compare among the different data sets, we obtained equal distributions of lengths between data sets, by trimming the abrupt and neutral data sets to the length of gradual ones. This means that as, on average, the waiting time for speciation is around 160,000 generations for abrupt data sets, and around 12,000 generations for gradual data sets, we kept only the 12,000 generations before speciation for the abrupt data sets and we kept only 12,000 generations from the neutral data sets. Figure 3 shows examples of abrupt and gradual data sets from the beginning of the simulation up to the time of speciation. Supplementary Figure S2 shows, in the same examples, only the portions of the data sets that were analyzed together with neutral data sets for comparison.

Finally, we performed analyses where the metrics of speciation we monitored (see next section for details) were recorded at resolutions of every 300, 100, and 30 generations. We report in the main text results obtained with the highest resolution (30 generations). Results obtained with lower resolutions are reported in Supplementary Figure S3 and were qualitatively similar.

Monitored metrics of speciation

The *BU2S* model outputs time series that provide information on the genetic characteristics of both populations, within each habitat, at each generation. The complete list of parameters is given in Supplementary Table S1. Here, for each simulation output, we analyzed six metrics that provide information on the genetic differentiation between the two populations. Each of the metrics is given for each population as a time series which constitute our data sets that were used to analyze EWS (abrupt, gradual, neutral data sets). Details are as follows:

Effective migration rate m_e : The effective migration rate m_e is the proportion of reproduction attributable to migrants. It is calculated as the gross migration rate multiplied by the proportion of immigrants that produce offspring. m_e drops at the time of speciation, as immigrants become unfit and thus exhibit reduced probability of contributing gametes to form the next generation.

Number of variable selected loci: Variable selected loci represent the loci that contribute to fitness and

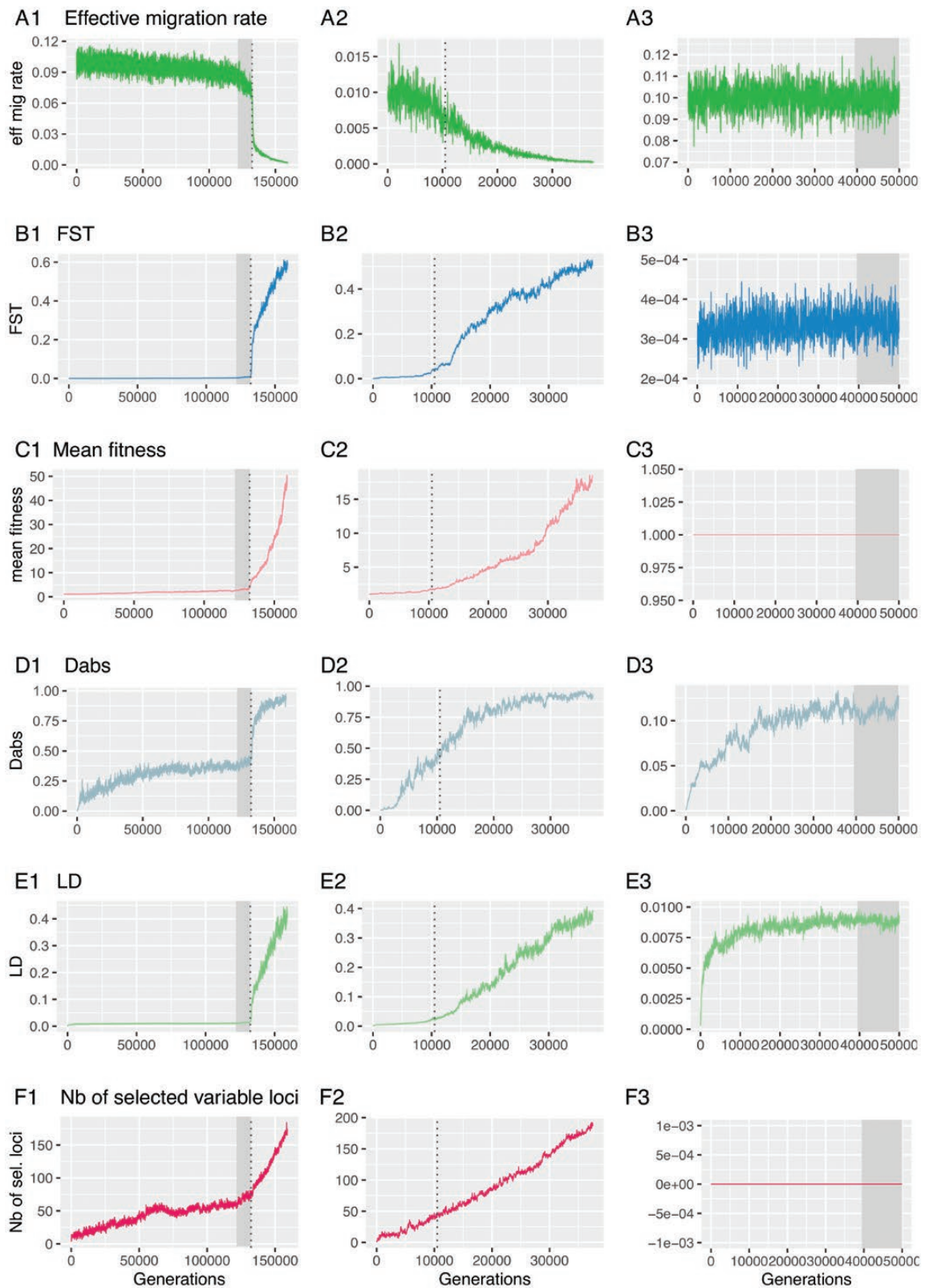


Figure 3. Metric dynamics before and after speciation. Left panels show abrupt data sets, middle panels show gradual data sets, and left panels show neutral data sets. Dotted vertical lines indicate the speciation event. Note the higher number of generations needed for speciation to occur in the abrupt data set when compared with the gradual data set, as expected given the higher migration rate in the abrupt data set. As speciation takes longer for abrupt data sets than gradual data sets, and to obtain data sets of equal length, we trimmed the abrupt data sets to the length of gradual ones by removing their excess data at the beginning of the simulation. In neutral data sets, there is no speciation event. The fitness of all individuals is set to 1, and there are no selected variable loci. This figure shows the entire time series. The parts analyzed correspond to the entire series for gradual data sets and to the gray-shaded areas for abrupt and neutral data sets. See [Supplementary Figure S2](#) for an example zooming in parts of the data sets (shaded area) that we used for estimating EWS.

adaptive divergence (as opposed to variable neutral loci, which do not affect fitness). Variable loci exhibit two different alleles and are created by spontaneously arising mutations. Depending on which environment they are in, alleles at selected loci will either be positively or negatively selected in a given population, meaning that they will either contribute a gain or a loss of relative fitness equal to s .

Mean fitness of a population: The fitness of an individual is determined by the cumulative effect of the selected loci in its genome, and the chances of survival and mating increase with higher fitness. As generations pass, the average fitness of residents rises as they adapt to their environment. In the output of the *BU2S* model, the fitness values of 200 individuals are given for each population as time series. The mean fitness of a population is estimated as the average of the 200 individual fitness values at each generation. As this is a soft selection model, the mean fitness is relative.

Linkage disequilibrium (*LD*) (Freeman & Herron, 2004): If allele A occurs with a frequency p_A at one locus and allele B occurs at frequency p_B at another locus, we define P_{AB} as the frequency with which A and B appear together in the same individual. The coefficient of linkage disequilibrium is then defined as $D_{AB} = P_{AB} - p_A p_B$. If $D_{AB} = 0$, alleles at the two loci are independent. As D rises, the association between the loci goes up. The correlation of allelic states between pairs of loci is then given by $r = \frac{|D_{AB}|}{\sqrt{p_A(1-p_A)p_B(1-p_B)}}$. In this study, we report

LD as the mean r over all pairs of variable loci.

Mean fixation index (F_{ST}): The fixation index (Wright, 1950) is a metric of relative differentiation between populations; in other words, it is based on both within and between-population variation. F_{ST} is usually based on allele frequencies, and in the *BU2S* model is calculated as follows: let H_T be the expected heterozygosity based on the average allele frequencies across populations at one time for one locus and H_S the average expected heterozygosity in each population. F_{ST} is calculated as $F_{ST} = \frac{H_T - H_S}{H_T}$ for each locus. We report here the mean F_{ST} over all variable loci (i.e., the mean of the single-locus estimates).

D_{abs} : We define D_{abs} , a metric analogous to D_{XY} defined by Nei and Li (1979) and referred to as π in their article. D_{XY} is a metric of absolute divergence. Unlike F_{ST} , it does not depend on intrapopulation variation. It is estimated as follows: take two populations X and Y. Suppose a locus i has two alleles, which we call “0” and “1.” Let p_i be the frequency of one of the alleles at this locus in population X, and let q_i be the frequency of that same allele at the same locus in population Y. Then, D_{XY} is $D_{XY} = \sum_{i=1}^N p_i(1 - q_i) + (1 - p_i)q_i$,

with N the number of loci in the genome. Because the *BU2S* model is an “infinite sites” model of genetic evolution, D_{XY} cannot be calculated over a specific number N of nucleotide sites for this model. As a result, we define D_{abs} , an analogous metric calculated as $D_{abs} = \frac{1}{N_v} \sum_{i=1}^{N_v} p_i(1 - q_i) + (1 - p_i)q_i$, with N_v the number of variable loci at the considered generation. D_{abs}

thus varies between 0 and 1 and is the expected fraction of variable sites that differ between two randomly chosen haplotypes from different populations.

Detecting EWS

To test for EWS we looked for critical slowing down (CSD), a sign of loss of resilience, in the time frame preceding speciation events in our simulations. Specifically, we focused on quantifying CSD through increases in autocorrelation at lag -1 (AR1) and increases in variability measured as standard deviation (SD) through time (Dakos et al., 2012). These two variables are referred to hereafter as indicators. Although changes in kurtosis (Biggs et al., 2009) and skewness (Guttal & Jayaprakash, 2008) of a time series can also arise, they are not connected to CSD and are less generic and sensitive than AR1 and SD (Dakos et al., 2012). We thus restrict our focus in the main text on AR1 and SD, but we do report results for kurtosis and skewness in Supplementary Figures S4–S6.

To estimate CSD, we followed methods detailed in Dakos et al. (2012). We analyzed, for each simulation output, the time series of the six metrics of speciation described in the previous section (effective migration rate, number of selected variable loci, mean fitness of residents, LD , F_{ST} , D_{abs}). For each data set type, outputs from 50 replicated simulations were analyzed. We report results by data set type.

Each time series was analyzed as follows: we first removed any underlying long-term trend to keep only the residual variation. CSD arises when the system starts taking longer to recover from small short-term perturbations from its main trend, and thus it should be detectable by analyzing short-term deviations from the main trend of a time series (i.e. residuals). We removed trends with a Gaussian filter that calculates a smoothed average trend from our noisy time series. Subtracting the resulting average trend from the initial time series returns the residuals. We detrended the data over window sizes (bandwidths) of size 5%, 10%, 15%, 20%, and 25% of the time series’ length. Window sizes were chosen experimentally by excluding smaller sizes that removed short-term variations of the time series (i.e., overfit) and the bigger sizes that did not render well the long-term variation of the time series (Supplementary Figure S7). We did this for each time series for all six metrics.

Second, for each residual time series, we computed the AR1 and SD within a rolling window of variable size. We used 11 rolling window sizes, ranging from 25% to 75% of the size of the time series with an increment of 5%. This means that for each time series, we estimated 55 records (from all combinations of 5 bandwidths and 11 rolling windows) showing the evolution of AR1 and SD, respectively, and we did so for all 50 outputs for each data set type. We thus obtained a total of 2,750 records for each of the 6 metrics, for each abrupt, gradual, and neutral data sets. A schematic representation of the above flow of work can be found in Supplementary Figure S8.

We then characterized whether each of the AR1 and SD records had an increasing or decreasing trend using the Kendall τ rank correlation coefficient between AR1 or SD and time. The Kendall τ rank correlation ranges between -1 to 1, with negative values indicating decreasing trends, positive values indicating increasing trends and values around zero indicating no trends. CSD being characterized by a rising AR1 and SD, we hypothesized positive Kendall τ ’s.

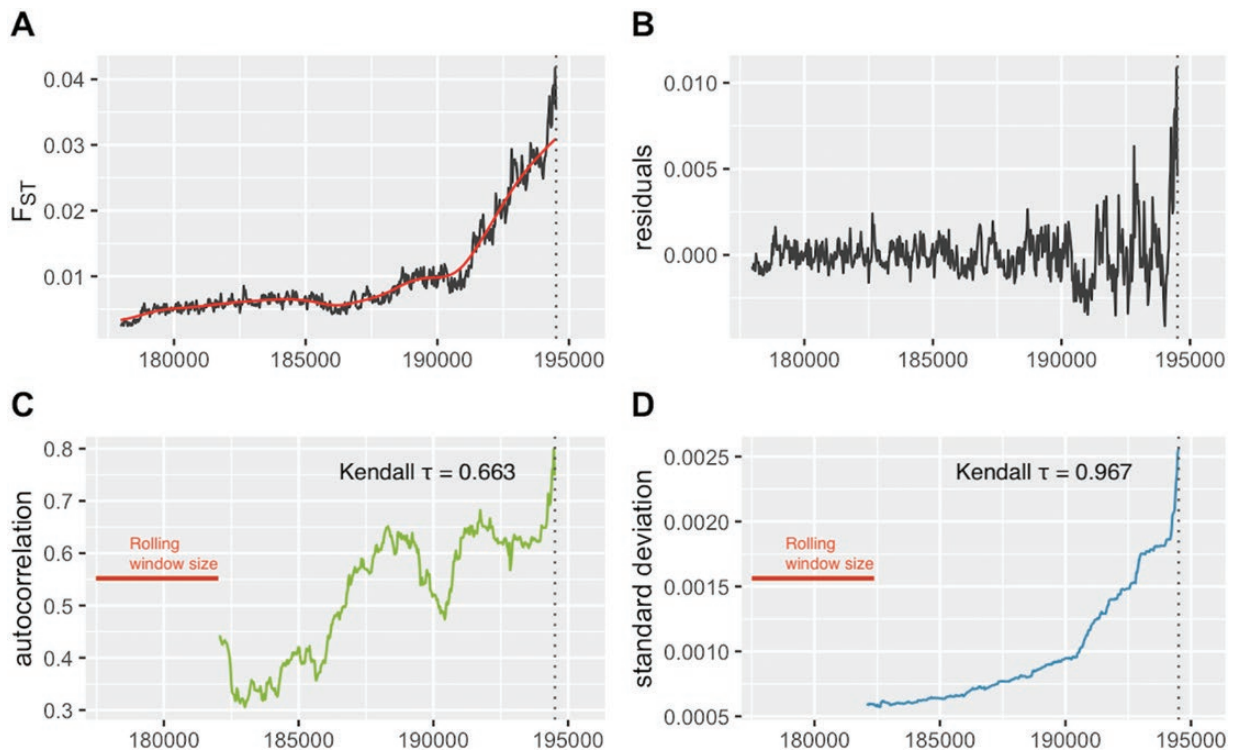


Figure 2. Example of estimating early warning signals in time series of a speciation metric. (A) F_{ST} (black) and Gaussian detrending (red, bandwidth = 10%). (B) Residuals after detrending. The statistical indicators are computed on the residuals: (C) autocorrelation at lag -1 , (D) standard deviation. All indicators are calculated within a rolling window equal to 25% of the length of the time series. Indicator trend is evaluated by the Kendall τ rank correlation coefficient. A Kendall τ value of close to 1 means a strongly increasing trend, a value close to -1 a strongly decreasing trend, and a value close to 0 the absence of a trend. A positive trend constitutes a sign of critical slowing down and can be used as early-warning signal for the speciation event.

Figure 2 demonstrates an example of estimating the EWS on the metric F_{ST} prior to speciation. After detrending (i.e., removing the long-term trend) of F_{ST} , we used the residuals (Figure 2B) to estimate the two EWS: AR1 (Figure 2C) and SD (Figure 2D). We then used the Kendall τ rank correlation to characterize the trend for each indicator. In this example, we found a strong increasing trend in standard deviation (Kendall $\tau = 0.967$, Figure 2D) and a moderate increasing trend in autocorrelation (Kendall $\tau = 0.663$, Figure 2C). In some of the abrupt data sets (like the example shown in Figure 2), a sharp increase in the metrics can be observed at the onset of speciation. Despite the fact that this sharp increase occurs technically before speciation (according to our definition), it nonetheless may be causing a strong positive trend in the indicators. To check that this is not the case, but there still is a positive trend, we also analyzed data sets where we removed such sharp increases by trimming 450 generations before speciation. We found similar results to those obtained without such trimming (Supplementary Figure S9).

We present summary results of trends in autocorrelation and standard deviation for residuals of the effective migration rate, number of selected variable loci, mean fitness of residents, LD , F_{ST} , and D_{abs} , estimated on 50 replicates of each abrupt, gradual, and neutral data sets. We report distributions of Kendall τ trends grouped by data set type, for all replicates, for all bandwidth and rolling window sizes (i.e., 2,750 Kendall τ per group), as a measure of the robustness of our results.

Receiver operating characteristic curves

We assessed the accuracy and sensitivity of our results using the area under curve (AUC) of receiver operating characteristic curves (ROC). Formally, ROC are a way of quantifying

the overlap between two distributions, which expresses the trade-off between accuracy (correctly detected EWS or true positives) and sensitivity (incorrectly detected EWS or false positives). We measured AUC from the overlap of Kendall τ distributions from two comparisons: (a) the distributions of Kendall τ from abrupt data sets were compared to those of neutral data sets. For instance, we compared the 50 trends of the AR1 of the F_{ST} of abrupt data sets to 50 AR1 trends computed from neutral data sets. In this comparison, neutral data sets served as control to test if our results were different from those obtained by chance; (b) the distributions of Kendall τ from abrupt data sets were compared with those of gradual data sets to assess whether the results found in abrupt data sets were characteristic of the dynamics of abrupt speciation events or solely of speciation events, regardless of their type.

To compute the AUC from ROC curves, we followed Boettiger and Hastings (2012) Boettiger and Hastings (2012) (Supplementary Figure S10). AUC ranges between 0 and 1, with values of 0.5 indicating that the null and real distributions are the same. An AUC close to 1 indicates that the observed distribution has higher values compared with the control. AUC values approaching zero indicate the contrary. When looking for signs of CSD, we expected to obtain higher Kendall τ values on abrupt data sets compared with neutral and gradual data sets, and hence expected AUC values above 0.5 when performing both comparisons.

Results

Metric dynamics before and after speciation

As expected, the differentiation metrics analyzed changed over time, but showed a sudden change of dynamics at

the time of speciation only for abrupt data sets (Figure 3). On neutral data sets, in the absence of selection, no change was visible in any of the metrics (Figure 3, A3–F3). Specifically, all metrics except the effective migration rate were rising prior to the speciation event in both abrupt and gradual data sets (Supplementary Figure S2). The effective migration rate was decreasing, as the fitness gap between residents and immigrants made the latter too unfit to contribute greatly to reproduction (Figure 3A, Supplementary Figure S1A). As new selected mutations arose through generations, the number of selected variable loci increased steadily (Figure 3F, Supplementary Figure S1F). Residents becoming better adapted to their environment over time translated into an increasing average fitness (Figure 3C, Supplementary Figure S1C). Our metrics of population genetic differentiation, namely F_{ST} (Figure 3B, Supplementary Figure S1B) and D_{abs} (Figure 3D, Supplementary Figure S1D), increased through time. Finally, LD (Figure 3E, Supplementary Figure S1E) slowly built up before jumping at the time of speciation for

abrupt runs, as expected in the presence of a positive feedback loop between LD and selection. But even if most of the metrics did change over time, this did not necessarily reflect whether or when speciation will occur, and whether it will be gradual or abrupt. It is EWS that might best provide this information, which we test below.

EWS before abrupt speciation

We compared Kendall τ values obtained for abrupt data sets to Kendall τ obtained for neutral data sets. The neutral data sets were used here as a control: the comparison aimed at assessing whether the results obtained for abrupt data sets were different from random. We detected evidence for EWS in abrupt data sets, but their robustness and accuracy varied among differentiation metrics and types of EWS. Robustness referred to the sensitivity of EWS to detrending bandwidths and window sizes we used, whereas accuracy referred to how different EWS were when compared with EWS computed in the control data sets.

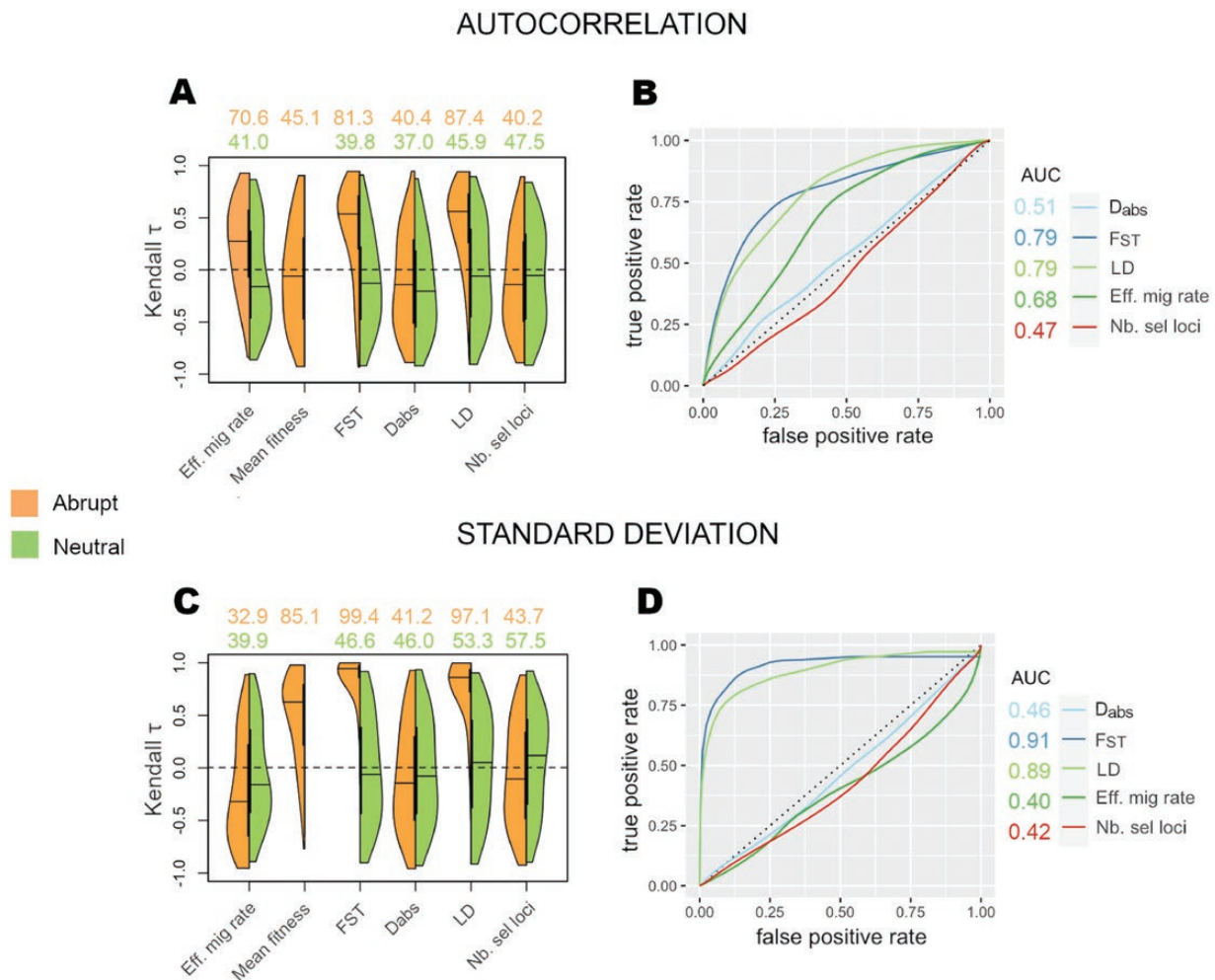


Figure 4. EWS of abrupt speciation. Summary results of Kendall τ correlations for different detrending and rolling window values (see Methods) for (A, B) autocorrelation and (C, D) standard deviation. (Left) Kendall τ distributions for abrupt and neutral data sets. Distributions skewed toward positive values indicate EWS. No Kendall τ trends are reported for the mean fitness of neutral data sets as all individuals in simulations with neutral parameters are characterized by a fitness of 1. (Right) ROC (receiver operating characteristic) curves used to calculate AUC values (area under curve) to compare abrupt and null distributions. AUC values close to 1 indicate that the trend (Kendall τ) measured in the abrupt data sets is substantially higher than the trend measured in the neutral data set. An AUC close to 0 indicates the opposite. An AUC value close to 0.5 indicates that the trends measured in the two distributions are similar. Black bars on violin plots (A, C) show the median of the distributions. Eff. mig rate = effective migration rate; Nb sel loci = number of variable selected loci.

Abrupt data sets showed robust EWS for F_{ST} and LD for autocorrelation (81.3% and 87.4% of positive Kendall τ , respectively, Figure 4A) and even more strongly for standard deviation (99.4% and 97.1% of positive Kendall τ , respectively, Figure 4C). We found an AUC of 0.79 for F_{ST} and of 0.79 for LD for autocorrelation, which indicates that the trends we estimated are far from the random expectations found in the control data sets (Figure 4B). Similarly, in the case of standard deviation, we observed even higher AUC values of 0.91 for F_{ST} and of 0.89 for LD (Figure 4D).

The rest of the metrics exhibited more variable trends, sometimes showing equally positive and negative trends. For example, the effective migration rate showed a robust increasing autocorrelation (70.6% positive Kendall τ , Figure 4A), but not standard deviation (32.9% positive Kendall τ , Figure 4C). The mean fitness of residents showed a robust increasing standard deviation (85.1% positive Kendall τ , Figure 4A), but not autocorrelation (45.1% positive Kendall τ , Figure 4C). For the mean fitness of residents, no AUC was calculated as the neutral data sets do not have a variable fitness by definition (fitness is set to 1 at all generations for all individuals). Table 1 provides a summary of the results.

Comparing EWS between abrupt and gradual speciation

We compared indicator trends between abrupt and gradual data sets to identify to what extent there were trends specific only to abrupt speciation events. Our results generally showed qualitatively similar trends between the two speciation types, but with differences in their robustness (Figure 5). Three indicators were particularly different between abrupt and gradual data sets and were also consistent with our expectations of higher Kendall τ for abrupt data sets: the autocorrelation of F_{ST} (AUC of 0.75), standard deviation of the effective migration rate (AUC of 0.81), and to a lesser extent the autocorrelation of the effective migration rate (AUC of 0.69) (Figure 5B and D). These results suggest that increasing trends in the autocorrelation of the F_{ST} and effective migration rate were indicative of an abrupt rather than a gradual speciation event, whereas a decreasing trend in the standard deviation of effective migration rate was indicative of gradual rather than abrupt speciation. We also observed some unexpected results: We found substantial differences between abrupt and gradual data sets in the standard deviation of D_{abs} (AUC of 0.24),

but this result was partly due to the decreasing trends found for abrupt data sets. In addition, interestingly, positive trends in the standard deviation of the mean fitness and F_{ST} were substantially higher for gradual rather than abrupt speciation (AUC of 0.21 and 0.23, respectively, Figure 5B and D).

For the rest of the metrics, we found modest differences between abrupt and gradual data sets. The number of selected variable loci notably showed no EWS for either data set type. In contrast, trends in the autocorrelation and standard deviation of LD provided clear EWS for both abrupt and gradual speciation, and thus were not specific to either speciation dynamic. Table 1 provides a summary of the results obtained when comparing abrupt to gradual data sets. We discuss the potential causes of these differences and similarities between speciation types in the Discussion section.

Discussion

Previous theoretical work (Flaxman et al. 2014; Nosil et al. 2017) on speciation dynamics through time has suggested that a positive feedback driven by linkage disequilibrium and divergent selection can generate a tipping point to abrupt speciation. Similar feedback effects of LD are also thought to affect coupling among loci across space in hybrid zones (Barton, 1983; Kruuk et al., 1999). Motivated by a characteristic hallmark of tipping points—namely the generic property of critical slowing down (CSD) (Scheffer et al., 2009)—we hypothesized that similar statistical signals of CSD would develop prior to abrupt speciation events. We thus searched for EWS preceding abrupt speciation events and particularly looked into potential differences between abrupt and gradual speciation. We here start by summarizing and discussing our results and then consider their implications for understanding speciation events.

As detailed in Introduction, our expectations are derived from past work (Flaxman et al., 2014; Nosil et al., 2017), which suggests that populations under divergent selection could exhibit alternative stable states. However, the model is analytically intractable, and other interpretations are possible. For example, it might be that there are no alternative states, but rather saddle points that would initially attract a trajectory starting with nondifferentiated populations before repelling it to the speciation equilibrium. Such saddle points are common in high-dimensional systems, and they could as well cause slowing down (Hastings et al., 2018). Moreover,

Table 1. Summary of the observed differences in early warning signals (EWS) between abrupt data sets versus neutral and gradual data sets. Summary of the AUC values computed when comparing abrupt data sets with neutral and gradual data sets. AUC values are a way of quantifying the overlap between two distributions, here Kendall τ characterizing abrupt data sets versus Kendall τ characterizing neutral or gradual data sets. An AUC ranges between 0 and 1, with a value of 0.5 indicating that the abrupt and gradual/neutral distributions are the same. An AUC close to 1 indicates that the abrupt distribution has higher values compared with the gradual or neutral one. An AUC approaching zero indicates the contrary. When looking for signs of CSD, we expected to obtain higher Kendall τ values on abrupt data sets compared with neutral and gradual data sets, and hence expected AUC values above 0.5 when performing both comparisons.

| | Autocorrelation | | Standard deviation | |
|-------------------------------|--------------------|--------------------|--------------------|--------------------|
| | Abrupt vs. neutral | Abrupt vs. gradual | Abrupt vs. neutral | Abrupt vs. gradual |
| Eff. migration rate | 0.68 | 0.69 | 0.40 | 0.81 |
| Mean fitness | / | 0.38 | / | 0.21 |
| F_{ST} | 0.79 | 0.75 | 0.91 | 0.23 |
| D_{abs} | 0.51 | 0.59 | 0.46 | 0.24 |
| LD | 0.79 | 0.45 | 0.89 | 0.45 |
| Nb. of selected variable loci | 0.47 | 0.49 | 0.42 | 0.44 |

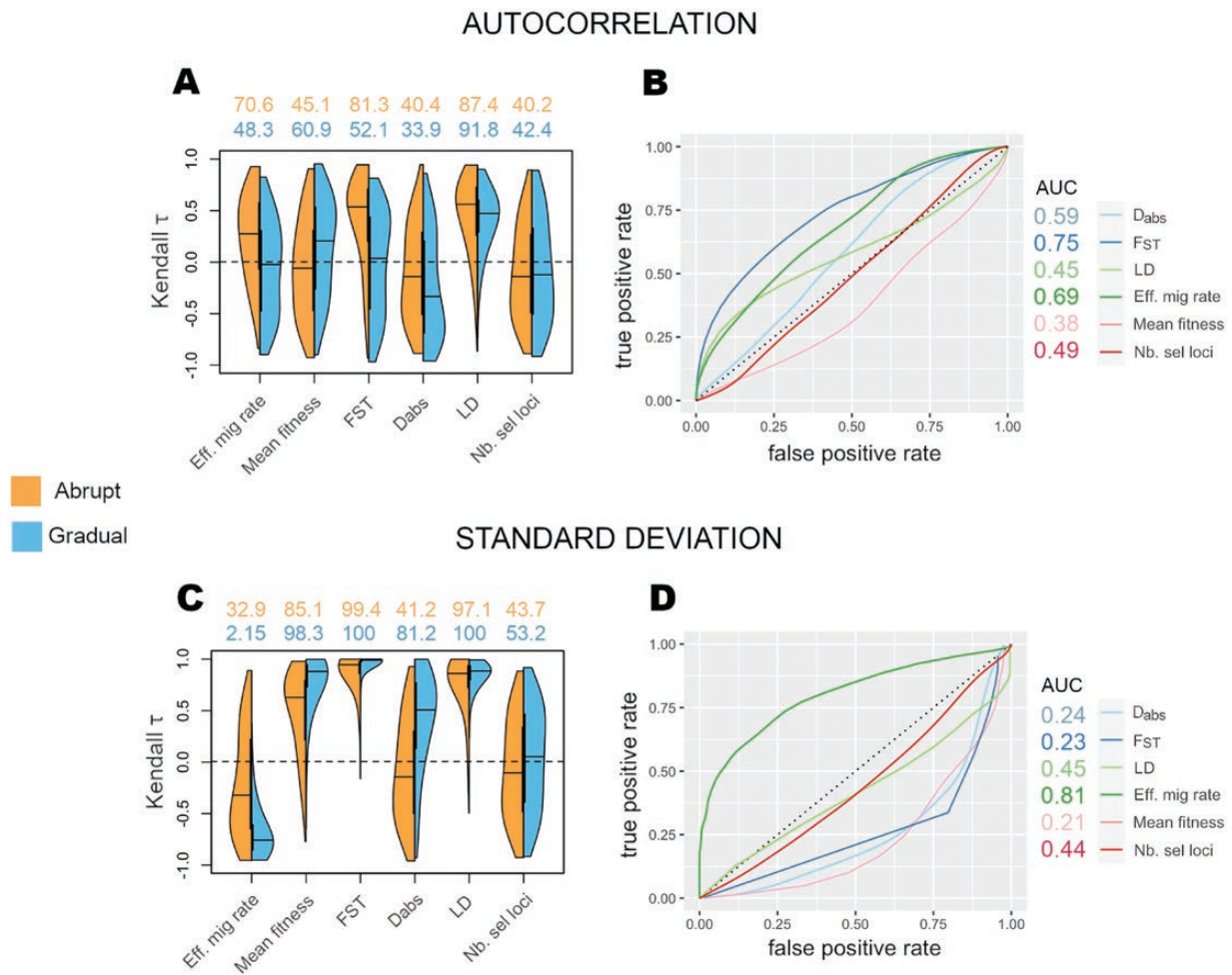


Figure 5. Comparing EWS between abrupt and gradual speciation. Summary results of Kendall τ correlations for different detrending and rolling window values (see Methods) for (A, B) autocorrelation and (C, D) standard deviation. (Left) Kendall τ distributions for abrupt and gradual data sets. Distributions skewed towards positive values indicate EWS. (Right) ROC (receiver operating characteristic) curves used to calculate AUC values (area under curve) to compare abrupt and gradual distributions. AUC values close to 1 indicate that the trend (Kendall τ) measured in the abrupt data sets is substantially higher than the trend measured in the gradual data set. An AUC close to 0 indicates the opposite. An AUC value close to 0.5 indicates that the trends measured in the two distributions are similar. Black bars on violin plots (A, C) show the median of the distributions. Eff. mig rate = effective migration rate, Nb sel loci = number of variable selected loci.

signals of increased autocorrelation and variability predicted for CSD could arise for reasons other than a loss of resilience near a tipping point. For example, because adaptive mutations are continuously added to the system, increased opportunities for *LD* among divergently selected loci as the system moves toward speciation could increase the stochastic variance in *LD* and thus in the selection experienced by the loci. Thus, increased autocorrelation and variability could be early-warning signals of speciation even if they do not indicate CSD per se. Even if the patterns we assess are not indicative of CSD, evidence of EWS would provide an important step forward with future work required to characterize the mechanistic basis of this heuristic signal.

EWS exist but vary among differentiation metrics

Although we detected clear evidence for EWS, our collective findings highlight heterogeneous results between the analyzed metrics (Table 1). We did find two indicators that are strong candidates for signals specific to abrupt speciation, namely a rising autocorrelation of F_{ST} and rising standard deviation of the effective migration rate (Table 1, Figure 5A). We propose

that given current understanding these are the most reliable and promising EWS of abrupt speciation. In fact, when testing (for a particular set of conditions) how early we could identify significant changes in AR1 or SD, we could find a clear early-warning only for *LD* and F_{ST} but not in any of the other metrics (Supplementary Figure S11). In particular, changes in SD become significant at earliest between 330 and 4,470 generations before speciation, making SD of *LD* perhaps the strongest early-warning candidate among all indicators we analyzed. Although the reasons for why these particular metrics are the most reliable require further study, their inherent link to reproductive isolation may be part of the explanation, since effective migration, as calculated here, is essentially a measure of reproductive isolation due to selection against first-generation migrants (Nosil et al., 2005).

Yet, other EWS differences between abrupt and gradual data sets contradicted our expectation of being stronger in abrupt data sets: standard deviation of mean fitness of residents, F_{ST} , and D_{abs} showed a stronger rising trend in gradual data sets than in abrupt ones. Nonetheless, these three indicators still show substantially different results when compared

with null expectations (Figure 4B, Table 1), which implies that they could serve as early warnings of speciation in general, irrespective of whether the speciation events are gradual or abrupt. In fact, EWS are not specific to tipping points associated only with abrupt transitions, but are more generic and can be identified also prior to gradual transitions that are related to noncatastrophic bifurcation points (Kéfi et al. 2013; Boettiger et al. 2013).

We also observed EWS that were common to both abrupt and gradual data sets, even though speciation in the gradual data sets is not inherently driven by a positive feedback. Moreover, LD , the key driver of the positive feedback, showed equally strong warning signals in both abrupt and gradual data sets: We reported rising autocorrelation and standard deviation approaching speciation for both data set types with similar strengths. This common trend for LD in both abrupt and gradual data sets may not be totally surprising as it reflects the generic behavior of LD as speciation approaches, regardless of the type of speciation (i.e., abrupt or gradual).

The most unexpected results were the decreasing trends in the standard deviation and autocorrelation of D_{abs} in abrupt data sets. At the same time, we reported increasing trends for F_{ST} (Figure 4). In this latter regard, Noor and Bennett (2009) noted that when F_{ST} and D_{XY} (here, D_{abs}) “give the same answer, one can have some confidence in the interpretation, but when they give different answers, then a bias is likely affecting one measure (either by overly deflating F_{ST} or by giving a high D_{XY} that does not reflect divergence occurring since the species split). The difficulty in the latter situation is interpreting which measure is biased or misinterpreted.” In the case of our simulations, the answer is likely an inflation of D_{abs} in earlier generations of the abrupt model due to variation (shared polymorphism) between populations. At earlier times during abrupt speciation, selected loci that establish, due to their having a minor effect on overall fitness, will be present at frequencies near 0.5 in both populations. In the formula for D_{abs} , this translates in values close to 0.5 for these loci. This will inflate the overall value of D_{abs} at an early state of differentiation when few loci are yet to differentiate. In contrast, F_{ST} will be near 0. Thus, D_{abs} is likely not as sensitive a metric for EWS as F_{ST} .

As for the effective migration rate, the standard deviation from the general trend reduced as populations approached speciation. A potential reason for the decreasing trend for the standard deviation may have to do with the way the parameter was measured in the simulations. Here, we estimated the effective migration as the proportion of immigrants from the most recent migration step that produced offspring (following Vuilleumier et al. 2010). This measure is a useful one to assess immediate reproductive isolation caused by selection against first-generation migrants. However, it does not take into account the effects of recombination in subsequent generations of hybrids that can have profound consequences for the introgression of genes beyond selection acting against immigrant parents. As a result, our means for calculating effective migration disconnected this metric to some extent from LD among selected loci, the latter we found to be a common currency for EWS in all our speciation models. Thus, the standard deviation of m_e from the general trend did not reflect the behavior of the LD , which was found to be rising.

The above consideration set aside, Figure 3 seemingly provides a general guide for the usefulness of different metrics as indicators of EWS during speciation: metrics whose values

are flat and close to baseline 0 up to the time of speciation (LD , the mean fitness of residents, and F_{ST}) were more informative in our analysis for EWS than metrics whose raw values were rising before speciation (D_{abs} and the number of selected variable loci). In terms of other potential properties that could provide EWS (i.e., skewness and kurtosis), the lack of clear trends in both data sets indicates that these metrics of variation do not appear highly informative for our system and are in line with equally mixed or inconclusive results from other studies of dynamics other than speciation (Guttal & Jayaprakash, 2008) (Supplementary Figures S3 and S4).

Although our findings identified F_{ST} , LD , D_{abs} , and effective migration rate as relevant signals for anticipating speciation events in some instances (Table 1), their heterogeneous behavior and discrepancies between abrupt and gradual data sets introduce nuance into their interpretation and use as EWS. Work on EWS in multivariate systems such as multispecies communities has shown that not all components of a system carry comparable signals of CSD (Dakos, 2018), and in some cases, they might not show such slowing down at all (Boerlijst et al., 2013). In our case, we estimated indicators based on metrics which are often derived from state variables that are dynamically changing during the simulations. For example, F_{ST} and mean fitness are calculated from time series of F_{ST} values for individual loci and a sample of fitness values from 200 randomly chosen individuals from a population, respectively. It is possible that analyses of the state variables and individual loci might yield a more refined understanding of EWS.

In fact, combining the EWS we calculated with the trends in the actual metrics could provide a better indication of abrupt speciation versus gradual speciation. For example, it is clear to see that in the case of gradual speciation almost all metrics show a linear change (Figure 3). Combining changes in the mean of the differentiation metrics with variance and autocorrelation could be straightforward to develop as it has been implemented in analogous work on monitoring the emergence of infectious disease (Brett et al., 2017) or population collapses (Clements & Ozgul, 2016).

Finally, our results are likely influenced by the fact that the $BU2S$ model is based on stochastic processes that introduce noise in the results. This is desirable when modeling evolution as it allows the realistic joint consideration of selection, random drift, and mutation. However, EWS and CSD indicators have mostly been developed for deterministic systems with stochastically perturbed equilibria. If noise is too strong, it can mask warning signals (Dakos et al., 2012). For example, in a stochastic model on the evolution of cooperation disrupted by tipping points to collapse, rising variance and autocorrelation were most significant only for a specific range of conditions (Cavaliere et al., 2014). Indeed, other studies have also reported mixed signals among different EWS depending on what variable EWS are estimated for (Boerlijst et al. 2013; Gsell et al. 2017). In summary, we detected promising potential EWS, while the observed heterogeneity described above forms a clear avenue for further investigation.

Future work and implications for understanding speciation

We here consider more explicitly potential future work on EWS in evolution, both theoretical and empirical. In terms of future theory, although our model of speciation is quite general, there are many others (Bolnick & Fitzpatrick, 2007; Coyne & Orr, 2004; Dieckmann & Doebeli, 2004; Gavrillets,

2004; Kirkpatrick & Ravigné, 2002; Orr, 1995), to which analyses similar to ours could be applied. Further research could also include an analysis of spatial clustering of variable loci along chromosomes. Indeed, nonrandom positioning of variable alleles is suspected to be an important marker of differentiation and to carry potential information on the stage of speciation (Nosil and Feder 2013; Wolf and Ellegren 2017), although other processes could also be involved (Cuickshank & Hahn, 2014). Linkage disequilibrium is more likely to appear between physically close loci, which are less prone to be separated by recombination than physically distant or unlinked loci. This process can sometimes create genomic “islands” of differentiation, which are suspected to play a role in shaping the speciation process in some scenarios (Feder et al., 2012). The *BU2S* model allows for spatial clustering of loci to build up in the genome as speciation approaches, and indeed some preliminary work implies that such islands can sometimes but not always contribute to speciation (Flaxman et al., 2014). Explicit future examination of the relationship between genomic islands and EWS is thus warranted. We note, however, that rapid transitions in speciation state may involve sudden increases of *LD* among loci across or spanning the genome (Flaxman et al., 2014), not just for spatially

linked loci, the details of which we can also investigate in the *BU2S* model.

Theory aside, how might one empirically test the ideas and results presented here? This relates to the bigger question of whether and how EWS can be used in practice. We acknowledge that this will be a challenge, but we do see two main realistic possibilities. First, microbes with short generation times could be suitable candidates to empirically test the results presented here using experimental evolution. Ideally, this would require microbes such as yeast that can undergo recombination during reproduction, a condition for variation in *LD* to appear. Second, one could focus on spatial EWS rather than temporal ones (Eby et al., 2017), by comparing statistical indicators not through time, but in a variety of environmental conditions (i.e., a “space-for-time substitution”). The increasing availability of genetic data from spatially distributed populations could facilitate comparisons based on such a space-for-time approach. Under such a context, diverging populations might be identified that are on the verge of an abrupt (or gradual) speciation event. Our most general finding that EWS of speciation do exist urges further such theoretical and empirical work.

Glossary

| Term | Definition |
|--------------------------------------|--|
| Tipping point | The point where accelerated change caused by a positive feedback generates a shift from the current system state towards a qualitatively different state. |
| Critical slowing down (CSD) | Increase in recovery time back to equilibrium after a perturbation. CSD translates in a rise of statistical indicators like autocorrelation or variance. |
| Speciation | Emergence of new species, here studied as the evolution of genetic differentiation between populations and reductions in gene flow (i.e., effective migration) between them. |
| Abrupt speciation | Nonlinear evolution of differentiation between populations of the same species. |
| Gradual speciation | Linear differentiation between populations of the same species. |
| Fitness | Measures the ability of an individual to survive and find a mate. The fitness depends on the sets of genes carried by the individual, positively selected genes yield higher fitness. |
| Variable loci | Genetic positions for which more than one allele exists. In the <i>BU2S</i> model, this implies that a mutation has occurred at a locus since the onset of the simulations, creating a second allele. |
| Selected/neutral loci | Selected loci contribute to the fitness by enhancing or diminishing it. Neutral loci do not contribute to the fitness. |
| Effective migration rate | Proportion of reproduction in a population attributable to migrants. |
| Linkage disequilibrium (<i>LD</i>) | Nonrandom association between loci. Practically, there is <i>LD</i> between two loci when alleles at the two loci occur together simultaneously in individuals more than expected by chance (i.e., more than expected based on allele frequencies at individual loci). |
| Fixation index, F_{ST} | Relative measure of genetic differentiation between two populations. F_{ST} values are thus dependent on the within-population variation. |
| D_{XY} | Absolute measure of genetic divergence. D_{XY} values do not depend on within-population variation. |

Supplementary material

Supplementary material is available online at *Evolution* (<https://academic.oup.com/evolut/qp054>).

Data availability

The code used in analysis and figure generation is available at: https://github.com/MaidieSinitam/ews_speciation. The raw simulation results are also publicly archived on Dryad (doi:10.5061/dryad.5qfttdz7d).

Author contributions

All authors conceived the project. S.F. generated the simulation data that V.D. and M.S. analyzed. M.S., P.N., and V.D. wrote the manuscript, with inputs from all coauthors.

Funding

This project received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement no. 770826 EE-Dynamics).

Conflict of interest: The authors declare no conflict of interest.

Acknowledgments

The authors thank Michael Kopp for the contribution to the review process of the manuscript.

References

- Alley, R. B., Marotzke, J., Nordhaus, W. D., Overpeck, J. T., Peteet, D. M., Pielke, R. A., Pierrehumbert, R. T., Rhines, P. B., Stocker, T. F., Talley, L. D., & Wallace, J. M. (2003). Abrupt climate change. *Science*, 299, 2005–2010.
- Angeli, D., Ferrell, J., & Sontag, E. (2004). Detection of multistability, bifurcations, and hysteresis in a large class of biological positive-feedback systems. *Proceedings of the National Academy of Sciences of the United States of America*, 101(7), 1822–1827.
- Barton, N. (1983). Multilocus clines. *Evolution*, 37(3), 454–471.
- Biggs, R., Carpenter, S., & Brock, W. (2009). Turning back from the brink: Detecting an impending regime shift in time to avert it. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 826–831.
- Boettiger, C., & Hastings, A. (2012). Quantifying limits to detection of early warning for critical transitions. *J R Soc Interface*, 9(75), 2527–539.
- Boerlijst, M., Oudman, T., & de Roos, A. (2013). Catastrophic collapse can occur without early warning: Examples of silent catastrophes in structured ecological models. *PLoS One*, 8(4), e62033.
- Boettiger, C., Ross, N., & Hastings, A. (2013). Early warning signals: The charted and uncharted territories. *Theoretical Ecology*, 3, 255–264.
- Bolnick, D., & Fitzpatrick, B. (2007). Sympatric speciation: Models and empirical evidence. *Annual Review of Ecology, Evolution, and Systematics*, 38, 459–487.
- Brett, T. S., Drake, J. M., & Rohani, P. (2017). Anticipating the emergence of infectious diseases. *Journal of the Royal Society Interface*, 14, 20170115. <https://doi.org/10.1098/rsif.2017.0115>
- Carpenter, S. R., & Brock, W. A. (2006). Rising variance: A leading indicator of ecological transition. *Ecology Letters*, 9(3), 311–318. <https://doi.org/10.1111/j.1461-0248.2005.00877.x>
- Cavaliere, M., Yang, G., Danos, V., & Dakos, V. (2014). Detecting the collapse of cooperation in evolving networks. *Scientific Reports*, 6, 30845.
- Charlesworth, B., & Jensen, J. (2022). Some complexities in interpreting apparent effects of hitchhiking: A commentary on Gompert *et al.* (2022). *Molecular Ecology*, 31(17), 4440–4443.
- Clements, C., & Ozgul, A. (2016). Including trait-based early warning signals helps predict population collapse. *Nature Communications*, 7, 10984.
- Coyne, J., & Orr, H. (2004). *Speciation*. Sinauer Associates.
- Cuickshank, T., & Hahn, M. (2014). Reanalysis suggests that genomic islands of speciation are due to reduced diversity, not reduced gene flow. *Molecular Ecology*, 23(13), 3133–3157.
- Dakos, V. (2018). Identifying best-indicator species for abrupt transitions in multispecies communities. *Ecological Indicators*, 94(1), 494–502. <https://doi.org/10.1016/j.ecolind.2017.10.024>
- Dakos, V., Carpenter, S., Brock, W., Ellison, A., Guttal, V., Ives, A. R., Kéfi, S., Livina, V., Seekell, D. A., van Nes, E. H., & Scheffer, M. (2012). Methods for detecting early warnings of critical transitions in time series illustrated using simulated ecological data. *PLoS One*, 7(7), e41010.
- Dakos, V., Van Nes, E., & Scheffer, M. (2013). Flickering as an early warning signal. *Theoretical Ecology*, 6, 309–317.
- Dent, L., Cumming, G., & Carpenter, S. (2003). Speciation as a positive feedback loop between postzygotic and prezygotic barriers to gene flow. *Proceedings of the Royal Society B: Biological Sciences*, 270(1523), 1473–1479.
- Dieckmann, U., & Doebeli, M. (2004). Adaptive dynamics of speciation: Sexual populations. In: Dieckmann U, Doebeli M, Metz JAJ, Tautz, D (eds.). *Adaptive speciation*. Cambridge University Press (pp. 76–111).
- Eby, S., Agrawal, A., Majumder, S., Dobson, A., & Guttal, V. (2017). Alternative stable states and spatial indicators of critical slowing down along a spatial gradient in a savanna ecosystem. *Global Ecology and Biogeography*, 26(6), 638–649.
- Endler, J. (1977). *Geographic variation, speciation and clines*. Princeton University Press.
- Feder, J., Egan, S., & Nosil, P. (2012). The genomics of speciation-with-gene-flow. *Trends in Genetics*, 28(7), 342–350.
- Flaxman, S., Feder, J., & Nosil, P. (2013). Genetic hitchhiking and the dynamic buildup of genomic divergence during speciation with gene flow. *Evolution*, 67(9), 2577–2591.
- Flaxman, S., Wacholder, A., Feder, J., & Nosil, P. (2014). Theoretical models of the influence of genomic architecture on the dynamics of speciation. *Molecular Ecology*, 23, 4074–4088.
- Freeman, S., & Herron, J. (2004). *Evolutionary analysis*. Pearson Prentice Hall.
- Gavrilets, S. (2004). *Fitness landscapes and the origin of species*. Princeton University Press.
- Gompert, Z., Egan, S., Barrett, R., Feder, J., & Nosil, P. (2017). Multilocus approaches for the measurement of selection on correlated genetic loci. *Molecular Ecology*, 26(1), 365–382.
- Gompert, Z., Feder, J. L., & Nosil, P. (2022). Natural selection drives genome-wide evolution via chance genetic associations. *Molecular Ecology*, 31(2), 467–481. <https://doi.org/10.1111/mec.16247>
- Gsell, A., Scharfenberger, U., Özkundakci, D., Walters, A., Hansson, L. A., Janssen, A. B., Nöges, P., Reid, P. C., Schindler, D. E., Van Donk, E., Dakos, V., & Adrian, R. (2017). Valuating early-warning indicators of critical transitions in natural aquatic ecosystems. *Proceedings of the National Academy of Sciences*, 113(50), E8089–E8095.
- Guttal, V., & Jayaprakash, C. (2008). Changing skewness: An early warning signal of regime shifts in ecosystems. *Ecology Letters*, 11(5), 450–460. <https://doi.org/10.1111/j.1461-0248.2008.01160.x>
- Hastings, A., Abbott, K., Cuddington, K., Francis, T., Gellner, G., Lai, Y., Morozov, A., Petrovskii, S., Scranton, K., & Zeeman, M. (2018). Transient phenomena in ecology. *Science*, 361(6406), eaat6412.
- Held, H., & Kleinen, T. (2004). Detection of climate system bifurcations by degenerate fingerprinting. *Geophysical Research Letters*, 31, L23207.

- Hendry, A., Day, T., & Taylor, E. (2001). Population mixing and the adaptive divergence of quantitative traits in discrete populations: A theoretical framework for empirical tests. *Evolution*, 55(3), 459–466.
- Hill, W., & Robertson, A. (1968). Linkage disequilibrium in finite populations. *Theoretical and Applied Genetics*, 38(6), 226–231.
- Hughes, T. (1994). Catastrophes, phase shifts, and large-scale degradation of a Caribbean coral reef. *Science*, 265(5178), 1547–1551.
- Kéfi, S., Dakos, V., Scheffer, M., Van Nes, E., & Rietkerk, M. (2013). Early warning signals also precede non-catastrophic transitions. *Oikos*, 122(5), 641–648.
- Kimura, M. (1971). Theoretical foundation of population genetics at the molecular level. *Theoretical Population Biology*, 2(2), 174–208. [https://doi.org/10.1016/0040-5809\(71\)90014-1](https://doi.org/10.1016/0040-5809(71)90014-1)
- Kirkpatrick, M., & Ravigné, V. (2002). Speciation by natural and sexual selection: Models and experiments. *American Naturalist*, 159(Suppl 3), S22–S35.
- Kruuk, L. E., Baird, S. J., Gale, K., & Barton, N. (1999). A comparison of multilocus clines maintained by environmental adaptation or by selection against hybrids. *Genetics*, 153(4), 1959–1971.
- Lande, R., & Arnold, S. (1983). The measurement of selection on correlated characters. *Evolution*, 37(6), 1210–1226.
- Lenton, T. (2013). Environmental tipping points. *Annual Review of Environment and Resources*, 38, 1–29.
- May, R., Levin, S., & Sugihara, G. (2008). Ecology for bankers. *Nature*, 451, 893–894.
- Mayr, E. (1942). *Systematics and the origin of species, from the viewpoint of a zoologist*. Columbia University Press.
- Nei, M., & Li, W. (1979). Mathematical model for studying genetic variation in terms of restriction endonucleases. *Proceedings of the National Academy of Sciences*, 76(10), 5269–5273.
- Noor, M., & Bennett, S. (2009). Islands of speciation or mirages in the desert? examining the role of restricted recombination in maintaining species. *Heredity*, 103, 439–444.
- Nosil, P., & Feder, J. (2013). Genome evolution and speciation: Toward quantitative descriptions of pattern and processes. *Evolution*, 67(9), 2461–2467.
- Nosil, P., Feder, J., Flaxman, S., & Gompert, Z. (2017). Tipping points in the dynamics of speciation. *Nature Ecology and Evolution*, 1, 1.
- Nosil, P., Flaxman, S., Feder, J., & Gompert, Z. (2020). Increasing our ability to predict contemporary evolution. *Nature Communications*, 11, 5592.
- Nosil, P., Vines, T., & Funk, D. (2005). Perspective: Reproductive isolation caused by natural selection against immigrants from divergent habitats. *Evolution*, 59, 705–719.
- Orr, H. (1995). The population genetics of speciation: The evolution of hybrid incompatibilities. *Genetics*, 139(4), 1805–1813.
- Price, T. (2007). *Speciation in birds*. Roberts and Company, Greenwood Village.
- Scheffer, M., Bascompte, J., Brock, W., Brovkin, V., Carpenter, S., Dakos, V., Held, H., van Nes, E. H., Rietkerk, M., & Sugihara, G. (2009). Early-warning signals for critical transitions. *Nature*, 461, 53–59.
- Scheffer, M., Carpenter, S. R., Lenton, T. M., Bascompte, J., Brock, W., Dakos, V., van de Koppel, J., van de Leemput, I. A., Levin, S. A., van Nes, E. H., Pascual, M., & Vandermeer, J. (2001). Catastrophic shifts in ecosystems. *Nature*, 413, 591–596.
- Scheffer, M., Carpenter, S., Lenton, T., Bascompte, J., Brock, W., Dakos, V., et al. (2012). Anticipating critical transitions. *Science*, 338(6105), 344–348.
- Scheffer, M., Hosper, S. H., Meijer, M. -L., Moss, B., & Jeppesen, E. (1993). Alternative equilibria in shallow lakes. *Trends in Ecology and Evolution*, 8, 275–279.
- Smith, J., & Haigh, J. (1974). The hitch-hiking effect of a favourable gene. *Genetics Research*, 23(1), 23–35.
- van Nes, E., & Scheffer, M. (2007). Slow recovery from perturbations as a generic indicator of a nearby catastrophic shift. *American Naturalist*, 169(6), 738–747. <https://doi.org/10.1086/516845>
- van Nes, E. H., Arani, B. M. S., Staal, A., van der Bolt, B., Flores, B. M., Bathiany, S., & Scheffer, M. (2016). What do you mean, ‘tipping point’? *Trends in Ecology and Evolution*, 31(12), 902–904. <https://doi.org/10.1016/j.tree.2016.09.011>
- Venegas, J. G., Winkler, T., Musch, G., Vidal Melo, M. F., Layfield, D., Tgavalekos, N., Fischman, A. J., Callahan, R. J., Bellani, G., & Harris, R. S. (2005). Self-organized patchiness in asthma as a prelude to catastrophic shifts. *Nature*, 434, 777–782.
- Vuilleumier, S., Goudet, J., & Perrin, N. (2010). Evolution in heterogeneous populations: From migration models to fixation probabilities. *Theoretical Population Biology*, 78(4), 250–258.
- Wolf, J., & Ellegren, H. (2017). Making sense of genomic islands of differentiation in light of speciation. *Nature Reviews Genetics*, 18(2), 87–100.
- Wright, S. (1950). Genetical structure of populations. *Nature*, 116, 247–249.