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Theoretical modelling of competitive microbial range expansion with heterogeneous mechanical interactions

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E-mail: lsanten@mx.uni-saarland.de**Keywords:** range expansion, competition, biofilm growth, Eden model, passive mobility, cell sorting, pushing

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Abstract

Microbial range expansion experiments provide insight into the complex link between dynamic structure, pattern formation and evolutionary dynamics of growing populations. In this work, we develop a theoretical model in order to investigate the interplay of growth statistics and mechanical interactions which are implemented as division driven pushing and swapping of cells. For the case of the competitive growth of a strongly and a weakly interacting strain we investigate the influence of different mean division times, as well as different mechanical interactions on the development of the colony. Our results show that the susceptibility to cell division induced pushing has a much stronger influence on the structure of the colony than cell sorting towards the colony's perimeter. Motivated by microbial range expansion experiments of *Neisseria gonorrhoeae* bacteria, we also consider the influence of mutating cells on the structure of the colony. We show that the outgrowth of the three different strains is strongly influenced by the relative strengths of their mechanical interaction. The experimentally observed patterns are reproduced for mechanical interactions of the mutants, which range between those of the strongly and weakly interacting strain.

1. Introduction

Microbial range expansion experiments are widely used to study ecological, population genetic and evolutionary dynamics. They provide insight into the complex link between dynamic structure, pattern formation and evolutionary dynamics of growing populations [1, 2]. Mechanical and genetic heterogeneity are known to be important factors in microbial expansions. These heterogeneities can lead to cell sorting, sector formation and gene surfing which increase the evolutionary fitness of otherwise disadvantaged sub-populations [3–5].

Microbial range expansion experiments and simulations have been used to study the influence of genetic drift in neutral population growth and for elucidating the development of advantageous or deleterious mutations inside expanding populations [4, 6, 7]. Also the influence of social interactions mediated by toxin or nutrient secretion and growth inhibition by direct contact has been investigated [8, 9]. Ultimately, all fitness differences in those studies, were mediated by differences in reproduction or death statistics.

However, it has been demonstrated experimentally that mechanical properties like reduced substrate adhesion or increased osmotic pressure influence the fitness inside a growing population [10, 11]. Additional mechanical interactions like pushing of microbes in growing colonies have been shown to reduce the power of natural selection [12, 13]. The corresponding increase in extinction time of a disadvantaged species facilitated evolutionary rescue in a changing environment. This sustained survival is relevant for the development of antibiotic resistance [12]. The influence of mechanical properties and interactions on the survival of mutants has been recently studied theoretically by Farrell *et al* [5].

Some bacteria, e.g. *Neisseria gonorrhoeae*, possess extracellular polymers named type IV pili, which lead in populations with and without pili to separation of both populations [14]. Zöllner *et al* [3] and Oldewurtel *et al* [14] introduced *N. gonorrhoeae* strains with different tunable mechanical interactions and reproduction statistics to study their influence on colony growth and range expansion. They used a strong interacting, fast growing strain and a slow growing, weakly interacting strain. The weakly

interacting strain could be sorted to the perimeter of the colony and therefore ‘surf’ on the colony front. Surfing in spatial population genetics refers to the effect that the offspring of individuals stay at the front of an expanding colony and, therefore, tend to be more successfully in reproducing than individuals from the bulk. Several mechanisms have been suggested to cause surfing, as for example initial cell sorting or pushing of cells by the bulk towards the colony’s surface [3].

In order to study the interplay of two sorting strains Dong and Klumpsp [15] introduced a lattice gas model. The modelling results confirm the predictions of the differential adhesion hypothesis [16] if the particle number is conserved. However, the predictions fail if cell division is considered as well. In this study, we address the role of division driving pushing in competitive range expansion in general, and apply our model to the particular experimental setup used in [3]. We focus on the influence of mechanical heterogeneous interactions, induced potentially by a population of piliated and non-piliated cells. To this end we implement selective cell division induced pushing of neighbouring cells into a lattice gas model. Within this model we investigate the influence of heterogeneous pushing on competitive growth from radial inoculations as well as sector formation from line inoculations. We demonstrate that in both cases heterogeneous mechanical interactions have strong influence on the composition of the growing colony.

2. Model

We model range expansion as a two dimensional cellular automaton with Eden-like growth [17] on a hexagonal lattice in continuous time.

2.1. Cell types and interactions

To study the interplay of mechanical heterogeneity and division statistics, we introduce three cell types with different interactions (corresponding to the degree of piliation) and mean division times. The strong interacting strain (SI-strain, red) has many pili and divides with scale parameter λ_r . The mutant strain (M-strain, yellow) originates from an SI-cell during division and inherits its division statistics. The mutant loses some of its pili and this leads to a weakening of the mechanical interactions in comparison to the SI-strain. Strong interacting cells and their mutants compete with cells from a weakly interacting strain (WI-strain, green), which has no pili and divides with different scale parameter λ_g .

2.2. Swapping

It is known that different degrees of piliation, i.e. different interaction strengths, lead to cell sorting [14]. In our model, we assume that the different interaction strengths lead locally to an optimisation of interaction energies, i.e. to an increase in the

number of the SI-strain SI-strain interactions. We implement this mechanism by swapping SI-cells with M- and WI-cells with rate $1/\mu_s$ (swapping of M- and WI-cells is not considered). Swapping is only allowed if it leads to an increase of neighbouring SI-cells (see figure 1(b)).

2.3. Cell division

Cell divisions are often modelled with exponential distributed waiting times between divisions. These statistics imply that the most likely time for a division is immediately after the last division. However, for real cells the minimal time between divisions is comparable to the mean division time [18]. In order to study systematically the influence of non-exponential waiting time distributions, we consider Weibull distributed waiting times (see appendix A). The probability density of the Weibull distribution is given by

$$\rho(t) = \frac{k}{\lambda} \left(\frac{t}{\lambda}\right)^{k-1} e^{-\left(\frac{t}{\lambda}\right)^k} \quad (1)$$

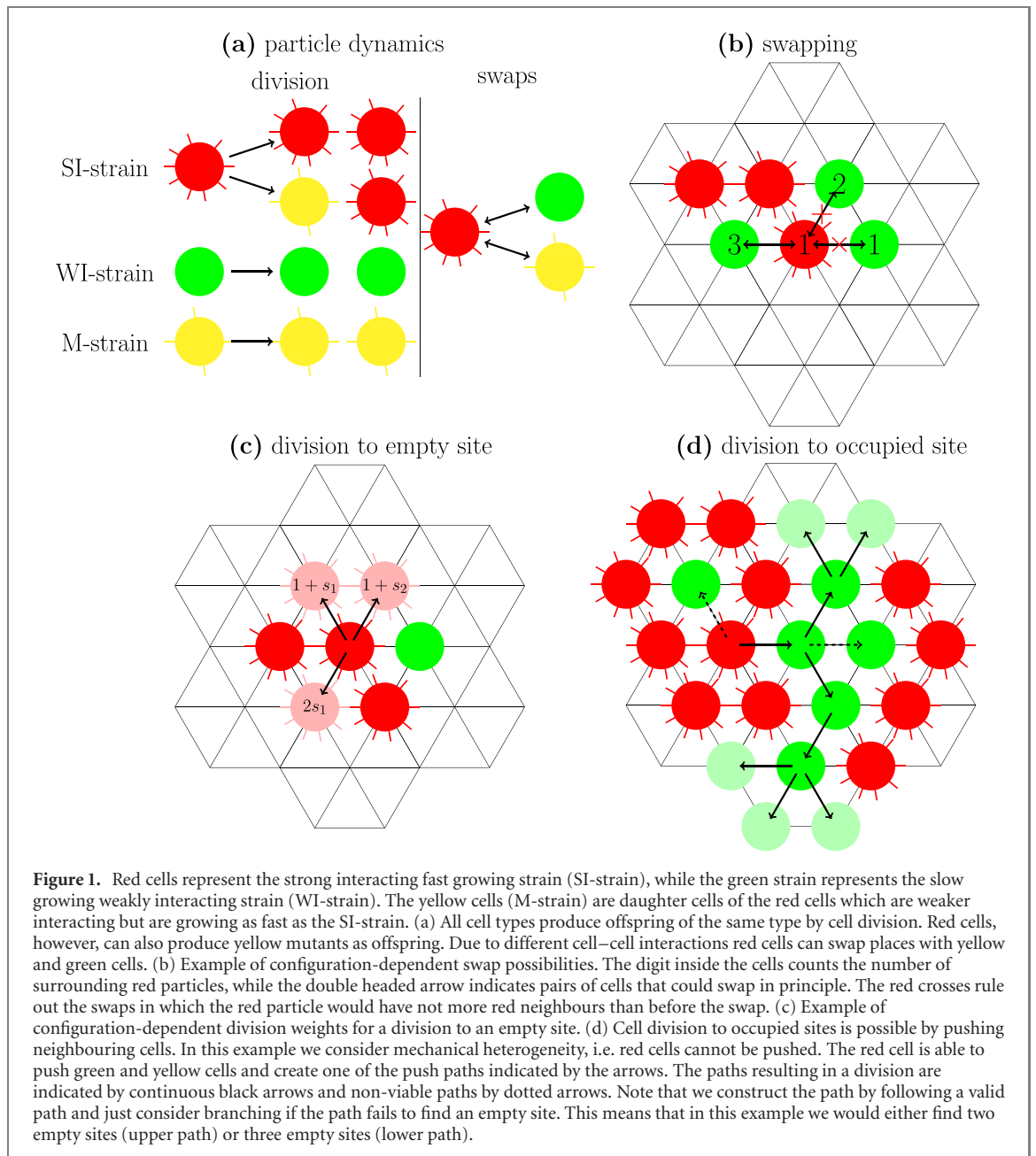
with scale parameter λ and form parameter k . This distribution reduces to the exponential distribution for $k = 1$ and therefore permits a systematic study of possible regularisation effects due to waiting times which are narrowly distributed around the mean value. In the experiments of Zöllner *et al* [3] the division statistics of the competing strains were regulated by antibiotics. In these experiments, the SI-strain was constructed to show only a weak dependence on the antibiotic concentration. Therefore, we use the scale parameter of the SI-strain as a reference time scale i.e. $\mu_s = r_s \cdot \lambda_r$, $\lambda_g = r_d \cdot \lambda_r$. Events (divisions, swaps) are selected analogously to the next reaction method of the stochastic simulation algorithm [19].

Cell division is always possible if a cell has an empty neighbour site (see figure 1(a)). In case more than a single neighbour site is empty one of the empty sites J is selected with relative weight

$$w_{I \rightarrow J}^d := \sum_j s_j \sum_{i \in \langle I, J \rangle} I_{S_i=P_j} + \sum_{i \in \langle I, J \rangle} I_{S_i=E}, \quad (2)$$

whereby $\sum_{\langle I, J \rangle}$ is the sum over common neighbour sites of site I and J . $I_{S_i=P_j}$ indicates whether a cell of type j is occupying the site and $I_{S_i=E}$ if the site is empty. The s_j control the stickiness of a given cell type by giving additional weight to a division next to it (see figure 1(c)). If the dividing cell is an SI-cell the newly placed cell mutates with probability p_m into an M-cell.

If all neighbouring sites of the cell are occupied, cell division may still be possible by pushing neighbouring cells. The cell can divide onto a neighbouring site if the translation of at most P particles leads to a valid configuration, i.e. the last particle of the chain occupies a previously empty site. The different interaction strengths of the strains are reflected by their influence on the pushing chain: SI-cells cannot be pushed, M-cells can only be pushed



to an empty site, and WI-cells can always be pushed. The construction of the pushing chain is implemented in the following way (see figure 1(d)): in the first layer we choose from the pushable (M-, WI-) neighbours of the dividing cell (0th layer), one random cell. The chosen cell has six neighbour sites from which three are not next neighbours to the dividing cell (0th layer). From the pushable of these sites the new position for the first layer cell is chosen at random and the chain continued such that the new position of the n th layer cell is chosen randomly from the three neighbours of the n th layer cell which are not common neighbours of the $(n - 1)$ th cell and are empty or occupied by a pushable cell. The construction of the chain ends if the maximal chain length P is reached or an empty site is found. The translation of the chain is accepted if a valid configuration is found. Otherwise we step back to the previous

layer and choose randomly a different neighbour to continue the chain. This method guarantees that an empty site in the distance reachable by the maximal amount of pushes P is always found.

3. Results and discussion

3.1. Competitive radial range expansion

To mimic typical experimental set-ups of radial range expansion we start with 500 cells of the SI- and WI-strain. The cells are initially randomly distributed in a circular patch of fixed density $\rho = 0.1$. Simulation parameters are listed in appendix C, table C1.

3.1.1. Effects of division induced pushing

First, we study the competition between the SI- and WI-strain. Different to the standard model configuration both strains are allowed to be pushed and

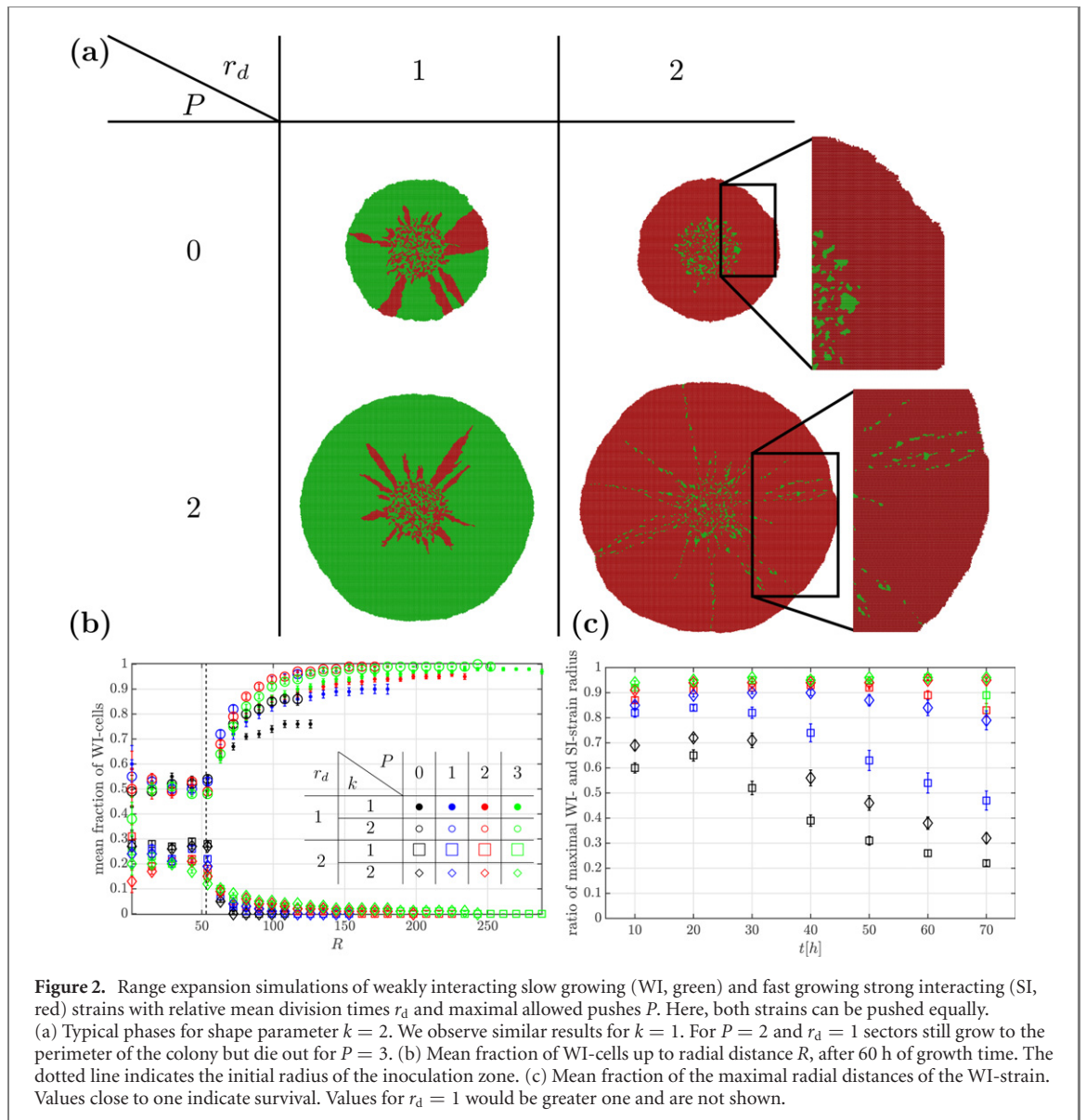


Figure 2. Range expansion simulations of weakly interacting slow growing (WI, green) and fast growing strong interacting (SI, red) strains with relative mean division times r_d and maximal allowed pushes P . Here, both strains can be pushed equally. (a) Typical phases for shape parameter $k = 2$. We observe similar results for $k = 1$. For $P = 2$ and $r_d = 1$ sectors still grow to the perimeter of the colony but die out for $P = 3$. (b) Mean fraction of WI-cells up to radial distance R , after 60 h of growth time. The dotted line indicates the initial radius of the inoculation zone. (c) Mean fraction of the maximal radial distances of the WI-strain. Values close to one indicate survival. Values for $r_d = 1$ would be greater one and are not shown.

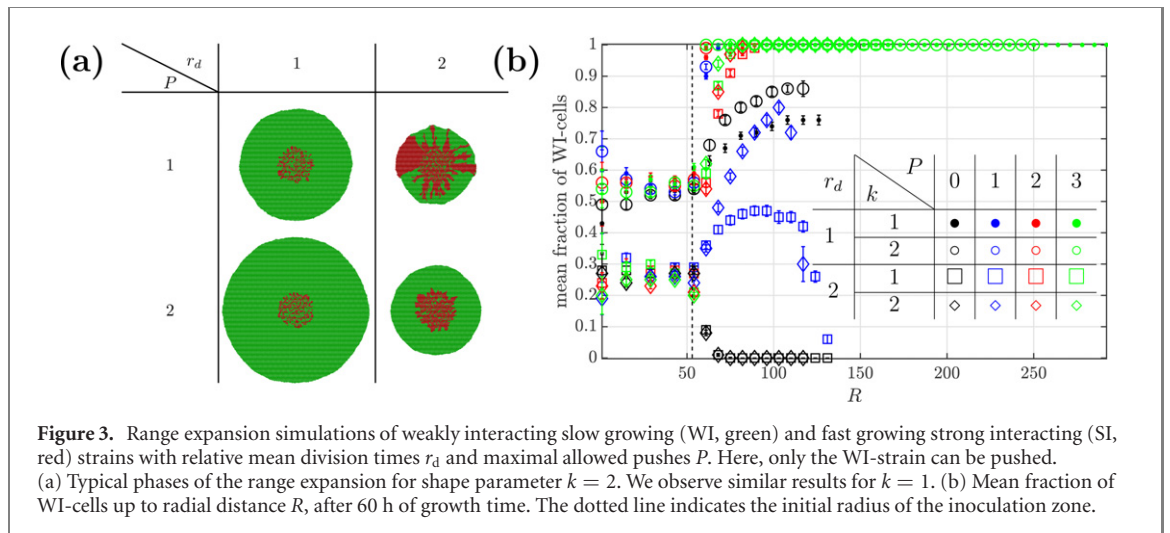
neither strain is mutating. Notice however, that the strong interactions of the SI-strain are still considered by swapping with the WI-strain (see section 2.2). The typical colony compositions after 60 h of growth time are shown in figure 2(a). We quantify the patterns by computing the mean fraction of WI-cells at radial distance R to the origin inside the inoculation zone (see figure 2(b)).

Competition of cells with equal mean division times:

If the strains have no divisional advantage ($r_d = 1$), we observe a compact ($\rho = 1$) random mixture of both strains inside the inoculation zone after 60 h of growth time. Inside the inoculation zone the mean fraction of WI-cells is 0.5 confirming that the inoculation zone is equally filled with both strains. Interestingly, outside the inoculation zone we observe a dominance of the WI-strain, with sectors of the SI-strain growing out of the inoculation zone. The increasing dominance of the WI-strain is quantitatively described by the monotonic increase of the mean fraction outside the inoculation zone.

This is different from the situation without swapping, where a constant mean fraction of 0.5 is predicted from symmetry as well as from stochastic continuum theory [2, 20]. We attribute this slow increase to the initial cell sorting, which grants the WI-strain a starting advantage originating from the swapping mechanism, which favours bonds between SI-cells. This leads to a systematic reduction of the number of neighbouring empty sites for the SI-strain. The aforementioned effect leads to a broken symmetry between WI- and SI-cells at the perimeter of the colony, giving the WI-strain the advantage to surf on the front of the expanding population. This asymmetry between SI- and WI-cells is also observed in experiments, where the WI-strain is always sorted towards the perimeter of the colony [14].

Swapping reduces the roughness of the interfaces between SI- and WI-strain sectors and thereby further stabilises the SI–WI sector boundaries. This leads to a slow increase of the mean fraction. However, if the cells are able to push, the WI-strain is able to



overcome the sector interfaces and therefore dominates the outgrowth even more. The dominance increases with P , but particular for small values of P we observe long living SI-strain sectors.

The regularisation ($k = 2$) of the waiting times between divisions enhances the symmetry breaking which is induced by swapping. This leads to a shift of the mean fraction to higher values, indicating a faster annihilation of the outgrowing sectors. Indeed, we see complete annihilation for $P = 2$, while for $k = 1$ the sectors still reach the colony frontier and get extinct for $P = 3$. Also somehow surprising, the maximal radial extension of the colony reaches smaller values. The mean value of the waiting times for $k = 2$ is $\sqrt{\pi}/2$ times smaller than for $k = 1$ (see appendix A, equation (A.4)), and therefore one would naively expect that the colony should grow faster and reach higher radial expansions. However, the actual time for the occupation of a vacant site is given by the minimal waiting time of the neighbouring cells. For a given mean value of the waiting time distributions this minimal time is significantly shorter for an exponential distribution ($k = 1$) than for higher values of k (see appendix A, equation (A.4)).

Impact of divisional advantage:

In the case of a substantial divisional advantage ($r_d = 2$) the strong interacting strain dominates the colony, as expected. Quantitatively, this is represented in a mean fraction value below 0.5 inside the inoculation zone. Outside the inoculation zone we observe a monotonic decrease to zero. In the case of $P = 0$ the dominance of the SI-strain leads to complete extinction of the WI-strain. Interestingly, if cells are allowed to push the expanding population of SI-cells transports a small population of WI-cells with it (see figure 2(a)). This leads to the chance of forming a standing variation of strains inside the expanding population and is not predicted by continuum theories. Since the population of WI-cells is quite small, and their radial position stochastic, the mean fraction of WI-cells is not a good quantity to characterise

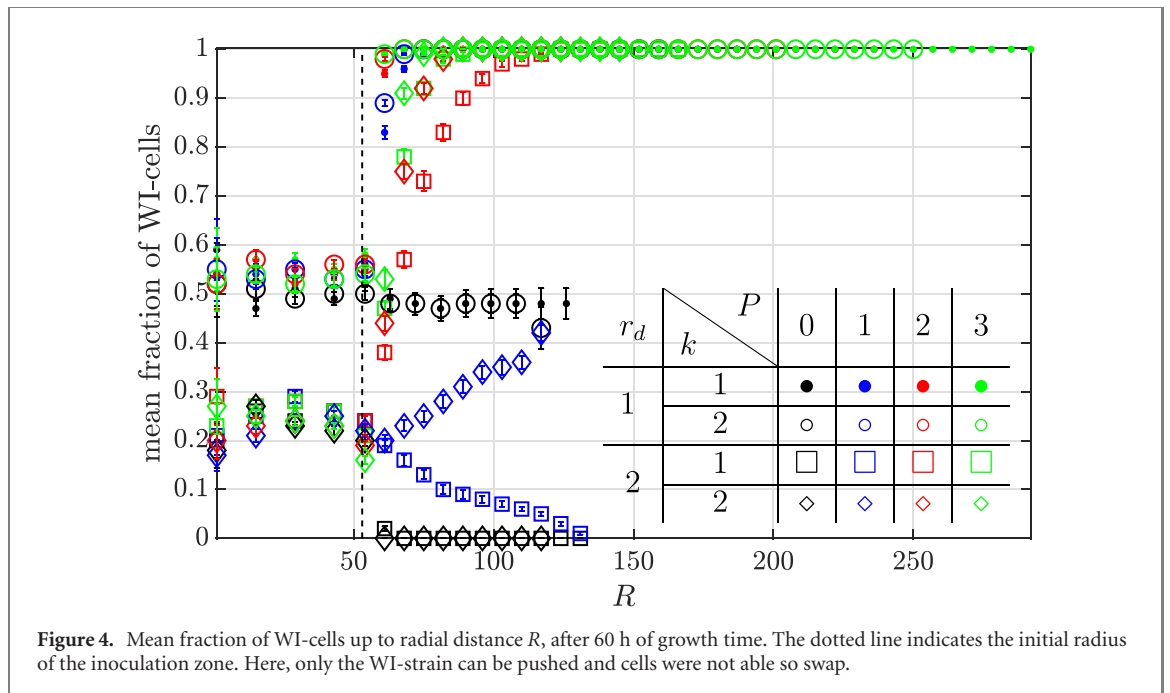
their survival. Therefore, we calculate the fraction of the maximal radial distances of all WI- and SI-cells for every colony. In figure 2(c) we show the mean values of this fraction for $r_d = 2$ at different times. Values close to one indicate a prolonged survival during subsequent range expansions. We observe for higher amount of pushes a sustained survival inside the colony. While the explanation for enhanced survival in the case of more allowed pushes is obvious, we also observe enhanced survival for the regularized distribution. This can be understood by comparing the probability of the WI-strain dividing slower than the SI-strain for arbitrary k (see appendix A, equation (A.3)). The probability for a slower division with $k = 1$ is higher than for $k = 2$, meaning that it is easier for the WI-strain to compete with the SI-strain.

3.1.2. Effects of mechanical heterogeneity

Mechanical heterogeneity is materialized by the different resistance of SI- and WI-cells with respect to pushing. Here, we consider that only the WI-strain can be pushed. In the case of $P = 0$ this reduces to the same scenario as in the previous section. As in section 3.1.1 we show the typical phases of the colony in figure 3(a) and quantify the composition by computing the mean fraction of WI-cells at radial distance R to the origin inside the inoculation zone (see figure 3(b)).

If we do not consider a divisional advantage for any strain ($r_d = 1$), the behaviour inside the inoculation zone is in accordance with the homogeneous case. However, the mean fraction of WI-strain increases more steeply outside the inoculation zone if selective pushing is applied. Remarkably, the mean fraction reaches one already for $R \gtrsim 57$. For $P \neq 0$ the parameters k and P have only little influence on the radial dependence of the mean fraction.

Now, we turn to the case, where mechanical inhomogeneous growth can compensate for a disadvantage in the reproduction statistics of individual



cells. For a divisional advantage of $r_d = 2$, which is comparable to the extreme case of the experimental setup of competitive microbial range expansion [3], we observe, as previously mentioned, a strong dominance of the SI-strain for $P = 0$. A very complex behaviour is observed for $P = 1$. In this case pushing supports the outgrowth of the WI-strain which have similar or higher mean fraction than the SI-strain below $R \lesssim 100$. The higher mean fraction is observed for $k = 2$, which means that the regularization supports the outgrowth of the WI-strain. The reason for this behaviour was already discussed in section 3.1.1. If we increase $P \geq 2$ the WI-strain dominates the colony almost in the same way than without divisional advantage.

Our results show that the higher passive mobility of the WI-cells, which is introduced by selective pushing, may lead to a dominance even in the case of an extreme divisional disadvantage. This dominance of a slower growing strain was observed by Zöllner *et al* [3] and studied with the help of simulations by Dong and Klumpp [15]. In their model, they incorporated cell division and cell sorting by swapping cells to energetically favourable positions and diffusion of cells to empty sites. Mechanical heterogeneity by pushing, however, has not been considered. Although these results show that cell swapping may lead as well to outcompetition despite divisional disadvantage, we notice that this effect strongly depends on the initial conditions. In particular, fast growing cells are contained in a single compact sector. This initial condition is not realised by the experimental setup of Zöllner *et al* [3], where a randomly mixed population is inoculated inside a circular domain. This discrepancy shows the

importance of pushing, which stabilises the dominance of the slow growing strain.

In order to characterise the importance of mechanical heterogeneity even further, we studied the competition between the different strains without swapping (see figure 4). First, we consider the reference case $r_d = 1, P = 0$, where both strains have identical properties and the value of the mean fraction is ≈ 0.5 , as expected. This result shows that the dominance of the WI-strain, observed for the same parameters in section 3.1.1, is caused by the asymmetry of the swapping rule. Remarkably, we observe comparable behaviour to the case without swapping if pushing is considered ($P > 0$). For $r_d = 1$ the mean fraction reaches one shortly after the inoculation zone, and only a weak dependence on the parameters k and P is observed. For $r_d = 2$ and $P = 1$, however, we observe a strong dependence of the waiting time distribution. While in the exponential case ($k = 1$) the mean fraction of WI-cells decreases, the mean fraction increases linearly for $k = 2$. This can be attributed to the different short time probabilities as discussed in the last paragraph of section 3.1.1. For $P \geq 2$ we observe, as with swapping, the dominance of the slow growing strain outside the inoculation zone. This demonstrates that the mechanical heterogeneity of the pushing rather than swapping is responsible for the outcompetition. Our results suggest that the outcompetition observed in the experiments by Zöllner *et al* [3] is caused by the heterogeneous transduction of division induced pushing forces, and not by the initial sorting of the WI-cells to the perimeter of inoculation zone. This hypothesis could be tested experimentally by using pilT knockout mutants of SI-cells. These knockout

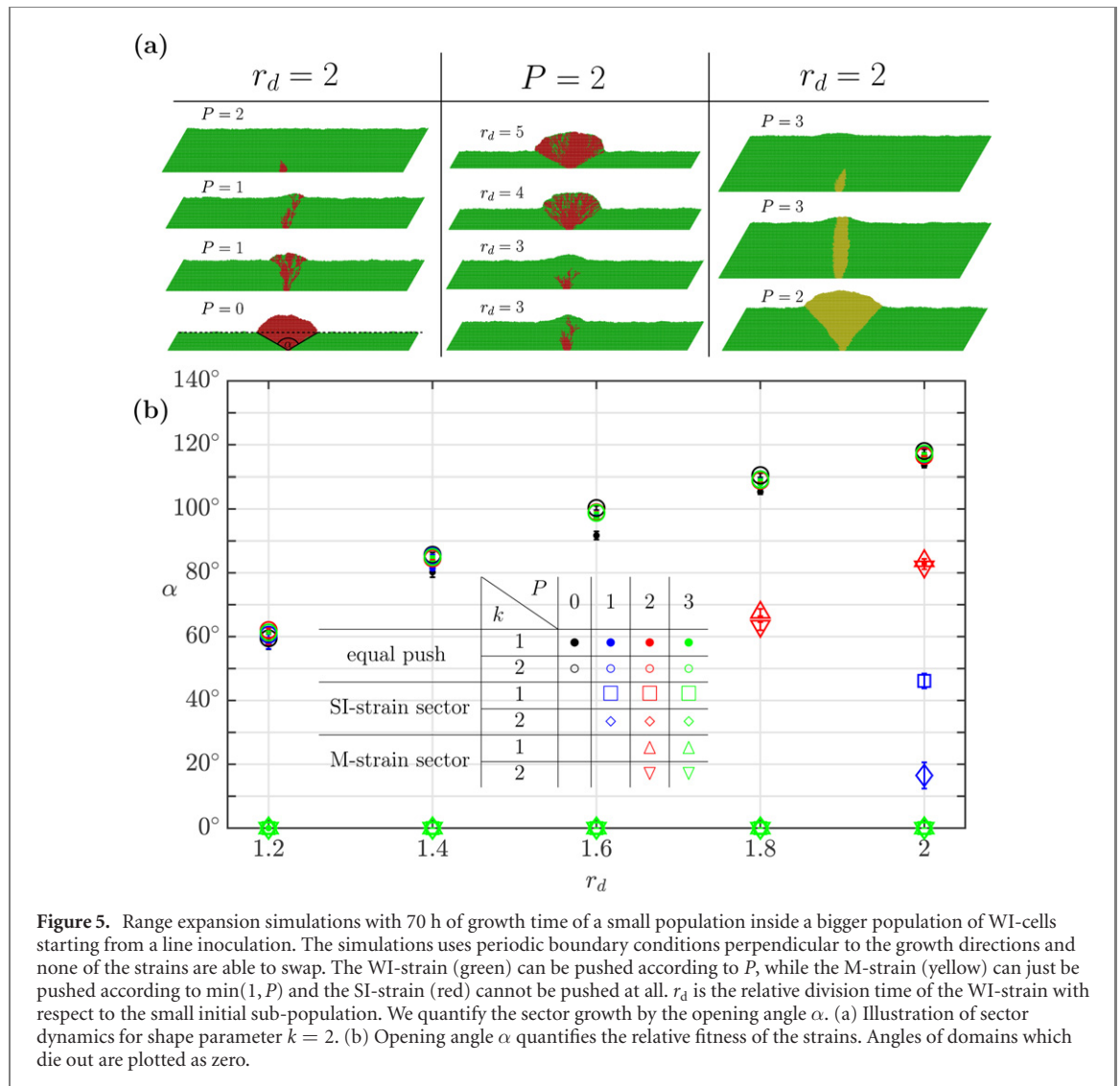


Figure 5. Range expansion simulations with 70 h of growth time of a small population inside a bigger population of WI-cells starting from a line inoculation. The simulations uses periodic boundary conditions perpendicular to the growth directions and none of the strains are able to swap. The WI-strain (green) can be pushed according to P , while the M-strain (yellow) can just be pushed according to $\min(1, P)$ and the SI-strain (red) cannot be pushed at all. r_d is the relative division time of the WI-strain with respect to the small initial sub-population. We quantify the sector growth by the opening angle α . (a) Illustration of sector dynamics for shape parameter $k = 2$. (b) Opening angle α quantifies the relative fitness of the strains. Angles of domains which die out are plotted as zero.

mutants lack the ability of pili retraction which inhibits cell-sorting by swapping [14, 21].

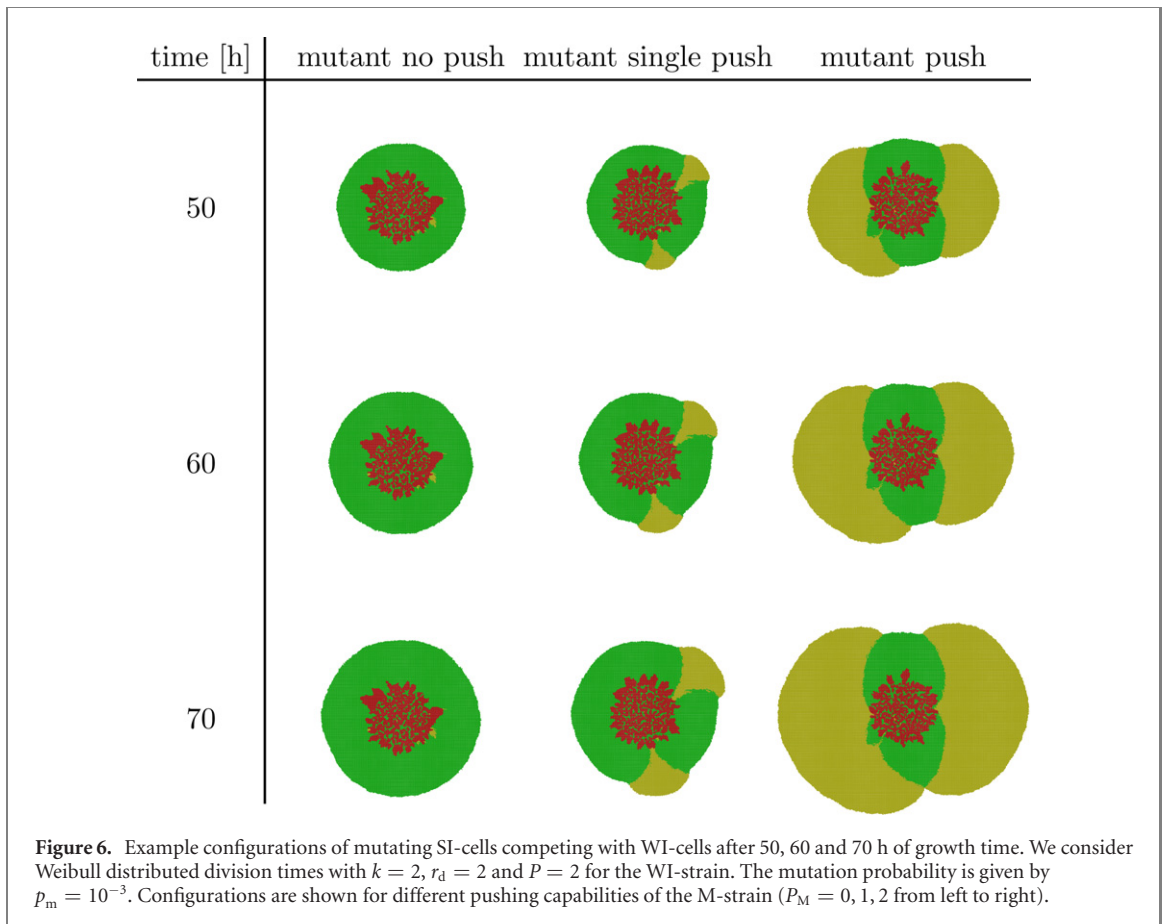
3.2. The fate of mutants

The previous section demonstrated that differential pushing is an important factor in colony growth. We now turn to the question how differential pushing influences the development of a small sub-population of cells, which is embedded in a large population of WI-cells. First, we study this with a deterministic flat initial condition and second we apply these results to a random circular inoculation as considered in the previous section. For the flat initial condition we consider the competition of an M- and SI-colony with the embedding WI-strain. In case of a circular inoculation zone both, where M-cells are created dynamically during the range expansion, both the SI- and M-strain compete with the WI-strain. As described in section 2.3 the SI-strain (red) cannot be pushed, while a single M-strain (yellow) cell can be pushed. The scale parameter of the SI-strain defines the reference time scale.

3.2.1. Flat front

In order to study the development of domains of different strains, we consider cells that are initially arranged along a line. The colony of the smaller population (M-/SI-cell, here 10 cells) is placed as compact segment inside a background of WI-cells. We use a two dimensional system with periodic boundary conditions perpendicular to the direction of growth (x -direction $x \in [0, 499]$) and a half open system in y -direction ($y \in [0, \infty)$). Here, we study the case that the cells are not allowed to swap positions. The other dynamic properties of SI-cells remain unchanged, i.e. they set the reference time scale and cannot be pushed. As already mentioned in section 2.3 the M-strain shares the division time distribution with the SI-strain but can be pushed according to $\min(1, P)$. Using this setup we study the influence of pushing and divisional advantage by varying P and r_d of the embedding WI-cells.

First, we studied the mechanical homogeneous case, i.e. every strain can be pushed equally. This is shown in figure 5(a) for $P = 0$ and $r_d = 2$. In this case,



we always observe a compact sector growing from the initial small population. We quantified these sectors by measuring the opening angle α (see appendix B). The opening angle is predominantly determined by the divisional advantage r_d , while P has only little influence (see figure 5(c)). The increase of the opening angle with increasing r_d is obviously due to the fact that faster dividing cells occupy the empty space earlier. Although the effect of pushing is much weaker than the r_d dependence, we still observe a systematic difference between $P = 0$ and $P \geq 1$: pushing increases the opening angle if it has any influence at all. Moreover, since pushing decreases the effective division time, it facilitates the occupation of space.

In the case of heterogeneous pushing, the dominance of the faster dividing cells is strongly reduced. For the case of WI-cells ($r_d = 2$) competing with SI-cells, we observe that the colonies generally die out for $P \geq 2$. In case of $P = 1$ we observe dendrite like shape and survival to at least 70 h of growth time. The shape of the sectors, however, complicates the interpretation of the opening angle, which is much smaller than for compact sectors. These results show that even a large divisional advantage is not sufficient to balance a small mechanical advantage. In order to quantify the necessary divisional advantage, we studied the competition of SI-cells competing with WI-cells for $P = 2$ and r_d in the range of three to five (see figure 5(a) middle column). Throughout our

simulations, we observe sector formation of the SI-strain for $r_d \geq 4$, which is difficult to realize experimentally [3]. Interestingly, these sectors show an inhomogeneous mixture of SI- and WI-cells despite the dominance of SI-strain. This high persistence of WI-cells inside the expanding SI-strain domain is caused by transportation of the mobile WI-cells towards the surface of the colony. This demonstrates that heterogeneous mechanical interactions can establish a standing heterogeneous population inside the growing sector, which is not observed for homogeneous mechanical interactions.

The third scenario under consideration is the competition of a small population of the M-strain with the WI-strain. Since we consider as pushing capabilities $\min(1, P)$ for the M-strain only the cases $P \geq 2$ constitute new scenarios. For $P = 2$ and $r_d \geq 1.6$ we observe stable sectors (see figure 5(b)). For larger passive mobility of the WI-strain ($P = 3$) and $r_d = 2$, we recover the dominance of the WI-strain background. Remarkably, although swapping is not considered, the domains of M-cells are compact irrespective whether the M-strain domain dies out or not.

3.2.2. Radial range expansion with mutants

Now we return to the experimental setup of Zöllner *et al* [3]. We initialize the system as in the previous section 3.1.2, i.e. SI- and WI-cells are placed initially at random positions in a circular

inoculation zone. Additionally, we consider a finite mutation probability $p_m = 0.001$ of SI- to M-cells. Zöllner *et al* [3] characterized the properties of the M-strain such that the division statistics remains unchanged from the SI-strain but their pili are lost. These properties suggest that M- and WI-strain share the same mechanical properties. The results of our simulations, however, show a fast growth of the M-strain sector with opening angles that are much larger than observed experimentally (see figure 6 right column). If the loss of pili would retain the mechanical properties of the SI-cell (no push) we observe that the M-strain domains die out fast. For the intermediate case (single push), however, we observe a stable outgrowth of M-strain sectors with an opening angle comparable to the experimental results.

4. Conclusion

Our work provides a coarse-grained model that contributes to the understanding of competitive microbial range expansion experiments. We focus on the role of division induced pushing with strain depended mechanical and growth speed specific properties. Moreover, we use initial conditions analogous to experiments, where a low density population of microbes are randomly distributed inside a circular inoculation zone. This enhances the general understanding of population genetic and evolutionary dynamics inside microbial populations.

For the competition between cells that possess the same mean division time (neutral case) and are unable to push, we observe that subtle differences in the swapping mechanism lead to a broken symmetry between WI- and SI-cells at the perimeter of the colony. The symmetry breaking can be attributed to the stronger clustering of SI-cells, which leads to an effective divisional advantage of WI-cells. This result is also valid if the pushing capabilities of both strains are identical. Therefore, our results demonstrate that the WI-strain dominates the outgrowths of the colony even in neutral case. Multiple cells compete for empty space, and therefore the regularization of division times, i.e. for a non-exponential distribution, reduces the growth speed of the colony and enhances the impact of different mean division times.

Independent of the regularization, the dominance of the WI-strain can only be compensated if the division times of the WI-cells are significantly larger. But even for the case, that the faster dividing SI-strain dominates the outgrowth of the colony, we observe that division induced pushing leads to a standing variation of slower dividing cells inside the outgrowth. These standing variations contribute to the development of antibiotic resistance and spread of microbial infections as argued by Kayser *et al* [12]: the sustained survival leads to evolutionary rescue in changing environments and promote accumulation of deleterious mutations inside a growing colony. This

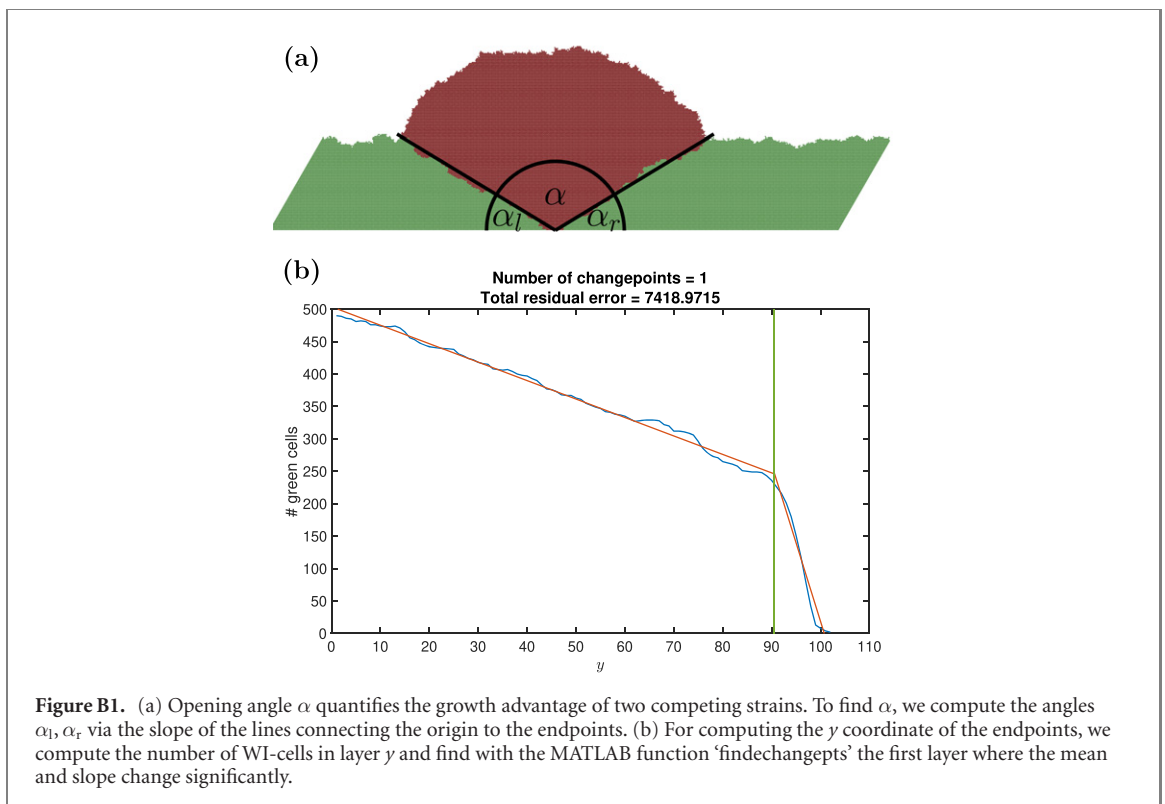
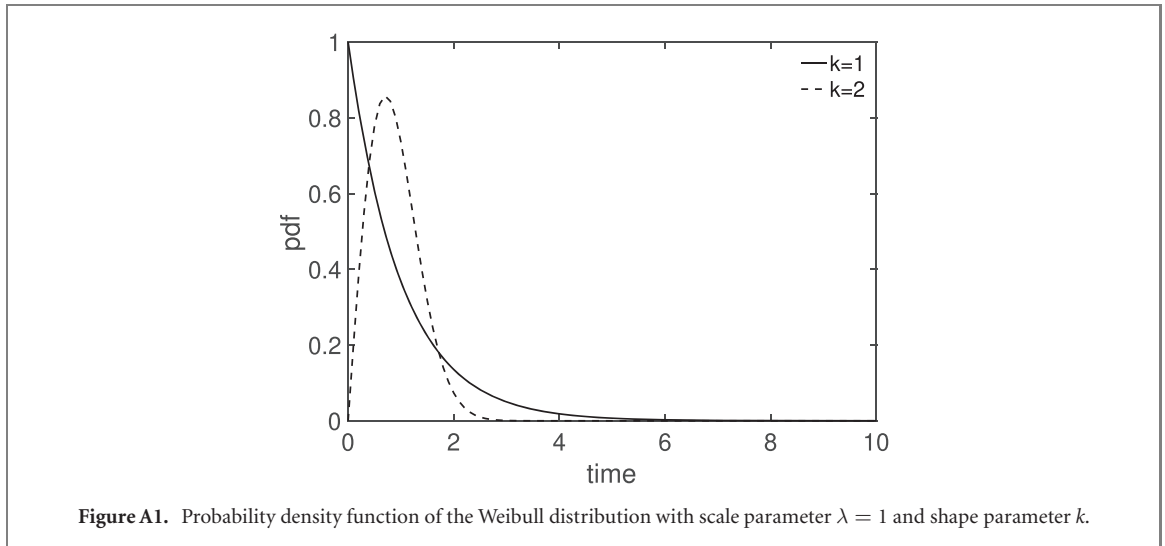
has interesting applications for e.g. the occurrence of antibiotic resistance inside a growing colony which usually comes at a cost in growth speed.

In the case that weak interactions of one strain lead to a susceptibility to pushes, we observe an even stronger dominance of the WI-strain. In this case, the outgrowth of the colony is populated by WI-cells even if the SI-cells divide two times faster. This observation is also valid in the absence of swapping because WI-cells are systematically pushed in direction of the colony perimeter. Motivated by the experiments of Zöllner *et al* [3], we also model the competition between three different interacting strains. In addition to SI- and WI-cells, we consider dynamically created M-cells that are partially piliated. The lower number of pili is materialized by a susceptibility to pushes, which lays between the susceptibility of WI- and SI-cell. Our simulation results show the experimentally observed WI-strain dominated outgrowth, which contains sectors of M-cells. It is important to notice, that the experimentally observed patterns cannot be reproduced if the mechanical interactions of the M-cells agree with the SI- or WI-strain. This can be understood by analysing the development of an initially small colony of SI- or M-cells inside a larger population of slowly dividing WI-cells. The competition of SI- and WI-cells generally leads to the formation of dendrite like structures or the extinction of the SI-strain domain. Compact SI-strain sectors are only observed if pushing of the embedding WI-cells is not considered. By contrast, the competition of M- and WI-cells always leads to compact sectors. Their opening angles depend on the pushing capabilities and divisional disadvantage of the embedding strain. These results suggest that the M-strain is not non-piliated but rather underpiliated. Comparing swapping and pushing mechanisms, we notice that the complete range of experimental results can be modelled by implementing heterogeneous strain depend susceptibility to pushing even without an explicit cell sorting mechanism (swapping).

Together, these results demonstrate the importance of passive mobility induced, by mechanical interactions inside expanding populations. These question the often used growth rate specific fitness definition in mechanical heterogeneous populations and therefore have interesting implications for the field of evolutionary systems and population genetics as a whole. In particular, it would be interesting to see, if indeed a sustained transport of a small sub-population during homogeneous and especially heterogeneous microbial expansion can be observed experimentally.

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Appendix A. Characteristics of the Weibull distribution

The Weibull distribution with scale parameter λ and form parameter k [Weib(λ, k)] is defined as ($t \geq 0$)

$$\rho(t) = \frac{k}{\lambda} \left(\frac{t}{\lambda}\right)^{k-1} e^{-\left(\frac{t}{\lambda}\right)^k}.$$

This distribution reduces to the exponential distribution for $k = 1$ (figure A1).

The cumulative distribution F and moments $\langle T^n \rangle$ are given by

$$F(t) = 1 - e^{-\left(\frac{t}{\lambda}\right)^k}$$

$$\langle T^n \rangle = \lambda^n \Gamma\left(1 + \frac{n}{k}\right)$$

where Γ is the Gamma function. Therefore, the relative moments of two independent Weibull random variables T_1, T_2 [Weib(λ_1, k), Weib(λ_2, k)] are $(\lambda_1/\lambda_2)^n$. The immediate consequence is that fixing relative mean values or scale parameters is identical, if one uses the same form parameter for both distributions. Furthermore, their minimum is again Weibull distributed with form parameter k but scale parameter $\lambda = 1/\sqrt[k]{\frac{1}{\lambda_1^k} + \frac{1}{\lambda_2^k}}$. The probability that T_1 was the smaller random variable is given by

$$P[T_1 \leq T_2] = \int_0^\infty \rho_{T_1}(1 - F_{T_2}) dx \quad (A.1)$$

$$\stackrel{u=\frac{t}{\lambda_1}}{=} \int_0^\infty k u^{k-1} e^{-u^k} \left(1 + \left(\frac{\lambda_1}{\lambda_2}\right)^k\right) du \quad (A.2)$$

Table C1. Reference parameters and symbols.

Initial number of SI-cells	500
Initial number of WI-cells	500
Initial density ρ_0	0.1
Scale parameter of SI- strain	1 h
Mean swap time relative to scale parameter of SI-strain r_s	0.1
Stickiness of M- and WI-strain s_g, s_y	1
Stickiness of SI-strain s_r	1
Mutation probability (in division) of SI- to M-strain p_m	0
Mean division time of WIS strain relative to mean division time of SIS strain	r_d
Maximal amount of cells that can be pushed by the WIS strain	P

$$= \frac{1}{1 + \left(\frac{\lambda_1}{\lambda_2}\right)^k}. \quad (\text{A.3})$$

Let X_k be the minimum of l independent random variables which are Weibull distributed with identical scale parameter λ and form parameter k . It is clear from induction that this variable is again Weibull distributed with form parameter k but scale parameter $\frac{\lambda}{\sqrt[l]{l}}$. Therefore, the fraction of the mean values of X_k and X_1 is

$$\frac{\langle X_k \rangle}{\langle X_1 \rangle} = \frac{l}{\sqrt[l]{l}} \Gamma\left(1 + \frac{1}{k}\right). \quad (\text{A.4})$$

Since for $k = 2$ $\Gamma\left(1 + \frac{1}{2}\right)$ is equal $\sqrt{\pi}/2$, the fraction is smaller one for $l = 1$, but larger one for $l \geq 2$.

Appendix B. Computation of sector angles

To compute the opening angles in section 3.2, we need to find the left and right endpoint of the sectors (see figure B1). From the coordinates (x_i, y) relative to the middle of the inoculation zone we can compute the left and right angle α_l, α_r , as

$$\alpha_i = \arctan \frac{y}{|x_i|}.$$

The opening angle α is then defined as $\alpha = 180^\circ - (\alpha_l + \alpha_r)$. To compute y , we count the number of WI-cells per layer and compute with the MATLAB function ‘findechangepts’ the first layer where the mean and slope change significantly. From the y value we compute the corresponding x values by finding the left and right closest points to the origin in layer y .

Remark. To compute the angles we change from hexagonal grid coordinates (x', y') to Cartesian coordinates by

$$x = x' + \frac{y'}{2} \quad y = \frac{\sqrt{3}}{2} y'.$$

Appendix C. Reference parameters

If not otherwise mentioned we used in the simulations the parameters of table C1.

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