Evolutionary principles promoting cooperation

Demographic fluctuations, population dynamics, and assortment

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Zusammenfassung

Leben zeigt verblüffende Formen von Komplexität. Das vielleicht fundamentalste und immer noch nicht gut verstandene Beispiel dieser biologischen Komplexität ist Kooperation. Das Zusammenwirken kooperativer Individuen erlaubt, um nur einige Beispiele zu nennen, Ressourcen besser zu erschließen, Gefahren abzuwehren oder höhere soziale Strukturen zu bilden. Allerdings ist die Entstehung von Kooperation nicht einfach zu erklären. Warum können sich Kooperatoren stabil in einer Population halten, wenn nicht-kooperierende Individuen den mit Kooperation verbundenen Aufwand umgehen können, gleichzeitig aber von Kooperatoren profitieren?

In dieser Arbeit werden verschiedene ökologische Faktoren untersucht, die die Entwicklung von Kooperation ermöglichen. Insbesondere wird der Einfluß von demographischen Fluktuationen, der Wachstumsdynamik, und die Einteilung in Unterpopulationen analysiert. Die drei Schwerpunkte der Arbeit werden im Folgenden kurz vorgestellt.

Im ersten Teil wird die Rolle von demographischen Fluktuationen betrachtet. Weil Geburts- und Sterbe-Ereignisse immanent stochastisch sind, ist auch die evolutionäre Dynamik in einer Population immer Fluktuationen unterworfen. Es werden die Auswirkungen von Fluktuationen auf Evolution betrachtet und mit dem Einfluß gerichteter Selektion von fitteren Individuen verglichen. Wir konzentrieren uns auf „evolutionäre Spiele“ und zeigen, dass es zwei abgegrenzte Bereiche gibt. In einem ausgedehnten Bereich der neutralen Evolution dominieren Fluktuationen die evolutionäre Dynamik, wohingegen im zweiten Bereich Fitnessunterschiede die treibende Kraft der Evolution sind und Fluktuationen ihre dominierende Bedeutung verlieren. Wir quantifizieren die Grenzen dieser beiden Bereiche.

Der zweite Teil betrachtet die Wechselwirkung der evolutionären Dynamik einer Population und deren Wachstumsdynamik. Beide Prozesse beruhen auf den gleichen Geburts- und Sterbe-Ereignissen und sind deswegen im Allgemeinen gekoppelt. Wir führen ein stochastisches Modell ein, um diese Kopplung zu untersuchen und diskutieren den Zusammenhang zu bekannten evolutionären Modellen, welche die Populationsgröße als konstant annehmen. Insbesondere betrachten wir das Kooperationsdilemma in wachsenden Populationen. Das Zusammenspiel zwischen demographischen Fluktuationen und der Populationsdynamik kann hier dazu führen, dass die Kosten der Kooperation überwunden werden und der Anteil an Kooperatoren zeitweise zunimmt. Dieser Effekt wird für verschiedene typische Wachstumsszenarien von Mikroben untersucht.

Im dritten Teil wird die Entstehung von Kooperation in strukturierten Populationen untersucht. Wir betrachten Populationen deren Individuen regelmäßig in Gruppen aufgeteilt werden. Das Modell dient als Grundlage um Kooperation in mikrobiellen Populationen zu untersuchen, welche regelmäßig Populationsengpässe durchlaufen. Verursacht werden können diese etwa durch das Durchlaufen eines Lebenszyklus oder durch komplexe Ausbreitungsmechanismen. Wir analysieren das Zusammenspiel von interner Evolution, Wachstumsdynamik

sowie Gruppenbildung und zeigen zwei Mechanismen auf, die Kooperation auf lange Sicht ermöglichen. Der „group-growth“-Mechanismus ermöglicht Kooperation durch das schnellere Wachsen von stärker kooperierenden Gruppen. Beginnend mit nur einer kooperativen Mutante ermöglicht er die stabile Koexistenz von Kooperatoren und nicht kooperierenden Individuen. Der „group-fixation“-Mechanismus basiert auf dem Vorteil von rein kooperativen Gruppen. Auf lange Sicht kann er zu rein kooperativen Populationen führen. Um unsere Vorhersagen zu überprüfen, führen Prof. Kirsten Jung und Prof. Heinrich Jung momentan Experimente am Lehrstuhl für Mikrobiologie der Ludwig-Maximilians Universität durch.

Die Arbeit ist gegliedert wie folgt: Kapitel 1 gibt eine kurze Einführung in die Evolutionstheorie und ordnet die Arbeit in den größeren Kontext ein. Die darauffolgenden Kapitel 2 und 3 führen in die Grundlagen der mathematischen Formulierung von Evolution und die Frage der Kooperation ein. Kapitel 4, 5 und 6 behandeln die spezifischen Fragestellungen dieser Arbeit. In Kapitel 4 werden demographische Fluktuationen und die Begrenzung neutraler Evolution untersucht. Die Kopplung zwischen der Populations- und der Evolutionsdynamik wird in Kapitel 5 diskutiert. Das letze Kapitel 6 behandelt den Einfluß der Populationsstruktur auf die Entwicklung von Kooperation. Hier wird auch das kooperative Verhalten von Mikroorganismen und deren Lebenszyklen analysiert.

Abstract

Life shows a stunning level of complexity. Understanding the emergence of this complexity and the functioning of intricate biological processes lies at the heart of modern biology. One major hallmark of biological complexity, including many forms of interacting organisms, is cooperation. Cooperating individuals are, by providing a benefit, capable to facilitate a better depletion of resources, a more efficient protection against threats, or the formation of social entities, to name but a few advantages. However, explaining cooperation is a major challenge of evolutionary theory: Why do cooperators persist if non-cooperative individuals can get away from paying the costs and benefit from faithful cooperators? This dilemma of cooperation emerges for a vast variety of life forms and on different levels of biological complexity.

This thesis focuses on the ecological factors promoting the evolution of cooperation. In particular, the role of demographic fluctuations, growth-dynamics and population structure is considered. Correspondingly, this thesis is divided into three main parts, briefly introduced in the following.

In the first part, the role of demographic fluctuations is studied. By the stochastic nature of the underlying birth and death events, the evolutionary dynamics of a population is always subject to demographic fluctuations. We here analyze their impact on the evolutionary outcome and compare it with the selection for fitter individuals. We focus on 'evolutionary games' and show that there are broad regimes of neutral-evolution where fluctuations dominate the dynamics. Furthermore, we quantify the edge of neutral evolution where fitness-differences become important and demographic fluctuations are only of minor relevance.

The second part considers the coupling of evolutionary and population dynamics. Growth and decline of a population as well as its internal evolution result from the same birth and death events and thus are coupled. We introduce a stochastic model to study this coupling and discuss the relation to common evolutionary models which assume a constant population size and hence do not take this coupling into account. As a particular example, we analyze the dilemma of cooperation in a growing population. We show that the interplay of demographic fluctuations and population dynamics can drastically influence the evolutionary outcome and lead to a transient increase of cooperation. We study this increase for different typical types of microbial growth dynamics.

In the third part, the evolutionary dynamics in structured populations is investigated. In particular, we consider group-structured populations where individuals are regularly assorted into new groups. The model serves as a null model to study cooperation in microbes under the permanent influence of population-bottlenecks. These can arise in nature due to life-cycles or migration events. We analyze the interplay of growth, internal evolution, and assortment dynamics and show that there are two mechanisms promoting cooperation: the group-growth

and the group-fixation mechanism. The group-growth mechanism is based on the faster growth of more cooperative groups and facilitates the evolution of cooperation from one single cooperating mutant on. The group-fixation mechanism rest upon the advantage of purely cooperative groups and can lead to entirely cooperative populations in the long run. Experiments to test our predictions and their dependence on the key parameters are currently performed by Prof. Kirsten Jung and Prof. Heinrich Jung at her chair of microbiology at the Ludwig-Maximilians University Munich.

The outline of this thesis is as follows. Chapter 1 gives a short introduction to evolutionary theory in general and states the broader context of this thesis. The following Chapters 2 and 3 provide an introduction to the mathematical formulations of evolutionary dynamics and the issue of cooperation, respectively. Chapters 4, 5, and 6 then consider the three main issues introduced before. Each of these chapters ends with a short discussion and a reprint of the corresponding papers and manuscripts. In Chapter 4, demographic fluctuations and the edge of neutral evolution are analyzed. Subsequently, the coupling between population dynamics and evolutionary dynamics is discussed in Chapter 5. Finally, the role of population structure is discussed in Chapter 6. It also considers microbial organisms and their life-cycles in detail.

Contents

1 Evolution and biological complexity

Life shows astonishing forms of complexity. This complexity steadily allows organisms to survive in a rough world. Furthermore however, life on earth is not only preserved but its complexity in terms of structure and dynamics has increased tremendously until this day: Life and the open system earth behave like the opposite of a closed thermodynamical system where the entropy increases over time and order (structure) is lost. Still, by the *theory of evolution*, the emergence of biological diversity, its ingenuity, and its change over time is assumed to be based on only a very few core-rules of natural selection. The challenge of evolutionary biology is to understand how these core-rules and the given biological and physical conditions give rise to the evolution of the biological complexity and diversity observed today.

In this thesis, mathematical models are applied to study certain aspects of evolutionary dynamics. In particular, biological and ecological factors promoting the evolution and maintenance of cooperation in microbial populations are studied. In this chapter, I give a personal perspective on the broader context of this thesis, i.e. the theory of evolution and the emergence of biological complexity. An outline of this thesis is given in Section 1.4 at the end of this chapter. The reader who prefers to start directly with the more specific aspects of this thesis may skip this chapter and continue directly with Chapter 2 where the basic mathematical formulations of evolution are introduced.

1.1 The minimal requirements of evolution

The theory of evolution as formulated by Charles Darwin and Alfred Russel Wallace [1, 2, 3, 4] is based on one key concept: *natural selection*. It acts on a population by the interaction of three constituents, *reproduction*, *heredity* and *variation*. In a most abstract formulation, the following *'minimal requirements'* must hold for selection to act:

- Variation: There are (phenotypic) differences between individuals in the population.
- Heredity: Variation is heritable such that an offspring resembles, in part and with higher probability than just by chance, its parents.
- Reproduction-differences: Different variants can have different contributions to later generations.

There are many similar formulations in the literature stating these necessary conditions, each with a slightly different focus. See for example [5], and [6] for a recent summary. However, while very concise, these minimal requirements are by no means sufficient and capable to explain the high diversity and complexity of life. Natural selection and the *survival of the fittest* lie at the root of evolutionary theory, but crucially, they act in a multifarious physical

and biological world. Only by this, the minimal requirements give rise to the tapestry of current life.

1.2 The tree of life and biological complexity

Before touching the additional factors promoting evolution of life, let us first consider the tree of life and a few examples of the complexity of *life*. It should be clear that this is a very selective overview which is only meant as a glimpse on the diverse forms of life evolution is acting on.

The theory of evolution is ultimately intertwined with the idea of a *most common ancestor*; the most common ancestor and a primordial population is the initial requirement for evolution to start with and stands at the beginning of the *tree of life*. Consequently the emergence of the first replicators and the *origin of life* are some of the most profound issues of evolutionary theory [7]. It comprises a whole field of research including questions about emergence and accumulation of organic molecules, the formation of the genetic code or the occurrence of first enzymes and cells, see e.g. [8, 9, 10, 11] for recent work.

Once having occurred, primordial populations gave rise to diverse forms of life. One of the first more detailed analysis of the phylogenetic relations between different species was given by Ernst Häckel. His notions of the tree of life are impressively shown in his book 'Generelle Morphologie der Organismen' [12], see Fig. 1.1. Later, with the dawn of molecular genetics, phylogenetic relations were not limited to the analysis of morphological traits anymore. Today, there is a stunning knowledge on phylogenetic relations considering often different molecular and morphological traits, like DNA-regions, rRNA and protein analysis, see for example the tree of life web project [13]. Without going into detail, these and also the data by fossil records stress two aspects: First, the phylogenetic data strongly supports the idea of a common ancestor. The branching of ancestral species towards more and more differentiated species seems to be ubiquitous. Second, the data suggests that biological complexity in terms of structure, regulation and signaling as well as multicellularity have increased strongly in the last 4 billion years.

But let us consider some of the most astonishing examples of biological complexity. Nowadays, one distinguishes between three different domains of life, archaea, bacteria, and eukaryotes [14]. All of them share striking similarities, like DNA as the same carrier of information and similar enzymes for protein synthesis. Thus, they are assumed to stem from the same ancestral strain. However, substantial differences have evolved, with each of the domains showing distinct forms of complexity.

For the less studied archaea, biologists only begin to realize the manifold intracellular structures and their interaction with the environment [15]. One stunning example is the interplay of the two archaea *Nanoarchaeum equitans* and *Ignicoccus hospitalis* [16]. *N. equitans* metabolically relies on *I. hospitalis* and a highly specialized association between both species has evolved. Depending on their growth state a different fraction of *I. hospitalis* cells are occupied by a varying number of *N. equitans* cells. See Fig. 1.2(a).

Bacteria with their capability of multicellular biofilm formation, sporulation and swimming show an astonishing level of complexity. One phenomenon is *competence* and the controlled

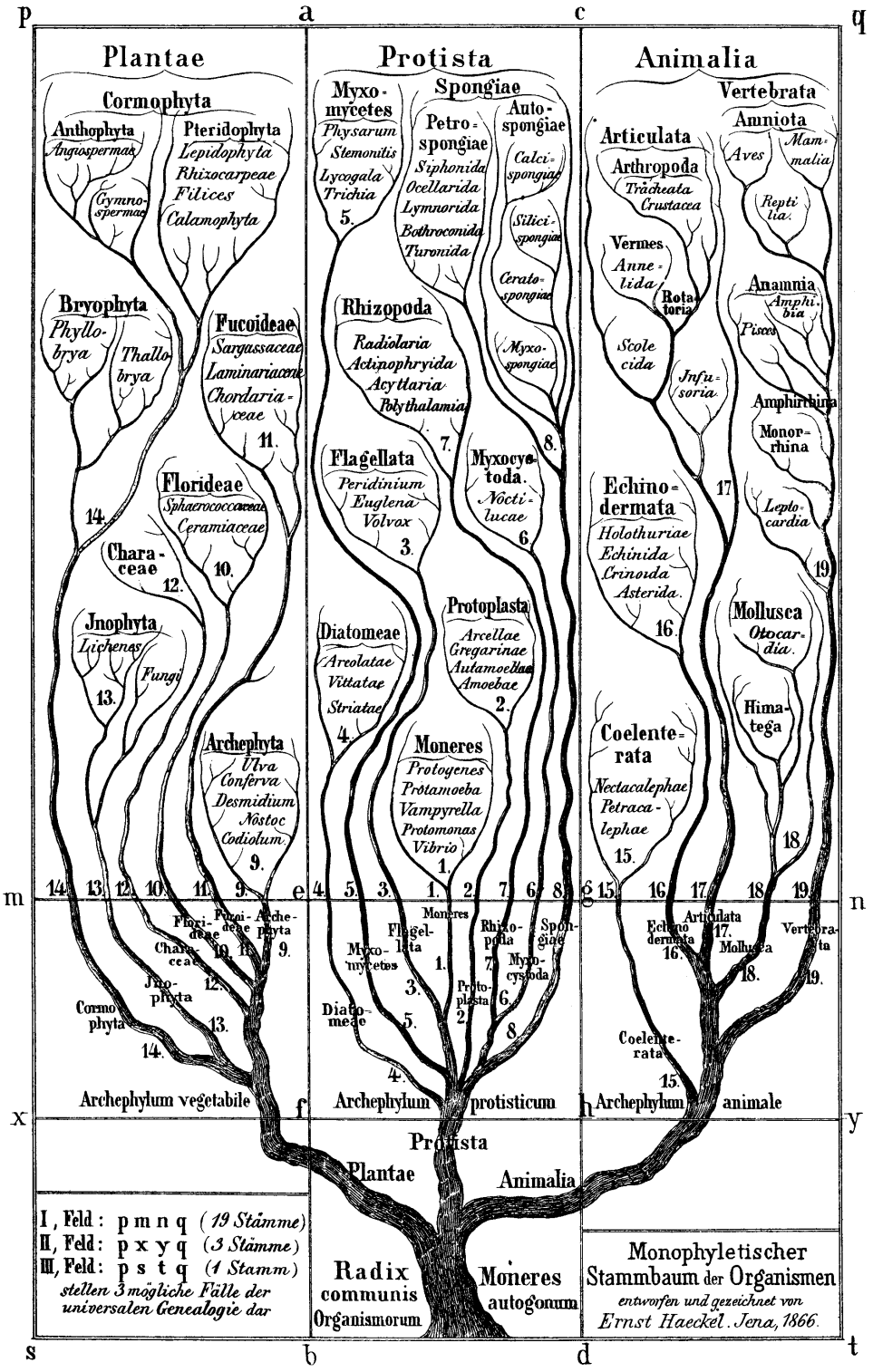

Figure 1.1: The stem-tree of organisms as seen by Ernst Häckel in his book 'Generelle Morphologie der Organismen' [12].

uptake of external DNA [17]. Schematically this is shown in Fig. 1.2(b) for *Bacillus subtilis*. For this organism uptake and switching between competent and non-competent states is highly regulated and controlled by more than a hundred proteins involved in the comK-regulation network. Fluctuations can play an important role for determining the phenotypic state [18, 19].

Eukaryotes show a very high intracellular level of compartmentalization. Most distinguished is the cell-nucleus and the organization of DNA in different chromosomes. In addition, many eukaryotes are multicellular organisms and have the capability for sexual reproduction. Thereby eukaryotes stand at the forefront of complexity. One example illustrating this complexity is the non-random formation of *chromosome territories* inside the cell nucleus [20], see Fig. 1.2(c). On DNA-structures below the chromosome level, DNA methylation, histone modifications and chromatin remodeling have been shown to play an important role for gene-regulation; there is a 'chromatin language' of regulation. However, the nuclear architecture and the spatiotemporal organization of whole chromosomes is not less important but might play a crucial role for the differentiation of the cell. Currently, several modes of such higher regulations are discussed. Another example is the process of meiosis. During cell division, homologous chromosomes exchange DNA sequences (chromosomal crossover). The process is very precise such that mainly matching regions interchange and cuts do not occur within gene-coding DNA sequences [14]. In addition, the process is highly effective and headed by the synaptonemal complex which serves as a scaffold for recombination, see Fig. 1.2(d).

1.3 Variation and selection in biology

With the natural history and biological complexity of currently living organisms in mind, let us come back to the conditions and reasons for biological diversity and complexity to evolve. With only the basic requirements of natural selection in mind, many more specific questions evolve: Why are there different species and why is there such an astonishing biodiversity on earth? Why is this still true on local scales? Why is there cooperation? Why are there multicellular organisms and how could they be phenotypically so different? These and similar questions [23] are of course at the core of evolutionary theory and we cannot nearly cover them here. However, very very roughly, there are two interrelated reasons: selection and variation in nature are by far not easy but very intricate processes.

First, regarding selection, evolution proceeds in close connection with the environment. The population undergoing natural selection is embedded in a multifaceted and dynamical physical world. Nutrients and other resources are diverse and heterogeneously distributed. Habitats are highly rutted and structured. Evolutionary dynamics itself is feeding back to the ecological dynamics and different species compete for limited resources in a couple of direct and indirect ways. Fitness advantages by differences in the reproduction rates can depend strongly on all of such details. Ecology and evolution are highly coupled. Evolutionary ecology and related fields try to uncover this interdependence and to figure out the schemes rendering the high diversity and complexity possible: What are the ecological factors driving adaption, coevolution, mutualism, or biodiversity?

Second, the many versatile and elaborate forms of variation are a main reason driving life towards higher biological complexity and diversity. Single cells and all higher forms of life are

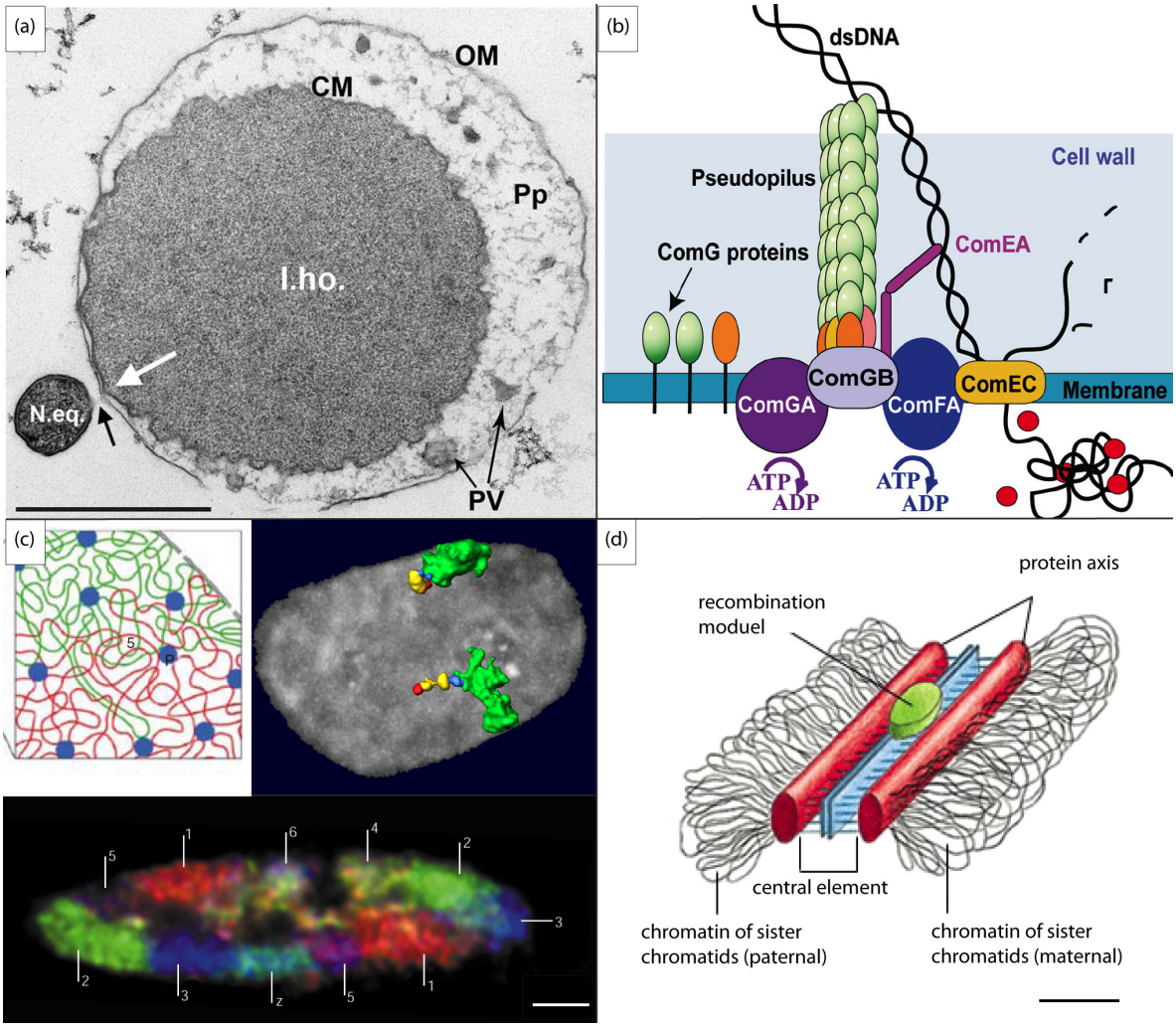

Figure 1.2: Selective examples illustrating the complexity and diversity of life. (a) The association of the two archaea *Nanoarchaeum equitans* (N.eq) and *Ignicoccus hospitalis* (I.ho). Scale bar corresponds to $1\mu m$; from [16]. (b) The membrane constituents of the comK network controlling competence in *B. subtilis*: Bacteria control their DNA uptake; from [21]. (c) Different chromosome in the nucleus of eukaryotic cells are arranged in chromosomal territories (CTs). Dynamical nuclear architecture is expected to be a major part of gene-regulation and differentiation in eukaryotic cells, see scheme. The 3D reconstruction plot shows the CTs of chromosome 11. The red and yellow areas denote the short ends of the chromome. The picture shows different CTs in a nucleus of a chicken cell. The scale bar corresponds to $2\mu m$. Note how it compares to the size of the archaea in (a); from [20, 22]. (d) The synaptonemal complex guiding the crossover of homologous chromosome region during meiosis. Genetic recombination is one major part of variation. Scale bar corresponds to $100nm$; from [14].

very structured, biochemically versatile entities. Mutations like point or frame-shift mutations, gene duplications or chromosomal translocations occur on vastly different time-scales. Further, recombination, sexual reproduction and meiosis are highly sophisticated processes increasing variation. Given the complex biology of the cell and the involved regulatory networks of gene expressions the mapping between geno- and phenotypes is subtle and even point mutations on the DNA can affect the phenotype in dramatic ways. How this complexity can push evolution is impressively shown in examples of developmental biology. Variations in the regulation of so-called toolbox genes can strongly affect the morphology of for example the fruit fly Drosophila melanogaster or vertebrates [24] and can therefore, in combination with selection, provoke the formation of new species. This interdependence between evolutionary and developmental biology is more and more recognized in the biological field of 'evo-devo'.

In total, both the generation of variation and the process of natural selection are by no means trivial but very complex processes. Further, these intricacies are essential for driving the evolution of complexity. In this sense, natural selection and the minimal requirements stated before form only the core-mechanism of the theory of evolution. To understand how organisms evolve in nature, additional factors, circumstances and constraints have to be included. Determining which factors are important is the major challenge of evolutionary theory.

As it is now, there is no convincing evidence that variation and selection should be directly linked in terms of a Lamarckian evolution, i.e. variation is not biased towards higher fitness and selection advantages. For example, it is known that bacteria can increase their variation rate by competence if fitness is low. However, there is no direct control mechanism such that only beneficial DNA is up-taken; selection must act afterwards to select for fitness-increasing variation. Variation and selection are related in an indirect manner and a separated consideration of selection and variation is sensible, at least in first order.

1.4 Outline of this thesis

In this thesis, we study selection. We focus on the evolutionary dynamics of microbes and the evolution and maintenance of cooperation for such organisms is considered. We setup and analyze mathematical models and try to understand the specific role of different ecological and biological factors. In particular, we consider three factors: growth, structure and demographic fluctuations (random drift). With this, we hopefully give a modest contribution to understand the role of drift, changing population sizes and population structure in a more general context.

In the two following Chapters 2 and 3, we introduce the mathematical and conceptual frameworks of this thesis. In Chapter 2, the basic mathematical concepts to describe natural selection are introduced. Cooperation and its role for the emergence of biological complexity are discussed in Chapter 3. The remaining Chapters 4, 5, and 6 discuss specific aspects in detail and include the reprinting of our publications and manuscripts. In Chapter 4, we consider the role of demographic fluctuations in evolutionary setups with a fixed population size. We then consider the role of population dynamics with the population size explicitly changing with time in Chapter 5. Here, demographic fluctuations can have a pronounced impact on the evolutionary dynamics. Finally, we consider the role of structure for cooperation in

Chapter 6. Both, demographic fluctuations as well as population dynamics can, interfering in a structured population, lead to the evolution of cooperation.

2 Natural selection in mathematical terms

The idea of natural selection can be stated in simple mathematical equations. Here, we introduce and discuss the Price equation as mathematical correspondence of the minimal requirements considered in Section 1.1. Further, we deduce the replicator dynamics which serve as a main description of evolutionary dynamics throughout this thesis.

Consider a population consisting of N individuals $i = 1...N$ at time t. Each individual is assumed to have one characteristic property, described by the number z_i; for example, z_i could be the height of individual i. The average characteristic property within the population is given by $\bar{z} = \sum_i z_i/N$. Individuals reproduce now for a certain time T. The number of offspring of an individual i created within that time, its *fitness*, is assumed to depend only on its characteristic property and is denoted as Φ_i. With this, the average character in the next generation is given by $\bar{z}' = \frac{1}{N}\sum_i \frac{\Phi_i}{\bar{\Phi}} z_i$, with $\bar{\Phi} = \sum_i \Phi_i/N$ being the average number of offsprings per individual. The average characteristic property has changed according to the characteristic properties of the individuals in the population and the fitness values related to these characteristic properties. The change of the average value, $\Delta\bar{z} = \bar{z}' - \bar{z}$ can be expressed as,

$$\bar{\Phi}\Delta\bar{z} = \mathrm{Cov}\left(\Phi_i, z_i\right). \tag{2.1}$$

This is the statement of natural selection in mathematical terms; the change in $\bar{z}$ is given by the covariance between the expected number of offspring and the character z_i.

Instead of considering single individuals separately, one can also change the description and use relative frequencies, i.e. the fraction of individuals belonging to a certain value z. Here, let us take the values of z to be discrete with values $\{z_l\}$ and each character z_l being represented by a relative frequency p_l within the population. Then the change in $\bar{z}$ is given by $\bar{\Phi}\Delta\bar{z} = \mathrm{Cov}_{p_l}\left(\Phi_l, z_l\right)$ where now covariance is taken with respect to the weights p_l. An illustration using this frequency based description is given in Fig. 2.1. If single individuals can in addition change their character, there is an additional term for the change of $\bar{z}$, now given by,

$$\bar{\Phi}\Delta\bar{z} = \mathrm{Cov}_{p_l}\left(\Phi_l, z_l\right) + \langle \Phi_l \Delta z_l \rangle_{p_l} \tag{2.2}$$

where Δz_l is the average change of individuals with character z_l and also the average $\langle \cdot \rangle_{p_l}$ is taken according to the weights p_l. In the context of evolution, this relation was first recognized by Price [25] and is called *Price equation* [26, 27, 28].

The Price equation (2.2) makes only statements about the average change within the population and not the change of the whole distribution. Furthermore, and crucial, the Price equation follows immediately from the underlying fitness-differences and the processes of variation and thereby makes only statements about how change is provoked, but not how fitness and variation terms come about; it mathematically describes natural selection if the minimal

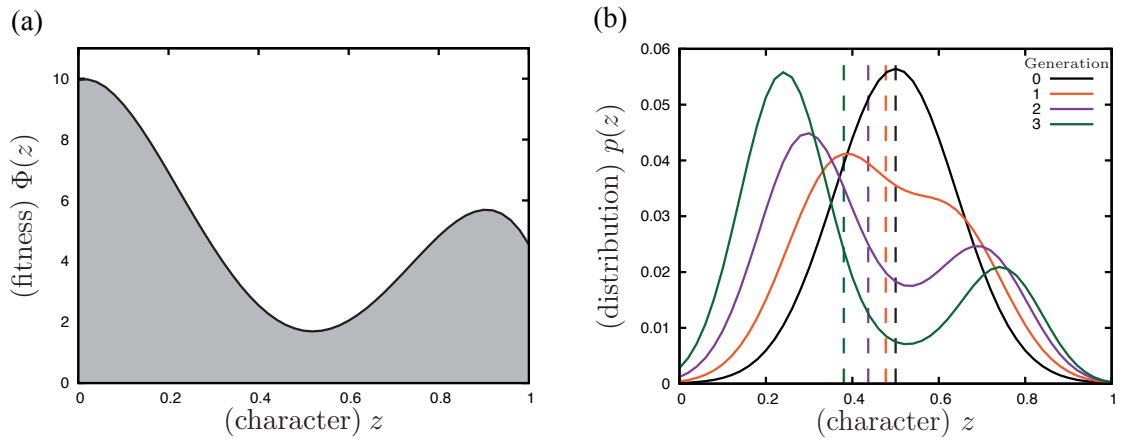

Figure 2.1: Natural selection. (a) The fitness-landscape, $\Phi(z)$, gives the expected number of offspring for a certain generation, depending on the character z of the individual. (b) A population, given by a distribution of character values, changes over time due to differences in fitness. Here, the population initially is mainly located in a fitness-valley, but then 'climbs up' the fitness landscape in the following generations. Fitter states, here given by smaller and larger z values are reached. The expected value $\bar{z}$ in the population is denoted by the dashed line, it decreases according to the Price equation (2.2). This equation does not make any predictions about the distribution of character values in the population, nor does it make any statements about the cause of underlying fitness-values.

requirements are fulfilled, cf. 1.1. But similar to those, it cannot explain any evolutionary process in biology alone. To understand the evolutionary dynamics for a given specific situation, one has to consider detailed biological and ecological factors and thereby try to establish the fitness functions for that given situation. It is exactly here, where modeling comes into play. To put it more descriptively: Let us say one has observed a whole population of *E. coli* over a certain time and knows the *actual reproductive process* of every individual during that time. Then one can of course calculate the change in the population a-posteriori by making use of the Price equation. However, nothing is learned by that about the actual reason of change. To understand evolution, one for example needs to know how *fitness*, i.e. the expected reproductive success, comes in: What is the role of nutrients? How do bacteria obstruct each other? How rutted is the environment? Many more microscopic details might play into the dynamics and hence understanding those factors is of course a very ambitious task. However, many aspects of evolution can already be understood by considering more coarse-grained descriptions and effective fitness-functions describing fitness on the population level. In agreement with these consideration and its prominence in evolutionary theory, the exact meaning of fitness is of course controversial, see e.g. [29, 30, 31, 32, 33].

The number of offsprings $w(z_l)$ depends on the character z_l; in evolutionary theory this functional dependence is called a *fitness landscape*. The possible number of states in this fitness landscape can be very large, and its exact form can range between very smooth and very rough extremes. For example, considering nuclear sequences with L bases, there are 4^L different states and due to the complex mapping between phenotype and genotypes the landscape can be very rugged.

Natural selection leads a population to 'climb up the fitness landscape' and to settle around states of high fitness. In contrast, variation broads the distribution by allowing the population to sample the fitness-landscape and to sense other fitness-peaks. Importantly, as mentioned before, the fitness of an individual depends strongly on the surrounding environment and therefore is highly coupled with the ecological dynamics. Moreover, fitness can be *frequency dependent* and change with changing composition of the population. Evolution thereby couples back to the fitness landscape. In total, the fitness-landscape thus depends on space and time and can also change drastically with evolution. To cast it colloquial, fitness-landscape is more a seascape [34, 35] with the underlying stream dynamics changing from sea to sea.

Many specific evolutionary situations have been considered and especially *population genetics* [36, 37] can successful explain many historically controversial aspects of evolutionary theory. For example, early population genetics has successfully contributed to the unification of Mendel's theory of inheritance and Darwin's theory of evolution. The original works by Fisher, Haldane and Wright [38, 39, 40] are now known as the theoretical contributions to *modern synthesis* [41]. A range of other aspects have been considered since then. More recent work includes for example the role of epistasis, mutation-accumulation, or sexual recombination [42, 43]. Further examples of more specific mathematical models include specification [44]. Often statistical physics contributed to the modeling [45].

Throughout this thesis we consider situations where there are only a few different *traits* within the population. By considering only these limited number of states within the fitness-landscape, the description is on a more coarse-grained level than for example for the nucleotide sequence mentioned before. One example is the expression of a certain constitutive gene. While one trait possesses a functioning gene, another one has mutations in the corresponding nuclear sequence and hence cannot express the gene anymore. A different genotype directly provokes a different phenotype. And selection is acting with respect to the differences in these phenotypes.

Let us here consider a situation with only two *traits* or *types*. In the context of evolutionary game theory, theses states are also called *strategies*. We assign these types A and B the character values $z_1 = 1$ and $z_2 = 0$ respectively. The relative abundance of both is denoted by $p_A = x$ and $p_B = 1-x$. With the fitness definitions stated above (or the Price equation (2.2)), the change in abundance is given by,

$$\bar{\Phi}\Delta x = \left(\Phi_A - \bar{\Phi}\right) x - \tilde{\mu}_{A\to B}\Phi_A x + \tilde{\mu}_{B\to A}\Phi_B(1-x). \tag{2.3}$$

Here, $\tilde{\mu}$ denotes the probability for an offspring to mutate to the other type with $\Delta z = \pm 1$. We can write this dynamics also in a continuos time formulation,

$$\frac{dx}{dt} = \frac{\phi_A - \bar{\phi}}{\bar{\phi}} x - \tilde{\mu}_{A\to B}\frac{\phi_A}{\bar{\phi}} x + \tilde{\mu}_{B\to A}\frac{\phi_B}{\bar{\phi}}(1-x) \tag{2.4}$$

This is the *replicator-mutator equation* [46]. Here, the fitness $\phi_l = \Phi_l/T$ is a rate giving the expected number of offsprings per time unit. $\bar{\phi} = \phi_A x + \phi_B(1-x)$ denotes the average fitness. The first term describes natural selection, x increases if the fitness of ϕ_A exceeds the average fitness $\bar{\phi}$. The other two terms describe mutations from B to A and vice versa. Without mutation, the equation,

$$\frac{dx}{dt} = \frac{\phi_A - \bar{\phi}}{\bar{\phi}} x \tag{2.5}$$

is termed *replicator equation* [47, 46, 48]. Similar equations follow for several different strategies $l = 1...S$ and their abundances $\mathbf{x} = (x_1, ..., x_S)$. The replicator approach describe evolution in a deterministic way. Stochastic formulations of the evolutionary dynamics which consider random drift are introduced in Section 4.2.

In this work, we focus on the case where fitness is frequency dependent, $f_l = f_l(\mathbf{x})$. In such a situation, Eq. (2.5) and its correspondent equations in higher dimensions are non-linear and many different scenarios can arise. In a first approach, frequency-dependence is described by a payoff matrix and evolutionary games. This formulation is introduced in Section 4.3.

3 Natural selection and cooperation

One aspect we focus on in this thesis is cooperation. In this chapter we explain, why evolution and maintenance of cooperation is challenging to explain from an evolutionary perspective and why it is of eminent importance for the evolution of biological complexity. We further state examples of cooperation for different tracts of biological life and introduce the main mechanisms promoting cooperation.

3.1 Cooperation and biological complexity

The biological complexity as exemplified in Chapter 1 is assumed to have occurred not in a continuous fashion with a slowly but steadily increasing level of complexity. Rather, evolution towards higher complexity is expected to have occurred via several larger steps, so called *major transitions* [49], see Fig. 3.1. Some of the most astonishing are certainly the formation of primordial cells and the evolution of the genetic code, the occurrence of eukaryotes with a separated cell-nucleus, the evolution of sex and a germ-line, the development of multicellular organisms, or the complex interactions of many individuals.

One aspect combining many of the major transitions is the formation of larger entities starting with smaller ones. This includes for example the gathering of several chromosomes, the origin of mitochondria or, most obvious, the attachment of several cells to a multicellular, chimeric organism. In fact, life is organized on different interacting levels. A schematic view of this level-organization is shown in Fig. 3.2.

Stunningly, the lower entities were, and often still are, able to reproduce autonomously. The different levels thus give immediately rise to the *levels of selection* debate and the question on which level selection is primarily acting on [50]. Regarding the major transitions, the question is how selection has shifted from lower to higher levels. Such issues were and still are discussed controversially within the theories of kin-, group-, and multi-level selection. We introduce and discuss these theories in Section 6.1.

Here, we want to stress one aspect: a working interplay of entities on a higher level is often linked to *cooperation* at the lower one. If lower entities can reproduce separately and are under permanent change by natural selection, then entities not involved into the formation of more complex structures might have fitness-advantages. Hence they might oppose the evolution of more complex structures involving higher levels. In fact, for many major transitions there is some form of cooperation required at the beginning. Thus, to understand transitions and the evolution of biological complexity in general, understanding the evolution and maintenance of cooperation is a major aspect. One example which involves two levels of selection and cooperation is biofilm formation in microbial populations. It is discussed in Section 6.2.

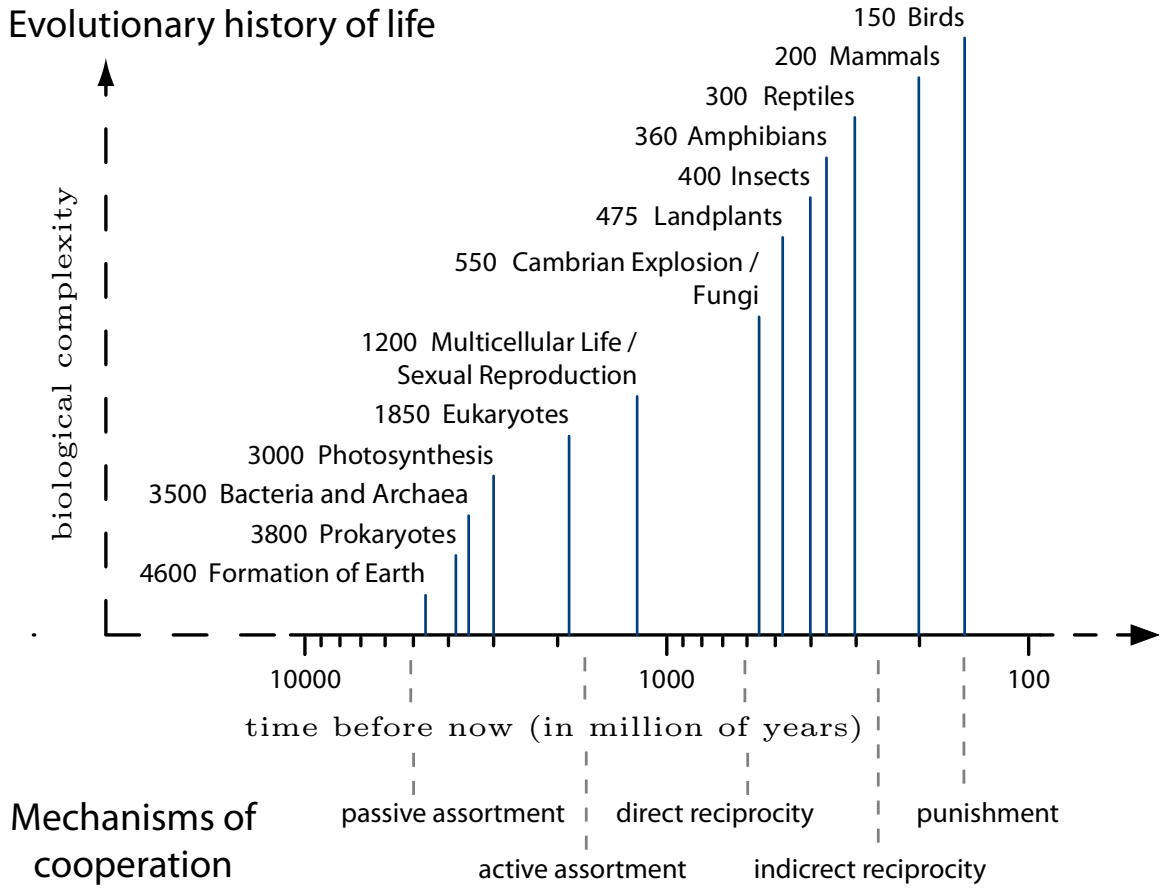

Figure 3.1: Major transitions, biological complexity and the evolution of mechanisms of cooperation. Evolutionary progress did not occur continuously but in major steps. In accordance with increasing complexity, more and more mechanisms to establish and maintain cooperation have evolved. Presumably only passive forms of assortment ensured cooperation for early forms of life. Only later, more active forms of assortment and the whole variety of complex mechanisms based on memory and recognition occurred.

3.2 Cooperation

Explaining cooperation has become a conundrum in evolutionary theory, and many evolutionary biologist see cooperation as one of the main challenges to be explained by evolutionary theory [51, 52]. Cooperation and evolution is considered by a lot of reviews [53, 54, 55]. Here I state my personal perspective of this issue.

Roughly speaking, cooperative behavior is given if an individual provokes a 'benefit' to another individual or its whole surrounding population by having some 'costs'. Subsequently, even if the benefit is much larger than the costs, non-cooperating individuals, i.e. *free-riders*, save the costs for providing the benefit and thereby have a selection advantage compared to cooperative-individuals: There is a *dilemma of cooperation*, without additional constraints only free-riders prevail. More formally, one might define cooperation as a behavior or trait which increases the fitness of other individuals but decreases the fitness of the cooperating

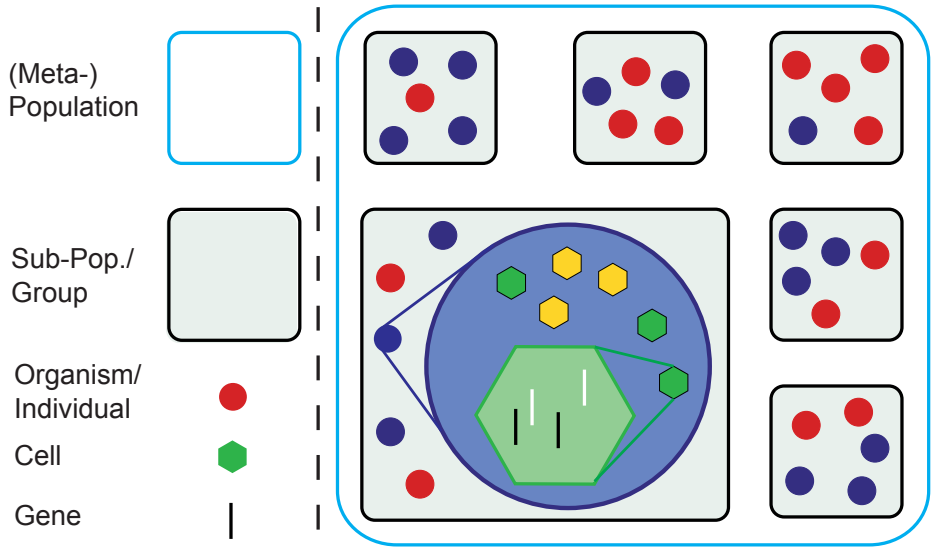

Figure 3.2: Biological life is arranged on different but interacting levels. Entities at lower levels may or may not be able to reproduce autonomously. A complex interaction on the higher level is often related with cooperation on a lower one. A major transition is often linked with a shift of selection from a lower to a higher level.

individual.

Throughout the literature, there are a lot of terms used to describe cooperative and free-riding behavior. Examples include altruists, and producers, opposing cheaters, free-loaders, and defectors respectively. Furthermore, a lot of slightly or strongly different meanings of the same terms are used. Many different classifications have been introduced to distinguish different forms of cooperation. This includes for example strong and weak-altruism, direct and indirect forms. Throughout this thesis, we use the terms *cooperators* and *free-riders*. Further, using the term altruism can be highly misleading since cooperation evolves and is maintained due to - in total - selection advantages and not by some sort of selflessness. Similar, the term cheater is not very adequate in many situations. Often no sophisticated intention is involved if not cooperating. Moreover, regarding the diversity of cooperative behavior, as introduced in the following, a complete classification of cooperation is probably not feasible but the exact way of cooperation becomes clear when considering specific examples.

3.3 The dilemma of cooperation and the prisoner's dilemma

To further illustrate the dilemma of cooperation let us consider one specific situation, the prisoner's dilemma [52]. Although certainly rather specific, it has become a mathematical metaphor for describing cooperative behavior [53, 56]. Individuals are either cooperators or free-riders and there is pairwise interaction described by a payoff matrix,

	Cooperator	Free-rider
Cooperator	$b-c$	$-c$
Free-rider	b	0

.

A cooperator is giving a benefit b to another individual by having some costs c, with $0 < c < b$. Thus, when interacting with another cooperator, both obtain the effective payoff $b - c$. In contrast, if a cooperator interacts with a free-rider, the free-rider obtains the benefit b, while the cooperator does not obtain any benefit but has to pay the costs c. Free-riders are always better off, in game-theoretic terms, free-riding is a Nash-equilibrium and and evolutionary stable strategy. For a repeated interaction in a population of N individuals only free-riders remain at the end. This occurs despite the fact that cooperation is beneficial in principle, and the whole population, i.e. the total payoff of the population, would be better off if every individual would cooperate: there is the dilemma of cooperation. The expected payoff of cooperators and defectors depends on their abundance in the population. If we assume that every individual interacts with all other individuals with equal probability, and if taking the expected payoff-values as expected fitness-values, the replicator equation (2.5) giving the change in the fraction of cooperators, x, has the following form,

$$\partial_t x = -c\, x(1-x) < 0. \tag{3.1}$$

The fraction of cooperators always declines because of the costs, c.

The prisoner's dilemma in its evolutionary formulation is one example of how to motivate a fitness-term on a macroscopic level. Further, it is one specific case of *evolutionary game theory*, a framework that will be considered in Section 4.3.1 in more detail. In the form stated, the prisoner's dilemma assumes detrimental conditions for the evolution of cooperation. In fact, the benefit cannot act at all and only the costs c occur in Eq. (3.1). In biology, cooperation does not follow the simple scheme of the prisoner's dilemma but different interaction scenarios have to be considered. Those interactions include other evolutionary games like the snowdrift game as will be introduced in Section 4.3.1. But the act of cooperation can also be different in its structure. Public good situations where the benefit of cooperation is split among all members of the population are entirely different from prisoner's dilemma interactions. Theories on cooperation consider these additional factors and try to uncover their impact on cooperation.

3.4 Examples of cooperation

In the following, some examples of cooperation, including different levels, are given. Moreover, the main pathways of how to overcome the dilemma of cooperation are stated in the following section. As obvious by the multi-level view and with the diversity of biological complexity in mind, there is no universal answer to this problem, but there exist different evolutionary pathways towards cooperation.

Let us start with the pretendedly highest level of life, the human being. Answering why humans persistently engage cooperation from the beginning of their life is of course a very stunning questions. Due to the outstanding mind and consciousness of *homo sapiens*, these questions shall mainly be considered in the context of sociology and psychology. There are a lot of heavily discussed issues in this field [57, 30]. Is cooperative behavior inherent within the human being? How important are early childhood and the first interactions with other humans? How does culture come in? Which role does punishment and the ability to form

institutions play? Which aspects are special for humans and in which respect does the cooperative behavior of *Homo sapiens* differ from other *Hominidae*?

Still, for very precisely given situations, insights into human cooperative behaviors may still be obtained by simple mathematical models or experiments with human subjects. Examples include simple setups of the tragedy of the commons [58], or the interacting of human subjects in well-defined laboratory situations [59]. Also in the context of economy, simple evolutionary setups might be proper to explain certain economical aspects and theoretical approaches might also tackle some basics of punishment [60, 61]. One must be aware, however, that also for very well defined conditions classical assumptions like in economy the rational, profit optimizing *Homo oeconomicus* might impressively fail. See for example the 'dictator game' [62]. In fact, the growing field of physiological economy is increasingly challenging the classical formulation of economical theory [63]. Further, cooperation in human behavior is often entirely different to what is assumed in common evolutionary models of cooperation simply because of the existence of contracts and enforced laws.

Also in the animal kingdom, cooperation is ubiquitous. Most common examples include the herd formation of gregarious animals [64]. While beneficial for the whole population, animals standing most outward must take the higher risk to be taken as prey. Also executing alarm calls, as observed for birds and monkeys, is a strong form of cooperation [64, 30]. The surrounding individuals are warned while at the same time the caller is strongly increasing the attention of the discovered predator. Another often stated extreme form of cooperation is the separation of working and reproducing individuals in insect populations, see e.g. [65]. Why for example are most of the individuals sterile female 'workers' or other specialized individuals supporting the reproduction of one or a few fertile 'queens'? The main reason for cooperation within such colonies or super-organisms is strong relatedness of kin. To speak in terms of the 'gene's eye view': by being genetical identical, working individuals reproduce their genes by supporting the queen. However, the precise reasons for cooperation in insect colonies, and the ways of protection against genetically different individuals are more subtle and for different species, different detailed mechanisms might act [50]. This includes kin-discrimination and reciprocity.

For unicellular organisms cooperation is widespread as well. Here, cooperation is often given by the production of a public good [66, 67]. Striking examples include the synthesis of matrix-proteins for biofilm formation, or the production of extracellularly acting enzymes for better nutrient or dietary mineral uptake. Cooperation and intracellular signal-transposition in biofilms is such pronounced that some researches see microbial populations even as social entities undergoing sophisticated properties like share of labor and communication [66, 68]. Another well studied example of cooperation in microbes is the formation of fruiting bodies, for example in the slime mold *Dictyostelium Discoideum* [69, 70]. While formation increases dispersal rates and therefore the exploitation of new nutrient resources, cooperation involves altruism as stalk cells cannot disperse but die. A more detailed description of cooperative behavior in microbes and the mechanisms promoting it is given in Section 6.2.

One example for cooperation on a more microscopic level is the evolution and maintenance of information by permanently replicating RNA sequences. Without error correcting enzymes, the maximum length of an RNA sequence which is selected during reproduction is limited due to a finite copying fidelity [71]; this *error catastrophe* forbids the coding of longer, error-

limiting enzymes and thus obstructs the evolution of a large genetic code. One way to still keep a larger amount of information stable over time is the hyper-cycle [72] where, arranged in a cycle, different RNA sequences catalytically promote the reproduction of the following one. Importantly, there can be 'parasites', i.e. mutators which are excellently replicated with the help of the foregoing sequence in the cycle but do not act catalytically for the reproduction of the following sequence. Thus, there is a dilemma of cooperation in the sense that cooperating replicators being part of the hyper cycle enhance the total reproduction rate in the system but mutators reproducing faster might not contribute to the enzymatic activity in the cycle. The total reproduction rate might break down. See [73, 74, 75] for further discussions and possible ways out of the dilemma.

3.5 The main principles promoting cooperation

What are the mechanisms and principles preventing cooperators from becoming exploited? Given the diversity of cooperation and the high biological complexity there is of course no universal answer to this question and the exact mechanism should be studied on a case by case basis. Nevertheless, one can roughly distinguish two main classes of mechanisms, *sophisticated forms of reciprocity* and *assortment*. Note however that this classification is by no means unique and other authors prefer to sort into different categories, see e.g. [50, 53, 54].

Reciprocity and other sophisticated mechanisms: If individuals have the capability to memorize behavior of other individuals and to control their own behavior, they can actively obstruct the exploitation of non-cooperators to themselves or others: cooperation is maintained by *reciprocity* [76]. In general, one differs between direct and indirect reciprocity. *Direct reciprocity* builds on repeated interaction. For example in the repeated prisoner's dilemma game it includes the famous tit for tat strategy [52], where individuals only continue cooperating when playing with another player if this other player was cooperating during the last engagement. *Indirect reciprocity* involves not only direct interaction between two individuals but also considers third parties and some sort of communication. More complex forms include punishment and policing [77, 62]. To be complete: Sophisticated mechanisms promoting cooperation include also evolved cultural rites and, considering humans, the foundation of institutions [78]. The necessary and sufficient conditions for reciprocity leading to the evolution and maintenance of cooperation can be intricate and have been considered in a lot of theoretical studies, e.g. [76, 30, 53].

Assortment of interacting individuals: For the second class of mechanisms, cooperation is rendered possible by a high relatedness among interacting individuals such that cooperators interact more likely with other cooperators than with non-cooperating free-riders. Importantly, additional ecological and biological factors are necessary to ensure assortment and a sufficient high relatedness. However, these conditions do not necessarily require sophisticated abilities like memory or visual recognition. In this thesis we consider the dilemma of cooperation in microbial populations and hence focus on this class of cooperation provoking mechanisms and the exact ecological details at play. More formally, relatedness and the evolution of cooperation can be considered in the theories of kin- and multi-level selection, as discussed in Section 6.1 in detail.

4 Neutral evolution and its edge

Demographic fluctuations have for long been acknowledged as a source for change during evolution. Its importance compared to selection by fitness-differences, however, has been controversial. In this chapter, two projects studying the role of demographic fluctuations in frequency-dependent fitness setups are presented.

In the following section, we give a short review of the role of random drift in biology and especially of the rise and fall of neutral theories which assume random drift being the main determinant of evolutionary change. The mathematical formulations of evolutionary dynamics taking demographic fluctuations into account are introduced in Section 4.2. Subsequently, frequency-dependent dynamics is introduced and discussed. We then shortly outline our contribution to this field. In the first manuscript, we consider the role of demographic fluctuations and its comparison with selection for frequency-dependent fitness terms. In the second project we study the interplay between random drift and mutations for a specific fitness-scenario: cyclic dominance.

4.1 Random drift and the theory of neutral evolution

The replicator equation (2.5) describes the evolutionary dynamics of different types in a deterministic manner. Change is rendered by differences in fitness, i.e. differences of the expected reproduction rates. Already since the work of Fisher, Wright and Haldane and the modern synthesis, demographic fluctuations have been recognized as an additional mechanism of change for evolution. Especially Wright emphasized its important role for evolutionary dynamics [40].

Due to the stochastic nature of birth and death events, there are aberrations from the expected deterministic dynamics. Thus, even without any differences in fitness-values, different strains can contribute differently to the next generation. These demographic fluctuations can then lead to substantial changes in the composition of the population on long time scales: there is *random drift*[1].

Change by random drift is not directed and has to work against selection by fitness-differences to show off. The role of random drift thus has been questioned by many, for example by Fisher [38]. However, with the increasing understanding in molecular biology, Kimura came up with his *neutral theory of evolution* stating that the majority of change on the DNA level is due to random drift [79], regardless of any fitness differences and natural selection. The theory has given rise to many debates, as many saw it as an open contradiction to

[1] In biology the terms allelic drift, genetic drift or drift are also used. As change by fluctuations is by no means directed and to distinguish it from a physical drift (see later), we always use the term 'random drift'.

Darwin's theory of evolution. However, as clearly stated by himself, Kimura did not deny the presence and importance of fitness-differences but rather made statements on the 'majority' of changes. However, accounting for the more recent progress in acknowledging the complexity of the phenotype genotype mapping, the understanding of gene regulation and the lapse of the junk-DNA picture, one has to admit that the abundance of truly neutral mutations on the DNA level cannot be determined reasonably.

In population genetics the neutral assumption is nevertheless the null model to start with. Building on neutral formulations, a lot of powerful methods have been established, most notably the coalescent theory introduced by Kingman [80]. Moreover, Kimura has established a standard description for evolutionary dynamics taking both, demographic fluctuations and fitness-differences into account: a continuos description by a diffusion-approximation as introduced in the next Section 4.2. It is used in a wide manner of contexts [37, 81].

In ecology, the neutral theory has recently aroused much attention in explaining biodiversity patterns. The theory of island biogeography was proposed by MacArthur and Edward Wilson to explain the diversity on separated habitats by a balance between migration and extinction of species [82]. Hubbell and others extended this approach and specifically considered neutral dynamics of individuals belonging to different species [83]. The approach is able to make analytical predictions for the *species abundance distribution* or *species area relations* which are central observables in biogeography, see e.g. [84, 85]. Moreover, the neutral theory of Hubbell was the first that could qualitatively explain some species abundance patterns observed in nature, like those observed for some tropical forests, as on Borro Colorado island, or coral reefs [84]. Strikingly, the theory is able to explain these abundance patterns without any complex assumptions on environment and interaction dynamics; taking merely the island-structure into account is sufficient. It thereby stands in contrast to the niche explanation [86, 87], which assumes each species to be specialized to a different but unique ecological niche. A niche is given by a certain combination of ecological conditions like nutrient level, light intensity, humidity, or soil composition. Diversity is explained by presence of multiple niches. These contradicting views could not coexist without vigorous debates and the role of fluctuations, in this context often called *ecological drift*, remains controversial. In the meanwhile, also niche models can explain the observed species abundance patterns which seem to have very universal characteristics and hence are not suited to confirm or disprove theories. However, as within population genetics, the neutral theory is a good null model to start with. Other theories going beyond it must convincingly prove to give a better description of observed biodiversity patterns.

Even if random drift cannot explain the bulk of evolutionary change, as is assumed in neutral theories, it certainly plays an important role in evolution. Especially if populations go through narrow bottlenecks, where population sizes drop to very low values, demographic fluctuations are high and random drift can be the main cause of change. Examples include the propagation of population fronts into unoccupied habitats [88]. Also, at the boundaries of habitats where environmental conditions change, demographic fluctuations are important [89]. Furthermore, speaking in terms of fitness landscapes, random drift can lead to a broader sampling of fitness-space. Thereby, fitter states, originally in 'far distance' beyond fitness valleys might be reached and be climbed up to by selection. See for example Wright and his *shifting balance theory* [40].

Roughly, the importance of random drift is given by the strength of fitness-differences compared to the strength of fluctuations. Consider a population of size N and the differences in fitness is given by the *selection strength* s. The strength of demographic fluctuations decreases with increasing N and hence fluctuations play only a minor role compared to selection by fitness differences for large N. As a rule of thumb, random drift is of minor importance for $sN \gg 1$ but dominates the dynamics for $sN \ll 1$. See also the following Section 4.2 where this relation is discussed in more detail.

To summarize, random drift alone is certainly not sufficient to substantially drive evolutionary progress in nature. However, it can be an important part and its role has to be determined from case to case. Here, we consider the role of fluctuations specifically for scenarios where fitness is frequency-dependent.

4.2 A stochastic description of evolutionary dynamics

To take demographic fluctuations in mathematical approaches into account, one has to go beyond the replicator model introduced in Sec. 2, and has to start with a stochastic model, based on birth and death events. We here introduce a common model, the *Moran process*, see [90, 91, 92, 93]. A similar but time-discrete description is given by the Fisher-Wright process [38, 94, 37, 81], a more detailed introduction can also be found in the Diploma thesis of the author, [95].

Let us again consider only two different traits A and B. The model assumes a fixed population size N in a well mixed population. The number of individuals belonging to type A and B are given by N_A and $N_B = N - N_A$ respectively. As illustrated in Fig. 4.1, the rates are given by,

$$\Gamma_{B\to A} = \frac{\phi_A}{\bar{\phi}} \frac{N_A}{N} \frac{N_B}{N}, \text{ and } \Gamma_{A\to B} = \frac{\phi_B}{\bar{\phi}} \frac{N_B}{N} \frac{N_A}{N}. \tag{4.1}$$

For example, an individual of type A replaces one individual of type B according to its abundance N_A and its fitness ϕ_A. Within a fixed time, the generation time, N such replacing events occur such that, on average, every individual in the population is replaced once during that time. The full stochastic dynamics is described by a master equation, giving the temporal change of the probability $P(N_A, N_B; t)$ for the population to consist of N_A individuals belonging to trait A. The dynamics can easily be expanded to cases involving more than two types, see for example [95].

In many circumstances, a diffusion-approximation, where the number of individuals belonging to Type A and B can be described by continuos variables and the dynamics follows a Fokker-Planck equation, works very well. Within this approach, the probability density $P(x;t)$ for a fraction $x = \frac{N_A}{N}$ of type A to be present in the system is described by the Fokker-Planck equation,

$$\partial_t P(x;t) = -\underbrace{\partial_x \alpha(x) P(x;t)}_{\text{selection}} + \underbrace{\frac{1}{2}\partial_x^2 \beta(x) P(x;t)}_{fluctuatons}, \tag{4.2}$$

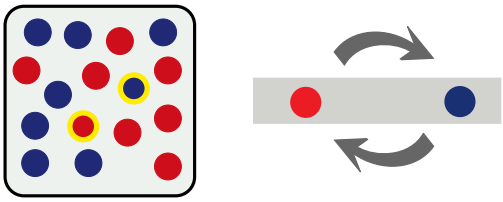

Figure 4.1: The Moran process. A fixed number N of individuals change the traits they belong to by replacing events. This can be illustrated by an urn-model. With respect to the fitness and abundance of different types, one individual is chosen for reproduction. The offspring individual then randomly replaces another individual. Here two different types are denoted as red and blue.

or a corresponding Langevin equation. With the rates, Eqs. (4.1), α and β are given by,

$$\alpha = \frac{\phi_A x - \phi_B(1-x)}{\bar{\phi}}, \text{ and } \quad \beta = \frac{1}{N}\frac{\phi_A x + \phi_B(1+x)}{\bar{\phi}}. \tag{4.3}$$

The first term describes *directed drift*. In the deterministic limit $N \to \infty$ this is the only remaining term and the dynamics is then given by the replicator equation (2.5), $\dot{x} = \alpha(x)$. The second term describes the impact of demographic fluctuations, here given by a diffusion term. It induces deviations from the deterministic solutions.

In this continuous description the role of demographic fluctuations is obvious: The strength of fluctuations scale with $1/\sqrt{N}$. Thus, for very large N, fluctuations (via the corresponding diffusion term) affect the dynamics only slightly, leading to centered distributions around the deterministic trajectories. Or, in the other marginal case, where the population size is very small, fluctuations completely dominate the dynamics and fitness differences (and the corresponding α term) are negligible. In the first extreme, one has *Darwinian selection*, while for the second case there is *neutral evolution*. In between, there is a crossover between both scenarios. It is given when both terms in Eq. (4.2) have about equal weights and balance each other. For the case of frequency independent fitness with a fitness difference $\phi_A - \phi_B = s$ and the average fitness $\bar{f} = 1$ this is given if,

$$sN \sim 1. \tag{4.4}$$

For $sN \ll 1$, evolution is effectively neutral, while for $sN \gg 1$, evolution is Darwinian. This condition has been stated by Kimura already [79]. In population genetics literature it is often stated as $2sN_e = 1$ [79, 36]. However, note that it only gives the rough position of the crossover. Further, if fitness-terms are more involved, more complex relations might hold. See also the first manuscript at the end of this chapter.

The diffusion approach based on the generalized Moran process, Eqs. (4.2) and (4.3), or the Kimura equation [79, 37],

$$\partial_t P(x,t) = -s\partial_x x(1-x) + \mu\partial_x(1-2x)P(x,t) + \frac{1}{2N_e}\partial_x^2 x(1-x)P(x,t), \tag{4.5}$$

which assumes frequency independent selection, $\phi_A - \phi_B = s$ with $\bar{\phi} \approx 1$ and includes mutations occurring with rate μ, are widely used to describe evolutionary dynamics. This includes also situations where the strict settings of the Moran process are not fulfilled.

Note that, although working well in many cases, this approach might fail in many others. For example, if the population size, N, changes rapidly, then the Kramers-Moyal expansion underlying the deviation of Eq. (4.2) might fail. In particular, one could not just substitute the population size by an effective one, $N = N_e$. Furthermore, the diffusion-approximation can fail for very small population sizes, see e.g. [95]. Nevertheless, in many situations, the diffusion approach works astonishingly well for intermediate population sizes.

In addition, the role of fluctuations has been studied also by other methodical approaches. For example, frequency-independent selection can be described by a statistical mechanics approach and an effective Hamiltonian similar to the one for paramagnet [96, 97]. Moreover, fluctuation theorems have been used to describe selection, adaptation, and fluctuations. [98].

4.3 Frequency-dependent scenarios

As introduced in Section 2, fitness can in principle be a very intricate quantity, depending on a lot of biological and ecological factors. In particular, the evolution of a population can couple back to the fitness and fitness may thus be *frequency dependent* with $\phi_l = \phi_l(\mathbf{x})$. For two types (or traits), and a deterministic description, the dynamics is given by the replicator equation (2.5),

$$\dot{x} = \left[\phi_A(x) - \bar{\phi}(x)\right] x. \tag{4.6}$$

Here, x denotes the frequency of type A. Due to the frequency-dependence, the replicator equation is now a non-linear ordinary differential equation.

4.3.1 Evolutionary dynamics and games

The exact functional form of $\phi(x)$ and its frequency-dependence follow from microscopic interactions, see for example Section 6.2 where cooperation and public good scenarios in microbial populations are discussed. Independent of such details however, one can study the impact of different forms of frequency-dependence on evolutionary dynamics. In a first approach, fitness may depend only linearly on the frequencies x in the population and therefore is described by a matrix $\mathcal{P}$. The fitness vector $\phi = (\phi_1, ..., \phi_S)$ is then given by,

$$\phi(\mathbf{x}) = 1 + \mathcal{P}\mathbf{x}. \tag{4.7}$$

Here, the *background fitness*, which is equal for each type, is one[2]. In evolutionary dynamics, $\mathcal{P}$ is often called a *payoff matrix* and the fitness is considered as emerging from underlying *games*. Consider for example only two types A and B and the Payoff matrix,

$$\mathcal{P} = \begin{pmatrix} \mathcal{R} & \mathcal{S} \\ \mathcal{T} & \mathcal{P} \end{pmatrix}. \tag{4.8}$$

[2]Often, a strength of selection ω, as additional factor before the payoff matrix is introduced in this context. For $\omega \ll 1$ one is in the limit of weak selection with $\omega = 0$ describing strict neutral dynamics.

Game	Payoff	Characteristics	Fixed points
Coordination game	$\mathcal{S}-\mathcal{P}<0, \mathcal{T}-\mathcal{R}<0$	Coexistence unstab.	$x_S^*=\{0,1\}$, $x_U^*\in(0,1)$
Prisoner's dilemma	$\mathcal{S}-\mathcal{P}<0, \mathcal{T}-\mathcal{R}>0$	Defection stable	$x_S^*=0$, $x_U^*=1$
Mutualism	$\mathcal{S}-\mathcal{P}>0, \mathcal{T}-\mathcal{R}<0$	Cooperation stable	$x_S^*=1$, $x_U^*=0$
Snowdrift game	$\mathcal{S}-\mathcal{P}>0, \mathcal{T}-\mathcal{R}>0$	Coexistence stable	$x_S^*\in(0,1)$, $x_U^*=\{0,1\}$

Table 4.1: Different types of two-player games and the fixed-point behavior of the replicator dynamics. In evolutionary theory, these games are often used to classify evolutionary dynamics also for more complex scenarios than two-player games in a well-mixed environment.

The entry $\mathcal{P}_{lk}=\mathcal{P}_{l\leftarrow k}$ is then the reward an individual of type l obtains when interacting with and individual of type k. The fitness of a given type l is thus the average reward that an individual of this type would get if 'playing' repeatingly with other individuals and thereby sampling interactions with the whole population.

The payoff conception is borrowed from game theory [99] and was introduced by Price and Maynard-Smith in the context of evolutionary dynamics [100, 49]. The replicator equation and other dynamical approaches involving a frequency dependent fitness are since often considered to belong to the field of *evolutionary game theory* [47, 49, 46, 56].

Here, we stress that evolution is a game in the sense that the fitness (success) of a certain type (strategy) can depend on the frequency of other types (strategies). However, as stated before, the underlying biological and evolutionary dynamics leading to a frequency dependence of fitness are much more involved than just sampling pairwise interactions. The payoff approach is therefore mainly useful to concisely classify the different situations which can occur if the fitness depends linearly on the frequencies.

4.3.2 Evolutionary games for two types

The replicator equation for two types, described by Eqs. (4.6), (4.7), and (4.8) is also called a *two-player game* scenario. In the context of 'social interactions', simple types of social dilemmas can be described with this approach [101]. The specific letters for the payoff matrix coefficients, see Eq. (4.8), are chosen according to these scenarios. The dynamics takes place in a one-dimensional state space, $x\in[0,1]$. Based on the stability analysis of the non-linear dynamics, four different games can be distinguished, see Table 4.1. There can be a stable coexistence fixed point, or the pure states with only a single type remaining can be stable. A more detailed introduction two two-player games and their classification can be found in [56, 95] and also in the first manuscript printed at the end of this chapter. Furthermore, note that a lot of different names are used to describe these different classes. E.g. the snowdrift game is also called *hawk and dove*.

The classification introduced above is based on replicator dynamics. Now, clearly, frequency-dependence is in general not simply linear, but, as stated before, emerges from the underlying microscopic details of the individuals interacting with their environment. To consider such microscopic details below the population-level, approaches of evolutionary game theory often study other types of dynamics. Most often, local or pairwise interactions are still described by payoff-matrixes and the idea of games, where the fitness of one individual depends on the

behavior of the surrounding ones, still holds. Additionally however, other update mechanisms and population structures are introduced and their global impact on the population is studied. In particular, the ensuing change of global frequencies and effective fitness functions ϕ are of interest. Examples are interaction on lattices [102, 103, 104, 105] and networks [106, 107] or structuring of the population into different sets [108, 109]. See also [110, 111] for recent reviews.

4.3.3 Evolutionary games for more than two types

In contrast to the two-player games discussed above, the replicator dynamics for more than two types do not only lead to stable coexistence or pure states with individuals belonging to only one single type. There can be limit cycles, chaos and other higher dimensional characteristics of non-linear dynamics. One additional scenario is cyclic dominance. Here, the frequency-dependence of three fitness terms is, for example, such that in pairwise interaction individuals of type A dominate those of type B, those of type B dominate individuals of type C and finally those of type C dominate individuals of type A. The scenario of cyclic dominance has been observed in populations of lizards and microbes [112, 113, 114]. Intriguingly, cyclic dominance in combination with motility can lead to stable abundance patterns of all three types [115, 116, 117, 118, 119]. In the second manuscript at the end of this chapter, we investigate the role of mutations for this coexistence.

4.4 Papers and manuscripts

4.4.1 The edge of neutral evolution in social dilemmas

In the paper 'The edge of neutral evolution in social dilemmas', *NJP* **11** 093029 (2009) by Jonas Cremer, Tobias Reichenbach, and Erwin Frey we consider the role of demographic fluctuations for the case where fitness-values depend linearly on the frequency of traits. More specifically, the project determines the edge between regimes where fluctuations dominate the dynamics and those in which fitness-differences are important. In detail, this is done by analytically and numerically determining *fixation probabilities* and *mean extinction times*, i.e. the probability to reach a pure state where only a certain type of individuals remains, and the times to reach these states. Our main result is that these variables show a crossover at a certain 'edge' discriminating between *neutral* and *Darwinian* regimes. These edges change with the difference in fitness and the strength of fluctuations which depend directly on the population size. As shown, the crossovers, and therefore the edges between neutral and Darwinian evolution change differently for different 'game-transitions'. We have classified these and the location of the edges.

4.4.2 Entropy production of cyclic population dynamics

In the paper 'Entropy production of cyclic population dynamics', *Phys. Rev. Lett.* **104**, 218102 (2010) by Benjamin Andrae, Jonas Cremer, Tobias Reichenbach, and Erwin Frey,

the balance between mutations and demographic fluctuations is studied for the case of cyclic dominance of three types. While mutations provoke an even coexistence of three types, demographic fluctuations counteract this dynamics. For small mutation rates, states close to pure states become occupied; the global frequency of one type is close to one. Here, we have studied the details of this transition between coexistence and the cease of two types by considering the entropy production in the steady state. Entropy production peaks close to the critical mutation rate separating the coexistence and the homogeneous regime where one type dominates. The work illustrates the usage of entropy production as quantity to analyze and understand stochastic systems, which do not reach detailed balance. Furthermore, it introduces the concept of entropy production to the description of evolutionary dynamics and helps to understand the interplay between mutations and random drift.

4.5 Discussion and outlook

In evolutionary dynamics, for a well mixed populations with a fixed size N, fluctuations play the pivotal role if the population size is sufficiently small. In contrast, for large populations, fluctuations have only a minor impact, while selection and mutations are important. The transitions between such regimes is smooth and expressed by crossovers in the evolutionary important variables like extinction times or the level of coexistence.

The discussed scenarios assume the population size to be fixed. In nature, however, population sizes are rarely constant. This is especially true on more local scales. A first approach to cover such scenarios is to replace the population size N by an efficient population size N_E, given by N averaged over time. However, the dynamics in N affects the strength of demographic fluctuations, hence such an approach the same crossover conditions as stated before can certainly not hold. Such a change in the population size and the thereby changing strength of random drift is considered in the next Chapter 5.

For more complex environmental conditions, the role of demographic fluctuations can change dramatically. Most importantly, demographic fluctuations can then always be a main determinant of evolution and not just for a small population size as local numbers of individuals can be very low. This is the case for many ecological situations. Examples are propagations and adaption at population fronts [88, 89]. Also for population bottlenecks and the occurrence of founder populations, fluctuations can play a crucial role, see also Chapter 6. Another example is the evolution of agents on a lattice, where interactions occur only between nearest neighbors [102, 103, 104, 105]. For example, mobility and the impact of fluctuations which in nature are always present, can dramatically alter the dynamics on these lattice games, see also [120]. To determine the role of demographic fluctuations in many other scenarios is a current challenge of evolutionary dynamics.

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The edge of neutral evolution in social dilemmas

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Abstract. The functioning of animal as well as human societies fundamentally relies on cooperation. Yet, defection is often favorable for the selfish individual, and social dilemmas arise. Selection by individuals' fitness, usually the basic driving force of evolution, quickly eliminates cooperators. However, evolution is also governed by fluctuations that can be of greater importance than fitness differences, and can render evolution effectively neutral. Here, we investigate the effects of selection versus fluctuations in social dilemmas.

By studying the mean extinction times of cooperators and defectors, a variable sensitive to fluctuations, we are able to identify and quantify an emerging 'edge of neutral evolution' that delineates regimes of neutral and Darwinian evolution. Our results reveal that cooperation is significantly maintained in the neutral regimes. In contrast, the classical predictions of evolutionary game theory, where defectors beat cooperators, are recovered in the Darwinian regimes. Our studies demonstrate that fluctuations can provide a surprisingly simple way to partly resolve social dilemmas. Our methods are generally applicable to estimate the role of random drift in evolutionary dynamics.

Contents

1. Introduction

Individuals of ecological communities permanently face the choice of either cooperating with each other, or of cheating [1]–[5]. While cooperation is beneficial for the whole population and essential for its functioning, it often requires an investment by each agent. Cheating is then tempting, yielding social dilemmas where defection is the rational choice that would yet undermine the community and could even lead to ultimate self-destruction. However, bacteria or animals do not act rationally; instead, the fate of their populations is governed by an evolutionary process, through reproduction and death. The conditions under which cooperation can thereby evolve are subject of much contemporary, interdisciplinary research [2], [6]–[11].

Evolutionary processes possess two main competing aspects. The first one is selection by individuals' different fitness, which underlies adaptation [12]–[14] and is, by neo-Darwinists, viewed as the primary driving force of evolutionary change. In social dilemmas, defectors exploit cooperators rewarding them a higher fitness; selection therefore leads to fast extinction of cooperation, such that the fate of the community mimics the rational one. A large body of work is currently devoted to the identification of mechanisms that can reinforce cooperative behavior [19], e.g. kin selection [15, 16], reciprocal altruism [17, 18], or punishment [5, 8, 20]. However, the evolution of cooperation in Darwinian settings still poses major challenges. The second important aspect of evolution is random fluctuations that occur from the unavoidable stochasticity of birth and death events and the finiteness of populations. Neutral theories emphasize their influence which can, ignoring selection, explain many empirical signatures of ecological systems such as species–abundance relations as well as species–area relationships [21]–[25]. The importance of neutral evolution for the maintenance of cooperation has so far found surprisingly little attention [26]–[29].

In this paper, we introduce a general concept capable of investigating the effects of selection versus fluctuations by analyzing extinction events. We focus on social dilemmas,

i.e. we study the effects of Darwinian versus neutral evolution on cooperation[3]. For this purpose, we consider a population that initially displays coexistence of cooperators and defectors, i.e. cooperating and non-cooperating individuals. After some transient time, one of both 'species' will disappear [23], simply due to directed and stochastic effects in evolution and because extinction is irreversible: an extinct species cannot reappear again. The fundamental questions regarding cooperation are therefore: will cooperators eventually take over the whole population, and if not, for how long can a certain level of cooperation be maintained?

We show that the answers to these questions depend on the influence of stochasticity. For large fluctuations, evolution is effectively neutral, and cooperation maintained on a long time-scale, if not ultimately prevailing. In contrast, small stochastic effects render selection important, and cooperators die out quickly if disfavored. We demonstrate the emergence of an 'edge of neutral evolution' delineating both regimes.

2. Models and theory

2.1. Social dilemmas

Consider a population of N individuals that are either cooperators C or defectors D. We assume that individuals randomly engage in pairwise interactions, whereby cooperators and defectors behave distinctly differently and thereby gain different fitnesses. The population then evolves by fitness-dependent reproduction and random death, i.e. a generalized Moran process [2, 30], which we describe in detail in the next subsection. Here, we present the different possible fitness gains of cooperators and defectors.

In the *prisoner's dilemma* a cooperator provides a benefit b to another individual, at a cost c to itself (with the cost falling short of the benefit). In contrast, a defector refuses to provide any benefit and hence does not pay any costs. For the selfish individual, irrespective of whether the partner cooperates or defects, defection is favorable, as it avoids the cost of cooperation, exploits cooperators and ensures not to become exploited. However, if all individuals act rationally and defect, everybody is, with a gain of 0, worse off compared to universal cooperation, where a net gain of $b - c$ would be achieved. The prisoner's dilemma therefore describes, in its most basic form, the fundamental problem of establishing cooperation.

We can generalize the above scheme to include other basic types of social dilemmas [31]. Namely, two cooperators that meet are both rewarded a payoff $\mathcal{R}$, while two defectors obtain a punishment $\mathcal{P}$. When a defector encounters a cooperator, the first exploits the second, gaining the temptation $\mathcal{T}$, while the cooperator only gets the sucker's payoff $\mathcal{S}$. Social dilemmas occur when $\mathcal{R} > \mathcal{P}$, such that cooperation is favorable, in principle, while temptation to defect is large: $\mathcal{T} > \mathcal{S}$ and $\mathcal{T} > \mathcal{P}$. These interactions may be summarized by the payoff matrix

	C	D
C	$\mathcal{R}$	$\mathcal{S}$
D	$\mathcal{T}$	$\mathcal{P}$

Hereby, the entries in the upper row describe the payoff that a cooperator obtains when encountering a cooperator C or a defector D, and the entries in the lower row contain the payoffs for a defector.

[3] Within this paper, we use the term 'Darwinian' to signify evolutionary dynamics mainly driven by selection, as assumed within the modern synthesis of evolution.

Table 1. Different types of social dilemmas. We consider a population of cooperators and defectors, and describe their interactions in terms of four parameters $\mathcal{T}$, $\mathcal{R}$, $\mathcal{S}$ and $\mathcal{P}$, see text. Depending on the payoff-differences $\mathcal{S}-\mathcal{P}$ and $\mathcal{T}-\mathcal{R}$, four qualitatively different scenarios arise.

	$\mathcal{S}-\mathcal{P}<0$	$\mathcal{S}-\mathcal{P}>0$
$\mathcal{T}-\mathcal{R}<0$	Coordination game	By-product mutualism
$\mathcal{T}-\mathcal{R}>0$	Prisoner's dilemma	Snowdrift game

Variation of the parameters $\mathcal{T}$, $\mathcal{P}$, $\mathcal{R}$ and $\mathcal{S}$ yields four principally different types of games, see table 1 and figure 3. The *prisoner's dilemma* as introduced above arises if the temptation $\mathcal{T}$ to defect is larger than the reward $\mathcal{R}$, and if the punishment $\mathcal{P}$ is larger than the sucker's payoff $\mathcal{S}$, e.g. $\mathcal{R}=b-c$, $\mathcal{T}=b$, $\mathcal{S}=-c$ and $\mathcal{P}=0$. As we have already seen above, in this case, defection is the best strategy for the selfish player. Within the three other types of games, defectors are not always better off. For the *snowdrift game* the temptation $\mathcal{T}$ is still higher than the reward $\mathcal{R}$ but the sucker's payoff $\mathcal{S}$ is larger than the punishment $\mathcal{P}$. Therefore, cooperation is favorable when meeting a defector, but defection pays off when encountering a cooperator, and a rational strategy consists of a mixture of cooperation and defection. Another scenario is the *coordination game*, where mutual agreement is preferred: either all individuals cooperate or defect as the reward $\mathcal{R}$ is higher than the temptation $\mathcal{T}$ and the punishment $\mathcal{P}$ is higher than the sucker's payoff $\mathcal{S}$. Lastly, the scenario of *by-product mutualism* yields cooperators fully dominating defectors since the reward $\mathcal{R}$ is higher than the temptation $\mathcal{T}$ and the sucker's payoff S is higher than the punishment $\mathcal{P}$. All four situations and the corresponding ranking of the payoff values are depicted in table 1 and figure 3.

2.2. The evolutionary dynamics

We describe the evolution by a generalized Moran process [2, 30], where the population size N remains constant and reproduction is fitness-dependent, followed by a random death event.

Let us denote the number of cooperators by N_C; the number of defectors then reads $N-N_C$. The individuals' fitness are given by a constant background fitness, set to 1, plus the payoffs obtained from social interactions. The fitness of cooperators and defectors thus read $f_C=1+\mathcal{R}(N_C-1)/(N-1)+\mathcal{S}(N-N_C)/(N-1)$ and $f_D=1+\mathcal{T}N_C/(N-1)+\mathcal{P}(N-1-N_C)/(N-1)$, respectively. In the following, we assume weak selection, i.e. the payoff coefficients are small compared to the background fitness. Note that within this limit, the self interactions of individuals are only of minor relevance. More important, in the case of weak selection, the evolutionary dynamics of the game depends only on the payoff differences $\mathcal{T}-\mathcal{R}$ and $\mathcal{S}-\mathcal{P}$. The different types of social dilemmas arising from these two parameters are listed in table 1.

In the Moran process, reproduction of individuals occurs proportional to their fitness, and each reproduction event is accompanied by death of a randomly chosen individual. As an example, the rate for reproduction of a defector and corresponding death of a cooperator reads

$$\Gamma_{C\to D}=\frac{f_D}{\langle f\rangle}\frac{N_C}{N}\frac{N-N_C}{N}, \tag{1}$$

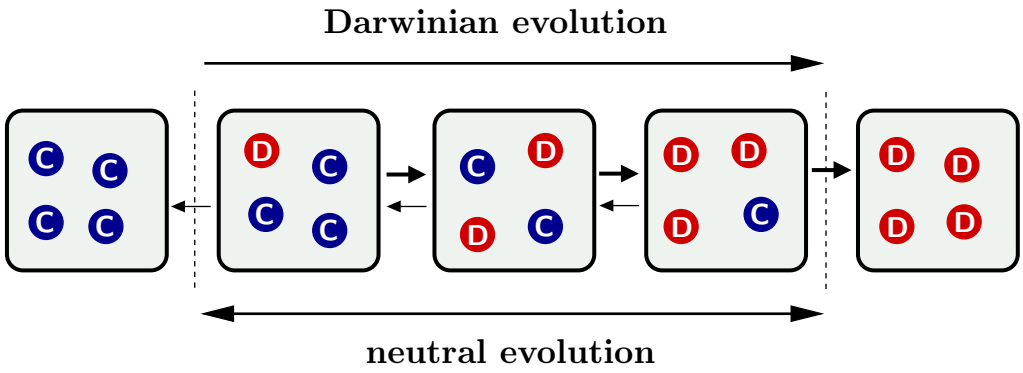

Figure 1. Phase space exemplified for the prisoner's dilemma. The evolutionary dynamics consists of a Darwinian, directed part caused by selection of defectors (D) against cooperators (C), and a neutral, undirected part due to fluctuations. Eventually, only one species survives.

whereby $\langle f \rangle = f_C N_C/N + f_D(1 - N_C/N)$ denotes the average fitness. The timescale is such that an average number of N reproduction and death events occur in one time step.

2.3. Distinguishing Darwinian from neutral evolution: extinction times

The evolutionary dynamics is intrinsically stochastic. Although defectors may have a fitness advantage compared to cooperators, the latter also have a certain probability to increase. This situation is illustrated in figure 1 for a population of four individuals and the dynamics of the prisoner's dilemma. Darwinian evolution, through selection by individuals' fitness, points to the 'rational' state of only defectors, while fluctuations oppose this dynamics and can lead to a state of only cooperators. In any case, upon reaching overall defection or cooperation, the temporal development comes to an end. One species therefore eventually dies out.

The mean extinction time, i.e. the mean time it takes a population where different species coexist to eventually become uniform, allows us to distinguish Darwinian from neutral evolution. Consider the dependence of the mean extinction time T on the system size N. Selection, as a result of some interactions within a finite population, can either stabilize or destabilize a species' coexistence with others as compared to neutral interactions, thereby altering the mean time until extinction occurs. Instability leads to steady decay of a species, and therefore to fast extinction [28, 29, 32]: the mean extinction time T increases only logarithmically in the population size N, $T \sim \ln N$, and a larger system size does not ensure much longer coexistence. This behavior can be understood by noting that a species disfavored by selection decreases by a constant rate. Consequently, its population size decays exponentially in time, leading to a logarithmic dependence of the extinction time on the initial population size. In contrast, stable existence of a species induces $T \sim \exp N$, such that extinction takes an astronomically long time for large populations [28, 29, 33]. In this regime, extinction only stems from large fluctuations that are able to cause sufficient deviation from the (deterministically) stable coexistence. These large deviations are exponentially suppressed and hence the time until a rare extinction event occurs scales exponentially in the system size N.

An intermediate situation, i.e. when T has a power-law dependence on N, $T \sim N^\gamma$, signals dominant influences of stochastic effects and corresponds to neutral evolution [34]–[36]. Here

the extinction time grows considerably, though not exponentially, in increasing population size. Large N therefore clearly prolongs coexistence of species but can still allow for extinction within biologically reasonable timescales. A typical neutral regime is characterized by $\gamma = 1$, such that T scales linearly in the system size N. This corresponds to the case where the dynamics yields an essentially unbiased random walk in state space. The mean-square displacement grows linearly in time, with a diffusion constant proportional to N. The absorbing boundary is thus reached after a time proportional to the system size N. Other values of γ can occur as well. For example, and as shown later, $\gamma = 1/2$ can occur in social dilemmas (regimes (2) in figure 3).

To summarize, the mean extinction time T can be used to classify evolutionary dynamics into a few fundamental regimes. Darwinian evolution can yield stable and unstable coexistence, characterized by $T \sim \log N$ and $T \sim \exp N$, respectively. Power law dependences, $T \sim N^\gamma$, indicate neutral evolution. Transitions between these regimes can occur and manifest as crossovers in the functional relation $T(N)$.

2.4. Analytical description

An approximate analytical description, valid for a large number N of interacting individuals, is possible. The quantity of interest is thereby the probability $P(N_C, t)$ of having N_C cooperators at time t. Its time evolution is described by a master equation specified by transition rates such as (1). For large population sizes N, the master equation can be approximately described within a generalized diffusion approach, where the fraction $x = N_C/N$ of cooperators is considered as a continuous variable. The temporal development of $P(x, t)$ is then described by a Fokker–Planck equation [27, 37, 38],

$$\frac{\partial}{\partial t} P(x,t) = -\frac{\partial}{\partial x}\left[\alpha(x) P(x,t)\right] + \frac{1}{2}\frac{\partial^2}{\partial x^2}\left[\beta(x) P(x,t)\right]. \tag{2}$$

Hereby, $\alpha(x)$ describes the Darwinian of the evolution, due to selection by fitness differences, and corresponds to the deterministic dynamics $\frac{\mathrm{d}}{\mathrm{d}t}x = \alpha(x)$. The second part, which involves the diffusion term $\beta(x)$, accounts for fluctuations (to leading order) and thereby describes undirected random drift. $\beta(x)$ decreases like $1/N$ with increasing population size. For the social dilemmas that we study in this article, α and β are given by

$$\begin{aligned} \alpha(x) &= x(1-x)\left[(\mathcal{S}-\mathcal{P})(1-x) - (\mathcal{T}-\mathcal{R})x\right], \\ \beta(x) &= \frac{1}{N}x(1-x)\left[2 + (\mathcal{S}-\mathcal{P})(1-x) + (\mathcal{T}-\mathcal{R})x\right] \\ &\approx \frac{2}{N}x(1-x). \end{aligned} \tag{3}$$

Here, the approximation of β given in the last line is valid since weak selection is assumed.

The prisoner's dilemma, specified by $\mathcal{T}-\mathcal{R} = \mathcal{P}-\mathcal{S} \equiv c > 0$ describes the situation where defectors have a frequency independent fitness advantage $f_D - f_C = c$ as compared to cooperators. This scenario is frequently studied in population genetics [37]; we briefly discuss it in the following. The directed part and diffusion coefficients are given by

$$\begin{aligned} \alpha(x) &= -cx(1-x), \\ \beta(x) &= \frac{1}{N}x(1-x)\left[2 - c(1-2x)\right] \approx \frac{2}{N}x(1-x). \end{aligned} \tag{4}$$

With these one can calculate the fixation probability $P_{\mathrm{fix,C}}$ to end up with only cooperators if starting with an equal fraction of cooperators and defectors. It has already been calculated in previous work [37, 38] and reads,

$$P_{\mathrm{fix,C}} = \frac{\mathrm{e}^{-Nc/2} - \mathrm{e}^{-Nc}}{1 - \mathrm{e}^{-Nc}}. \tag{5}$$

The probability for fixation of defectors follows as $P_{\mathrm{fix,D}} = 1 - P_{\mathrm{fix,C}}$. Within the Darwinian regime ($Nc \to \infty$) defectors fixate ($P_{\mathrm{fix,D}} = 1$), whereas for the neutral regime ($Nc \to 0$) both strategies have the same chance of prevailing ($P_{\mathrm{fix,C}} = P_{\mathrm{fix,D}} = 1/2$).

The fixation probability gives no information about the typical time needed for extinction of one of the two species. However, this time is important to determine whether extinction happens within the timescale of observation. We turn to this question in the following.

2.5. Analytical calculation of mean extinction times

The above analytical description, in the form of the Fokker–Planck equation (2), can be employed for computing the mean extinction time $T(x)$. The latter refers to the mean time required for a population initially consisting of a fraction $x = N_{\mathrm{C}}/N$ of cooperators to reach a uniform state (only either cooperators or defectors). It is given as a solution to the corresponding backward Kolmogorov equation [39, 40],

$$\left[\alpha(x)\frac{\partial}{\partial x} + \frac{1}{2}\beta(x)\frac{\partial^2}{\partial x^2}\right] T(x) = -1, \tag{6}$$

with appropriate boundary conditions. This equation can be solved by iterative integration [39]. In detail, the mean extinction time, $T = T(x = 1/2)$, if starting with an equal fraction of cooperators $x = 1/2$ is given by

$$T = 2\left[\left(\int_0^{1/2} \mathrm{d}u/\Psi(u)\right)\int_{1/2}^{1} \mathrm{d}y/\Psi(y)\int_0^y \mathrm{d}z\Psi(z)/\beta(z) - \left(\int_{1/2}^{1} \mathrm{d}u/\Psi(u)\right)\int_0^{1/2} \mathrm{d}y/\Psi(y)\int_0^y \mathrm{d}z\Psi(z)/\beta(z)\right]\left[\int_0^1 \mathrm{d}u/\Psi(u)\right]^{-1}, \tag{7}$$

where $\Psi(x)$ is given by $\Psi(x) = \exp(\int_0^x \mathrm{d}y\, 2\alpha(y)/\beta(y))$. We have performed these integrals for the general Moran process and show the results in the following.

For the special case of the prisoner's dilemma, specified by $\mathcal{T} - \mathcal{R} = \mathcal{P} - \mathcal{S} \equiv c > 0$, (frequency independent fitness advantage), equation (7) can be solved exactly. The solution reads,

$$T = \frac{1}{N}\left[P_{\mathrm{fix,C}}\left\{-\ln(cN) - \gamma + \mathrm{Ei}(cN/2) + \mathrm{e}^{cN}\left[\mathrm{Ei}(-cN) - \mathrm{Ei}(-cN/2)\right]\right\} + P_{\mathrm{fix,D}}\left\{\ln(cN) + \gamma - \mathrm{Ei}(-cN/2) + \mathrm{e}^{-cN}\left[\mathrm{Ei}(cN/2) - \mathrm{Ei}(cN)\right]\right\}\right], \tag{8}$$

where $\mathrm{Ei}(x)$ denotes the exponential integral $\mathrm{Ei}(x) = \int x^{-1}\exp(x)\mathrm{d}x$ and $\gamma \approx 0.577$ is the Euler Mascheroni constant. $P_{\mathrm{fix,C}}$ and $P_{\mathrm{fix,D}}$ denote the fixation probabilities of cooperators and defectors, given by equation (5). The analytical solution of the mean extinction time as a function of N is shown and compared to stochastic simulations in figure 2. For a further discussion of $T(N)$ (equation (8)) and its impact on evolutionary dynamics we defer the

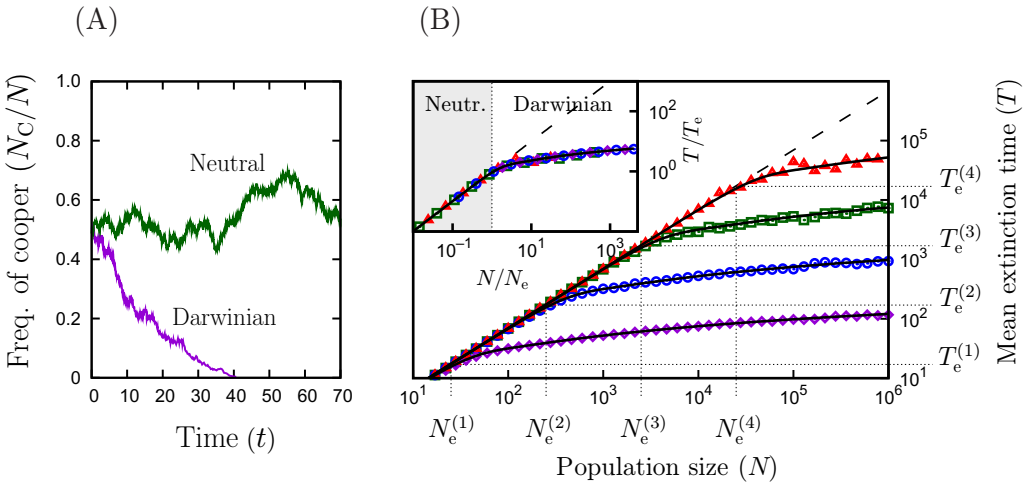

Figure 2. The prisoner's dilemma. Defectors save the cost c of cooperation and therefore have a fitness advantage of c compared to cooperators. (A) Exemplary evolutionary trajectories. A high selection strength, i.e. a high fitness difference $c = 0.1$ (purple), leads to Darwinian evolution and fast extinction of cooperators, while a small one, $c = 0.001$ (green), allows for dominant effects of fluctuations and maintenance of cooperation on long time-scales. We have used $N = 1000$ in both cases. (B) The dependence of the corresponding mean extinction time T on the system size N. We show data from stochastic simulations as well as analytical results (solid lines) for T, starting from equal abundances of both species, for different values of c (see text): $c_1 = 0.1$ (◇), $c_2 = 0.01$ (○), $c_3 = 0.001$ (□) and $c_4 = 0.0001$ (△). The transition from the neutral to the Darwinian regime occurs at population sizes $N_e^{(1)}$, $N_e^{(2)}$, $N_e^{(3)}$ and $N_e^{(4)}$. They scale as $1/c$: $N_e \approx 2.5/c$, as is confirmed by the rescaled plot where the data collapse onto the universal scaling function G, shown in the inset.

reader to section 3. Here, just note that the asymptotic behavior, of $\mathrm{Ei}(x)$ is given by $\mathrm{Ei}(x) \approx \log(|x|) + \gamma + x$ for $x \to 0$, and $\mathrm{Ei}(x) \approx \pm\log(|x|) + \exp(x)/x$ for $x \to \pm\infty$. With this, the well-known asymptotic solutions for high and low population size N, $T = \log(2)N$ and $T \sim \log N$ are obtained.

For general social dilemmas with arbitrary payoff values $\mathcal{T}, \mathcal{P}, \mathcal{R}, \mathcal{S}$, we need to rely on some approximations. Using the drift and diffusion coefficient given by equation (3) we now linearize the fraction α/β, i.e. we write $\alpha(x)/\beta(x) \approx g(x - x^*)$. Hereby $x^* = (\mathcal{S} - \mathcal{P})/(\mathcal{S} - \mathcal{P} + \mathcal{T} - \mathcal{R})$ denotes the fixed point of the deterministic dynamics, where $\alpha(x^*) = 0$ and $g = -N(\mathcal{S} - \mathcal{P} + \mathcal{T} - \mathcal{R})/2$. As an example, in the situation $\mathcal{S} - \mathcal{P} + \mathcal{T} - \mathcal{R} > 0$, $|x^*| \gg 1/\sqrt{g}$ and $|1 - x^*| \gg 1/\sqrt{g}$, we obtain the mean extinction time

$$\begin{aligned} T = \frac{N\ln(2)}{g}&[\mathrm{erfi}[\sqrt{g}\,(1-x^*)] + \mathrm{erfi}(\sqrt{g}x^*)]^{-1} \\ &\times \left\{\mathrm{erfi}(-\sqrt{g}x^*)[-\mathcal{F}\,(g\,(1-x^*)) + \mathcal{F}\,(g\,(1/2-x^*))]\right. \\ &- \mathrm{erfi}\left(\sqrt{g}\,(1-x^*)\right)\left[\mathcal{F}\,(g\,(1/2-x^*)) - \mathcal{F}\,(g\,(x^*))\right] \\ &\left.+\mathrm{erfi}\left(\sqrt{g}\,(1/2-x^*)\right)\left[\mathcal{F}\,(g\,(1-x^*)) - \mathcal{F}\,(g\,(x^*))\right]\right\}. \end{aligned} \tag{9}$$

Here, $\mathrm{erfi}(x) = \frac{2}{\sqrt{\pi}} \int_0^x \mathrm{d}y \exp(y^2)$ denotes the complex error function and $\mathcal{F}(x) \equiv x\mathsf{F}_{1,1;3/2,2}(x)$ involves a generalized hypergeometric function. For graphical representation of equation (8) see figure 4(A, upper branch). As before, the correct asymptotic behavior can also be calculated for this case. Note that the asymptotic behavior of $\mathcal{F}(x)$ is given by $\mathcal{F}(x) \approx x$ for $x \to 0$ and $\mathcal{F}(x) \approx \mathrm{erfi}(\sqrt{x}) - \log(|x|)/2 - 1$ for $x \to \infty$. For small population size, the mean extinction time scales again like $T = \log(2)N$. For asymptotically large system sizes, the scaling depends on the value of the fixed point x^*. For an internal fixed point $x^* \in (0, 1)$, as arises in the snowdrift game, T scales as expected like $T \sim \exp(N)$.

In section 3, we analyze the properties of the analytical form of the mean extinction time, equations (8) and (9), together with numerical simulations, and demonstrate how it defines an emerging edge of neutral evolution.

2.6. Edges of neutral evolution

In section 3, we show that the mean extinction time, equation (9), exhibits different regimes of neutral and Darwinian dynamics. Here, we provide further information on how the boundaries between these regimes can be obtained analytically. For this purpose, we further approximate the dynamics. Let us, firstly, focus on the edge of the regime, where $T \sim N$ emerges. We note that, before unavoidable extinction of one species occurs, a quasi-stationary distribution may form around the fixed point x^*. Following the generic behavior of an Ornstein–Uhlenbeck process, its shape is approximately Gaussian [41]. Its width is given by $w \sim \sqrt{1/|g|}$. x^* and g are specified in the preceding section. Now, for small width, $w \ll 1$, the Darwinian evolution dominates the behavior, meaning $T \sim \ln(N)$ or $T \sim \exp(N)$. In contrast, if $w \gg 1$ the dynamics is essentially a random walk, and $T \sim N$ emerges. The edge of neutral evolution therefore arises at $w \sim 1$. Remembering that g is given by $g = -N(\mathcal{S} - \mathcal{P} + \mathcal{T} - \mathcal{R})/2$, it follows that the edge between both regimes for $\mathcal{S} - \mathcal{P}$ and $\mathcal{T} - \mathcal{R}$ is described by $(\mathcal{T} - \mathcal{R}) = d/N - (\mathcal{S} - \mathcal{P})$. Numerical simulations yield a good agreement with this prediction. As discussed later (see figure 2), they reveal that the crossover between the two regimes is remarkably sharp. The constant d which specifies the exact position of the crossover can therefore be estimated as $d \approx 5$. It follows that the regime of $T \sim N$ therefore corresponds to the square circumscribed by straight lines connecting the points $(\mathcal{T} - \mathcal{R}, \mathcal{S} - \mathcal{P}) = (5/N, 0), (0, -5/N), (-5/N, 0), (0, 5/N)$ as shown in figure 3.

A similar argument allows to determine the crossover from the other neutral regime, with $T \sim \sqrt{N}$, to the Darwinian regimes. The neutral regime emerges if the fixed point x^* is close to the boundaries, such that $w \sim |x^*|$ or $w \sim |1 - x^*|$ denotes the crossover to the Darwinian regimes. From these relations, it follows that the shapes of this second neutral regime are described by $\mathcal{T} - R \approx -(\mathcal{S} - \mathcal{P}) + (\mathcal{S} - \mathcal{P})^2 N$ and $\mathcal{S} - \mathcal{P} \approx -(\mathcal{T} - \mathcal{R}) + (\mathcal{T} - \mathcal{R})^2 N$. The proportionality constant has again been estimated from numerical simulations. From the latter, we have also found that the parabolic curves constitute a valid approximation to this second edge of neutral evolution.

3. Results

We employ the analytical expression, equations (8) and (9), for the mean extinction time, as well as computer simulations, to show how regimes of Darwinian and neutral evolution can be

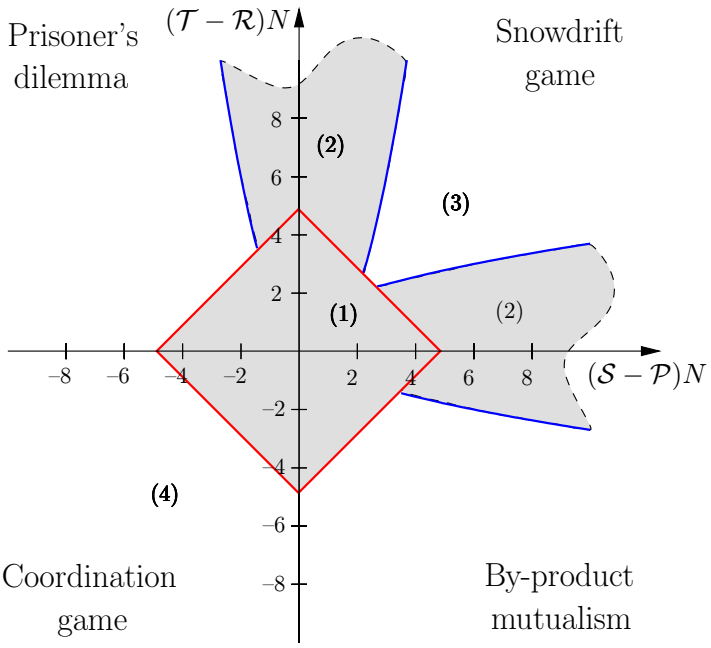

Figure 3. Social dilemmas. Depending on the sign of the payoff differences $\mathcal{T}-\mathcal{R}$ and $\mathcal{S}-\mathcal{P}$, a prisoner's dilemma, snowdrift game, by-product mutualism or coordination game arises. Two regimes of neutral evolution, (1) and (2) shown in grey, intervene two Darwinian regimes, (3) and (4), depicted in white. Coexistence of cooperators and defectors is lost after a mean time T which discriminates the distinct regimes: In (1), we encounter $T \sim N$, while $T \sim \sqrt{N}$ emerges in (2), $T \sim \exp N$ in (3), and $T \sim \ln N$ in (4). In the prisoner's dilemma and the coordination game, neutral evolution can thus maintain cooperation at a much longer time than Darwinian evolution. The edges of neutral evolution, red and blue curves, scale as $1/N$ (see text). We therefore show them depending on $(\mathcal{T}-\mathcal{R})N$ and $(\mathcal{S}-\mathcal{P})N$, where they adopt universal shapes.

distinguished. We demonstrate that neutral evolution can maintain cooperation on much longer timescales than Darwinian, even if cooperation has a fitness disadvantage.

3.1. Prisoner's dilemma

We start with the special case of the prisoner's dilemma where defectors have a frequency independent fitness advantage c compared to cooperators. The fixation probabilities, equation (5), provides first insight into the dynamics. When the population size N is large and selection by fitness differences dominates the dynamics, i.e. when $cN \gg 1$, the probability that defectors ultimately take over the whole population tends to 1. Cooperators are guaranteed to eventually die out. This is the regime of *Darwinian* evolution; the resulting outcome equals the one of rational agents. However, in the situation of small populations and small fitness difference, i.e. $cN \ll 1$, both cooperators and defectors have an equal chance of $1/2$ of fixating. In this regime, fluctuations have an important influence and dominate the evolutionary dynamics, leaving fitness advantages without effect, evolution is *neutral*.

Further quantification of the regimes of Darwinian and neutral evolution is feasible by considering the mean extinction time, given by equation (8). It is compared to stochastic simulations in figure 2(B) for different costs (fitness advantages) c. The excellent agreement confirms the validity of our analytic approach. Regarding the dependence of T on the population size N and the fitness difference c, the mean extinction time can be cast into the form,

$$T(N, c) = T_e \mathsf{G}(N/N_e), \tag{10}$$

with a scaling function G. T_e and N_e are characteristic timescales and population sizes depending only on the selection strength c. Analyzing its properties, it turns out that G increases linearly in N for small argument $N/N_e \ll 1$, such that $T \sim N$, cf figure 2(B). This is in line with our classification scheme and the expected behavior. It indicates [28, 29] that for small system sizes, $N \ll N_e$, evolution is *neutral*. Fluctuations dominate the evolutionary dynamics, while the fitness advantage of defectors does not give them an edge, cf figure 2(A). Indeed, in this regime, cooperators and defectors have an equal chance of surviving, see equation (5). The $T \sim N$ behavior shows that the extinction time considerably grows with increasing population size; a larger system size proportionally extends the time cooperators and defectors coexist. As expected, a very different behavior emerges for large system sizes, $N/N_e \gg 1$, where G increases only logarithmically in N, and therefore $T \sim \ln N$, again in correspondence with our classification scheme of the mean extinction time. The extinction time remains small even for large system sizes, and coexistence of cooperators and defectors is unstable. Indeed, in this regime, selection dominates over fluctuations in the stochastic time evolution and quickly drives the system to a state where only defectors remain, cf figure 2(A). The evolution is *Darwinian*.

As described above, the regimes of neutral and Darwinian evolution emerge for $N/N_e \ll 1$ and $N/N_e \gg 1$, respectively. The cross-over population size N_e delineates both scenarios. Further analyzing the universal scaling function G, as well as comparison with data from stochastic simulations, see figure 2(B), reveals that the transition at N_e is notably sharp. We therefore refer to it as the *edge of neutral evolution*.

The crossover time T_e and the crossover population size N_e, which define the edge of neutral evolution decrease as $1/c$ in increasing cost c. This can be understood by recalling that the cost c corresponds to the fitness advantage of defectors and can thus be viewed as the selection strength. The latter drives the Darwinian dynamics, which therefore intensifies when c grows, and the regime of neutral evolution diminishes. On the other hand, when the cost of cooperation vanishes, evolution becomes neutral also for large populations. Indeed, in this case, defectors do not have a fitness advantage compared to cooperators; both do equally well. Our approach now yields information about how large the cost may be until evolution changes from neutral to Darwinian. From numerical inspection of G, we find that neutral evolution is present for $cN < 2.5$, and Darwinian evolution takes over for $cN > 2.5$. This resembles a condition previously derived by Kimura, Ohta and others [38, 42, 43] for frequency independent fitness advantages. The edge of neutral evolution arises at $N_e = 2.5/c$ and $T_e = 2.5/c$.

As a consequence we note that, though selection pressure clearly disfavors cooperation, our results reveal that the ubiquitous presence of randomness (stochasticity) in any population dynamics opens a window of opportunity where cooperation is facilitated. In the regime of neutral evolution, for $cN < 2.5$, cooperators have a significant chance of taking over the whole population when initially present. Even if not, they remain on timescales proportional to the system size, $T \sim N$, and therefore considerably longer than in the regime of Darwinian evolution, where they become extinct after a short transient time, $T \sim \ln N$.

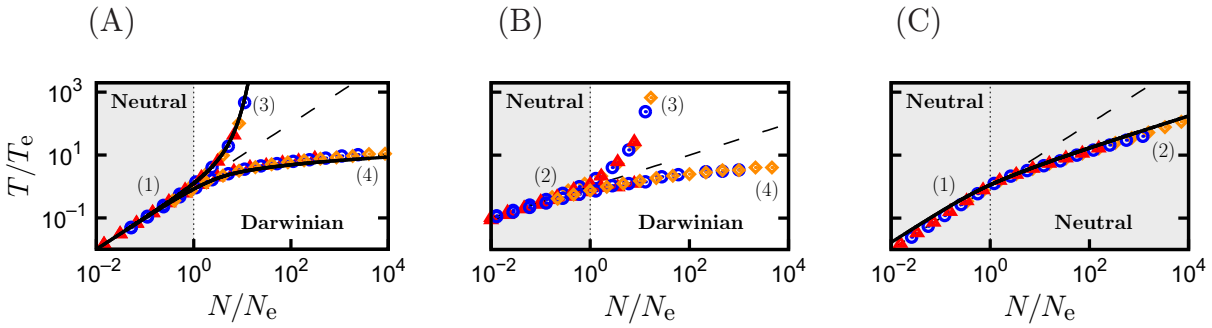

Figure 4. Transitions and universal scaling. We show the rescaled mean extinction time, T/T_e, depending on N/N_e, for different transitions emerging in social dilemmas (cf figure 3). (A) Transition from the neutral regime (1), where $T \sim N$ emerges, to the Darwinian regimes (3) ($T \sim \exp N$) as well as (4) ($T \sim \ln N$). (B) From neutral dynamics in regime (2) ($T \sim \sqrt{N}$) to the Darwinian regimes (3) ($T \sim \exp N$) and (4) ($T \sim \ln N$). (C) Transition between the two neutral regimes (1) ($T \sim N$) and (2) ($T \sim \sqrt{N}$). Analytical calculations are shown as black lines, and symbols have been obtained from stochastic simulations for large (△), medium (○), and small (◇) values of $\mathcal{S}-\mathcal{P}$ and/or $\mathcal{T}-R$. The data collapse onto universal curves revealing the accuracy of the scaling laws. In (A), we have used $\mathcal{S}-\mathcal{P}=\mathcal{T}-\mathcal{R} \in \{-0.1, -0.01, -0.001, 0.001, 0.01, 0.1\}$, while $\mathcal{S}-\mathcal{P} \in \{-0.1, -0.01, -0.001, 0.001, 0.01, 0.1\}$, $\mathcal{T}-\mathcal{R}=1$ in (B), and $\mathcal{S}-\mathcal{P}=0$, $\mathcal{T}-\mathcal{R} \in \{0.001, 0.01, 0.1\}$ in (C).

3.2. General social dilemmas

Let us now consider the influence of fluctuations within the more general form of social dilemmas, given by the parameters $\mathcal{T}, \mathcal{P}, \mathcal{R}$ and $\mathcal{S}$. We employ the analytical form of the mean extinction time, equation (9), as well as results from stochastic simulations. Examples for different paths in parameter space are shown in figure 4. Again, the approximative analytical results agree excellently with numerics.

Concerning the dependence of the mean extinction time on the population size, different behaviors emerge, reflecting the different regimes of evolutionary dynamics. Two regimes of Darwinian evolution form, depicted white in figure 3. The first one occurs within the snowdrift game, where the extinction time increases exponentially in the population size, $T \sim \exp N$, and coexistence of cooperators and defectors is stable. The second regime comprises parts of the prisoner's dilemma, the coordination game and by-product mutualism. There, either defectors or cooperators eventually survive, and the mean extinction time of the other strategy is small, and obeys a logarithmic law $T \sim \ln N$. We have encountered this regime already in the particular case of the prisoner's dilemma specified by $\mathcal{T}-R=P-S \equiv c>0$. These two Darwinian regimes are separated by two regimes of neutral evolution, shown in grey in figure 3. Firstly, for small N and small differences in the payoffs (i.e. around the point where the four types of games coincide) a $T \sim N$ behavior emerges. Secondly, at the lines where the snowdrift game turns into the prisoner's dilemma, respectively, by-product mutualism, the mean extinction time increases as a square-root in the population size, $T \sim \sqrt{N}$.

Similar to the prisoner's dilemma, we now aim at identifying the edge of neutral evolution, i.e. the crossover from the Darwinian regimes to the regimes of neutral evolution. We have calculated the boundaries of both neutral regimes, $T \sim N$ and $T \sim \sqrt{N}$ analytically, see section 2.6. They are described by straight lines for the first one and by parabola-shaped lines for the second one, see figure 3.

Both edges of neutral evolution scale proportional to the system size N. Therefore, while increasing the system size changes the payoff parameters where the crossovers appear, the shape and relations of the different regimes are not altered. Concerning the dependence of the edges of neutral evolution on the characteristic strength of selection s, meaning the average contribution of the fitness-dependent payoff to the overall fitness, different scaling laws arise. For the crossover from the neutral regime $T \sim N$ to the other regimes, T_e and N_e scale as $1/s$. In contrast, a scaling law $N_e \sim 1/s^2$ for crossovers between the neutral regime with $T \sim \sqrt{N}$ and the Darwinian regimes emerges. This different scaling behavior arises, for example, for $\mathcal{T} - \mathcal{R} = 1$ and varying $s = \mathcal{S} - \mathcal{P}$ as shown in figure 4(B).

4. Discussion

Cooperation is often threatened by exploitation and therefore, although beneficial, vulnerable to extinction. In evolutionary dynamics, this mechanism comes in through selection by individuals' fitness, the driving force of Darwinian evolution. However, evolution also possesses stochastic aspects. Employing a standard formulation of social dilemmas, we have shown that fluctuations can support cooperation in two distinct ways. Firstly, they can lead cooperators to fully take over the population. Secondly, neutral evolution considerably increases the time at which cooperators and defectors coexist, i.e. at which a certain level of cooperation is maintained. To emphasize the importance of the second point, we note that in real ecological systems the rules of the dynamics themselves change due to external [44] or internal [45] influences, setting an upper limit to the timescales at which evolution with constant payoffs, as we study here, applies. In particular, these times can be shorter than the times that would be needed for extinction of either cooperators or defectors, such that it may be less important to look at which of both would ultimately remain, but what the timescales for extinction are.

Quantitatively, we have shown the emergence of different Darwinian and neutral regimes. In the Darwinian regime of the prisoner's dilemma, cooperators are guaranteed to become extinct; the same is true for the second neutral regime, where $T \sim \sqrt{N}$. However, in the other neutral regime, with $T \sim N$, a random process determines whether cooperators or defectors prevail. Cooperators may therefore take over due to essentially neutral evolution. Moreover, even if cooperators eventually disappear, they remain for a considerably longer time in the neutral regimes than in the Darwinian regime. Indeed, in the regimes of neutral evolution, coexistence of cooperators and defectors is maintained for a mean time T obeying $T \sim N$, respectively, $T \sim \sqrt{N}$. For medium and large population sizes, this time exceeds by far the time $T \sim \ln N$ at which cooperation disappears in the Darwinian regimes of the prisoner's dilemma or of the coordination game (if defectors happen to dominate in the latter case). Neutral evolution can therefore maintain cooperation on a much longer timescale than Darwinian evolution. This effect is relevant as the neutral regimes considerably extend into the prisoner's dilemma as well as the cooperation game region. There, a form of neutrally maintained cooperation evolves.

Our results have been obtained by applying a general concept based on extinction times that allows us to classify evolutionary dynamics into regimes of Darwinian and neutral character, separated by an emerging edge of neutral evolution. Apart from the social dilemmas under consideration here, we believe that our quantitative analytical approach can be versatilely applied to disentangle the effects of selection and fluctuations in various ecological situations where different species coexist [46]–[50]. Encouraged by our findings, we expect such studies to reveal further unexpected effects of fluctuations on ecology and evolution.

Acknowledgments

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Entropy Production of Cyclic Population Dynamics

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Entropy serves as a central observable in equilibrium thermodynamics. However, many biological and ecological systems operate far from thermal equilibrium. Here we show that entropy production can characterize the behavior of such nonequilibrium systems. To this end we calculate the entropy production for a population model that displays nonequilibrium behavior resulting from cyclic competition. At a critical point the dynamics exhibits a transition from large, limit-cycle-like oscillations to small, erratic oscillations. We show that the entropy production peaks very close to the critical point and tends to zero upon deviating from it. We further provide analytical methods for computing the entropy production which agree excellently with numerical simulations.

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The study of complex systems with a large number of interacting particles requires global observables that characterize their behavior. Modern statistical mechanics has successfully identified, interpreted, and applied such observables for equilibrium systems. One of these observables is the entropy which allows for predictions of a system's behavior through the second law of thermodynamics—an isolated system's entropy cannot decrease. Identifying similar principles for nonequilibrium systems, however, proves elusive. Neither a characteristic global observable nor a universal principle has been identified in a general way. While also in nonequilibrium the entropy production has been proposed as a useful observable [1,2], and different principles governing its behavior have been suggested [3,4], problems arise from different employed definitions of entropy and approaches to nonequilibrium dynamics [2,5,6].

In this Letter we demonstrate that entropy production can successfully characterize ecological systems with cyclic competition. Ecological systems display a wide variety of nonlinear and nonequilibrium behavior. Random interactions between individuals and the finiteness of the population lead to intrinsic stochasticity. Nonequilibrium results when interactions between individuals of different species include cyclic dependencies where a species A_1 benefits from and suppresses a species A_2, while A_2 benefits from and suppresses a species A_3, and so on, with some species A_k of the resulting chain benefiting from and suppressing species A_1. Such cycles can lead to erratic or limit-cycle oscillations in the steady state of the population dynamics [7–16]. Experimental observations of cyclic dynamics and corresponding oscillations have, amongst others, been documented for mating behavior of lizards in costal California [17] and in microbial laboratory communities [18].

The dynamics of ecological systems can be conveniently described as a Markovian stochastic process through a master equation,

$$\partial_t P_i(t) = \sum_j [\omega_i^j P_j(t) - \omega_j^i P_i(t)], \tag{1}$$

in which $P_i(t)$ denotes the probability of finding the system in a certain state i at time t and ω_i^j is the transition probability from state j to state i. The associated mean entropy production $\dot{S}$ of the system follows as

$$\dot{S} = \frac{1}{2}\sum_{i,j} [\omega_i^j P_j(t) - \omega_j^i P_i(t)] \ln\left[\frac{\omega_i^j P_j(t)}{\omega_j^i P_i(t)}\right]. \tag{2}$$

Equation (2) can be obtained through considering the difference between forward and backward entropy per unit time of the stochastic process, Eq. (1) [19]. Equation (2) follows also as the temporal derivative of the system's Gibbs entropy together with a term describing the total increase of thermodynamic entropy in the reservoirs to which the system is coupled [20]. For steady states defined by $\partial_t P_i(t) = 0$, as we consider in this Letter, the entropy production simplifies to

$$\dot{S} = \frac{1}{2}\sum_{i,j} [\omega_i^j P_j - \omega_j^i P_i] \ln\left[\frac{\omega_i^j}{\omega_j^i}\right]. \tag{3}$$

It follows from Eq. (2) that the entropy production vanishes if and only if the system obeys detailed balance, $\omega_i^j P_j = \omega_j^i P_i$. Indeed, detailed balance represents the notion of thermodynamic equilibrium in the framework of the master equation. Cyclic population dynamics violates detailed balance; the computation and discussion of the associated entropy production is the scope of this Letter.

Consider a simple model for cyclic population dynamics of three species A, B, and C. Interactions are formulated as chemical reactions:

$$\begin{aligned} AB &\xrightarrow{k} AA, & A &\xleftrightarrow{m} B, \\ BC &\xrightarrow{k} BB, & B &\xleftrightarrow{m} C, \\ CA &\xrightarrow{k} CC, & C &\xleftrightarrow{m} A. \end{aligned} \tag{4}$$

The reactions on the left describe cyclic competition: A outperforms B but is beaten by C, and C is taken over by B in turn. The reactions on the right correspond to spontaneous mutations between the three species.

The population model defined by the reactions (4) exhibits a critical mutation rate that, in the resulting nonequilibrium steady state, delineates large oscillations in the species densities from only small ones. Let us introduce this critical mutation rate first. The reactions (4) conserve the total number N of interacting individuals. The densities a, b, and c of species A, B, C therefore sum up to one, $a + b + c = 1$, and the population's state space is the simplex S_3 (see Fig. 1). Numerical simulations indicate that small values of the mutation rate m lead to large oscillations between the densities of the three species; the probability distribution is highest close to the corners of the simplex [Fig. 1(a)]. Large values of m, on the contrary, lead to an approximately Gaussian probability distribution around the simplex center [Fig. 1(b)]. Erratic oscillations occur at small amplitudes [9].

The system's behavior can be analytically described by an approximate Fokker-Planck equation. A systematic expansion in the system size N yields an equation for the temporal evolution of the probability distribution $P(\boldsymbol{s}, t)$ of the densities $\boldsymbol{s} = (a, b)$ at time t:

$$\partial_t P(\boldsymbol{s}, t) = -\partial_i[\alpha_i(\boldsymbol{s})P(\boldsymbol{s}, t)] + \tfrac{1}{2}\partial_i\partial_j[\beta_{ij}(\boldsymbol{s})P(\boldsymbol{s}, t)], \tag{5}$$

in which the indices i, j run from 1 to 2; the summation convention implies summation over them. The density c follows as $c = 1 - a - b$. The coefficients read

$$\begin{aligned} \alpha_i(\boldsymbol{s}) &= [m(1 - 3s_i) + ks_i(s_{i+1} - s_{i+2})], \\ \beta_{ii}(\boldsymbol{s}) &= N^{-1}[m(1 + s_i) + ks_i(s_{i+1} + s_{i+2})], \\ \beta_{ij}(\boldsymbol{s}) &= -N^{-1}[m(s_i + s_j) + ks_i s_j] \quad \text{for } i \neq j, \end{aligned} \tag{6}$$

where the indices are understood as modulus 3 and $s_3 = c$. The terms containing α describe the deterministic part of the temporal evolution. In the absence of fluctuations, the reactions for cyclic dominance lead to neutrally stable oscillations around the internal fixed point $\boldsymbol{s}_* = (1/3, 1/3, 1/3)$, while the spontaneous mutations render the internal fixed point stable. Demographic fluctuations are, for large system sizes N, inversely proportional to $\sqrt{N}$ and enter the Fokker-Planck equation (5) through the terms containing β. They induce a stochastic drift away from the internal fixed point towards the boundaries of the phase space. The Fokker-Planck equation (5) shows that the competition between the deterministic and the stochastic effects leads, at a critical mutation rate $m_c = k/(2N)$, to a uniform probability distribution. Certain deviations from the uniform distribution occur near the phase space boundaries where the discreteness of the phase space becomes relevant and the continuous formulation through the Fokker-Planck equation does not hold. For a small mutation rate, $m < m_c$, fluctuations dominate and drive the system towards the boundary. In the absence of mutations the corner states are absorbing and the system goes extinct [21]. An arbitrary small mutation rate, however, leads to sustained species coexistence and oscillations. In the opposite case, when $m > m_c$, the deterministic dynamics centers the probability distribution around the internal fixed point.

The cyclic population dynamics yields a nonequilibrium steady state that is characterized by oscillations, large or small, around the internal fixed point. What is the resulting entropy production and how does it relate to the regimes of small, critical, and large mutation rates outlined above?

To tackle this question we have carried out extensive numerical simulations of the stochastic system employing the Gillespie algorithm [22]. Throughout our simulations we have considered $k = 1$ which defines the time scale. Numerical results from computer simulations of the stochastic system show that the entropy production peaks at a certain value $m_{\max}$ of the mutation rate (Fig. 2). The value $m_{\max}$ approximately equals the critical mutation rate, $m_{\max} \approx m_c$ (Fig. 2 inset). Small deviations from this behavior arise because the probability distribution at the critical mutation rate is not uniform near the boundaries as mentioned above.

Analytical understanding of the entropy production in the regimes of small, critical, and large mutation rates is feasible through the Fokker-Planck equation (5). To this end we employ a continuous version of the entropy pro-

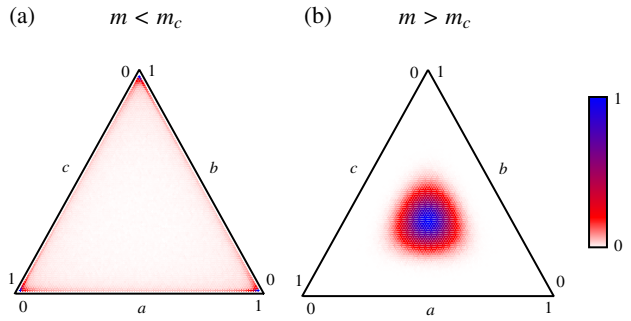

FIG. 1 (color online). Probability distributions ($k = 1$, $N = 100$). (a) For a mutation rate $m = 0.003$ smaller than $m_c = k/(2N)$ the probability distribution is concentrated near the edges and particularly near the corners of the phase space. (b) A mutation rate $m = 0.1$ larger than m_c leads to a Gaussian distribution around the center.

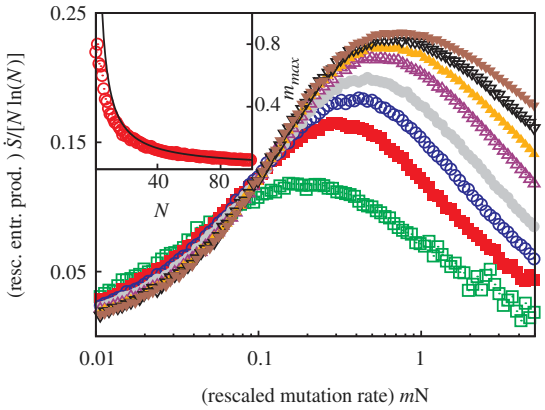

FIG. 2 (color online). Entropy production in the steady state for different system sizes (□, $N = 2$; ■, $N = 5$; ○, $N = 10$; ●, $N = 20$; △, $N = 50$; ▲, $N = 100$; ▽, $N = 200$; ▼, $N = 400$). The entropy production vanishes for very high and very low mutation rates and exhibits a maximum at an intermediate value $m_{\max}$. The value $m_{\max}$ is near the critical mutation rate as shown in the inset where the black line indicates $m_c + 0.001$, and red circles represent data obtained from simulations.

duction (3),

$$\dot{S} = \frac{1}{2}\int d\boldsymbol{r}\int ds[\omega_s^r P(\boldsymbol{r}) - \omega_r^s P(s)]\ln\left(\frac{\omega_s^r}{\omega_r^s}\right), \quad (7)$$

where integration is over all states $\boldsymbol{r}$, $\boldsymbol{s}$ of the phase space.

The entropy production in the form of Eq. (7) can readily be evaluated at the critical mutation rate m_c. The probability distribution is uniform according to the Fokker-Planck equation (5); we obtain

$$\dot{S}_{m=m_c} = \frac{3}{144}kN[12\ln(N) - 13 + 6\ln(4)]. \quad (8)$$

For moderate and large N the term $N\ln(N)$ on the right-hand side dominates the entropy production. Stochastic simulations confirm this behavior (Fig. 2).

In the regime of large mutation rates, $m > m_c$, we need to calculate the probability density in the steady state to compute the entropy production. We obtain the probability density by using polar coordinates (r, ϕ) centered at the internal fixed point. We then simplify the Fokker-Planck equation (5) through a van Kampen approximation for the coefficients (6) in which the coefficients are approximated by their value at the internal fixed point. The resulting Fokker-Planck equation is then solved by the Gaussian distribution

$$P(r,\varphi) = \frac{1}{2\pi\sigma^2}\exp\left(\frac{-r^2}{2\sigma^2}\right), \quad (9)$$

where $\sigma = \sqrt{(k + 6m)/36mN}$. The entropy production follows from Eq. (7) where the integral is evaluated by setting the upper boundary of the integral to ∞ and an average over the angular dependence is taken:

$$\dot{S}_{m\gg m_c} = \frac{kN}{3}\ln\left(\frac{k}{3m} + 1\right). \quad (10)$$

This result agrees excellently with numerical simulations [Fig. 3(b)]. The entropy production (10) depends linearly on the system size N. This behavior arises because the typical area in phase space explored by the dynamics is proportional to $\sigma^2 \sim 1/N$ and thus contains $N^2\sigma^2 \sim N$ states. The continuity approximation employed in the Fokker-Planck equation (5) holds for arbitrary large m, since the width σ of the probability distribution (9) remains finite as $m \to \infty$.

Expanding (10) for large values of m results in $\dot{S}_{m\gg m_c} = k^2N/(9m)$. The entropy production vanishes as m/k increases. Indeed, only the cyclic dynamics at rate k underlies the nonequilibrium behavior and therefore entropy production, while the mutations at rate m obey detailed balance.

When the mutation rate is small, $m \ll m_c$, the probability distribution is concentrated near the boundaries of the phase space [Fig. 1(a)]. The dynamics occurs predominantly along the boundary and can therefore be approximately described by considering only the boundary states. Because of the threefold symmetry it suffices to regard only one edge of the simplex with periodic boundary conditions. The concentration x of one of the three species increases along this edge from 0 to 1 such that the cyclic dynamics drives the system to $x = 1$. The deterministic part of the dynamics is given by

$$\partial_t x = m(1 - 2x) - k(x - x^2) \quad (11)$$

and features a fixed point at $x_* = [(2m + k) - \sqrt{4m^2 + k^2}]/(2k)$. In the range of $m \ll m_c$, this fixed point

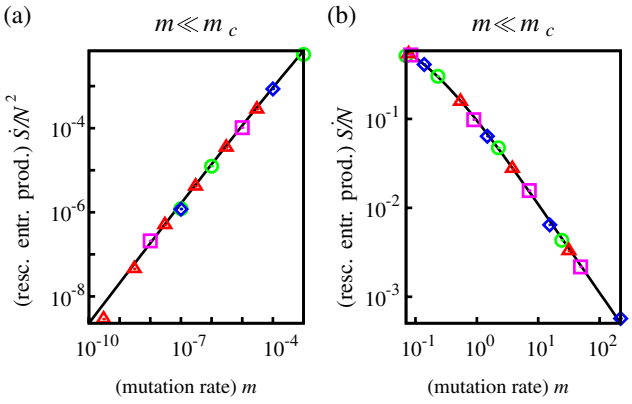

FIG. 3 (color online). Entropy production in the limiting cases $m \ll m_c$ (a) and $m \gg m_c$ (b). Analytical results (black lines) agree excellently with simulations (○, $N = 30$; △, $N = 100$; □, $N = 200$; ◇, $N = 400$). The data confirm that the entropy production is proportional to the squared system size N^2 for small mutation rates and proportional to N for large mutation rates. The simulation results further confirm that the entropy production decays as m for $m \to 0$ and as $1/m$ for $m \to \infty$.

is closer to 1 than the distance $1/N$ between two discrete states. We conclude that fluctuations will cause the system to exhibit a constant circular current in the steady state. The probability distribution $P(x)$ for $x \in [\frac{1}{N}, 1-\frac{1}{N}]$ can therefore be obtained as a solution to the Fokker-Planck equation $0 = -\partial_x\{[m(1-2x) - k(x-x^2)]P(x)\}$ where fluctuations have been ignored:

$$P(x) = \mathcal{N}\frac{1}{m - 2mx - kx + kx^2}, \tag{12}$$

with a normalization coefficient $\mathcal{N}$. To determine the probability P_0 of a corner state, which turns out to be finite, fluctuations have to be included. P_0 can be obtained using the master equation and the values of $P(x = 1/N)$ and $P(x = 1 - 1/N)$. The normalization $\mathcal{N}$ follows from

$$3\left[\int_{1/N}^{1-(1/N)} P(x)dx + \frac{2}{N}P_0\right] = 1. \tag{13}$$

The factor 3 arises because the phase space simplex possesses three edges. For moderate and large system sizes N we obtain $P_0 = \mathcal{N}/(2m)$ which dominates the left-hand side of Eq. (13), such that $\mathcal{N} = Nm/3$. The resulting probability density can again be inserted into (7) to provide an analytical result for the entropy production in the regime $m \ll \frac{k}{2N} \ll 1$:

$$\dot{S}_{m \ll m_c} = mN^2 \ln(m/k), \tag{14}$$

in perfect agreement with simulations [Fig. 3(a)]. The entropy production for small mutation rates is proportional to the squared system size. Decreasing m lowers the entropy production in proportion because mutations are the process that restarts the cyclic dynamics once a corner state has been reached. Mutations therefore limit the dynamics to a time scale proportional to m.

In conclusion, we have examined the global entropy production in the steady state of a cyclic population model. At a critical mutation rate the system undergoes a transition from large oscillations along the phase space's boundary to small erratic oscillations around an internal fixed point. The entropy production peaks very near the critical mutation rate and decreases to zero away from it. We believe that, in a similar manner, the entropy production can yield valuable information about the nonequilibrium steady state of other stochastic systems. Indeed, in a recently studied model, because of a nonfixed system size and the extensivity of the entropy production, the *slope* of the entropy production peaks near a critical point [23]. Within our approach of a fixed system size we have investigated a stochastic system that displays a supercritical Hopf bifurcation. We found that the entropy production predicts the scale of the critical mutation rate: it peaks near the Hopf bifurcation, at a mutation rate of about $1/4$ of the critical one [24]. Understanding the certain discrepancy between the maximum and the critical value may open a route to a more general understanding of the role of entropy production. Because of the universality of the Hopf bifurcation we conclude that our approach is valid for a wide class of nonequilibrium systems, namely, those that exhibit a transition from small, erratic oscillations to limit-cycle-like ones, including systems with spatial degrees of freedom [25].

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Entropy production of cyclic population dynamics

Benjamin Andrae, Jonas Cremer, Tobias Reichenbach, and Erwin Frey

Supplementary EPAPS Document: Entropy production and Hopf bifurcation

Entropy production can characterize the behavior of a broad class of nonequilibrium systems. In this Supplementary Material we underpin this point through consideration of a nonequilibrium stochastic system that exhibitis a Hopf bifurcation. We show that the entropy production peaks in the vicinity of the bifurcation, where the behavior changes from noisy, erratic oscillations to larger limit-cycle oscillations. We conclude that the entropy production generally characterizes the behavior of systems with limit cycles that fall into the universality class of the Hopf bifurcation.

Consider a stochastic system with species A, B, C and empty sites $\oslash$ that obey the following reactions:

$$\begin{aligned} AB &\xrightarrow{k} A\oslash\,, & A\oslash &\xrightarrow{l} AA\,, & A &\xleftrightarrow{m} B\,,\\ BC &\xrightarrow{k} B\oslash\,, & B\oslash &\xrightarrow{l} BB\,, & B &\xleftrightarrow{m} C\,,\\ CA &\xrightarrow{k} C\oslash\,, & C\oslash &\xrightarrow{l} CC\,, & C &\xleftrightarrow{m} A\,. \end{aligned} \tag{15}$$

The reactions with rates k and l can represent cyclic dominance of three species [11]. The corresponding deterministic rate equations have first been proposed and analyzed by R. M. May and W. J. Leonard [16]. The reactions with rate m describe spontaneous mutations between the three species.

The deterministic equations for the temporal evolution of the concentrations a, b, c of species A, B, C follow from the reactions (15) as

$$\begin{aligned} \partial_t a &= a[l(1-\rho) - kc] + m(b + c - 2a)\,,\\ \partial_t b &= b[l(1-\rho) - ka] + m(a + c - 2b)\,,\\ \partial_t c &= c[l(1-\rho) - kb] + m(a + b - 2c)\,. \end{aligned} \tag{16}$$

Linear stability analysis reveals the existence of a reactive fixed point at $(a_*, b_*, c_*) = l/(3l + k) \cdot (1, 1, 1)$. This fixed point changes its stability at a critical mutation rate $m_c = kl/6/(3l + k)$ from a stable spiral point (above m_c) to an unstable spiral point (below m_c). Further analysis that takes the leading nonlinearities into account reveals that a supercritical Hopf bifurcation arises at m_c. Above the critical mutation rate, for $m > m_c$, the stochastic system performs noisy erratic oscillations around the reactive fixed point. The steady-state probability distribution is

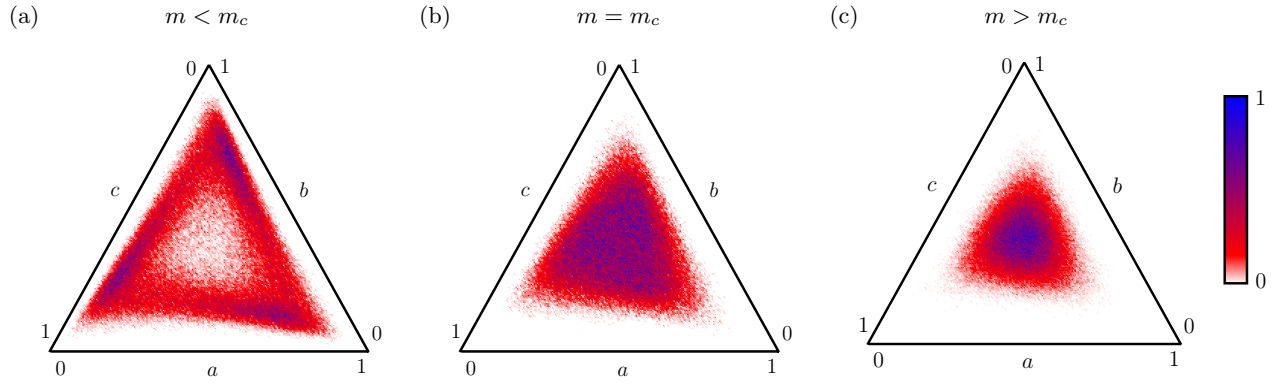

FIG. 1: (color online) Steady-state probability distributions for $k = l = 1$, $N = 100$, projected on the plane spanned by $(a, b, c) = (1, 0, 0), (0, 1, 0), (0, 0, 1)$. (a) For a mutation rate $m = 0.022$ smaller than $m_c \approx 0.042$ the probability distribution is concentrated along the limit cycle. (b) At the critical mutation rate m_c a broad probability distribution centered around the reactive fixed point arises. (c) A mutation rate $m = 0.062$ larger than m_c leads to a narrow, gaussian distribution around the reactive fixed point.

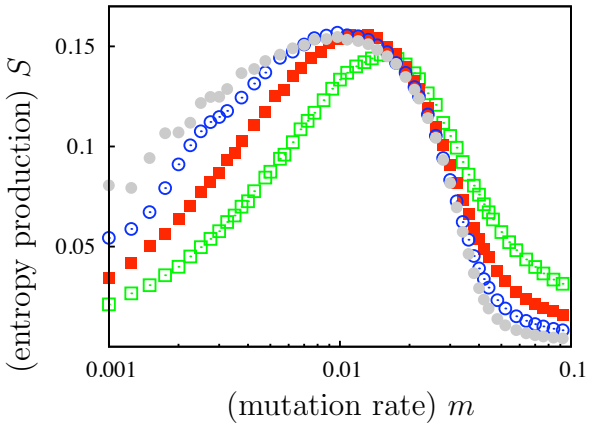

FIG. 2: (color online) Entropy production in the steady state. Results for different system sizes (□, $N = 100$; ■, $N = 200$; ○, $N = 400$; ●, $N = 800$) show that the entropy production peaks at a mutation rate $m_{\max} \approx 0.01$ near the critical mutation rate $m_c \approx 0.042$. The entropy production vanishes both for smaller and higher mutation rates.

approximately gaussian around the reactive fixed point, see Fig. 1 (c) for a projection of the system's steady state onto the simplex spanned by the densities a, b, c. Below the critical mutation rate, for $m < m_c$, a stable limit cycle forms. The stochastic dynamics leads to noisy trajectories along the limit cycle, see Fig. 1 (a). At the critical mutation rate, as the linear terms in the deterministic equations vanish, a relatively broad, non-gaussian probability distribution centered at the reactive fixed point arises [Fig. 1 (b)]. This behavior is similar to the one recently reported in Ref. [13] where higher order nonlinearities render a spiral point stable while the linear terms vanish.

We have performed extensive stochastic simulations of the stochastic system defined by the reactions (15). In these simulations we have left the rates k, l constant at $k = l = 1$, defining the time-scale, and systematically varied the mutation rate m as well as the system size N. In principle, a divergence in the entropy production can arise when the system reaches the boundary of the phase space. However, because the probability of these boundary states is exponentially suppressed, this effect can be ignored.

For all considered system sizes the resulting entropy production exhibits a maximum near the critical mutation rate m_c, see Fig. 2. For system sizes above about $N = 200$ the maximum of the entropy production arises at a value $m_{\max} \approx 0.01$, about 1/4 of the value of the critical mutation rate $m_c \approx 0.042$. For mutation rates much smaller and much larger than $m_{\max}$ the entropy production tends to zero. The system's behavior therefore resembles the one reported in the main part of this Letter, underpinning the general usefulness of entropy production in characterizing nonequilibrium steady states. Understanding the certain discrepancy of $m_{\max}$ and m_c will yield further insight into the relation between entropy production and critical nonequilibrium behavior.

5 Evolution and population dynamics

The standard approaches to describe evolution assume the population size to be constant. For example, for the Moran Process, which was introduced in Section 4.2, only replacing events are considered such that the death of an individual is directly coupled to the birth of another one. In general however, the population size is not fixed but can vary tremendously. Here, we consider the role of population dynamics for the outcome of evolution. First, the most important growth scenarios are reviewed. We go on to discuss the coupling between population dynamics and evolution, and introduce a stochastic approach to study this coupling. We end this chapter with a short discussion of our work.

5.1 Growth and population dynamics

5.1.1 The growth laws by Malthus and Verhulst

Although familiar, let us recall basic growth laws. If each individual of a population reproduces with a constant *per-capita* growth rate r, then the total number of individuals, N, increases exponentially. With the dawn of differential calculus the exponential growth law was first formulated by Malthus in the now most common, time-continuous notation [121]:

$$\frac{dN}{dt} = rN. \tag{5.1}$$

Regarding the world population of humans, the growth rate within the last thousand years has even been super-exponential with $r = r(t)$ increasing over time. With this equation in mind, Malthus conclusively stated the *dilemma of growing populations* in a prosaic way: populations increase geometrically in size while food supply increases arithmetically. Thus growth must be limited by a *carrying capacity* K, which is the maximum population size the environment can sustain. Verhulst was the first describing this in mathematical terms, by the logistic equation [122],

$$\frac{dN}{dt} = r(1 - N/K)N, \tag{5.2}$$

see also Fig. 5.1(a).

Historically, Malthus' work was crucial for both, Darwin and Wallace to think in terms of limited resources and to come up with the idea of natural selection [4].

5.1.2 General population dynamics

In general, population size is determined by the impact of a highly dynamical and diverse environment which itself is coupled to the temporal development of the population. In population biology, evolution within the population is often neglected and the population size is modeled by equations of the form,

$$\frac{dN}{dt} = \mathcal{F}(N;t). \tag{5.3}$$

Here, $\mathcal{F}$ can explicitly depend on time. A lot of different specific situations have been studied, see [123, 124, 125] for many examples. Famous scenarios are predator-prey situations, first studied by Lotka and Volterra [126, 127]. In this case, the population size of, for example, prey depends on the temporal dynamics of predators and the growth and decline of the predator population occurs with a certain phase-delay compared to growth and decline of the prey population, see also Fig.5.1(b). Studied examples include fish populations or lynxes chasing snow rabbits [128].

In these scenarios, the population dynamics of one species is coupled to the dynamics of other species and hence there is frequency dependence on the species level[1]. In contrast to that, the internal evolutionary change within a species and frequency-dependence within the population is typically not considered. This simplification is assumed to work since evolutionary change is expected to occur on much longer time-scales than ecological change. As discussed in Section 5.2 however, this does not have to be true.

5.1.3 Growth dynamics of microbes

The ecological and evolutionary dynamics of microbial organisms will be introduced in Section 6.2 in detail. Here, we already introduce the growth scenarios of such microbial populations. For typical situations[2], the growth dynamics of microbes within an initially nutrient-rich environment resembles, at least roughly and for not too long time scales, the logistic dynamics and may be described by Eq. (5.2) as proposed by Verhulst. More generally, growth dynamics is separated into four different growth-phases [129], cf. Fig. 5.1(c).

First, there is the *lag phase*. When placing microbes in a new environment they typically need some time to adjust to the environment and to start their growth. The second phase is the *exponential phase*[3], where growth is following Eq. (5.1). This phase prevails until a lack of nutrients occurs or when worsening environmental conditions start to harm the bacteria. Growth then slows down until saturation is reached, as *stationary phase*. The exact behavior of microbes can be quite diverse and may depend on a lot of details. For example, cells may be able switch into a *dormant* state by stopping metabolic activity. Or growth might continue and outbalance the death of cells [130, 131]. In the long run, if no nutrients are

[1] The analogy with frequency dependent evolution described by a payoff matrix, as introduced in Section 4.3, can be stressed that far that generalized Lotka Volterra equations resemble replicator dynamics [46].

[2] This especially includes bacteria and standard setups in the laboratory, for example the usage of a chemostat.

[3] In microbiology it is common to call this phase also the 'log-phase'; when plotting on a semi-logarithmic scale, the growth curve is a straight line.

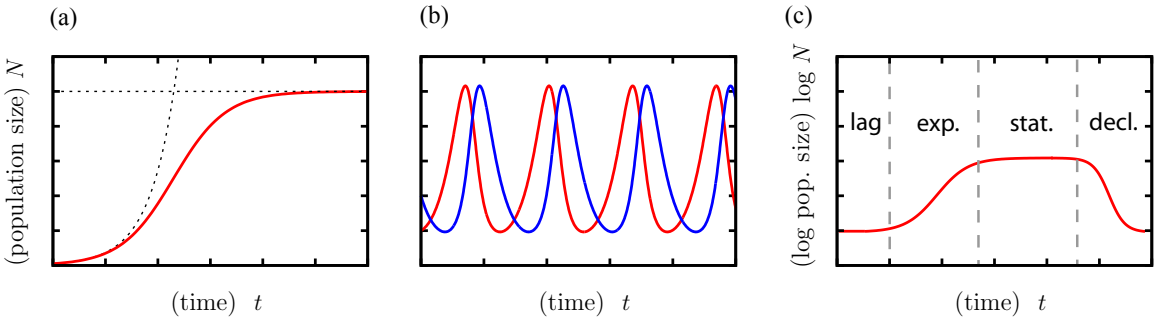

Figure 5.1: Different types of population dynamics. (a) The growth laws; Logistic growth (red line) compared to exponential growth and a constant population size (grey lines). (b) A predator-prey scenario with oscillating prey (red line) and predator populations (blue line). (c) Typical growth phases of bacteria. Roughly, there are four different phases.

resupplied, cells cannot maintain their vital functions and die; the *decline phase* is reached. In the second paper at the end of this chapter we have studied and compared different kinds of growth-dynamics.

5.2 The coupling of evolution and population dynamics

Evolution and population dynamics are based on per capita birth and death events. Hence, grounded on the same biological process, one should not expect a separated approach to work in general. Population dynamics can depend on the internal evolution and hence be much more complex than Eq. (5.3). Similar, the evolutionary dynamics can be strikingly different compared to the standard replicator approach, (2.5), when N changes rapidly.

The reason why a separated approach is working in many cases is a sharp separation of time scales. On the one hand, evolutionary change is often much slower than ecological change such that the change within the population does not have to be considered for short time scales and population dynamics. On the other hand, when considering evolution in a population with a vastly changing population size then one might approximate the population size N by an average or effective population size N_E.

However, both assumptions may fail dramatically. For example, the intricacies of evolution and population dynamics have been shown for rotifers and algae standing in a predator prey interaction [132, 133]. Here, the evolutionary change within the algae population has been shown to affect the oscillations between the number of rotifers as predators and algae as prey. Resistant algae mutants have a fitness advantage if predators are highly abundant while non-resistant strains prevail if predators are rare. Growth dynamics and evolutionary change occur on the same timescale and hence are coupled.

Another case of coupling is given if demographic fluctuations are large and growth dynamics is fast. In the two manuscripts attached at the end of this chapter, we show this aspect to be important for the evolution of cooperation in microbial, rapidly growing populations.

To describe the coupling between population dynamics and evolution and to correctly include demographic fluctuations, we have introduced an alternative stochastic description as outlined

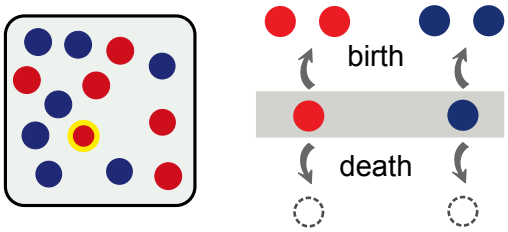

Figure 5.2: A general stochastic update process for a population of individuals belonging to two types, A and B. In contrast to the Moran process, cf. Fig. 4.1, the population size is not fixed and individuals are subject to separated birth and death events. The dynamics is described by per-capita birth and death rates.

in the manuscripts at the end of this chapter. In this description, birth and death events are not strictly coupled as in the Moran process introduced in Section 4.2, but are considered separately. Thereby, N is not fixed a priori but may change with time. Individuals belonging to type S reproduce by per-capita birth and death rates,

$$G_S = g(\mathbf{x}, N) f_S(\mathbf{x}), \text{ and } \quad D_S = d(\mathbf{x}, N) w_S(\mathbf{x}), \tag{5.4}$$

see also Fig. 5.2. While the *birth-fitness* f_S gives the fitness of type S during growth-phases, the *weakness* w_S gives the viability of type S during phases of population decline. The effective fitness ϕ follows by the interplay of evolutionary and population dynamics. The model and its full stochastic dynamics are introduced and discussed in the manuscripts at the end of this chapter.

5.3 Papers and manuscripts

5.3.1 Evolutionary game theory in growing populations

In the paper 'Evolutionary game theory in growing populations', *Phys. Rev. Lett.* **105**, 178101 (2010) by Anna Melbinger, Jonas Cremer, and Erwin Frey we introduce the mentioned stochastic model. As an example, we study the dilemma of cooperation in growing populations following a Verhulst dynamics. Populations start out with a small size N_0 and a certain fraction of cooperators, x_0. Due to cooperation, the global growth rate of the population, $g = 1 + px$, which we denote as global fitness, depends on the fraction of cooperators x; the parameter p here scales the impact of cooperation on population growth. In contrast, because of the selection advantage s of free-riders, the fraction of cooperators is expected to decline in populations. We consider an ensemble of populations and study the impact of fluctuations. We show that the global fraction of cooperators mat increase, since fluctuations at the beginning favor cooperation. Initial fluctuations are amplified by growth. The global level of cooperation, considering all populations, can then increase due to the growth advantage of more cooperative populations. Taken together, fluctuations are *amplified asymmetrically* and can help to overcome the direct selection advantage of free-riders.

The condition for cooperation to increase, at least transiently ,is derived analytically and is given by,

$$sN_0 < \frac{p}{1+px_0}. \tag{5.5}$$

To correctly consider the temporal change of the population size N in analytical calculations we performe a system size expansion as introduced by Van Kampen [134].

5.3.2 Evolutionary and population dynamics: a coupled approach

In the manuscript 'Evolutionary dynamics and population size: a coupled approach' by Jonas Cremer, Anna Melbinger, and Erwin Frey, we have extended the stochastic model introduced before to more general cases. We discuss the role of frequency-dependent birth-fitness and weakness terms affecting the birth and death rates, respectively. Furthermore, we treat the stochastic model introduced before in detail and discuss the mapping to standard models of evolutionary dynamics, which have been introduced in Sec. 4.2. In addition we study the evolution of cooperation in growing populations in more detail. We fully consider the role of the parameters p, x_0 and N_0 and also study global fitness functions which do not depend linearly on the fraction of cooperators, x. The asymmetric amplification mechanism provoking cooperation turns out to be robust and the condition for an initial increase can be stated more generally as,

$$sN_0 < \frac{g'(x)|_{x_0}}{g(x_0)}, \tag{5.6}$$

with $g'(x)$ being the slope of $g(x)$. We consider different growth scenarios and also cases where individuals can swap to a *dormant* state, maintaining only the vital metabolic functions and therefore provoking birth and death-rates to be almost zero for very long times.

5.4 Discussion and outlook

In evolutionary theory, the population size is often assumed to be constant at an effective population size N_E. However, the interplay between population dynamics and evolution can be an important issue and the notion of an effective population size, often used without care or even as a fitting parameter, can fail. This is especially the case when population dynamics is strong and when fitness-terms are frequency-dependent. We have considered one example, where the growth-rate of populations is frequency dependent and where fluctuations have strong effects on the evolutionary dynamics and standard evolutionary approaches fail. Besides the scenarios considered in this thesis, there exist many other situations where we expect the interplay of population and evolutionary dynamics in combination with demographic fluctuations to strongly affect the evolutionary outcome.

One example is the interplay between frequency-independent birth fitness, f, and weakness terms, w, with the first affecting the birth rate of individuals, and the second affecting the death rates. In growth and shrinkage phases of the population, individuals are selected

according to one or the other term respectively: in growth phases individuals with higher birth-fitness have a selection advantage, while in shrinkage phases, individuals with a lower weakness have a selection advantage. It would be interesting to study the effective fitness ϕ of individuals which follows by some convolution between the fitness terms with the population dynamics. As a starting point of this topic, simple fitness and weakness scenarios have been considered where the effective fitness difference $\Delta\phi$ between two types changes sign during logistic growth [135].

For more complex forms of population dynamics, like oscillatory population sizes provoked for example by a predator-prey scenario, studying the impact of frequency-dependent fitness and growth terms is another interesting issue. It includes predator-prey scenarios where prey species can evolve and increase their ability to persist against predators. Further, as for the approaches with constant population size, the role of population structure and the impact of inevitably small numbers, would be interesting to be studied in such a context. One example, the assortment of a population into locally well mixed groups is considered in the next Chapter 6. In a broader context, the role of time-dependent fitness and weakness terms, and finally the evolution of aging [136, 137] is of interest to be studied with such stochastic approaches.

Evolutionary Game Theory in Growing Populations

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Existing theoretical models of evolution focus on the relative fitness advantages of different mutants in a population while the dynamic behavior of the population size is mostly left unconsidered. We present here a generic stochastic model which combines the growth dynamics of the population and its internal evolution. Our model thereby accounts for the fact that both evolutionary and growth dynamics are based on individual reproduction events and hence are highly coupled and stochastic in nature. We exemplify our approach by studying the dilemma of cooperation in growing populations and show that genuinely stochastic events can ease the dilemma by leading to a transient but robust increase in cooperation.

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Commonly, Darwinian evolution in terms of reproduction, selection, and variation is described in frameworks of population genetics and evolutionary game theory [1–3]. These approaches model the internal evolutionary dynamics of a species' different strategies (or traits) in a relative perspective. Namely, they compare fitness terms and focus on the relative advantage and abundance of different traits. In such a setup, the time evolution of the relative abundance x of a certain strategy is frequently described by a replicator equation,

$$\partial_t x = (f - \langle f \rangle)x. \tag{1}$$

A trait's relative abundance will increase if its fitness f exceeds the average fitness $\langle f \rangle$ in the population.

While in these evolutionary approaches the dynamics of the population size N is mostly left unconsidered or assumed to be fixed [3], in population ecology the dynamical behavior of a species' population size is studied. Models of population dynamics [4,5] usually describe the time development of the total number of individuals N by equations of the form

$$\partial_t N = \mathcal{F}(N, t). \tag{2}$$

$\mathcal{F}(N, t)$ is in general a nonlinear function which includes the influence of the environment on the population, such as the impact of restricted resources or the presence of other species. By explicitly depending on time, a changing environment such as, for example, the seasonal variation of resources can be taken into account.

The internal evolution of different traits and the dynamics of a species' population size are, however, not independent [6]. Actually, species typically coevolve with other species in a changing environment, and a separate description of both evolutionary and population dynamics is in general not appropriate. Not only population dynamics affects the internal evolution (as considered, for example, by models of density-dependent selection [7]), but also vice versa. Illustrative examples of the coupling are biofilms which permanently grow and shrink. In these microbial structures diverse strains live, interact, and outcompete each other while simultaneously affecting the population size [8]. So far, specific examples of this coupling have been considered by deterministic approaches only, e.g., [9,10]. However, classical and recent work have emphasized the importance of fluctuations for internal evolution which are only accounted for by stochastic, individual-based models, e.g., [11–14].

In this Letter, we introduce a class of stochastic models which consider the interplay between population growth and its internal dynamics. Both processes are based on reproduction events. A proper combined description should therefore be solely based on isolated birth and death events. Such an approach also offers a more biological interpretation of evolutionary dynamics than common formulations like the Fisher-Wright or Moran process [1,3,12,15]. That is to say, fitter individuals prevail due to higher birth rates and not by winning a tooth-and-claw struggle where the birth of one individual directly results in the death of another one. The advantage of our formulation is illustrated by the dilemma of cooperation where a transient increase in cooperation can be found [which does not exist in standard approaches, Eq. (1)].

In the following, we consider two different traits, A and B, in a well-mixed population; however, generalizing the model to more traits is straightforward. The state of the population is then described by the total number of individuals $N = N_A + N_B$ and the fraction of one trait within the population $x = N_A/N$. The stochastic evolutionary dynamics is fully specified by stochastic birth and death events with rates

$$\Gamma_{\varnothing \to S} = G_S(x, N)N_S, \qquad \Gamma_{S \to \varnothing} = D_S(x, N)N_S, \tag{3}$$

where $G_S(x, N)$ and $D_S(x, N)$ are per capita reproduction and death rates for an individual of type $S \in \{A, B\}$, respectively. We consider these rates to be separable into

a global and relative part, meaning a trait-independent and trait-dependent part:

$$G_S = g(x, N) f_S(x), \qquad D_S = d(x, N) w_S(x). \tag{4}$$

The global population fitness $g(x, N)$ and the global population weakness $d(x, N)$ affect the population dynamics of all traits in the same manner. For example, they account for constraints imposed by limited resources or how one strategy impacts the whole population. In contrast, the relative fitness $f_S(x)$ and the relative weakness $w_S(x)$ characterize the relative advantage of one strategy compared to the other. They are different for each trait and depend, in a first approach, only on the relative abundance x [16]. The relative fitness terms $f_S(x)$ affect the corresponding birth rates, and the relative weakness functions $w_S(x)$ describe the chances for survival of distinct traits.

While in evolutionary game theory only the relative fitness is considered [2], and common models of population dynamics take only the global functions into account, we consider here both global and relative fitness and show how their interplay determines the evolutionary outcome of a system. In the following, we set $w_A(x) = w_B(x) = 1$ in order to compare our unifying approach with standard formulations [2]. Though the full stochastic dynamics are given by a master equation, it is instructive to disregard fluctuations for now and examine the corresponding set of deterministic rate equations:

$$\partial_t x = g(x, N)(f_A(x) - \langle f \rangle)x, \tag{5a}$$

$$\partial_t N = [g(x, N)\langle f \rangle - d(x, N)]N, \tag{5b}$$

where $\langle f \rangle = x f_A + (1 - x) f_B$ denotes the average fitness. Equation (5a) has the form of a replicator equation [2]. However, in Eq. (5a) there is an additional factor, namely, the global population fitness $g(x, N)$. This leads to a coupling of x and N whose implications we will discuss later on. Similarly, Eq. (5b) describing population growth is coupled to the internal evolution, Eq. (5a). Note that for frequency-independent global functions, $g(x, N) \equiv g(N)$ and $d(x, N) \equiv d(N)$, Eqs. (5) resemble Eqs. (1) and (2). Only then, the deterministic dynamics reduces to the common scenario [12,13,15], where a changing population size is immaterial to the evolutionary outcome of the dynamics [3]. For the full stochastic dynamics the strength of fluctuations scales as $\sqrt{1/N}$ [3,11,14] and thereby is strongly affected by population growth.

In more realistic settings, the global fitness and weakness functions, $g(x, N)$ and $d(x, N)$, can also depend on the relative abundance x. This implies an interdependence of population growth and internal evolution. In the following, we focus on one particular but very important example: the dilemma of cooperation in a growing population. There is an ongoing debate in sociobiology regarding how cooperation within a population emerges in the first place and how it is maintained in the long run [8,17]. Microbial biofilms serve as versatile model systems [8,18–20]. There, cooperators are producers of a common good, usually a metabolically expensive biochemical product. For example, for the proteobacteria *Pseudomonas aeruginosa*, cooperators produce iron-scavenging molecules (siderophores). Released into the environment, these molecules strongly support the iron uptake of each individual in the population [20]. Cooperators thereby clearly increase the global fitness of the population as a whole, leading to a faster growth rate and a higher maximum population size [20]. In such a setting, however, nonproducers (''cheaters'') have a relative advantage over cooperators as they save the cost of providing the common good, e.g., the production of siderophores. Hence, their relative fraction is expected to increase within the population, implying that the global fitness of the population declines. Surprisingly, as we show in the following, a coupling between growth and internal evolution can overcome this dilemma transiently, and the average level of cooperators can increase despite a disadvantage in relative fitness.

We model the internal evolutionary dynamics by the prisoner's dilemma game [2,17]. Within this standard approach, individuals are either cooperators (A) or cheaters (B). While cooperators provide a benefit b to all players at the expense of a (metabolic) cost $c < b$, a cheater saves the cost by not providing the benefit. The relative fitness of these traits is given by $f_A(x) = 1 + s[(b - c)x - c(1 - x)]$ and $f_B(x) = 1 + sbx$, respectively, where the frequency-independent and dependent parts are weighted by the strength of selection s [12]. Analyzing the prisoner's dilemma *per se*, defectors are always better off than cooperators because of their advantage in relative fitness, $f_A(x) < f_B(x)$ [17]. In the following, we choose for specificity $b = 3$ and $c = 1$; however, our conclusions are independent of the exact values.

Importantly, cooperation positively affects the whole population by increasing its global fitness, e.g., by production of a common good such as siderophores. Here, we consider bounded population growth with a growth rate increasing with the cooperator fraction x. In detail, we choose an x-dependent global fitness, $g(x) = 1 + px$, and an N-dependent global weakness, $d(x, N) = N/K$, accounting for limited resources. For $p = 0$, one obtains the well-known dynamics of logistic growth [21] with a carrying capacity K. For $p > 0$, the carrying capacity, $K(1 + px)$, depends on the fraction of cooperators. For instance, for *P. aeruginosa* [20], the iron uptake, and hence the birth rates, increase with a higher siderophore density and therefore with a higher fraction of cooperators.

To analyze the evolutionary behavior of our model we performed extensive simulations of the stochastic dynamics given by the master equation determined by the birth and death rates, Eq. (3). All ensemble averages were performed over a set of 10^4 realizations. In Fig. 1 the average population size N and the average fraction of cooperators x are shown for different initial population sizes N_0. The influence of a frequency-dependent growth on the population is twofold. First, starting in the regime of

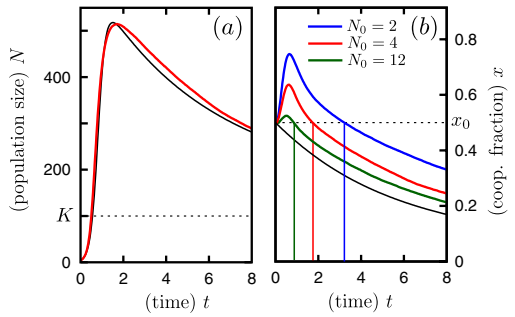

FIG. 1 (color online). The dilemma of cooperation in growing populations. (a) Average population size over time. Because of a cooperation-mediated growth advantage, it can show an overshoot. The gray (red) line corresponds to simulation results while the black line is obtained by evaluating Eqs. (6). (b) The average level of cooperation increases transiently for times $t < t_c$, especially if the initial population size is small meaning fluctuations are large. The parameters are given by $x_0 = 0.5$, $b = 3$, $c = 1$, $s = 0.05$, $K = 100$, and $p = 10$. In (a), N_0 is 4. In (b), the gray lines correspond to $N_0 = 2$ (blue), 4 (red), and 12 (green), from top to bottom. The black line is obtained by evaluating Eqs. (6) for $N_0 = 4$. Cooperation times t_c are denoted by thin lines.

exponential growth, the frequency-dependent global fitness may cause an overshoot in the population size [Fig. 1(a)]. Second, and more strikingly, the selection disadvantage of cooperators can be overcome and a transient increase of cooperation emerges [Fig. 1(b)]. It is maintained until a time t_c, which we term as the cooperation time.

Both phenomena rely on a subtle interplay between internal evolution, with a selection pressure towards more defectors, and population growth, with a growth rate increasing with the fraction of cooperators. While the overshoot in population size can already be understood on the basis of the rate equations,

$$\partial_t x = -s(1 + px)x(1 - x), \tag{6a}$$

$$\partial_t N = [(1 + px)\langle f\rangle - N/K]N, \tag{6b}$$

the transient increase of cooperation is a genuinely stochastic event as discussed in detail below. A first impression of the antagonism between selection pressure and growth can already be obtained by examining the characteristic time scales. While the fraction of cooperators changes on a time scale $\tau_x \propto 1/s$, the population size evolves on a time scale $\tau_N \propto 1$. Hence, the strength of selection s regulates the competition between population growth and internal dynamics. For $s \gg 1$, selection is much faster than growth dynamics. Therefore, the rapid ensuing extinction of cooperators cannot be compensated for by the growth advantage of populations with a larger fraction of cooperators. In contrast, in the limit of weak selection ($s \ll 1$), growth dynamics dominates selection and both an overshoot in the population size and a transient increase of cooperation become possible (see below). In the following we focus on this latter, more interesting, scenario of weak selection ($\tau_N < \tau_x$).

Let us first consider the overshoot in the population size [Fig. 1(a)]. It is caused by a growth rate and a carrying capacity which are increasing functions of the fraction of cooperators (here we use $p = 10$ as observed in microbial experiments [19]). For $t < \tau_x$, a small population [$N \ll K(1 + px_0)$] with an initial fraction of cooperators x_0 grows exponentially towards its comparatively large carrying capacity $K(1 + px_0)$. During this initial time period the fraction of cooperators evolves only slowly and can be considered as constant. On a longer time scale, $t > \tau_x$, however, selection pressure drives the fraction of cooperators substantially below its initial value x_0, leading to a smaller carrying capacity, $K(1 + px)$. Finally, cooperators go extinct and the population size decreases to K. This functional form of $N(t)$ is well described by the rate equations (6); see black line in Fig. 1(a).

In contrast, the transient increase of cooperation, cf. Fig. 1(b), cannot be understood on the basis of a simple deterministic approach, where $\partial_t x \leq 0$ holds strictly [see black line in Fig. 1(b)]. It is a genuinely stochastic effect, which relies on the amplification of stochastic fluctuations generated during the initial phase of the dynamics where the population is still small. In more detail, for small populations, the fraction of cooperators is subject to strong fluctuations and differs significantly from one realization to another. Crucially, due to the coupling between the growth of a population and its internal composition, these fluctuations are amplified asymmetrically, favoring a more cooperative population; i.e., growth, set by the global fitness $g(x)$, is amplified by an additional cooperator while it is hampered by an additional defector. This implies that the ensemble of realizations becomes strongly skewed towards realizations with more cooperators. If this effect is strong enough the ensemble average $x(t) = \sum_i N_{A,i}(t)/\sum_i N_i(t)$, which describes the mean fraction of cooperators when averaging over different realizations i, increases with time. Because of a subsequent antagonism between selection pressure towards more defectors and asymmetric exponential amplification of fluctuations during growth phase, there is only a transient increase of cooperation in a finite time window, $t \in [0, t_c]$. These findings are illustrated in a movie in [22] showing the time evolution of the probability distribution for an ensemble of stochastic realizations.

Additional qualitative and quantitative insights can be gained from analytic calculations via a van Kampen approximation [23]; see the supplementary material [22]. Thereby starting with a master equation given by Eq. (3), first and higher moments of the fluctuations can be obtained. They show that fluctuations during the first generation (i.e., doubling the initial population size on average) are by far the dominant source for the variance in the composition of the population. In addition (see below), these calculations give a strictly lower bound on the parameter regime where the cooperation time is finite and thus quantify the magnitude of fluctuations necessary to overcome the strength of selection acting against cooperators.

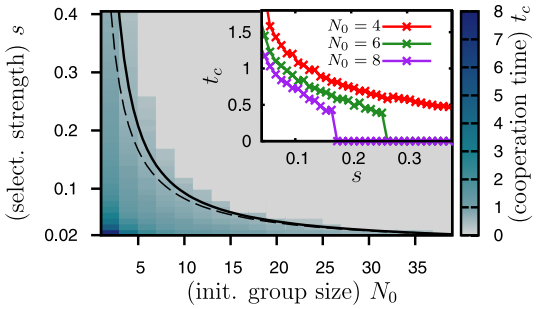

FIG. 2 (color online). Dependence of the cooperation time t_c on the strength of selection s and the initial population size N_0. There exist two distinct phases: the phase of transient maintained cooperation (where $t_c > 0$ holds) and the phase of extinction of cooperation (where $t_c = 0$). The boundary of both phases (solid line) is approximately given by $sN_0 \approx p/(1 + px_0)$ (dashed line). The cooperation time t_c is shown for varying s but fixed N_0 in the inset. See text and [22].

Figure 2 shows the cooperation time t_c with varying selection strength s and initial population size N_0. For large s and N_0 (light gray area), t_c is identical to zero; i.e., the fraction of cooperators always decreases as predicted by the deterministic replicator dynamics, Eq. (6a). In contrast, if s and N_0 are sufficiently small, t_c is finite. The transition between these regimes is discontinuous and is marked by a steep drop in the cooperation time from a finite value to zero; see Fig. 2 (inset). A strictly lower bound for the phase boundary (Fig. 2, solid line) can be derived analytically by comparing the antagonistic effects of drift and fluctuations; see [22]. Its asymptotic behavior for large N_0 is given by $sN_0 \approx p/(1 + px_0)$ (Fig. 2, dashed line). This behavior resembles the condition for neutral evolution [11,14]. Indeed, for $sN_0 < p/(1 + px_0)$, fluctuations dominate and the system evolves neutrally. It is this neutral evolution leading to sufficiently large fluctuations which in turn—by asymmetric amplification—result in a transient increase of cooperation.

In summary, we introduced a general approach, which couples the internal evolution of a population to its growth dynamics. Both processes originate from birth and death events and are therefore naturally described by a unifying stochastic model. The standard formulations of evolutionary game theory and population dynamics emerge as special cases. Importantly, by including the coupling, our model offers the opportunity to investigate a broad range of phenomena which cannot be studied by standard approaches. We have demonstrated this for the prisoners' dilemma in growing populations. Here, a transient regime of increasing cooperation can emerge by a fluctuation-induced effect. For this effect, the positive correlation between global population fitness and the level of cooperation is essential. Similar to the Luria-Delbrück experiment [24], initial fluctuations in the fraction of cooperators are exponentially amplified. Here, this renders it possible for cooperators to overcome the selection advantage of defectors.

In biological settings, growth is ubiquitous: populations regularly explore new habitats, or almost go extinct by external catastrophes and rebuild afterwards. For a realistic description, it is therefore necessary to relax the assumption of a decoupled population size. Especially for bacterial populations undergoing a life cycle with a repeated change between dispersal and maturation phases [8,18–20], a transient increase in cooperation may be sufficient to overcome the dilemma of cooperation.

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Evolutionary game theory in growing populations

Anna Melbinger, Jonas Cremer, and Erwin Frey

Supplementary EPAPS document: conditions for the transient increase of cooperation

The transient increase of cooperation emerges if initial fluctuations in the evolutionary dynamics are sufficiently large such that the asymmetrical amplification of those can overcome the selection advantage of cheaters. In this Supplementary Material we derive the conditions for the transient increase. In particular, we give an analytical expression for the phase boundary in Fig. 2 (black line).

The full stochastic dynamics is given by the master equation determined by the birth and death rates, Eq. (3),

$$\begin{aligned}\frac{dP(A,B)}{dt} = \quad & \Gamma_{\emptyset\to A}(A-1,B)(A-1)P(A-1,B) + \Gamma_{\emptyset\to B}(A,B-1)(B-1)P(A,B-1) \\ & + \Gamma_{A\to\emptyset}(A+1,B)(A+1)P(A+1,B) + \Gamma_{B\to\emptyset}(A,B+1)(B+1)P(A,B+1) \\ & - \left[\Gamma_{\emptyset\to A}(A,B)A + \Gamma_{\emptyset\to B}(A,B)B + \Gamma_{A\to\emptyset}(A,B)A + \Gamma_{B\to\emptyset}(A,B)B\right] P(A,B).\end{aligned} \tag{7}$$

Here, $A \equiv N_A$ and $B \equiv N_B$ stand for the number of individuals of both traits. We approximate the master equation upon performing a van Kampen expansion [1]. To this end, we consider A and B as extensive variables which we write as

$$\begin{aligned}A &= \Omega a(t) + \sqrt{\Omega}\xi\,, \\ B &= \Omega b(t) + \sqrt{\Omega}\mu\,.\end{aligned} \tag{8}$$

Here, Ω is of the order of the actual system size, and deterministically evolving densities $a(t)$ and $b(t)$ are corrected by fluctuations $\xi(t)$ and $\mu(t)$. By this Ansatz the strength

of fluctuations is correctly considered; their relative impact decreases like $1/\sqrt{\Omega}$ with increasing system size. In the following, we consider the initial dynamics of the population when starting with a small population size N_0. Then, Ω is of the order $\Omega \approx N_0$. Death events can be neglected as the initial population size is far below the carrying capacity, $N_0/K \approx 0$.

To proceed, we expand Eq. (7) in orders of $1/\sqrt{\Omega}$. The deterministic equations follow to leading order, $\mathcal{O}\left(\sqrt{\Omega}\right)$, see Eqs. (6) with $N/K \to 0$ and $x(t) = a(t)/\left[a(t)+b(t)\right]$. The next leading order, $\mathcal{O}(\Omega^0)$, results in a Fokker-Planck equation for the probability distribution of the fluctuations, $\Pi(\xi,\mu)$. The dynamics in $\Pi(\xi,\mu)$ is coupled to the deterministic equations and can be extended to include higher orders, $\mathcal{O}\left(1/\sqrt{\Omega}\right)$. From the Fokker-Planck equation for $\Pi(\xi,\mu)$, differential equations for the first moments of ξ and μ can be obtained. They have the following functional form,

$$\begin{aligned}\partial_t\langle\xi\rangle =& C_1\langle\xi\rangle + C_2\langle\mu\rangle + \frac{1}{\sqrt{\Omega}}(C_3\langle\xi^2\rangle + C_4\langle\xi\mu\rangle + C_5\langle\mu^2\rangle) + \mathcal{O}\left(\frac{1}{\Omega}\right),\\ \partial_t\langle\mu\rangle =& D_1\langle\xi\rangle + D_2\langle\mu\rangle + \frac{1}{\sqrt{\Omega}}(D_3\langle\xi^2\rangle + D_4\langle\xi\mu\rangle + D_5\langle\mu^2\rangle) + \mathcal{O}\left(\frac{1}{\Omega}\right).\end{aligned} \tag{9}$$

The constants C_i and D_i with $i \in \{1,2,3,4,5\}$, depend on the parameters s , b, c, p, the *deterministic* parts of the composition of the population, $x(t) = a(t)/\left[a(t)+b(t)\right]$, and the population size $n(t) = a(t)+b(t)$ (in units of Ω), respectively. Importantly, the second moments couple into the dynamics only through $\mathcal{O}\left(1/\sqrt{\Omega}\right)$ corrections.

Neglecting these second and higher order moments, the ensuing linear equation has an unstable fixed point at $(\langle\xi\rangle,\langle\mu\rangle)^* = (0,0)$. The eigendirection with the larger (positive) eigenvalue has a component in the ξ-direction which is significantly larger than its component in the μ-direction. As a consequence, the fluctuations in the number of coop-

erators (ξ) are amplified more strongly than those of the defectors (μ); fluctuations are asymmetrically amplified.

Next, we analyze the effect of the second moments on the dynamics. Consider a single initial state without any variance (and all other higher moments identically zero), starting the dynamics in the fixed point, $(\langle\xi\rangle, \langle\mu\rangle)^* = (0, 0)$. Then, since the first moments are zero, only higher orders in Eq. (9) lead to deviations from the (linearly unstable) fixed point. Once such deviations are generated these are amplified *exponentially* by the (linearly) unstable dynamics, i.e. the first moments in Eq. (9). In more detail, consider the differential equations of the second moments which, for $t \to 0$, have the following asymptotic form:

$$\begin{aligned}
\partial_t\langle\xi^2\rangle =& n(1+px)\left[1+s(bx-c)\right]x, \\
\partial_t\langle\xi\mu\rangle =& 0, \\
\partial_t\langle\mu^2\rangle =& n(1+px)(1+sbx)(1-x).
\end{aligned} \tag{10}$$

Starting with zero at $t = 0$, both, $\langle\xi^2\rangle$ and $\langle\mu^2\rangle$ increase linearly in time (note that the fitness of a cooperator $1 + s(bx - c) > 0$ since otherwise the birth rate would be negative). Within one generation, $t_g = 1/\left[(1+px)(1+s(b-c)x)\right]$ (compare Eq. (6b)), i.e. doubling the population size on average, finite variances $\langle\xi^2\rangle_g$ and $\langle\mu^2\rangle_g$ are generated. This variance can be taken as a *lower bound*. We even expect this lower bound to be a reasonable estimate for the actual value since the impact of the variance created in following generations on Eqs. 9 is strongly suppressed by the exponential increase in population size.

Upon inserting the values $\langle\xi^2\rangle_g$ and $\langle\mu^2\rangle_g$ into Eq. (9) one can now calculate the time

evolution of the first moments, $\langle\xi\rangle$ and $\langle\mu\rangle$. This allows to determine the conditions necessary for a transient increase of cooperation by analyzing the fraction of cooperators $\langle\frac{A}{A+B}\rangle$; see Eqs. (8). The phase boundary separating the regimes of transient increase and immediate decrease of cooperation is defined by the condition of an initially stationary fraction of cooperators: $\partial_t\langle\frac{A}{A+B}\rangle = 0$ at $t \approx 0$.

The ensuing phase boundary is plotted in Fig. 2 (black line). The deviation from the actual (numerically determined) transition line is small for intermediate Ω and goes to zero for larger Ω. By evaluating the expression in orders of s/p, the lower bound of the transition line can be further simplified. To first order one finds

$$s = \frac{p}{n\Omega(1+px)}, \tag{11}$$

with $\Omega n = N_0$; see Fig. 2, dashed line. Note that this expression gives the asymptotically correct results for large Ω.

It is instructive to compare this result with the theory of neutral evolution [2] where a condition $sN_0 \propto 1$ separates regimes of neutral and selection-dominated evolution [2, 3]. In the present case, for the transient increase of cooperation to occur, the system has to evolve neutrally in the initial phase to create a large enough variation in the fraction of cooperators. Then, after being asymmetriclly amplified, these fluctuations can overcome the selection pressure towards more defectors. This is mathematically reflected in Eqs. (9) and (10). Initially, the second moments increase, Eqs. (10), which then feed into Eqs. (9) and lead to an increase in the first moments. Finally, the good agreement of the phase boundary with its lower bound, reassures that the variation in cooperators fraction is mainly generated at the beginning of the dynamics.

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Evolutionary and Population Dynamics: A Coupled Approach

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We study the interplay of population growth and evolutionary dynamics using a stochastic model based on birth and death events. In contrast to the common assumption of an independent population size, evolution can be strongly affected by population dynamics in general. Especially for fast reproducing microbes which are subject to selection, both types of dynamics are often closely intertwined. We illustrate this by considering different growth scenarios. Depending on whether microbes die or stop to reproduce (dormancy), qualitatively different behaviors emerge. For cooperating bacteria, a permanent increase of costly cooperation can occur. Even if not permanent, cooperation can still increase transiently due to demographic fluctuations. We validate our analysis via stochastic simulations and analytic calculations. In particular, we derive a condition for an increase in the level of cooperation.

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I. INTRODUCTION

The time evolution of size and internal composition of a population are both driven by discrete birth and death events. As a consequence, population dynamics and internal evolutionary dynamics are intricately linked. The biological significance of this coupling has previously been emphasized [1–9]. Those studies mostly employ density-dependent fitness functions to phenomenologically derive sets of coupled deterministic equations for the size and composition of populations in various ecological contexts. While those studies correctly describe the evolutionary dynamics of large population sizes, they do not account for stochastic effects arising at low population sizes. These demographic fluctuations are naturally described in the theoretical framework of stochastic processes based on elementary birth and death events as recently introduced [10]. In particular, this approach allows to explore the role of fluctuations in populations with a time-varying population size.

To understand such interdependence of population and evolutionary dynamics, it is instructive to first review the decoupled and deterministic formulations of both. *Evolutionary game theory* is a well defined framework to describe the temporal development of different interacting traits or strategies [11, 12]. It has been established as a standard approach to describe evolutionary dynamics if the fitness is frequency-dependent, i.e. if the fitness of a certain strategy depends on the abundance of other strategies within the population. Within the most basic setup, well-mixed populations are assumed and the evolution of strategies is solely determined by fitness advantages. The temporal development of the abundance x_S of a trait S follows a *replicator dynamics* [11–13],

$$\partial_t x_S = \left(\phi_S - \bar{\phi}\right) x_S. \tag{1}$$

A trait's abundance increases if its fitness ϕ_S exceeds the average fitness $\bar{\phi}$ of the population. The frequency dependence, with ϕ_S a function of the abundances $\vec{x}$ of all strategies, provoke non-linearities in Eq. (1). Starting from this standard approach, many specific examples and extensions thereof have been studied [12–14]. This comprises, for example, the prisoner's dilemma, the snowdrift-game and other games in well-mixed populations [11–13, 15]. It further ranges from the role of spatial arrangements and network interactions [16–25] via cyclic dominance [7, 26–33], structured populations [34, 35], modified update-rules [36, 37], multi-player games [38] and evolutionary algorithms [39] to the influence of internal and external fluctuations [40–45]. While these models consider a wide range of evolutionary aspects, they mostly rely on one key assumption, a decoupled, constant population size.

In contrast, *population dynamics* focus on the time evolution of the population size and how it is determined by environmental impacts like limited resources or seasonal variations. The dynamics is typically described by differential equations of the form [46–48]

$$\partial_t N = \mathcal{F}(N;t), \tag{2}$$

where $\mathcal{F}(N;t)$ may explicitly depend on time [46]. The most prominent example is logistic growth [49]. While a small population grows exponentially, the growth rate decreases with increasing population size due to limitations of resources and the population size is bounded below a maximum carrying capacity.

Illustrative examples of dynamical changes in the population size comprise bacterial and other microbial populations [50–52]: A surplus in nutrients or other metabolism related factors, can lead to an immediate and strong growth of the population while resource limitations or antibiotics and other detrimental factors can imply a stop in growth or even an abrupt death of single individuals. Even for only slightly varying environmental conditions, a fixed population size is thus rather the exception than the rule.

But microbes not only show rich population dynamics, they are also subject to diverse evolutionary forces [53–57]. Microbes live in interacting collectives of different traits. Evolution is ubiquitous and strong forms of frequency-dependence can be observed. Public good scenarios where a metabolically costly biochemical product is shared among individuals are of particular interest from an evolutionary perspective, see e.g. [51, 55, 58–60]. This includes, for example, nutrient uptake, like disaccharides in yeast [61–63], collective fruiting body formation [64, 65], or the active formation of biofilms [52, 57, 66, 67]. An example regarding iron uptake is considered below in more detail [68–70]. Furthermore, synthetical microbial systems have been considered [71, 72].

Motivated by these recent studies of microbial systems, we here investigate the consequences of such an interdependence between evolutionary and populations dynamics. Employing a previously introduced theoretical approach [10], we study the influence of different growth scenarios in combination with demographic fluctuations.

The outline of this article is the following. In Section II we discuss the stochastic dynamics and its deterministic approximation. Further, we consider the limits in which the model maps to standard (deterministic and stochastic) formulations of evolutionary dynamics. In Section III we consider the dilemma of cooperation in growing populations. Here, an increase of cooperation can be observed which is analyzed in detail. In particular, we discuss the outcomes for two different growth scenarios, i.e. a reproduction-dynamics which either is balanced by death events or simply arrests in the stationary case. Finally, we close with a short conclusion in Section IV.

II. COUPLING OF EVOLUTIONARY AND POPULATION DYNAMICS

A. Microscopic Model

We consider a population of M different traits. Each trait S is represented by N_S individuals, such that the state of the population is given by $\vec{N} = (N_1, N_2, ..., N_M)$. We further denote the frequencies of all different traits by $\vec{x} = \vec{N}/N$ with $N = \sum_S N_S$ being the total population size. The stochastic evolutionary dynamics is formulated in terms of per capita birth and death rates, G_S and D_S, respectively. The total rate for the abundance of trait S to increase or decrease by one individual is given by

$$\Gamma_{S\to 2S} = G_S N_S, \quad \Gamma_{S\to\emptyset} = D_S N_S. \tag{3}$$

The various biological factors determining each rate can be split up into two parts, a global and a relative contribution. While the global term is trait-independent and affects all traits in the same manner the relative term is trait-dependent and sets the differences between traits. We write

$$G_S = g(\vec{x}, N) f_S(\vec{x}), \quad D_S = d(\vec{x}, N) w_S(\vec{x}), \tag{4}$$

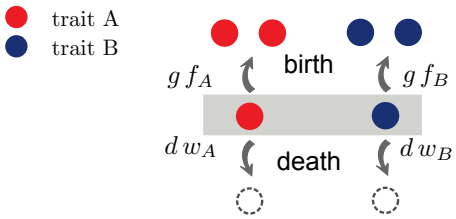

FIG. 1: The per capita birth and death rates for two different traits, A and B. Each rate depends on a global, trait-independent and a relative, trait-dependent part. While the global and relative fitness terms, g and $f_{A/B}$ affect the birth rates, the global and relative weakness terms d and $w_{A/B}$ determine the death rates.

and refer to $g(\vec{x}, N)$ and $d(\vec{x}, N)$ as *global birth-fitness* and *global weakness*, respectively. The trait-dependent terms are the *relative birth-fitness* $f_S(\vec{x})$ and the *relative weakness* $w_S(\vec{x})$[100]. While birth-fitness terms affect the birth rates, weakness terms determine the expected survival times of individuals and hence their viability. A short illustration of the stochastic processes is given in Fig. 1 for the case of two different traits.

To specify the relative fitness terms, we follow the standard approach of evolutionary game theory [11], and assume them to depend linearly on the frequencies $\vec{x}$. Let $\mathcal{P}$ be the payoff matrix for birth events. Then, the corresponding fitness vector for all traits is defined as

$$\vec{\phi} = 1 + s\mathcal{P}\vec{x}\,. \tag{5}$$

Following standard formulations, the *selection strength* s defines the relative weight of a frequency-dependent part with respect to a background-fitness set to 1 [40, 43]. As will become clear in the following, it is convenient to make use of normalized fitness values,

$$\vec{f} = \vec{\phi}/\bar{\phi}, \tag{6}$$

where $\bar{\phi} = \sum_S \phi_S x_S$ such that $\bar{f} = \sum_S f_S x_S = 1$. Without loss of generality, this choice separates global and relative parts in such a way that the dynamics of the population size depends only on the global functions g and d; see also the following Eq. (8a). An analogous approach with a payoff matrix $\mathcal{V}$ for death events can be used to obtain the frequency-dependent weakness functions w_S, which are also taken as normalized, $\sum_S w_S x_S = 1$. Of course, a more general, non-linear frequency-dependance for both relative functions can readily be taken into account. For example, in microbial systems the fitness of an individual or the whole community depends in an intricate way on a plethora of factors, e.g. the abundance of individuals, secretion and detection of signaling molecules, toxin secretion leading to inter-strain competition and changes in environmental conditions. Non-linear frequency-dependent fitness-functions might help to account for such factors, see e.g. [58, 62].

In general, the global terms $g(\vec{x}, N)$ and $d(\vec{x}, N)$ depend on the population size and are frequency-

dependent. Limited growth is one example of size-dependence. In such a setting, small populations starts to grow exponentially but growth is bounded due to limited resources, e.g. $d(\vec{x}, N)$ increases with N. Frequency-dependent terms can, for example, occur in public good situations, as discussed in Section III.

B. Dynamics

The per-capita birth and death rates, Eqs. (4), define a continuous-time Markov process [73, 74]. It is described by a master equation for the probability density $P(\vec{N};t)$ to find the population in state $\vec{N}$ at time t:

$$\frac{dP(\vec{N};t)}{dt} = \sum_S \left[(\mathbb{E}_S^- - 1)G_S N_S + (\mathbb{E}_S^+ - 1)D_S N_S\right] P(\vec{N};t). \quad (7)$$

Here, $\mathbb{E}_S^\pm$ are step operators increasing/decreasing the number of individuals of trait S by one [74], e.g.

$$\mathbb{E}_S^\pm P(\vec{N};t) = P\left(N_1, ..., N_S \pm 1, ..., N_M; t\right).$$

For a reference it is instructive to first consider a deterministic limit where both, fluctuations and correlations, can be neglected. Then, upon factorizing higher moments of the probability density [73, 74], one finds a closed set of equations for the expected frequencies x_S and the total population size N:

$$\partial_t N = \left[g\left(\vec{x}, N\right)\bar{f} - d\left(\vec{x}, N\right)\bar{w}\right]N, \quad (8a)$$

$$\partial_t x_S = g(\vec{x}, N)\left[f_S(\vec{x}) - \bar{f}\right]x_S - d(\vec{x}, N)\left[w_S(\vec{x}) - \bar{w}\right]x_S, \quad (8b)$$

where $\bar{f} = \bar{w} = 1$ according to Eq. (6). To unclutter notation, we have not explicitly marked the expectation values in Eqs. (8) but use the same notation as for the stochastic variables.

This set of coupled non-linear equations resembles other deterministic approaches [1–4, 6–8] and has a simple interpretation. Eq. (8a) describes the population dynamics. As it is typical for a deterministic approach, the dynamics does not depend on the global birth-fitness, g, and the global weakness, d, separately, but only on their difference. Eq. (8b) describes the internal evolution of the population: The time evolution of the frequency of a strategy S is given by the interplay between a growth and a death term. Each of them consists of a relative term measuring the surplus of the fitness/weakness relative to the corresponding population average. The weight of these terms are given by the respective global fitness functions, g and d. During phases of population growth, where $g > d$ holds (see Eq.(8a)), the growth term and hence differences in relative birth fitness dominate the internal evolution of the population. Similarly, weakness differences are the main evolutionary driving forces during population decline.

From these considerations it follows that both, the time scale of population and evolutionary dynamics have a crucial impact on the dynamics. This is obvious if the time-scales are similar. Such biological situations have been observed in many examples, see e.g. [75–78]. But also if evolution happens on longer time-scales than ecology this coupling can affect the evolutionary outcome as we show in the following.

Importantly, fluctuation cannot be ignored in general but can change evolutionary dynamics dramatically. Then, the deterministic approach given by Eqs. (8) is not adequate. This regards for example fixation and extinction events but also the evolution of first and higher moments of a trait's abundance. For a proper description, one has to take the full stochastic dynamics and master equation (7) into account. One example, where fluctuations drastically change the outcome is given in the following Section III.

C. Mapping to Standard Approaches: Replicator Dynamics and the Moran Process

We now consider in which limits and to what extent our stochastic approach resembles the standard approaches of evolutionary dynamics. Let us first consider the special case where the global rates $g(\vec{x}, N) \equiv g(N)$ and $d(\vec{x}, N) \equiv d(N)$ are frequency-independent and the ensuing deterministic dynamics exhibits a stable fixed point N^* in the population size. Then, birth and death events exactly balance each other, $g(N^*) = d(N^*)$, such that N^* is fixed, $\partial_t N^* = 0$. This is, for example, the case if the population size evolves according to a logistic growth law and the carrying capacity has been reached. In the deterministic limit, the internal dynamics, Eq. (8), simplifies to

$$\partial_t x_S = g(N^*)\left[f_S(\vec{x}) - \bar{f} - w_S(\vec{x}) + \bar{w}\right]x_S. \quad (9)$$

The fraction x_S evolves like in a standard replicator equation, similar to Eq.(1). It is the difference of both relative terms, the effective fitness $f_S - w_S$, which determines internal evolution. Compared to Eq. (1), the additional constant prefactor $g(N^*)$ in Eq. (9) just rescales the time-scale on which internal evolution occurs [41].

Furthermore, also the full stochastic formulations of our model and the standard stochastic approaches with a fixed population size resemble each other. In those standard approaches, the birth of one individual is directly coupled to the death of another one. The dynamics is described by *update rules*. For example, for the time-continous formulation used here, the stochastic dynamics can be described by the Moran process [40, 41, 43, 44, 79–81] [101]. In our formulation, this process holds in the limit where the fixed point of the population size, N^*, is linearly stable with a large stability coefficient [102]. Then, a birth event is directly followed by a death event and vice versa. The effective rate for such a combined

birth-death event is given by,

$$\tilde{\Gamma}_{S\to S'} = \Gamma_{S'\to 2S'}\Gamma_{S\to\emptyset} + \Gamma_{S\to\emptyset}\Gamma_{S'\to 2S'}. \quad (10)$$

The strength of fluctuations is of the order $1/\sqrt{N^*}$ and the transition rate $\tilde{\Gamma}_{S\to S'}$ follows by the logic of an urn-model where, fitness-dependent, individuals reproduce to substitute other, randomly chosen, individuals [40, 41, 43, 79, 80].

Beyond the Moran process, however, if N^* is not linearly stable with sufficiently high stability coefficients, then birth and death events do not strictly follow each other and N is not strongly confined within the range $N^* \pm 1$. Depending on the stability of the fixed point, evolutionary paths deviating from N^* by more than one individual have to be taken into account to derive an effective rate for a combined birth-death event.

In general, the population size changes with time, $N = N(t)$. For frequency-independent global rates, the deterministic limit of the internal evolutionary dynamics resembles the form of a replicator equation,

$$\partial_t N = [g(N) - d(N)]N, \quad (11a)$$
$$\partial_t x_S = \{g(N)\left[f_S(\vec{x}) - \bar{f}\right] \quad (11b)$$
$$- d(N)\left[w_S(\vec{x}) - \bar{w}\right]\}x_S. \quad (11c)$$

However, in contrast to Eq. (1), both relative fitness terms, f and w, are now weighted by the global rates. This has important implications. While in growth phases with $g > d$ the relative birth fitness f_S dominates the dynamics, the relative weakness functions w_S dominate during population-decline, $g < d$. Moreover, the time-varying population size also leads to a changing strength of fluctuations $\sim 1/\sqrt{N(t)}$. In particular, when fitness differences are weak and the dynamics is close to neutral evolution, such a change might have strong consequences [41, 43, 45, 82, 83].

III. THE DILEMMA OF COOPERATION IN GROWING POPULATIONS

To exemplify the importance of coupling and fluctuations offered by our approach, we here study the dilemma of cooperation in growing populations. This is motivated by the dynamics observed in microbial biofilms where strong forms of cooperation can be observed [51, 55, 57, 59, 60, 67]. Single individuals produce metabolically costly products which they release into the environment to support, for example, biofilm formation or nutrient depletion. As these products are available for other bacteria in the colony, the cooperating individuals are producers of a public good, and, by having the extra load of production, permanently run the risk to be undermined by non-producing free-riding strains. An example is provided by the proteobacterium *Pseudomonas aeruginosa* [68–70]. To facilitate the metabolically important iron-uptake, these microbes produce siderophores which they release into the environment. Given the high binding affinity to iron, these proteins are capable to scavenge single iron atoms from larger iron clusters. The iron-sideorophore complex can then be taken up by the bacteria, ensuring their iron supply. However, as every bacterium, not only the producing ones, can take advantage of the released siderophores there is a dilemma of cooperation: While it would be optimal for the whole population to cooperate, cooperators are endangered due to their reproduction disadvantage.

In addition to the evolutionary dynamics, microbial colonies are also subject to strong changes in population size [50–52, 84]. While in the presence of nutrients, small colonies grow exponentially, growth is bounded due to limitations in resources or deteriorating environmental conditions. This includes insufficient amounts of nutrients, a lack of oxygen or a poisoning by metabolites. Eventually the colony size remains constant or even declines again [50]. Given by the exact interplay of these detrimental and other environmental factors, and differing from species to species, growth dynamics varies between two scenarios[85, 86]. First, bacteria can switch into a dormant state where individuals stay alive but regulate reproduction rates and metabolic activity towards zero (*dormancy scenario*). Depending on environmental conditions dormancy can increase survival chances. For example, in the presence of antibiotics, this downgraded metabolism can make bacteria less vulnerable leading to persistence [87–90], or dormancy might hedge a population against strongly fluctuation environments [86, 90, 91]. Second, environmental conditions can lead to death rates increasing with the population size N while birth rates are only slightly affected [92]. The population, therefore, reaches a state of dynamical maintained population size with the death rates exactly balancing the birth rates (*scenario of balanced growth*). In many populations, a situation in-between both scenarios is observed. In pathogenes like *P. aeruginosa*, the fraction of individuals transferring to the dormancy state varies between 20% and 80% [93]. In the following we consider both scenarios and their impact on internal evolution separately.

A. The Balanced Growth Scenario

Let us first study the balanced growth dynamics where, in the stationary state, birth and death events are both present, but exactly balance each other such that the population size is about constant. We consider a population which consists of two traits, cooperators (C) and free-riders (F). The total number of individuals in the population is given by $N = N_C + N_F$ and the fraction of cooperators by $x \equiv x_C = N_C/N$. The relative birth fitness, f_S (ϕ_S, if not normalized), accounts for the reproduction disadvantage of cooperating individuals. We

study the well-know prisoner's dilemma [11]:

$$\begin{aligned}\phi_C =& 1 + s(\tilde{b}x - \tilde{c}),\\ \phi_F =& 1 + s\tilde{b}x,\\ \bar{\phi} =& 1 + s(\tilde{b} - \tilde{c})x.\end{aligned} \tag{12}$$

As introduced in Section II, the frequency-dependent part is weighted with the strength of selection s. Individuals obtain a benefit $\tilde{b}$ from direct interaction with cooperators, while only cooperating individuals have to pay the cost $\tilde{c}$ for producing the public good. For the resulting normalized fitness functions, $f_S = \phi_S/\bar{\phi}$, the inequality $f_C < f_F$ always holds; within the same population, the reproduction rate of cooperators is always smaller than the one of free-riders.

In the following, we take the payoff parameters to be constant, $\tilde{c} = 1$ and $\tilde{b} = 3$. Then, s directly sets the time scale of the internal evolution. The relative weakness is assumed to be trait-independent and constant, $w_C = w_F = 1$; free-riders and cooperators have equal survival chances.

Further, because cooperators are the producers of a public good, the overall growth condition of a population improves with a higher level of cooperation. We here choose the global birth fitness to increase linearly with the level of cooperation,

$$g(x) = 1 + px. \tag{13}$$

The parameter p scales the positive impact of the presence of public good on the population. In the scenario of balanced growth, we consider death rates increasing with the population size. For specificity, we assume logistic growth [49] and set

$$d(N) = N/K. \tag{14}$$

K scales the maximal size a population can reach (carrying capacity) as discussed in detail below.

The master equation (7) describing the full stochastic dynamics then takes the form

$$\begin{aligned}\frac{dP(N_C, N_F)}{dt} =& \left[(\mathbb{E}_C^- - 1)gf_C N_C + ((\mathbb{E}_F^- - 1)gf_F N_F\right.\\ &+ (\mathbb{E}_C^+ - 1)d\,N_C + \left.(\mathbb{E}_F^+ - 1)d\,N_C\right] \times\\ &P(N_C, N_F).\end{aligned} \tag{15}$$

To explore the dynamics, we performed extensive stochastic simulations. They were obtained by simulating $i = 1, \ldots, R$ different realizations with the Gillespie algorithm [94], according to the master equation (15). In Fig. 2, we show the ensemble averages of the population size $\langle N\rangle$ and the fraction of cooperators $\langle x\rangle$ given by

$$\langle N\rangle = \sum_i N_i(t)/R, \tag{16a}$$

$$\langle x\rangle = \sum_i N_{C,i}(t)/\sum_i N_i(t). \tag{16b}$$

This choice for the average naturally accounts for the fact that realizations with a larger populations size provide a larger statistical weight. Starting with a small population, the system size grows exponentially (*exponential phase*), reaches a maximum size and then declines again. Furthermore, and more strikingly, the disadvantage of cooperators can be overcome and a transient increase of cooperation can emerge. Even though the transient increase is caused by demographic fluctuations, it is instructive to examine the deterministic equations first. They not only describe the overshoot in the population size well, but also give insights into the relevant time scales of the dynamics:

$$\partial_t x = -s(1 + px)x(1 - x)., \tag{17a}$$

$$\partial_t N = \left(1 + px - \frac{N}{K}\right) N \tag{17b}$$

The first equation describes the change in the average fraction of cooperators. The dynamics occurs on the time scale $\tau_x \sim 1/s$, i.e. the strength of selection sets the time-scale of internal evolution. Note that $\partial_t x \leq 0$ always holds and therefore the deterministic approximation cannot give rise to any transient increase of cooperation. In contrast, the dynamics of the total population size is well described deterministically, see Fig. 2(a). It resembles the well known equation of logistic growth [49] with a frequency-dependent maximal population size $K(1 + px)$ (carrying capacity). During growth, changes in the population size occur on a time-scale $\tau_N \sim 1 + px$, c.f. Eq. (17b). In the limit of weak selection, τ_N is comparably smaller than the time scale τ_x, on which selection occurs. This and the frequency dependent carrying capacity are the reason for the overshoot: At the beginning the maximal population size is given by $K(1+px_0)$. Because cooperators go extinct, the size decreases with time. As this reduction is happening on a faster time scale than selection, $\tau_N < \tau_x$, the population size grows towards a larger carrying capacity, and then subsequently drops with decreasing carrying capacity due to a decline in cooperation.

B. A Transient Increase of Cooperation

The stochastic dynamics of the average fraction of cooperators $\langle x\rangle$ is qualitatively different from its deterministic limit. We observe a transient increase in the level of cooperation during a time window $(0, t_C)$. The magnitude of the *cooperation time*, t_C, strongly depends on the initial population size N_0, cf. Fig. 2. The origin of this transient increase in cooperation is a genuine stochastic effect: demographic fluctuations during the initial phase are subsequently asymmetrically amplified by the population dynamics. Heuristically, this can be understood as follows; for a detailed mathematical analysis employing a van Kampen expansion see the next section.

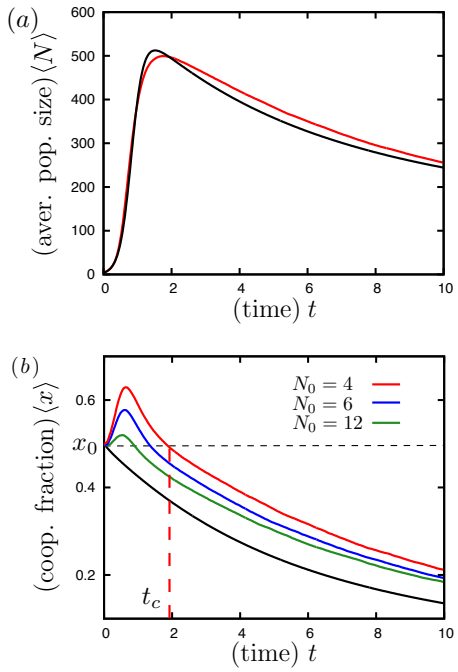

FIG. 2: (color online) Cooperation in growing populations. Temporal development of ensemble averages. (a) The population size. Starting with $N_0 = 4$, the system grows exponentially until the carrying capacity is reached. It then falls again due to selection and a decreasing carrying capacity, see text. The full stochastic solution, grey (red) line, is described well by the deterministic approximation, black line. (b) The fraction of cooperators. It initially increases due to asymmetric amplification of fluctuations, and then falls again due to selection, see text. The level of cooperation, x, falls below its initial value, x_0 at the cooperation time, t_C. The transient increase is stronger for larger fluctuations and thus is stronger with a smaller initial population size N_0, see grey (colored) lines. The deterministic approximation do not account for this behavior, cf. black line. Parameters are $s = 0.1$ and $p = 10$t.

For a small initial population size N_0 demographic fluctuations are effectively symmetric, i.e., the occurrence of an additional cooperator or an additional free-rider are equally likely. However, the consequences of these two directions of demographic fluctuations differ strongly: In the exponential phase, an additional cooperator amplifies the growth of the population, while an additional free-rider hampers it. In other words, fluctuations towards more cooperators imply a larger growth rate and hence a larger population size. Therefore, those realizations of the stochastic dynamics have a larger weight in the ensemble average, Eq. (16b), and enable an increase in the overall fraction of cooperators. With these considerations, a criterion for the transient increase of cooperation can be obtained: Demographic fluctuations, which are of size $\sqrt{N}$ [41], have to be large enough to overcome the selection pressure towards free-riders. This can already be inferred from Fig. 2(b), where curves for three different values of the initial population size are shown. For the smallest N_0 the effect is the strongest because fluctuations are large at the beginning.

C. Van Kampen Expansion

As discussed above the transient increase of cooperation is caused by fluctuations which are asymmetrically amplified. In order to quantify these findings analytically, we employ an Omega expansion in the system size according to van Kampen [74] of the master equation (15). For generality, we perform these calculation for arbitrary global growth function $g(x)$. The deterministic solutions are separated from fluctuations by the following ansatz:

$$\begin{aligned} N_C &= \Omega c(t) + \sqrt{\Omega}\xi, \\ N_F &= \Omega f(t) + \sqrt{\Omega}\mu. \end{aligned} \tag{18}$$

$c(t)$ and $f(t)$ correspond to the deterministic solutions, as shown below. ξ and μ are fluctuations in the number of cooperators and free-riders. The relative strength of fluctuations and the deterministic parts are weighted by powers of Ω which scales with the current system size. Hence, this ansatz accounts for the fact that fluctuations scale as $1/\sqrt{N}$ [73]. Eq. (15) is expanded in orders of $1/\sqrt{\Omega}$. With Eq. (18), the step operators $\mathbb{E}_S^+$, $\mathbb{E}_S^-$ are given by

$$\begin{aligned} \mathbb{E}_C^{\pm} &= 1 \pm \frac{1}{\sqrt{\Omega}}\partial_\xi + \frac{1}{2\Omega}\partial_\xi^2 + \mathcal{O}(\Omega^{3/2}), \\ \mathbb{E}_F^{\pm} &= 1 \pm \frac{1}{\sqrt{\Omega}}\partial_\mu + \frac{1}{2\Omega}\partial_\mu^2 + \mathcal{O}(\Omega^{3/2}). \end{aligned} \tag{19}$$

Employing these and Eqs. (18) in Eq. (15) leads to

$$\begin{aligned} \partial_t P(\xi,\mu) - \sqrt{\Omega}(\dot{c}\partial_\xi + \dot{f}\partial_\mu) = \Big[&-\sqrt{\Omega} g\Big(\frac{\phi_C}{\bar{\phi}} c\partial_\xi + \frac{\phi_F}{\bar{\phi}} f\partial_\mu\Big) \\ &+\Omega^0(...) + \frac{1}{\sqrt{\Omega}}(...) + \mathcal{O}(\Omega^{-3/2})\Big] P(\xi,\mu), \end{aligned} \tag{20}$$

where terms of the order Ω/K and higher are neglected. Initially, starting with a small population, these higher orders are very small because $\Omega \approx N_0$ and $N_0 \ll K$ holds. The orders Ω^0 and $1/\sqrt{\Omega}$ depend on c, f, s, $\tilde{b}$, $\tilde{c}$, g, ∂_ξ, ∂_μ, ξ, μ and are not written out in this equation for clarity. By collecting terms of order $\sqrt{\Omega}$ and using the identities $n = c(t) + f(t)$ and $x = c(t)/[c(t) + f(t)]$ the determinstic equations, Eqs. (17), are obtained (for $K \to \infty$). Higher orders of Eq. (20) lead to a Fokker-Planck equation for $P(\xi,\mu)$. From this Fokker-Planck equation, differential equations for the first and second moments of the fluctuations can

be obtained. The first moments are given by

$$\begin{aligned}\langle\dot{\xi}\rangle =&\left[\frac{g\phi_C}{\bar{\phi}}+x(1-x)\partial_x\frac{g\phi_C}{\bar{\phi}}\right]\langle\xi\rangle-x^2\partial_x\frac{g(x)\phi_C}{\bar{\phi}}\langle\mu\rangle\\&+\partial_x^2\frac{g\phi_C}{\bar{\phi}}\frac{1}{\sqrt{\Omega}}\left[(1-x)^2\langle\xi^2\rangle-2x(1-x)\langle\xi\mu\rangle+x^2\langle\mu^2\rangle\right],\\\langle\dot{\mu}\rangle =&(1-x)^2\partial_x\frac{g\phi_F}{\bar{\phi}}\langle\xi\rangle+\left[\frac{g\phi_F}{\bar{\phi}}-x(1-x)\partial_x\frac{g\phi_F}{\bar{\phi}}\right]\langle\mu\rangle\\&-\partial_x^2\frac{g\phi_F}{\bar{\phi}}\frac{1}{\sqrt{\Omega}}\left[(1-x)^2\langle\xi^2\rangle-2x(1-x)\langle\xi\mu\rangle+x^2\langle\mu^2\rangle\right].\end{aligned}\tag{21}$$

Note that the second moments only couple at order $1/\sqrt{\Omega}$. Neglecting these higher orders, Eq. (21) is linear and has an unstable fixed point at $(\xi,\mu)^*=(0,0)$.

Next, we analyze the impact of the second moments on the dynamics. Their coupling into Eq. (21) is only important for small times, when the first moments are still at the initial condition, the unstable fixed point $(\xi,\mu)^*=(0,0)$. Therefore, it is appropriate, to examine the second moments for small times, $t\to 0$. They then have the asymptotic form

$$\begin{aligned}\partial_t\langle\xi^2\rangle =&ng\frac{\phi_C}{\bar{\phi}}x,\\\partial_t\langle\xi\mu\rangle =&0,\\\partial_t\langle\mu^2\rangle =&ng\frac{\phi_F}{\bar{\phi}}(1-x).\end{aligned}\tag{22}$$

Due to the inhomogeneity of the differential equations, the second moments $\langle\xi^2\rangle$ and $\langle\mu^2\rangle$ immediatly start to grow. These non-zero second moments now couple back into the first moments, Eqs. (21), and push them out of the unstable fixed point. To quantify this, the solution of Eqs. (22) is employed in Eqs. (21). The resulting equations are solved for small times. As fixed time we here consider the doubling time of the initial population $t_d=1/g(x)$. This means that only fluctuations during the time interval $[0,t_d]$ are considered. Hence, this approximation leads to a lower bound for the strength of fluctuations. Further, the initial conditions are given by $\langle\xi_0\rangle=\langle\mu_0\rangle=\langle\xi_0^2\rangle=\langle\mu_0^2\rangle=0$.

If the initially generated and asymmetrically enhanced fluctuations are large enough to overcome the selection disadvantage, the transient increase of cooperation arises. To quantify this, the total fraction of cooperators in the system has to be examined:

$$\begin{aligned}\frac{d}{dt}\langle\frac{N_C}{N_C+N_F}\rangle =&\frac{\dot{x}+1/\sqrt{\Omega}\langle\dot{\xi}\rangle}{n+1/\sqrt{\Omega}(\langle\xi\rangle+\langle\mu\rangle)}\\&-\frac{(xn+1/\sqrt{\Omega})(\langle\dot{\xi}\rangle+\langle\dot{\mu}\rangle)}{(n\sqrt{\Omega}+1/\Omega(\langle\xi\rangle+\langle\mu\rangle))^2}.\end{aligned}\tag{23}$$

For $\frac{d}{dt}\langle\frac{N_C}{N_C+N_F}\rangle>0$ the transient increase of cooperation is present. The condition $\frac{d}{dt}\langle\frac{N_C}{N_C+N_F}\rangle=0$ leads, to first order in s, to the transition line

$$s=\frac{\partial_x\ln[g(x)]}{n(1/g(x))\Omega}\Big|_{x_0}=\frac{\partial_x g(x)}{n(1/g(x))\Omega g(x)}\Big|_{x_0}.\tag{24}$$

For smaller s there is a transient increase in cooperation, while for larger s the level of cooperation decreases immediately. This resembles the condition for neutral evolution, e.g. [45, 82]; evolution is only neutral for $sN\lesssim const.$ Thus, only if fluctuations are strong during the initial phase of the dynamics, such that the system behaves neutrally, they are sufficient to overcome the selection pressure towards free-riders. The phase boundary and thereby the strength of the transient increase depends on $\partial_x g(x)|_{x_0}$ and $g(x_0)$. Both terms have antagonistic impacts on the transition line. The reason for this behavior is that the initial doubling time, i.e. the time during which fluctuations are the most pronounced, decreases with increasing $g(x_0)$. The positive enhancement relies on the growth advantage of more cooperative realizations, which depends on $\partial_x g(x)|_{x_0}$ at the beginning. Note, that for non-linear growth functions, where $\partial_x g(x)|_{x_0}$ also depends on x_0, the transient increase can even be reduced by accounting for higher orders. This behavior was also experimentally observed in recent studies with microbes, where the growth advantage of cooperators was tuned [72]. In the next paragraph, we show that the calculated phase boundaries match our simulation results very well for several distinct global growth functions.

D. Phase Diagrams

In the following we consider how the duration t_C of the transient increase in cooperation depends on the system parameters for the specific global growth function $g(x)=1+px$, cf. Fig. 3. Then, the transition line between a transient increase, $t_C>0$, and an immediate decrease, $t_C=0$, given by Eq. (24), now reads,

$$s=\frac{p}{n\Omega(1+px_0)}.\tag{25}$$

For smaller selection strength, $s<\frac{p}{n\Omega(1+px_0)}$, the asymmetric amplification of fluctuations is sufficient to overcome the selection disadvantage of cooperators while for larger selection strength, $s>\frac{p}{n\Omega(1+px_0)}$, free-riders prevail.

In Fig. 3, we compare this result of the analytical calculations with the stochastic simulations. We observe that upon increasing the strength of selection, s, which sets the advantage of free-riders, the cooperation time t_C decreases. In contrast, stronger demographic fluctuations, their strength scales as $1/\sqrt{N_0}$, prolong the duration of the transient increase, i.e., t_C increases with decreasing N_0, cf. Fig. 3(a). These two antagonistic effects lead to a sharp phase boundary between the regimes of transient increase ($t_C>0$) and immediate decrease ($t_C=0$); see inset of Fig. 3(a). Here, the cooperation time steeply drops to zero if the strength of selection exceeds a critical value. The boundary line is in good agreement with Eq. (25), cf. black line in Fig. 3(a).

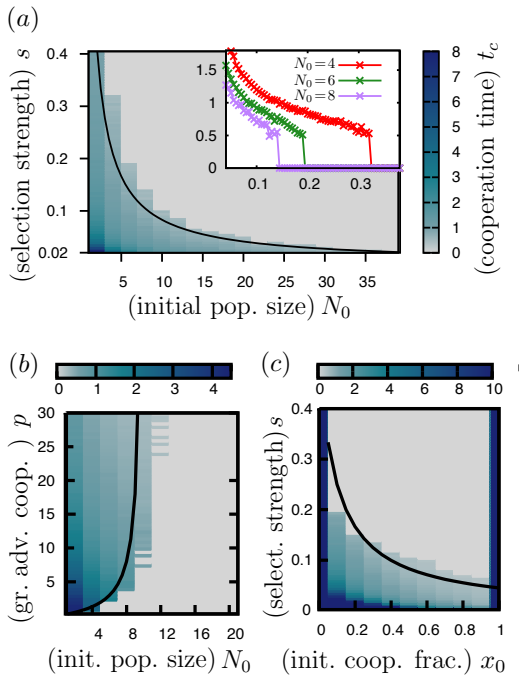

FIG. 3: (color online) The transient increase of cooperation and its dependence on parameters. Encoded in grey (colored) scale, the cooperation time t_C is plotted for three different pairs of parameters: $\{N_0, s\}$, $\{N_0, p\}$, and $\{x_0, s\}$ in (a), (b), and (c) respectively. The boundary between the regimes of transient increase and immediate decrease are in good agreement given by Eq. (24), plotted as black lines. In the inset of (a), the cooperation time is shown for varying selection strength s: t_C sharply drops at the boundary. Not varied parameters are given by $p = 10, x_0 = 0.5$ in (a); $s = 0.05$ and $x_0 = 0.5$ in (b); $p = 10, N_0 = 6$ in (c).

In Fig. 3(b), the cooperation time is shown for varying initial population size N_0 and strength of the global fitness advantage due to cooperators, p. Now, the phase boundary is determined by the interplay between the size of demographic fluctuations and its amplification due to the global fitness advantage of more cooperative populations. N_0 has to be small enough for the asymmetric amplification mechanism to be effective. Again, the phase boundary is in good agreement with Eq. (24); see solid black line in Fig. 3(b).

In Fig. 3(c), the cooperation time is plotted for varying initial cooperator fraction, x_0, and selection strength, s. We find that the cooperation time decreases with increasing x_0. Remarkably, for small x_0, the amplification mechanism is especially pronounced and therefore able to compensate comparably large selection strengths s. This is again well described by Eq. (25), see Fig. 3(c) (solid black line). The observation is of possible relevance for the evolution of cooperation since it allows a small initial fraction of cooperators to proliferate in the population.

Taken together, our analytical calculations provide a mechanistic understanding for the transient increase of cooperation and its dependence on the system parameters s, p, x_0, and N_0. We have quantitatively calculated the phase boundary and gained insights into the basic nature of the transient increase: First, the probability distribution in the cooperator fraction $\langle x \rangle$ is broadened due to neutral evolution; note that Eq. (25) resembles the condition for neutral evolution [45, 82]. Second, these initially generated fluctuations are asymmetrically amplified and can, therefore, cause an increase in the level of cooperation.

E. The Dormancy Scenario

Let us now consider the dormancy scenario where the ability to reproduce decreases with increasing population size. For specificity, we assume the global birth and death functions to be given by

$$g(x, N) = 1 + px - \frac{N}{K}, \text{ and } d = 0. \tag{26}$$

In this scenario individuals do not die but the birth rates decrease towards zero as the population size reaches its carrying capacity. The relative functions, f_S and w_S, are the same as before; the weakness terms are constant and the fitness terms given by Eq. (12).

To understand the differences in the evolutionary outcome, we again study the deterministic rate equations first. They are given by

$$\partial_t N = \left(1 + px - \frac{N}{K}\right) N, \tag{27a}$$

$$\partial_t x = -s \left(1 + px - \frac{N}{K}\right) x(1 - x). \tag{27b}$$

The equation describing population growth is formally identical to the corresponding equation in the balanced growth scenario, Eq. (17b). Differences arise because in the present case there is mutual feedback between internal and population dynamics. This coupling implies that both arrest once the population size reaches its carrying capacity. In the arrested state there is a relation between population size N^* and composition x^*: $1+px^* = N^*/K$. Thus, the reached stationary state, (x^*, N^*), depends on the initial values x_0 and N_0. The precise mapping depends on the selection strength s. For weak selection (small s), the population dynamics is much faster than the internal dynamics and hence the population size reaches a stationary state while the composition is still at its initial value x_0, i.e., $N^* = K(1 + px_0)$. In contrast, for strong selection, cooperators go extinct quickly with $x^* = 0$ such that the stationary population size becomes $N^* = K$. An example for the deterministic dynamics is shown as solid black line in Fig. 4. As for balanced growth, the deterministic dynamics exhibits a strictly monotonous decrease in the cooperator fraction, with the difference that now the asymptotic value is arrested at some finite value. These differences are also

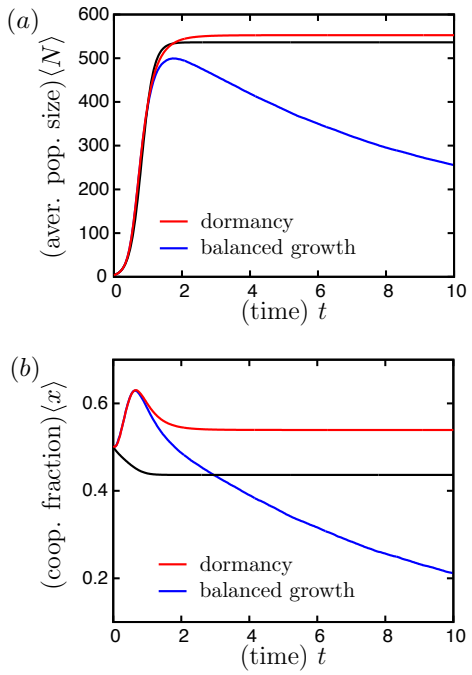

FIG. 4: The dilemma of cooperation in the dormancy scenario (color online). (a) The growth dynamics. Initially, the small population grows exponentially until growth is stopped, cf. light grey (red) line. This behavior is well described by the deterministic equation (27a), see black line. In contrast, for the balanced growth scenario, the dynamics continue and, due to selection, the population size falls again, see dark grey (blue) line. (b) The fraction of cooperators. Equal to the balanced growth scenario, dark gray (blue) line, there is an initial increase of cooperation due to asymmetric amplification within the dormancy scenario. Again, this is not described by the deterministic approximation, Eq. (27b). However, in contrast to the balanced growth scenario, the higher level of selection is latter fixed due to the stop in growth dynamics. Parameters are given by $s = 0.05$, $p = 10$, and $N_0 = 4$.

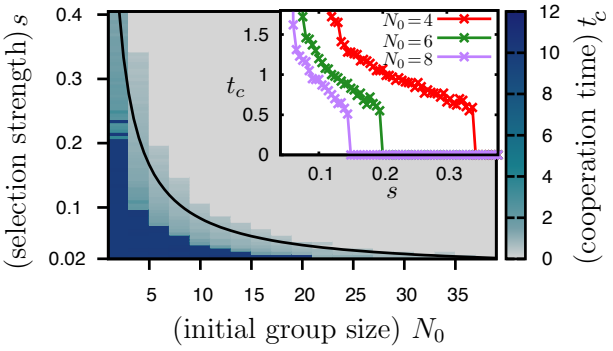

FIG. 5: (color online) The transient increase of cooperation for the dormancy scenario. The cooperation time t_C depending on the initial population size, N_0, and the strength of selection, s. The condition for a transient increase of cooperation to occur is still given by Eq. (24), black line. In addition, due to the stop in growth dynamics, there is an additional regime, where the increase becomes permanent, dark grey (dark blue) area. The permanent increase is also shown in the inset, where the cooperation time is shown for varying strength of selection. If, for a given initial population size, selection is sufficiently slow compared to fixation of the growth dynamics, the increase of cooperation becomes permanent. Parameters are given by $p = 10,\ x_0 = 0.5$.

reflected in the stochastic dynamics, where the asymmetric amplification mechanism is acting, cf. Fig. 4. In the initial phase of the dynamics, this mechanism affects the time evolution of the cooperator fraction in the same way as for balanced growth, namely it leads to an initial increase of cooperation. Differences in birth and death rates, Eq. (13) and Eq. (26), are negligible for small population size. The arrest of the dynamics only becomes effective at later times where an increase in population size implies a significantly declining birth rate. As a consequence even the stochastic dynamics becomes arrested such that the initial rise in cooperator fraction may become manifested as a permanent increase. This will be the case if the dynamics becomes arrested during the time window where the asymmetric amplification mechanism acts; see red line in Fig. 4(b).

In summary, there are now three scenarios for the dynamics, cf. Fig. 5. In addition to the immediate decline and transient increase there is now also a *permanent increase* in cooperator fraction. The analytical expression separating the regimes of transient increase and immediate decline still holds, Eq. (25), because it is due to the same mechanism as before. We did not manage to derive an explicit expression for the transition line to permanent increase. However, as the existence of a permanent increase in cooperator fraction depends on the asymmetric amplification mechanism, the regime of permanent increase is bounded by a hyperbolic line beneath the one given by Eq. (24). The latter is a necessary but not a sufficient condititon for the permanent increase to occur.

IV. CONCLUSION

In this article, we have given a synthesis of evolutionary and population dynamics. This is based on the understanding that birth and death events are the driving forces underlying changes in the size as well as the composition of a population [10]. Both processes are inherently stochastic and inevitably lead to demographic fluctuations whose magnitude depends on the population size. The ensuing stochastic formulation thereby naturally accounts for the coupling between internal evolutionary dynamics and population dynamics. The evolutionary outcome of the dynamics is determined by the interplay between selection pressure and random drift caused by demographic fluctuations. Since our approach allows to study evolutionary dynamics with varying population size we can explore ecological situations where the

relative impact of deterministic and stochastic evolutionary forces change with time. Thereby demographic fluctuations may lead to a dynamics which is qualitatively different from the corresponding deterministic dynamics: Beyond creating a broad distribution in size and composition, the coupling can strongly distort the distribution and thus strongly influence average values. For the public good scenario, discussed in this paper, this corresponds to an asymmetric amplification mechanism which yield a transient increase in the level of cooperation.

In the absence of a coupling between internal evolution and population dynamics, the impact of population size on the internal evolutionary dynamics reduces to a modulation in the strength of demographic fluctuations. If, in addition, the deterministic population dynamics exhibits a strongly attractive fixed point at a finite population size, our model maps to a standard description of evolutionary dynamics, i.e. the Moran process.

The general observations made for the coupled stochastic dynamics are exemplified by the dilemma of cooperation in growing populations. Here, fluctuations in combination with growth lead to a transient increase of cooperation. Origin of this increase is the asymmetric amplification of fluctuations. As the presence of cooperators increases the growth rates, fluctuations towards those are enhanced. Therefore growth dynamics cannot be ignored but can be an essential part in evolution. Further, the details of the growth dynamics can be crucial in determining the evolutionary outcome. As we have considered for the dilemma of cooperation and two extremes of microbial growth dynamics, cooperation can either increase only transiently or the higher level can even fixate due to dormancy. Our analytical derived transition line provides the same sufficient condition for the transient increase in both scenarios. Further, the same line is also a necessary condition for the permanent increase for the dormancy scenario. In actual populations, both scenarios are present with a fraction of 20% to 80% dormant bacteria [93]. While the transient increase does not depend on this fraction, the permanent increase is smaller than for purely dormant bacteria. The discussed scenarios for the increase of cooperation, rely on demographic fluctuations which are especially pronounced during population bottlenecks. Such bottlenecks may be caused by seasonal changes of the environment, migration into new habitats and range expansion, e.g. [46, 95–99]. Also if the permanent increase is not present, repeated bottlenecks provoking regular occurring growth phases can favor cooperative behavior by stabilizing a former transient increase. This becomes especially important in the context of biofilms where population structure and involved restructuring mechanisms can drastically change evolutionary outcome [66, 71, 72].

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[100] In this work, we assume the relative parts to be independent of the system size. However, including an density dependent part also in the relative terms is straightforward.
[101] Similarly, the stochastic dynamics is described by a Fisher-Wright process for discrete time-steps. Other update-rules are based on other fitness-functions or the way one individual replaces another one
[102] To strictly ensure N to vary around N^* with ± 1, the fixed point has to be linear stable with additional higher orders supporting the stability.

6 Structure and the evolution of cooperation

As broadly discussed in Chapter 3, cooperation is ubiquitous in nature but difficult to explain from an evolutionary perspective. To overcome the direct selection advantage of non-cooperating individuals which save the cost for providing the benefit of cooperation, additional mechanisms are necessary. Here, we focus on assortment and the structure of a population. We especially consider cooperation in microbes.

In the following, we review the concepts of kin-, group- and multi-level selection theory and the general biological and ecological factors promoting cooperation in structured populations. Subsequently, the biology and ecology of microbes, their life-cycles and the formation of biofilms and colonies are discussed. Our work, which analyzes the evolutionary and growth dynamics in structured populations is shortly introduced and we end this chapter with a discussion setting directions for future work.

6.1 Assortment and the theories of kin- and multi-level-selection

As noted in Section 3.5, the principles promoting cooperation can be roughly divided into two categories: *reciprocity* and *assortment*. Here, we focus on the second category.

By assortment, cooperators preferentially interact with other cooperators. They hence benefit from the other cooperators while at the same time running a lower risk to be exploited by non-cooperating free-riders. Importantly however, free-riders are still better off than neighboring cooperators and hence assortment has to be safeguarded continuously to ensure cooperation to be maintained: additional principles are required.

6.1.1 Biological and ecological factors promoting cooperation

Assortment can be provoked by a number of biological and ecological factors. The details differ from situation to situation but the factors can be roughly divided into two classes: *active assortment* and *passive assortment*. Note however, that, as for the classification of the more general mechanisms promoting cooperation, other authors might prefer different classification schemes, e.g. [53, 138, 139].

For *active forms of assortment*, individuals contribute actively to a positive assortment; cooperators 'preferentially' engage with other cooperators. This requires the capability of cooperators to identify other cooperators, e.g. *kin-discrimination*[1]. Obviously, kin-discrimination is

[1] If kin is meant in the 'weak' sense, then kin-discrimination simply means recognition of other cooperators; the meaning of kin is discussed in more detail in Section 6.1.3.

present in higher developed organisms, like animal populations [64]. But it also occurs for less sophisticated forms of life[2]. Examples are green-beard genes [140, 51, 141, 142] as observed for microbial organisms [143, 144]: The green-beard gene directly encodes for cooperation, kin-discrimination and some sort of assortment mechanism, such that, induced by some activity of the organism, there is sufficiently high assortment of cooperators for cooperation to be maintained. See also Section 6.2.3 for a specific example in *Dictyostelium discoideum*. Furthermore, note that green-beard mechanisms must be stable against cheating mutants which pretend to be cooperators, see e.g. [145, 146, 141, 142].

For *passive forms of assortment*, cooperators more often engage with other cooperators due to the external environmental conditions, there is no active part of the organisms involved. One important ecological factor passively promoting assortment is *limited dispersal* [140]. For example, in microbial populations, the viscosity of the surrounding media can hinder mobility and hence individuals 'interact' only with neighboring ones. Often these individuals share the same genes as they stem from the same cell lineage. In general, populations can be highly heterogenous, and passive forms of assortment can permanently sustain sub-populations in which cooperators engage with other cooperators more often than in well mixed populations.

More formally, assortment is described by the theories of inclusive fitness, kin-, group- and multi-level-selection. As the details of assortment and the exact meaning of terms is often controversial, we here first present a *two-level setup* where there is a strict assortment of individuals into distinct groups. This example also illustrates that, for active as well as passive forms of assortment, the advantage for cooperators by positive assortment has to act against the selection advantage of free-riders for cooperation to be maintained.

6.1.2 A two level setup

Consider two types of individuals, A, and B. Individuals are assigned to (assorted into) different groups, $m = 1...M$, see Fig. 6.1(a). Individuals are able to reproduce but fitness also depends on the group's composition. Natural selection is then in principle determined by two levels: *intra-* and *inter-group evolution*. First, if different types of individuals in a group possess different reproduction rates, there is selection towards higher reproduction rates within groups. Second, regarding inter-group evolution, groups can do better or worse depending on their internal composition. The total evolutionary outcome depends on both levels. If both, intra- and inter-group evolution favor one type of individuals compared to the other then the evolutionary outcome is obvious and the interplay between both levels only sets the time-scale of selection. In contrast, if both levels favor different types, than the interplay is important. In particular it sets the sign of change: Whether type A or type B increases its global fraction in the population depends on the exact interplay of intra- and inter-group evolution. Many forms of cooperation discussed in Section 3 resemble such a scenario: there is a selection disadvantage of cooperators within each group due to the the costs for providing cooperation, while at the same time, groups benefit from cooperation.

Mathematically, the interplay of both levels can be described by the Price equation approach as introduced in Chapter 2. For the two-level setup it was first introduced by Price and

[2] Again, especially when 'kin' is used in the weak form.

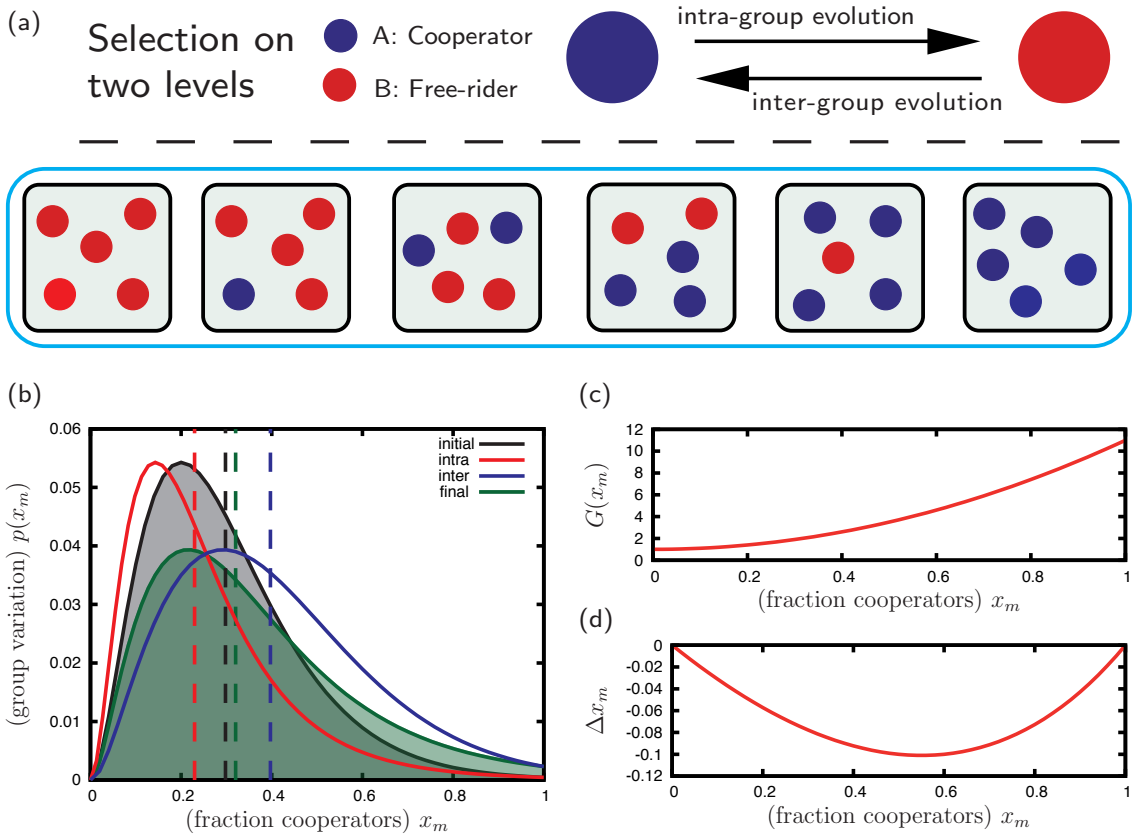

Figure 6.1: Selection on two levels. (a) The meta population consists of individuals assorted into groups. There is intra- and inter-group evolution. For the public-good scenario considered here, intra-group evolution selects for free-riders while inter-group evolution selects for cooperators. (b) The evolutionary outcome depends on the exact interplay of both processes. Here it is plotted for a whole ensemble of groups and a specific intra- and inter-group evolution. The black line shows the initial distribution of group-compositions, the average level of cooperation is shown as dashed line. In a given time interval this distribution and the average change according to the group fitness and the change within each group. The group fitness is shown in (c) and is higher for more cooperative groups. If only inter-group selection is considered, then one obtains the new distribution and average shown in blue in (b). The change within each group is shown in (d), the level of cooperators declines in each group due to the selection advantage of free-riders. If only intra-group selection is considered, then one obtains the distribution and the average value shown red in (b). The total outcome following by both processes is shown in green in (b). Cooperation has increased, the average level of cooperation here is larger than the initial value. In general, this change is described by the Price equation (6.2). Hamilton's rule, (6.6), states if the change is larger or smaller than zero. In addition, not only the average, but also the distribution of group-compositions changed in this example. In particular, the fraction of cooperation declined within every group. Thus, if the advantage on the group-level should be sufficient to overcome intra-group evolution also for several generations, additional impacts are required to maintain highly cooperative groups. Note that one generation here means the time for which the group-fitness and the direct fitness within groups are constructed.

Hamilton [25, 26]. We here review this work, see also [147, 27, 28, 148]. The following considerations do not rely on specific fitness forms. However, it is instructive to think of a specific example, the dilemma of cooperation with individuals of type A being cooperators and those of type B being free-riders. Cooperation is assumed to be linked with a public good, beneficial to *all* individuals in the group.

Furthermore note that the two-level system considered above suggests that a strict separation of groups is required for the mechanism to work. However, this is not the case as the notion of a group can be used in a much more general sense, i.e. arbitrary forms of structure assorting into *sub-populations*. Examples include individuals interacting with neighboring individuals on lattices or on network-structures.

Intra-group evolution

Let us first consider the evolution within one specific group m. In that group, the two different types, A and B are presented with the abundance x_m and $1-x_m$, respectively. The evolutionary change within the group (intra-group evolution) depends on the *direct fitness* Φ_A and Φ_B, i.e. the expected reproduction rate of the individuals belonging to the two types within the group[3]. The expected change can be described by a Price equation, see also Section 2 and Eq. (2.3). Here the change $\Delta x_m = x'_m - x_m$ of the fraction of type A in group m is given by,

$$\bar{\Phi}_m \Delta x_m = \mathrm{Cov}_m(\Phi_{i,m}, x_{i,m}) = [\Phi_A - \Phi_B]\, x_m(1-x_m). \tag{6.1}$$

$\bar{\Phi}_m = \Phi_A x_m + \Phi_B(1-x)$ denotes the average direct fitness within the group. As in Section 2, this is the change within a fixed time-interval[4]. i denotes the possible characteristic properties of individuals and here only takes the two values 0 and 1 (corresponding to the two types A and B)[5]. Compared to Eq. 2.2, there is no second term as we ignore processes like migration or mutation which directly (and not fitness mediated) drive the change of x_m within a group. When considering the dilemma of cooperation, the fitness of cooperators A is lower than the one of non-cooperators B, $\Phi_A < \Phi_B$. Thus, the fraction of cooperators, x_m, declines within every group. For example, for frequency independent fitness-terms, $\Phi_A = 1$ and $\Phi_B = 1+s$ with a selection advantage s of free-riders, change in x_m is given by $\Delta x_m = -s x_m(1-x_m)$ in the weak selection limit with $s \ll 1$ and $\bar{\Phi} \approx 1$.

Inter-group evolution and total change

Up to now, we have only considered intra-group evolution. Inter-group evolution can be taken into account by a Price-equation acting on the group level. Let us consider the global fraction x of individuals belonging to type A. It follows from the local fractions x_m within every group by $x = \sum_m x_m p_m$. Here, p_m describes the statistical weight of group m for

[3] To avoid confusion, note that there are two different fitness functions involved in this setup: direct- and group-fitness.

[4] We denote the new state by prime, $'$.

[5] If taking other values, then there is an additional conversion factor between the average character and the fraction of cooperators.

the composition of the total population. In the easiest case it is directly proportional to the group-size N_m, but other weights, like for example survival probabilities of groups, can also be considered. Importantly, these weights can change because of inter-group evolution: groups are doing differently well. If we assign a *group-fitness* G_m to each group, the new weight of group m after evolution during the fixed time interval is given by $p'_m = G_m p_m / \langle G_m \rangle$ where $\langle G_m \rangle = \sum G_m p_m$ is the expected group fitness.

Let us now consider the global change of x. In addition to the change of individuals within each group, the global change of x also depends on the change of the statistical weights of the groups, $\{p_m\}$. It is described by the Price equation,

$$\langle G_m \rangle_{p_m} \Delta x = \underbrace{\mathrm{Cov}_{p_m}(G_m, x_m)}_{\text{inter-group}} + \underbrace{\langle G_m \Delta x_m \rangle_{p_m}}_{\text{intra-group}}. \tag{6.2}$$

The first term describes the influence of inter-group evolution. It is determined by the covariance between group-fitness and the composition of groups, $\{x_m\}$. The second term describes intra-group evolution. The change within every group is described by Eq. (6.1) and couples to the global change according to the group weights $\{p_m\}$.

Hamilton's rule

For the dilemma of cooperation, the group-fitness G_m increases with the level of cooperation x_m, while the change of cooperation within each group, Δx_m, is negative, the defectors B have a selection advantage in direct fitness. Such a scenario is illustrated in Fig. 6.1 (b), (c) and (d). Cooperation in the total population can increase if inter-group evolution prevails over intra-group evolution and hence, following Eq. (6.2) and Eq. (6.1), if,

$$\mathrm{Cov}_{p_m}(G_m, x_m) + \langle G_m \mathrm{Cov}_m(\Phi_{i,m}, x_{i,m}) \rangle_{p_m} > 0. \tag{6.3}$$

This condition is a generalized form of *Hamilton's rule*. Following Price, it is usually stated in a different form by writing the covariance of two stochastic variables as $\mathrm{Cov}(A, B) = \beta(A, B)\mathrm{Var}(A)$, with β being a regression coefficient. With that, Eq. (6.3) is given by,

$$\beta(G_m, x_m)\mathrm{Var}_{p_m}(x_m) + \langle \beta_m(\Phi_{i,m}, x_{i,m})\mathrm{Var}_m(x_{i,m}) \rangle_{p_m} > 0. \tag{6.4}$$

If groups do not differ in structure such that the group-fitness only depends on its internal composition, than β_m is the same for each group and we can write,

$$\beta(G_m, x_m)\frac{\mathrm{Var}(x_g)}{\langle \mathrm{Var}(x_{i,m}) \rangle} + \beta_m(\Phi_{i,m}, x_{i,m}) > 0. \tag{6.5}$$

If we introduce the *relatedness*, $\mathcal{R} \equiv \frac{\mathrm{Var}(x_g)}{\langle \mathrm{Var}(x_{i,m}) \rangle}$, recall that $\mathcal{C} \equiv -\beta_m(\Phi_{i,m}, x_{i,m})$ is larger than zero because of the costs and $\mathcal{B} \equiv \beta(G_m, x_m)$ describes the benefit on the group level[6], then we can phrase this condition in the most famous way, Hamilton's rule,

$$\mathcal{B}\mathcal{R} > \mathcal{C}. \tag{6.6}$$

[6] not to be confused with the payoff-values, used in Section 4.3.1.

This is the mathematical correspondence of the statement that inter-group evolution can in principle dominate intra-group evolution: For an increase in cooperation, the benefit weighted by the relatedness has to exceed the costs. Note however, that all three variables are functions which depend on $\{x_{i,m}\}$ and hence on the current state of the system. As pointed out by Chuang et al. in [148], $\mathcal{B}$, $\mathcal{R}$, and $\mathcal{C}$ can only be assumed to be numbers if the fitness terms $\Phi_{i,m}$ and G_m depend linearly on the frequencies $\{x_m\}$.

Importantly, Hamilton's rule is not a fixed condition which always promotes cooperation once it is satisfied, but the variables and functions involved can change over time. Thus, while the condition can always be stated for a specific situation at a certain time, its predictive power for analyzing evolutionary outcome is limited. This is not surprising, as the Price-equation itself says nothing about the detailed dynamics but describes the change during a fixed time interval, given the fitness-values for that certain time-window. See also the discussions in Section 2. Furthermore, as stated above, additional requirements are needed to ensure a permanent assortment of cooperators (a sufficient high relatedness $\mathcal{R}$) and thereby cooperation to be stable. For a full understanding the specific mechanisms promoting assortment and how those provoke changes of the state $\{x_{i,m}\}$ have to be considered. In the manuscript at the end of this chapter, we perform this approach for a specific scenario: growing microbial populations in structured populations.

The setup introduced above can be extended to several levels as schematically shown in Fig 3.2, see e.g. [26, 28]. This framework is hence often called *multi-level selection theory*: Selection acts on several levels, with different levels being differently importance for the evolutionary outcome. Of prominent interest are the conditions which can lead to a *shift in the level of selection*, i.e. the conditions which crucially change the relative impact of different levels. Such shifts are assumed to be involved in many major transitions towards higher biological complexity [50, 28], see Section 3 for further discussion. One example is the evolution of multi-cellularity which has been considered for different model organisms [149, 150] and in a number of theoretical models, e.g. [151, 152].

6.1.3 The controversial debate on kin- and group-selection

The idea that assortment can promote cooperation has led to controversial debates between proponents of kin- and group-selection. In the following, we outline the history of both theories and highlight the different attitudes in this debate as well as the semantic confusion which has evolved over time. It is probably this semantic confusion which makes it so difficult to settle this debate. Historical aspects of this debate are given in [28, 153, 154]. See also [155] and [54] for reviews written from the group-selection and kin-selection perspective, respectively.

Kin-selection

In many contexts the idea that assortment of individuals can promote cooperation is called *kin-selection* [140, 156, 157, 158]. However, the mechanism does not rely on the presence of 'real kin' like family members, but kin is often meant in a 'weaker' sense. This stands in contrast to the historical usage of the term, we here give a brief historical overview.

In its original form, kin-selection, the idea that interactions with relatives to increase their reproduction success on the costs of one's own is beneficial, has already been acknowledged by Fisher and Haldane [38, 39]. Cooperative behavior supports close relatives sharing the same genes. Thereby, cooperation promotes the spreading of related genes. Nowadays, it is often introduced by stating a shortened quote from Haldane [159], for example:

> You can jump into the river and risk your life to either save two brothers or eight cousins.

What sounds reasonable if thinking in terms of genes to be transmitted to future generations, cannot work without additional requirements. One should extend the quote mentioning several constraints, for example still thinking of human behavior:

> You can jump into the river to either save two brothers or eight cousins, provided that you can reliable recognize the people in the river as your brothers and cousins and you are sure there are no cuckoo's eggs involved.

Haldane was very aware that additional requirements are needed to ensure kin-selection to work and therefore stated [159]:

> But on the two occasions when I have pulled possibly drowning people out of the water (at an infinitesimal risk to myself) I had no time to make such calculations.

Hamilton formalized the idea of kin-selection and especially used it to study cooperation in hymenoptera like ants or bees [160, 140]. There, relatedness on a genetic level is high and kin-selection[7] is certainly involved in promoting cooperation. In his approach, he distinguished factors directly and indirectly influencing the fitness. While direct factors, e.g. the metabolical cost for providing a benefit, immediately affect the fitness of the individual at focus (direct fitness), the indirect fitness describes how an individual benefits from related individuals. The relatedness is measured by a quantity $r \in [0, 1]$ which scales the impact of related individuals on the indirect fitness. Mathematically, the interplay between direct and indirect-fitness are described by *inclusive fitness*.

For the dilemma of cooperation, the direct fitness of cooperators is lower than that of non-cooperators because of the costs, while the benefit of cooperation is given to the related individuals. Cooperation can increase in such a setup if Hamilton's rule is fulfilled,

$$b \cdot r > c. \tag{6.7}$$

This is the original formulation of Hamilton's rule, which is a special case of the more general formulation given before, Eq. (6.6). In the original sense of kin-selection and the formulation by Hamilton, relatedness r means the similarity of genes and the genome; 'relatives belong to the same family'[8]. However, relatedness is ambiguous and often misunderstood. Let us for example consider a situation where cooperation is encoded by a single gene. Then, although

[7] Kin-selection in the strict sense as considered below.

[8] Terming in the *gene's eye view*, cooperative genes are selected because they are also reproduced in other, related individuals. This view, however, might be problematic, selection is mainly acting on phenotypes and not on the level of genes.

genetically very similar, individuals highly related to cooperators might not show the cooperative behavior anymore [9]. Thus, while promoting the spreading of relatives, cooperation is not promoted by such a kin-selection mechanism and its level is expected to decrease. It follows: For kin-selection to promote cooperation, a sufficient high relatedness has to be ensured not for the whole genome but for the specific trait (or gene) which promotes cooperation.

For kin-selection to act, relatedness in a 'weak sense' is sufficient[10], i.e. cooperators preferentially engage with other cooperators independent of the degree of relationship regarding other traits. The approach by Price, stated in Section 6.1.2 for the two-level setup, exactly makes use of this more generalized understanding: assortment of cooperators is needed but real kinship is not necessary. Hamilton later acknowledged Price's approach as more general and adopted it. For example, he introduced the two-level approach as considered before [26].

As pointed out by a number of authors, the original formulation of inclusive fitness theory by Hamilton [140] and Price's two-level approach [25] are formally equivalent for standard situations and can be mapped to each other. This especially includes cases where fitness terms depend linearly on frequencies, see e.g. [28, 161, 162]. Importantly, the notion of inclusive fitness is nowadays mostly used in a more general sense, corresponding to the approach by Price [25] and the more recent work by Hamilton [26]. In particular, it does not rely on linear fitness terms.

If meant in the stronger sense, kin-selection is probably only of minor importance to explain cooperation in populations, however it is of major importance for multicellular organisms: In fact, the evolution of a separated *germ-line* and the start of development with a single zygote prevents multicellular organisms from permanently being threatened by non-cooperative cells [163]. At least in this sense, Wilson's manuscript title 'Kin Selection as the Key to Altruism: Its Rise and Fall' is highly overdramatized [164].

In total, kin-selection in the presented weaker sense resembles the approach by Price. And if one is aware of this notion of kin, then nothing is wrong with using the kin-selection or inclusive fitness theory. Although, regarding kin-selection, it is not typical to term mechanisms by their consequence instead of their cause.

Group-selection

With the origin of evolutionary theory, the idea of groups being the entities of selection was bound to occur and Darwin had already proposed to consider such scenarios in his book 'The Descent of Man' [165]. A first mathematical model investigating group-selection was introduced by Wright [94, 40]. Already since then, the concept of group-selection has been a controversial issue, since it focuses on selection on the group level and, at least in its original formulations, did not pay too much attention on selection within groups (intra-group evolution). Despite that, the theory of group-selection was widely used uncritically and especially put forward by Wynne-Edwards [166] in the mid of the 20th century. For many the

[9] One point mutation on the cooperation encoding DNA sequence might be sufficient to lose cooperation while the total relatedness remains high.

[10] Or, depending on the point of view, in an even more strict sense, since relatedness has to occur specifically regarding the cooperative trait.

dilemma of cooperation was solved: there is cooperation because an advantage on the group level; *species selection* was a presentable term.

However, this did not hold for long. With critics formulated drastically by Williams [167], the group-selection idea was abandoned: There is selection within the group, and this level is expected to dominate the dynamics. This view was shared by Maynard-Smith who tried to corroborate it by a mathematical model taking both levels of selection in groups into account, the haystack model [168]. Since then the line of thinking was: group-selection is possible in principle but not practically. If group-selection is meant in the strict sense of Wynne-Edwards then this statement is presumably true. However, as illustrated by the two-level setup considered before, selection on the upper-level can have a substantial influence on evolution and can provoke cooperation. Of course, the conditions must be such that the upper level dominates the dynamics. These are the same conditions which are also needed for kin-selection to work.

In total, when studying selection on the level of groups, one always has to take selection within groups into account and has to check which level dominates. The Price equation approach, see Section 6.1.2, and reliable mathematical approaches modeling specific situations are exactly doing that. Many different variants of selection involving group-structures have been modeled. See e.g. [169, 170, 171, 172, 173, 174, 145, 175, 176, 177, 178, 179].

Finally, if one denotes such a process where both levels are involved as a new form of group-selection, then nothing is wrong with the term group selection.

The debate goes on

The historical debate provoked a lot of semantic confusion [180] being stably upheld today [181]. Further, different people are still appraising the importance of the two perspectives differently. See for example the discussion between Traulsen et al. [176] and Lehmann et al. [182] or West et al. [180, 138] and Wilson [183] or Wade et al. [184] and Wild et al. [185, 186]. Most recently for this thesis, Nowak et al. doubted the generality of inclusive fitness [187]. This provoked heavy objection by the biological community working on issues of cooperation, see [188, 189, 190, 191, 192] and the reply [193].

Nevertheless, the majority (including the majority of the authors cited before) agrees that assortment (or whatever one likes to call it) is the key to cooperation and that multi-level selection theory (or group-selection in a careful sense including intra-group evolution) and kin-selection theory, (with kin in a weak sense, or inclusive fitness theory) are just different perspectives of the same mechanism promoting cooperation.

Despite this consensus within a large part of the community, the debate between some advocates of group- and kin-selection continues. We hope also those will soon agree that each side is right and that only the perspective differs. To phrase it colloquially, it is time to uncover the last page in David McKees' brilliant picture book 'The two monsters' [194]. Moreover, neither the Price-equation approach on multiple levels, nor the generalized forms of Hamilton's rule and the inclusive fitness approach can explain any form of cooperation without taking more microscopic details into account. And, if details are considered with a specific

biological context at hand, then there is hopefully less to debate about as terms should be clear.

Here, we want to understand the specific conditions driving cooperation in microbial populations. Microbes serve as starting point to understand the evolution of cooperation also for biologically more complex organisms. Already for microbes however, the additional ecological and biological factors promoting cooperation can be very diverse and include more sophisticated mechanisms as will be reviewed in the next Section 6.2. In this chapter ,we specifically consider the evolution of microbes in structured populations and the role of demographic fluctuations, growth dynamics and bottlenecks.

6.2 Microbes

Already for a long time, microbial organisms have been used to study evolution. Their short reproduction times, the ability to cultivate them under controllable laboratory conditions, as well as the possibility to 'freeze' strains to analyze them later on, make those organisms the ideal candidates for studying evolution experimentally [195]. Such experiments serve as a broad testing field for the modern synthesis and, in combination with theoretical models, can hopefully lead to a better understanding of many general aspects like mutation-accumulation, random drift or long-time evolution. One of the most prominent examples is the Luria-Delbück experiment showing that mutations occur spontaneously and are not induced by changing selection pressures [196]. Long-term evolution in *Escherichia coli*, as studied by Lenski and others, is a further convincing example [197]. Moreover, as it increasingly becomes clear, microbes interact in very complex ways with each other and the environment. They can form highly organized colonies which even process through different stages of a life-cycle [198, 199]. Understanding the evolution of such more complex behavior in microbial organisms can therefore help to understand the evolution of complexity in higher organisms. Aspects include the evolution of cooperation and competition [67, 200, 201], the emergence of multicellularity [202, 203] and even aspects of aging [204, 205]. In the following sections, we give a short overview of the microbial world and especially consider cooperation of microbes and the dynamics in life-cycles.

6.2.1 Microbial colonies and biofilms

In nature, microbes typically do not occur as single cells, fairly separated from others but within large colonies. These colonies are not just simple aggregations of cells but can show an enormous complexity in terms of structure and dynamics. First, the composition of the colonies can be very heterogeneous with individuals belonging to different species, the same species but different genotypes, or also different phenotypes of the same genotypes (*phenotypic heterogeneity* [202]. Second, microbes are capable of intercellular signaling. By such an interchange of information, microbes are able to adjust their gene-expression patterns and thus the physiological behavior with respect to others [206, 207]. One famous example is *quorum sensing* where the metabolical response of single microbes depends on the density and size of the surrounding colony[11]. Third, microbes engage in the formation of *biofilms* by actively

[11] See quorum sensing and bioluminescence of *Vibrio fisheri* for an impressive example [208].

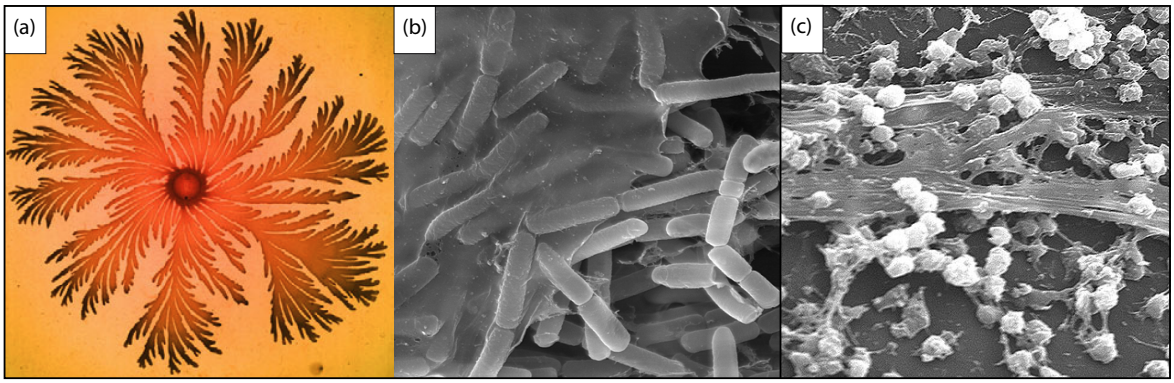

Figure 6.2: Bacterial colonies in nature occur in a variety of forms. (a) A macro colony of about 10^{10} individuals of *P. dendritiformis*. When growing on a surface, complex branching patterns can be formed [209]. (b) *Bacillus* bacteria and the production of matrix proteins. Photo by Dennis Kunkel Microscopy. (c) *Staphyloccocus aereus* biofilm on a catheter. Picture by Rodney M. Donlan and Janice Carr.

releasing proteins, lipids, smaller metabolites or other bio-molecules into the environment. These biofilms are highly abundant in nature and show an astonishing diversity [199]. By the production of matrix proteins, biofilms are cohesive entities which are strongly attached to surfaces. They can be highly structured, optimized for example for nutrient uptake and disposal of waste. The formation of biofilms can dramatically improve the survival rates of the involved microbes. By the formation of a protecting protein shield and the fixed adjustment on a surface, microbes can better sustain and survive in diverse environments: Biofilms are forearmed against for example drought, biocidal agents, or antibiotics. With respect to this complexity, people have called microbial population to show forms of 'social' behavior comprising aspects like communication, cooperation, or even division of labor, see e.g. [66, 68]. Independently of the details, cooperation and the production of public goods is an important requirement for the formation and maintenance of biofilms.

6.2.2 Cooperation in microbial populations

Cooperation in microbes is often related to the production of a public good which increases the growth or survival rates of neighboring individuals or of the whole colony. While cooperators are *producers* of the public good bearing the metabolical costs for its provision, free-riding *non-producers* save the costs of production while still benefitting from the public good of cooperators.

Environmental conditions can strongly change in nature. In particular, costs and benefit of production can widely vary, and many public goods are simply needed to survive. Thus, it is not easy to untangle the precise role of cooperation in such microbial systems. To better unveil cooperation and the precise factors promoting it, people have studied cooperation in highly controlled setups in the laboratory. Synthetic systems have also been studied providing even more control [210, 148]. In the following, we shortly review some of the organisms and the specific public-good situations which have been considered.

One prominent example of cooperation is the iron-uptake in *Pseudomonas aeruginosa* [211, 212, 213]. There, cooperators are producers of *siderophores*, i.e. iron-scavenging molecules. Due to their high binding affinity with iron, these molecules can effectively bind single iron-atoms when released into the environment and when taken up again strongly support the iron-uptake of each individual. However, production is related to metabolical costs, producers have a selection disadvantage compared to non-producing free-riders. Different experimental situations have been considered, e.g. [214, 215, 216, 217, 218].

Another example is the sucrose uptake in the budding yeast *Saccharomyces cerevisiae* [219, 220, 221]. Budding yeast is not able to take up sucrose into the cell but extracellularly has to split it into glucose and fructose. This is performed by the enzyme *invertase* which expressing cells release into the environment where it then can act. Importantly, about 99% of the glucose and fructose diffuse away [220] (in a chemostat where diffusion is high). Non-expressing strains should benefit by saving the metabolical costs for its production. Interestingly, in the experimental setup of Gore et al., they applied a chemostat and thus populations are well-mixed. Nevertheless, coexistence of producers and non-producers with a large fraction of producers can be stable. One possible reason for this is the non-linearity of the growth function [220]. If the concentration of invertase is low, then glucose level in the cell is low, and it strongly pays off to produce invertase despite the high dispersal rate of the cellular suitable sugar.

Further examples of cooperation include the formation of matrix-proteins which, when released from the cell, induce biofilm formation and thereby help the colony for example to attach to surfaces or to protect them against draining. One example is the *wrinkly spreader* strain in *Pseudomonas fluorescens* [222]. Here, matrix-formation does not prevent draining but rather the opposite, the production prevents from drowning: Wrinkly spreaders contribute to the formation of a cellulose sheath which, on a water-air surface, can prevent colonies to sink and hence ensure good oxygen supply. In the context of microbial systems, group-selection was first experimentally studied with this system [223]. See also Section 6.1.3 and the discussion on group-selection. Further, see [224] for another example involving *P. fluorescens*.

Another form of cooperation is the emergence of altruistic stalk-cells during fruiting body formation [149, 225]. Here, the benefit of cooperation is not directly linked to the growth rate or survival probability of the surrounding populations, but given by an increase in dispersal rates. See also the discussion in Section 6.2.3.

Similar to cooperation in other organisms, there is no universal solution to the dilemma of cooperation in microbial populations, cf. Sec. 3. If colonies are clonal then there is no dilemma of cooperation. Speaking in the framework of group-selection, selection is only on the group level, and cooperation clearly increase the fitness. Although isogenic, not all individuals have to be the producers of a common good but there can be *phenotypic noise* [226]. However, independent of such details and as discussed before in Section 3.5, additional requirements are needed to ensure isogenic populations and thereby cooperation in the population. What prevents a non-cooperating mutant to spread in the population? More sophisticated mechanisms like punishment are discussed to occur in microbial populations, but the main pathway towards cooperation is assortment [227, 228, 229, 67, 203, 226, 230, 231, 232, 233]. The ecological and biological factors ensuring this assortment persistently in microbial populations can be

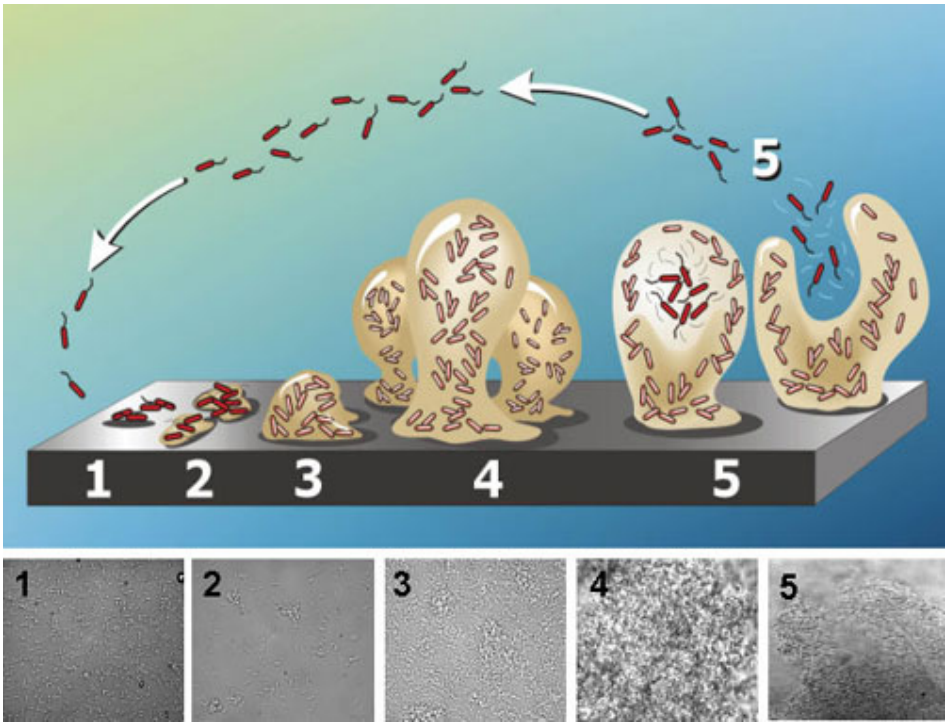

Figure 6.3: Different steps of bio-film formation as widespread in procaryotes. At the top, schematical view of the life-cycle. The dynamics can be divided into five different steps, (1) loose attachment, (2) adhesion, (3) aggregation into micro-colonies, (4) growth and maturation, (5) and dispersal. The pictures at the bottom show the corresponding observation in a biofilm of *Pseudomonas aeruginosa* [234]. Cartoon by P. Dirckx and D. Davies, Montana State University, see also [198].

multifarious. One example is the permanent growth of bacterial fronts. Demographic fluctuations at the front can here lead to heterogenous fronts and areas of cooperation can form [200]. Especially nutrient dynamics and its interplay with population growth can play a crucial role. Another important aspect in microbial populations is the structure of the population and the separation of the population into sub-colonies. Selection can be strong and non-cooperating sub-colonies simply not viably. But non-cooperative groups might also survive. To provoke cooperation in such setups, a permanently regrouping among sub-populations is needed. In the manuscript at the end of this chapter, we study reoccurring bottlenecks where populations or sub-populations are subject to massive population decline and pass states with very small population-sizes. As discussed in the following, such bottlenecks can occur quite often in microbial populations as many microbial organisms undergo highly evolved life-cycles and bottlenecks are genetically conceived within the dynamics of the organism.

6.2.3 Dispersal and life-cycles

Associated with the rapid improvement of observation methods and the knowledge how to more naturally cultivate microbes in the laboratory, it became obvious that many microbes and collectives of them process through different steps of a life-cycle. Especially, different

complex forms of dispersal have been observed.

Bacterial biofilms

As discussed in Section 6.2.1 many bacterial species form biofilms. Interestingly, many of these organisms process through different developmental steps while arranged within a biofilm. Roughly, biofilm formation can be divided into five steps [234, 198]; cf. Fig. 6.3. First, bacteria loosely attach to a surface. Second, there is strong adhesion to that surface. In a third step, bacteria aggregate into micro-colonies, followed by, 4th, a growth and maturation phase. The final 5th step is given by a dispersal step. These steps have been observed experimentally for example for *P. aeruginosa* [234] and the schematic view in Fig. 6.3 is directly deduced from these observations. The proposed steps of a life-cycle seem to be rather conserved in prokaryotes. However, the exact dispersal mechanisms are very diverse [199]. Besides passive forms involving dispersal of single microbes or whole clumps of the biofilm mediated by the surrounding fluid, there are also active forms. This includes swimming of single microbes or gliding on a surface. Sporulation and the formation of fruiting bodies is also observed in microbial populations. For example, this is studied very well in the proteobacterium *Myxococcus xanthus* [225].

Dictyostelium discoideum

Another prominent example of cooperation and a complex life-cycle is observed in the fruiting-body formation of the slime mold *Dictyostelium discoideum*. This 'social amoeba' has become a model organism in biology to understand cell-signaling, phagocytosis, chemotaxis, differentiation and multicellularity [235, 149]. While living as single cells in the presence of prey bacteria, a complex aggregation-process is triggered in the absence of nutrients. Mediated by cyclic AMP, single amoebae attach to each other by chemotaxis. The formed aggregate consists of 10^5 to 10^6 cells in the laboratory, and starts to differentiate. Via many intermediate steps and after approximately 20 hours, a fruiting body is formed, cf. Fig. 6.4. As the aggregate is formed from different cells in the surrounding environment, fruiting bodies are in generally not clonal but chimeric, i.e. cells belong to different genotypes. Thus, and in contrast to multicellular organisms emerging from a single cell, there is a strong dilemma of cooperation: Cells forming the stalk of the fruiting-bodies do not disperse but die [236, 237, 69]. Therefore strains not contributing their fair share to stalk-formation are free-riders exploiting the stalk-formation mainly promoted by other strains. A lot of cheating strains are known [70]. Kin-discrimination during chemotaxis and the differentiation process plays a major role for cooperative strains to sustain in nature [238, 239]. For example, the *csA* gene has been identified as green-beard gene [143]. The gene encodes membrane proteins which lead to the preferential attachment of other individuals also producing this protein.

Parasites and hosts

Complex forms of life-cycles are also known for many parasites. One intriguing example is given by *Plasmodium falciparum* and other *Plasmodia* strains. *P. falciparum* is the pathogen

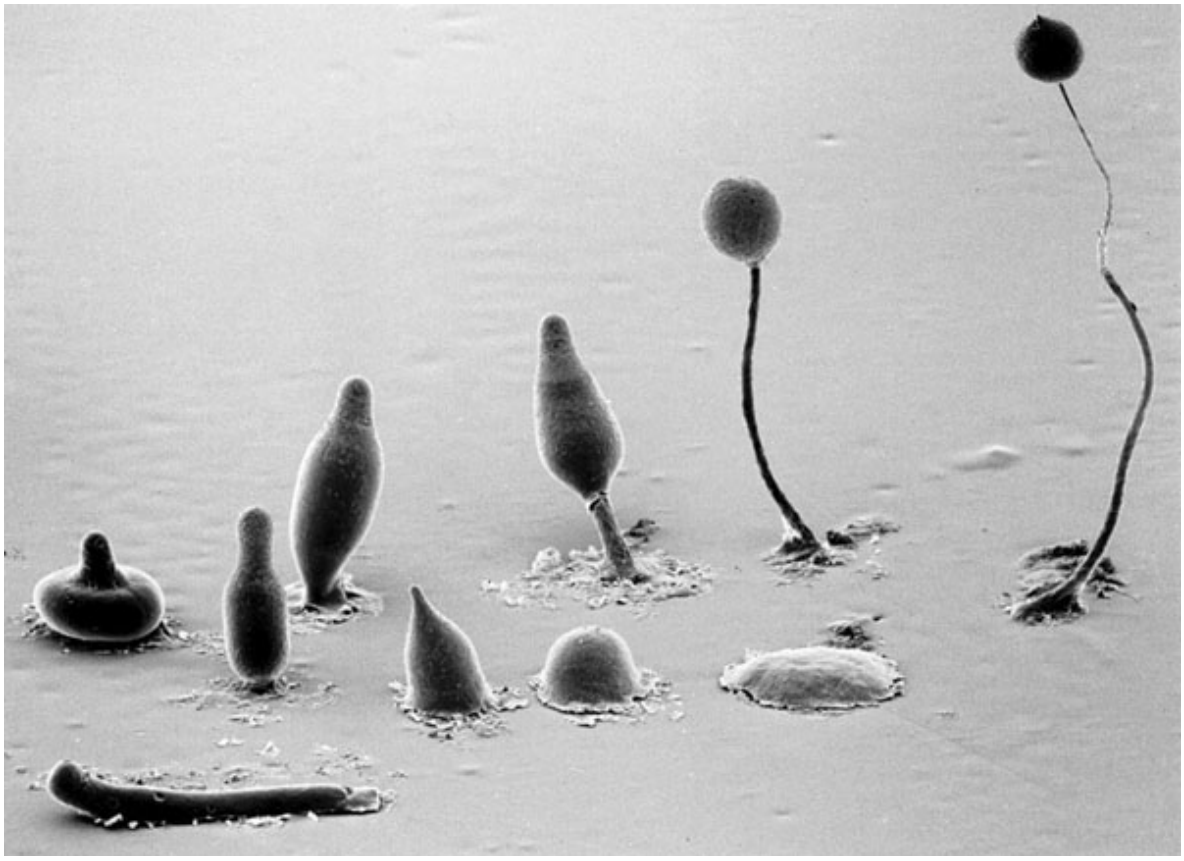

Figure 6.4: Fruiting body formation of *Dictyostelium discoideum*. Triggered by the lack of nutrients, single amoebae start to aggregate and within approximately 20 hours differentiate into a 'slug' and then into a full fruiting body with approximately 20% of stalk and 80% of spore cells. Stalk cells do not disperse but die and are therefore 'altruistic'. The life-cycle of *D. discoideum* is given by alternating phases of aggregation and single-amoeba states. Picture from the website dictyBase where resources on *Dictyostelia* [240] are collected. Copyright by M.J. Grimson and R.L. Blanton, Texas Tech University.

of malaria tropica, the most abundant and lethal form of malaria [241]. To account of the seriousness of malaria, the life-cycle of *P. falciparum* has been studied very well. The parasite process through up to twelve different steps in its life-cycle, cf. Fig. 6.5. Steps of growth, non-growth, and dispersal steps take turn in humans as hosts and *Anopheles* as vectors. There are several different sexual and asexual stages. Evolutionary aspects of malaria have been studied [242]. For example, already Haldane considered coevolution with humans and the occurrence of thalassemia [243], a blood disease promoting resistance against Malaria. One further example for a parasite with a complex life-cycle is *Dicrocoelium dendriticum*, a parasite fluke which mainly lives in cattle. In this organisms, even three hosts are involved: cattle (mainly sheep and cows), the snail *Cochlicopa lubrica*, and ants like *Formica fusca*. Similar to other eukaryotic organisms like *D. discoideum* and *P. falciparum*, sexual stages occur in the life-cycle. Amazingly, *D. dicrocoelium* manipulates the behavior of ants by sacrificing individuals; there is a dilemma of cooperation. Cooperation has been studied by models of group-selection [169]. Interesting from an evolutionary perspective, the life-cycles of parasites

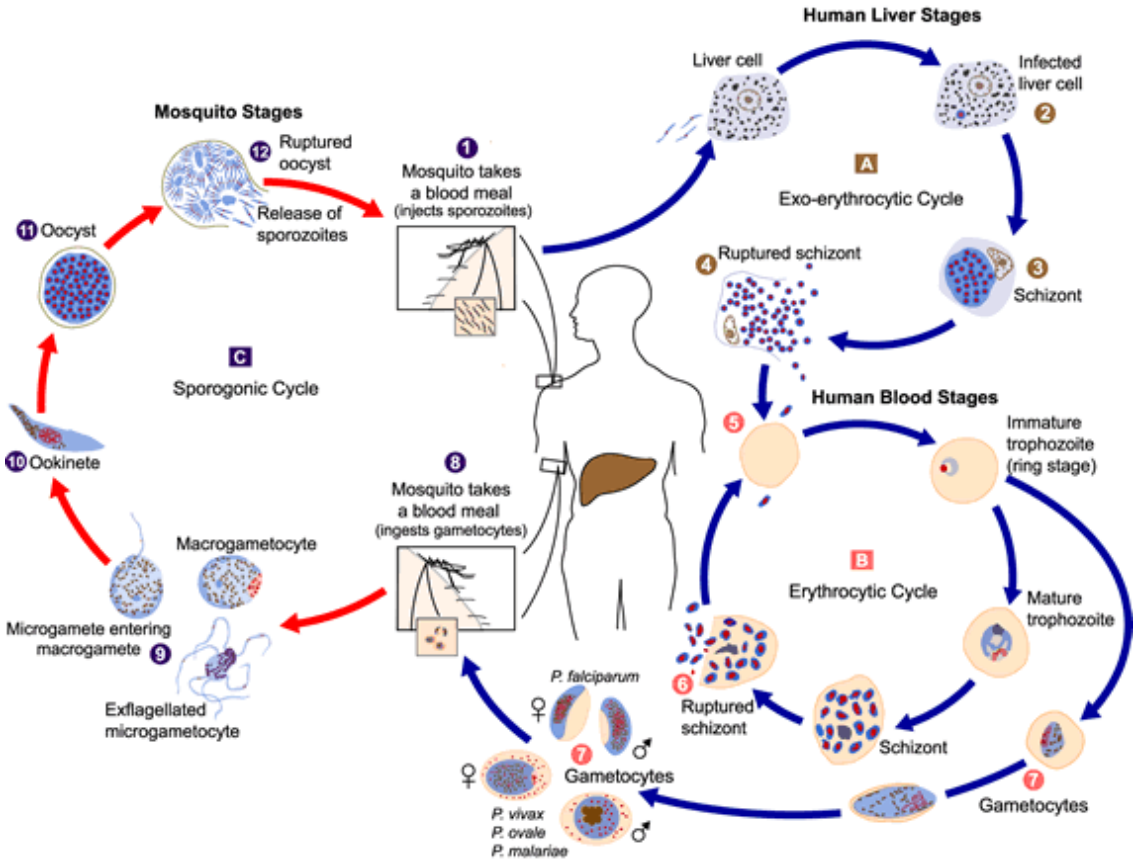

Figure 6.5: The life cycle of *Plasmodia*, the pathogens of malaria. It involves many different steps interchanging between sexual and asexual states, see also text. Cartoon is adapted from the Centers for Disease Control and Prevention of the US government. Information to the different steps and additional images can be found on their website on parasites, DPDx [244].

involve small population sizes during several steps and therefore might have contributed to the evolution of cooperation in these organisms.

6.2.4 Evolution and bottlenecks in experiments

The role of bottlenecks for the evolution and maintenance of cooperation in microbial populations has been studied experimentally. The main idea is to specify a well-defined life-cycle and thereby to study evolution of cooperation under controled conditions. In the following, two main experiments are shortly described.

Griffin, West, and Buckling have studied the role of competition for the evolution of cooperative siderophore production in *Pseudomonas aeruginosa* [214], as introduced in Section 6.2.2. In their experimental setup consisting of several sup-populations and cooperative and free-riding strains, they changed the relatedness of sub-populations, i.e. the ratio how individuals

in a sub-population resemble each other, by adjusting the numbers of individuals founding the sub-colony. Furthermore they differentiate between two different competition setups. For global competition, sub-populations use the same nutrient resources, while for local competition, sub-populations grow separated in different environments. With their setup Griffin et al. showed that high relatedness leads to cooperation, while local competition favors free-riders. In addition, if competition is too local, then even a high relatedness cannot ensure the maintenance of cooperation.

Chuang, Rivoire and Leibler [210, 148] have studied the evolution of cooperation for a synthetical system in a group-structured setup. In their synthetic approach they have integrated components from the *Pseudomonas aeruginosa* Rhl system into plasmids of *E. coli* strains. Cooperators are producers of Rhl autoinducers which they release into the environment. Uptake of Rhl autoinducers by producers and non-producing free-riders triggers the resistance against the antibiotic chloramphenicol. By regulating the chloramphenicol concentration and the external concentration of autoinducers, they can control, in game theoretical terms, benefits and costs of the system. The authors performed regrouping experiments, where they regularly mixed groups and formed new populations. While within groups cooperation declined, they showed that cooperation can increase over time for narrow population bottlenecks during regrouping. In the logic of Price's two level approach selection on the group-level can dominate selection within groups.

These and other experiments [216, 218] stress the role of narrow bottlenecks (in terms of high relatedness or small sizes of founder populations). With these experiments in mind and the ubiquitous presence of life-cycles in microbial populations, we have studied the dynamical aspects of growing populations divided into sub-populations.

6.3 Demographic fluctuations promote the evolution of cooperation

In the manuscript 'Demographic fluctuations promote the evolution of cooperation' by Jonas Cremer, Anna Melbinger, Erwin Frey, which has been submitted for publication, we study the role of repetitive fragmentation into sub-populations for the evolution of cooperation. Similar to the two-level setup in Section 6.1.2, we consider different, locally well mixed groups consisting of cooperators and free-riders. Groups are regularly mixed with each other and individuals are assorted into new groups. We explicitly take the growth and evolutionary dynamics into account and thereby go beyond the Price equation approach and Hamilton's rule. Extending our approach to describe the coupling between evolution and population dynamics, introduced in Section 5.3, we study the impact of demographic fluctuations, size of bottlenecks, frequencies of regrouping events and variation in the growth parameters. We uncover two mechanisms which promote cooperation, the *group-fixation* and the *group-growth* mechanism. The first relies on the fixation of groups and the large advantage of purely cooperative ones, which in the long run can lead to purely cooperative or purely free-riding populations. The second is related to the growth advantage of more cooperative groups and leads to coexistence between cooperators and free-riders. Remarkably, this mechanism also acts for initially very small fractions of cooperators and therefore promotes the evolution of

cooperation when starting with a single cooperating mutant. In the manuscript we discuss the interplay of both mechanisms and their dependence on the dynamical parameters. Our results highlight the importance of a dynamical approach for a full understanding of the evolutionary dynamics. Furthermore, they confirm the experimental results by [245, 210, 148] introduced before and make predictions which can be tested by new experiments. Currently, experiments are performed at the chair of microbiology at the Ludwig-Maximilians-Universität by Prof. Kirsten Jung and Prof. Heinrich Jung.

6.4 Discussion and Outlook

Our introduced dynamical approach to study evolution of cooperation in structured populations assumes random assortment during the group-formation step. It thereby involves only a minimal form of assortment, detrimental for cooperation. In further considerations, the role of biased, non-random assortment is interesting to study. How does a more complex assortment-dynamics change the evolutionary outcome in the long run? Furthermore, assortment in nature does not occur in a highly synchronized way but rather in a continuous manner, regarding only a limited fraction of the population and with a whole distribution of regrouping times. We expect the observed group-growth and group-fixation mechanisms to be stable against such variations, but the details shall be studied in future work.

In addition, we assumed mutation of individuals to other types and migration events between groups to occur only on much longer time-scales then the regrouping dynamics. In contrast, if migration and mutation events are highly abundant then clearly the group-fixation mechanism is not able to act and the evolutionary outcome in the long run changes dramatically. Maynard Smith initially even denied group-selection because of such invasion events [168]. Strikingly however, the group-growth mechanism is very robust against rather high mutation and migration rates as we have confirmed by first studies. The exact impact of both processes remains to be studied, but we expect our dynamical framework to be ideally suited to approach this issue.

The evolution of life-cycles is another fascinating problem to investigate. How can, starting with a very simple dynamics, more and more complex life-cycles emerge. Can one for example explain the original formation of a life-cycle by ecological conditions, which are then increasingly promoted by active, genetically-controlled forms of life-cycle formation? One primitive example of a life-cycle has been proposed for the wrinkly spreader mutants in *P. fluorescens* [246]. Here, the permanent formation and draining of biofilms on the liquid-air surface might give rise to an oscillating dynamics. It is interesting to study the detailed aspects of this dynamics.

Finally, in a broader context, can one take the simple model as starting point also to analyze the more complex life-cycles of parasites? How does the theoretical results compare with the dynamics observed for parasites like *D. dendriticum* or *P. falciparum*. As these have been studied extensively, they might prove to be good model organisms for more quantitative studies of evolutionary dynamics.

Population dynamics and the evolution of cooperation in group-structured populations

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Abstract

Microbes providing public goods are widespread in nature despite running the risk of being exploited by free-riders. However, the precise ecological factors required for the evolution and maintenance of cooperation are still puzzling. Here, we consider the role of population growth and the repetitive fragmentation of populations into small colonies, as also studied in recent experiments. Individual-based modeling reveals that demographic fluctuations, which lead to a large variance in the composition of colonies, promote cooperation. Biased by population dynamics these fluctuations result in two qualitatively distinct regimes of stable cooperation. First, if the level of cooperation exceeds a threshold, cooperators will take over the whole population. Second, cooperators can also emerge from a single mutant leading to a stable coexistence between cooperators and free-riders. We find the frequency and size of population bottlenecks as well as growth dynamics to be the major ecological factors determining the regimes and thereby the evolutionary pathway towards cooperation.

Author Summary

While cooperative traits are widespread in nature, cooperation can be threatened by selfish individuals which save the costs of cooperation. Therefore cooperators go extinct in simple scenarios of Darwinian evolution and it is an enormous challenge to explain why cooperative traits could be maintained, or even introduced in the first place. Recently, microbial systems have been increasingly applied to uncover the evolutionary pathways towards cooperative behavior in the absence of sophisticated mechanisms like recognition or memory. Here we study the intertwined coupling between growth and selection dynamics

in microbial populations which are subdivided into colonies. We investigate how this coupling affects cooperation. In particular we show that the growth advantage resulting from the presence of cooperators in a colony can lead to a robust pathway promoting cooperation. This evolutionary pathway does not only prevent the extinction of cooperators but also enables the evolution of cooperation starting with one single mutant. Once established, cooperative behavior might in turn be stabilized further by additional mechanisms based, for example, on memory and recognition.

Introduction

One pivotal question in evolutionary biology is the emergence of cooperative traits and their sustainment in the presence of free-riders [1–6]. By providing a public good, cooperative behavior of every single individual would be optimal for the entire population. However, non-contributing free-riders may take evolutionary advantage by saving the costs for providing the benefit and hence jeopardize the survival of the whole population. In evolutionary theory kin selection [1, 7–9], multi-level selection [10–13], and reciprocity [14] have been found to provide conceptual frameworks to resolve the dilemma [4–6]. For higher developed organisms, stable cooperation is generally traced back to specific mechanisms like repeated interaction [2,14], punishment [15,16], and kin discrimination [1,6,17,18]. But how can cooperation emerge in the first place and be maintained without abilities like memory or recognition? Answering this question is especially important within the expanding field of biofilm formation [19–23]. There, a successfully cooperating collective of microbes runs the risk to be undermined by non-producing strains saving the metabolically costly supply of biofilm formation [18, 20, 23]. Sophisticated social behavior cannot be presumed to explain the high level of cooperation observed in nature and experiments [18–20, 24–30]. Instead, different forms of limited dispersal, such as spatial arrangements, or fragmentation into groups are essential to resolve the dilemma of cooperation among such microbial organisms [1, 31, 32].

Recent experiments address this question by studying microbial metapopulations of cooperators and free-riders [24,25,27,28,30]. In these setups small founder colonies differing in composition were cultivated in separate habitats like several Petri dishes. When these colonies were repeatedly merged and reformed, an increase in the overall level of cooperation was observed even though free-riders have a growth advantage within every colony. However, the precise conditions under which cooperation is favored are subtle [8, 9, 11, 13, 30, 32–40]. A possible theoretical explanation for the observed increase in cooperation

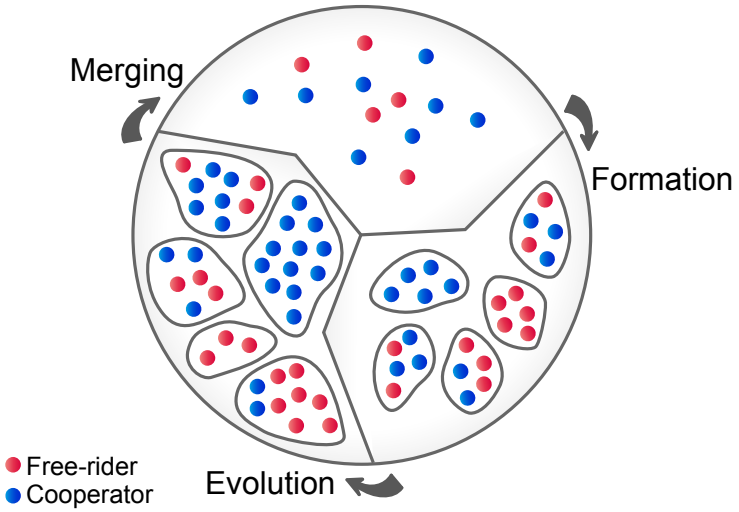

Figure 1. Repetitive cycle of population dynamics. The time evolution of a population composed of cooperators (blue) and free-riders (red) consists of three cyclically recurring steps. *Group formation step:* we consider a well-mixed population which is divided into M separate groups ($i = 1, \ldots, M$) by an unbiased stochastic process such that the initial group size and the fraction of cooperation vary statistically with mean values n_0 and x_0, respectively. *Group evolution step:* groups grow and evolve separately and independently; while the fraction of cooperators decrease within each group, cooperative groups grow faster and can reach a higher carrying capacity. *Group merging step:* after a regrouping time, T, all groups are merged together again. With the ensuing new composition of the total population, the cycle starts anew.

is antagonism between two levels of selection, as widely discussed in the literature [12]. Here, these levels, *intra-* and *inter-group* evolution, arise as population dynamics alternates between independent evolution in subpopulations (groups) and global competition in a merged well-mixed population. Due to the dilemma of cooperation, free-riders are always better off than cooperators within each group (intra-group evolution). In contrast, on the inter-group level, groups with a higher fraction of cooperators are favored over groups with a lower one.

In this article, we study the interplay between the dynamics at the intra- and inter-group evolution and how it may provoke the maintenance or even the emergence of cooperation. We propose a generic individual-based model which includes three essential elements: a growth disadvantage of cooperators within each group, an advantage of groups incorporating more cooperative individuals, and regularly occurring regrouping events; cf. Fig. 1. Well-known from the theories of kin [1, 7, 9, 40] and multi-level selection [12, 28, 40, 41], cooperation can increase in principle: While, within a group i, the fraction of

cooperators, ξ_i, decreases, groups also change their size, n_i, such that the fraction of cooperators in the total population, given by the weighted average, $x = \sum_i n_i \, \xi_i \, / \sum_i n_i$, may still increase. For this to occur, a decreasing fraction of cooperators, ξ_i, within groups must be compensated by changing weights, n_i/N, in the total population of size $N = \sum_i n_i$, i.e. by a sufficiently high positive correlation between a group's size and its fraction of cooperators [41]. Here we want to go beyond stating this mathematical fact and reveal the ecological factors underlying these correlations. To this end the full stochastic dynamics at the intra- and inter-group level will be analyzed. A key element will be the intricate coupling between the dynamics of the composition and the dynamics of the overall size of a group. This applies in particular to microbial populations where the reproduction rate of microbes strongly depends on environmental conditions and thereby on the composition of the population [42]. Therefore, a proper theoretical formulation has to account for a dynamics in the group size [43] rather than assuming it to be constant as in most classical approaches [44–46]. Such a dynamic formulation will allow us to uncover ecological mechanisms for the evolution and maintenance of cooperation.

Motivated by the aforementioned experiments [24, 25, 27, 28, 30], we consider a population of cooperators and free-riders and its evolution in a repetitive cycle consisting of three consecutive steps [32], cf. Fig. 1. In the *group formation step*, the total population with a fraction of cooperators, x_0, is divided into a set of M groups by an unbiased stochastic process such that the group size and the fraction of cooperation vary statistically with mean values n_0 and x_0, respectively. Subsequently, the groups evolve independently (*group evolution step*). In each group, both the fraction of cooperators and the group size vary dynamically and change over time. Independent of the specific details, the groups' internal dynamics has the following characteristic features: First, because of the costs for providing the benefit, cooperators have a selection disadvantage, s, compared to cheaters in the same group. In particular, cooperators reproduce slower than cheaters and hence the fraction of cooperators decreases within each group (intra-group evolution). Second, considering the benefit of cooperation, groups with more cooperators grow faster and can reach a higher maximum size (carrying capacity) than groups of mainly cheaters (inter-group evolution) [43]. For details see also the materials and methods section. For specifity, we assume typical experimental conditions comparable to those observed in reference [28]. After evolving separately for a certain time $t = T$, all groups are merged (*group merging*), and the cycle restarts by forming new groups according to the current fraction of cooperators, x, in the whole population. It is the interplay of these three steps, characterized by the initial group size, n_0, the selection strength, s, and

the regrouping time, T, which determines the long-term evolution of the population.

Results

Fig. 2**A** shows the time evolution of the overall fraction of cooperators during a group evolution step. We find three distinct scenarios: decrease (red), transient increase (green), and permanent increase of cooperation (blue). Their origin can be ascribed to two ecological mechanisms: more cooperative groups grow faster (*group-growth mechanism*) and purely cooperative groups can reach a larger carrying capacity (*group-fixation mechanism*).

A permanent increase of cooperation can be explained on the basis of the *group-fixation* mechanism: for asymptotically long times the intra-group evolution reaches a stationary state, where each group consist solely of either cooperators or free-riders. Which state is favored depends on the interplay between selection pressure and stochastic effects. Because cheaters have a relative fitness advantage, they tend to outcompete cooperators in groups with a mixed initial composition. However, there are two stochastic effects leading to purely cooperative groups. First, the stochastic process of group formation results in a distribution of group compositions also containing a fraction of groups which consist of cooperators only. Second, random drift [47, 48], which is most pronounced during a population bottleneck where group sizes are small, can cause a group to become fixed in a state with cooperators only. Due to the benefit of cooperators for the whole group, these purely cooperative groups reach a much higher carrying capacity than those left without any cooperator. Hence, although inferior in terms of number of groups, purely cooperative groups through their large group size contribute with a large statistical weight to the total composition of the population, and thereby ensure maintenance or even increase of the level of cooperation for long times, cf. Fig. 2**A** blue curve.

In order for the group-fixation mechanism to become effective the evolutionary dynamics has to act for time scales longer than the selection time, $t_s := 1/s$, which measures the time scale on which selection acts. For smaller times, a temporary increase in cooperation level is observed provided the initial group size is small enough, cf. Fig. 2**A**. The initial rise is caused by the *group-growth mechanism*. Given a distribution of initial group compositions, it asymmetrically amplifies the size of those groups which contain more cooperators. This effect becomes stronger with a broader distribution, or, equivalently, a smaller initial group size n_0. Eventually the initial rise has to decline since, due to the internal selection advantage of

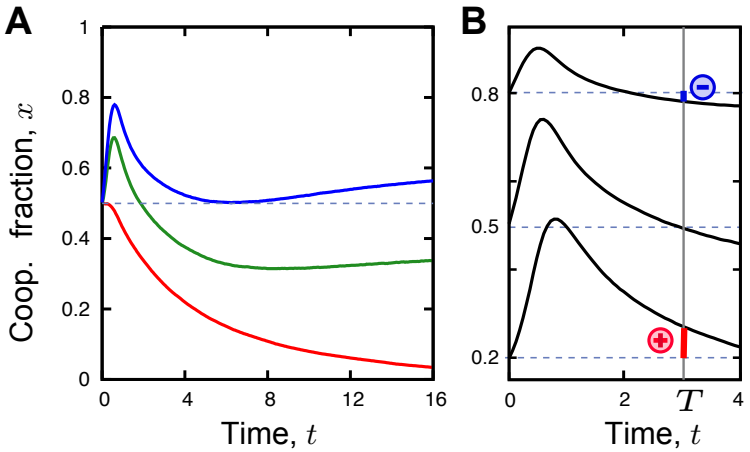

Figure 2. Evolution of the cooperator fraction while individuals are arranged in groups (group-evolution step). **A** Population average of cooperator fraction, x, as a function of time t. Depending on the average initial group size, n_0, three different scenarios arise: *decrease of cooperation* (red line, $n_0 = 30$), *transient increase of cooperation* (green line, $n_0 = 6$) and *permanently enhanced cooperation* (blue line, $n_0 = 4$). These three scenarios arise from the interplay of two mechanisms. While the *group-growth mechanism*, due to faster growth of more cooperative groups, can cause a maximum in the fraction of cooperators for short times, the *group-fixation mechanism*, due to a larger maximum size of purely cooperative groups, assures cooperation for large times. Both mechanisms become more efficient with decreasing initial group sizes. **B** The strength of the group-growth mechanism decreases with an increasing initial fraction of cooperators. This is illustrated by comparing the time evolution for three different initial fractions of cooperators and a fixed initial group size $n_0 = 5$. After a fixed time, here $t = 3.03$, the fraction of cooperators is larger than the initial one for $x_0 = 0.2$, equal to it for $x_0 = 0.5$, and eventually becomes smaller than the initial value, as shown for $x_0 = 0.8$. In both figures the selection strength is taken to be $s = 0.1$.

free-riders, the fraction of cooperators is always decreasing within each mixed group. As a consequence, the overall benefit of cooperators through faster growth of more cooperative groups is only transient. After a certain time, the cooperation time, t_c, the fraction of cooperators, $x(t)$, falls again below its initial value, x_0, unless the group-fixation mechanism is strong enough to ensure a permanent increase. Finally, if group-internal selection is too strong compared with the growth advantage of cooperative groups, the level of cooperation cannot increase even transiently, cf. Fig. 2**A**, red curve.

Combining all three steps of the cycle we now ask for the evolutionary outcome after many iterations, k, of the cycle. Depending on the relative magnitude of the *regrouping time* T, and the *selection time*, t_s, we find two fundamentally distinct scenarios, as shown in Fig. 3**A**. For large regrouping times, $T \gg t_s$, there is a threshold value, x_u^*, for the initial cooperator fraction, x_0, above which cooperators take over the whole population and below which they go extinct. In contrast, for regrouping times smaller than the selection time, $T \leq t_s$, independent of the initial value, x_0, the population reaches a stationary state where cooperators are in stable coexistence with free-riders. As explained next, these two scenarios are closely tied to the group-growth and group-fixation mechanisms; for an illustration see the supporting videos S1 and S2.

The threshold value for maintenance of cooperation at large regrouping times is a consequence of group-fixation and the larger carrying capacity of purely cooperative groups. Since for $T \gg t_s$ the intra-group dynamics has reached a stationary state, fixation leaves the population with groups consisting of either cooperators or defectors only. The probability of fixation in the respective state and hence the fraction of purely cooperative groups after completing one cycle strongly depends on the initial cooperator fraction. Now, if the initial cooperator fraction becomes too low, the number of cooperative groups will be too rare such that even their larger maximum group size is no longer sufficient for them to gain significant weight in the total population, and the overall cooperator fraction in the population will decline. Thus there must be a critical value for the cooperator fraction, x_u^*, below which, upon iterating the cycle the fraction of cooperators will decline more and more, see Fig. 3**A** (red line). In contrast, above the critical value purely cooperating groups are becoming more frequent upon regrouping, and therefore cooperators will eventually take over the population completely, cf. Fig. 3**A** (blue line).

When groups are merged during the phase of transient increase of cooperation, $T \leq t_s$, the stationary level of cooperation does not depend on the initial one. This striking behavior is due to the non-monotonous dependence of the change of the cooperator fraction during one cycle, Δx, on the initial

fraction, x_0; see Fig. 2**B**. As we have already eluded to in the discussion of the group-growth mechanism, stochasticity during group formation and during the initial neutral phase of the group evolution dynamics results in a broad distribution of group compositions. The evolutionary dynamics is acting on this distribution in an antagonistic fashion. While, due to the higher growth rate of more cooperative groups, the distribution develops a positive skew leading to an increase in the average overall cooperation, the group-internal selection pressure is counteracting this effect by reducing the cooperator fraction within each group. The relative strength of the former effect is largest for small initial cooperator fraction since this allows the largest positive skew to develop. Hence, for a given regrouping time, if the change in overall cooperator fraction Δx is positive for small x_0 it must become negative for sufficiently large x_0, as illustrated in Fig. 2**B**. For a more detailed mathematical discussion of these effects we refer to the supporting text S1. As a consequence, in populations with a small initial fraction of defectors, the defectors increase in frequency. At the same time, when the initial fraction of cooperators is low, they also increase in number, finally leading to stable coexistence of cooperators and defectors at some fraction x_s^*. This stationary fraction of cooperators is independent of the starting fraction and solely determined by the parameters of the evolutionary dynamics.

The interplay of both the group-growth and group-fixation mechanism leads, depending on the regrouping time, to different scenarios for the levels of cooperation. These are summarized in the bifurcation diagram Fig. 3**B**, where the stable and unstable fixed points of the cyclic dynamics, x_s^* and x_u^*, are shown as functions of the regrouping time. According to the evolutionary outcomes of standard two-player games [49], but genuinely distinct from them in their underlying mechanisms, the phenomenology of the cyclic regrouping dynamics can be classified as follows. For large regrouping times, $T \gg t_s$, the group-fixation mechanism leads to bistable behavior resembling the *stag hunt game*. With decreasing T, the fixation mechanism loses ground while the group-growth mechanism becomes more prominent. An intriguing *intermediate regime* emerges which lies outside the scope of the classification scheme for standard two-player games: the dynamics is bistable with full cooperation as well as coexistence as stable fixed points. For even smaller times, only the group-growth mechanism remains effective and, similar in phenomenology to the *snowdrift game*, the rare strategy here always outperfoms the common one such that each strategy can invade but not overtake the other. Finally, for $T \ll t_s$, cooperators always take over the population, effectively leading to *mutual cooperation*.

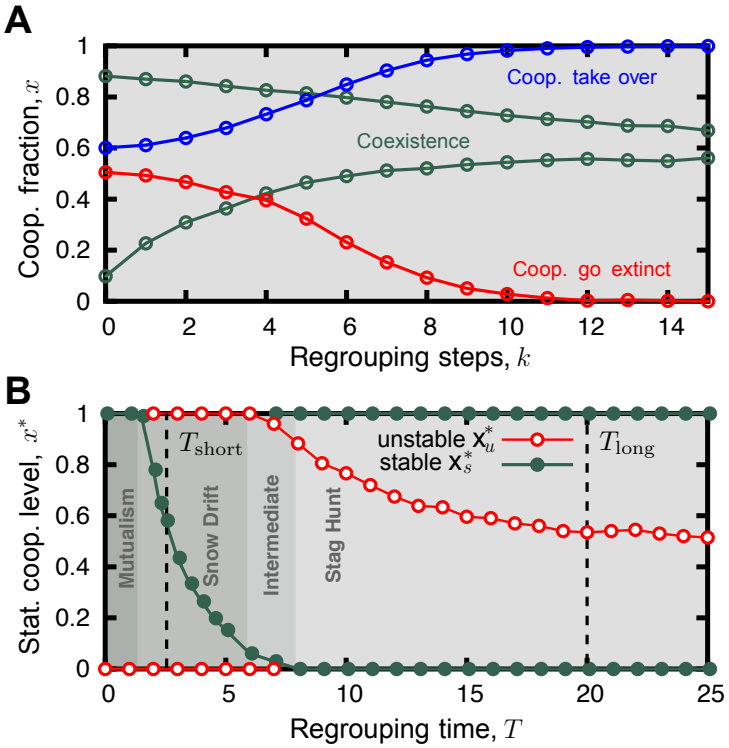

Figure 3. Evolution of the overall cooperator fraction under repeated regrouping. A After many iterations, k, of the evolutionary cycle, a stationary level of cooperation is reached. Depending on the relative efficiency of the group-growth and group-fixation mechanism two qualitatively different regimes emerge. While the group-growth mechanism leads to stable coexistence of cooperators and free-riders (green lines), the group-fixation mechanism can lead to a pure state of either only cheaters (red line) or only cooperators (blue line). The relative impact of these mechanisms depends strongly on the regrouping time T. For short regrouping times ($T_{\text{short}} = 2.5 < t_s$, green lines), the group-growth mechanism is effective, while for sufficiently long regrouping times ($T_{\text{long}} = 20 > t_s$, blue and red lines) the group-fixation mechanism acts more strongly. **B** The detailed interplay of the group-growth and group-fixation mechanisms is summarized in a bifurcation diagram showing the stationary levels of cooperation as a function of the regrouping time T. Depending of the relative efficiency of both mechanism, four different regimes arise. Their phenomenology resemble those of standard two-player games: mutualism, snow-drift game, and stag hunt game. In addition, an intriguing intermediate regime outside of the scope of the classification scheme for two-player games arises. Parameters are given by $s = 0.1$, $n_0 = 5$. In **A**, the initial fractions of cooperators are given by $x_0 = \{0.1$ (green), $x_0 = 0.9$ (green)$\}$ and $x_0 = \{0.5$ (red), $x_0 = 0.6$ (blue)$\}$ for $T_{\text{short}} = 2.5$ and $T_{\text{long}} = 20$, respectively.

Discussion

In this article, we have studied the influence of population dynamics and fluctuations on the evolution and maintenance of cooperation. Following recent microbiological experiments [24,25,27,28,30], we have considered the following ecological scenario: An initially well-mixed population is fragmented into a set of small subpopulations which are evolving independently for some fixed time period T. During this time, we consider the full stochastic dynamics of both, the fraction of cooperators and the size of a subpopulation. Subsequently, these groups are merged into a again well-mixed population, and the cycle starts anew with the next fragmentation event. With this general formulation of restructuring, the model serves as a null-model for cooperation in rearranging populations [24, 25, 27, 28, 30], e.g. during microbial and parasitic life-cycles [50–53], and bacterial biofilm formation [54, 55]. The final outcome of the dynamics depends on the interplay between the time evolution of size and composition of each subpopulation. While a growth advantage of more cooperative groups favors the evolution of cooperation, it is counteracted by the evolutionary advantage of free-riders within each subpopulation. We have investigated the stochastic population dynamics and the ensuing correlations between these two opposing factors. Our theoretical analysis identifies demographic noise as one of the main determinants favoring both the maintenance and the evolution of cooperation. These fluctuations strongly affect the dynamics due to two basic ecological factors: First, demographic noise during population bottlenecks creates a broad distribution in the relative abundance of cooperators and free-riders within the set of subpopulations. The growth advantage of more cooperative subpopulations implies an asymmetric amplification of fluctuations and possibly yields to an increase of cooperation in the whole population (group-growth mechanism). Our analysis shows that this can enable a single cooperative mutant to spread in the population which then, mediated by the dynamics, reaches a stationary state with coexisting cooperators and free-riders. Second, if the founder populations contain only very few individuals, demographic fluctuations strongly enhance the fixation probability of each subpopulation which then consists of cooperators or free-riders only. Purely cooperative groups can reach a much higher carrying capacity. However, only if the relative weight of purely cooperative groups is large enough, this effect leads to an increase in the level of cooperation in the whole population (group-fixation mechanism). From our theoretical analysis of the population dynamics we conclude this to be the case only if the initial fraction of cooperators is above some threshold value.

In summary, we have uncovered the origin of the correlations between group size and composition,

which promote cooperation. The nature of these correlations is strongly affected by population dynamics: Depending on whether groups are merged while they are still exponentially growing or already in the stationary phase, two qualitatively different mechanisms are favored, the group-growth and the group-fixation mechanism. These findings can be tested experimentally using microbial model systems. Previous experiments [24,28] have shown that, in accordance with our theoretical analysis, an increase in the level of cooperation is possible; see Supporting Information. However, to clarify how population dynamics promotes cooperation and leads to two distinct mechanisms, additional experiments are necessary: For example, by varying easily accessible parameters like the initial group size or the regrouping time T, the relative influence of both mechanisms can be tuned. Thereby, they can be distinguished and the resulting level of stable cooperation can be quantitatively compared with our theoretical predictions.

As we assume the worst case scenario for cooperators, e.g randomly formed groups and no additional assortment, our findings are robust: The discussed pathways towards cooperation based on a growth-advantage of more cooperative groups and restructuring are expected to stay effective when accounting also for other biological factors like positive assortment, spatial arrangements of groups, mutation, or migration. Overall, our theoretical investigations emphasize and quantify the role of ecological factors and demographic fluctuations on the evolution of cooperation.

Materials and methods

We used a stochastic, individual-based model where each individual is either a cooperator or a free-rider. In the group formation step groups are formed at random. The initial group size, $\nu_{0,i}$, is Poisson distributed (with mean n_0). Given this size, the fraction of cooperators $\xi_{0,i}$ follows by a binomial distributed number of cooperators. During the evolution step, each individual is subject to random birth and death events. The dynamics is given by a time-continuos Markov process where the change of the probability, $\partial_t P(\nu_i, \xi_i; t)$, is given by a master equation. In detail, the basal per capita birth rate of each individual depends linearly on the group level of cooperation ξ_i, while the per capita death rate increases linearly with the group size ν_i the individual belong to. In addition, free-riding individuals have a higher birth-rate where the strength of selection s measures the advantage of freeriding individuals. Full details are given in the Supporting Material. The time scale is such that a small population of only free-riders initially grows exponentially with the average size $\nu_{i,0} \exp t$. To investigate the dynamics and both evolutionary

mechanisms we performed extensive computer simulations by employing the Gillespie algorithm. Group size is $M = 5 \cdot 10^3$ in Fig. 2, and $M = 5 \cdot 10^4$ in Fig. 3. In addition, to gain further insights on the functioning of both mechanisms and their robustness, we have approximated the dynamics for some limits and did analytic calculations, see the Supplementary Information.

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Supporting Files

Supporting Text S1 In this supporting text, we give a more detailed discussion of our model. In particular, we focus on the stochastic dynamics underlying the group evolution step. Furthermore, both, the group-growth and group-fixation mechanism are analyzed mathematically.

Supporting Video S1. Evolution of cooperation, caused by the group-growth mechanism. The video shows the probability distribution for groups of size N containing a fraction of cooperators, x and how it changes with time during the group evolution step. The green dot indicates the mean fraction of cooperators. For several regrouping steps the evolutionary outcome depends strongly on the relative impact of the growth and fixation mechanisms. Here, the regrouping time $T = 2.5$ is fairly small and the group-growth-menchanism dominates. Thus, a single cooperating mutant can spread in the population. Starting from a very low initial fraction of cooperators, the level of cooperation increases during every regrouping step until a stable level of cooperation is reached. This behavior is caused by the faster growth of more cooperative groups as illustrated in the video by the strong correlation between the level of cooperation within a group and its speed of growth. Parameters are $T = 2.5$, $N_0 = 5$, $s = 0.1$, and $M = 5000$.

Supporting Video S2. Reaching purely cooperative behavior, caused by the group-fixation mechanism. Similar to video S2 this video shows the temporal evolution of the probability distribution for groups of size N to contain a fraction of cooperators x. In this video however, the regrouping time $T = 20$ is fairly large such that the group-fixation mechanism dominates. Thus, above a certain treshold value in the level of cooperation, cooperators can overtake the entire population since purely cooperative groups are present and can make use of their advantage in reaching a higher maximum group size even though almost all initially mixed groups are taken over by cheaters only. Parameters are $T = 20$, $N_0 = 5$, $s = 0.1$, and $M = 5000$.

Supporting Text
Population dynamics and the evolution of cooperation in group-structured populations

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In this supplementary document, we give a more detailed discussion of our model. In particular, we focus on the stochastic dynamics underlying the group evolution step. Furthermore, both, the group-growth and group-fixation mechanism are analyzed mathematically.

1 The Model

Here, we give details on the consecutive steps of the "life-cycle" of the meta-population. We first specify the group formation step before considering the dynamics within groups (group evolution step).

1.1 The Group Formation Step

Starting with an initial fraction of cooperators x_0 in the population, M groups are formed. Both, group size and group composition, are randomly distributed. Each group $i \in [1, M]$

initially consists of $\nu_{0,\,i}$ individuals where $\nu_{0,\,i}$ follows a Poisson distribution,

$$P(\nu_{0,\,i}) = \frac{n_0^{\nu_{0,\,i}}}{\nu_{0,\,i}!} \exp\left(-n_0\right), \tag{S1}$$

with mean n_0. Further, the initial composition of each group is also formed randomly. The probability for $\zeta_{0,\,i}$ cooperators in a group i is assumed to be given by a Binomial distribution

$$P(\zeta_{0,\,i}) = \binom{\nu_{0,\,i}}{\zeta_{0,\,i}} x_0^{\zeta_{0,\,i}} (1 - x_0)^{\nu_{0,\,i} - \zeta_{0,\,i}} \tag{S2}$$

with mean $x_0 \nu_{0,i}$. The initial fraction of cooperators $\xi_{0,\,i}$ within each group is thereby given by $\xi_{0,\,i} = \frac{\zeta_{0,\,i}}{\nu_{0,\,i}}$.

By this we assume the groups to be formed at random without any bias. This corresponds to a worst case scenario for cooperators which gain no additional advantage due to positive assortment. Note, that the same initial distribution of group compositions is reached if one assumes both, the initial number of cooperators (C) and free-riders (F), to be Poisson distributed with mean values λ_C and λ_F, respectively. The mean values are related by $n_0 = \lambda_C + \lambda_F$ and $x_0 = \lambda_C/(\lambda_C + \lambda_F)$.

1.2 The Group Evolution Step

After the groups were formed randomly, they grow and evolve separately. In the following, we consider the dynamics within one specific group i in detail. As emphasized in the main text, we include two essential requirements experiments on microbial systems have in common. First, in each group cooperators (C) grow slower than free-riders (F). Second, groups with a higher fraction of cooperators grow faster and are bounded by a higher maximum group size (carrying capacity) than groups with a lower one. To account for these facts, the growth rates have to consist of a group related and a trait/type specific part [1]. We, therefore, denote the per capita growth rate of an individual of type $S \in$

$\{C, F\}$ within group i as

$$G_S(\xi_i) = g(\xi_i)\frac{f_S(\xi_i)}{\langle f\rangle}, \tag{S3}$$

where $g(\xi_i)$ is the group related, $f_S(\xi_i)$, $S \in \{C, F\}$ is the species related part, and $\langle f\rangle = \xi_i f_C(\xi_i) + (1-\xi_i) f_F(\xi_i)$ is the average fitness. The normalization of the fitness, $f_S(\xi_i)/\langle f\rangle$, is a convenient choice to disentangle the influence of global and relative parts more easily. Further, the group related part, $g(\xi_i)$, which accounts for the growth advantage of more cooperative groups, is assumed to increase linearly with ξ_i. For specificity, we use experimental conditions similar to those presented in reference [2, 3]. In these experiments, a purely cooperating population growth to an about ten times higher population size than a purely defecting one. In our model, the maximum population size scales with g and therefore we set

$$g(\xi_i) = r(1 + p\xi_i). \tag{S4}$$

Here r determines the overall time scale for growth and defines our units of time, i.e. it is set to one unless specified otherwise. In the main text we have used $p = 10$ for specificity; see also section 3.3 where we compare with the experimental data by Chuang et a. [2].

Note, however, that the qualitative findings, especially both evolutionary mechanisms, do not depend on the exact form of $g(\xi_i)$ but only on the fact that $g(\xi_i)$ is monotonically increasing with the fraction of cooperators. The trait specific part, $f_S(\xi_i)$, includes the different growth rates of cooperators and free-riders within group i. We here employ the standard formulation of evolutionary game theory and assume it to be given by the payoff matrix of a Prisoner's dilemma game [4, 5]. The trait specific parts are given by

$$\begin{aligned} f_C(\xi_i) =& 1 + s\left[b\xi_i - c\right], \\ f_F(\xi_i) =& 1 + sb\xi_i, \end{aligned} \tag{S5}$$

and the fitness advantage of free-riders $\Delta f = f_F(x) - f_C(x) = -sc$ is frequency independent. For specificity, we set $b = 3$ and $c = 1$. Thereby, the selection strength s is the only free parameter controlling the fitness difference, Δf, which corresponds to the advantage of free-riders within each group. In the experiments [2, 3], the selection strength was of the order $s \sim 0.05$. In our manuscript, we set $s = 0.1$ as an upper approximation of this value.

To model growth bounded by restricted resources we further introduce per capita death rates which increase linearly with the number of individuals in a group,

$$D_S(\nu_i) = \frac{\nu_i}{K}. \tag{S6}$$

These are independent of the specific type S and lead to logistic-like growth within each group. K sets the scale of the maximum group size [6]. In detail, for purely defecting groups the carrying capacity is K while it is $(1+10)K$ for purely cooperating ones. For the discussed results, only the ratio of group sizes and not their absolute values are important. Hence, for numerical convenience, we set K to a constant value, $K = 100$.

The full stochastic dynamics follows a master equation which can be derived by the per capita growth and death rates, Eqs. (S3) and (S6). This master equation gives the temporal evolution of $P(\xi_i; \nu_i; t)$, the probability for group i to consist of ν_i individuals with a fraction of ξ_i cooperators at time t. We use the Gillespie algorithm to perform stochastic simulations [7].

While fluctuations strongly affect the dynamics, it is still instructive to look at the deterministic description where fluctuations during the group-evolution step are neglected. This deterministic dynamics within each group, i, is then given by rate equations for the

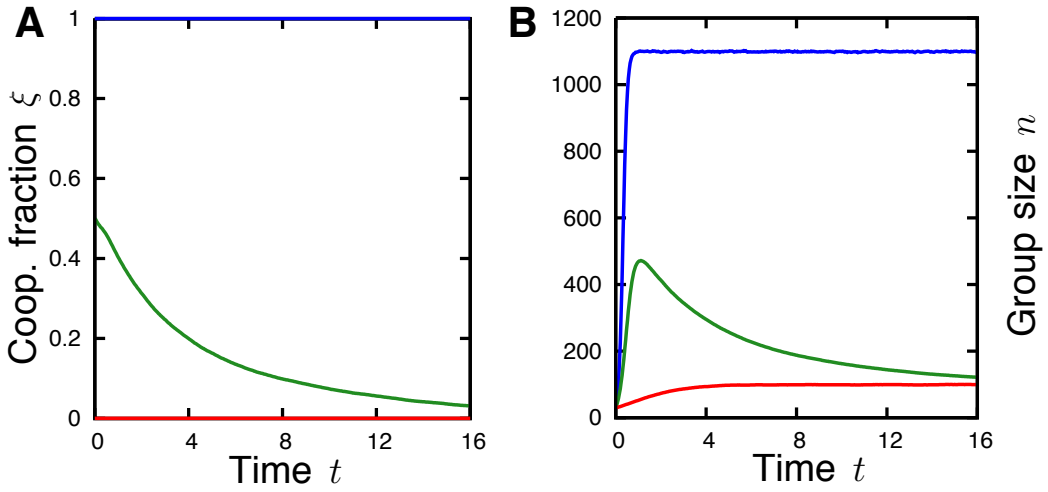

Figure S1: Dynamics in single groups. **A** Evolution of cooperation. For a mixed group (green), the fraction of cooperators declines due to the fitness advantage of free-riders while it stays constant for purely cooperating (blue) or defecting (red) groups. **B** Logistic like growth of the group size. For pure groups, the group-related advantage of more cooperative groups is most visible. Purely cooperating groups (blue) grow faster and reach a larger maximum carrying capacity than groups of only free-riders (red). A mixed group (green) grows faster than a group of only free-riders at the beginning. However also in the initially mixed group only free-riders can remain in the long run, and the carrying capacities of both groups become the same. Parameters are $n_0 = 40$ and $s = 0.1$, ξ_0 is equal to 0 (red), 0.5 (green), and 1 (blue).

fraction of cooperators ξ_i and the total group size ν_i:

$$\begin{aligned} \partial_t \xi_i &= -s(1+10\xi_i)\xi_i(1-\xi_i), \\ \partial_t \nu_i &= (1+10\xi_i - \nu_i/K)\nu_i. \end{aligned} \tag{S7}$$

Thus, in a deterministic manner, intra-group evolution is described by a replicator-like dynamics while the size of each group follows logistic growth (with a ξ_i dependent growth rate and carrying capacity). We illustrate this dynamics in Fig. SS1 for three different initial conditions.

2 The Group-Fixation Mechanism

We now give an analytical description of the group-fixation mechanism and discuss its dependence on the initial fraction of cooperators in more detail. As eluded to in the main text, the mechanism relies on the presence of purely cooperating groups. These groups remain cooperative, and reach a carrying capacity larger than all other groups. Thus, the probability for the emergence of a purely cooperating group, P_C, at the group formation step plays an essential role for the strength and the existence of the mechanism. Assuming a fixed initial size $\nu_{0,i} \equiv n_0$ for every group, this probability is given by $x_0^{n_0}$. For group sizes following a Poisson distribution it is even larger and found to be

$$P_C = \frac{e^{n_0 x_0} - 1}{e^{n_0} - 1}.$$

Let us now consider the fraction of cooperators in the whole population for very long times such that each group has reached its stationary state. Then, groups consist of either cooperators or free-riders only, with a group size of K or $11K$, respectively. In a first approximation, the fraction of purely cooperative groups remains constant during group evolution. The new fraction of cooperation within the whole population, x', is thus given by

$$x' = \frac{11(e^{n_0 x_0} - 1)}{10e^{n_0 x_0} + e^{n_0} - 11}. \tag{S8}$$

If $x' > x_0$ holds, the group-fixation mechanism is strong enough to cause an increase in the fraction of cooperators after one cycle even for very large regrouping times T. As x' clearly increase with increasing x_0, there is a threshold value x_u^* where $x' = x$. For $x_0 < x_u^*$, the new fraction of cooperation x' is smaller than x_0 while it is larger for $x > x_u^*$. Note that this threshold value depends only on the initial group size n_0 and not on the strength of the selection s. Furthermore, note that the analytical description above

Table S1: Per capita growth rates of cooperators and free-riders in two groups

	group 1	group 2
fraction of cooperators ξ_i	3/4	1/4
per capita growth rate cooperators, $g(\xi_i)f_C(\xi_i)/\langle f\rangle$	8.31	3.33
per capita growth rate free-riders, $g(\xi_i)f_F(\xi_i)/\langle f\rangle$	9.05	3.58

Two groups, $i = 1$ and $i = 2$ in comparison. While the per capita growth rates of cooperators are smaller than the per capita growth rates of free-riders within every group, the per capita growth rate of cooperators in the more cooperative group 1 strongly exceeds the per capita growth rate of free-riders in the less cooperative group 2 due to the group related fitness $g(\xi_i)$. The strength of selection is given by $s = 0.1$.

gives the right qualitative picture of the mechanism but underestimates its strength since demographic fluctuations, which are not accounted for in Eq. (S8), increase the chance for the occurrence of purely cooperating groups.

3 The Group-Growth Mechanism

As stated in the main text, the group-growth mechanism relies on the faster growth of more cooperative groups. Even though cooperators reproduce slower compared to free-riders in the same group, the positive effect on group-growth can outbalance this disadvantage. For an illustration see the specific example given in Table SS1.

3.1 The growth advantage of more cooperative groups

First, we quantify the growth advantage of more cooperative groups. For this, we consider only short times $t \ll 1/s$. Then, and in the limit of weak selection, $s \ll 1$, the deterministic time evolution, given by Eqs. (S7), is

$$\begin{aligned}\xi_i =& \xi_{0,i}\\ \nu_i =& \nu_{0,i} \exp\left[g(\xi_{0,i})t\right].\end{aligned}$$

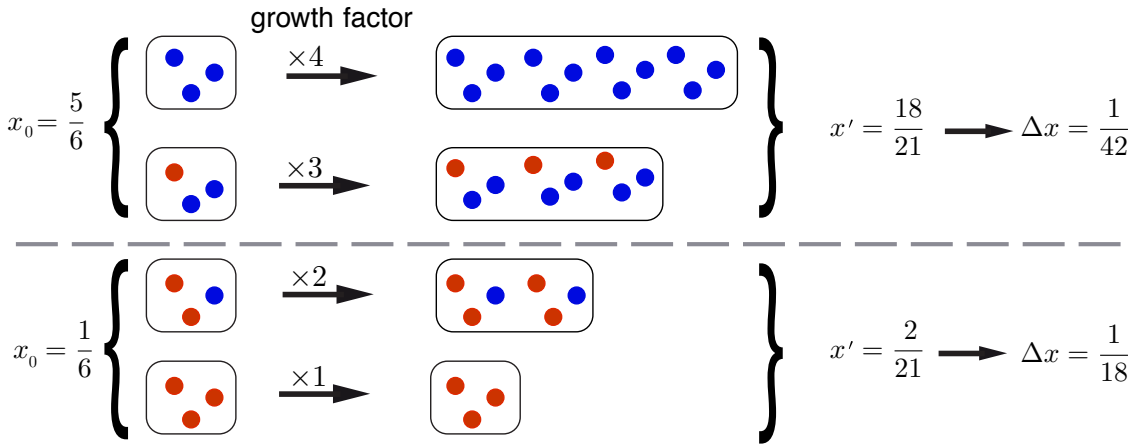

Figure S2: How the group-growth mechanism depends on the fraction of cooperators. Two sets of two groups are compared, one with a low fraction of cooperators (bottom) and one with a high one (top). Both groups evolve for a certain time, here with $g \propto 1+3x$ and no selection advantage for free-riders, $s = 0$. As can be readily seen, the change in the fraction of cooperators is larger for groups with a smaller initial fraction of cooperators.

The overall fraction of cooperators can be calculated by averaging over all possible initial group compositions,

$$x(t) = \frac{\sum_i P(\xi_{0,i};\nu_{0,i})\xi_i\nu_i}{\sum_i P(\xi_{0,i};\nu_{0,i})\nu_i}.$$

By differentiating with respect to time t, we find the following expression

$$\frac{d}{dt}x = \mathrm{Cov}(x, g(x)). \tag{S9}$$

This corresponds to a Price equation on the group level [8, 9], here stating that an increase in the fraction of cooperators is possible in principle if there is a positive correlation between x and the group related growth $g(x)$. However, for longer times $t > 1/s$ the selection advantage of free-riders counteracts the group-growth mechanism such that it can only act transiently.

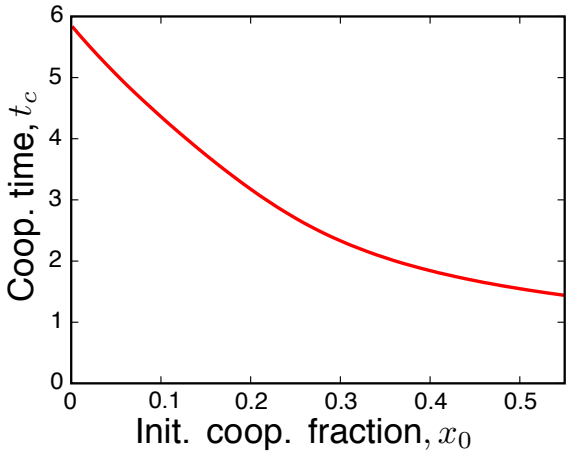

Figure S3: The group-growth mechanism decreases with larger initial fractions of cooperators. The larger the initial fraction of cooperators the smaller the cooperation time. The parameters are $n_0 = 5$, and $s = 0.1$

3.2 The Group-growth mechanism and its dependence on the initial fraction of cooperators

The strength of the group-growth mechanism depends strongly on the initial fraction of cooperators. This is illustrated in Fig. SS2.

A more comprehensive understanding can be gained by analyzing Eqs. (S7). In detail, we evaluate them for all initial conditions and weighted the solutions with the probability distribution for each set of starting values according to the group-formation step. Even though demographic fluctuations are not considered in this approach, it agrees well with the full stochastic dynamics: the solutions underestimate the positive effect on cooperators but give the right parameter dependences. To characterize the strength of the group-growth mechanism, we specifically evaluate the cooperation time, t_c, i.e. the time until the fraction of cooperators drops under its initial value. In Fig. SS3, the cooperation time is shown for different initial fraction of cooperators, x_0. With increasing x_0 the cooperation time strongly decreases, meaning the group-growth mechanism is stronger

for smaller initial fractions of cooperators.

3.3 Comparison with experiments on synthetic microbial system by Chuang, Rivoire and Leibler

We have compared our theoretical analysis with recent experiments by Chuang et al. [2] on a synthetic microbial model system. They have studied regrouping populations with initial population size n_0 in the range between 2 and 3, an initial cooperator fraction of $x_0 = 0.86$, and a regrouping time $T = 12 - 13$ h. Other model parameters were estimated as follows. The inherent fitness advantage of free-riders relative to cooperators was observed to be in the range between 1.04 and 1.05. In our model this translates to

$$f_C = 1\,, \tag{S10}$$

$$f_D = 1.05\,, \tag{S11}$$

where in contrast to equation (S3) we did not normalize the species related part, i.e. $\langle f \rangle \equiv 1$. The growth curves for different compositions of the population (see Fig.S3 in [2]) give access to the overall growth rate and its frequency dependence. From Fig.S3 in [2] we estimate:

$$r = 6.8 \times 10^{-4}\,\mathrm{min}^{-1}\,, \tag{S12}$$

$$p = 6.6\,. \tag{S13}$$

Employing these parameters in our model we have simulated the regrouping dynamics and find good agreement with the experimental results, cf. Fig. S4a. Since the population dynamics is still within the exponential growth phase at the regrouping time, we interpret the observed increase of cooperation as a group-growth mechanism. However, because of the particular set of experimental parameters, the resulting stationary cooperator fraction is very close to one which makes it difficult to observe coexistence between cooperators

and free-riders. We can now use our theoretical model to explore the effects of an increase in the regrouping time. Changing the regrouping time from $T = 12.5$ h to $T = 375$ h we find that the time evolution of the cooperator fraction remains qualitatively similar, despite the fact that now cooperation increases because of the group-fixation mechanism, cf. Fig. S4b. Thus even by changing the regrouping time these small values of n_0 do not allow to distinguish between the two mechanisms. However, as discussed in the main text, larger values of n_0 (in the range of $4-6$) give a clear signature of each of the mechanisms upon varying the regrouping time.

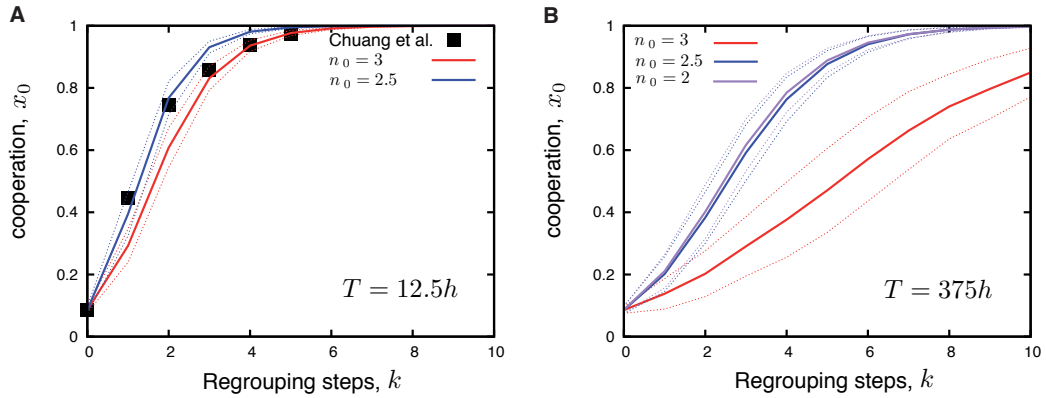

Figure S4: Increase in the level of cooperation for conditions resembling those examined by Chuang et al. [2]. **A** Short regrouping time, $T = 12.5h$. The measurements by Chuang et al. (black points) in comparison with the predictions of our model. Solid lines denote the expected level of cooperation. The dashed lines show the corresponding mean plus/minus the standard deviation. **B**, Large regrouping time $T = 375h$. For similar conditions, but a longer regrouping time, the outcome is qualitatively the same and only cooperators prevail. For both parts of the figure parameters are $x_0 = 0.086$, $r = 6.8 \times 10^{-4}\,\mathrm{min}^{-1}$, $f_C = 1$, $f_D = 1.05$, $p = 6.6$. In **A**, $K = 1.5 \times 10^6$. In **B**, $K = 1.5 \times 10^5$.

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