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<http://lukaseigentler.github.io>

Competition and coexistence in bacterial range expansion: the role of founder cells and spatial heterogeneities

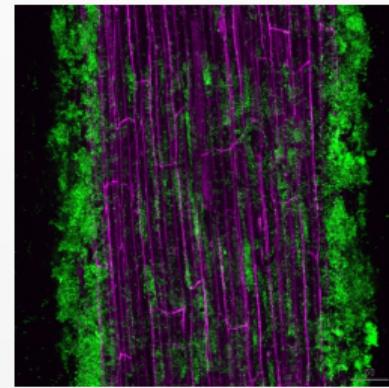
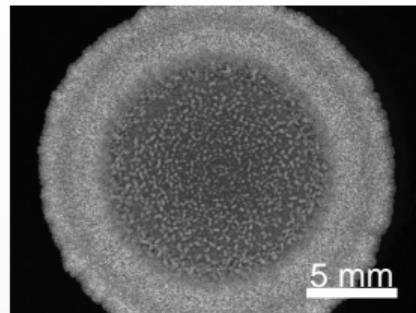
Spatial ecology workshop, Sheffield

11/07/2023

Lukas Eigentler (Universität Bielefeld)

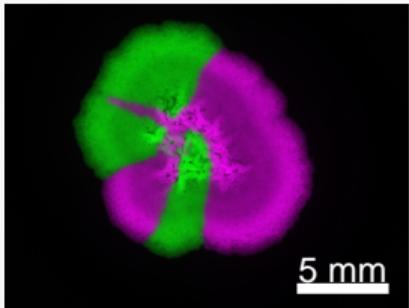
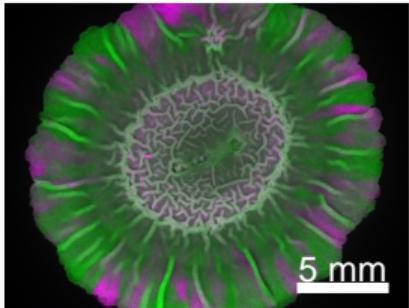
Biofilms

- Bacterial biofilms are surface-adhering multicellular collectives embedded in a self-produced extracellular matrix.
- Biofilms can have both beneficial and detrimental effects on the surrounding environment.
- Example: the soil-dwelling bacterium *Bacillus subtilis* forms biofilms on the roots of plants, where some strains promote the growth of plants.
- To fully realise their potential as biocontrol agents, **strains need to be capable of coexisting with (or outcompeting) other biofilm-forming strains** in the rhizosphere.



Competition within biofilms

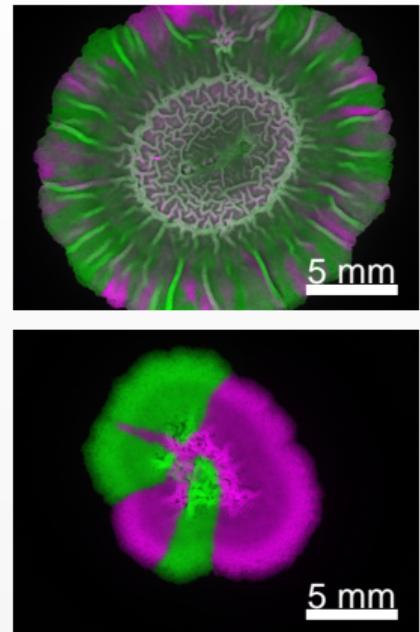
- Competition in biofilms is underpinned by kin discrimination.
- Many mechanisms of kin discrimination require spatial co-location of strains.
- Take a step back: **need to understand the role of spatial structure first.**
- Often studied through the “colony biofilm model”^a



^aEigentler, L. et al.: *Open Biol.* 12.220294 (2022).

Competition within biofilms

- Spatial structure is best studied using **isogenic strains**: all other competitive mechanisms (e.g. kin discrimination) are excluded from the model system by design.
- Isogenic strains: Low founder densities promote spatial segregation and formation of spatial sectors.^{1,2}
- Questions: **How does spatial structure arise and how does it affect competitive interactions?**

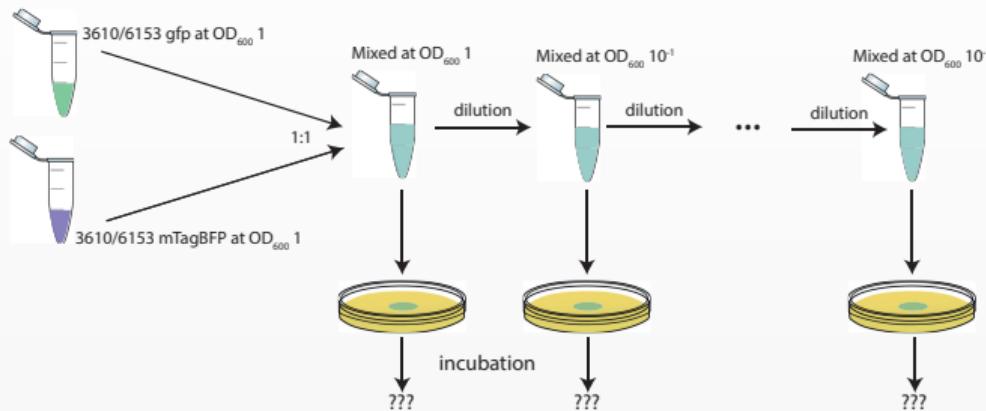


¹van Gestel, J. et al.: *ISME J.* 8.10 (2014)

²Martinez-Garcia, R. et al.: *PLoS Comput. Biol.* 14.4 (2018)

Methods

Experimental assay:



Tested for

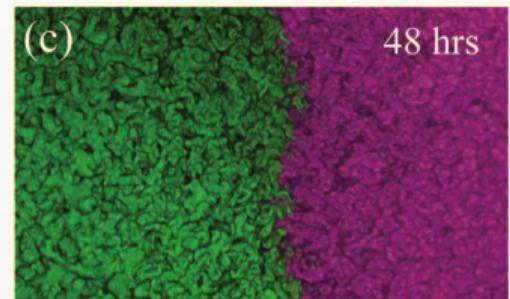
- *B. subtilis* NCIB3610 ("standard" lab strain).
- *B. subtilis* NRS6153 (isolated from garden soil in Tayport, Fife, UK).

Methods

Mathematical model for isogenic strain pair:

$$\frac{\partial B_1}{\partial t} = \nabla \cdot ((1 - (B_1 + B_2)) \nabla B_1) + B_1 (1 - (B_1 + B_2)),$$
$$\frac{\partial B_2}{\partial t} = \nabla \cdot ((1 - (B_1 + B_2)) \nabla B_2) + B_2 (1 - (B_1 + B_2)).$$

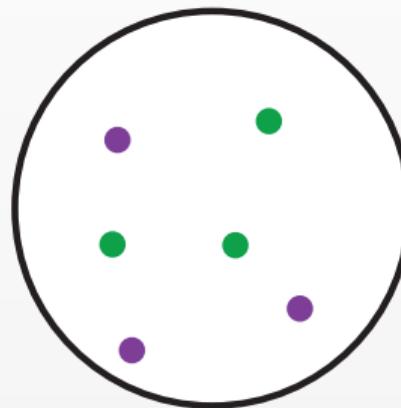
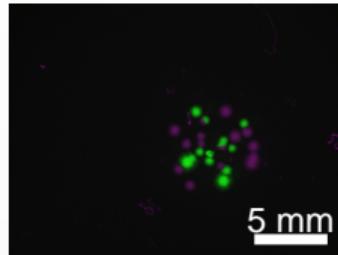
- Circular domain $\Omega = \{x \in \mathbb{R}^2 : \|x\| \leq R\}$.
- Logistic growth
- Diffusion with density-dependent diffusion coefficient, motivated by experimental observation that initially separated colonies abut rather than merge¹.



¹Matoz-Fernandez, D. et al.: *Soft Matter* 16.13 (2020)

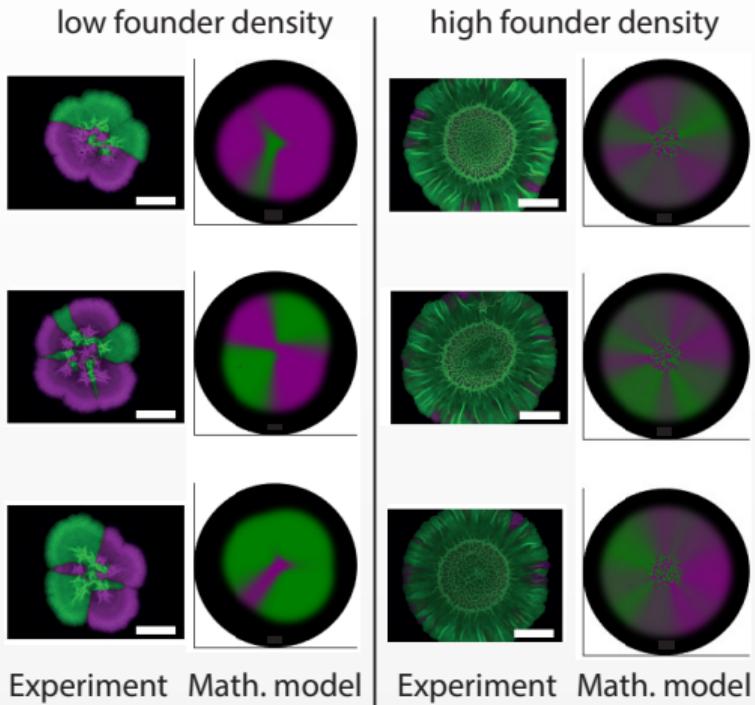
Initial conditions

- What are appropriate initial conditions?
- In experiments, **cells settle at random locations** within the initial spot and grow to small micro-colonies.
- In the model, we position **initial “cell patches” at random locations** in the domain centre $\Omega_0 = \{x \in \mathbb{R}^2 : \|x\| \leq R_0\} \subset \Omega$.
- Each model patch represents 1 microcolony \Rightarrow tool to modulate founder density.



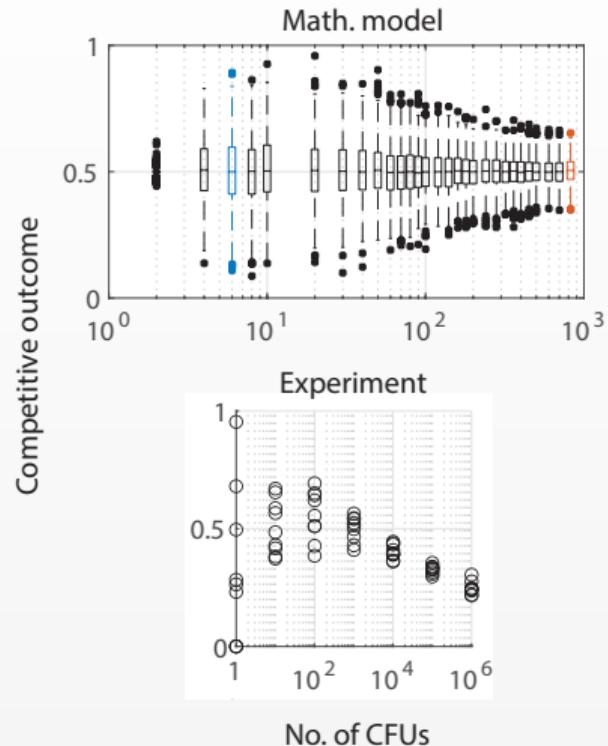
Variability in competitive outcome

- High founder density: no spatial structure and initial strain ratio consistently determines competitive outcome.
- Low founder density: spatial segregation occurs. Large variability in competitive outcome for fixed initial strain ratio.



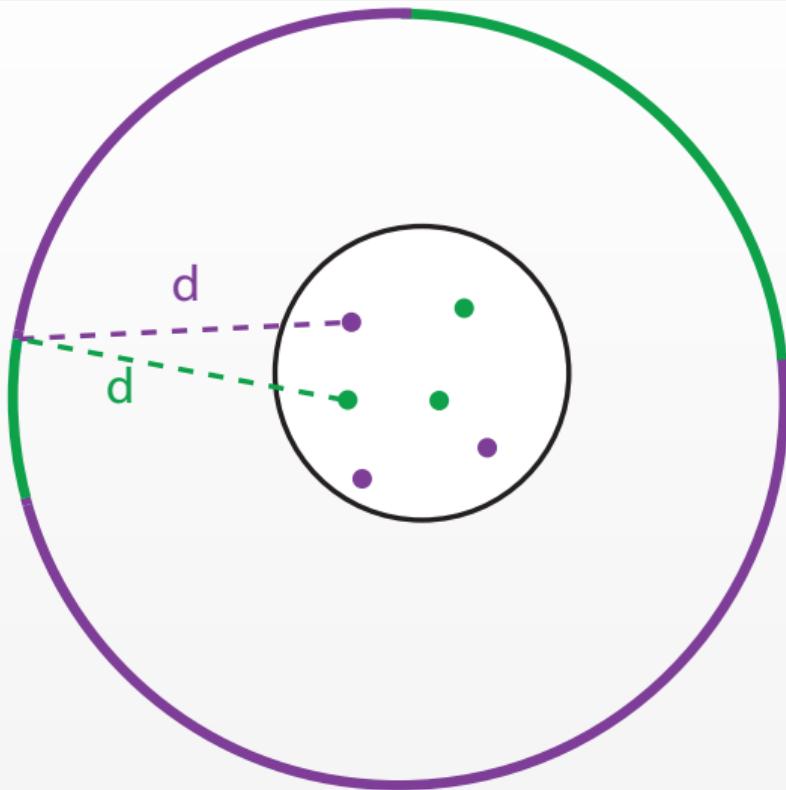
Variability in competitive outcome

- Founder density significantly affects phenotype and variability in competitive outcome.
- Variability increases with decreasing founder density.



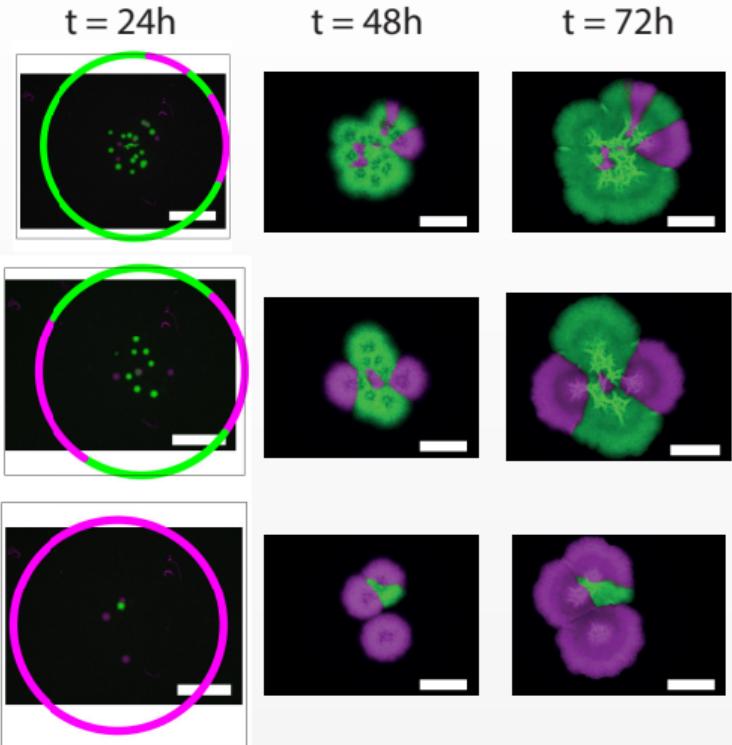
Disentangling variability

- Hypothesis: only initial patches that can drive the biofilm's radial expansion contribute to outcome density.
- We define a quantity that, based on the initial cell locations, **measures a strain's "access to free space"**



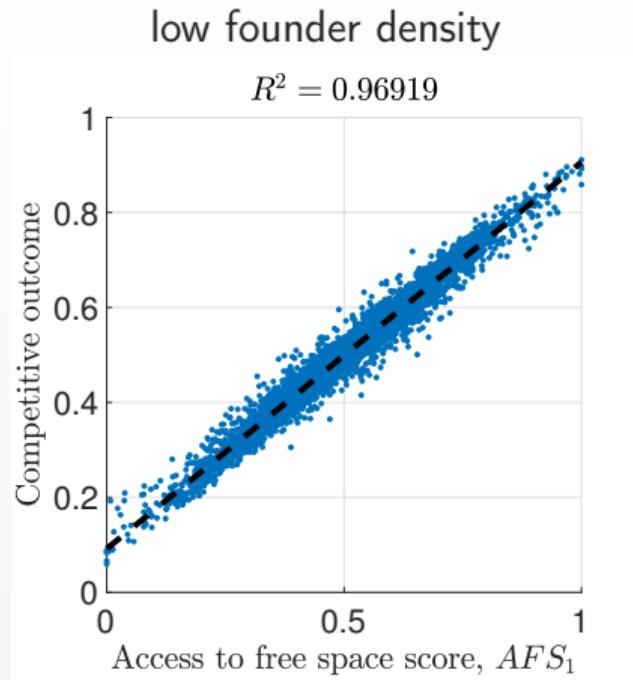
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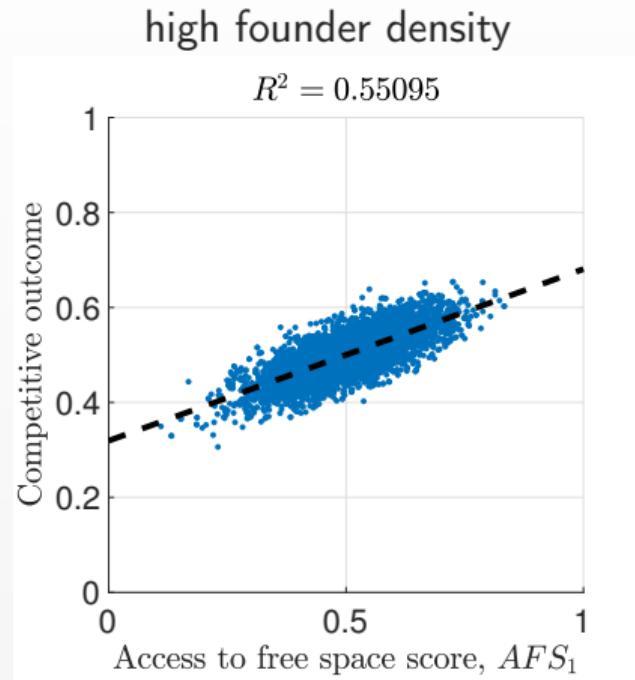
Access to free space predicts outcome

- Access to free space determines competitive outcome in the absence of any other competitive dynamics (isogenic strains).



Access to free space predicts outcome

- Access to free space determines competitive outcome in the absence of any other competitive dynamics (isogenic strains).
- Slope of relation between access to free space and competitive outcome depends on founder density.



Non-isogenic strains

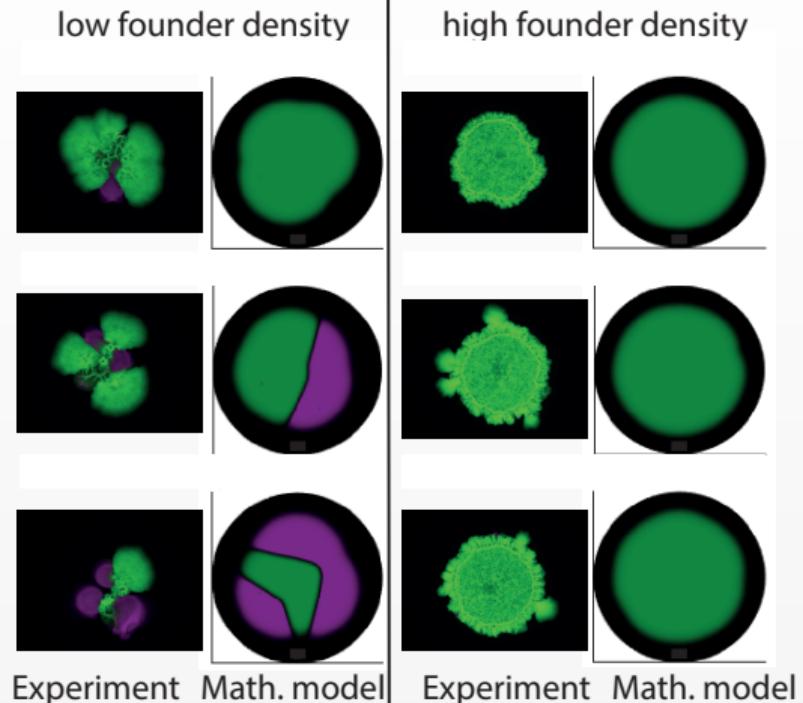
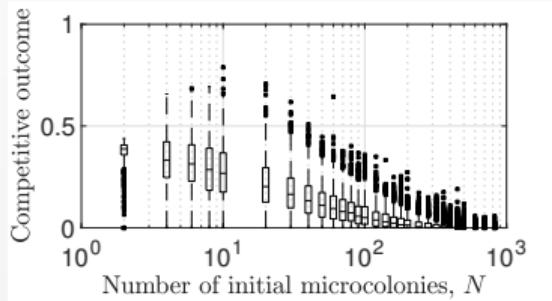
- Do these results also hold if **strains are non-isogenic and interact through local antagonisms?**

$$\frac{\partial B_1}{\partial t} = \nabla \cdot \left(\left(1 - \frac{B_1 + B_2}{k} \right) \nabla B_1 \right) + B_1 \left(1 - \frac{B_1 + B_2}{k} \right) - B_1 B_2,$$
$$\frac{\partial B_2}{\partial t} = \nabla \cdot \left(d \left(1 - \frac{B_1 + B_2}{k} \right) \nabla B_2 \right) + r B_2 \left(1 - \frac{B_1 + B_2}{k} \right) - c B_2 B_1.$$

Nondimensional model, i.e. d, r, c are ratios of corresponding dimensional parameters.

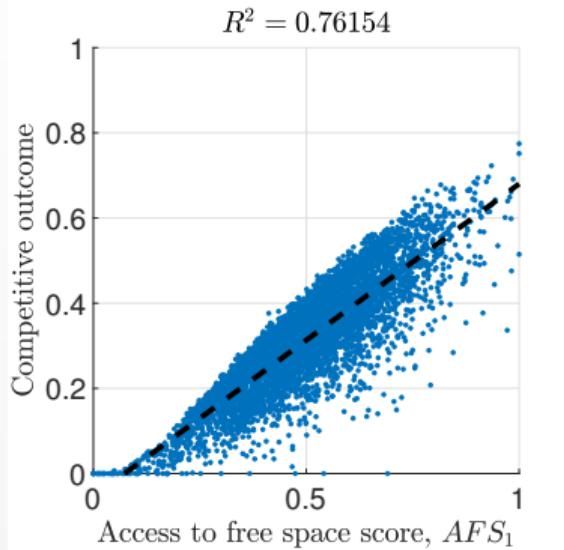
Non-isogenic strains

- High founder density: competitive exclusion.
- Low founder density: spatial segregation enables coexistence.
- Decreases in founder density cause (i) increased variability in competitive outcome, (ii) higher (on average) densities of weaker strain.



Access to free space predicts outcome

- Access to free space remains a reliable predictor of competitive outcome for low founder densities.
- **Competition for space is the dominant mode of interaction for low founder densities.**



Impact of spatial heterogeneity

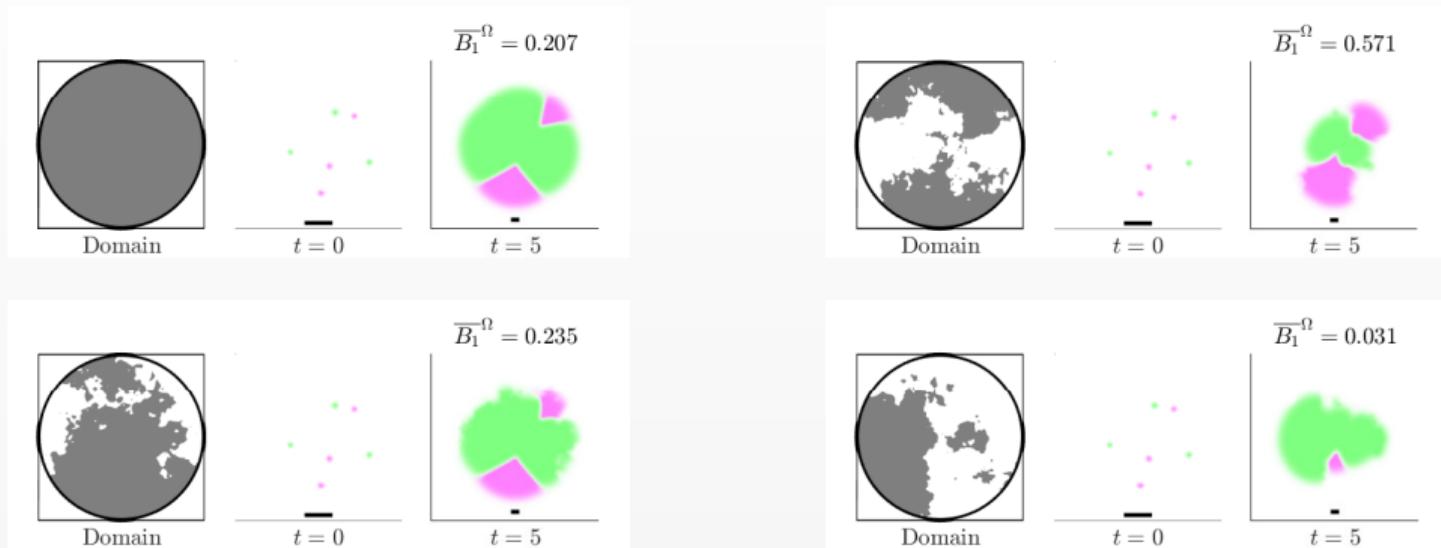
Q: What if environmental conditions are spatially heterogeneous?

$$\frac{\partial B_1}{\partial t} = \nabla \cdot \left(\mathbf{d}_1(\mathbf{x}) \left(1 - \frac{B_1 + B_2}{k} \right) \nabla B_1 \right) + \mathbf{r}_1(\mathbf{x}) B_1 \left(1 - \frac{B_1 + B_2}{k} \right) - c_{12} B_1 B_2,$$

$$\frac{\partial B_2}{\partial t} = \nabla \cdot \left(\mathbf{d}_2(\mathbf{x}) \left(1 - \frac{B_1 + B_2}{k} \right) \nabla B_2 \right) + \mathbf{r}_2(\mathbf{x}) B_2 \left(1 - \frac{B_1 + B_2}{k} \right) - c_{21} B_1 B_2.$$

Impact of spatial heterogeneity

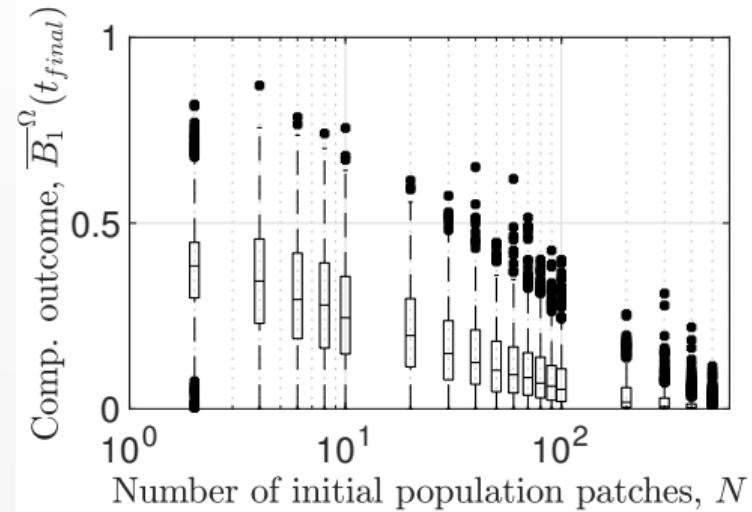
Q: What if environmental conditions are spatially heterogeneous?



A: Spatial heterogeneity adds more variability \Rightarrow Access to free space score cannot make accurate predictions.

Impact of spatial heterogeneity

Q: Which source of variability (low founder density or spatial heterogeneous environmental conditions) dominates?



A: Low founder density determines variability in competitive outcome.

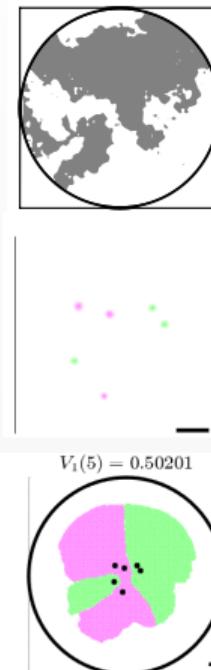
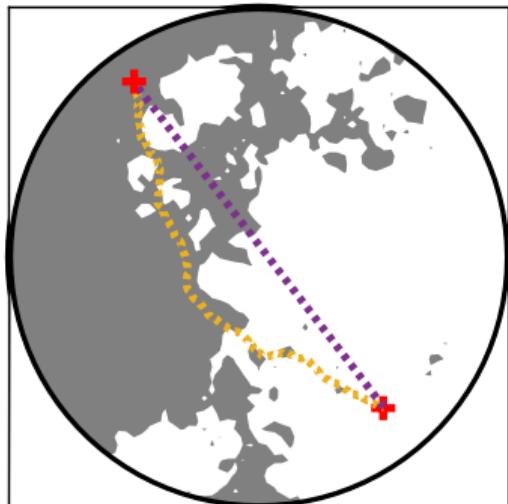
Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions of competitive outcome?

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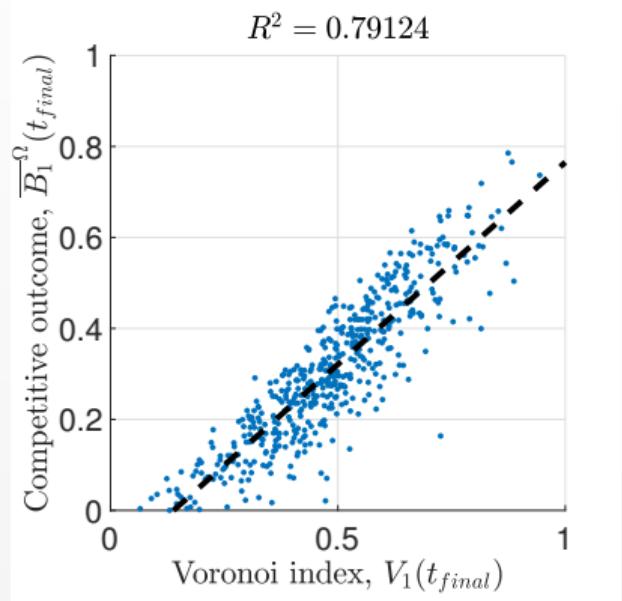
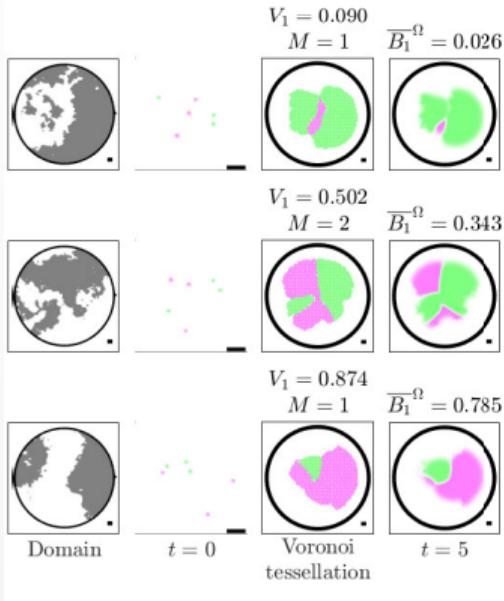
A: Yes, using Voronoi tessellations based on an appropriate metric.



Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions for competitive outcome?

A: Yes, using Voronoi tessellations based on an appropriate metric.



Conclusions

- Large variability in competitive outcome occurs for biofilms inoculated at low founder density, induced by the random positions of founder cells within the inoculum.
- Competition for space is the dominant mode of competition for low founder densities.
- Antagonistic interactions determine competitive outcome for high founder densities.
- Impact on applications (e.g. use of *B. subtilis* as biofertilizer): Competitive success across all founder densities can only be guaranteed if a strain spreads fast and kills efficiently.

Discussion

- How to test the results on spatially heterogeneous domains in empirical systems?
- Experimental approaches?
- Data-driven approaches?
- Nothing in my models is microbe-specific - just a phenomenological system of range expansion.
- Extensions to eco-evolutionary dynamics?

Acknowledgements

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of Dundee

References

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- [1] Eigentler, L., Davidson, F. A. and Stanley-Wall, N. R.: 'Mechanisms driving spatial distribution of residents in colony biofilms: an interdisciplinary perspective'. *Open Biol.* 12.220294 (2022).
- [2] Eigentler, L., Kalamara, M., Ball, G., MacPhee, C. E., Stanley-Wall, N. R. and Davidson, F. A.: 'Founder cell configuration drives competitive outcome within colony biofilms'. *ISME J* 16.6 (2022), pp. 1512–1522.
- [3] Eigentler, L., Stanley-Wall, N. R. and Davidson, F. A.: 'A theoretical framework for multi-species range expansion in spatially heterogeneous landscapes'. *Oikos* 2022.8 (2022), e09077.

Additional slides

Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions for competitive outcome?

Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions for competitive outcome?

A: Yes, using **Voronoi tessellations based on an appropriate metric**.

Let $\mathcal{P}(x, y) := \{P = p([0, 1]) \subset \Omega, \text{ where } p : [0, 1] \rightarrow \Omega : p \in C^1 \text{ a.e.}, p(0) = x, p(1) = y\}$ be the set of all paths from x to y . For a given path $P \in \mathcal{P}(x, y)$, the time taken to move along the path is given by

$$I(P) := \int_P \frac{1}{c(x)} ds = \int_0^1 \frac{1}{c(p(\tau))} \|p'(\tau)\| d\tau,$$

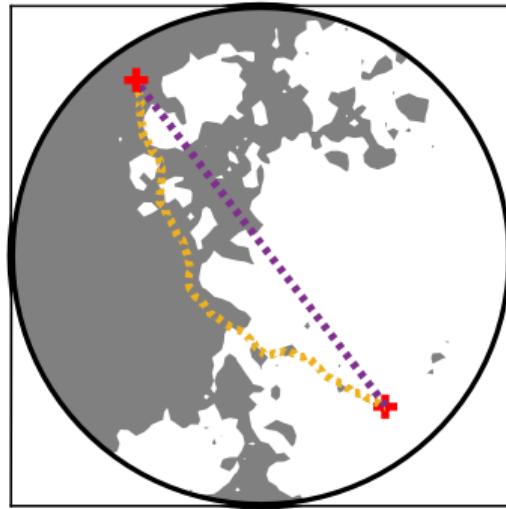
where $0 \leq c(x) < \infty$ represents the propagation speed along the path P . We define the *front propagation metric* from x to y as

$$t_{FP}(x, y) := \inf_{P \in \mathcal{P}(x, y)} I(P).$$

Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions of competitive outcome?

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Voronoi tessellation of whole domain:

$$\Delta_{B_i}^\Omega := \left\{ x \in \Omega : \min_{x_i \in B_i} t_{FP}(x, x_i) \leq \min_{x_j \in B_j} t_{FP}(x, x_j), i \neq j \right\},$$

where $B_i := \{x \in \{x_1, \dots, x_N\} : B_i(x, 0) > 0\}$, $i = 1, 2$.

Restrict to area expected to be occupied by time t :

$$\Delta_{B_i}(t) := \left\{ x \in \Delta_{B_i}^\Omega : \min_{y \in B_i} t_{FP}(x, y) \leq t \right\}, \quad i = 1, 2.$$

Voronoi index:

$$V_i(t) := \frac{\text{Area}(\Delta_{B_i}(t))}{\text{Area}(\Delta_{B_1}(t)) + \text{Area}(\Delta_{B_2}(t))}, \quad i = 1, 2,$$

