Population dynamics and genetics in inhomogeneous media

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Aquatic environments are a natural ecosystem for a large variety of living organisms. In such ecosystems the level of inhomogeneities is high and inhomogeneities can influence the dynamics and the genetics of a population that is growing and expanding in such an environment. Moreover, displacement due to self-propulsion can sum up with turbulent dispersion at larger scales to influence the local densities and thus population and genetic dynamics. In this work the expansion of a population, consisting of two subpopulations differing for neutral alleles, in inhomogeneous environments is investigated numerically using a discrete particle model with certain rules for birth, death by competition and displacement by diffusion.

First the focus is on ‘internal’ inhomogeneities, induced by self-propulsion of interacting and reactive particles and modeled as a density-dependent motility of individuals. In this case spatial structures develop in the population in the form of high and low density regions. The clustering dynamics and the influence of the spatial structures on the genetics is explored numerically. The genetics is measured by means of standard statistical observables such as fixation time, that is found to be strongly influenced by the level of communication between high density peaks.

Secondly the situation of front propagation in a medium with ‘external’ inhomogeneities is investigated. When the population duplication time is much larger than the turnover time of eddies, a turbulent area can be modeled by replacing the microscopic diffusion coefficient by an enhanced effective total diffusivity. Numerical simulations with a non-homogeneous diffusion coefficient are employed to explore the effect of inhomogeneities on the population dynamics and genetics. Initially the effect of single modified areas is analyzed, then a quenched random medium is also considered. The front dynamics is characterized in terms of front shape and front speed and the genetic dynamics is characterized in terms of heterozygosity and fixation time. It was found that inhomogeneities accelerate the decay of the heterozygosity and reduce the global fixation time. Finally the connection between roughness of the front and the genetic boundaries motion is clarified in expanding populations. Special attention is given to the role of enhanced roughness in defining the fate of species correlation in random media.
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<td>Selective advantage of species $A$</td>
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<td>Macroscopic selective advantage of species $A$</td>
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<tr>
<td>$c$</td>
<td>The concentration of a chemo-attractant $L^{-d}$</td>
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<td>$c_i(x,t)$</td>
<td>The concentration of species $i$</td>
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<td>$\mathcal{D}_g$</td>
<td>The genetic diffusion constant $T^{-d}$</td>
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<td>$d$</td>
<td>The dimensionality</td>
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<td>$D, D_s$</td>
<td>The spatial diffusion coefficient $L^{dT^{-1}}$</td>
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<td>$D_g$</td>
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<td>$\mathcal{F}_{ex}$</td>
<td>Excess free energy</td>
<td>24</td>
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<tr>
<td>$f(t)$</td>
<td>The frequency of one species at time $t$</td>
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<td>$f_{energy}(\rho)$</td>
<td>The free energy density $JL^{-d}$</td>
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<tr>
<td>$H(x,t)$</td>
<td>The heterozygosity which is the probability of two individuals at distance $x$ and time $t$ to be of a different type</td>
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<td>$K(t)$</td>
<td>The function that computes the chance in the local chemoattractant concentration</td>
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<td>The size of a local fixated domain $L$</td>
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<td>$n(r)$</td>
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<td>$N_l$</td>
<td>The number of individuals in deme $l$ in the SSM</td>
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<td>$P(t,f)$</td>
<td>The probability density function for $f(t)$ at time $t$ measured in generation</td>
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<td>$p(x,t)$</td>
<td>The probability density of one particle</td>
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<td>$p_{ss}$</td>
<td>The steady-state probability density</td>
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\( q \) Wave vector \( L^{-1} \) page 42

\( R(x, t), L(x, t) \) The probability densities of finding a particle at position \( x \) and time \( t \) and moving respectively rightwards or leftwards page 22

\( T^1(x) \) The mean first passage time of a trajectory \( T \) page 33

\( V \) The drift speed \( LT^{-1} \) page 22

\( v \) The swim speed of a run-and-tumble particle \( LT^{-1} \) page 21

\( v_s \) The steady state passage rate of the front \( Ls^{-1} \) page 67

\( v_r \) The velocity inside a high diffusion area \( LT^{-1} \) page 62

\( v_s \) The sedimentation speed \( LT^{-1} \) page 22

\( w \) characteristic length which is used to calculate the density \( L \) page 25

\( X_i \) A discrete particle of type \( i \) page 14

\( (Z) \) The effective carrying capacity page 16

**Greek Letters**

\( \alpha \) The tumble rate of a run-and-tumble particle \( T^{-1} \) page 21

\( \Delta \) The interparticle distance \( L \) page 29

\( \delta \) Length of the interaction domain \( L \) page 14

\( \epsilon \) The perturbation of the front velocity page 66

\( \Gamma(x, t) \) A white zero mean Gaussian nose which is delta correlated in space and time page 9

\( \kappa \) Surface tension parameter that control the gradient in the bacterial density page 41

\( \lambda_{ij} \) The macroscopic death rate of death by competition \( T^{-1} \) page 14

\( \tilde{\lambda}_{ij} \) The microscopic death rate by competition \( T^{-1} \) page 14

\( \mu_i \) The growth rate of species \( i \) \( T^{-1} \) page 9

\( \omega \) The front roughness \( L \) page 71

\( \rho(r) \) The bacterial density at position \( r \) \( ML^{-d} \) page 23

\( \sigma \) The standard deviation of a Gaussian probability distribution page 37
\( \tau_f \) The local fixation time \( T \) page 12

Subscripts

\( i \) \( i \) represents species \( A \) or \( B \) page 13
\( j \) \( j \) represents species \( A \) or \( B \) page 13
\( l \) The deme number in the Stepping Stone Model page 13
Introduction

Population growth requires new space and resources, such as nutrients. When both factors are available populations will expand, which is quite common in natural ecosystems. During such an expansion individuals inside a population can interact due to cooperation or competition, but even neutral mutations display a non-trivial dynamics. In this work the focus is on the case where this expansions happen in non homogenous media, having in mind, the dynamics of micro-organisms living in an aquatic environment. Such an aquatic environment can for example include turbulent flows. So far most research on turbulent transport includes passive particles [33]. In this research particles are not passive but active, since they can reproduce, die and sometimes even swim. The combination of active particles and inhomogeneities in the domain creates a challenging research field and the goal of this work is to understand expanding populations of active particles in inhomogeneous media.

Dynamics and genetics in population expansions

Population expansions are common in biology, with species invading new territories starting form their homeland. In this work the main question is how inhomogeneities in the domain influence the dynamics and the genetics of such an expanding population. Genetics is the study of species diversity, which is influenced by evolutionary processes as natural selection and mutations. This work has an application to the dynamics of marine organisms like phytoplankton and thus the focus will be on modeling dynamics and genetics that can happen in that context. In figure 1 a photo of a plankton bloom in the ocean near Iceland is shown. Different phytoplankton species can compete in the same ecosystem for resources, while being advected by oceanic currents and being mixed by turbulence. It is well known that even passive tracers can develop patches in turbulent environments [7]. Here the competition between transport and growth makes the problem even more complex and challenging.

To investigate the dynamics of an expanding population the focus is on two main features. The first one is the development of spatial structures in a population, which can be caused by both internal and/or external factors. An example of an external factor is turbulence, which leads to patchiness of a phytoplankton population as shown in [7]. In this work also internal factors are included, since it is found that motility of the phytoplankton organisms increases the patchiness. Motility is the ability of organisms to move actively and is an internal factor, which should be modeled as a property of the particles themselves.

The second characteristics for the dynamics of population expansions are the front shape and the front velocity. Inhomogeneities in the domain can change the velocity of organisms locally and therefore influence the front shape and behavior. The expansion of organisms can be blocked by obstacles in the environment, but a velocity increase is also possible. When the time scale for reproduction of organisms is much larger than the time scale of turbulence a turbulent region can act as an effective mixing mechanism and can be seen as an effective increase of the swimming speed and associated diffusivity.

In a population expansion the focus is on the dynamics at the front, since only the offspring of organisms at the front will occupy the new territory. Therefore the local population density, which includes only individuals at the front, is much smaller then the total population density.
This density reduction in the front, as sketched in figure 2a, enhances the effect of genetic drift, which is the fluctuation in a species frequency due to randomness. When two species are equally fit and randomly distributed in the front by chance, i.e. due to randomness one of the two species might leave behind more offspring in the updated front. Therefore the next generation will include more organisms of the 'lucky' species. As a result sectors consisting of one species develop, which is called local fixation, and eventually one of the two species can take over the whole front, which is called global fixation. An example of an experiment in which the effect of genetic drift in the front is observed is shown in figure 2b. The experiment shows a radial expansion of a bacterial population of the \textit{E. Coli} bacterium, on the scale of millimeters, on an agar plate. The bacteria are genetically modified such that they can express different fluorescent proteins. With a fluorescent microscope both proteins can be distinguished and in figure 2b they are indicated with red and green. The development of well defined red and green sectors due to genetic drift is clearly observed. The interfaces between the red and green segments wander around and this dynamics is important for local and global fixation.

A major part of the theoretical models and the experiments done so far are in the well mixed limit. In a well-mixed population no spatial structure are present and all the individuals are equally likely to interact with each other. Research in this well-mixed limit increases the understanding of for example genetic drift, however it does not provide a complete picture since spatial structures are neglected and genetic drift is underestimated. Moreover most earlier studies focus on population expansions in homogeneous media, while in this work the focus is on inhomogeneous media. Domain inhomogeneities can increase the role of genetic drift at the front, therefore a model that allows for fluctuations and includes spatial structures is used to investigate the influence of inhomogeneities on population dynamics and population genetics.
Figure 2: In panel (a) a sketch of a population front expanding in time is shown in which two species are present that are neutral variants of each other. The population density decreases at the front, which increases the role of fluctuations. This is also of importance at the front of the expanding bacterial population shown in panel (b). Here a fluorescent image of a bacterial colony consisting of two types of bacteria that are neutral variants of each other but express different fluorescent proteins, indicated with red and green in this picture, is shown. The experiment is performed by F. Tesser.

Report layout

Population dynamics and genetics in inhomogeneous media are mostly studied numerically. In this work the focus is on how the dynamics and the genetics of a population is influenced by spatial non-homogeneities. The first chapter of this report is an introduction to the theory of population dynamics and genetics, which is the fundament for the numerical model used in this research. The numerical model is then introduced and results are presented to show that the model does correctly reproduce the same basic theoretical predictions for population dynamics as well as genetics. In the same chapter the concepts of motility and external perturbations in the environment are introduced and it is explained how these concepts can be implemented in the numerical model. Again results are given to validate the model.

In the second chapter the focus is on the development of spatial non-homogeneities in a population, caused by internal or external inhomogeneities. First the state of the art of research on pattern formation in populations is given. Then results concerning the pattern formation dynamics and the influence of such patterns on the genetic dynamics are presented.

In chapter 3 the focus is on population expansions in inhomogeneous media. The influence of such non homogeneities on the front dynamics and the population genetics of an expanding population is investigated numerically. Starting from the simple geometry corresponding to one single region with high or low diffusivity, the situation of a quenched distribution of inhomogeneities is ultimately considered. To model an expanding population in such a quenched disorder in an efficient way, a simple event driven model for the front dynamics is developed. With this model front shape and front velocity for the propagation in a random medium can be explained and compared to analytical results. Finally also the genetics of a population expanding in a random medium is investigated numerically in chapter 3. In chapter 4 conclusions are drawn with recommendation and suggestions for further research in the field of population dynamics and genetics, especially for what concerns the possibility to experimentally validate the case of the perturbations.
Chapter 1

Theoretical background

1.1 Population dynamics and genetics

In this work the influence of inhomogeneities on population dynamics and population genetics is studied numerically using a discrete particle model, with certain rules for birth, death and displacement by diffusion.

1.1: Population genetics

Population genetics is a scientific discipline that studies how evolutionary forces, such as Darwinian selection, mutations and genetic drift, influence the genetic diversity of a population. In a population different species and genes are present. A gene is the heredity of living organisms and an allele is a specific type of a gene. A neutral mutation mutates an allele without changing its ability to survive or reproduce. By random drift such a neutral mutation can survive and change the allele frequency in a gene pool, which is called neutral selection [18].

In this chapter the theoretical background of population dynamics and genetics is given, with the description of several well-known population models and the underlying theory. Some of these models include spatial structures while others do not. A model without spatial structures is the well-mixed model. In this model all individuals are equally likely to interact with each other. An example of a population in a well-mixed cylindrical cell is shown in figure 1.2a. A model that does include spatial structures is the Stepping Stone Model (SSM). In the SSM the domain is discretized into multiple well-mixed cells, as sketched in figure 1.2. Both the well-mixed model and the SSM are introduced in section 1.1.1. Moreover it is explained how the extinction dynamics can be characterized in a statistical way via the two point correlation function, the so called heterozygosity, and how it behaves as a function of time and space. In the last part of section 1.1.1 it is described how an expanding population can be described as a Fisher wave with its corresponding Fisher speed.

After giving the theoretical background on population modeling the model used in this work is introduced. This individual based model, with certain rules for birth and death, was first introduced in [28] and is similar in spirit to the SSM, however the model allows for density fluctuations in the population while in the SSM the density is constant. At the end of this section it is investigated numerically if above introduced theories of heterozygosity and Fisher speed are still valid for this fluctuating density model.
1.1.1 Theoretical introduction to population dynamic and genetics

The well-mixed population model

1.2: Genetic drift

Genetic drift is the change in a species frequency due to random fluctuations. In figure 1.1 the frequency of one species of a population consisting of two species, which are neutral variants of each other, is shown in time for a well-mixed population of size $N = 100$ and $N = 10$. The Moran process is used to model birth-and-death, which will be explained below. In the Moran process the population size is fixed. The random fluctuations in $f(t)$ are visible and it is moreover observed that the fluctuations are more important in the smaller population. This means that the role of genetic drift is stronger when the population size is smaller. A measure for the fluctuations in the species frequency is the genetic diffusion constant, which equals $D_g = \frac{2\mu}{N}$, where $\mu$ is the growth rate and $N$ is the global population density. [21]

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{The frequency, $f(t)$, of species $A$ in a well-mixed population consisting of two species, species $A$ and species $B$ for $N = 10$ and $N = 100$.}
\end{figure}

The classical results for population dynamics in (well-mixed) homogeneous environments date back to the works of Wright, Fisher, Haldane, and Kimura amongst the others [5]. The theoretical descriptions given in this section of both the well-mixed model and of the spatial Stepping Stone Model are mainly taken from the review of Korolev et al [21].

In a well-mixed population model no spatial structures are present and every individual is equally likely to interact with any other individual. The well-mixed model provides the simplest context in which mutation, selection and genetic drift can be studied. The well-mixed model has disadvantages associated to its simplicity. First, the role of genetic drift is underestimated. In reality an organism can only interact with its neighbors and the number of neighboring individuals is much smaller than the total number of individuals in the population and the role of genetic drift is stronger in smaller populations. Second, the spatial structure of the population is completely neglected. Such structures do often exist and can influence the evolutionary processes significantly [21].

To investigate population genetics using a well-mixed model certain rules for birth and death should be imposed on the discrete particles. A simple model of such birth-and-death reactions is the Moran model [21]. In the Moran model it is assumed that two different species $A$ and $B$ are present. At each time step two individuals are randomly selected; one of these individuals is chosen to reproduce and the other one is chosen to die. The fraction of one species in the total population, of global size $N$, at time $t$ is called the frequency, $f(t)$. The expectation value of this frequency at time $t + 1$ is

$$\langle f(t + 1) \rangle = f(t),$$

(1.1)
where the average is taken with respect to the random choice of individuals for reproduction and death and time \( t \) is measured in generation time. The above equations imply that \( f(t) \) behaves as an unbiased random walk in the space of species frequencies, with a frequency-dependent diffusion coefficient. Some examples of this unbiased random walk are shown in figure 1.1, where the frequency, \( f(t) \), is shown in time. In the continuum limit the random walk of the frequency follows the following Fokker-Planck equation:

\[
\frac{\partial P(t, f)}{\partial t} = \frac{D_g}{2} \frac{\partial^2}{\partial f^2} [f(1 - f) P(t, f)],
\]

where \( P(t, f) \) is the probability density function for the frequency \( f(t) \) at time \( t \) and \( D_g \) is the genetic diffusion constant. In the Moran model this genetic diffusion constant is

\[
D_g = \frac{2}{N \tau_g},
\]

where \( \tau_g \) is the generation time and \( N \) the number of particles in the volume. In equation (1.3) it is assumed that no selective advantage is present.

### 1.3: Selective advantage

When an individual or a species has a selective advantage it is more fit to the environment and therefore has a higher probability to survive compared to other individuals or species.

A selective advantage can be implemented as well in the model by simply introducing different growth rates for the different species, i.e. the probability of reproduction for species \( A \) in the Moran model is changed from \( f \) to \( \frac{\mu_A f}{\mu_A f + \mu_B (1 - f)} \), where \( \mu_A \) and \( \mu_B \) are the growth rates of species \( A \) and species \( B \) respectively. The resulting expectation value for the frequency is now biased:

\[
\langle f(t + 1) \rangle = f(t) + \frac{f(t)[1 - f(t)](\mu_A - \mu_B)}{N[\mu_A f(t) + \mu_B (1 - f(t))]}.
\]

In the weak selection limit, that is for \( |\mu_A - \mu_B| << \mu_A + \mu_B \), the above equation reduces to

\[
\langle f(t + 1) \rangle = f(t) + \frac{\tilde{a}}{N}[1 - f(t)],
\]

with

\[
\tilde{a} = \frac{2(\mu_A - \mu_B)}{\mu_A + \mu_B}.
\]

When \( \tilde{a} \) is positive, the species \( A \) has a selective advantage and when \( \tilde{a} \) is negative the selective advantage is for the species \( B \). The corresponding Fokker-Planck equation is given by

\[
\frac{\partial P(t, f)}{\partial t} = -a \frac{\partial}{\partial f} [f(1 - f) P(t, f)] + \frac{D_g}{2} \frac{\partial^2}{\partial f^2} [f(1 - f) P(t, f)],
\]

where \( a = \frac{\tilde{a}}{\tau_g} \). An alternative formulation is a stochastic differential equation, which is more easy to generalize to spatial models. In the case of a Moran process with selective advantage this stochastic equation for the evolution of \( f(t) \) is

\[
\frac{df(t)}{dt} = af(t)[1 - f(t)] + \sqrt{D_g f(t)[1 - f(t)]} \Gamma(t) \quad (\text{Itô}),
\]

where \( \Gamma(t) \) is a zero mean Gaussian noise, white in time, i.e. \( \langle \Gamma(t_1) \Gamma(t_2) \rangle = \delta(t_1 - t_2) \). The Itô prescription is necessary to remove the ambiguity in the interpretation of the stochastic term. It is appropriate in population genetics, because a random change on the frequencies depends only on the genetic composition at the time before the change.
Figure 1.2: In panel (a) a sketch of a population inside a well-mixed cylindrical cell is given. Two species are present in a well-mixed test tube obeying the Moran rules for birth and death. In panel (b) a sketch of the Stepping Stone Model is shown. The domain is discretized into well-mixed demes, such as sketched in panel (a). The deme number $l$ is defined as $l = -\infty, \ldots, -1, 0, 1, \ldots, \infty$ and the population within one deme is indicated with $N_l$. The arrows indicate migration of one deme to its nearest neighbor, which occurs with a migration rate $m$.

Stepping Stone Model

An example of a model in which a spatial structure is implemented in an easy and efficient way is the Stepping Stone Model (SSM), which was introduced by Kimura in 1953 [19]. This subsection is an introduction to the SSM closely based on the review of Korolev et. al [21]. In the SSM the domain is discretized into a number of islands, called demes. Inside these demes the population is assumed to be well mixed. It is further assumed that each deme is saturated to its maximal sustainable population size and therefore the number of organisms in one deme, denoted by $N_l$, is constant and equals the carrying capacity of that deme. In the SSM birth-and-death reactions, described by the Moran model, take place within a single deme while spatial displacement only occurs as exchange of particles between neighboring demes. This exchange is called migration and occurs with a rate $m$ as sketched in figure 1.2. The frequency of one species inside deme $l$ is $f_l(t)$. In the continuum limit the stochastic differential equation for the evolution $f_l(t)$ in the case of a selective advantage $a$ is

$$\frac{df_l}{dt} = \frac{m}{2} (f_{l-1} + f_{l+1} - 2f_l) + af_l (1 - f_l) + \sqrt{D_g f_l (1 - f_l)} \Gamma_l,$$

(1.10)

where $\Gamma_l$ is a white zero mean Gaussian noise which obeys $\langle \Gamma_{l_1}(t_1) \Gamma_{l_2}(t_2) \rangle = \delta_{l_1l_2} \delta(t_1 - t_2)$. Introducing a spatial coordinate $x = ls$, where $s$ is the deme size, reshapes this equation to

$$\frac{df}{dt} = D_s \frac{\partial^2 f}{\partial x^2} + af(1 - f) + \sqrt{D_g f(1 - f)} \Gamma,$$

(1.11)

where the spatial diffusion constant is $D_s = \frac{ms^2}{2}$ and the genetic diffusion constant is $D_g = sD_g$. Equation (1.11) includes a spatial diffusion term and is known as the stochastic Fisher-Kolmogorov-Petrovsky-Piscounov equation (FKPP-equation).
Heterozygosity

1.4: Heterozygosity

The heterozygosity quantifies the probability, in statistical sense, of finding two individuals of a different type at distance $x$ for a given time $t$. The heterozygosity is used to investigate the statistics of the genetics and the fixation inside a population. More precisely the heterozygosity $H(x,t)$ is defined as

$$H(x,t) = \langle 2f(x,t)[1-f(x,t)] \rangle.$$ (1.12)

An important parameter for the population genetics is the heterozygosity. When extinction of one of the species occurs the heterozygosity goes to zero. In the neutral Stepping Stone Model with a fixed population size, $H(x,t)$ behaves according to the following differential equation:

$$\frac{\partial H(x,t)}{\partial t} = D\nabla^2 H - D_g H(x,t) \delta(x),$$ (1.13)

where $D$ is the spatial diffusion coefficient. Equation (1.13) can be derived from the stochastic equation for the species frequency in the neutral case, equation (1.11) with $\alpha = 0$, as shown in [21]. As shown in [21] equation (1.13) can be solved explicitly in 1D. The solution is:

$$H(x,t) = H_0 - D_g \int_0^t dt' e^{-x^2/4D(t-t')} \frac{H(t',0)}{\sqrt{8\pi D(t-t')}},$$ (1.14)

in which $H(0,t)$ is the local heterozygosity defined as $\lim_{x \to 0} H(x,t)$. The expression for this local heterozygosity is

$$H(t,0) = H_0 \text{erfc} \left( \sqrt{\frac{D_g t}{8D}} \right) e^{D_g t/8D},$$ (1.15)

where $H_0$ is the initial heterozygosity, which is one half in the case of a random mixed population at $t = 0$ and erfc($x$) is the complementary error function. For $t \geq 8D/D_g^2$ equation (1.15) becomes

$$H(t,0) = H_0 \left( \frac{\pi D_g^2 t}{8D} \right)^{-1/2} + O(t^{-3/2}).$$ (1.16)

The local heterozygosity can be used to characterize the local fixation of the species, since if $H(t,0) \ll 1$ the demes are fixed to one of the two species locally and the population appears demixed in sectors occupied only by a single species.

From equation (1.16) it is shown that in 1D the local heterozygosity $H(0,t)$ decays as $t^{-1/2}$ at long times, which is connected to the probability of merging of two genetic interfaces (the interface between two different species), that perform a Brownian walk in 1D. In two dimensions this decay is much slower and goes as $H(0,t) \sim \frac{1}{\ln t}$. Also front roughness influences the decay of the local heterozygosity at the front. When a population is expanding in time in a homogeneous domain undulations in the population front can develop because of noise. These undulations can bias the direction of the genetic interface motion locally, which changes the survival probability of locally fixed sectors and therefore the decay of the heterozygosity. It is found experimentally by Hallatschek, in the case of non-motile E. Coli bacteria expanding on an agar plate, that the motion of the genetic interface is indeed biased and can be characterized as superdiffusive [10]. In [24] this superdiffusive behavior is found numerically and it was shown that the local heterozygosity decays as $H(0,t) \sim \frac{1}{\tau^{3/2}}$ in the case of rough front propagation.
1.5: Fixation

Fixation is the situation in which one species takes over a population that initially consists of two or more species. Local and global fixation are distinguished. Local fixation describes the process of the development of sectors consisting of just one species, which decreases the heterozygosity locally as a result of the genetic drift. After local fixation has occurred, eventually a population fixates globally, such that only one type of individuals is present in the species. This process is connected to the way the borders of genetic sectors merge while wandering. In figure 1.3 an experiment is shown in which local fixation is observed by the development of red and green sectors.

Figure 1.3: A fluorescent image of a bacterial colony consisting of two types of bacteria that are neutral variants of each other but express different fluorescent proteins, indicated with red and green in this picture. The experiment is performed by F. Tesser.

From equation (1.16) it is seen that local fixation occurs at long times, since \( \lim_{t \to \infty} H(0, t) = 0 \). The characteristic fixation time for local fixation is:

\[
\tau_f = \frac{8D}{\pi D g} \sim N_l^2, \tag{1.17}
\]

where \( N_l \) is the population size in a deme in the SSM. The characteristic length scale for the local fixated segments, \( l(t) \), can be obtained from the solution \( H(x, t) \) of equation (1.13) as shown in [21]:

\[
l = \frac{\sqrt{2\pi Dt}}{2f_0(1 - f_0)} \tag{1.18}
\]

Expanding populations as Fisher waves

In the presence of space and resources populations can start to expand. It is known that such a population expansion in a homogeneous medium can be described by a Fisher wave. In [6] it is shown how an expression for the Fisher velocity in the low and high noise regime can be derived from the Fisher-Kolmogorov-Petrovsky-Piscounov equation. Here a short version of this derivation is given. As mentioned in section 1.1.1 the dynamics of the species frequency can be described by the FKPP-equation in continuous time and space. The stochastic FKPP-equation is

\[
\frac{df(x,t)}{dt} = D\frac{\partial^2 f}{\partial x^2} + af(1 - f) + \sqrt{D_s f(1 - f)\Gamma(x,t)} \quad \text{(Ito)}, \tag{1.19}
\]

where the second term on the right-hand-side is the logistic growth term, for which the ordinary differential equation is

\[
\frac{df}{dt} = af(1 - f). \tag{1.20}
\]

This equation has two stationary solutions, one unstable solution for \( f = 0 \) and one stable solution corresponding to the fixed point \( f = 1 \). In the SSM spatial structures are implemented by migration between demes, which results in an diffusion term in the FKPP-equation:

\[
\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2} + af(1 - f), \tag{1.21}
\]
with \( 0 \leq f \leq 1 \) and initial conditions \( \lim_{x \to -\infty} f(x,t) = 1 \) and \( \lim_{x \to +\infty} f(x,t) = 0 \). This FKPP equation describes the invasion of the stable state \( f = 1 \) into the regions of the unstable extinct phase \( f = 0 \). The propagation of the front associated to this invasion has a constant velocity, which can be found from the traveling wave solutions. The traveling wave solutions of the FKPP-equation are of the form:

\[
f(x,t) = F(z) = F(x - v_f t), \tag{1.22}
\]

where \( v_f \) is the Fisher speed in positive \( x \) direction and \( F(z) \) is an equation for the front shape. To derive an expression for the Fisher speed \( v_f \), the traveling wave solution is substituted in the FKPP-equation which results in the following ordinary differential equation

\[
DF''(z) + v_f F'(z) + aF(z)(1 - F(z)) = 0, \tag{1.23}
\]

with the corresponding initial conditions \( \lim_{z \to -\infty} F(z) = 1 \) and \( \lim_{z \to +\infty} F(z) = 0 \). This differential equation can be compared to the dynamics of a body of convenient mass moving in the potential \( V(F) = \frac{1}{2}F^2 - \frac{1}{3}F^3 \). Oscillations around 0, near \( f = 0 \), should be prevented, which means that \( v_f \) (the friction coefficient in the case of a mass moving in a potential) should be sufficiently high so that the stable fixed point \((f, f') = (0, 0)\) is a node and not a spiral. This results in the condition \( v_f \geq 2\sqrt{D\mu} \). For sufficiently sharp initial fronts at time \( t = 0 \) the minimum speed is selected [20], which leads to the following expression for the Fisher speed in the case of a sharp initial front:

\[
v_f = 2\sqrt{aD}. \tag{1.24}
\]

Moreover it is found that this sharp front will broaden to a width of order \( \sqrt{D/\mu} \) [9]. Since the above expression for the Fisher speed is derived from the FKPP-equation without noise it can only be applied in the weak noise limit, which is the regime in which \( N\sqrt{D/\mu} \gg 1 \). Outside this weak noise regime there is no exact expression known for the front velocity in the interacting particle model, which obeys the stochastic FKPP equation. However for the strong noise limit a velocity expression can be found as will be explained below.

In the strong noise limit, i.e. when \( N\sqrt{D/\mu} \leq 1 \), the stochastic FKPP is dual to a diffusion-controlled particle reaction [6]. It is known that for the wave-front in the diffusion-limited process the velocity is exactly \( v = D\rho_{eq} \), where \( \rho_{eq} \) is the equilibrium density. In the discrete particle model this equilibrium density is the number of particles per cell, which equals \( \rho_{eq} = \frac{2a}{x_g} \). Now the velocity of stochastic FKPP wave in the strong noise limit is

\[
v_f = D\rho_{eq} = \frac{2aD}{D_g}. \tag{1.25}
\]

The two expressions found for the Fisher velocity in the low and high noise limit are in agreement with numerical simulations as shown in [6]. In figure 1.4 the result from [6] for the Fisher wave as a function of the dimensionless noise strength is shown. The velocity is normalized by the minimum no-noise speed \( 2\sqrt{aD} \).

### 1.1.2 Numerical method for population dynamics and genetics

**Model with density fluctuations**

The model that is used in this research is based on the Stepping Stone Model, however now the density is allowed to fluctuate locally as well as globally, as explained below. This model with fluctuating deme density is described in the paper of Pigolotti et al [28] about growth and competition in spatial population genetics.

Individuals are assumed to diffuse in continuous space with a diffusion constant \( D \), obeying the following equation of motion:

\[
x(t + \delta t) = x(t) + L(t)\sqrt{2D\delta t}, \tag{1.26}
\]
Figure 1.4: The velocity of the traveling wave in the sFKPP equation, normalized by the minimum velocity, $2\sqrt{Da}$, as a function of the dimensionless noise strength. Two regimes are distinguished: the weak- and the strong-noise regime. The figure is reproduced from [6].

where the mean of $L(t)$ is zero and the correlation function is $\langle L(t)L(t') \rangle = \delta(t-t')$ [36].

Also the equations for the birth-and-death processes differ from the Moran process, since now the deme population is not fixed anymore. The birth-coagulation process is described by the following equations:

$$X_i \xrightarrow{\mu_i} 2X_i \quad \text{(reproduction)} \quad (1.27)$$
$$X_i + X_j \xrightarrow{\tilde{\lambda}_{ij}} X_i \quad \text{(death by competition)} \quad (1.28)$$

In this case the indices $i$ and $j$ correspond to either species $A$ or species $B$ and $\tilde{\lambda}_{ij}$ is the death rate by competition inside an interaction range $\delta$. Unlike in the Moran process the population size is not fixed and the density of the organisms fluctuates both locally and globally. [28]

To derive the stochastic equations the number densities $n_A(x,t)$ and $n_B(x,t)$ are introduced. From this number densities the concentrations can be defined as $c_A(x,t) = n_A(x,t)/N$ and $c_B(x,t) = n_B(x,t)/N$, where $N$ is a constant parameter that represents a particle density and is assumed to be of the same order of magnitude as $n_A$ and $n_B$. A constant density $c = 1$ thus corresponds to a uniform distribution of $N$ individuals in a segment of length 1 (in 1D). $N$ has a similar role as the deme population size $N_l$ in the SSM, however $N_l$ is a number of particles and $N$ represents a particle density. The macroscopic equations describing the evolution of the concentrations $c_A$ and $c_B$ are

$$\frac{\partial}{\partial t} c_A = D\nabla^2 c_A + c_A(\mu_A - \lambda_{AA}c_A - \lambda_{AB}c_B) + \sqrt{\frac{c_A(\mu_A + \lambda_{AA}c_A + \lambda_{AB}c_B)}{N}} \Gamma, \quad (1.29)$$
$$\frac{\partial}{\partial t} c_B = D\nabla^2 c_B + c_B(\mu_B - \lambda_{BA}c_A - \lambda_{BB}c_B) + \sqrt{\frac{c_B(\mu_B + \lambda_{BA}c_A + \lambda_{BB}c_B)}{N}} \Gamma, \quad (1.30)$$

where $\lambda_{ij}$ is the macroscopic death rate, which equals $\lambda_{ij} = N\delta \tilde{\lambda}_{ij}$, and $D_g$ is the genetic diffusion constant which is $D_g = \frac{2\mu}{N}$. As mentioned before the parameter $\delta$ represents the size of the interaction domain within which particles compete. A convenient choice for the interaction length $\delta$ is $\delta = 1/N$. In this case there is one particle per interaction cell present and $\lambda_{ij} = \tilde{\lambda}_{ij}$. Like in equation (1.9) $\Gamma$ represents a Gaussian noise which is delta correlated in space as well as in time, $\langle \Gamma(x,t)\Gamma(x',t') \rangle = \delta(t-t')\delta(x-x')$, that should be interpreted according to the Itô prescription. There are three biological relevant choices for the birth- and death rates $\mu_i$ and $\lambda_{ij}$. The three cases are described below:
**Neutral theory**

In this case the two species are neutral variants of each other, which means that they are equally fit to the environment and that their growth rates and their death rates are the same. The parameter choice in this case is $\mu = \mu_A = \mu_B$ and $\lambda = \lambda_{AA} = \lambda_{AB} = \lambda_{BA} = \lambda_{BB}$. When the neutral case is used the species will demix as time progresses. Eventually fixation of one species occurs because of coalescence of the domain boundaries. An example of a simulation in the neutral case is shown in figure 1.5a. It is seen that the species are indeed demixed and that fixation will eventually occur.

**Reproductive Advantage**

A reproductive advantage is given to one of the species by changing the growth rate. In this case $\mu_A = \mu(1 + a)$, which means that species $A$ has a selective advantage if $a > 0$ and a disadvantage if $a < 0$. Furthermore $\lambda = \lambda_{AA} = \lambda_{AB} = \lambda_{BA} = \lambda_{BB}$ like in the neutral case. When one of the species has a selective advantage there is a high probability that this species eventually takes over the full domain, also when initially the advantageous species occupies a minority of the total space. This result is shown in figure 1.5b, where a simulation with species $A$ having an advantage over species $B$ is shown with species $A$ being the minority in the initial condition.

**Mutualistic Setting**

In this setting the competition between the two species $A$ and $B$ is reduced as a consequence of mutualistic interactions. This is achieved by choosing $\mu = \mu_A = \mu_B$, $\lambda = \lambda_{AA} = \lambda_{BB}$, $\lambda_{AB} = \lambda(1 - \epsilon_A)$ and $\lambda_{BA} = \lambda(1 - \epsilon_B)$. The death rates should be nonnegative and therefore it is assumed that $\epsilon_A, \epsilon_B \leq 1$. In this setting mixing of the two species is promoted since the competition is reduced. In figure 1.5c the result of a simulation in the mutualistic setting is shown and it is indeed observed that the species remain mixed over a long time. In this figure the parameters are $\mu = 1, \lambda = 1$ and $\lambda_{AB} = \lambda_{BA} = 0.3$, that results in $\epsilon_A = \epsilon_B = 0.7$. If the system is large enough the two species will remain mixed indefinitely in contrast to the neutral setting and the selective advantage case [28].

In the model described above density fluctuations play a significant role. This spatial variation in the species frequency can also result in a reduction in the average carrying capacity.
The carrying capacity of a population is the maximal population size that the environment can sustain indefinitely. Noise in the form of density fluctuations influence the carrying capacity of a system. In figure 1.6 the evolution of the number of particles is shown for a simulation of front propagation in 2-dimensional space in the neutral case. It is observed that from $t \approx 150$ the population size reaches the carrying capacity.

The effective average carrying capacity is defined as $\langle Z \rangle = \left\langle \frac{n(t)}{N} \right\rangle$, where $n(t)$ is the actual number of particles present at time $t$ per unit length and the average, indicated by $\langle \rangle$, is taken over time. From equation (1.30) it is calculated that without fluctuations this carrying capacity $\langle Z \rangle$ should equal unity. Significant deviations from this prediction indicate that the system is in the strong noise limit, where fluctuations are dominant. This strong noise limit corresponds to $N \sqrt{D/\mu} \leq 1$. This can be understood by the fact that the diffusion scale $\sqrt{D/\mu}$ can be considered as an ‘effective deme size’, since populations are mixed by diffusion. When many particles are present in such a deme, i.e. $N \sqrt{D/\mu} \gg 1$, the role of fluctuations is not very important. This case is called the ‘weak noise limit’. In the ‘strong noise limit’ the number of particles present in one deme is small and the role of fluctuations becomes much more important [28].

In the model different types of boundary conditions can be implemented. The most used boundary conditions is the periodic boundary condition. A periodic boundary condition implies that a particle passing one of the boundaries is reappearing on the opposite boundary. Periodic boundary conditions are a convenient choice when simulating a large system and are therefore used in most of the simulations performed in this research. When using periodic boundary conditions the number of genetic interfaces is always even. Sometimes it is desirable to have an odd number of interfaces since new phenomena can arise, for example, the fixation time can become longer when only one interface is left [27]. In this case periodic boundary conditions are not adequate. A simple alternative is then to simply disregard particles moving outside the domain: this boundary conditions is called an open boundary condition. A mix of both condition is also possible. For example when a population is expanding in a linear space periodic boundary conditions are only used in the lateral direction and open boundary conditions are used in the propagation direction. The type of boundary condition can influence the noise level in a simulation. In figure 1.7 the effective average capacity $\langle Z \rangle$ is plotted as a function of the non-dimensional noise parameter $N^{1/4} \sqrt{D/\mu}$ (with $d$ being the dimensionality) for both open and periodic boundary conditions. It is seen that the weak and strong noise limits introduced before are indeed observed, since for small values of $N^{1/4} \sqrt{D/\mu}$ the average carrying capacity is much smaller than the saturation value and for larger values of $N^{1/4} \sqrt{D/\mu}$ the effective carrying capacity approaches the saturation value. Moreover it is observed that in the case of open boundary conditions the curve for $\langle Z \rangle$ is shifted downwards, however the behavior of the carrying capacity is similar. This is expected since in the case of open boundary conditions particles crossing the domain boundary disappear, so an outwards flux results in a smaller population size and therefore in a lower average carrying capacity.
The average effective carrying capacity $\langle Z \rangle$ as a function of the noise level, $N \sqrt{D/\mu}$, in 1 dimension for periodic boundary conditions and open boundary conditions.

Heterozygosity in the discrete particle model

Heterozygosity is an important measure for the extinction dynamics of a population. In the model used in this work the heterozygosity is computed by first introducing a bin size $h$, which is equal to the interaction distance $\delta$. Then the number of individuals separated with a distance between $r$ and $r + h$ and being of a different types is calculated. The heterozygosity is now calculated as the ratio between this number of individuals and the total number of pairs within this separation range. In figure 1.8a the heterozygosity $H(x, t)$ is shown as a function of $x$ in 1D for three different times $t$. In the same figure the solution from equation (1.13) is shown as a solid line. It is seen that the data points follow this line, which indicates that the heterozygosity computed from simulations recovers the analytical solution. In figure 1.8 also the decay for the local heterozygosity, $H(0, t)$ is shown for both 1D and 2D. As explained in section 1.1.1 this decay is expected to go as $H(0, t) \sim \frac{1}{t^{1/2}}$ in 1D and as $H(0, t) \sim \frac{1}{\ln(t)}$ in 2D. From the fits performed on the data for the local heterozygosity in figure 1.8b and figure 1.8c this expected decay is indeed observed.

Since the heterozygosity characterizes the fixation dynamics the fixation time and the fixation length can be derived from the expression for the heterozygosity. It is found that the fixation time is proportional to the square of the deme population, as shown in equation (1.17). To validate if this equation is valid for the model used in this work the evolution of a 1D population for different values of population size $N$ is shown in figure 1.9. It is observed that the local fixation time is lower for lower population sizes as expected from equation (1.17). Substituting the three different values of population size $N$ is shown in figure 1.9. It is observed that the local fixation time is lower for lower population sizes as expected from equation (1.17). Substituting the three different values of population size $N$, $N = 1000$, $N = 2000$ and $N = 4000$, in equation (1.17) result in the following local fixation times: $\tau_f = 16$, $\tau_f = 64$ and $\tau_f = 255$. In figure 1.9 the black dashed lines show these local fixation times. From equation (1.18) it is expected that the size of the fixated segments does not depend on the number of particles $N$. From figure 1.9 it is indeed observed that the pattern size is similar for all three values of $N$. Using equation (1.18) the fixation length at $t = 400$ is calculated as $l = 0.5$. The segments shown in figure 1.9 are of this order of magnitude.

Fisher wave

Both a population expansion in empty space and an advantageous species invading a domain filled with the other disadvantageous species can be described by a Fisher wave. In the first case the initial condition is a thin layer of particles in an empty domain. When this particle layer starts to invade the empty domain a Fisher wave evolves in the direction of the empty domain. For a population expanding in an empty domain the logistic growth term $a$ in the FKPP equation (equation (1.21)) is equal to the birth rate $\mu$. In the second case initially a thin layer of particles consisting of an advantageous species $A$ is implemented in a domain filled with
Figure 1.8: Plots of the heterozygosity $H(x,t)$ as a function of $x$ and the local heterozygosity $H(0,t)$ as a function of $t$ in both 1D and 2D. In panel (a) the heterozygosity $H(x,t)$ is plotted as a function of $x$ for three different times in 1D. The dots represent simulation data and the solid lines represent the solutions of equation (1.13). In panel (b) the decay of the local heterozygosity in time is shown on a logarithmic scale in 1D. A linear fit is performed on the data which shows that the decay goes as $H(0,t) \sim t^{1/2}$. In panel (c) the decay of the heterozygosity in 2D is shown on a semi-log scale. Using a linear fit it is shown that the heterozygosity decay in 2D goes as $H(0,t) \sim \frac{1}{\ln(t)}$.

Figure 1.9: Three simulations of a 1D population expanding in time in the neutral case with $\mu = 1$ and $D = 2.5 \times 10^{-5}$ for different population sizes $N = 1000$, $N = 2000$ and $N = 4000$. The black dashed lines represent the corresponding local fixation time which are calculated as $\tau_f = 16$, $\tau_f = 64$ and $\tau_f = 255$ for $N = 1000$, $N = 2000$ and $N = 4000$ respectively.
particles of a disadvantaged species $B$. Since species $A$ has a selective advantage it will invade the rest of the domain. In this case the logistic growth term $a$ in equation (1.21) is the selective advantage as defined in equation (1.7). The initial conditions of both cases are sketched in figure 1.10. To investigate whether our model recovers the derived expressions for the Fisher speed, an invading population front is simulated both in the high- and in the low-noise regime. First a simulation with an advantageous species invading a domain occupied by a disadvantaged species is performed in the strong noise limit, where $N^{1/2} \sqrt{D/\mu} \approx 1 \leq 1$. The result of this simulation is shown in figure 1.11, where the velocity of the expansion of the advantageous species $A$ is plotted as a function of the selective advantage $a$. In a model that follows the stochastic FKPP equation the Fisher velocity is expected to be proportional to $a$ with the slope being $\frac{2D}{\mu} \approx 0.005$, calculated from equation (1.25). The slope found from the fit in figure 1.11 is $0.0052 \pm 0.0002$, which means that for the model used in this work the Fisher velocity in the strong noise limit matches the velocity computed from equation (1.25), unless that the stochastic equations (equation (1.30)) are slightly different from the stochastic FKPP equation.

To check if also equation (1.24) is recovered with our model a simulation with a Fisher wave in the weak noise limit is performed with $N^{1/2} \sqrt{D/\mu} = 15$, since $N = 90000$, $D = 2.5 \cdot 10^{-4}$ and $\mu = 0.1$. The traveling population wave is the result of population expansion in an empty two dimensional domain as sketched in figure 1.10a. The resulting front speed is computed from the linear growth of the number of particles in time. This evolution of the number of particles in time is shown in figure 1.12. A fit is performed on the linear part of the curve with resulting slope $690 \pm 4$. This slope corresponds to the growth of particles per unit time and should be normalized with the carrying capacity density in order to compute the front speed. The carrying capacity density is $N_{sat} = 6.9 \cdot 10^4$, with $L = 1$ and the resulting front velocity is $v_f = 0.010 \pm 0.001$. The Fisher speed in the weak noise limit expected from theory is calculated as $v_f = 0.01$ from equation (1.24), with $D = 2.5 \cdot 10^{-4}$ and $\mu = 0.1$. It is found that the Fisher speed determined from the simulation matches this theoretical expectation perfectly.
**Figure 1.11:** The Fisher speed of a domain boundary as a function of the selective advantage, $a$, of species A. A linear fit is performed on the data, with a resulting slope $(5.2 \pm 0.2) \cdot 10^{-3}$. The parameters used for the simulations are $\lambda = 1$ and $D = 2.5 \cdot 10^{-5}$.

**Figure 1.12:** The evolution of the number of particles in time for an expanding population wave in an empty two dimensional domain with $N = 90000, D = 2.5 \cdot 10^{-4}$ and $\mu = \lambda = 0.1$. A linear fit is performed on the linear part of the curve with the resulting slope $690 \pm 5$. The black line indicates the saturation value which is $N_{sat} = 6.9 \cdot 10^4$. 
1.2 Motility induced phase separation

Patterns can develop in populations by external factors, as nutrient levels, but also by internal factors, as motility, as experimentally observed in a motile E. Coli population in [32]. Motility is the ability of bacteria to move actively. To investigate how motility can lead to phase separation into high and low density regions the discrete particle model, defined in section 1.1.2, is extended with self-propulsion of particles that depends on the interaction between individuals.

In this section first the theoretical background of phase separation induced by motility is given. Then it is described how the discrete particle model is extended with density dependent motility of particles. Simulation results with these interacting motile particles, that do not die or reproduce yet for simplicity, are provided to investigate if the pattern formation occurs as expected from [2]. Subsequently birth-and-death processes are included to show that also the combination of logistic growth and motility can induce spatial structures in the population as expected from [3]. Since there are a lot of parameters that can be varied in this situation, at the end of this section the influence of varying each of these parameters is discussed in detail.

1.2.1 Theoretical introduction to motile particles

The mechanism that motile bacteria use to swim depends on the specific species of bacteria. A simple example is the mechanism of the Escherichia coli. These bacteria use their flagella (lash-like appendages) to rotate or swim in a straight direction. This movement can be modeled by a run-and-tumble mechanism, in which two different types of movements are distinguished. The first movement is when bacteria swim in a straight line with swimming speed $v$, called a ‘run’. The second movement is the ‘tumble event’, which is the rotational movement that changes the swimming direction. These tumble events occur with a rate $\alpha$. In figure 1.13 a sketch of the run-and-tumble movement is given. It is reasonable to assume that the duration of a run is Poisson-distributed and that a tumble is instantaneous compared to the duration of a run. In the simple case, in which the swim speed $v$ and tumble rate $\alpha$ do not depend on environmental factors, like space and density, and the run-and-tumble events are independent of previous states the bacteria perform a random walk, with an effective diffusion constant

$$D = \frac{v^2}{\alpha d}, \quad (1.31)$$

where $d$ is the spatial dimensionality. This effective diffusion constant is hundreds of times larger than the Brownian diffusion constant of colloidal particles of the same size suspended in a fluid.

For time and length scales much larger than $1/\alpha$ and $v/\alpha$, respectively, the motion of run-and-tumble particles can be mapped on a system with Brownian diffusion, which obeys a detailed balance that restores time-reversal symmetry in thermal equilibrium. At mesoscopic length scales mapping is possible only when the parameters $\alpha$ and $v$ do not vary in space. When these parameters do vary in space the movement of the bacteria is a biased process which has no detailed balance. In the following paragraph a simple 1D model for independent motile particles with space-dependent motility parameters will be explained.

Figure 1.13: A sketch of a run-and-tumble motion in which the blue arrows represent a straight run and the stars represent a tumble motion which changes the direction of the movement.
A model for independent run-and-tumble particles in 1D

In this section a 1D model with right-and-left moving particles is introduced, following [2]. The particles are confined to the $x$-axis and $R(x,t)$ and $L(x,t)$ are the probability densities of finding a particle at position $x$ and time $t$ moving rightwards or leftwards respectively. The motility parameters $\alpha_{R,L}$ and $v_{L,R}$ can be different for right- and left-moving particles depending, for example, on environmental factors. Now the equations of motion for the particles are:

$$\frac{\partial R}{\partial t} = -\frac{\partial v_{LR}}{\partial x} - \frac{\alpha_{R,R}}{2} + \frac{\alpha_{L,L}}{2},$$

$$\frac{\partial L}{\partial t} = -\frac{\partial v_{LR}}{\partial x} + \frac{\alpha_{R,R}}{2} - \frac{\alpha_{L,L}}{2},$$

(1.32)

(1.33)

(1.34)

with the factor $\frac{1}{2}$ the result of half of the tumbles, the tumbles from $R$ to $R$ and from $L$ to $L$, being ineffective. Now the model is coarse-grained and the resulting diffusion-drift equation for the probability density, $p \equiv R + L$, of one single particle is:

$$\frac{\partial p}{\partial t} = \frac{\partial}{\partial x} \left( D(x) \frac{\partial p}{\partial x} - V(x)p \right),$$

(1.35)

where $V(x)$ is the drift velocity. The equation above needs an explicit expression for $D(x)$ and $V(x)$ as a function of $\alpha_{R,L}$ and $v_{L,R}$. In [31] these expressions are derived as

$$D \equiv \frac{v_{RL}}{\alpha},$$

$$V \equiv \frac{\alpha_L v_R - \alpha_R v_L}{2\alpha} - \frac{\alpha (v_{RL} / \alpha)}{2\alpha},$$

(1.36)

(1.37)

where $\alpha \equiv \frac{1}{2}(\alpha_L + \alpha_R)$ and $v \equiv \frac{1}{2}(v_L + v_R)$ and $'$ is the derivative in space. The choice of the run-and-tumble parameters is important for the resulting steady state. Below the steady state probability function is derived in three cases with important applications in physics and biology. The first case is the symmetrical case in which $v_R = v_L = v(x)$ and $\alpha_R = \alpha_L = \alpha(x)$. In [30] the resulting steady state, $p_{ss}(x)$, is derived as

$$p_{ss}(x) = p_{ss}(0) \frac{v(0)}{v(x)},$$

(1.38)

where $p_{ss}(0)$ and $v(0)$ are the steady state density and the swim speed at $x = 0$, which is an arbitrary chosen reference point. The probability density is inversely proportional to the speed of individuals, which means that the individuals accumulate wherever they move slower. Moreover the steady state density does not depend on the tumble rate, but this only holds for instantaneous tumbles.

A second interesting result is that of sedimentation. Instead of left- and right-moving particles up- and down-moving particles are distinguished. Moreover the system is bounded by a wall, which is the bottom of the domain. The velocities of up- and down-moving particles differ according to $v_{L,R} = v \pm v_s$, where $v_s$ is the sedimentation speed. The resulting steady state is

$$p_{ss}(x) = p_{ss}(0) \exp[-x / \eta],$$

(1.39)

where $\eta$ is the decay length defined as $\eta = (v^2 - v_s^2) / \alpha v_s$. Equation (1.39) also holds for Brownian particles under sedimentation. In this case $\eta \equiv D / \alpha v_s$, which is proportional to the inverse of the gravity acceleration, $g$, since $v_s = D m g / k_B T$, with $m$ the buoyant mass. Now the thickness of the sedimented layer goes to zero as gravity goes to infinity. In the run-and-tumble case the layer thickness goes to zero for $v_s \to v$. This means that the collapse of the system occurs at a finite gravity threshold. A special case is the case $v_s > v$. Now all particles move downwards and there is only a steady state if all particles are in contact with the bottom wall.

The third interesting steady-state density is a result of harmonic trapping. Particles are confined to a harmonic potential in a way that they cannot escape beyond a horizon at $r^*$. At this radius the
outwards oriented swim speed is balanced by the inwards movement caused by the confining force, which is pulling the particles inwards. Two regimes are distinguished, weak trapping for \( \alpha r^* \gg v \) and strong trapping for \( \alpha r^* \ll v \). In the case of weak trapping the particles rarely reach the event horizon \( r^* \) and in steady state most particles are trapped in the center. For strong trapping (when a tumble is rare) the particle will soon reach \( r^* \) and wait there until the next tumble event. Now the maximum density is at radius \( r^* \). The above described dynamics is applicable in 1D as well as in higher dimensions. However when only the tumble rate depends on the position and on the swimming direction, the behavior changes for higher dimension. This can be understood by considering the low-order multipole expansion of the tumble rate: \( \alpha = \alpha_0 + \alpha_1(\mathbf{r}) \cdot \hat{\mathbf{v}} \). When the vector field \( \alpha_1 \) is conservative and obeys \( \alpha_1 = \nabla \phi \) the steady state density becomes

\[
p_{ss}(r) \propto \exp[-\phi(r)/v]. \tag{1.40}\]

In 1D \( \alpha_1 \) is always conservative, but in higher dimensions this condition is not always met. In this case the mapping on a thermal equilibrium system is not possible and equation (1.40) can no longer be used.

### Chemotaxis

An important application of above model for individual run-and-tumble particles is chemotaxis. Chemotaxis determines the response of bacteria to external chemical stimuli, for example nutrients. Chemotactic bacteria move themselves up a chemical gradient \( \nabla c \), where \( c \) is the concentration of a chemo-attractant or chemo-repellent. In case of a repellent the sign of the effect is reversed. So far the observation of spatial structures in a bacterial population is often used as an indicator of the presence of chemotaxis. Chemotaixxs can be modeled using a coarse-grained model with run-and-tumble particles in which the chemo-attractant is shown in the drift velocity, \( V = \xi \nabla c \), with \( \xi \) a constant that may depend on the diffusion coefficient \( D \). The chemotactic behavior is modeled in the equation for the tumble rate, since a tumble can change the direction of the movement and modulation of the tumble rate can make the bacteria move towards the chemoattractant. The tumble rate is modulated according to

\[
\alpha = \alpha_0 - \int_{-\infty}^{t} K(t-t')c(t')dt', \tag{1.41}\]

where \( \alpha_0 \) is the tumble rate corresponding to \( \nabla c = 0 \). \( K(t) \) is a function which computes the change in the local chemoattractant concentration \( \Delta c \) over a time scale \( \tau_c \). This time scale should be of the order \( \tau_c \alpha_0 \sim 1 \). At times much larger than \( 1/\alpha_0 \) the integral over \( K(t) \) ceases to be informative about the orientation of the bacterium and at much shorter times the detection of weak gradients can become inefficient. When straight runs are assumed and equation (1.41) is expanded in weak concentration gradients a steady state probability density can be derived. This steady state density obeys the following Boltzmann-like description

\[
p_{ss}(r) \propto \exp[\psi c(r)]. \tag{1.42}\]

In this equation \( \psi \) is defined from the expansion of equation (1.41), \( \alpha(t) = \alpha_0 - \psi v \cdot \nabla c \). It can be mapped on a Brownian equilibrium system in the same way as equation (1.40) [2]. Despite pattern formation on the density of bacteria growing on an agar plate can be explained by chemotactic behavior [30], we will follow a different mechanism as suggested in [3] and introduced below.

### Density dependent motility

So far the parameters \( v \) and \( \alpha \) did only depend on position and particles are treated as independent particles. In this section the case of density dependent run-and-tumble parameters is described. This problem is a typical many-body problem in which bacteria cannot be treated independently. In a many-body problem the density \( \rho \) is a collective density field given by \( \rho(\mathbf{r}) = \Sigma_i \delta(\mathbf{r} - \mathbf{r}_i) \),
Figure 1.14: The construction of the effective free energy density \( f(\rho) \) in the mapping from 1D interacting run-and-tumble particles onto a fluid with interacting Brownian particles. In the left figure an example of a velocity function \( v(\rho) \) is shown and in the right figure the corresponding free energy density \( f(\rho) \) is shown. If \( v(\rho) \) decreases rapidly enough \( f(\rho) \) has a negative curvature. Then the system shows spinodal instability with the coexistence of two binodal densities \( \rho_1 \) and \( \rho_2 \) in the global equilibrium state. The condition for instability, \( f'' < 0 \), translates into the geometric construction in \( v(\rho) \) shown in the left figure: when a line is drawn from the origin to any point on the curve and reflected in the vertical axis the system is unstable if the slope of this reflected line is higher than the slope of the function \( v(\rho) \). The figure is reproduced from [2].

with the sum taken over \( N \) particles. A system with density dependent motility can be mapped on a set of Brownian particles if and only if a function \( F_{ex}(\rho) \) exist such that

\[
\frac{V(\rho,x)}{D(\rho,x)} = -\frac{\partial}{\partial x} \left[ \frac{\delta F_{ex}(\rho)}{\delta \rho(x)} \right]. \tag{1.43}
\]

When this equation is applicable the system behaves like a fluid with excess free energy \( F_{ex} \). This is only true in the symmetrical case, where left and right moving particles have the same swim speed and the same tumble rate. Moreover the run-and-tumble parameters should depend on the density in a purely local way. The free energy density \( f_{\text{energy}} \) of such a system is

\[
f_{\text{energy}}(\rho) = \rho(\ln \rho - 1) + \int_0^{\rho} \ln v(u) du. \tag{1.44}
\]

From this equation it is found that the local free energy density has a negative curvature if \( v(\rho) \) is a sufficiently decreasing function of \( \rho \), which can be quantified as

\[
\frac{dv}{d\rho} < -\frac{v}{\rho}. \tag{1.45}
\]

Now there is an intermediate range of densities at which the system shows a spinodal instability, which separates the system into domains of coexisting binodal densities \( \rho_1 \) and \( \rho_2 \). This construction is shown in figure 1.14, which can originally be found in [2]. The phase separation process can also be understood physically. Run-and-tumble particles accumulate wherever they move slower (equation (1.38)) and since it was found that \( v \) should be a sufficiently decreasing function of \( \rho \), bacteria slow down in high density region. These two phenomena create a positive feedback loop that will induce phase separation [2] [31].

1.2.2 Numerical method for motile particles

Modeling run-and-tumble particles

In this section the numerical model used to explore pattern formation by density dependent motility is described. The model is an extension on the individual particle model introduced in section 1.1.2. The rules for birth-and-death are the same as described in that section, however the rules for the displacement of particles are changed in order to create a density dependent movement of particles.
Figure 1.15: The normalized function $g(r)$, shown in equation (1.46), that is used for the density calculation for $w = 3.5$. From the plot it is seen that $\rho \ll 1$ for $r > w$.

How this density dependent displacement is implemented in the model is explained below. The movement of the particles is modeled as a run-and-tumble movement with density dependent swimming velocity, $v(\rho)$, and constant tumble rate $\alpha$. To model the density dependent velocity a mechanism to determine the local particle density has to be implemented. Inspired by [4] the density is computed as the convolution of the number density field $\Sigma_i \delta(r - r_i)$ with the function $g(r)$:

$$g(r) = C_{norm} \exp \left[ \frac{-1}{1 - \frac{w^2}{r^2}} \right],$$  \hspace{1cm} (1.46)

where $w$ is a characteristic length that is used to calculate the density and $C_{norm}$ is a normalization constant. In figure 1.15 the function $g(r)$ is plotted as a function of $r$ for $w = 3.5$. From this figure it is clear that particles within a distance $w$ are considered to calculate the density, which means that all particles within a distance $w$ separated from an individual particle at some position $x$ influence the self-propulsion of that particle, while particles outside this interaction range $w$ do not.

This swimming speed of the interacting run-and-tumble particles, $v(\rho)$, should be a decreasing function of $\rho$ as explained before. The velocity profile used in the numerical model is

$$v(\rho) = v_0 \exp \left[ -\gamma \phi \arctan(\rho/\phi) \right],$$  \hspace{1cm} (1.47)

with $\phi$ and $\gamma$ the velocity parameters. The velocity profile decreases exponentially at low densities and reaches a saturation velocity $v_{sat} = v_0 \exp(\gamma \phi^2/2)$ at high densities. The latter is necessary since if the velocity vanishes at high densities, the density in the dense phase diverges when excluded-volume interactions are absent as in our case [31]. Now the diffusion coefficient is $D = \frac{v(\rho)^2}{\alpha \sigma}$ and the displacement of the particles due to this density dependent velocity is modeled using Langevin dynamics:

$$\frac{\partial r}{\partial t} = \frac{v}{2\alpha D} \nabla v + \sqrt{2D \Gamma(r, t)},$$  \hspace{1cm} (1.48)

where the first term on the right-hand side is a drift term induced by the density dependent velocity, and $\Gamma(r, t)$ is a white Gaussian noise term which is delta correlated in space and in time [31]. In 1 dimensional space the gradient should be replaced by a derivative and $r$ should be replaced by $x$. A necessary condition for phase separation is given in equation (1.45). When substituting equation (1.47) in this equation the condition can be rewritten as $\frac{\gamma \rho \phi^2}{\rho^2 + \phi^2} < 1$.  

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Development of spatial structures by interacting run-and-tumble particles

Using the model described above pattern formation caused by motility is investigated. To focus purely on the pattern formation dynamics birth-and-death processes are neglected here. First a simulation in 2-dimensional space is done to see if our model can reproduce the results shown in [4], in which run-and-tumble particles cluster in high density droplets. This formation of high-density ‘droplets’ in an otherwise low-density background is indeed observed in figure 1.16, where the result of a 2D simulation with run-and-tumble particles is shown at three different times. In the same figure the results of [4] of simulations with similar parameters and a similar velocity profile are shown and it is found that our model provides similar results, which means that the model works as expected using the velocity profile and density calculation as introduced in section 1.2.2.

The next step is to investigate numerically the influence of varying different parameters as the domain length $L$ and the interaction length $w$. To check if the finite volume effects are present we detect that the number of peaks is proportional to the domain length, $L$. The results of simulations with interacting run-and-tumble particles for $L = 40$, $L = 80$ and $L = 120$ and initial density $\rho_0 = 7.5$ are shown in figure 1.17. From that figure it can be is seen that the number of peaks is indeed proportional to $L$, of course when the initial density is kept the same. Moreover the peak length is the same in all three figures, meaning that only the number of peaks depends on $L$ while the peak size does not.

Another important length scale in the model is the interaction length $w$, introduced in equation (1.46). This length $w$ is the length below which particles can feel each others presence and can thus interact, since $\rho \ll 1$ when $d > w$, with $d$ the separation distance, as seen in equation (1.46) and figure 1.15. It is expected that this length influences the pattern size significantly, and indeed this is the case as it is shown in figure 1.18, were the evolution of run-and-tumble particles in time
Figure 1.17: The evolution of run-and-tumble particles in time in 1D with $w = 3.5$, $\alpha = 1.25$, $v_0 = 3$, $\gamma = 0.4$ and $\phi = 30$ for three different domain lengths $L = 40$, $L = 80$ and $L = 120$. The number of particles is chosen such that the initial density is $\rho_0 = 7.5$ and the colors of the particles correspond to the local density.

Figure 1.18: The result of three simulations of run-and-tumble particles in 1D for $w = 1$, $w = 2$ and $w = 4$ respectively. The other parameters are $\alpha = 1.25$, $v_0 = 3$, $\gamma = 0.4$ and $\phi = 30$. The initial number of particles is 300 and the color of the particles represents the local density.

in 1D is shown for different values of $w$. We found that by increasing the interaction length, $w$, it results in lower peak density and a smaller peak size. The number of particles is the same in all three simulations and is fixed in time, which explains why the peak density is lower when they occupy a bigger part of the domain.

Arrested phase separation by logistic growth and motility

In order to investigate the influence of spatial structures on the extinction dynamics, birth-and-death processes are also included. When combining logistic growth and motility the model has an increase in computational costs and thus simulations are performed only in 1-dimensional space in this section.

Parameter selection

When logistic growth and motility are combined, the number of parameters that can be varied in the model becomes very large. Therefore it is important to discuss the influence of varying these parameters in detail. First a convenient choice for the birth-and-death rates should be found. Therefore simulations are performed for different values of $\mu$ and $\lambda$, while keeping $w$ and $\alpha$ fixed and for convenience similar to the values used in the simulations with run-and-tumble particles obtained in the previous section. The results for $\mu = \lambda = 0.001$, $\mu = \lambda = 0.01$ and $\mu = \lambda = 0.1$ are
Figure 1.19: A 1D population of active particles that can reproduce and die evolving in time for three different birth-and-death rates $\mu = \lambda = 0.001$, $\mu = \lambda = 0.01$ and $\mu = \lambda = 0.1$. The other parameters are $\alpha = 1.25$, $v_0 = 3$, $\gamma = 0.4$, $\phi = 30$, $w = 3.5$ and $\rho_0 = 7.5$.

Figure 1.20: The expansion of a 1D population of run-and-tumble particles that can reproduce and die in time for two different domain lengths $L = 40$ and $L = 120$. The parameters are $\mu = \lambda = 0.01$, $\alpha = 1.25$, $v_0 = 3$, $\gamma = 0.4$, $\phi = 30$, $w = 3.5$ and $\rho_0 = 7.5$. In panel (a) and (b) the evolution of the population in time is shown, with green en red indicating the two different species.
shown in figure 1.19. It is found that $\mu = \lambda = 0.01$ is a convenient choice, since for higher birth-and-death rates no pattern formation is observed and for lower birth-and-death rates the effect of logistic growth on the pattern formation is not visible since the result is comparable to the result for run-and-tumble particles that can not die neither reproduce. This can be explained by comparing the corresponding time scales of the pattern formation and the birth-and-death processes: when $\mu$ is too small pattern formation has already set in before the logistic growth towards the carrying capacity is visualized, since the time scale for logistic growth is higher. On the other hand when $\mu$ is high the carrying capacity is reached so fast, that pattern formation into high- and low-density regions does not have the chance to occur.

As in the previous section, the influence of the domain length $L$ is investigated. In figure 2.3 the result of a 1D simulation with $w = 3.5$, $\alpha = 1.25$ and $\mu = 0.01$ is shown for two different domain lengths $L = 40$ and $L = 120$. It is seen that high and low density regions occur. These regions have a fixed length and the number of peaks is proportional the domain length $L$ as expected.

In the simulations shown in figure 1.20 the interaction length for the death process, which is the cell size $\delta = \frac{L}{\alpha}$, with $N$ the number of cells, is much smaller than the interaction length for the density calculation, $w$. As a result both phenomena are modeled as two completely separated processes. To couple the processes it is convenient to model the death rate explicitly with the local density instead of using a fixed range within which particles compete as done so far. This fixed interaction range was equal to the cell size, so the death of particles was depending on the number of particles in the corresponding cell. If the competition is modeled using the local density, the death of particles becomes proportional to the local density $\rho$ of particles in the corresponding cell. If the competition is modeled using the local density, the death of particles was depending on the number of particles in the corresponding cell.

Now the influence of changing $w$, which is the length within which particles can interact, is analyzed. In the previous subsection it is already shown that, in the case without logistic growth, $w$ influences the pattern size significantly. Also in this case, were active motion is combined with logistic growth, the influence of $w$ is investigated. Results of simulations in this case of $w = 1$, $w = 2$ and $w = 3$ are shown in figure 1.21. It is seen that the pattern shape and size are completely different for $w = 1$ but comparable for $w = 2$ and $w = 3$. In the result for $w = 1$ the development of several bigger peaks consisting of multiple smaller peaks is observed. A possible explanation is that a small value of $w$ results in a very small pattern length $l$ and that for $w = 1$ this pattern length $l$ is even smaller than the interparticle distance, which means that the simulation is not reliable. For $w = 2$ and $w = 3$, $l$ is bigger than the interparticle distance, so this problem is not present. From the panels in the center of figure 1.21 it is observed that the density inside the peaks is different for different values of $w$. A smaller value of $w$ leads to a higher peak density, which could be the result of the decreased pattern length only if the eventual number of particles is constant. On the bottom of figure 1.21 the evolution of the number of particles in time is shown for the three values of $w$ and it is indeed observed that the number of particles saturates to approximately the same value of 170. Moreover it is seen that saturation is reached faster for larger $w$.

It is already mentioned that $w$ should be bigger than the interparticle distance $\Delta$, since when $w$ is smaller than $\Delta$ particles will not feel each other anymore. As a result the calculated density will be underestimated. To perform a reliable density calculation all neighboring particles should be taken into account. To clarify this the density in a domain with an almost uniform distribution of particles is calculated using different values of $w$. The number of particles is $N = 5000$ and the size of the domain is $40 \times 40$, so the resulting density is approximately $\rho \approx 3.1$. The results of this density calculation for $w = 1$, $w = 2$, $w = 3$ and $w = 5$ are shown in figure 1.22. It is observed that for $w = 1$ the resulting density profile is noisy and the density is locally underestimated or
Figure 1.21: The result of three simulations of a 1D population of run-and-tumble particles that can reproduce and die evolving in time for $w = 1$, $w = 2$ and $w = 3$. In all three simulations the density is used as a measure for the competition and the parameters are $v_0 = 3$, $\gamma = 0.4$, $\psi = 30$, $\mu = 0.01$ and $\lambda = 0.0005$. In the top panels the evolution of both species $A$ (green) and species $B$ (red) is shown. In panel (d), (e) and (f) the same population evolution in time is shown, but now the color represents the local density of the particles. In the bottom panels the evolution of the number of particles in time is shown.
overestimated. For $w = 2$ or higher, the results are less noisy and although the density profiles are not equal they are similar.

There is not only a lower limit for $w$, but also an upper limit. When $w$ is too large, the processes in the high density peaks will not be captured accurately. This means that the interaction length $w$ should be smaller than the peak length $l$, which leads to the constraint $\Delta \ll w < l$. From the simulations shown in figure 1.21 it can be found that $w = 3$ is a convenient choice. In this case the interparticle distance in the peaks is approximately $\Delta \approx 0.1$, so the first condition, $\Delta \ll w$, is met. The peak length can be calculated using equation (2.7) and equals $l \approx 5$, so also the second condition, $w < l$, is met. To map the range in which the birth-and-death rates $\mu$ and $\lambda$ can be varied for a fixed $w = 3$, a plot of $w$, $l$ and $\Delta$ as a function of the saturation density $\rho_0$ is created.

In this plot the condition $\gamma \rho_0^2 + \phi > 1$, which is introduced in section 2.2, is also taken into account. Using $\gamma = 0.4$ and $\phi = 30$ this condition becomes $\rho_0 > 2.5$. The carrying capacity density was introduced as $\rho_0 = \frac{1}{w \lambda}$. The plot of $w$, $\Delta$ and $l$ as a function of $\rho_0$ is shown in figure 1.23. In this plot the birth rate $\mu$ is a fixed parameter and equals $\mu = 0.01$, since it is known that larger values of $\mu$ do not result in pattern formation and that for lower value the effects of the logistic growth are not clearly visible anymore. From figure 1.23 it is seen that the condition $\Delta \ll w < l$ is met for $2.5 < \rho_0 < 11.6$. Since $\mu = 0.01$, $w = 3$ and $\rho_0 = \frac{1}{w \lambda}$ this corresponds to $0.00029 < \lambda < 0.0013$. A reliable set of parameters is thus $\gamma = 0.4$, $\phi = 30$, $w = 3$, $\mu = 0.01$ and $0.00029 < \lambda < 0.0013$. In upcoming simulations the parameters choice will be close to this optimal parameter set to ensure that the results are reliable.
Figure 1.23: The interaction length, $w$, the interparticle distance, $\Delta$, and the pattern length, $l$, as a function of the density, $\rho_0$, for $w = 3, v_0 = 3$, and $\gamma = 0.4$. The birth rate $\mu$ is 0.01 in both cases and $\rho_0$ is defined as $\rho_0 = \frac{1}{w} \frac{\mu}{\lambda}$.

1.3 The influence of external inhomogeneities on the population expansion

In the previous section the focus was on motility, which is an internal property of the particles themselves. In this section the focus is on external inhomogeneities that can be present in the ecosystem, since it is expected that also external inhomogeneities can change the spatial properties of a population. Such an environmental inhomogeneity can for example be a mountain, which behaves as an obstacle for the expanding population. In this chapter it is explained how to integrate the stochastic equation when inhomogeneities are present. Moreover it is shown how these external inhomogeneities can be implemented in our numerical model. At the end of this section simulation results of a population expansion around an obstacle are given and compared to results of earlier studies to validate the model in which external inhomogeneities are included.

1.3.1 Theoretical background of population expansion in inhomogeneous media

Inhomogeneities in the domain can have an impact on the displacements of individual particles. The local displacement of particles is controlled in our model by the diffusion coefficient $D$ and in general, spatial dependence can be considered so that $D$ is function of $x$, $D = D(x)$. Here it is explained how this situation differs from the situation of a constant diffusion coefficient. When diffusion is continuous in space the particles perform a Brownian motion with variance $\langle \Delta x^2 \rangle = 2D\Delta t$. The stochastic equation for the displacement of the particle is then

$$\frac{dx}{dt} = \sqrt{2D}L(t), \quad (1.49)$$

where $L(t)$ is a noise term with $\langle L(t) \rangle = 0$ and $\langle L(t_1)L(t_2) \rangle = \delta(t_1 - t_2)$. When integrating a stochastic equation different interpretations are available among which mainly Itô calculus and Stratonovich calculus are used as described in [36].
1.7: Itô and Stratonovich calculus

When integrating a stochastic equation, several interpretations for the stochastic term are available, among them the Itô and Stratonovich convention are the most famous choices. To show the differences between the two integration methods we consider the stochastic process

\[ dx = f(t) \, dg(t), \]  

(1.50)

where \( g(t) \) is a Wiener process with \( \langle dg \rangle = 0 \) and \( \langle dg^2 \rangle = dt \). The difference between the two methods becomes clear when writing the Riemann integral for \( dx \):

\[ \int_0^t f(t) \, dg(t) = \lim_{n \to \infty} \sum_{j=1}^n f(\tau_j) (g(\tau_{j+1}) - g(\tau_j)). \]  

(1.51)

The Itô convention requires \( \tau_j = t_j \) in above equation, while in the Stratonovich convention considers \( \tau_j = (t_j + t_{j+1})/2 \).

When integrating equation (1.49) both methods lead to the same result, namely \( \langle \Delta x \rangle = 0 \) and \( \langle \Delta x^2 \rangle = 2D \Delta t \), since \( D \) is constant and therefore the noise is additive. However when \( D = D(x) \) the noise becomes multiplicative and Itô and Stratonovich give different results as shown in [22]:

\[ \langle \Delta x \rangle = \zeta dD \frac{dx}{dx} \Delta t \{ \begin{array}{ll} \zeta = 0 & \text{Itô} \\ \zeta = \frac{1}{2} & \text{Stratonovich} \end{array} \} \]  

(1.52)

When deriving the Fokker-Plank equation the choice between Itô and Stratonovich also leads to different equations. For the forward Fokker-Planck equation the equations are:

\[ \frac{\partial P}{\partial t} = -\frac{\partial}{\partial x} [A(x) + \zeta C(x)C'(x)] P + \frac{1}{2} \frac{\partial^2}{\partial x^2} (C(x))^2 P \{ \begin{array}{ll} \zeta = 0 & \text{Itô} \\ \zeta = \frac{1}{2} & \text{Stratonovich} \end{array} \} \]  

(1.53)

where \( ' \) is a derivate with respect to \( x \), \( C^2(x) = 2D(x) \), and \( A(x) \) is the drift term in the corresponding Langevin equation [35]. The backward Fokker-Planck equations for a diffusion process in the Itô and the Stratonovich convention are

\[ \frac{\partial P}{\partial t} = \zeta \frac{\partial D(x)}{\partial x} \frac{\partial P}{\partial x} + D(x) \frac{\partial^2 P}{\partial x^2} \{ \begin{array}{ll} \zeta = 0 & \text{Itô} \\ \zeta = \frac{1}{2} & \text{Stratonovich} \end{array} \} \]  

(1.54)

[36].

To show the difference between the Itô and the Stratonovich convention in the case \( D = D(x) \), simulations are performed using both integration methods. From these simulations the mean first passage time \( T^1(x_0) \) is measured, which is the average time that it takes for a particle to be absorbed in one of the domain boundaries \( x = 0 \) or \( x = L \), starting from a given position \( x = x_0 \). To determine the mean first passage time the operator of the backwards Fokker-Planck equation is used. This operator is:

\[ L_{FP} = \zeta \frac{1}{2} \frac{\partial D(x)}{\partial x} \frac{\partial}{\partial x} + D(x) \frac{\partial^2}{\partial x^2}. \]  

(1.55)

From [34] it is know that for the mean first passage the following equation holds:

\[ L_{FP}(x_0)T^1(x_0) = -1 \]  

(1.56)

With this equation the mean first passage time can be derived analytically for both the Itô and the Stratonovich convention. The position, \( x(t) \), of particles moving according to the Langevin equation, shown in equation (2.9), is integrated in both the Itô and the Stratonovich convention in order to measure the average first passage, \( T^1(x_0) \) in both cases and to point out the differences. This is analog to simulating the genetic interface between two different species, which performs a Brownian motion with diffusion.
Figure 1.24: A sketch of a genetic interface that starts in $x = x_0$ and ends up in $x = 0$. The mean first passage time, $T^1(x_0)$, measures the time that it takes for such an interface to be absorbed in $x = 0$ or $x = L$, starting from $x = x_0$.

Coefficient $D$, equal to the diffusion coefficient for the displacement of individual particles, in 1D. This statement is confirmed for the model used in this work by determining that the local heterozygosity decays as $H(0,t) \sim \frac{1}{\sqrt{t}}$, as shown in section 1.1.2. In the simulations performed in this section the interface position $x$ is initially at $x_0$. Now the mean first passage time is determined as the time that it takes for the genetic interface that starts at $x = x_0$ to end up in one of the domain boundaries $x = 0$ or $x = L$, or in other words the time that it takes for one of the two species to take over the whole domain. This procedure is sketched in figure 1.25a

First the situation of a sharp edge between two different diffusion coefficients $D_1$ and $D_2$ is investigated. The expression for $D(x)$ is $D(x) = D_1 + (D_2 - D_1)H(x - x_c)$, where $H(x)$ is a Heaviside step function and the sharp transition is positioned at $x = x_c$. Now the mean first passage time as a function of the initial interface position $x_0$ is determined both analytically and numerically using both the Itô integral and the Stratonovich integral. In the simulations the Stratonovich case is modeled by giving the particles a 'kick' when passing $x = x_c$, corresponding to the drift term in equation for the particle displacement. The results of a simulation with $D_1 = 0.1, D_2 = 0.001$ and $x_c = 10$ in both the Itô and the Stratonovich convention is shown in figure 1.25a. For the Itô process also the analytical computation is shown. From figure 1.25a it is seen that both curves are similar, however the values for $T^1(x_0)$ are lower for the Stratonovich result.

A second example is presented with diffusion coefficient that depends linearly on $x$: $D(x) = D_1 \cdot x$. Again the mean first passage time is determined for both an Itô and a Stratonovich convention. The results for $D_1 = 0.001$ for both Itô and Stratonovich integration are shown in figure 1.25b. In the same figure the analytical solutions are shown. For the Itô process this analytical solution for $T^1(x_0)$ is

$$T^1_{\text{Itô}}(x_0) = \frac{x_0 \log L - x_0 \log x_0}{D_1}. \quad (1.57)$$

In the Stratonovich case this expression is

$$T^1_{\text{Stratonovich}}(x_0) = \frac{2(\sqrt{Lx_0} - x_0)}{D_1}. \quad (1.58)$$

From figure 1.25b it is seen that in both cases the result of the simulation follows the analytical expression. However the results for the Itô and Stratonovich processes are different: the peaks of the curves are at a different position and again the values for $T^1(x_0)$ in the Stratonovich case are higher.

As in [31] Itô calculus is used to integrate the stochastic equation for the particle displacement in our model. In this work space-dependency of the diffusion coefficient is always implemented as a sharp edge between regions with different diffusion coefficients and it was found that in this case the results for both conventions were similar.
1.3.2 Numerical methods for population expansion in inhomogeneous media

To investigate population expansion in inhomogeneous media the discrete particle model introduced in section 1.1.2 is used. There are different ways of implementing external domain inhomogeneities in this model. A first option is to make the birth rate space-dependent. In a real biological environment this higher or lower growth regions can be the result of different nutrient levels or different temperatures [29]. Another way of implementing inhomogeneities is using a space-dependent diffusion coefficient, which changes the displacement of the particles, $\langle \Delta x \rangle$, locally, as explained in detail in the previous section. A space-dependent diffusion coefficient is used to model front propagation around an obstacle as will be described below.

Population expansion around an obstacle

To model population expansion around an obstacle a diamond shaped area in which the diffusion coefficient, $D_1$, is zero is implemented in the domain. The case of front propagation around an obstacle is already explored both numerically as experimentally [26]. In that work the obstacle was diamond shaped and it was characterized by a zero growth region instead of a zero diffusivity region. They found that Fermat’s principle of least time could be used to describe the front dynamics. Moreover it was found that using the principle of least time, only the fastest particles survive and as a consequence particles that approach the obstacle cannot survive in the front. In this chapter it is investigated whether simulations of front propagation around an obstacle using our model lead to similar results.

The result of a simulation of an expanding population around a zero diffusion obstacle is shown in figure 1.26. In this figure it is observed that after the front has has passed the obstacle its shape is not flat anymore, but a cusp has developed at the height of the obstacle. In [26] the principle of least time, Fermat’s principle in optics, is used to explain the cusp. All points at the front are reached in minimal time. For the points in the cusp this minimal time trajectory bends around the corner of the obstacle. This bended trajectory is shown with a red line in figure 1.27a, where a sketch of the front propagation around the obstacle is given. A particle that goes straight ahead
Figure 1.26: The expansion of a population around a diamond shaped obstacle with \(D_{\text{obstacle}} = 0\) at six different times. Initially two types of particles are distributed homogeneously in a front layer of thickness 0.05. Outside the obstacle the diffusion coefficient is \(D = 2.5 \cdot 10^{-5}\). The birth-and-death rates are \(\mu = \lambda = 1\) and the initial number of particles is \(N = 2000\).

and does not have to bend because of the obstacle, will travel a longer distance in the same time that particles need to travel the refracted trajectories. Therefore the part of the front right after the obstacle is slowed down compared to the part that can go straight ahead, which explains the cusp in the front.

It is possible to calculate the cusp angle, indicated by \(\phi\) in figure 1.27a, and express the tangent of this angle as a function of time \([26]\). For this derivation it is assumed that \(R(t)\) increases with velocity \(v\), which means that \(R(t)^2 = (R(0) + vt)^2 = (x - R_0)^2 + y^2\), with \(R_0 = \frac{L}{\sqrt{2}}\). Now the derivative \(\frac{dy}{dx}\) is

\[
\frac{dy}{dx} = \frac{R_0 - x}{y} = \tan(\phi).
\]  

(1.59)

The resulting equation for the development of \(\phi\) in time at the position \(x = 0\) is

\[
\tan(\phi) = f(t) = \frac{L}{\sqrt{L^2 + 4Lvvt + 2v^2t^2}}.
\]  

(1.60)

To compare the analytical result from this equation to the numerical results the tangent of the cusp angle, determined from simulations, is plotted as a function of time. The result is shown in figure 1.27b. In this figure also the theoretical curve, corresponding to equation (1.60), is shown. The data points follow the theoretical prediction which means that equation (1.60) is indeed valid for the simulated situation. Moreover it means that the refraction of particle trajectories around the obstacle can indeed be compared to refraction of light rays around an obstacle.

Apart for measuring the cusp angle it is also possible to show the ancestor lines to explore the refraction of the population front around the obstacle. To achieve this the algorithm is extended with a particle tracking mechanism.
Figure 1.27: In panel (a) a sketch of the front propagation around a diamond shaped obstacle is shown. The cusp and the cusp angle $\phi$ are sketched and the lengths $R(t)$ and $L$ are shown. The red line shows a trajectory that is refracted because of the obstacle. In panel (b) the tangent of the cusp angle as a function of time is plotted. The blue dots are the data points gathered from simulations and $f(t)$ represents the analytical prediction for $\tan(\phi)$ from equation (1.60).

1.8: Tracking ancestor lines

In order to follow the ancestor lines of particles, a particle tracking mechanism is developed and implemented in the discrete particle model. All particles are registered under a unique name, which makes it possible to keep track of all the birth events during a simulation. Starting from particles in the front at some time $t$ the ancestor lines are created by tracing back all the mothers of the particle until ending up in the initial condition at $t = 0$.

The ancestor trajectories of eight particles at the front at $t = 260$ are shown in figure 1.28. Lengths scales are chosen such that fluctuations in the trajectories are small compared to the obstacle size. Particles that are initially right in front of the obstacle will never be able to reach the front according to the principle of least time, since they always have a longer route to travel than other particles. In other words: only the fastest trajectories survive [26].

After analyzing the front dynamics the focus is on the influence of the obstacle on the genetics. The simulations start with a population consisting of two species that are initially randomly mixed and that are neutral variants of each other. From figure 1.26 it is observed that the red and green particles are first separated by the obstacle and that the genetic interface between red and green appears right at the center of the obstacle at $y = 0.5$, after the front has passed the obstacle, independent of where the interface hits the obstacle initially. When full statistics is computed of the $y$–position of the interface right after the obstacle a peak around $y = 0.5$ is expected. In figure 1.29 the result of these statistics is shown and indeed a peak occurs at $y = 0.5$, confirming the visual impression from figure 1.26. A Gaussian curve with the mean $\bar{y}_{\text{interface}} = 0.48$ and the standard deviation $\sigma = 0.18$ is giving the best fit to the data.
Figure 1.28: The trajectories of eight particles at the front at $t = 260$ in a domain with a diamond shaped obstacle, with $D = 2.5 \cdot 10^{-5}$ and $\mu = \lambda = 1$. The particles are tracked by identifying the ancestors starting from the front. The black dotted line represents the population front at $t = 260$.

Figure 1.29: Statistics on the $y$–position of the genetic interface after the front has passed the diamond shaped obstacle at $t = 94$. 100 realizations are used to create the histogram performed with $D = 2.5 \cdot 10^{-5}$ and $\mu = \lambda = 1$. A Gaussian curve is fitted through the histogram with resulting mean $\bar{y}_{\text{interface}} = 0.48$ and $\sigma = 0.18$. 
1.4 Summary

In this chapter the theoretical background of population dynamics and genetics is given and the numerical models used in this work have been introduced. First the focus was on population genetics and dynamics. An important concept in population genetics is genetic drift. Genetic drift is the random change in a species frequency due to fluctuations and can result in local fixation of species and eventually even in global fixation. A statistical measure for the genetic diversity is the heterozygosity. The heterozygosity is the probability of finding two individuals of a different type at distance $x$ for a given time $t$. From the heterozygosity fixation times and lengths of the local fixated domains can be characterized. To explore population genetics numerically a discrete particle model is used with certain rules for birth and death. In this chapter numerical results for the heterozygosity have been presented and it was found that our numerical model recovers the theoretical predictions. In this work population dynamics is characterized by the front of an expanding population. Such a population expansion can often be described as a Fisher wave. Fisher speeds in the low- and high-noise regime have been introduced in this chapter. Moreover it has been validated that these expressions can be used for population expansions simulated using our discrete particle model.

The second part of this chapter focuses on inhomogeneities, caused by motility that depends on the interaction between particles. This has been implemented in the discrete particle model as a run-and-tumble motion with a density-dependent swimming speed. It has been validated that this density-dependent swimming speed indeed results in pattern formation in the population. The last part of this chapter describes how external inhomogeneities can be implemented in the domain by a space-dependent diffusion coefficient. Using our discrete particle model with space-dependent diffusion an obstacle with zero diffusivity was implemented in the domain and population expansion around this obstacle was explored numerically. It has been found that the front dynamics can be explained by Fermat’s principle of least time.
Pattern formation in populations

Pattern formation in a population can occur because of external inhomogeneities in the environment, such as turbulence, or by internal inhomogeneities caused by properties of the organisms itself, such as self-propulsion [7]. Pattern formation caused by motility is experimentally investigated in [32], where spatial structures are observed in a motile bacterial population growing on an agar plate. In this section the dynamics of pattern formation is investigated numerically using the discrete particle model extended with self-propulsion of particles, given in section 1.2.2. Using this model also the combination of logistic growth and self-propulsion is investigated based on the ideas in [2] that it can result in very stable and long-living patterns. Now that birth-and-death processes are included the influence of spatial structures on the fixation probability is explored. Moreover, at the end of this chapter, pattern formation in expanding populations caused by external factors is simulated and again the influence of these patterns on the fixation dynamics is analyzed.

2.1 Arrested phase separation by the combination of motility and logistic growth

So far the observation of patterns was often linked to the presence of chemotaxis, however in [3] it is stated that also logistic growth, resulting from the birth-and-death processes, together with motility can induce pattern formation, which means that the observation of spatial structures is not necessarily an indicator of chemotaxis. Moreover this means that pattern formation is not necessary due to external factors, as food levels, but can also be the result of purely internal properties, as a density dependent velocity. In [3] a continuum model for the density evolution in time is used. The contribution of the logistic growth due to birth-and-death processes to the density evolution in this continuum limit is described as:

\[
\frac{\partial \rho(r,t)}{\partial t} = \beta \rho \left(1 - \frac{\rho}{\rho_0}\right),
\]

where \(\beta\) is the logistic term which results in growth of the population from \(\rho < \rho_0\), or death from \(\rho > \rho_0\), until the stable state \(\rho_0\).

The density dependent motility is introduced in the equation for the swim speed \(v\), which is a decreasing function of \(\rho\) as found in section 1.2.1. The diffusion coefficient in this system is \(D = \frac{v^2}{\alpha^2}\) (equation (1.31)). Moreover a mean drift velocity is induced: \(V = -\frac{v}{\alpha} \nabla v = -\frac{D'(\rho)\nabla \rho}{2}\), with \(\frac{d}{d\rho}\) the derivative in \(\rho\). In the continuum model used in [3] the full dynamics is now given by

\[
\frac{\partial \rho(r,t)}{\partial t} = \nabla \cdot [D_e \nabla \rho(r,t)] + \beta \rho(r,t) \left(1 - \frac{\rho(r,t)}{\rho_0}\right) - \kappa \nabla^4 \rho(r,t),
\]

where the effective diffusivity is \(D_e = D(\rho) + \frac{vD'(\rho)}{2}\) and \(\kappa\) is a surface tension parameter (\(\kappa > 0\)) that controls the gradient in the bacterial density. In the discrete particle model used here the
surface tension parameter $\kappa$ does not exist. In this continuum equation noise in the birth-and-death processes is neglected, however this noise may be important [3]. For phase separation the inset of a spinodal instability is a necessary condition. This instability occurs only for $\frac{d\rho}{d\rho} < -\frac{\kappa}{\rho}$ (equation (1.45)), which implies $D(\rho) + \frac{\rho D'(\rho)}{2} < 0$. We notice that this term can be negative even for positive diffusion coefficient $D$.

The motility dependent diffusion separates the system into high- and low-density regions. Moreover from equation (2.1) it is known that individuals tend to die in high-density regions and tend to reproduce in low-density regions. Consequently a transport between the two regions is necessary to maintain a steady state. At typical length- and time-scale the diffusion-drift transport and birth-and-death processes balance and as a consequence domain coarsening will no longer progress. The patterns that are formed at that characteristic time are expected to be stable and to stay fixed for a long time. In figure 2.1a a result of this pattern formation, modeled using equation (2.2), from [3] is shown.

In [3] the onset of the instability is understood by linearizing equation (2.1) and by introducing the Fourier space. The density is now defined as

$$\rho(\mathbf{r}) = \rho_0 + \sum_q \delta \rho_q \exp[iq \cdot \mathbf{r}], \quad (2.3)$$

where $q$ is the wave vector. Now the following equation can be derived:

$$\dot{\delta \rho_q} = \Lambda_q \delta \rho_q, \quad (2.4)$$

$$\Lambda_q = -\beta - q^2 \mathcal{D}_c(\rho_0) - \kappa q^4.$$  

Note that the flat profile $\rho = \rho_0$ is stable for $\Lambda_q \leq 0$ and unstable for $\Lambda_q > 0$. The conditions for instability are therefore

$$\Phi \equiv -\frac{\rho_0 D'(\rho_0)}{2D(\rho_0)} \geq 1$$

$$-\frac{\mathcal{D}_c(\rho_0)}{\sqrt{\beta \kappa}} \geq 2. \quad (2.5)$$

In figure 2.1b the wavelength $\Lambda_q$ is shown as function of the wave vector $q$. The original plot can be found in [3]. It is seen that at the onset of the instability the only unstable mode is $q_c = \sqrt{\frac{2\beta}{|\mathcal{D}_c(\rho_0)|}}$.

When the instability is set the unstable modes lie in a band $q_1 < q < q_2$ with $q_1 \simeq \sqrt{\frac{\beta}{|\mathcal{D}_c(\rho_0)|}}$ and $q_2 \simeq q_\kappa \equiv \sqrt{\frac{|\mathcal{D}_c(\rho_0)|}{\kappa}}$. The length scale of the formed patterns now obeys

$$l = \frac{2\pi}{q_c} = 2\pi \sqrt{\frac{|\mathcal{D}_c(\rho_0)|}{\beta}} \quad (2.7)$$
Figure 2.1: In panel (a) a simulation results presented in [3] is shown, where a perturbation in the initial condition grows towards pattern with high- and low-density peaks. For the simulation equation (2.2), with $\beta = \kappa = 0.01$ and $\rho_0 = 15, D = 1$ is used. In panel (b) three plots of the wavelength $\Lambda_q(q)$ as a function of the wave vector $q$ for $\frac{|D|}{\sqrt{2\pi}} = 1, 2, 3$ (from bottom to top) are shown. The plot is reproduced from [3].

2.2 Simulations

2.2.1 Development of spatial structures by interacting run-and-tumble particles

To investigate numerically pattern formation due to motility, the model described in section 1.2.2 is used. In this model the swimming velocity of the run-and-tumble particles, $v(\rho)$ is:

$$v(\rho) = v_0 \exp \left[ -\gamma \phi \arctan(\rho/\phi) \right],$$

with $\phi$ and $\gamma$ the velocity parameters. The displacement of particles as result of this density dependent velocity is modeled using the Langevin equation:

$$\frac{\partial r}{\partial t} = \frac{v}{2aD} \nabla v + \sqrt{2D} \Gamma(r, t).$$

where the first term on the right-hand side is a drift term, $D = \frac{2v^2}{\gamma}$ and $\Gamma(r, t)$ is a white Gaussian noise term which is delta correlated in space and in time [31]. More details of the used model and the particle dynamics can be found in section 1.2.2.

In this section, as initial case, particles are not allowed to die or reproduce, so that the focus is purely on the role of motility in the development of spatial structures. In figure 2.2 the result of a simulation of run-and-tumble particles in one dimensional space is show. It is seen that while evolving in time high and low density regions are formed as expected. Moreover it is observed from figure 2.2b that the density is the highest in the peak center which agrees with the results obtained in [3], which are shown in figure 2.1a.

From figure 1.17 it is observed that, at some times, two peaks merge together, like at $t \approx 5000$ in figure 1.17a. This merging happens after a period in which the peak seems to lose particles and not because of a collective motion of the peak. Moreover, it is found that an eventual diffusion coefficient of the peak is very low compared to the diffusion of the individual particles. Therefore the peaks hardly move and are unlikely to meet each other at these time scales. To understand this behavior the density profile of the 1D population of active particles in figure ?? is investigated. It is seen that the density at the top of the disappearing peak is much smaller than the density in the rest of the peak. From equation (1.47) we know that at lower densities the velocity of the particles is higher. The high velocity makes it possible for particles to escape towards a neighboring peak. This process becomes more clear when the trajectory of one single particle, starting from the disappearing peak, is followed, like in figure 2.2c. In this plot the particle color indicates its
velocity. It is seen that the velocity of this particle increases significantly at the top of the peak so that the particle can jump to the neighboring peak. Since the velocity does not vanish for high densities this jumping behavior repeats itself multiple times. If the velocity would vanish at high densities a particle is more likely to stay inside a peak for longer periods of time.

2.2.2 The influence of spatial structures on the extinction dynamics

In the previous section birth-and-death processes were neglected and the focus was on the density profiles and the pattern shapes, however in this section the focus is on how the spatial structures influence the fixation dynamics and birth-and-death processes are included. In figure 2.3 the result of a 1D simulation with $w = 3$, $\alpha = 1.25$ and $\mu = 0.01$ is shown. The evolution of the population, consisting of two species, the density profile, the density as a function of $x$ and the number of particles as a function of time are shown. From figure 2.3c it is observed that all the peaks have the same length and a periodic wave-like behavior of peaks is found. From equation (2.7) the peaks size is calculated as $l = 12$ for the used parameters, which does indeed correspond to the peak size observed in figure 2.3c. From figure 2.3d it is seen that the eventual number of particles is much lower than the initial number of particle. With only density dependent diffusion the population size is fixed in time and with only logistic growth with $\mu = 0.01$ the population size will fluctuate around the carrying capacity, which is $N = \rho_0 L = \frac{1}{w} x L$. The increased number of death events causing the decrease in the population size is probably due to the balancing between the logistic growth and the diffusive transport.
Figure 2.3: The evolution of a 1D population of run-and-tumble particles that can reproduce and die in time with parameters are \( \mu = \lambda = 0.01 \), \( \alpha = 1.25 \), \( v_0 = 3 \), \( \gamma = 0.4 \), \( \phi = 30 \), \( w = 3 \) and \( \rho_0 = 7.5 \). In panel (a) the evolution of the population in time is shown, with green and red indicating the two different species. In panel (b) the same evolution is shown, however now the color represents the local density. In figure (d) the density as a function of \( x \) is shown and in panel (g) the evolution of the total population size in time is shown.
Local and global fixation

### 2.1: Meta-population dynamics

A meta-population consists of multiple subpopulations which are spatially separated and can interact at some level. Inside a subpopulation processes as reproduction and death by competition are present and moreover species can go extinct because of genetic drift. The empty space that is left behind by such a subpopulation that dies out, can be reoccupied by another subpopulation and as a result the total meta-population is stable. Moreover a subpopulation can rescue another subpopulation from extinction by sending emigrants when the subpopulation size is getting small [15].

In figure 2.3a it is seen that within the peaks species stay well-mixed until global fixation of the whole 1D population occurs. It is expected that the run-and-tumble dynamics can separate the initially mixed population into subpopulations each consisting of just one of the two species. This means that the fixation dynamics experiences two processes: local fixation of one single peak and, as a result of communication between peaks, eventually global fixation of the whole population. In figure 2.3a this dynamics is not observed and a possible explanation for the absence of local fixated subpopulations is that the particle velocity is too high. As a consequence peaks continuously exchange particles with each other, which makes local fixation within one peak unlikely to occur.

In figure 2.2c a single trajectory of a particle that starts inside a peak is shown, with its color indicating its velocity. It shows, indeed, that the particle continuously moves from peak to peak. Therefore to observe local fixation of one single peak the velocity should be decreased, such that particles spent more time within a peak. This velocity decrease is achieved by decreasing \( v_0 \) from 3 to 2 and increasing \( \gamma \) from 0.4 to 0.6. In the two right panels of figure 2.4 the velocity profile with \( v_0 = 3 \) and \( \gamma = 0.4 \) and the velocity profile with \( v_0 = 2 \) and \( \gamma = 0.6 \) are shown as a function of \( \rho \) to show how the velocity decrease is achieved. When \( v \) is decreased the pattern length also decreases, which allows for decreasing \( w \) without disobeying the condition \( l < w \). A lower \( w \) will result in a larger density difference between the peaks, which will make it easier to observe single peaks and the communication between them. To make sure that the chosen parameter set is in the regime in which \( \Delta \ll w < l \) is plotted as function of \( \rho_0 \) and also the line \( w = 2 \) is shown. It is observed that for \( 1.67 < \rho_0 < 7.5 \) we are in the regime in which \( \Delta \ll w < l \).

Using \( \rho_0 = \frac{1}{w} \), \( \mu = 0.01 \) and \( w = 2 \) this results in the following condition for the death rate: \( 0.00067 < \lambda < 0.003 \).

To investigate if fixation of individual peaks is indeed observed when the new decreased velocity profile is used a simulation is performed with \( v_0 = 2, \gamma = 0.6, w = 2 \) and \( \lambda = 0.00075 \). Note that \( \lambda \) is in the regime set in the previous paragraph. The result of this simulation is shown in figure 2.4c and it is indeed observed that fully red and fully green peaks have developed. Since the velocity goes to a non-zero saturation value \( v_{sat} \) for high densities particle exchange between peaks is allowed. Moreover it is seen that peaks wander through the domain and meet frequently. The communication between peaks is quantified by the flux of particles from peak to peak and it is expected that because of this communication, eventually the whole system fixates globally into one of the two species. A simulation until this global fixation is shown in figure 2.6a for a domain length \( L = 60 \). The system in which fully green and fully red peaks develop can be compared to a meta-population.

Now that the dynamics of local and global fixation is understood it is interesting to investigate whether the spatial structures stimulate or suppress extinction. To investigate this, simulations are performed with a population of interacting run-and-tumble particles, in which patterns will develop, and with a population of independent diffusive particles in which there is no pattern formation. In the latter case the global fixation is quantified using the heterozygosity at \( x = L, H(L,t) \). When this quantity is zero, \( H(L,t) = 0 \), global fixation is reached. For both simulations the same birth-and-death rates, \( \mu = 0.01 \) and \( \lambda = 0.00075 \) are used and also the same number
Figure 2.4: Simulation results of 1D population evolutions of a run-and-tumble population for two different velocity profiles. In the top panels the velocity parameters are $v_0 = 3$, $\gamma = 0.4$ and $\phi = 30$. In panel (a) the result of a simulation performed with $w = 3$, $\alpha = 1.25$, $\mu = 0.01$ and $\lambda = 0.0005$ is shown and in panel (b) the velocity as a function of $\rho$ is plotted. In the bottom panels the velocity parameters are $v_0 = 2$, $\gamma = 0.6$ and $\phi = 30$. In panel (c) the result of a simulation performed with $w = 2$, $\alpha = 1.25$, $\mu = 0.01$ and $\lambda = 0.00075$ is shown and in panel (d) the velocity as a function of $\rho$ is plotted.

Figure 2.5: The interaction length, $w$, the interparticle distance, $\Delta$, and the pattern length, $l$, as a function of the density, $\rho_0$, for $w = 2$, $v_0 = 2$, and $\gamma = 0.6$. The birth rate $\mu$ is 0.01 and $\rho_0$ is defined as $\rho_0 = \frac{1}{w \lambda}$. 
of particles $N = 400$ is used. The diffusion coefficient used in the simulations with non-motile particles is calculated from equation (1.31) as $D = 0.0012$ using the fact that $\rho = \frac{N}{L} \approx 6.67$, with $L = 60$. Multiple simulations are performed in both cases to create a histogram of the global fixation time for multiple realizations. In figure 2.6c and figure 2.6d the resulting histogram for run-tumble particles with $v = v(\rho)$ and independent diffusive particles, with $v = 0$, are shown both on linear an semilogarithmic scale. In the case of interacting run-and-tumble particles 100 simulations are performed and the peak of the histogram is at $t_{fix} \approx 1 \cdot 10^4$. In the case of particles with zero swim speed 100 simulations are performed and the peak is at $t_{fix} \approx 5 \cdot 10^4$. It is seen that the tail of the histogram is much longer for non-motile particles which leads to a higher average fixation time. The average global fixation times for run-and-tumble particles with $v = v(\rho)$ and particles with $v = 0$ are respectively $t_{fix} \approx 2.6 \cdot 10^4$ and $t_{fix} \approx 1.8 \cdot 10^5$. This means that in 1D the motility induced spatial structures stimulate fixation. A possible explanation is that the balancing process between transport and logistic growth decreases the number of particles below the expected carrying capacity, $N = \rho_0 L = \frac{1}{\mu} \frac{\mu}{\lambda} L$. This is shown in figure 2.6b where the evolution of the number of particles in time is shown for both the simulation with interacting run-and-tumble particles and the simulation with independent diffusive particles. From equation (1.17) it is seen that fixation time is proportional to the number of particles and therefore a lower fixation time is expected when less particles are present, as in the simulations with interacting run-and-tumble particles. Apart from the population size the fixation time also depends on the communication between peaks. In the simulation shown in figure 2.6a peaks communicate at a high level, however when the communication is suppressed it also possible that the development of spatial structures increases the fixation time.
Figure 2.6: In panel (a) a simulation result of a 1D population of interacting run-and-tumble particles that can die and reproduce is shown. The parameters are $w = 2, \alpha = 1.25, v_0 = 2, \gamma = 0.4, \phi = 30, \mu = 0.01, \lambda = 0.00075$ and $L = 60$. In panel (b) the evolution of the number of particles in time is shown for both types of particles. In panel (c) and (d) the pdf of the corresponding fixation time is shown on a linear scale and on semilogarithmic scale respectively after 100 simulations for both interacting run-and-tumble particles and independent particles with zero swim speed. The parameters for the simulations with zero swimming speed are $w = 2, \mu = 0.01, \lambda = 0.00075$, $D = 0.0012$ and $L = 60$. 
2.2.3 Pattern formation by externally imposed non-homogeneities

In the previous section the influence of pattern formation on the fixation dynamics is explained. It is stated that the fixation depends on the communication level between the peaks and therefore on the peak size and the size of the low density area between peaks, which modulate the flux of particles from peak to peak. When motility and logistic growth are combined the system becomes very complex and peaks are not stable which makes it hard to measure the communication level. It is expected that peak formation by external factors leads to more stable patterns and therefore allows for measuring the effect of communication between peaks.

External factors that can cause pattern formation are, for example, non-homogeneities in the temperature or in the nutrient concentration as explained in [32]. Temperature is an external factor that changes the growth rate of bacteria [29], which is the motivation for implementing a space-dependent growth rate in the ecosystem to investigate whether stable patterns develop in the population as expected. Simulations are performed with a simple geometry in which strips of width $L_s$ with a lower birth rate, $\mu_s$, are implemented in the domain as shown in figure 2.7. The result of a population expansion in such a domain with periodic boundary conditions in the lateral direction is shown in figure 2.8. It is seen that, indeed, stable high density peaks are formed inside the high growth regions, where $\mu = \mu_f$, of width $L_f$. Again fixation of single peaks and global fixation appear as different processes, well separated with respect to time scales. First each individual peak fixates locally at the front and because of communication eventually the front fixates globally. To quantify the local and global fixation times statistics is performed on multiple realizations with $L_s = 0.05$ and $L_f = 0.2$. In figure 2.9a the probability density function of the local fixation time is shown after 197 realizations and in figure 2.9b the pdf for the global fixation time is shown after 1000 simulations. To create the pdf for the local fixation time, each peak is considered as an individual realization. The average global fixation time is found to be $t_{fix} = (8.8 \pm 7) \cdot 10^2$ and the average local fixation time is $t_{fix} = (5.3 \pm 4) \cdot 10^1$. The large errors can be explained by the shape of the histogram, which includes a very long ‘tail’.

The communication can be characterized by the two lengths $L_s$ and $L_f$, so to analyze the influence of the communication level on the fixation dynamics, the average global fixation time is measured as a function of $\frac{L_s}{L_f}$. In figure 2.10a the probability density functions are shown for three different levels of communication, $\frac{L_s}{L_f} = 0.25$, $\frac{L_s}{L_f} = 0.43$ and $\frac{L_s}{L_f} = 1.0$, with the number of realizations being 1000, 350 and 258 respectively. From figure 2.10a it is observed that the distributions show progressively a low peak and a longer tail, so that the mean fixation time is higher for higher ratios of $\frac{L_s}{L_f}$ or, in other words, for lower communication levels. To clarify the relation between fixation time and communication even further in figure 2.10b the average global fixation time is plotted as a function of $\frac{L_s}{L_f}$. It is seen that fixation time indeed increases when communication is decreased.
Figure 2.7: A sketch of a domain with alternating high and low growth regions. The low growth regions have length $L_s$ and growth rate $\mu_s$ and the high growth regions have length $L_f$ and growth rate $\mu_f$. $L_s < L_f$ and $\mu_s < \mu_f$. The initial front consisting of a random distribution of red and green particles is sketched in the figure.

Figure 2.8: The result of simulations of a population expanding through a domain with alternating high and low growth regions at different times $t$. The low growth regions have length $L_s = 0.05$ and growth rate $\mu_s = 0.2$ and the high growth regions have length $L_f = 0.2$ and growth rate $\mu_f = 1$, so $\mu_s = \frac{1}{5} \mu_f$. The used death rate is $\lambda = 1$. 
Figure 2.9: In panel (a) the pdfs of local fixation time after 197 realizations is given and in panel (b) the histogram of global fixation after 1000 simulations is given. The realizations are performed with $L_s = 0.05$ and $L_f = 0.2$.

Figure 2.10: In panel (a) the histograms for the global fixation time for $\frac{L_s}{L_f} = 0$, $\frac{L_s}{L_f} = 0.43$ and $\frac{L_s}{L_f} = 1.0$ are shown after respectively 197, 303 and 211 realizations. In panel (b) the mean global fixation time is given as a function of $\frac{L_s}{L_f}$.
2.3 Conclusion

In this chapter motility driven phase separation is investigated. It is shown that active particles with a velocity that is a decreasing function of the density will form high density clusters [3]. First pattern formation is observed in the case of run-and-tumble particles that can not die or reproduce. From the results it is observed is that peaks can merge together. This is due to density fluctuations in the peak. Sometimes the density decreases because of such fluctuations, which leads to a higher particle velocity. This increased velocity makes particles escape to neighboring peaks. When particles are allowed to die and reproduce the dynamics of communication between peaks changes. Now peaks show a wandering motion through the domain and when they meet, they communicate by particle exchange.

To change the particle exchange to a level at which subpopulations, consisting of just one of the two species, develop the velocity profile is decreased. With this new velocity profile the development of fully red and fully green peaks is indeed observed in a 1D population evolution of run-and-tumble particles. The genetic process is characterized by local and global fixation. First local fixation within single peaks occurs and because of communication between these single peaks eventually the whole domain fixates globally into one species. Whether fixation is stimulated or suppressed depends on the communication rate between peaks. To measure this communication rate, front propagation in a region with alternating low and high growth strips is simulated. The ratio between the size of the low and high growth strips indicates the level of communication and it is indeed found that the fixation time increases when the communication is decreased by increasing this ratio. The situation described above is comparable to meta-population dynamics, where a population consist of multiple subpopulations that are spatially separated and communicate at some level.
Chapter 3

Population expansion in inhomogeneous media

In the previous chapter it is explained how homogeneity can be spontaneously broken by motility, that can lead to the development of spatial structures in a population in an otherwise homogeneous environment. However, very often spatial structures can be the result of external factors, for example non homogeneity in the nutrients level in different parts of the domain. Not only can externally imposed non-homogeneities lead to stable patterns, but they will also influence the dynamics of the population and its genetics significantly, especially when a population is expanding in this inhomogeneous environment. To investigate how populations expand in inhomogeneous media we performed a number of numerical investigations. The non-homogeneities are included in the population model, introduced in section 1.1.2, at the microscopic level of individuals by means of spatially dependent diffusion. Using this model the influence of the inhomogeneities on the population front shape and on its velocity is explored. Moreover a more efficient event driven model is introduced for the front dynamics. In addition to the front dynamics we investigate the influence of the inhomogeneities on the population genetics. Since it is known from literature that front roughness influences the extinction dynamics the coupling between the front shape, that is changed by the inhomogeneities, and the genetic processes is analyzed.

3.1 Front propagation in turbulence: two regimes

In this thesis the focus is on front propagation in inhomogeneous media in the field of biology. However front propagation in inhomogeneous media occurs in many other scientific areas, such as combustion. In [1] the front speed in a turbulent media is investigated in the case of combustion and since they also consider the Fisher/KPP equation, solved in the presence of a turbulent flow, the results are applicable to a much broader field, such as population expansions in inhomogeneous media.

In turbulent premixed combustion the Damköhler number is of great importance. In [1] this number is defined as the ratio of the turnover time of the eddies, \( (u_{rms}k_t) \), to the chemical reaction time, \( \tau_c \):

\[
Da = (-\tau_c u_{rms} k_t)^{-1},
\]

where \( u_{rms} \) is the root-mean-square velocity of the turbulence and \( k_t \) is wave number of the energy-carrying eddies. The Damköhler number distinguishes two regimes for the front speed: small-scale and large-scale turbulence. The first regime is characterized by small Damköhler numbers and in this regime the turbulent front thickness is much broader than the scale of the turbulent eddies. Because of this good scale separation the flame speed can be computed using a new effective total diffusivity, \( D_t \), which is the sum of the microscopic and turbulent diffusion. This effective
diffusivity can be simply substituted in the equation for the laminar flame speed, $S_L$, which obeys $S_L \sim \left( \frac{D}{t_c} \right)^{1/2}$, where $t_c$ is the chemical time scale. For the turbulent flame speed this means:

$$S_L \sim \left( \frac{D_t}{t_c} \right)^{1/2}.$$  

(3.2)

When the Damkohler number is large, in the large-scale turbulence regime, the turbulent front thickness is smaller than the scale of the turbulent eddies. In this case the effective diffusion can no longer be used to determine the turbulent flame speed and there is no clear definition for the front speed in turbulence.

In this work we are interested in how spatial inhomogeneities on the diffusion (and $v_f$) affect the population and its genetics while propagating. We assume that the population is propagating at small Damkohler numbers, so that $v_f$ is still defined and the effect of a turbulent environment is included changing the microscopic diffusivity of individuals from $D$ to an effective total diffusion coefficient $D_t$.

### 3.2 Optical theories for front propagation in inhomogeneous media

In section 1.3.2 front propagation around an obstacle is explained. Based on [26] the front dynamics was described using the principle of least time, called Fermat’s principle in optics. Fermat based his principle on Huygen’s principle for light ray propagation. Huygens stated that every point on a propagating wavefront is the source of a secondary spherical wave. The result is that the wavefront at later time is the envelope of all these spherical waves [12]. This is applicable to front propagation as modeled in this work, since every individual particle is assumed to spread out its offspring isotropically. In other words when starting with one single bacterium in an empty domain a colony will start to grow radially. Sketches of a radial and linear Huygen’s front are shown in figure 3.1a. Huygens’ principle is used to derive the laws of refraction and reflection, however it could not explain the concept of interference. Fresnel successfully modified Huygens’ theory by including assumptions about the amplitude and phase of the secondary waves such that also interference is included. The Huygens-Fresnel principle is used to explain diffraction of light around an obstacle or an edge.

Fermat used Huygens’ principle to derive his theory of least time, which implies that a light beam travels the path that is traversed in the least time. According to Fermat’s principle the ray of light traveling from $A$ to $B$ leaves the optical length stationary under variation of the family of nearby ray paths. In equation form this is described as

$$0 = \delta L = \delta \int_A^B n(r(s)) \sqrt{\frac{dr}{ds} \cdot \frac{dr}{ds}} ds,$$

(3.3)

where $L$ is the optical length and $n(r)$ the refractive index. Furthermore $r(s)$ describes the path, where $s$ is the arc-length parameter. With the use of $ds^2 = dr(s) \cdot dr(s)$ and $|\dot{r}| = 1$ this results in

$$\frac{d}{ds} \left( n(r) \frac{dr}{ds} \right) = \frac{\partial n}{\partial r},$$

(3.4)

which is called the general eikonal equation in optics [13]. The scalar description of this equation is

$$|\nabla S|^2(r) = n^2(r),$$

(3.5)

with $S(r)$ a level set of the wave front. For refraction of light on the interface between two media Fermat’s principle leads to Snell’s law. In figure 3.1b a sketch of refraction of a light ray is shown. When this path is minimized in time the following equation is found for the refraction angles:

$$\frac{\sin \theta_1}{\sin \theta_2} = \frac{v_1}{v_2} = \frac{n_2}{n_1},$$

(3.6)
where \( v_i \) is the velocity and \( n_i \) the refraction index of medium \( i \). Therefore \( \theta_1 \) is the angle of incidence and \( \theta_2 \) is the angle of refraction. Fermat’s principle can be derived from Huygens’ principle only in the limit of small wavelengths. When we want to apply optics on the refraction of particle trajectories and genetic interfaces the limitation is not the wavelength but the fluctuations on the trajectories. Therefore we can only apply geometrical optics to the front propagation in the limit of small fluctuations, compared to the size of the non-homogeneities.

\[
\begin{align*}
\text{Figure 3.1:} & \quad \text{In panel (a) a sketch of Huygens’ principle is given. Every point at a front is the source of a radial wave and the front at later time is the envelop of all wavelets. The front and the wavelets are sketched for a linear and radial front. The original figure can be found in [8]. In panel (b) refraction of a light ray on the interface between medium 1 and medium 2 is sketched. The angle of incidence is indicated with } \theta_1 \text{ and the angle of refraction is indicated with } \theta_2. \text{ The velocity and the refractive index for medium } i \text{ are } v_i \text{ and } n_i, \text{ with } n_2 > n_1.
\end{align*}
\]

3.3 Simulations

3.3.1 High- and low-diffusion areas

Refraction of the genetic interface

In the limit of small fluctuations it is expected that refraction of a genetic interface can be observed on the border between different front velocities, since in a population expansion as well as in optical light ray propagation, the direction of propagation is perpendicular to the front. In the case of refraction of a genetic interface the diffusion coefficient \( D \) would play the role of the refractive index, since it changes the front velocity locally. To measure refraction in the case of a front expansion the genetic interface between a red and a green segment is followed while approaching an interface between two different diffusion regimes. The domain used for this simulations, consisting of two different diffusion regimes is sketched in figure 3.2a. The population front is initially filled with red species for \( y > 0.5 \) and green species for \( y < 0.5 \). In figure 3.2b the result of such a population expansion in the described domain is shown at \( t = 550 \). It is seen that the interface is indeed refracted at the edge between \( D_1 \) and \( D_2 \). To average out fluctuations the interface path is averaged over 200 realizations. The resulting average path of the genetic interface is shown in figure 3.3. In the same figure the theoretical prediction of the path is shown as a red dashed line, which is calculated using Snell’s law, equation (3.6), with \( \theta_1 = 17^\circ, v_1 = 0.0013 \) and \( v_2 = 0.0029 \). The resulting angle of refraction is \( \theta_2 = 37^\circ \). It is seen that the path computed from simulations does follow the theoretical prediction, which means that the refraction of the genetic interface can
Figure 3.2: In panel (a) a sketch of a domain with two different diffusion coefficients \(D_1\) and \(D_2\) separated by a straight line which is tilted under an angle \(\theta_1 = 17^\circ\) is shown. In panel (b) the result of a simulation of a population expansion in such a domain at \(t = 550\) is shown. The simulation is performed with \(D_1 = 2.5 \cdot 10^{-6}\), \(D_2 = 5 \cdot 10^{-6}\) and \(\mu = \lambda = 10\). It is seen that the interface between red and green particles is refracted upwards at the edge between the two diffusion coefficients.

indeed be explained by Snell’s law, when fluctuations on the interface motion are smaller than the domain size.

Low diffusion area

Now that it is known that optical theory can be used to describe the front dynamics on an interface between different diffusion coefficients, many different geometries of space dependent diffusion can be modeled. In this subsection the situation of a low diffusion area is modeled, in which the front will travel with a lower velocity, \(v_{\text{obs}}\), compared to the front velocity in the rest of the domain, \(v_f\). A comparison to optics leads to a possible explanation for the front shape. All the particles spread their offspring as a radial wave and according to Huygens’ principle the front is the envelope of all these wavelets. The front will experience different velocities in the domain and as a result the part of the front that is in the region with \(D = D_1\) is ahead of the front that is in the region with \(D = D_2\), since \(D_1 > D_2\). Using Huygens’ principle this means that the front will develop both in the propagation direction and in the lateral direction. A simple geometry to study this situation consist in simulating a rectangular domain with a low diffusion coefficient, with respect to the rest of the domain, as sketched in figure 3.4a. In figure 3.4b the result of a population, which is initially mixed randomly, expanding in this domain is shown. Because the front velocities outside and inside of the rectangular region are different, an angle \(\psi\) will develop between the faster and slower parts of the front as shown in figure 3.4b. This angle should equal the ratio of the two velocities in the lateral and perpendicular direction. Using \(v \sim \sqrt{D}\) the expression for \(\psi\) becomes

\[
\tan(\psi) = \frac{v_{\text{obs}}}{v_f} = \sqrt{\frac{D_2}{D_1}}.
\]

(3.7)

To verify this relation several simulations with a constant \(D_1\) but different \(D_2\) are performed. The front angle \(\psi\) is determined and the tangent of \(\psi\) is plotted as a function of the ratio between \(D_2\) and \(D_1\). The result of this plot is shown in figure 3.5. The red line in this figure represents the function \(\tan(\psi) = \sqrt{\frac{D_2}{D_1}}\), which agrees well with the measured data points. However not all the points are on the predicted line, which can be explained by the fact that the velocity is not exactly \(2\sqrt{\mu D}\) since the simulations are not exactly performed in the weak noise limit, since the non-dimensional noise strength is \(N^{1/2} \sqrt{D/\mu} \lesssim 1\) and does not obey \(N^{1/2} \sqrt{D/\mu} > 1\).
Figure 3.3: The path of the genetic interface computed numerically and analytically. The blue line is the numerical result which is the average interface path over 200 simulations with \( D_1 = 2.5 \cdot 10^{-6} \) and \( D_2 = 5 \cdot 10^{-6} \). The red dashed line is the analytical prediction determined using equation (3.6) with \( \theta_1 = 17^\circ, v_1 = 0.0013 \) and \( v_2 = 0.0029 \). The resulting angle of refraction \( \theta_2 = 37^\circ \).

Figure 3.4: In panel (a) the simulated geometry consisting of a domain with a rectangular shaped area with a lower diffusion coefficient \( D_2 = \frac{D_1}{2.5} \) is shown. In panel (b) the corresponding simulation result of a population front expanding outside, while also invading the rectangular domain is shown for \( D_1 = 2.5 \cdot 10^{-5}, D_2 = 1 \cdot 10^{-5} \) and \( \mu = \lambda = 1 \). In the plot the angle \( \psi \) is sketched.
The tangent of $\psi$ as a function of the square root of the ratio between $D_2$ and $D_1$. The red line represents the function $\tan(\psi) = \sqrt{\frac{D_2}{D_1}}$, corresponding to the solution of the geometric optics with velocities $v_2$ and $v_1$ equal to the velocities of light propagation in different media.

High diffusion area as a diverging lens

In the case of a zero diffusion area it was found that a cusp in the front develops as explained in section 1.3.2. However the opposite behavior is also thinkable, namely a high diffusion area in which the front will move faster. In an aquatic environment such a region can be compared to a turbulent region if the time scales of the smaller eddies are much smaller than the generation time. In this case the turbulent region can be modeled by replacing the microscopic diffusion coefficient $D$, by the enhanced total diffusion coefficient $D_t$.

To simulate this situation we consider a circular region with diffusion coefficient $D_t$, which is higher than the microscopic diffusion coefficient $D$. It is expected that the front directly after the high diffusion area is ahead of the rest of the front. Six snapshots of simulations of a front propagating through this domain at different times are shown in figure 3.6. It is observed that the high diffusion area behaves as a diverging lens. To show the divergence of trajectories the ancestor lines of eight different particles in the front at $t = 94$ are shown in figure 3.7, where the size of the high diffusion region is chosen such that it is larger than the fluctuations in the particle trajectories. It is observed that all eight particles are offspring of just one particle that was in the center of the initial front. This means that a particle starting in front of the high diffusion area has an advantage and its offspring will occupy a bigger part of the eventual front giving an effective enhance in the survival probability.

The diverging lens behavior lead to the development of a blob in the front. The front shape can be regarded as the sum of a linear part, caused by linear front propagation with the Fisher velocity outside the circular high diffusion area, and a circular part, caused by radiation of the high diffusion region from its center. This behavior can be explained by Huygens’ principle. The front is a collection of circular waves and when undulations in the front occur radiation from these points lead to front propagation in different directions. The front that develops around a high diffusion area is the combination of the radial and linear Huygens’ fronts sketched in figure 3.1a. Since the noise level in the simulations is not exactly in the strong or weak noise limit, $N \sqrt{D/\mu} \approx 1$, the Fisher velocity cannot be determined using (1.24) or equation (1.25) but has to be measured from simulations. With the use of this measured velocities it is possible to derive an expression for both parts of the front. The linear part of the front can easily be described using $x = x_{int} + v_ft$, where $x_{int}$ is the initial $x$–position of the front. The description of the circular part of the front is more complex and two different situations should be taken into account. In figure 3.6 it is seen that the filling of the particles occurs almost instantaneously. This means that the radiation from the center starts as soon as the linear front hits the circle shaped high diffusion region and this is referred to as the situation of instantaneous filling. The equation for the circular front in this case
Figure 3.6: The expansion of a population in a domain with a circularly shaped high diffusion region in which the diffusion coefficient is $D_t = 10 \cdot D$ at six different time instants. The initial condition is a layer of thickness 0.5 consisting of red species for $y > 0.5$ and green species for $y < 0.5$. Outside the high diffusion area the diffusion coefficient is $D = 2.5 \cdot 10^{-5}$, the birth-and-death rates are $\mu = \lambda = 1$ and the initial number of particles is $N_{\text{start}} = 2000$.

Figure 3.7: The trajectories of eight particles at the front that propagates in a domain with a high diffusion area, indicated with the black circle, at $t = 94$. The simulation is performed with $D = 2.5 \cdot 10^{-5}$ and $D_t = 10 \cdot D$. The birth-and-death rates are $\mu = \lambda = 1$. 

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Figure 3.8: A sketch of a domain with a circular high diffusion area. The length scales $x_0, x_1, r_0, R_1(t)$ and $R_2(t)$ are given and the front experiences two different velocities $v_1$ and $v_2$.

is:

$$R(t) = r_0 + v_f \left( t - \frac{x_1}{v_f} - \frac{2r_0}{v_r} \right)$$

$$= r_0 + v_f \left( t - \frac{x_1}{v_f} \right)$$

(3.8)

(3.9)

where $x_1$ is the distance between the initial position of the front and start of the high diffusion region at $y = 0.5$, $r_0$ is the radius of the high diffusion region and $v_r$ is the velocity inside the high diffusion region, as sketched in figure 3.8. Equation (3.9) follows from (3.8) using $v_r \gg v_f$ and $x_1 \sim r_0$. In optics an eikonal equation is used to describe the front dynamics, which follows from Fermat’s principle of least time. Above expressions for the front shape can be seen as an ‘ad hoc’ solution for the eikonal equation in the case of population expansion in the simple geometry of one high diffusion area.

When the filling time is finite the phase delay of the circular wave is as if it had been triggered by the movement of the planar wave through the center of the high diffusion area. Now the expression for the radial part of the front knows two cases, the case in which the front is still in the high diffusion region and the case in which the front is outside the high diffusion region. The expressions are

$$x_0 < x < x_0 + r_0$$

$$x > x_0 + r_0$$

$$R(t) = r_0 + v_f \left( t - \frac{x_1}{v_f} - \frac{2r_0}{v_r} \right),$$

$$R(t) = v_r \left( t - \frac{x_1}{v_f} - \frac{r_0}{v_r} \right),$$

(3.10)

(3.11)

where $x_0$ is the x-coordinate of the center of the high diffusion region. Now that the equations for the linear and the circular part of the front are derived, it is possible to predict the front shape for different velocities. Moreover the time at which the radiation started can be found. This time is called the explosion time, $t_{\text{explosion}}$, and corresponds to $R(t) = 0$. The top figures in figure 3.9 show that both the front equation for instantaneous filling and the front equation for finite filling do indeed predict the circular part of the front. The calculated explosion times are respectively $t_{\text{explosion}} = 56$ and $t_{\text{explosion}} = 60$. In the bottom figures snapshots of the simulations at these times are shown and they indeed correspond to the starting of the radiation from the high diffusion region. For instantaneous filling this is when the linear front hits the high diffusion region first and in the case of finite filling this is when the center of the circular high diffusion area is touched. Similar behavior is expected for other shapes of the high diffusion area. Based on a multiple expansion the resulting front will be as if an effective circle is present.

So far the focus was on the influence of the high diffusion area on the front dynamics, however also the genetics is influenced by an area of inhomogeneity. An important measure for the genetics
Figure 3.9: On top the analytical predictions for the front using equation (3.9) and (3.11) is shown together with the numerical result. In panel (a) the case of instantaneous filling is shown with $D_t = 2.5 \cdot 10^{-4}$ and panel (b) the case of finite filling is shown with $D_t = 5 \cdot 10^{-5}$. On the bottom snapshots of the simulation at the predicted explosion time are shown for both cases. All simulations in this figure are performed with $D = 2.5 \cdot 10^{-5}$ and $\mu = \lambda = 1$. 

is the lateral motion of the genetic interface, which is the interface between sectors of different species. In figure 3.6 it is seen that the interface is refracted and pushed toward the intersection between the flat front and the circular one, pinned at a cusp. Depending on whether the interface is initially, in the upper half or lower half of the domain, it will be refracted downwards or upwards. Even when an interface does not hit the obstacle it will experience the drift. When statistics is done on the interface position after the high diffusion area two peaks are expected. Moreover the peaks are expected to be equally far from the center of the high diffusion circle. In figure 3.10 it is seen that indeed two peaks are found in the histogram of the \( y \)-position of the interface at \( t = 94 \) using 240 realizations and that they are equally far separated from the center of the high diffusion area, \( y = 0.5 \). Moreover it is shown in figure 3.11 that the genetic interface indeed follows the black line drawn through these intersection points. It has to be noted that this is only true if the high diffusion region is filled almost instantaneous with the type of species that is entering the high diffusion area first. In this case particles entering the high diffusion region have an advantageous over the other species and will occupy a bigger part of the final front, despite both types of particles having the exact same characteristics. When the ratio between \( D_t \) and \( D \) is lower and the filling of the high diffusion area is finite, both species can be present in the high diffusion area. In this case it takes longer for one of the two species to take over the whole front.

### 3.3.2 Front propagation in a random medium

#### Front velocity in inhomogeneous media

An aquatic environment, such as the ocean, is characterized by a high level of non-homogeneities. So far the focus was on a single non-homogeneity in the domain but in this section we consider a quenched distribution of high diffusion areas throughout the domain. These high diffusion areas can be seen as turbulent regions with some effective diffusivity, \( D_t \), when the length scales of the eddies is much smaller than the front thickness. To measure the front velocity of a population expansion through such a random medium accurately, a large domain size is needed. Using the discrete particle based model, the simulation of this situation, with a sufficient large domain size and a sufficient high population size, is expensive. Therefore it is more efficient to model just the motion of the front itself, since it was found to be described by the eikonal equation, which was solved ‘by hand’ for the simple case of a single high diffusion area. The solution is presented in equation (3.11) and can be used to build a simple event driven model for a front propagating in a medium with a quenched disorder of high diffusion areas. These high diffusion areas are modeled as ‘scattering centers’, which are activated as soon as they are touched by the propagating front. This is based on the result of the previous section, where it was found that a high diffusion area
Figure 3.11: The result of a simulation of a population expansion in a domain with a circular high diffusion region with $D = 2.5 \cdot 10^{-5}$, $D_r = 2.5 \cdot 10^{-4}$ and $\mu = \lambda = 1$ at six different times. The blue lines show the analytical predictions of the linear and the radial part of the front. The black dots represent the intersection point of both parts of the front.

started to ‘radiate’ as soon as its center was touched by the propagating front. The scattering centers form the centers of circles of radius $R_0$ in which the front velocity is higher than in the rest of the domain. Outside the scattering circles the front propagates with the Fisher speed, $v_f$, and inside a scattering area the front speed is $v_r$ with $v_r > v_f$. The initial condition is a linear front that will start to propagate from $x = 0$ with velocity $v_f$. The resulting front is a collection of this linear front and all radial fronts, that are the result of radiation from the activated scattering centers. In figure 3.12 several snapshots of a simulation with this new event driven model are shown, in which the activation of scattering centers is shown.

To determine the velocity of the front propagating in this random medium, first a standard homogenization procedure is used to derive an effective velocity based on the volume fractions of the high and low diffusion areas:

$$v_{\text{eff}} = \frac{v_r S_r + v_f S_f}{S_r + S_f},$$

(3.12)

where $S_r$ is the total area occupied by the scattering circles in which the velocity is $v_r$ and $S_f$ is the area in which the velocity is $v_f$. It is found numerically that the eventual average front speed exceeds this effective velocity.

To find an expression for the final front velocity $v_*$, the study in [25] is used. In this study the front speedup or slowdown of a Huygens front, due to velocity perturbation is investigated. In [25], a speedup of a Huygens front is found, scaling with the velocity perturbations according to a certain power law. This scaling is derived solving a first passage problem for the front. This means that all the particles in the front represents first arrivals and correspond to the fastest trajectory out of all possible trajectories. Now the dynamics of the trajectories is described as

$$\frac{dx}{dt} = v_n,$$

(3.13)

where $v$ is the front velocity and $n$ is the unit vector normal to the front. For the first passage problem a necessary condition is

$$\frac{dn}{dt} = -P_n (\nabla v),$$

(3.14)
Figure 3.12: The result of a simulation with the event-driven model of a front propagating through a random medium. The random medium is modeled as a quenched sequence of scattering centers. The used parameters are $R_0 = 0.1, v_r = 0.028, v_f = 0.0067$ and $\nu = 0.5$, where $\nu$ is the mean distance between the scattering centers. The velocities correspond to $D = 2.5 \cdot 10^{-5}, D_t = 10D$ and $\mu = 1$.

where $P_n$ is the projection orthogonal to $n$. Equation (3.13) and equation (3.14) are equal to the ray equations for geometrical optics. Just like in optics a generalized ‘eikonal’ equation can be derived. This eikonal equation for the first arrival time $T^1(x)$ is

$$v(T^1(x), x) \frac{\nabla T^1(x)}{\nabla T^1(x)} = 1.$$  \hspace{1cm} (3.15)

Since $T^1$ is a constant over a front, $\nabla T^1$ is perpendicular to the front. To derive an expression for the scaling of the velocity with the perturbation method, the velocity is assumed to fluctuate around some mean value. For convenience this mean value is assumed to be unity, which means that the front velocity can be described as

$$v(t, x) = 1 + \epsilon V(\epsilon t, x, y),$$  \hspace{1cm} (3.16)

where $V$ is a homogeneous isotropic random velocity field and $\epsilon$ is the perturbation that goes to zero. In this expression the scalar $x$ can be seen as a time-coordinate, since the front propagates in this direction and the part of the domain that is already traversed by the front is not of interest. From earlier studies [16] [17] it is expected that the front reaches a statistically steady state after traveling a distance of order $\epsilon^{-2/3}$ and that the eventual front velocity exceeds unity by $\epsilon^{4/3}$. Guided by this expectation the following rescaled parameters are defined

$$\xi = \epsilon^p y,$$

$$\tau(\xi, y) = \epsilon^{-p} [T^1(x, y) - x].$$  \hspace{1cm} (3.17, 3.18)

The consequence of this rescaling is that if $\nabla_x \tau$ reaches a steady value $-C$, than $\nabla_x T^1$ averages to $1 - C \epsilon^{2p}$ after a characteristic distance $y \sim \epsilon^{-p}$. For the passage rate, or the front velocity, of the medium this leads to

$$v_* = 1 + C \epsilon^{2p},$$  \hspace{1cm} (3.19)
The front speedup \( v_* - \langle v \rangle \), computed numerically using the event driven model, is shown for different values of the velocity perturbation \( \epsilon \). In panel (a) the results in the weak fluctuation limit are shown on a logarithmic scale. A fit is drawn through the data points and the resulting slope is 1.29 ± 0.12. In panel (b) a larger range of results is shown on a normal scale. The fit resulting from the figure in panel (a) is also shown in this figure. It is seen that only the data points in the weak fluctuation limit follow the fit.

Figure 3.13: The front speedup \( v_* - \langle v \rangle \), computed numerically using the event driven model, is shown for different values of the velocity perturbation \( \epsilon \). In panel (a) the results in the weak fluctuation limit are shown on a logarithmic scale. A fit is drawn through the data points and the resulting slope is 1.29 ± 0.12. In panel (b) a larger range of results is shown on a normal scale. The fit resulting from the figure in panel (a) is also shown in this figure. It is seen that only the data points in the weak fluctuation limit follow the fit.

after a Taylor expansion around \( \epsilon = 0 \). The next step is to show that statistically steady state is indeed reached for \( p = \frac{4}{3} \). To prove this, the velocity, as described in equation (3.16), is substituted in the eikonal equation (3.15) using the rescaled parameters. For \( \frac{1}{2} < p < 1 \) and \( \epsilon \to 0 \) this results in the following simplified expression for the eikonal equation:

\[
\nabla \xi \tau + \frac{1}{2} |\nabla \tau|^2 = -\epsilon^{1-2p} V(0, \epsilon^{-p} \xi, x) \equiv \eta(\xi, y).
\]  

(3.20)

In this expression the prefactor \( \epsilon^{1-2p} \) will diverge if \( \epsilon \) goes to zero, however the dependency on \( \xi \) will become more rapid in this limit. It is found that for \( p = \frac{4}{3} \) these processes balance and a steady state is reached.

Since it was found that the population fronts modeled in this work can be described using Huygens’ principle, it is interesting to find if the results found in [25] for the front speedup are similar to the results for the front velocities using the event driven model.

To investigate if this scaling principle is indeed applicable the front velocity should be defined as in equation (3.16). This is achieved by forcing the high diffusion area to occupy half of the total surface, such that the mean velocity is simply \( v = \frac{v_f + v_r}{2} \). The perturbation is now defined as \( \epsilon = v_r - v = v - v_f \), assuming \( V = 1 \). Simulations are then performed for different values of \( \epsilon \) such that the eventual front velocity \( v_* \) can be plotted as a function of the perturbation \( \epsilon \). The scaling is expected to hold only in the small perturbation limit, which means that \( \epsilon \) should not be chosen too high compared to \( \langle v \rangle \). A proper way to determine the scaling of the front velocity with \( \epsilon \) is to plot \( v_* - \langle v \rangle \) as the function of \( \epsilon \) on a logarithmic scale. If equation (3.19) is indeed valid, the data points will show a linear behavior with slope \( 2p \). In figure 3.13a this plot is shown and it is found that the data in the weak fluctuation limit do indeed follow the linear behavior and the slope of this line is determined with a linear fit as 1.29 ± 0.12. From theory it is expected that the slope is \( 2p = \frac{8}{3} \), so the numerical result for the speedup scaling matches the analytical expectation within the uncertainty. In figure 3.13b the speedup is plotted for a wider range of perturbations \( \epsilon \). It is seen that indeed only for small \( \epsilon \) the found scaling is valid. Moreover it is seen that for larger perturbations \( v_* - \langle v \rangle \) becomes negative which means that the front is slowed down. In this case the front velocity outside the scattering areas is almost zero and when scattering areas do not overlap the front will propagate very slow.
Population genetics in a random medium

The event driven model presented above gives results concerning the front shape and front speed, but the discrete particle model is necessary to investigate the fluctuating dynamics of genetic interfaces. Therefore to explore the influence of non homogeneities on genetic processes, such as extinction probability, the discrete particle model introduced in section 1.1.2 is used. To perform accurate measurements on extinction probabilities the domain size should be large, compared to the size of the high diffusion areas and the mean distance between high diffusion areas. However, with the discrete particle model, modeling a large domain size and modeling multiple high diffusion areas is very expensive. To prevent high computational costs the model should be adapted. Since the focus is on the genetic processes in the front and not on the processes in the wake of the front the model is adapted such that only a certain width of the front is modeled. This width should be larger than the interparticle distance and the interaction length, so that all processes in the front are captured. Particles in the wake of the front are considered to be static, so that they cannot die, reproduce or move anymore. The result of a simulation with the discrete particle model of a front expansion through a quenched sequence of high diffusion areas of size \( R_0 = 0.1 \) and mean separation distance \( \nu = 0.5 \) is shown in figure 3.15. These parameters are equal to the parameters used for the simulation with the event driven model shown in figure 3.12. Inside the high diffusion areas the diffusion is 10 times higher then outside. It is seen that undulations in the front occur because of the high diffusion areas. To check if the front behaves in the exact same way as the front does using the event driven model, both front results are plotted in the same figure as shown in figure 3.15f and they are found to match. From figure 3.15 it is observed that the genetic diversity in the front decreases in time. This effect is due to genetic drift and might be enhanced by the high diffusion regions. To check the last statement the fixation time of a front that propagates in a homogeneous medium is compared to the fixation time of a propagating front in a random medium. Fixation is reached as soon as the outer front layer consist of only one type of species. In figure 3.16 the probability density functions of the fixation time for a front propagating through a domain with and without inhomogeneities are shown. The fixation time is determined after 100 simulations and it is checked that indeed half of the times the red species win and the other half of the times the green species win as expected. For the random medium \( D = 2.5 \cdot 10^{-5} \) and \( D_i = 2.5 \cdot 10^{-4} \) and for the homogeneous medium \( D = 5.3 \cdot 10^{-5} \), which is the effective diffusivity corresponding to the volume fractions of the turbulent areas in the random medium. From the figure it is found that the peaks of both histograms are approximately at the same value, \( t_{fix} \approx 240 \). However the tail of the histogram is much longer for the domain without inhomogeneities, which means that the average fixation time is longer in this case. The average fixation times for a front propagating through a domain with and without inhomogeneities are respectively \( t_{fix} \approx 709 \pm 656 \) and \( t_{fix} \approx 319 \pm 158 \). The large tails of the pdfs are causing the big errors. Apart from the fixation times also the genetic interface motion is analyzed in order the understand the genetic processes. From figure 3.15 it is seen that often the interface is pinned in a cusp, for example the interface at \( y \approx 1.4 \) in figure 3.15d. This can be explained by the fact that in a valley there is a drif present, pushing the interface towards the center of the valley. This behavior of the interface in a rough front is better illustrated by the concepts of inflation and deflation as described in [23]. Inflation occurs at a curved frontier, for example in a radial expansion. The perimeter of the front will increase in time, which suppresses the effect of genetic drift because it makes genetic interfaces move away from each other. However the opposite occurs in the case of deflation. Deflation occurs for example in the case of a population ring that expands inwards towards the center of the ring. Now the perimeter of the front decreases and interfaces are more likely to meet, which speeds up the fixation process [23]. For the undulated front this implies that a genetic interface will move away from positive curvatures and will be stuck inside negative curvatures in the front, where an inwards drift is present. The latter phenomenon is sketched in figure 3.14a. This observations regarding to the interface motion are of interest, since it can be used to implement the genetics in the simple event driven model that was derived for the front dynamics. If the relation between the motion of the interface at the front and the front dynamics is completely understood the genetics could be implemented by updating the interface position at the front. The interface motion could be modeled as a Brownian motion along the front, with a drift in a preferred direction.
given by the local curvature of the front.

Figure 3.14: In panel (a) the motion of a genetic interface in a valley is sketched, where an inwards drift is present. Because of Brownian motion the interface will first move in the lateral direction with \( \delta \) and then it will move in the perpendicular direction with the front velocity \( \Delta \) as a result of the expansion. In panel (b) the superdiffusive character of a genetic interface on a rough front is sketched. The roughness induces a tilt, which changes the direction of the displacement of the genetic interface at the front, as sketched in the figure. Figure (a) is reproduced from [10].

3.3.3 Front roughness

Domain inhomogeneities change the front shape, as observed and described in detail in the previous section. It is important to understand the influence of this changing front shape on the genetic processes. It is known from [24] that front roughness changes the wandering motion of the genetic interface at the front and therefore influences the fixation dynamics of the population. If the front would be flat, for example in the case of a 1D population evolving in time, the so-called 1+1D case, the genetic interface will perform a Brownian motion in time [28]. In this case the variance of the Brownian motion behaves as \( \sigma^2 \sim D t^{2 \zeta} \), with \( \zeta \) the wandering exponent that equals \( \zeta = \frac{1}{2} \). However when a front propagates in a homogeneous 2D domain, the so-called 2+1D case, undulations may develop because of noise, inducing a transverse drift on the genetic interface motion. In figure 3.14b a sketch of the magnitude and direction of this transversal drift compared to the rough front is shown [10]. The genetic interface will inherit this drift, caused by front roughness, and consequently show a different behavior then in the 1+1D case. In [10] a superdiffusive behavior for the genetic interface motion is found experimentally, characterized with \( \zeta > \frac{1}{2} \), with \( \zeta \) the wandering exponent of the random interface motion.

To understand this superdiffusive behavior the transverse drift term is quantified, using a roughness exponent, \( \chi \), and a dynamical exponent, \( z \), which characterize the front roughness as proposed in [10]: A segment of the rough front of dimension \( L \) shows a displacement of order \( L^x \) from a straight line and saturates on time scale \( L^z \). The transverse drift acting on the tip of the genetic interface is now proportional to \( L^{x-1} \sim t^{(x-1)/z} \) as shown in figure 3.14b, using that the characteristic time-scale is \( t \sim L^z \) as mentioned before. As a result the transversal displacement of the fluctuating random walk of the interface, which is the drift velocity multiplied by time, scales as \( t^{1+(x-1)/z} \), so the wandering exponent \( \zeta \) is:

\[
\zeta = 1 + \frac{(x-1)}{z}.
\]  

This means that the variance of the random genetic interface walk, \( \sigma^2 \), obeys \( \sigma^2 \sim D t^{2 \zeta} = D t^{2(1+(x-1)/z)} \).
Figure 3.15: A simulation of a population expanding in a random medium is shown for different times \( t \). Two types of particles are present and the circles with radius \( R_0 = 0.1 \) indicate high diffusion areas in which \( D_t = 10 \cdot D \). \( D \) is the diffusion coefficient outside these circular region and equals \( D = 2.5 \cdot 10^{-5} \). Furthermore the mean distance between circular regions is \( \nu = 0.5 \) and the birth-and-death rate are \( \mu = \lambda = 1 \). The blue line in the figure in panel (f) is the front resulting from a simulation with the event driven model with the exact same parameters.

Figure 3.16: In panel (a) the pdf for the fixation time after 100 realizations for both front propagation in a homogeneous and an inhomogeneous medium are shown on a linear scale. In the panel (b) the same pdf is shown on a linear scale. Fixation has occurred as soon as the front consist of only one of the two species.
3.1: KPZ equation

In [11] it is found that different models for stochastic growth lead to the same characteristics for what concerns the dynamical and the roughness exponents of the front. This class of models is called the Kardar-Parisi-Zhang (KPZ) universality class and underlying it there is a non-linear stochastic differential equation, known as the KPZ equation.

The front roughness, $\omega$, in the KPZ universality class obeys the following equation:

$$\omega \sim f_{KPZ}(t) \left( \frac{t}{L^2} \right), \quad (3.22)$$

where $L$ is the domain length and the KPZ scaling function, $f_{KPZ}(x)$, behaves as $x^3$, with $\beta = \chi/z$, for small $x$ and approaches a constant value for large $x$ [11].

Based on the KPZ universality in [14] front roughness is analyzed for one of the simplest growth models, the Eden model, in which a cluster of particles grows by random accumulation at the cluster boundary. As a result the roughness exponent, $\chi$, and the dynamical exponent, $z$, are determined as $\chi = \frac{1}{2}$ and $z = \frac{3}{2}$, leading to a wandering exponent of $\zeta = \frac{2}{3}$, using equation (3.21), for the case of front propagation in 2+1D [14]. To check if our model falls in the KPZ universality class, the dynamical and the roughness exponent are measured, by analyzing the front roughness $\omega$ as a function of time. From equation (3.22) it is expected that the front roughness initially grows as $\omega \sim t^\beta$, with $\beta = \frac{2}{3}$, and eventually saturates to a level that scales with $L$ as $L^\chi$. The saturation level, $L^\chi$, is given by a finite size effect and it scales with the domain size $L$, compared to a fix interparticle distance, $\frac{z}{L}$. In our model we vary the number of particles per cell by changing the ratio between the birth-and-death rate, $\frac{\lambda}{\mu}$, in order to make the same analysis.

In figure 3.17a the roughness is shown as a function of time for seven different values of $\frac{\lambda}{\mu}$. When the same data is plotted on a logarithmic scale the scaling of the initial growth can be determined by performing a linear fit on the data for early times (approximately until $t = 100$). The results of these fits are shown in figure 3.17b and it is seen that for all the different values of $\frac{\lambda}{\mu}$ the initial growth of the front roughness obeys $\omega \sim t^{0.31}$. From literature this growth exponent is expected to be $\beta = \frac{2}{3}$ so the value determined from these simulations is close to this theoretical prediction for the KPZ universality class [11] [14]. Now $\beta = \frac{2}{3}$ is known, the next step is to determine the roughness exponent $\chi$ from the saturation values of the roughness. Since the noise level changes when varying $\frac{\lambda}{\mu}$ the saturation of the front roughness is measured as a function of the eventual number of particles per unit length, $\sqrt{N_{eff}}$. Increasing $L$ in equation (3.22) has the same effect as increasing $(N_{eff})^{-1/2}$, so the saturation level of the front roughness, $\omega_{sat}$, is plotted as a function of $(N_{eff})^{-1/2}$. The result of this plot on logarithmic scale is shown in figure 3.17c. A fit is performed on the data and the resulting roughness exponent is $\chi = 0.50 \pm 0.02$, which is exactly as expected from theory. Now that it is found that $\beta \approx 0.31$ and $\chi = \frac{2}{3}$ it is confirmed that the results of the discrete particle model follow in the KPZ universality class. Moreover the resulting wandering exponent, computed from equation (3.21), of the genetic interface motion is expected to be $\zeta = 1 + (x^{-1})/z = \frac{2}{3}$.

This wandering exponent $\zeta$ should be visible in the local heterozygosity decay, which is expected to go as $H(0,t) \sim \frac{t}{L^2}$ for a rough front propagating in a homogeneous medium. To numerically measure this decay the heterozygosity is determined for different times, performing simulations of front expansion in the homogeneous case. Since it is hard to determine the heterozygosity at the front, because of its irregular shape, the heterozygosity is determined along a cut with fixed $x$-coordinate. Since the front propagates in the $x$-direction, the $x$-coordinate is comparable to the time coordinate. In figure 3.18a the heterozygosity, $H(y,t)$, is shown at different $x$-positions (or in other words at different times) as a function of separation distance $y$ for front propagation in a system with $D = 5.3 \cdot 10^{-5}$. This diffusion coefficient $D$ is chosen such that it equals the effective diffusion coefficient for the random domains. In figure 3.18c the corresponding scaling of the local heterozygosity, $H(0,t)$ is shown in blue on a logarithmic scale. A linear fit is performed on the data, regarding to the power law behavior. The result of the fit is a power law that behaves as $H(0,t) \sim t^{-0.66 \pm 0.02}$. From [24] the decay for a 2D rough front is also expected to go as $H(0,t) \sim t^{-\frac{3}{4}}$, which means that the result matches the theory. The decay exponent is
Figure 3.17: In panel (a) the front roughness, $\omega(t)$, is shown as a function of time for seven different values of $k = \xi$ and $L_y = 1, N = 100$ and $D = 2.5 \cdot 10^{-5}$. In panel (b) the same data is shown on a logarithmic scale. Linear fits are performed on the data until $t = 100$ and the resulting slopes are shown in the legend. In panel (c) the saturation of the roughness, $\omega_{\text{sat}}$, is shown as a function of $\frac{\mu}{\lambda}$. The saturation value is determined by averaging the data points from the figure in panel (a) from $t = 250$ till $t = 600$. 
strongly coupled to the wandering exponent of the genetic interface motion, $\zeta$, since the decay of the heterozygosity is determined by the encounter and merging of genetic interfaces.

To confirm the superdiffusive motion for the genetic interface expected from [14], the variance of the random walk of the genetic interface is determined as function of time, by starting with a front that consists half of red particles and half of green particles with the interface at $y = 0.5$. For 50 simulations with $D = 2.5 \cdot 10^{-5}$ the genetic interface motion is followed and the variance of this interface position compared to its initial position is computed. In figure 3.19a the variance, $\sigma^2$, is shown as function of time for a population expansion in a homogeneous domain, in blue, on a logarithmic scale. On the data points a linear fit is performed with resulting slope $1.33 \pm 0.07$. Since the variance is expected to scale with $t^{2\zeta}$, this result matches the scaling expected from theory, $2 \cdot \frac{2}{3} \approx 1.34$. Moreover the prefactor $C$ of the fit is found to be $C = (2.6 \pm 0.7)10^{-5}$ which matches the diffusion coefficient used for the simulations as expected. From these results it is found that the coupling between the local heterozygosity decay and the random walk of the genetic interface is exactly as expected from theory.

So far the focus was on front propagation in a homogeneous domain, where front roughness develops due to noise. It is found that this front roughness influences the fixation dynamics of populations. Since it is known that inhomogeneities in the environment of a population increases
the front roughness even further it should be investigated if the fixation probabilities are changed as well. Therefore the heterozygosity is also measured for the case of front propagation through a quenched distribution of high diffusion areas. The result of this heterozygosity, \( H(y,t) \), measured at different times in the case of a random domain is shown in figure 3.18b. From this data the decay of the local heterozygosity, \( H(0,t) \), can be found and this result is shown in figure 3.18c in red. It is seen that the decay is changed compared to the situation of front propagation in a homogeneous domain from \( H(0,t) \sim t^{-0.66 \pm 0.02} \) to \( H(0,t) \sim t^{0.97 \pm 0.06} \), which means that the decay of the local heterozygosity is compatible with \( H(0,t) \sim \frac{1}{t} \), when the mean distance between high diffusion areas is \( \nu = 0.5 \). This can be explained by the fact that the interfaces are pushed together when meeting a high diffusion area, as observed in figure 3.15, where a simulation result for \( \nu = 0.5 \) is shown. This ballistic behavior causes the wandering motion of the genetic interfaces to be proportional to time. To verify this the variance of the genetic interface motion is plotted as a function of time in the case of front propagation in a random medium. The result is shown in figure 3.19 in red, where it is found that \( \sigma^2 \sim t^{1.86 \pm 0.10} \), which means that \( 2\zeta = 1.86 \pm 0.17 \), so the wandering exponent \( \zeta \) is again found to be compatible with 1 within uncertainties as expected from the ballistic behavior. It is expected that this ballistic behavior is found if the size of the local fixated segments is of the same order as the radius of the high diffusion areas and the distance between high diffusion areas, as in the simulation shown in figure 3.15 for \( \nu = 0.5 \).

### 3.4 Conclusion

In this chapter population expansions in inhomogeneous media are explored numerically. First some simple geometries of high or low diffusion areas are considered and the influence of such a single inhomogeneity on front shape and genetic interface position is investigated. It was found that Fermat’s principle of least time can be used to describe the front dynamics after an inhomogeneity. The same principle could be applied to the genetic interface motion which characterizes the genetic dynamics.

After modeling these simple geometries a quenched disorder of high diffusion areas is considered. To analyze the front shape and the front dynamics a simple event driven model is used which is based on an eikonal equation. In this model the high diffusion areas are regarded as scattering centers that start to radiate as soon as they are touched by the front. By comparing the resulting front from the event driven model to the front resulting from the discrete particle model it was found that the front shape can be predicted very accurately using this efficient event driven model. Moreover the resulting front speed is compared to an analytical prediction. It is found that for small perturbations the font velocity exceeds the average front velocity with \( \epsilon^{1.29 \pm 0.12} \), where \( \epsilon \) is
the velocity perturbation, as expected from literature. Then the influence of the inhomogeneities on the fixation probability is investigated. From literature it is expected that front roughness changes the random walk of genetic interfaces from a diffusive motion to a superdiffusive motion. Front roughness can be induced by noise in the case of front propagation in a homogeneous domain. In this case the wandering exponent for the random walk of genetic interfaces was found, both from the local heterozygosity decay and from following directly the random walk of an interface, to be $\zeta = \frac{2}{3}$ within uncertainties as expected from literature. Since non homogeneities induce an enhanced front roughness it was analyzed whether this enhanced roughness changes the random walk of the genetic interface even further. It was found that when the length of local fixated segments is of the order of the radius of high diffusion areas and the distance between high diffusion areas, so $l \sim R_0 \sim \nu$, the wandering exponent is $\zeta = 1$ within uncertainties. This exponent differs from the result for a homogeneous domain and is explained by the fact that the high diffusion areas push the interfaces towards each other as a ballistic process. The latter process also explains the reduced average fixation time for fixation at the front, when propagating through a random medium compared to a homogeneous medium.
Chapter 4

Conclusions and recommendations

4.1 Conclusions

In this work the influence of non-homogeneities on population dynamics and genetics is investigated numerically. The model used in this work is a discrete particle model with certain rules for birth, death and displacement by diffusion, which was already been developed by Pigolotti et al. [28]. Specific individual rules from that model have been modified in this work in order to implement inhomogeneities at different levels. First, the case of non-homogeneities induced by self-propulsion of interacting particles is explored. We implemented the run-and-tumble mechanism with density dependent swim speed in the discrete particle model, as introduced in [4]. As expected from [3] spatial structures develop, when performing both 1D and 2D simulations with interacting and reactive run-and-tumble particles. To investigate the influence of these spatial structures on the genetic processes the fixation dynamics is analyzed in a 1-dimensional system. It was found that this dynamics is characterized by two processes: first local fixation occurs within single peaks and by communication between the peaks eventually the whole population fixates globally. In the case of interacting run-and-tumble particles the peaks show a wandering motion through the domain and continuously merge and split. The level of this communication determines whether fixation is suppressed or stimulated. This situation can be compared to the concept of meta-populations, in which a population is spatially separated into sub-populations that communicate at some level. However, the whole dynamics appears to be complicated, since the peaks are not stable. Therefore we developed a simplified ‘ad hoc’ system in the same spirit of the above situation by a space-dependent growth rate in a 2D population expansion. In this case it is observed that stable peaks develop that do not move but communicate purely by particle exchange. The communication is measured by the ratio between the length of low- and high-growth regions and it was found that global fixation increases when communication is decreased.

Secondly, the focus is on front propagation through non-homogeneous media. First some simple geometries of a single high- or low-diffusion area are investigated for what concerns front dynamics and genetics. To explore the dynamics of individual particles an algorithm is developed to follow ancestor lines and it was found that Fermat’s principle of least time can be used to explain particle trajectories and predict front shape as already stated in [26]. This means that the front shape can be predicted by solving an eikonal equation. Based on the solution of the eikonal equation we developed an efficient event driven model for the front propagation. Using this model the front speed was investigated in a quenched distribution of high diffusion areas. Such a high diffusion area can be seen as the global effect of a region of enhanced turbulence, when the time scales of the birth-and-death processes are much larger than the turnover time of the turbulent eddies. In this case propagation in this turbulent area can be modeled by replacing the microscopic diffusion coefficient $D$, by an enhanced effective total diffusivity $D_t$. The total front speed in the medium with a quenched order of this so called ‘turbulent regions’, was found to exceed the average front velocity, computed by a homogenization procedure. This velocity speedup scales with the velocity
perturbations, $\epsilon$, as $\epsilon^{\nu}$, as expected from [25].

To analyze the influence of inhomogeneities on the population genetics the discrete particle model is used directly in the case of single inhomogeneous islands and in the quenched random media. Since simulations with a sufficient large domain size using the discrete particle model are expensive, an additional algorithm is implemented in the original code such that only particles in a region behind the front die and reproduce, which reduces computational costs significantly, without compromising the results related to the dynamics of the front. For front propagation in the quenched medium it was observed that the genetic interface, which is the interface between clusters of different species, is often pinned in a region of negative curvature at the front. This behavior can be explained both macroscopically using Fermat’s principle of least time and locally connecting the interface motion to the local curvature of the front. Indeed it is expected that in regions with negative curvature an inwards drift is present pushing the interface towards the valley in the front. From that we understand that another way of exploring the influence of inhomogeneities on the genetics is to focus on front roughness and how it is perturbed by inhomogeneities. First front propagation in a homogeneous 2 dimensional domain is considered where front roughness develops because of noise. From [10] it is expected that the motion of the genetic interface shows a superdiffusive behavior in the case of front propagation in a homogeneous 2D domain. This is confirmed in our simulations, where it was found that the genetic interface performs a superdiffusive random walk with wandering exponent $2\zeta = 1.33 \pm 0.07$. Moreover the corresponding local heterozygosity decay was found to go as $H(0,t) \sim t^{-\zeta}$, as expected from literature [14] [23]. Since the high diffusion areas will induce an extra front roughness it is investigated whether the genetic interface motion is changed even further. It was found that when the length scale of the fixed segments in the population is comparable to the mean distance between high diffusion areas the variance of the genetic interface motion goes as $\sigma^2 \sim t^{2\zeta}$, with $2\zeta = 1.86 \pm 0.10$, and the local heterozygosity decay goes as $H(0,t) \sim t^{-\zeta}$. This is expected to be the result of high diffusion areas pushing the interfaces towards each other, therefore inducing a ballistic behavior and suppressing coexistence of species.

4.2 Recommendations for further research

Now that the theoretical frame for the prediction of front shape and front speed in inhomogeneous media has been understood, as well a the connection between local front curvature and genetic interface wandering, the next step in this research could be the implementation of the genetic properties in the simple event driven model for the front. The ideas of the motion of a genetic interface on a curved front could be used to model the interface position at the front itself, without solving the problems with all individual dynamics. When including genetics in the event driven model the model becomes complete, since then not only front shape and velocity can be investigated but also genetic properties as fixation time and heterozygosity. Moreover a deeper analysis on the scaling of heterozygosity in the random medium is of interest. The study of different regimes connected to the length scales involved in the problem has to be completed.

On top of the numerical work done on this topic it would be interested to perform experiments in the future. Experiments could be done using the fact that the growth rate of bacteria is temperature dependent. Bacteria could be grown on an agar plate with a locally heated spot in which they can grow faster. This is comparable to the situation of a population expansion in a domain with a circular higher diffusion area, which is investigated numerically in this work. Another option would be to create a manifold on the agar, modulating the surface with mountains and valleys. In both cases there is an increase in traveling distance compared to the flat case and this would act as a net slowed front after the obstacle. The resulting front and the influence of the front shape on the genetics of two neutral variants of bacteria growing in this scenario could be investigated.
Bibliography


