CHALMERS

A model for the evolution of local adaptation of a subdivided population

Master's Thesis in Complex Adaptive Systems

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Abstract

The ecotypes of *Littorina saxatalis* are believed to be intermediate steps in an ongoing speciation process. *L. saxatalis* is therefore of scientific interest as a model organism for speciation by local adaptation. In order to understand the genetic patterns that arise from the local adaptation, temporal and spatial adaptation dynamics in a model with two partly isolated sub-populations are analysed. The model is implemented by means of individual-based stochastic simulations and deterministic approximations. We obtain qualitative understanding of the mechanisms underlying local adaptation by investigating how a mutant allele (beneficial in one sub-population) is accepted in a system already containing two alleles (each adapted to opposite sub-populations) with frequencies in steady state. The sizes of the original alleles describe the level of local adaptation before the mutation event. We find the parameter regions where the mutant allele replaces one original allele and investigate the dynamics further within this region. We investigate the replacement probability of the mutant allele. We show that the replacement probability increases with increasing mutation effect size, decreases with increasing degree of local adaptation and decreases with increasing value of the migration rate. We investigate the improvement in average phenotype that results from a replacement of one of the original alleles by the mutant allele, and we investigate the amount of deleterious alleles within each sub-population (the gene flow). We find that the gene flow between the sub populations decrease with increased level of adaptation. By allowing for recombination between two loci, we derive results that implies that a concentrated genetic architecture is preferred by the system in certain parameter regions.

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1 Introduction

Understanding evolution is critical for understanding genetic variation within and between species. Evolution refers to the changes of genotype frequencies over time. The requirements for such changes are genetic variation and the existence of a driving force.

sources of genetic variation:
mutations
recombination
immigrants

Genetic variation is created by mutations, recombination and migration. Mutations are occasional mistakes during the creation of sperm and eggs that give rise to new genes and hence new genotypes. Recombination does not give rise to new genes, but it regulates which genes are inherited together and thus creates new genotypes. Sometimes, migration is also accounted for as a source of genetic variation. For an almost isolated population, immigrants bring in new genotypes.

evolutionary driving forces:
selection
genetic drift

Whether the genetic variants established by mutations, recombination and migration are maintained in the population or not depends on the driving forces of evolution, namely selection and random genetic drift. Selection means that fitter genotypes have a higher survival probability compared to less fit genotypes. The effect of selection was first described by Charles Darwin (1859). The other driving force is random genetic drift which is a stochastic effect that arises due to finite population size. As a consequence of the driving forces acting on the genetic variation new species arise.

speciation is a result of evolution

ongoing speciation
Littorina saxatalis

Speciation is the evolutionary process by which new species are formed. It may occur provided that sub-populations are isolated for long enough and especially if the inhabitants are selected for different phenotypes (Johannesson, 2007). In the field it is desirable to study speciation when it is ongoing.

observed ecotypes: intermediate step

The sea-snail *Littorina saxatalis* is believed to be undergoing a speciation process. Today it forms ecotypes as a consequence of local adaptation to specific shore microhabitats and these are believed to be intermediate steps to a full speciation (Johannesson et al., 2010). *L. saxatalis* can therefore be viewed as a model organism for speciation and this is one of the reasons for the scientific interest in studying it.

the crab and wave ecotypes

In Sweden, Spain and in the UK contrasting *L. saxatalis* ecotypes are present in either crab-rich or wave-swept habitats, see Figure 1. The ecotypes in the crab-rich habitats face strong predation from crabs. They are therefore relatively larger and thick-shelled because the smaller individuals are more likely to be eaten. The ecotypes on the cliffs exposed to heavy waves are instead smaller and have a large foot hole to prevent them from being flushed away by waves (Johannesson et al., 2010).

The speciation process can be intuitively understood by considering

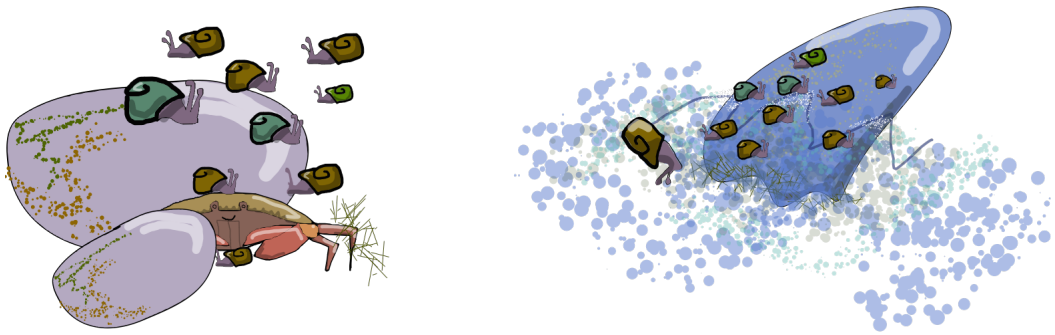


Figure 1: The ecotype-forming snail *Littorina saxatalis* is a model organism for ongoing speciation. The snails live in different habitats where they are either under predation of crabs and therefore selected to be large and thick shelled, or on wave exposed cliffs where they are selected to be small and have a large foot-hole (Johannesson et al., 2010).

the different habitats as two isolated sub-populations where the inhabitants are selected for opposite phenotypes, such as large and small shell size. However, the sub-populations are not isolated in real life. In the field it is observed that the snails migrate between the habitats (in reality there are also intermediate habitats, so called "hybrid zones"), and that some immigrants mate and produce viable offspring. When immigrants mate and produce viable offspring, there is gene flow between the sub-populations.

the mixing effect of gene flow prevents speciation

Gene flow between the habitats creates a so called mixing effect that may prevent speciation. Yet it is believed, as previously mentioned, that the ecotypes of *L. saxatalis* are currently undergoing speciation. The selective pressure described earlier however disfavours hybrids and hence creates a barrier to gene flow for the loci that are under selection. There are also reasons to believe that additional barriers to gene flow may further develop (Johannesson et al., 2010). An additional barrier to gene-flow could be genetically encoded such as a mating or habitat preference. But, before inserting such a feature in a model it is necessary to understand the genetic patterns that arise from the ecotype formation with selection-migration balance alone. This is the objective of this study.

developing barriers to gene flow

The objective of this study is to qualitatively understand how the joint effect of selection-migration balance, recombination and mutations affect the expected genetic patterns arising from local adaptation by means of stochastic individual-based modelling and mathematical anal-

objective: *qualitative understanding of genetic patterns arising from local adaptation*

ysis. The hope is that the insights may be used to interpret empiric sequence data from experiments with *L. saxatalis* such as for example RAD-sequencing and genomic F_{st}-patterns comparing the different ecotypes, see glossary for explanation.

Similar questions have been targeted by model studies and computer simulations carried out by for example Yeaman and Whitlock (2011) and Yeaman and Otto (2011). In these models each individual is assigned a genotype, and the genotype is composed of loci (positions on chromosomes) comprised by different alleles that are characterized by their different allelic effect sizes (numbers at the positions). The phenotype is a function of the genotype and the fitness is a function of the phenotype of an individual and of an optimal phenotype specific for the environment the individual is in.

Yeaman and Otto (2011)

Yeaman and Otto (2011) investigated a model that explored the dynamics of one locus and two alleles, see Figure 2. They found that mutant adaptive alleles of larger allelic effect size had a higher probability to remain in the system than alleles of smaller effect size. In addition, mutant alleles had a much higher probability to remain in the system when selection was stronger. In all cases the probability for mutant alleles to remain in the system decreased with increased migration rate, because the rare allele spent an increasing amount of time in the patch where it was disfavoured. Assuming symmetrical migration between the demes and infinite population size Yeaman and Otto (2011) found that the steady state with coexistence of two allelic types was stable for all migration rates.

For a local adaptation to be successful the conditions described by Yeaman and Otto (2011) must be met since polymorphism needs to be maintained in the system. The polymorphic system with two different alleles favoured in two different habitats can be thought of as a partly locally adapted system. In this study we investigate how the local adaptation proceeds by investigating the conditions under which an additional mutant allele is accepted into a system with an already established stable dimorphic state. The method and results are explained in this report.

Yeaman and Whitlock (2011)

Yeaman and Whitlock (2011) extended the single locus model of Yeaman and Otto (2011) to a multi locus model in order to make qualitative predictions about the evolution of genetic architecture. The genetic architecture is the relationship of allelic sizes between many loci and can thus not be studied in a one locus model. Yeaman and Whitlock (2011) predict that multi-locus traits evolving with migration are more tightly

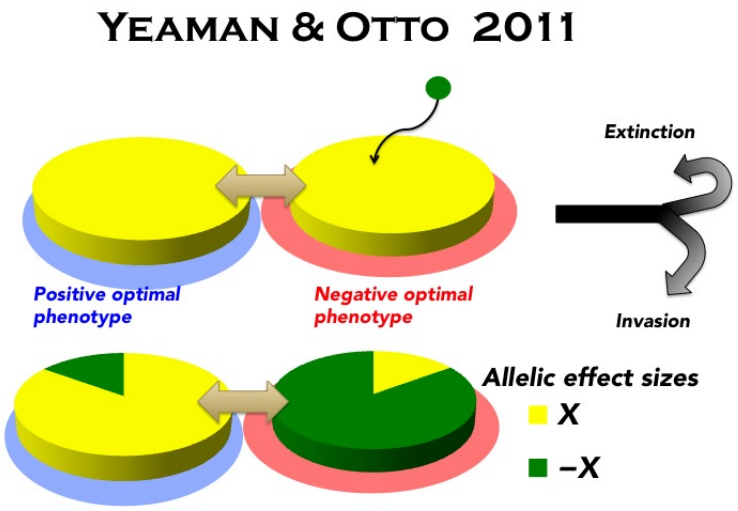


Figure 2: A one locus, two-alleles model as used by Yeaman and Otto (2011). The two sub-populations are connected through migration and are initially inhabitated with only one allelic type (X in the figure). Yeaman and Otto investigated the conditions under which polymorphism (coexistence of X and -X) is likely to be maintained.

linked than if there were no migration. The results were observed in experiments performed by means of individual-based simulations.

We have derived results that agree with those by Yeaman and Whitlock (2011) but with a method and a simplified model that allows us to understand the mechanisms of the bias towards large alleles in more detail.

report structure

The remainder of this report is structured as follows. Section 2 contains a presentation of the model (Subsection 2.1) and delimitations of the model (Subsection 2.2). Section 3 gives information about the numerical simulations of the model (Subsection 3.1), and an explanation of an approximation of the model (Subsection 3.2). The results are presented and discussed in Section 4. Conclusions and future outlooks are given in Section 5.

2 A Model for local adaptation

2.1 Description

Our model describes the dynamics of two-locus diploid genotypes in two sub-populations connected by migration. Each sub-population is assumed to be well mixed and there is no distinction between males and females. The generations are assumed to be discrete and non overlapping.

reproduction
selection

The individuals reproduce by random mating locally within the sub-populations. Due to viability selection, only a fraction of juveniles survive to maturity. In our model, the number of juveniles surviving to maturity is assumed to be constant in time, and we denote it by N.

migration

We denote the migration rate per generation per individual per sub-population by m. We assume that only adult virgin individuals migrate, which means migration occurs after viability selection but before mating. The life cycle of individuals in our model is schematically illustrated in Fig. 4.

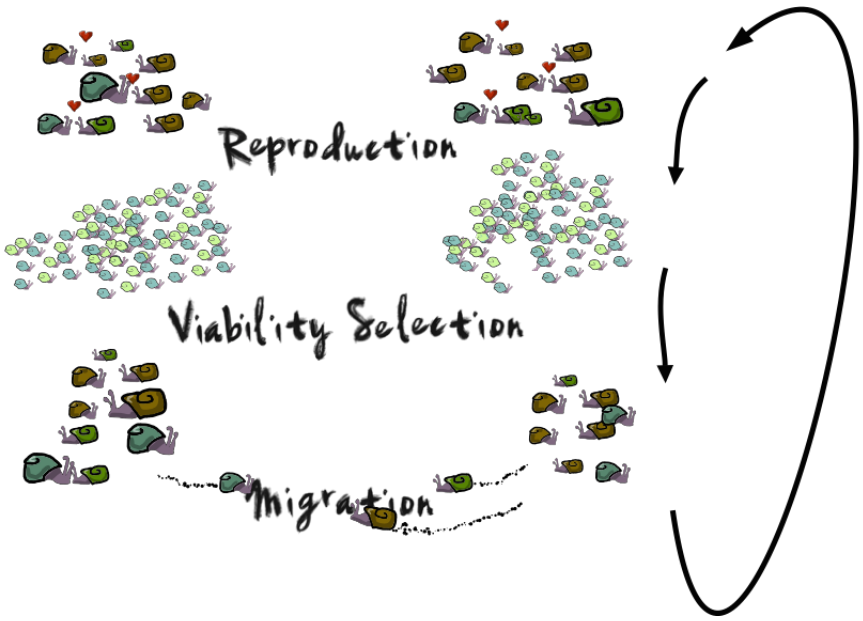


Figure 3: Life cycle of individuals in our model. Adults mate and reproduce locally within their sub-popoulation. The juveniles undergo viability selection so that only N juveniles survives to maturity. Adults then migrate to the other sub-population with probability m.

Each individual is associated with a two-locus diploid genotype (note that this reduces to one locus when recombination rate $r = 0$, in which case it is referred to as a one-locus model). Each locus contains an allele with an allelic effect size. Throughout this report the term allelic effect size is used to refer to the value stored at a specific locus. The ecological phenotype z_i of an individual i is assumed to be determined by the genotype and is given by the sum over all allelic effect sizes in an individual divided the number of loci n_l.

diploid genotype

phenotype

$$z_i = \sum_{j=1}^{2n_l} \frac{a_j^i}{n_l} \tag{1}$$

The number of alleles considered for each individual is the number of loci duplicated, because of diploidity.

The fitness w_i of an individual is assumed to depend on the ecological phenotype and an optimal phenotype θ that is constant in time.

the fitness function

$$w_i = e^{-\frac{(z_i-\theta)^2}{2\sigma^2}} \tag{2}$$

Note that the fitness function places the difference between z and θ on a Gaussian function so that the larger the difference, the smaller the fitness. When $z_i = \theta$ the fitness of the individual i is 1. The parameter σ determines the selection strength by scaling the width of the Gaussian function (the smaller the σ the stronger the selection).

The optimal phenotype is different in the two sub-populations. For simplicity, θ is positive in one sub-population and negative in the other, and the two are symmetric around zero. We assume random mating locally within each sub-population. We assume that the survival probability for a given juvenile is equal to its fitness divided by the total fitness within the same sub-population. An illustration of the relationship between alleles, genotype, phenotype, fitness and survival probability can be seen in Figure 4.

the two sub-populations have different optimal phenotypes

During reproduction, the two loci recombine with the recombination probability r per locus per generation. However, in all cases except for when it is explicitly needed in order to study the impact of recombination, r is set to zero and thus the model reduces to a one locus model.

recombination

Mutations are assumed to occur with the mutation probability μ per locus per individual per generation. When a mutation occurs, a mutation of effect size ε is drawn from a normal distribution with standard deviation σ_μ and added to the allelic value at the locus. Each mutation event thus gives rise to a new allele. However, in many simulations

mutations

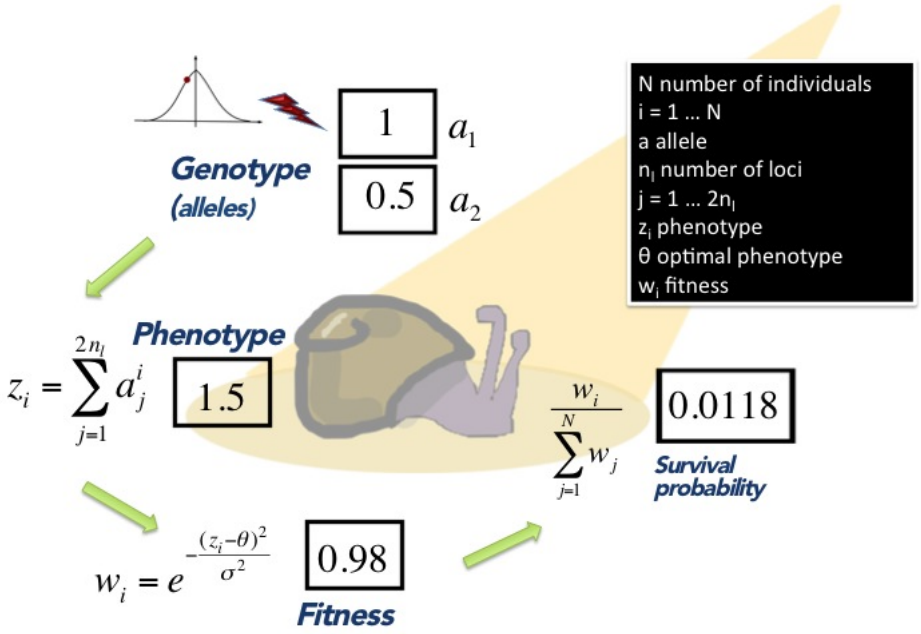


Figure 4: Relation between genotype, phenotype, fitness and survival probability for one individual (with inserted dummy-numbers).

we let $\mu = 0$ and approximate the model by repeated initializations as described in Section 3.

2.2 Delimitations and other models

spatial structure: *two linked sub-populations*

The simplest model is a well-mixed model without any spatial distinctions. The spatial structure of our model system is two coupled sub-populations, which is the simplest model which allows for migration between sub-populations. When the probability for an individual to migrate is 0.5 between two sub-populations our model reduces to one well mixed population. The dynamics in well mixed models have been extensively studied (Felsenstein, 1981; Barton and de Cara, 2008; Wang, 2013), as well as systems of more complicated spatial structures (Sadedin et al., 2009; Bierne et al., 2013).

mutations drawn from continuous distribution

Another distinction between models is whether they allow for a finite (Yeaman and Otto, 2011; Bierne et al., 2013) or for an infinite (Yeaman and Whitlock, 2011; Sadedin et al., 2009) set of alleles per locus. A small finite set of alleles has the advantage of easy derivation of deterministic approximations of the population dynamics in the limit of large population sizes. An infinite set is needed when using the standard way of inferring mutations with effect sizes from a continuous normal function. We have considered an infinite set of possible alleles for our model system, then we approximate the results in the limits where we can use a small finite set of alleles.

number of loci considered: *two, which reduces to one when $r = 0$*

When deciding upon how many loci to consider in the model, there are clear distinction between assuming a single locus model (Yeaman and Otto, 2011), or a multi locus model (Yeaman and Whitlock, 2011; Griswold, 2006; Bierne et al., 2013). The difference is how many positions containing alleles each individuals phenotype is associated with. Often it is assumed that the phenotype of an individual is proportional to the sum over all allelic effect sizes in the individual that corresponds to a given trait. Under this assumption and if recombination between the loci is negligible, the phenotypic changes of adaption will be the same for a multi locus and a single locus model. But when recombination is taken into account in the multi-locus model the genetic architecture, which describes the relation between different allelic effect sizes on a chromosome, differs. The important difference between a single locus and a multi loci model difference is thus the effect of recombination in the multi loci case.

There are different ways of modelling selection, but it is usually done with a fitness function. The fitness function given by Eq. (2) was also used in Sadedin et al. (2009) (but where additional selection pressures were applied) and in Wang (2013). It is also a special case of the fitness function used by Griswold (2006) and Yeaman and Whitlock (2011).

3 Method

3.1 Individual-based simulations of the local adaptation model

The individual-based simulations were carried out as follows:

1. The individuals were initialised so that each individual was associated with a diploid genotype. The individuals were assigned to one of the two sub-populations randomly, and so that each sub-population consisted of N individuals.

2. Individuals migrated to the other deme with probability m.

3. Within each deme the local genotype pool consisted of all genotypes within the deme. The phenotype and fitness of each genotype was computed, as well as the local average fitness.

4. The survival probability of each genotype was computed.

5. Within each sub-population, $2N$ "successful parents" were chosen with replacement from the local genotype pool based on their survival probabilities, thus constructing the parental genotypes pool.

6. Recombination was executed in the parental genotype pool with probability r per generation per genotype. When a recombination event occurred, the alleles on the same locus changed place between the two sister haplotypes in a genotype.

7. Within each deme, each parental genotype contributed with one haplotype (half the diploid genotype) to form the new generation.

8. A mutation of effect size ϵ was added to each locus with probability μ per locus per generation.[1]

9. Steps 2-8 were repeated in each generation. For a space-time plot of one realisation, see Figure 5. For more realisations and different parameter settings, see Appendix C.

[1]The observant reader will note that this implies that the mutations are added on already viability selected adults as in Griswold (2006).

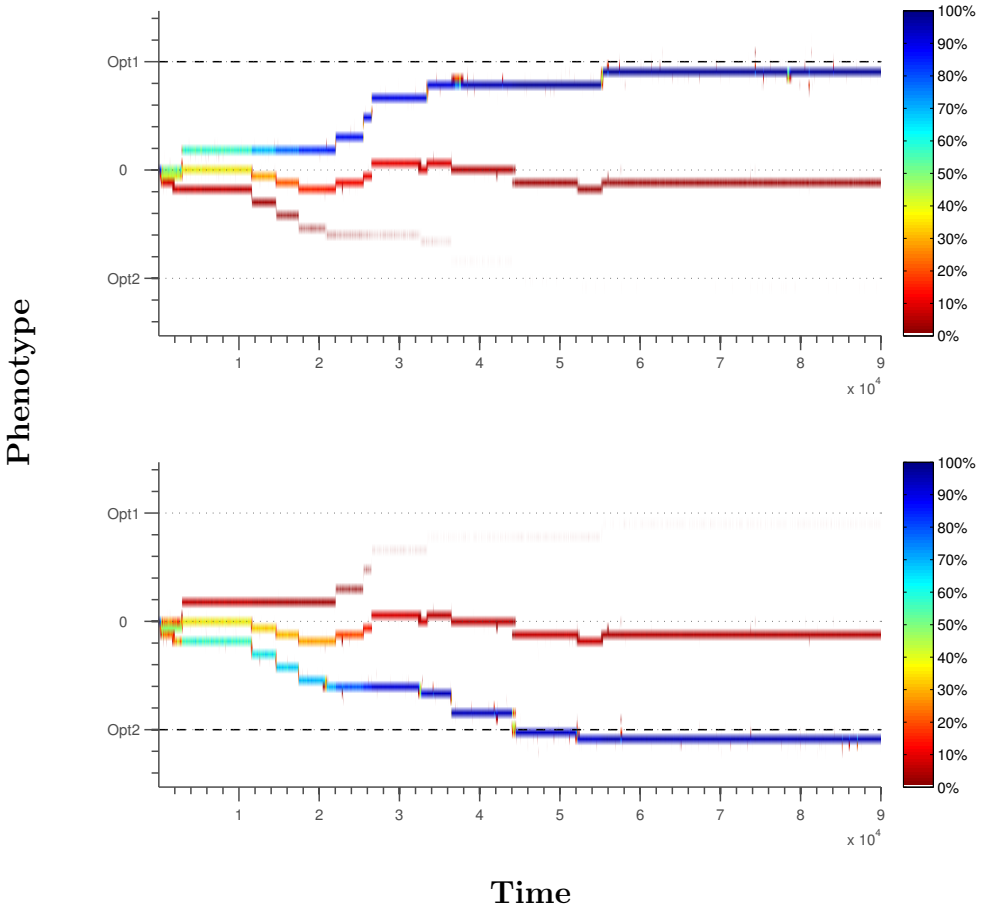


Figure 5: Space-time plot of an adaptation showing the frequencies of colour coded phenotypes sub-populations in separate panels. All individuals were initialised with the allelic effect sizes 0. The phenotype frequencies are colour coded so that blue means that all (or almost all) share the same phenotype, and dark red that only a few have the same phenotype. The blue "lines" in the plots show the well adapted homozygotes of the population. The individuals that have phenotypes around zero are the heterozygote offspring of well-adapted homozygotes in one sub-population and deleterious immigrants from the other sub population. The rather thin red "line" of maladapted individuals of low frequencies in both populations are homozygote offspring of immigrants. A dashed line marks the optimal phenotype in the local population. Note that this trajectory is from one single run. $\theta = \pm 2$, $\sigma = 2$, $\mu = 2 \cdot 10^{-5}$, $\sigma_\mu = 0.1$, $m = 0.1$, $N = 200$.

3.2 Approximation of the local adaptation model

In order to analyse the dynamics in realisations such as in Figure 5 simplifications are required. We note that the local adaptation proceeds stepwise, and approximately symmetrically in the sub-populations. In the limit where mutation rate μ is small, the system will always reach a monomorphic or dimorphic state (only one or two allelic types present) before a new mutation appears, similar to the the polymorphic state described by Yeaman and Otto (2011) that were discussed in Section 1, see Figure 2.

dimorphic system with allelic types X and $-X$

We assume that a dimorphic state consists of alleles of size X and $-X$ (when $X = 0$, the system is in a monomorphic state). From comparison to Figure 5 we understand that in a given time the allelic effect size X can be seen as a parameter describing how far adapted the sub-population are.

allelic effect size X a measure of divergence

We aim to explain the dynamics in our model by analysing what happens when a mutation of size ϵ hits a system with frequencies of alleles of effect size X and $-X$ already in steady state. By increasing the value of X from 0 we approximate the dynamics of a local adaptation when mutations appear rarely (μ small).

mutation ϵ hits a dimorphic system with frequencies in steady state

The steady states for a system with allelic types $X + \epsilon$, X and $-X$ were derived by iteration of deterministic approximations in the limit where $N \to \infty$ (for equations see Appendix B). The regions in parameter space where the adaptive mutant allele of effect size $X + \epsilon$ deterministically "wins" over the allele of effect size X was found (frequency of $X \to 0$). This region is referred to as the region of deterministic advantage for the mutant allele, this is the region that is investigated in this study.

region of deterministic advantage for the mutant allele

If a system is in the steady state with only alleles of sizes X and $-X$ and a mutation of effect size ϵ hits and creates one copy of a mutant allele of effect size $X + \epsilon$, then a population of finite size will inevitably reach the state with the mutant allele extinct or having replaces the original one (see Figure 6). Extinction will happen due to stochastic effects as a consequence of finite population sizes. The mutant allele only exists with a frequency of $\frac{1}{2N}$ the first time step and is therefor vulnerable to stochastic fluctuations especially in the beginning. Replacement will happen when the mutant allele takes over as a consequence of its selective advantage. We investigate the probability of a replacement as well as the change in average phenotype in the system when a replacement occurs.

two possibilities for mutant allele: *extinction replacement*

In order to understand the mechanisms causing a preference for

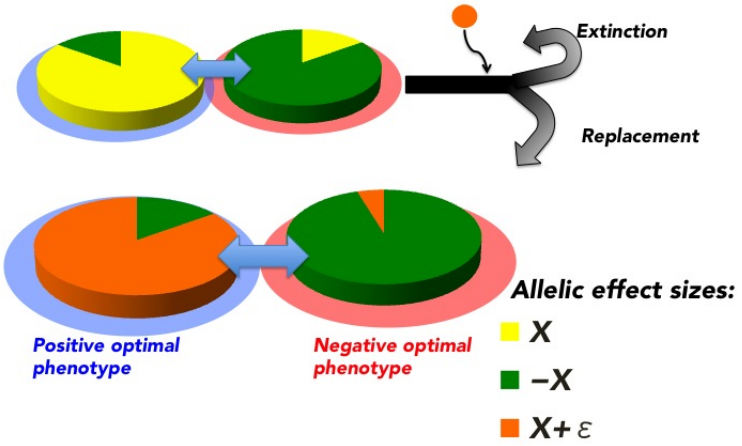


Figure 6: Two sub-populations connected by migration. The pie-charts show the steady state frequencies of alleles with different effect size. The two only possible outcomes after a mutation event where mutant allele of effect size $X + \epsilon$ is created are extinction or replacement. The three observables (described in Subsection 3.3) are p_r probably of replacement, I^* is the improvement which is the decrease in distance to optimal phenotype for the local average phenotype, and γ is the fraction of $-X$ in the sub-population with positive optimal phenotype or one minus the fraction of $-X$ sub-population with negative optimal phenotype.

two loci $r \neq 0$

tightly linked loci under selection in the genetic architectures as observed by Yeaman and Whitlock (2011) it is necessary to consider more than one locus ($r \neq 0$). In the case where recombination $r \neq 0$ the system becomes more complicated. Rater than initialising with only two alleles the system is initialised with only two alleles *per locus*. Namely with allelic effect sizes Y and $-Y$ for one locus, and $Y+\alpha$ and $-(Y+\alpha)$ for the other where $\alpha > 0$ is a parameter which allows us to analyse the effect of alleles of larger versus smaller effect sizes at different loci.

one "large" and one "small" locus

more haplotypes when $r \neq 0$

Because of recombination more halplotypes will be created even though the system like before are initialised with haplotype effect sizes[2] X and $-X$ where $X = 2Y + \alpha$, see Figure 7. A mutation of effect size ε can then either hit the "large locus" containing allele $Y + \alpha$ or the

[2]For a one-locus genotype, the haplotype effect size is the same as the allelic effect size. When more than one locus is considered a distinction is needed.

"small locus" containing allele Y. In either case the phenotype of an individual which obtains the mutation is $z_i = \frac{4Y+\epsilon}{2}$. We investigate how the average phenotype of the system is affectd by the placement of the mutation.

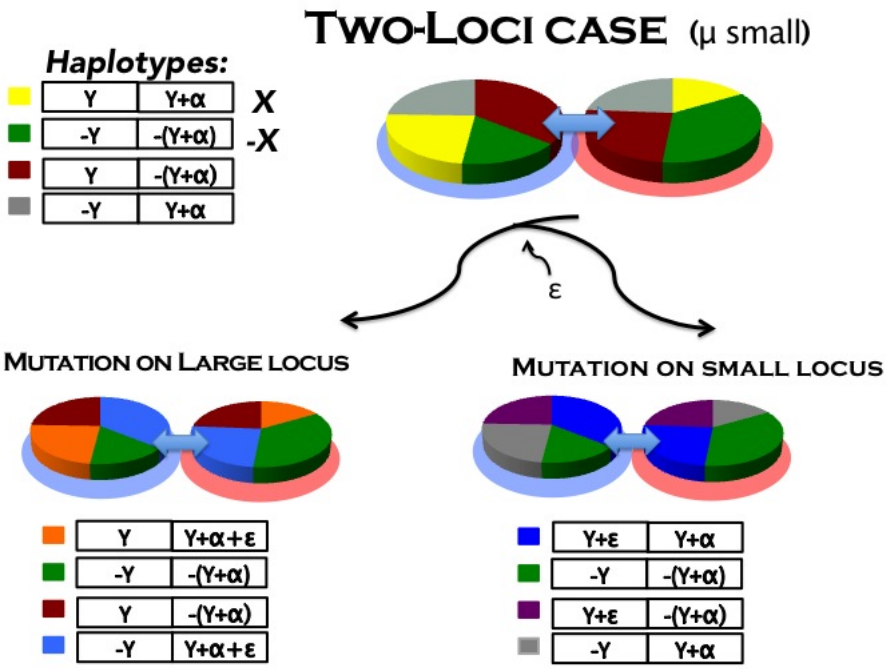


Figure 7: Steady state system where $r \neq 0$. The top steady state system is similar to the top system in Figure 6, with the difference that recombinations can create more possible haplotypes. The effect sizes in the original haplotypes are constructed so that one locus has larger values than the other. In the case of a replacement the system ends up in one of the bottom two states, depending on the placement of the mutation.

3.3 Observables (p_r, I^*, γ)

the replacement probability p_r

The replacement probability is the probability that a mutant allele does not become extinct but replaces the original allele it hit, and we denote this by p_r. We investigate this by stochastic individual-based simulations (as described in Subsection 3.1, with $r = 0$ and $\mu = 0$). We initialise system of two sub-populations connected with migration with only two possible alleles of effect size X and $-X$, and the system is allowed to relax into the steady state. Then a mutation is added to one allele with allelic effect size X in the deme with positive optimal phenotype to create a single copy of a mutant allele of effect size $X + \epsilon$. The simulation is then allowed to run until either extinction or replacement occurs. We estimate the replacement probability p_r by the ratio of replacement events relative to the total number of independent trials.

the improvement I^*

A replacement event results in a new steady state with the two allelic effect sizes $X + \epsilon$ and $-X$. The average phenotype in this steady state will be closer to (or possibly further from) the optimal phenotype in a sub-population, compared to the original X and $-X$ steady state. This difference in distance of the average phenotype to the optimum is called improvement (so that a positive value means closer to the optimum) and denote it with I^*. We compute the improvement by comparing the average phenotype for a system in the steady state with alleles of effect sizes X and $-X$, with the average phenotype of a system in the steady state with allelic effect sizes $X+\epsilon$ and $-X$. The steady states are obtained iteratively from deterministic approximations (see equations in Appendix B).

the amount of deleterious alleles γ

In order to understand the improvement we define γ as the amount of deleterious alleles (alleles reducing fitness) within the sub-populations. If $f(-X)$ is the frequency of allele $-X$ in a sub-population, then $\gamma = f(-X)$ in the sub-population with positive optimal phenotype and $\gamma = 1 - f(-X)$ in the sub-population with negative optimal phenotype. γ is also an estimate of the gene flow between the sub-populations.

4 Results and discussion

4.1 Regions of deterministic advantage of the mutant allele

Because of the migration, a mutant allele that is beneficial in one sub-population is deleterious in the other sub-population and is thus not necessarily beneficial to the whole population. The region where the adaptive mutant allele of effect size $X + \epsilon$ deterministically "wins" over the allele of effect size X (frequency of $X \to 0$) is referred to as the region of deterministic advantage of the mutant allele, see Figure 8 and 9.

critical migration rate

The mutant allele has a deterministic advantage for small migration rates. There is a critical migration rate above which the mutant allele is not beneficial to the whole system. This can be seen in the region between the region of deterministic advantage and disadvantage of the mutant allele in Figure 8.

depenence on σ and X

The critical migration rate decreases with increasing X (Figure 8). The reason is that for a given migration rate, the selective *dis*advantage of the mutant allele in the opposite sub-population increases with increasing X. When the selective strength is stronger (σ smaller) the critical migration rate becomes larger, see Figure 9. For very strong selection the mutant allele has a deterministic advantage for any value of the migration rate.

Outside the region of deterministic advantage of the mutant allele a mutation is expected to have a very low probability of maintaining in the system. Not only does the mutant allele have a selective disadvantage, but the initial single copy of the mutant allele also have to withstand the stochastic effects (for finite population sizes).

in this study we investigate the dynamics within the region

For small values of m most values of X are within the region of deterministic advantage of the mutant allele. Because estimated values of the migration rate between the habitats of *Littorina saxatalis* are small (Johannesson et al., 2010), we argue that the region of deterministic advantage of the mutant allele is biologically relevant. In this study we only investigated the dynamics within the region of deterministic advantage of the mutant allele.

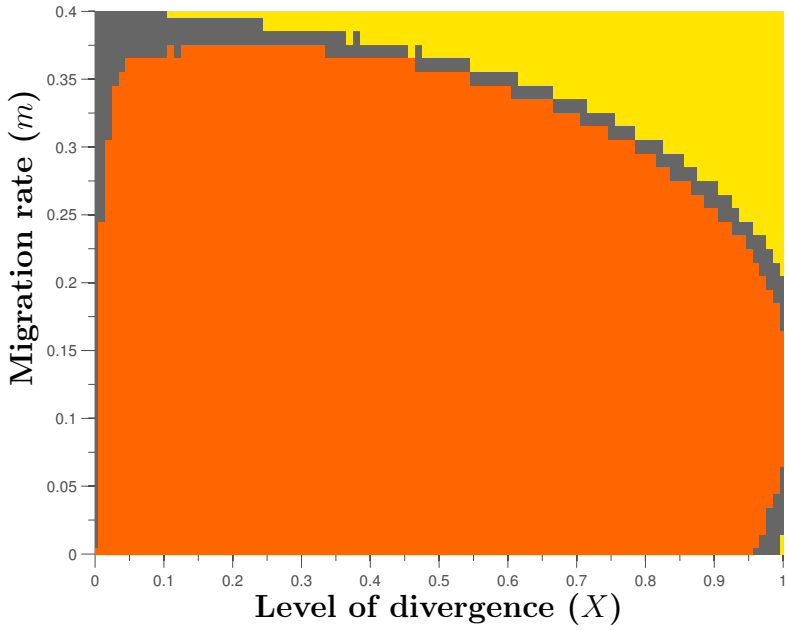


Figure 8: A phase plot showing the regions of deterministic advantage for the mutant allele. A datapoint is orange whenever the steady state frequencies of X in both sub-populations were $< 10^{-5}$. A datapoint is yellow whenever the steady state frequencies of $X + \epsilon$ were $< 10^{-5}$. The condition for steady state was that all frequencies should be the same with a precision of 3 decimals for 1000 time-steps. The simulation was run 10^6 time-steps at most. $\theta = \pm 2$, $\sigma = 2.5$, $\epsilon = 0.05$.

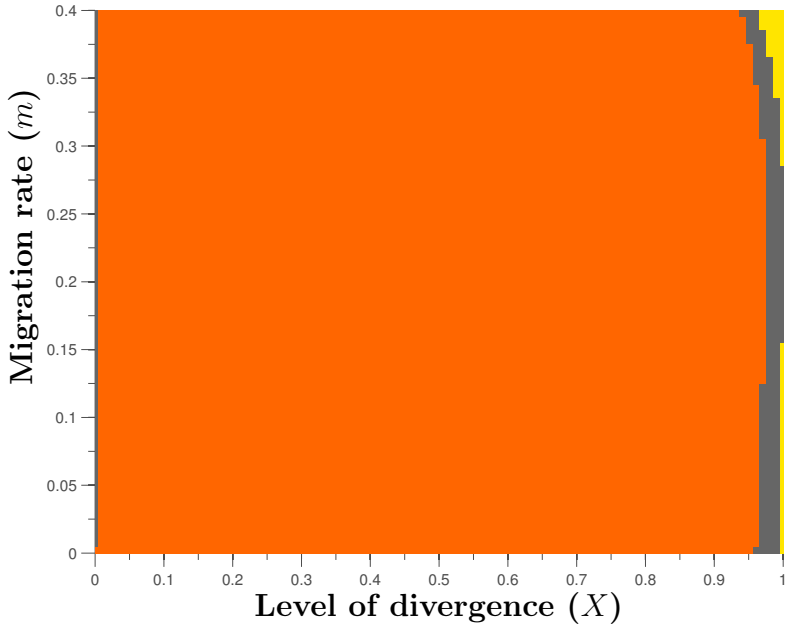


Figure 9: Same as in Figure 8, but for $\sigma = 1.73$.

4.2 Replacement probability when $r = 0$ (one locus)

The replacement probability is the probability that a mutated allele of effect size $X + \epsilon$ replaces the original allele of size X in a coupled system with alleles X and $-X$ in the steady state, see Figures 10 and 11. We have only investigated the replacement probability p_r for values of X and ϵ such that the phenotypes of the individuals never exceed the positive optimal phenotype.

theoretical approximation of p_r ($m = 0$)

In the case when the sub-populations are isolated from each other (migration rate $m = 0$) and selection is weak, the replacement probability can be approximated by the fixation probability as derived by Kimura (1957) (for more details see Appendix A). As Figures 10 and 11 show, the approximation agrees well with the data points even for relatively strong selective strength. As a consequence of the fitness function (Eq. (2), Section 2) the selective advantage of the adaptive mutant allele decreases as the distance of the average phenotype to the optimum decreases.

selective advantage decreases as the sub-population approaches the optimal phenotype

p_r decreases with increasing migration probability

The replacement probability decreases with increasing migration as Figures 10 and 11 show. The reason for lower replacement probabilities with increasing migration is the increased amount of time spent in the "wrong" sub-population when migration is frequent, which causes the mutant allele to go extinct more often. This result is in qualitative agreement with the results of Yeaman and Otto (2011) but was not explicitly shown for the conditions of a mutation arriving in already locally adapted populations.

initial curvature connected to I^*

We observe a curvature in the p_r curves that is stronger for higher migration rates, see Figures 10 and 11. We argue that the curvature can be connected to the improvement that the sub-populations gain by $X + \epsilon$ replacing X (measured by the quantity I^*). This is discussed in Subsection 4.3.

preference for mutations of large effect sizes

We have not observed any qualitative difference in replacement probability as a consequence of different mutation effect sizes (compare Figure 10 and 11). However, the replacement probability is quantitatively lower for smaller mutation effect sizes. The reason is again the difference in selective advantage which is larger for mutations of larger effect size. This can be expressed as a preference for mutations of large effect sizes in the system. This preference is more potent in the beginning of adaptation and decreases the closer to the optimum the average phenotype becomes, because the selective advantage decreases. Large beneficial mutations are, however, a lot rarer than beneficial mutations of small effect size.

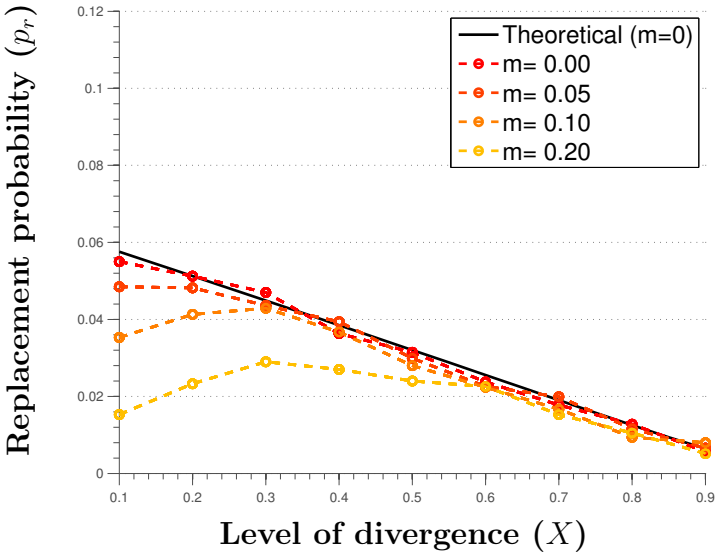


Figure 10: Replacement probability, p_r, for different migration rates. $\sigma = 1.73$, $N = 200$, $\theta = \pm 2$, $\epsilon = 0.05$.

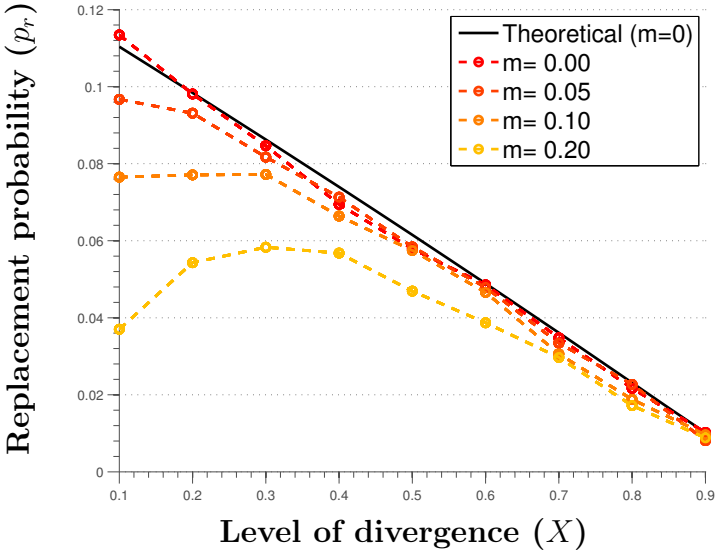


Figure 11: Same as in Figure 10, but for $\epsilon = 0.1$.

4.3 Improvement when $r = 0$ (one locus)

selection shuts down gene flow more efficiently towards the end of adaptation

Selection reduces gene-flow more efficiently the more well adapted the two sub-populations become, which can be observed in the general trend that γ decreases with increasing X, see Figures 12**a** and 13**a**. This is expected because the better adapted the individuals are to their own sub-population the more mal-adapted they are to the other, and thus their offspring die easier after migration.

In the sub-population with positive optimal phenotype the values of I^* are always positive, see Figure 12. This is expected as that sub-population experiences the replacement of an adaptive mutant allele $(X + \epsilon)$. I^* increases with increasing X (or saturates for high X), because, as explained above, the amount γ of deleterious alleles in the sub-population decreases with X.

a cost in the beginning of adaptation relates to p_r

However, accepting a mutation that is beneficial in one sub-population (I^* is positive in Figure 14) comes with a cost in the sub-population with negative optimal phenotype in the beginning of adaptation (seen as the negative values for low values of X in Figure 13 b). The cost of accepting a mutation in the beginning is a plausible explanation to the curvature with lower p_r values in the beginning of adaptation when $m \neq 0$, as discussed in Subsection 4.2. The system overcomes the cost of accepting the mutant allele in in the vicinity of the maximum replacement probability (in respect to the parameter X). This suggests that the replacement probability is qualitatively influenced by I^*.

For larger values of X there are improvement of the average phenotype even in the sub-population with negative optimal phenotype (Figure 13 b). The improvement is again explained by the decrease in γ (Figure 13 a). That is, even though $X + \epsilon$ is more deleterious than X the sub-population with negative optimal phenotype, the average phenotype still becomes closer to the optimum because of the reduced amount of deleterious alleles in the sub-population.

Notably, the total improvement (the sum of the improvements observed in individual sub-populations) is positive for all values of X (Figure 14).

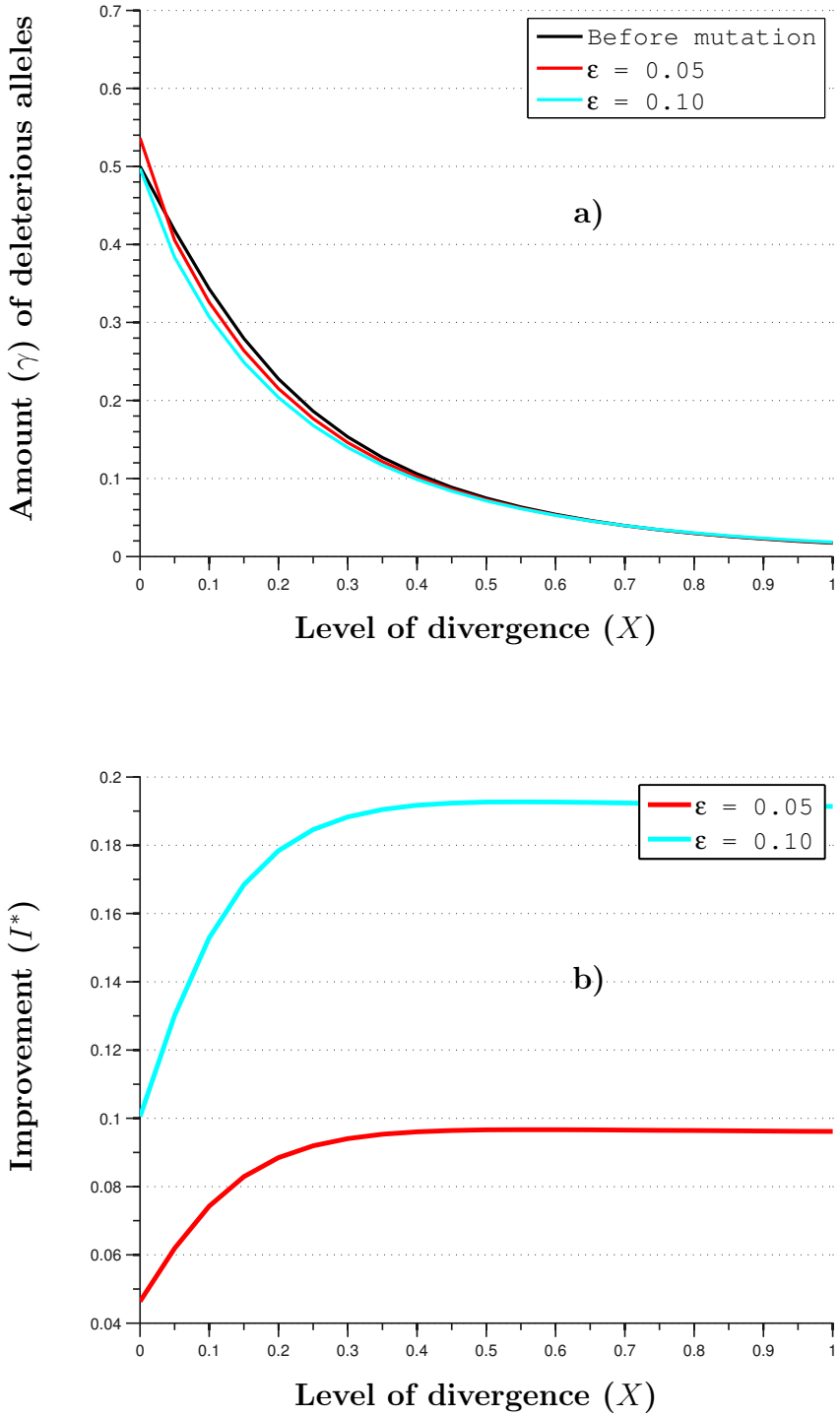
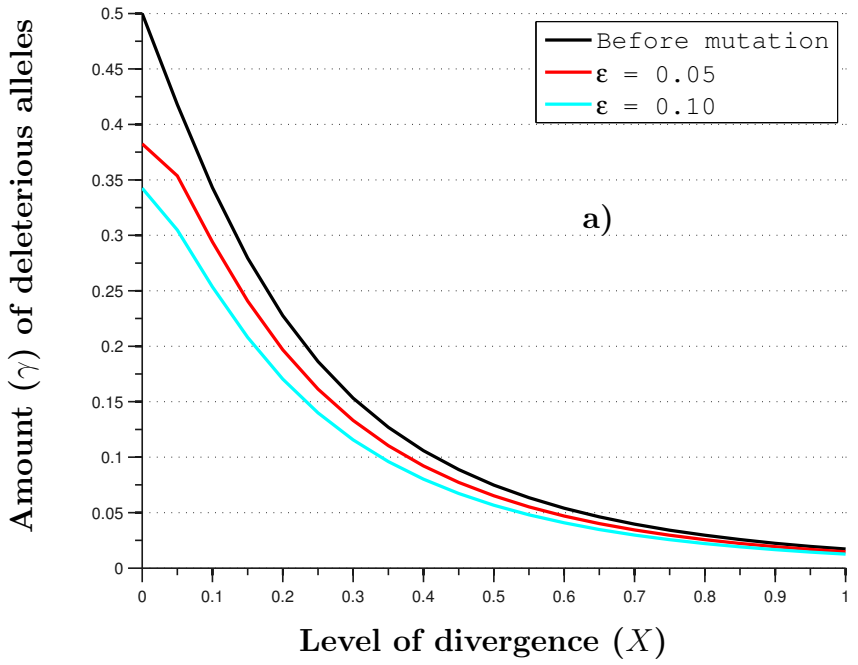


Figure 12: γ and I^* as a function of X in the sub-population with positive θ. $\sigma = 1.73$, $m = 0.1$, $\theta = \pm 2$.



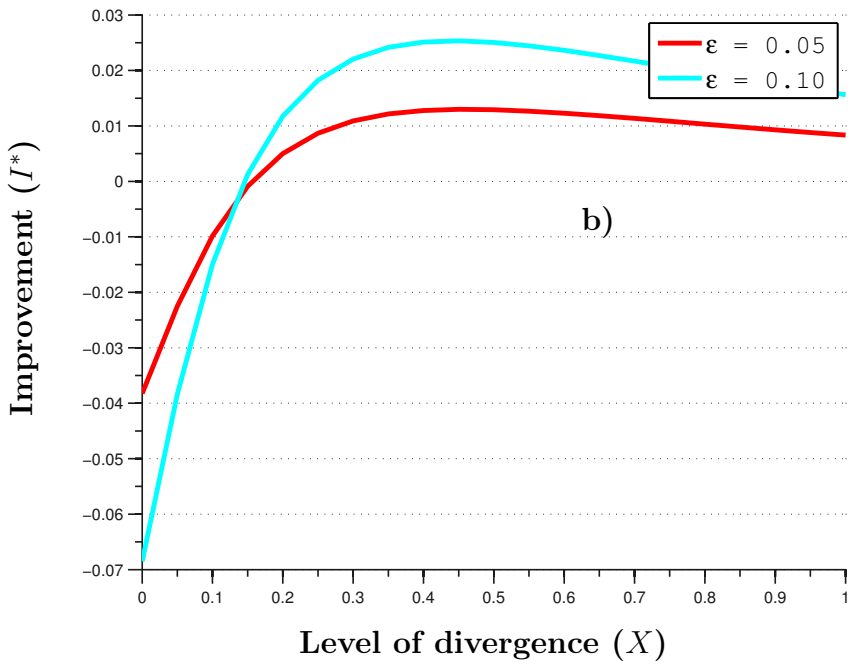


Figure 13: Same as in Figure 12 but in the sub-population with negative θ.

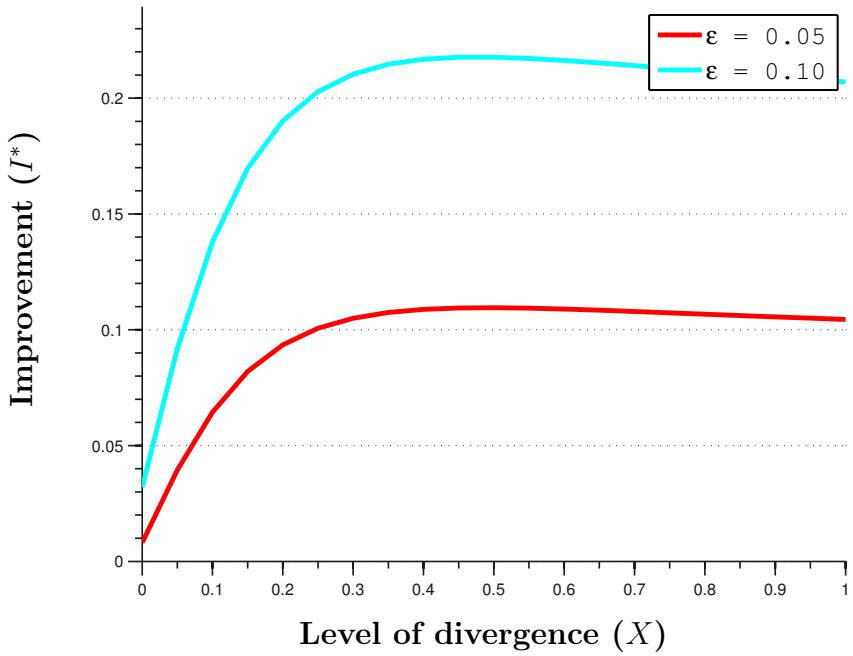


Figure 14: Same as in Figure 12**b** and 13**b**, but for the total population (both sub-populations).

4.4 Improvement depending on the placement of a mutation ($r \neq 0$)

In order to investigate the effect of the placement of a mutation in a multi locus case, I^* was measured when a mutation was placed on the large and when a mutation was placed on the small locus (as explained in Section 3.2). In analogy to the qualitative understanding of the replacement probability in terms of improvement (in the one-locus case, see Section 4.3), we expect that the system has a preference for "stacking" mutations on top of each other when the improvement is larger for a mutation placed on the large locus compared to on the small.Results are shown in Figures 15 and 16.

larger improvement for mutation on large locus → preference for "stacking"?

When selection is relatively weak ($\sigma = 2.5$, Figure 15) the system seems to have a preference for "stacking" mutations throughout the local adaptation. For stronger selection however, ($\sigma = 1.73$, Figure 16) there is a transition such that for X larger than ≈ 0.6 the improvement becomes slightly larger when a mutation is placed on the small locus. This transition is not further investigated in this study.

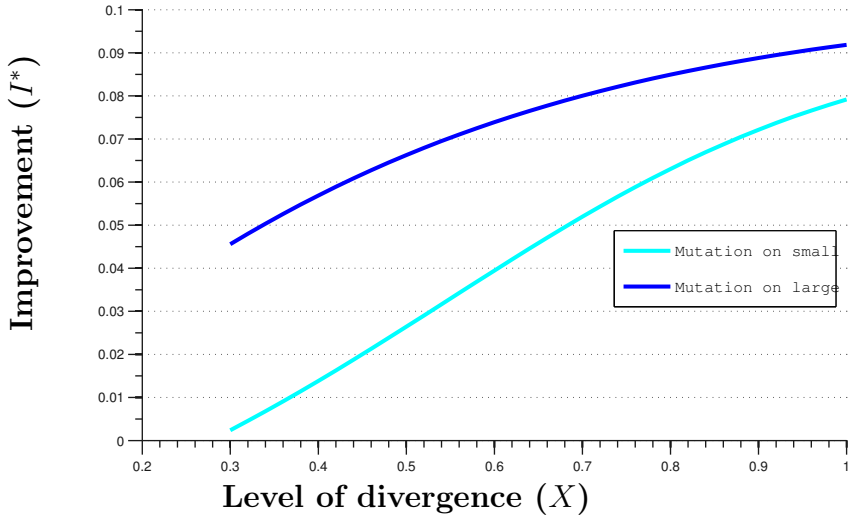


Figure 15: I^* in both sub-populations when av mutation is placed on the large versus the small locus. $\epsilon = 0.05$, $\alpha = 0.3$, $r = 0.1$, $m = 0.1$, $\theta = \pm 2$, $\sigma = 2.5$.

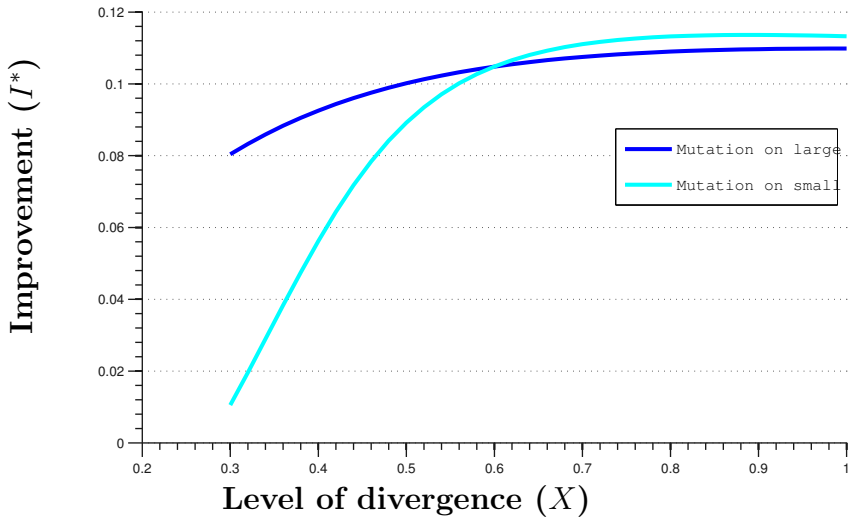


Figure 16: Same as in Figure 15, but for $\sigma = 1.73$.

5 Conclusions and future outlook

We studied local adaptation in a model with two partly isolated sub-populations with different optimal phenotypes, in order to understand the mechanisms underlying local adaptation. The objective of this study was to qualitatively understand how the joint effect of selection-migration balance and recombination and mutations influences the expected genetic patterns, by means of stochastic individual-based modelling and mathematical analysis. In what follows the qualitative understanding obtained is summarised.

objective: *qualitative understanding of genetic patterns arising from local adaptation*

We analysed how the local adaptation proceeds from partially locally adapted sub-populations. This was done by investigating how a mutant allele (beneficial in one sub-population) is accepted in a system already containing two alleles (each adapted to opposite sub populations) with frequencies in steady state.

We found a parameter region where the mutant allele have a deterministic advantage. Within the region the mutant allele is expected to replace the original allele if the population size is infinite. For finite populations however, the mutant allele may become extinct rather than replacing the original allele due to stochasticity and random genetic drift. The mutant allele is especially sensitive to fluctuations shortly after its appearance when there are only few copies in the population. We estimated the probability of replacement by measuring the number of replacement events versus total number of trials in stochastic individual-based simulations.

deterministic advantage of mutant allele

Our results show that the probability for a mutant allele to replace the original allele increases as the mutant effect size increases, and is larger in the beginning of adaptation than towards the end. In either case the selective advantage of the mutant allele increases. The mutant allele also becomes extinct more often when migration rate is high. All our results regarding the replacement probability are in qualitative agreement with those by Yeaman and Otto (2011) (although they studied a different and more restricted system).

p_r increases with selective advantage of mutant allele

A replacement event causes changes in the average phenotypes in the sub-populations. We computed the change in the average phenotype caused by a replacing mutant allele. A mutant allele is beneficial in one sub-population and deleterious in the other. In the sub-population where the mutant allele is beneficial our results show that the replacement always causes an improvement in the average phenotype. The improvement increases (and then saturates) the more locally adapted the system becomes. Our results show that the reason for the increase

in improvement lies in reduced gene-flow due to selection. In the beginning of local adaptation, the improvement in the sub-population where the mutant allele is beneficial comes with a cost in the other sub population where the mutant allele is deleterious (when migration rate $m \neq 0$). This may explain why the replacement probability does not strictly decrease as the degree of local adaptation increases (a strictly decreasing trend is observed for $m = 0$). The system overcomes the cost of accepting the mutant allele (because of reduced gene flow) in in the vicinity of the maximum replacement probability (with respect to the parameter X).

selection reduces gene-flow

In order to investigate the effect of recombination we studied two-loci genotypes. We compared the improvement in average phenotype after a mutation hit a large versus a small allele. We expect that the system is likely to prefer to "stack" mutations on large loci if the improvement is larger when a mutation is placed on a large versus a small allele. Our results show that this is the case for many parameter settings. This result is in qualitative agreement to what Yeaman and Whitlock (2011) observed in their multi-locus model.

indication of preference for "stacking" of mutations in certain regions

Our two-locus model, however, should still be further investigated. In order to further explain how the placement of a mutation influences its chances of replacing the original allele and consequently the preference to "stack" mutations on a large locus, the replacement probability should be estimated. Furthermore, in order to understand the difference in barriers to gene flow between the two loci, the gene flow should be measured for the two loci separately.

As already mentioned, the degree of gene flow between the sub-populations saturates as the local adaptation proceeds. It would be interesting to investigate other mechanisms for further reduction of gene flow. One possibility is to extend our model with a locus that is responsible for an assortative mating trait.

In order to understand which of the effects explained in this thesis are of most importance for the local adaptation of biological populations, and especially of *Littorina saxatalis*, estimates of the model parameters are needed.

parameter estimations

6 Glossary

Adaptive allele: Alleles enhancing fitness

Allele: One out of a number of alternative forms of a gene or genetic locus.

Allelic effect size: In this report used to refer to the number stored at a specific locus. It can be thought of as the contribution to a measurable trait of interest caused by a gene (or several tightly linked genes).

Assortative mating: Non-random mating where some individuals are more likely to mate with each other.

Barriers to gene flow: No exchange of genetic material. Can for example be due to geographical barriers or distance or incompatibility, or due to some mating preference.

Deleterious allele: Allele reducing fitness.

Dimorphic: Only two allelic types.

Ecotype: The two ecotypes of *Littorina saxatalis* are the ones that live in crab-rich boulder shores versus on wave-swept cliffs.

F_{st} is a comparison in variation of allelic types between and within subpopulations. Estimates of F_{st} for many loci along the genome can be used identify regions of that have been under selective pressure. It is reasonable to assume that all loci have experienced the same demographic history and thus loci that are showing unusually large amounts of diversification indicate regions that have been under diversifying selection, such as local adaptation to two habitats (Holsinger and Weir, 2009). A long term goal is to be able to look at the genome wide F_{st}-patterns and from that infer the adaptive history of the ecotypes of *Littorina saxatalis*.

Gene flow: Exchange of genetic material.

Genotype: What is inherited and underlies a phenotype, which can be observed.

Habitat: An ecological area that are inhabited by a specific type of organism such as species or ecotype.

Haplotype: Half of the diploid genotype. In the case of a one locus-genotype, a haplotype is the same as an allele.

Improvement: We have used the word improvement to describe a quantity that corresponds to a change in average phenotype in our model system, caused by the invasion of a mutation.

Monomorphic: Only one allelic type.

Mutation effect size: In the model system the mutation effect size is the value added to an allelic effect size due to a mutation event. In reality it would translate into the of the specific trait of interest.

Population Group of individuals that mate more frequently with each other than with other individuals.

RAD restriction site associated DNA (RAD) techniques is an option to genotyping and to find genetic differences between ecotypes. Roughly, one uniformly samples small pieces of DNA rather than looking at the whole genome which makes it quicker, easier and cheaper (Miller et al., 2007).

Random mating: All individuals are equally likely to mate with each other.

Recombination: the process by which genetic material is broken and joined to other genetic material.

Replacement: In this report used to describe the outcome when a mutant allele replaces the original allele after a replacement event, see Section 3.2

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A Approximation of p_r for m = 0

An approximation of the fixation probability for an allele A_1 in a well mixed system with only possible alleles A_1 and A_2 has been derived by Kimura (1957, 1962).

$$p_{fix}(A_1) = \frac{1 - e^{-4Nsp}}{1 - e^{4Ns}}. \tag{3}$$

Here, p is the frequency of the mutant allele in the beginning, which is $p = \frac{1}{2N}$ when a mutation appear in a diploid population.

s is written on the form such that the relation ship between the fitnesses of the three genotypes are:

$$w_{11} = 1 \tag{4}$$

$$w_{12} = 1 + s \tag{5}$$

$$w_{11} = 1 + 2s \tag{6}$$

Our model reduces to two independent well mixed populations $m = 0$. The replacement probability when $m = 0$ is thus the same as the fixation probability of an advantageous allele in a well mixed population of size N. In order to use Kimuras formula, we to derive s for the genotypes in our system. If $A_1 = X + \epsilon$ and $A_2 = X$, then the possible phenotypes are:

$$z(A_1A_1) = z_{11} = 2X \tag{7}$$

$$z(A_1A_2) = z(A_2A_1) = z_{12} = 2X + \epsilon \tag{8}$$

$$z(A_2A_2) = z_{11} = 2X + 2\epsilon. \tag{9}$$

The fitnesses are:

$$w_{11} = e^{-\frac{(2X-\theta)^2}{2\sigma^2}} \tag{10}$$

$$w_{12} = e^{-\frac{(2X+\epsilon-\theta)^2}{2\sigma^2}} \tag{11}$$

$$w_{22} = e^{-\frac{(2X+2\epsilon-\theta)^2}{2\sigma^2}}. \tag{12}$$

In order to make w_{11} as in Equation (4), we divide all fitnesses with w_{11}:

$$\frac{w_{12}}{w_{11}} = e^{-\epsilon(4X+\epsilon+2\theta)} \overset{\sigma<<1}{\approx} 1 - \frac{\epsilon(\epsilon + 4X - 2\theta)}{2\sigma^2} = 1 + \frac{\epsilon(2\theta - \epsilon - 4X)}{2\sigma^2} \quad (13)$$

and

$$\frac{w_{22}}{w_{11}} = e^{-\epsilon(4X+\epsilon+2\theta)} \overset{\sigma<<1}{\approx} 1 - \frac{2\epsilon(2\epsilon + 4X - 2\theta)}{2\sigma^2} = 1 + 2\frac{\epsilon(2\theta - \epsilon - 2X)}{2\sigma^2}. \quad (14)$$

From this s is derived:

$$s = \frac{\epsilon(2\theta - \epsilon - 4X)}{2\sigma^2}. \quad (15)$$

B Deterministic approximations

- $x_{ij}^{(a)}(t)$ denotes frequency of haplotype A_iB_j in deme a. $i, j \epsilon \{1, 2, 3\}$
- $w_{ijkl}^{(a)}(t)$ is the fitness of an individual in deme a with haplotype indices i, j, k and l. Note that the order of the indices in the fitness variable has no meaning, $w_{ijkl} = w_{klij} = w_{ljki}$ etc.
- The two different demes are denoted $a = 1$ and $a = 2$ respectively.

$$b = \frac{1 + (-1)^{a-1}}{2} + 1, \tag{16}$$

  which means that b is the "other deme".

- m is the fraction of individuals in deme a that migrated from deme b.

The weighted average fitness of individuals in deme a is given by Eq. (17).

$$\begin{aligned} \widetilde{w}^{(a)}(t) = (1-m) \sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}\sum_{l=1}^{3} x_{ij}^{(a)}(t) x_{kl}^{(a)}(t) w_{ijkl}^{(a)}(t) \\ + m \sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}\sum_{l=1}^{3} x_{ij}^{(b)}(t) x_{kl}^{(b)}(t) w_{ijkl}^{(a)}(t) \end{aligned} \tag{17}$$

The deterministic approximation of haplotype frequencies of individuals in deme a is then given by Eqs. (18)-(26). Because of convenience $x_{ij}^{(a)}$ and $w_{ijkl}^{(a)}$ are used instead of $x_{ij}^{(a)}(t)$ and $w_{ijkl}^{(a)}(t)$ respectively.

$$
\begin{aligned}
&x_{11}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{11}^{(a)}x_{11}^{(a)}w_{1111}^{(a)} + [x_{11}^{(a)}x_{12}^{(a)} + x_{11}^{(a)}x_{21}^{(a)}]w_{1112}^{(a)} + [x_{11}^{(a)}x_{13}^{(a)} + x_{11}^{(a)}x_{31}^{(a)}]w_{1113}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{11}^{(a)}x_{22}^{(a)}w_{1122}^{(a)} + [x_{11}^{(a)}x_{23}^{(a)} + x_{11}^{(a)}x_{32}^{(a)}]w_{1123}^{(a)} + x_{11}^{(a)}x_{33}^{(a)}w_{1133}^{(a)}\Big] \\
&\qquad + r\Big[x_{12}^{(a)}x_{21}^{(a)}w_{1122}^{(a)} + [x_{12}^{(a)}x_{31}^{(a)} + x_{13}^{(a)}x_{21}^{(a)}]w_{1123}^{(a)} + x_{13}^{(a)}x_{31}^{(a)}w_{1133}^{(a)}\Big]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{11}^{(b)}x_{11}^{(b)}w_{1111}^{(a)} + [x_{11}^{(b)}x_{12}^{(b)} + x_{11}^{(b)}x_{21}^{(b)}]w_{1112}^{(a)} + [x_{11}^{(b)}x_{13}^{(b)} + x_{11}^{(b)}x_{31}^{(b)}]w_{1113}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{11}^{(b)}x_{22}^{(b)}w_{1122}^{(a)} + [x_{11}^{(b)}x_{23}^{(b)} + x_{11}^{(b)}x_{32}^{(b)}]w_{1123}^{(a)} + x_{11}^{(b)}x_{33}^{(b)}w_{1133}^{(a)}\Big] \\
&\qquad + r\Big[x_{12}^{(b)}x_{21}^{(b)}w_{1122}^{(a)} + [x_{12}^{(b)}x_{31}^{(b)} + x_{13}^{(b)}x_{21}^{(b)}]w_{1123}^{(a)} + x_{13}^{(b)}x_{31}^{(b)}w_{1133}^{(a)}\Big]\Bigg)
\end{aligned}
\tag{18}
$$

$$
\begin{aligned}
&x_{12}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{12}^{(a)}x_{11}^{(a)}w_{1112}^{(a)} + x_{12}^{(a)}x_{12}^{(a)}w_{1122}^{(a)} + x_{12}^{(a)}x_{13}^{(a)}w_{1123}^{(a)} + x_{12}^{(a)}x_{22}^{(a)}w_{1222}^{(a)} + x_{12}^{(a)}x_{32}^{(a)}w_{1223}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{12}^{(a)}x_{21}^{(a)}w_{1122}^{(a)} + x_{12}^{(a)}x_{23}^{(a)}w_{1223}^{(a)} + x_{12}^{(a)}x_{31}^{(a)}w_{1123}^{(a)} + x_{12}^{(a)}x_{33}^{(a)}w_{1233}^{(a)}\Big] \\
&\qquad + r\Big[x_{11}^{(a)}x_{22}^{(a)}w_{1122}^{(a)} + x_{11}^{(a)}x_{32}^{(a)}w_{1123}^{(a)} + x_{13}^{(a)}x_{22}^{(a)}w_{1223}^{(a)} + x_{13}^{(a)}x_{32}^{(a)}w_{1233}^{(a)}\Big]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{12}^{(b)}x_{11}^{(b)}w_{1112}^{(a)} + x_{12}^{(b)}x_{12}^{(b)}w_{1122}^{(a)} + x_{12}^{(b)}x_{13}^{(b)}w_{1123}^{(a)} + x_{12}^{(b)}x_{22}^{(b)}w_{1222}^{(a)} + x_{12}^{(b)}x_{32}^{(b)}w_{1223}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{12}^{(b)}x_{21}^{(b)}w_{1122}^{(a)} + x_{12}^{(b)}x_{23}^{(b)}w_{1223}^{(a)} + x_{12}^{(b)}x_{31}^{(b)}w_{1123}^{(a)} + x_{12}^{(b)}x_{33}^{(b)}w_{1233}^{(a)}\Big] \\
&\qquad + r\Big[x_{11}^{(b)}x_{22}^{(b)}w_{1122}^{(a)} + x_{11}^{(b)}x_{32}^{(b)}w_{1123}^{(a)} + x_{13}^{(b)}x_{22}^{(b)}w_{1223}^{(a)} + x_{13}^{(b)}x_{32}^{(b)}w_{1233}^{(a)}\Big]\Bigg)
\end{aligned}
\tag{19}
$$

$$
\begin{aligned}
&x_{13}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{13}^{(a)}x_{11}^{(a)}w_{1113}^{(a)} + x_{13}^{(a)}x_{12}^{(a)}w_{1123}^{(a)} + x_{13}^{(a)}x_{13}^{(a)}w_{1133}^{(a)} + x_{13}^{(a)}x_{23}^{(a)}w_{1233}^{(a)} + x_{13}^{(a)}x_{33}^{(a)}w_{1333}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{13}^{(a)}x_{21}^{(a)}w_{1123}^{(a)} + x_{13}^{(a)}x_{22}^{(a)}w_{1223}^{(a)} + x_{13}^{(a)}x_{31}^{(a)}w_{1133}^{(a)} + x_{13}^{(a)}x_{32}^{(a)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{11}^{(a)}x_{23}^{(a)}w_{1123}^{(a)} + x_{11}^{(a)}x_{33}^{(a)}w_{1133}^{(a)} + x_{12}^{(a)}x_{23}^{(a)}w_{1223}^{(a)} + x_{12}^{(a)}x_{33}^{(a)}w_{1233}^{(a)}\right]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{13}^{(b)}x_{11}^{(b)}w_{1113}^{(a)} + x_{13}^{(b)}x_{12}^{(b)}w_{1123}^{(a)} + x_{13}^{(b)}x_{13}^{(b)}w_{1133}^{(a)} + x_{13}^{(b)}x_{23}^{(b)}w_{1233}^{(a)} + x_{13}^{(b)}x_{33}^{(b)}w_{1333}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{13}^{(b)}x_{21}^{(b)}w_{1123}^{(a)} + x_{13}^{(b)}x_{22}^{(b)}w_{1223}^{(a)} + x_{13}^{(b)}x_{31}^{(b)}w_{1133}^{(a)} + x_{13}^{(b)}x_{32}^{(b)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{11}^{(b)}x_{23}^{(b)}w_{1123}^{(a)} + x_{11}^{(b)}x_{33}^{(b)}w_{1133}^{(a)} + x_{12}^{(b)}x_{23}^{(b)}w_{1223}^{(a)} + x_{12}^{(b)}x_{33}^{(b)}w_{1233}^{(a)}\right]\Bigg)
\end{aligned}
\tag{20}
$$

$$
\begin{aligned}
&x_{21}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{21}^{(a)}x_{22}^{(a)}w_{2221}^{(a)} + x_{21}^{(a)}x_{21}^{(a)}w_{1122}^{(a)} + x_{21}^{(a)}x_{23}^{(a)}w_{1223}^{(a)} + x_{21}^{(a)}x_{11}^{(a)}w_{1112}^{(a)} + x_{21}^{(a)}x_{31}^{(a)}w_{1123}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{21}^{(a)}x_{12}^{(a)}w_{1122}^{(a)} + x_{21}^{(a)}x_{13}^{(a)}w_{1123}^{(a)} + x_{21}^{(a)}x_{32}^{(a)}w_{1223}^{(a)} + x_{21}^{(a)}x_{33}^{(a)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{22}^{(a)}x_{11}^{(a)}w_{1122}^{(a)} + x_{22}^{(a)}x_{31}^{(a)}w_{1223}^{(a)} + x_{23}^{(a)}x_{11}^{(a)}w_{1123}^{(a)} + x_{23}^{(a)}x_{31}^{(a)}w_{1233}^{(a)}\right]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{21}^{(b)}x_{22}^{(b)}w_{1222}^{(a)} + x_{21}^{(b)}x_{21}^{(b)}w_{1122}^{(a)} + x_{21}^{(b)}x_{23}^{(b)}w_{1223}^{(a)} + x_{21}^{(b)}x_{11}^{(b)}w_{1112}^{(a)} + x_{21}^{(b)}x_{31}^{(b)}w_{1123}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{21}^{(b)}x_{12}^{(b)}w_{1122}^{(a)} + x_{21}^{(b)}x_{13}^{(b)}w_{1123}^{(a)} + x_{21}^{(b)}x_{32}^{(b)}w_{1223}^{(a)} + x_{21}^{(b)}x_{33}^{(b)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{22}^{(b)}x_{11}^{(b)}w_{1122}^{(a)} + x_{22}^{(b)}x_{31}^{(b)}w_{1223}^{(a)} + x_{23}^{(b)}x_{11}^{(b)}w_{1123}^{(a)} + x_{23}^{(b)}x_{31}^{(b)}w_{1233}^{(a)}\right]\Bigg)
\end{aligned}
\tag{21}
$$

$$
\begin{aligned}
&x_{22}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{22}^{(a)}x_{22}^{(a)}w_{2222}^{(a)} + [x_{22}^{(a)}x_{21}^{(a)} + x_{22}^{(a)}x_{12}^{(a)}]w_{1222}^{(a)} + [x_{22}^{(a)}x_{23}^{(a)} + x_{22}^{(a)}x_{32}^{(a)}]w_{2223}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{22}^{(a)}x_{11}^{(a)}w_{1122}^{(a)} + [x_{22}^{(a)}x_{13}^{(a)} + x_{22}^{(a)}x_{31}^{(a)}]w_{1223}^{(a)} + x_{22}^{(a)}x_{33}^{(a)}w_{2233}^{(a)}\Big] \\
&\qquad + r\Big[x_{21}^{(a)}x_{12}^{(a)}w_{1122}^{(a)} + [x_{21}^{(a)}x_{32}^{(a)} + x_{23}^{(a)}x_{12}^{(a)}]w_{1223}^{(a)} + x_{23}^{(a)}x_{32}^{(a)}w_{2233}^{(a)}\Big]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{22}^{(b)}x_{22}^{(b)}w_{2222}^{(a)} + [x_{22}^{(b)}x_{21}^{(b)} + x_{22}^{(b)}x_{12}^{(b)}]w_{1222}^{(a)} + [x_{22}^{(b)}x_{23}^{(b)} + x_{22}^{(b)}x_{32}^{(b)}]w_{2223}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{22}^{(b)}x_{11}^{(b)}w_{1122}^{(a)} + [x_{22}^{(b)}x_{13}^{(b)} + x_{22}^{(b)}x_{31}^{(b)}]w_{1223}^{(a)} + x_{22}^{(b)}x_{33}^{(b)}w_{2233}^{(a)}\Big] \\
&\qquad + r\Big[x_{21}^{(b)}x_{12}^{(b)}w_{1122}^{(a)} + [x_{21}^{(b)}x_{32}^{(b)} + x_{23}^{(b)}x_{12}^{(b)}]w_{1223}^{(a)} + x_{23}^{(b)}x_{32}^{(b)}w_{2233}^{(a)}\Big]\Bigg)
\end{aligned}
\tag{22}
$$

$$
\begin{aligned}
&x_{23}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{23}^{(a)}x_{22}^{(a)}w_{2223}^{(a)} + x_{23}^{(a)}x_{21}^{(a)}w_{1223}^{(a)} + x_{23}^{(a)}x_{23}^{(a)}w_{2233}^{(a)} + x_{23}^{(a)}x_{13}^{(a)}w_{1233}^{(a)} + x_{23}^{(a)}x_{33}^{(a)}w_{2333}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{23}^{(a)}x_{12}^{(a)}w_{1223}^{(a)} + x_{23}^{(a)}x_{11}^{(a)}w_{1123}^{(a)} + x_{23}^{(a)}x_{32}^{(a)}w_{2233}^{(a)} + x_{23}^{(a)}x_{31}^{(a)}w_{1233}^{(a)}\Big] \\
&\qquad + r\Big[x_{22}^{(a)}x_{13}^{(a)}w_{1223}^{(a)} + x_{22}^{(a)}x_{33}^{(a)}w_{2233}^{(a)} + x_{21}^{(a)}x_{13}^{(a)}w_{1123}^{(a)} + x_{21}^{(a)}x_{33}^{(a)}w_{1233}^{(a)}\Big]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\Big[x_{23}^{(b)}x_{22}^{(b)}w_{2223}^{(a)} + x_{23}^{(b)}x_{21}^{(b)}w_{1223}^{(a)} + x_{23}^{(b)}x_{23}^{(b)}w_{2233}^{(a)} + x_{23}^{(b)}x_{13}^{(b)}w_{1233}^{(a)} + x_{23}^{(b)}x_{33}^{(b)}w_{2333}^{(a)}\Big] \\
&\qquad + (1-r)\Big[x_{23}^{(b)}x_{12}^{(b)}w_{1223}^{(a)} + x_{23}^{(b)}x_{11}^{(b)}w_{1123}^{(a)} + x_{23}^{(b)}x_{32}^{(b)}w_{2233}^{(a)} + x_{23}^{(b)}x_{31}^{(b)}w_{1233}^{(a)}\Big] \\
&\qquad + r\Big[x_{22}^{(b)}x_{13}^{(b)}w_{1223}^{(a)} + x_{22}^{(b)}x_{33}^{(b)}w_{2233}^{(a)} + x_{21}^{(b)}x_{13}^{(b)}w_{1123}^{(a)} + x_{21}^{(b)}x_{33}^{(b)}w_{1233}^{(a)}\Big]\Bigg)
\end{aligned}
\tag{23}
$$

$$
\begin{aligned}
&x_{31}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{31}^{(a)}x_{33}^{(a)}w_{1333}^{(a)} + x_{31}^{(a)}x_{31}^{(a)}w_{1133}^{(a)} + x_{31}^{(a)}x_{32}^{(a)}w_{1233}^{(a)} + x_{31}^{(a)}x_{11}^{(a)}w_{1113}^{(a)} + x_{31}^{(a)}x_{21}^{(a)}w_{1123}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{31}^{(a)}x_{13}^{(a)}w_{1133}^{(a)} + x_{31}^{(a)}x_{12}^{(a)}w_{1123}^{(a)} + x_{31}^{(a)}x_{23}^{(a)}w_{1233}^{(a)} + x_{31}^{(a)}x_{22}^{(a)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{33}^{(a)}x_{11}^{(a)}w_{1133}^{(a)} + x_{33}^{(a)}x_{21}^{(a)}w_{1233}^{(a)} + x_{32}^{(a)}x_{11}^{(a)}w_{1123}^{(a)} + x_{32}^{(a)}x_{21}^{(a)}w_{1233}^{(a)}\right]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{31}^{(b)}x_{33}^{(b)}w_{1333}^{(a)} + x_{31}^{(b)}x_{31}^{(b)}w_{1133}^{(a)} + x_{31}^{(b)}x_{32}^{(b)}w_{1233}^{(a)} + x_{31}^{(b)}x_{11}^{(b)}w_{1113}^{(a)} + x_{31}^{(b)}x_{21}^{(b)}w_{1123}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{31}^{(b)}x_{13}^{(b)}w_{1133}^{(a)} + x_{31}^{(b)}x_{12}^{(b)}w_{1123}^{(a)} + x_{31}^{(b)}x_{23}^{(b)}w_{1233}^{(a)} + x_{31}^{(b)}x_{22}^{(b)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{33}^{(b)}x_{11}^{(b)}w_{1133}^{(a)} + x_{33}^{(b)}x_{21}^{(b)}w_{1233}^{(a)} + x_{32}^{(b)}x_{11}^{(b)}w_{1123}^{(a)} + x_{32}^{(b)}x_{21}^{(b)}w_{1233}^{(a)}\right]\Bigg)
\end{aligned}
\tag{24}
$$

$$
\begin{aligned}
&x_{32}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{32}^{(a)}x_{33}^{(a)}w_{2333}^{(a)} + x_{32}^{(a)}x_{31}^{(a)}w_{1233}^{(a)} + x_{32}^{(a)}x_{32}^{(a)}w_{2233}^{(a)} + x_{32}^{(a)}x_{12}^{(a)}w_{1233}^{(a)} + x_{32}^{(a)}x_{22}^{(a)}w_{2223}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{32}^{(a)}x_{13}^{(a)}w_{1233}^{(a)} + x_{32}^{(a)}x_{11}^{(a)}w_{1123}^{(a)} + x_{32}^{(a)}x_{23}^{(a)}w_{2233}^{(a)} + x_{32}^{(a)}x_{21}^{(a)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{33}^{(a)}x_{12}^{(a)}w_{1233}^{(a)} + x_{33}^{(a)}x_{22}^{(a)}w_{2233}^{(a)} + x_{31}^{(a)}x_{12}^{(a)}w_{1123}^{(a)} + x_{31}^{(a)}x_{22}^{(a)}w_{1233}^{(a)}\right]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{32}^{(b)}x_{33}^{(b)}w_{2333}^{(a)} + x_{32}^{(b)}x_{31}^{(b)}w_{1233}^{(a)} + x_{32}^{(b)}x_{32}^{(b)}w_{2233}^{(a)} + x_{32}^{(b)}x_{12}^{(b)}w_{1233}^{(a)} + x_{32}^{(b)}x_{22}^{(b)}w_{2223}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{32}^{(b)}x_{13}^{(b)}w_{1233}^{(a)} + x_{32}^{(b)}x_{11}^{(b)}w_{1123}^{(a)} + x_{32}^{(b)}x_{23}^{(b)}w_{2233}^{(a)} + x_{32}^{(b)}x_{21}^{(b)}w_{1233}^{(a)}\right] \\
&\qquad + r\left[x_{33}^{(b)}x_{12}^{(b)}w_{1233}^{(a)} + x_{33}^{(b)}x_{22}^{(b)}w_{2233}^{(a)} + x_{31}^{(b)}x_{12}^{(b)}w_{1123}^{(a)} + x_{31}^{(b)}x_{22}^{(b)}w_{1233}^{(a)}\right]\Bigg)
\end{aligned}
\tag{25}
$$

$$
\begin{aligned}
&x_{33}^{(a)}(t+1) = \\
&\frac{(1-m)}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{33}^{(a)}x_{33}^{(a)}w_{3333}^{(a)} + [x_{33}^{(a)}x_{31}^{(a)} + x_{33}^{(a)}x_{13}^{(a)}]w_{1333}^{(a)} + [x_{33}^{(a)}x_{32}^{(a)} + x_{33}^{(a)}x_{23}^{(a)}]w_{2333}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{33}^{(a)}x_{11}^{(a)}w_{1133}^{(a)} + [x_{33}^{(a)}x_{12}^{(a)} + x_{33}^{(a)}x_{21}^{(a)}]w_{1233}^{(a)} + x_{33}^{(a)}x_{22}^{(a)}w_{2233}^{(a)}\right] \\
&\qquad + r\left[x_{31}^{(a)}x_{13}^{(a)}w_{1133}^{(a)} + [x_{31}^{(a)}x_{23}^{(a)} + x_{32}^{(a)}x_{13}^{(a)}]w_{1233}^{(a)} + x_{32}^{(a)}x_{23}^{(a)}w_{2233}^{(a)}\right]\Bigg) \\
&+ \frac{m}{\widetilde{w}^{(a)}(t)}\Bigg(\left[x_{33}^{(b)}x_{33}^{(b)}w_{3333}^{(a)} + [x_{33}^{(b)}x_{31}^{(b)} + x_{33}^{(b)}x_{13}^{(b)}]w_{1333}^{(a)} + [x_{33}^{(b)}x_{32}^{(b)} + x_{33}^{(b)}x_{23}^{(b)}]w_{2333}^{(a)}\right] \\
&\qquad + (1-r)\left[x_{33}^{(b)}x_{11}^{(b)}w_{1133}^{(a)} + [x_{33}^{(b)}x_{12}^{(b)} + x_{33}^{(b)}x_{21}^{(b)}]w_{1233}^{(a)} + x_{33}^{(b)}x_{22}^{(b)}w_{2233}^{(a)}\right] \\
&\qquad + r\left[x_{31}^{(b)}x_{13}^{(b)}w_{1133}^{(a)} + [x_{31}^{(b)}x_{23}^{(b)} + x_{32}^{(b)}x_{13}^{(b)}]w_{1233}^{(a)} + x_{32}^{(b)}x_{23}^{(b)}w_{2233}^{(a)}\right]\Bigg)
\end{aligned}
\tag{26}
$$

C Additional plots

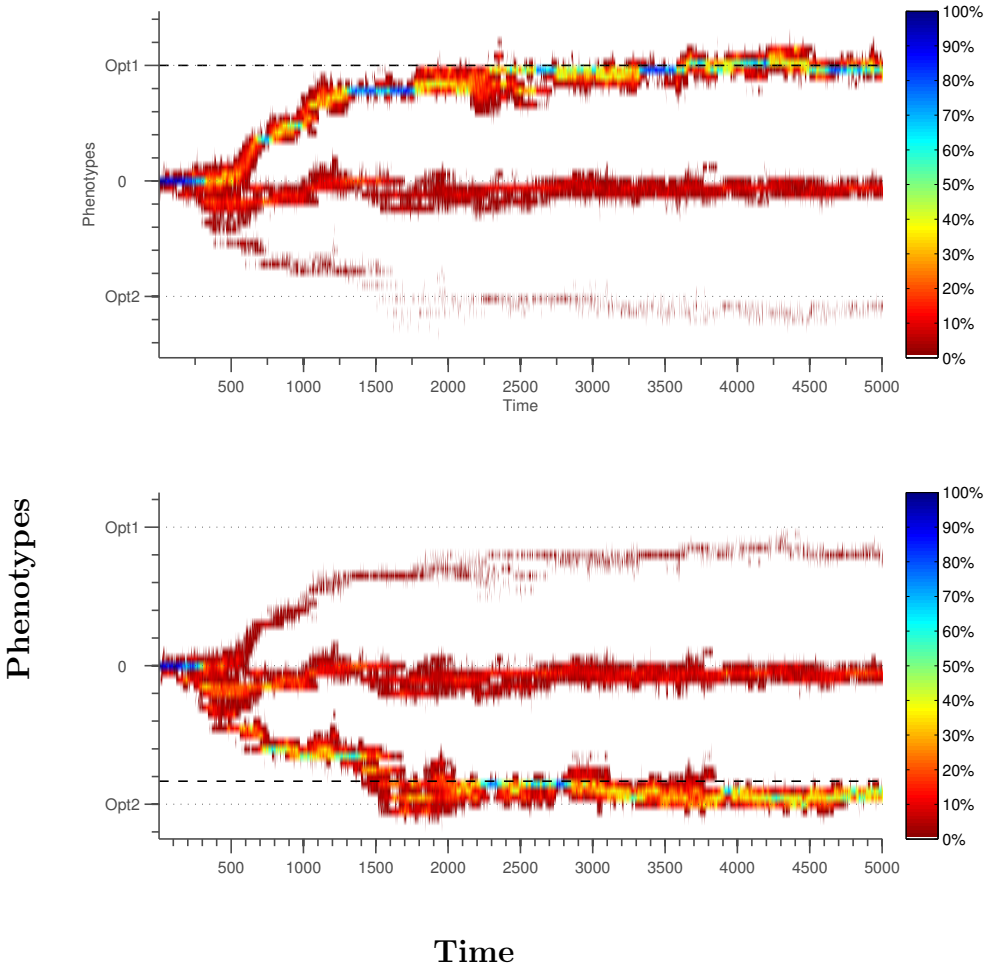

Figure 17: Colour-coded phenotypic frequencies versus time. $\sigma = 1.73$, $\mu = 0.002$, $\sigma_\mu = 0.1$, $r = 0$, $m = 0.1$, $\theta = \pm 2$

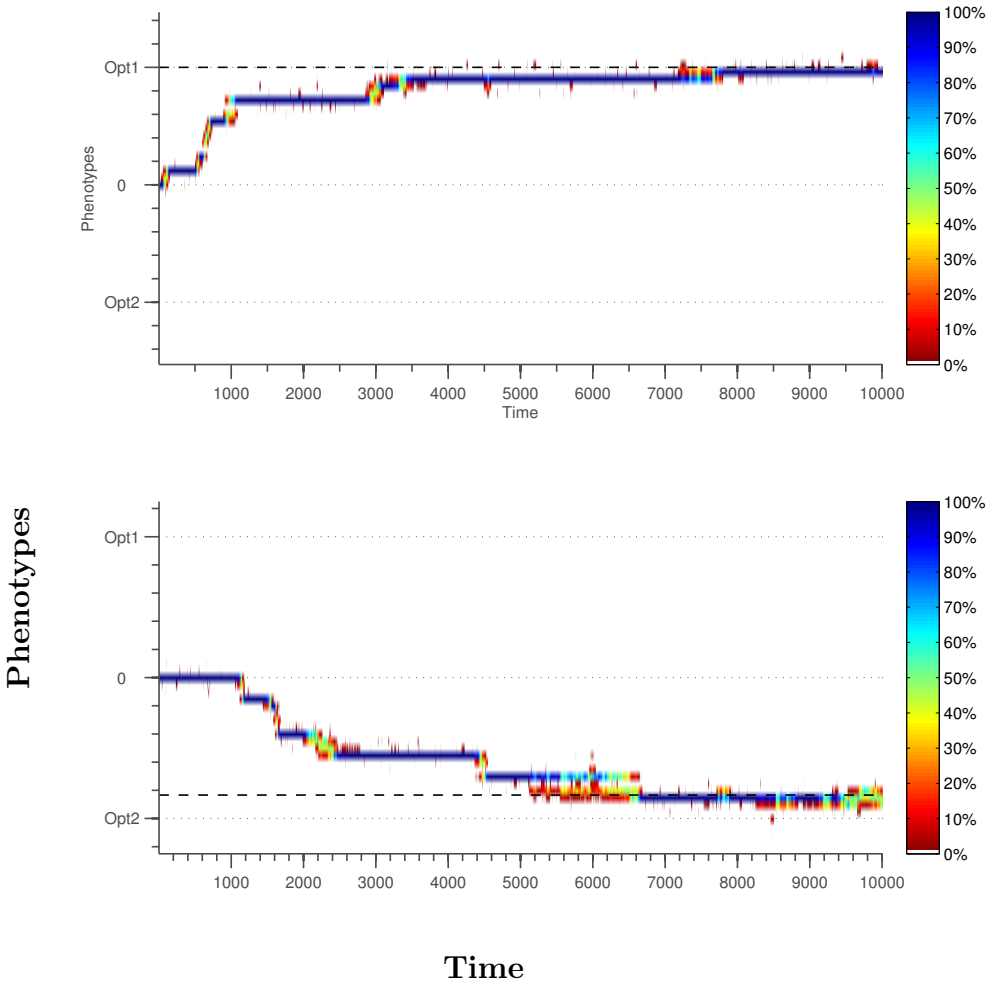

Figure 18: Colour-coded phenotypic frequencies versus time. $\sigma = 1.73$, $\mu = 0.0002$, $\sigma_\mu = 0.1$, $r = 0$, $m = 0$, $\theta = \pm 2$