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

StAMBio Seminar

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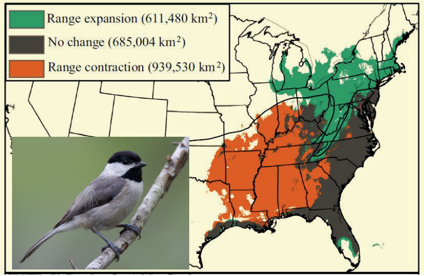
Range expansion

- Range expansion refers to the spread of a population into previously unoccupied habitats.
- Occurs in early evolutionary history of species, but is also induced by climate change because habitable environments shift polewards (or to higher altitudes).
- Examples include ecological invasions, spread of epidemics, human migration, growth of microbial populations, ...

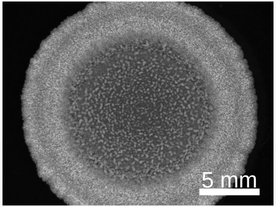


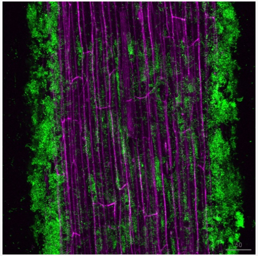
Range expansion of Carolina chickadee (*Poecile carolinensis*)[1]

[1] McQuillan, M. A. and Rice, A. M.: *Ecology and Evolution* 5.21 (2015)

Biofilms

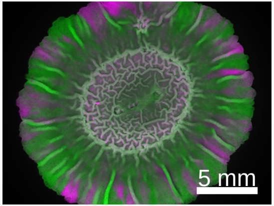
- Bacterial biofilms are surface-adhering multicellular collectives embedded in a self-produced extracellular matrix.
- Biofilms can have both beneficial and detrimental effects on the surrounding environment.
- Example: the soil-dwelling bacterium *Bacillus subtilis* forms biofilms on the roots of plants, 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.

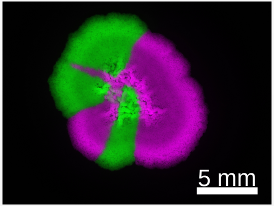




Competition within biofilms

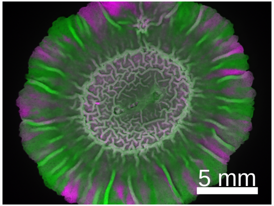
- Competition in biofilms is underpinned by kin discrimination.
- Many mechanisms of kin discrimination require spatial co-location of strains.
- Take a step back: need to understand the role of spatial structure first.

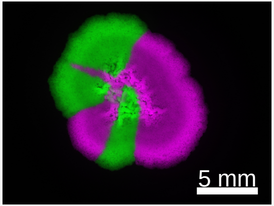




Competition within biofilms

- 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?

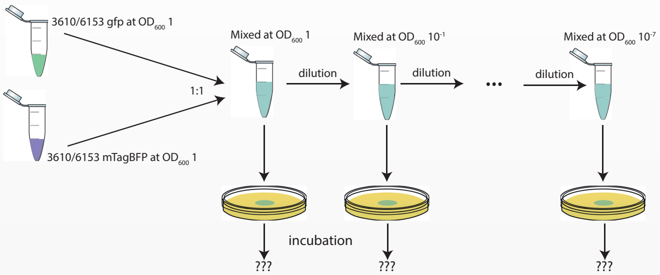




[1] van Gestel, J. et al.: *ISME J.* 8.10 (2014)
[2] Martinez-Garcia, R. et al.: *PLoS Comput. Biol.* 14.4 (2018)

Methods

Experimental assay:



Tested for

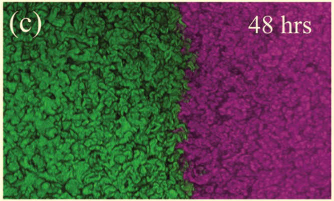
- *B. subtilis* NCIB3610 (“standard” lab strain).
- *B. subtilis* NRS6153 (isolated from garden soil in Tayport, Fife).

Methods

Mathematical model for isogenic strain pair:

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

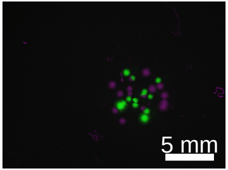
- Circular domain $\Omega = \{x \in \mathbb{R}^2 : \|x\| \leq R\}$.
- Logistic growth
- Diffusion with density-dependent diffusion coefficient, motivated by experimental observation that initially separated colonies abut rather than merge[2].

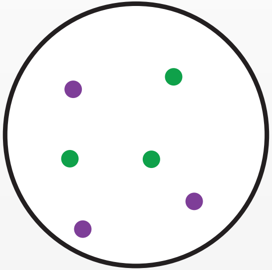


[2] Matoz-Fernandez, D. et al.: *Soft Matter* 16.13 (2020)

Initial conditions

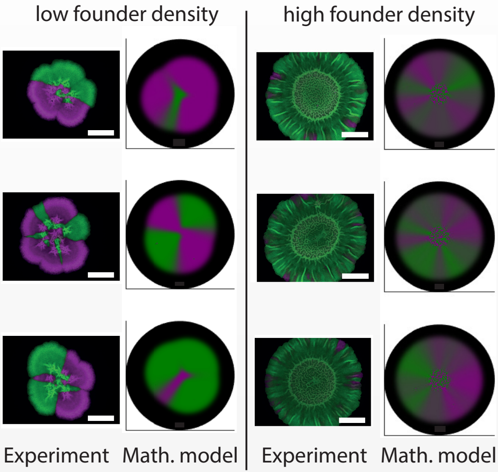
- What are appropriate initial conditions?
- In experiments, cells settle at random locations within the initial spot and grow to small micro-colonies.
- In the model, we position initial "cell patches" at random locations in the domain centre $\Omega_0 = \{x \in \mathbb{R}^2 : \|x\| \leq R_0\} \subset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





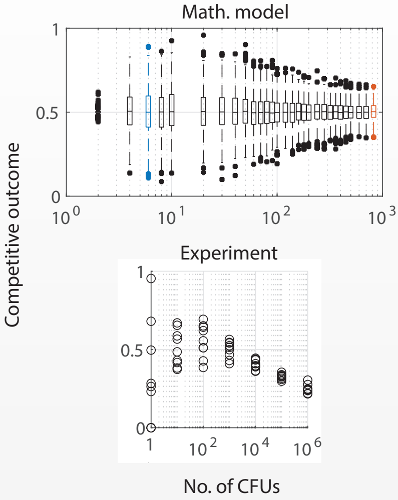
Variability in competitive outcome

- 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.
- Founder density significantly affects phenotype and variability in competitive outcome.



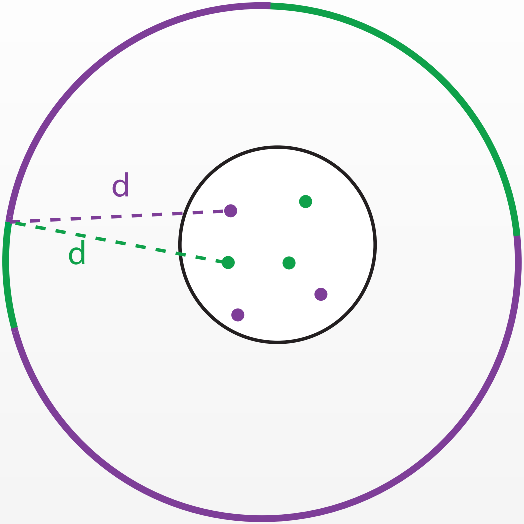
Variability in competitive outcome

- Founder density significantly affects phenotype and variability in competitive outcome.
- Variability increases with decreasing founder density.
- Note the computational power of the mathematical model: 1000 model simulations each vs 12 technical replicates each of experimental assay.



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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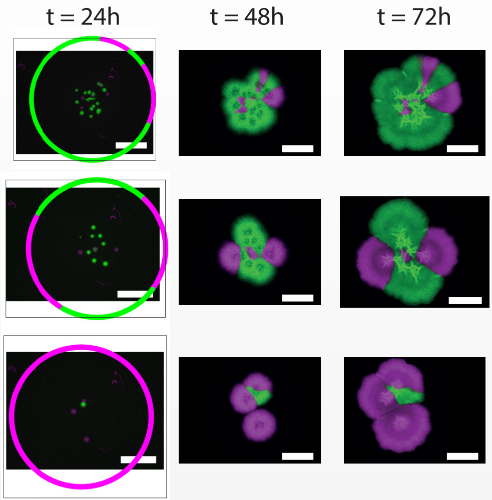
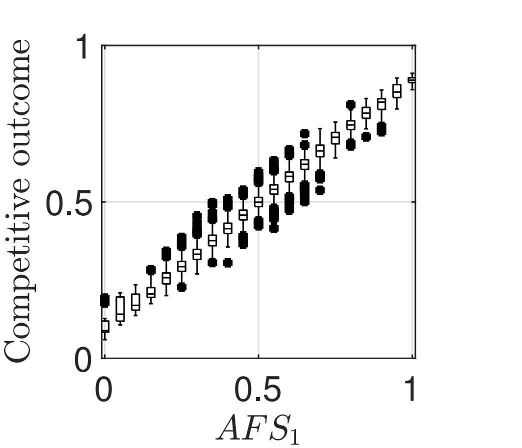


Access to free space predicts outcome

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

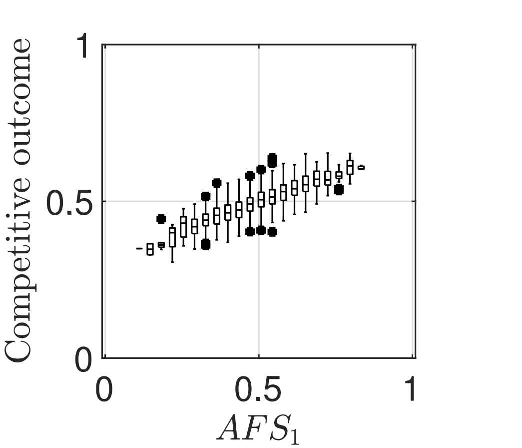
low founder density



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.

high founder density



Non-isogenic strains

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

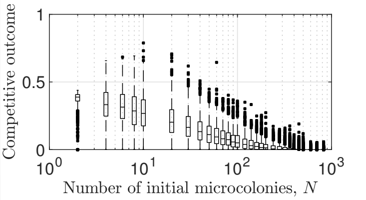
$$\frac{\partial B_1}{\partial t} = \nabla \cdot \left(\left(1 - \frac{B_1 + B_2}{k} \right) \nabla B_1 \right) \quad + B_1 \left(1 - \frac{B_1 + B_2}{k} \right) - B_1 B_2,$$

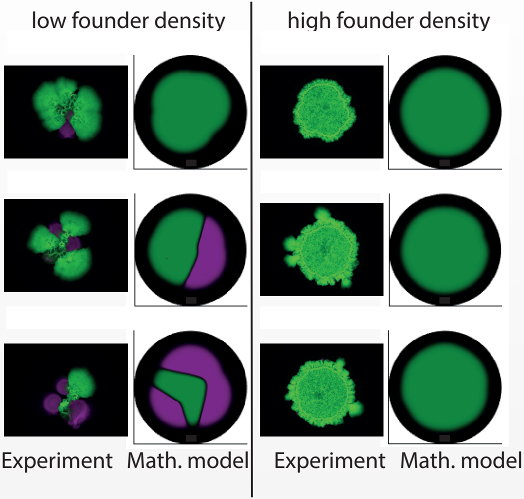
$$\frac{\partial B_2}{\partial t} = \nabla \cdot \left(d \left(1 - \frac{B_1 + B_2}{k} \right) \nabla B_2 \right) + r B_2 \left(1 - \frac{B_1 + B_2}{k} \right) - c B_2 B_1.$$

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

Non-isogenic strains

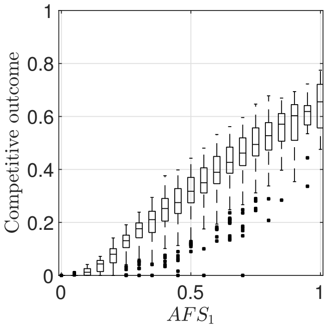
- High founder density: competitive exclusion.
- Low founder density: spatial segregation enables coexistence.
- Decreases in founder density cause (i) increased variability in competitive outcome, (ii) higher (on average) densities of weaker strain.





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

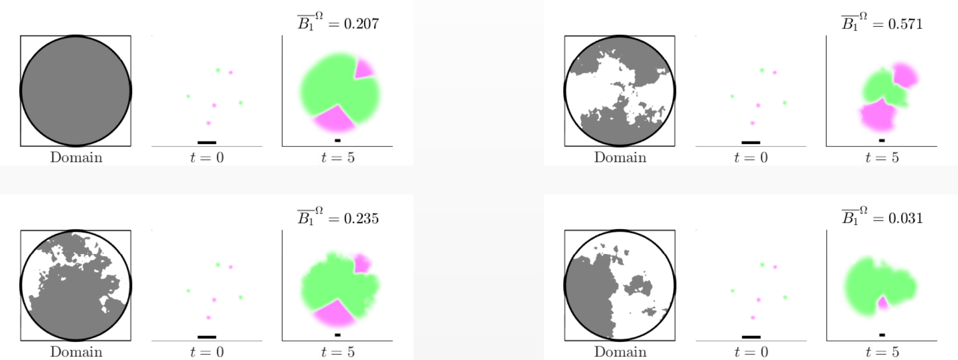
Q: What if environmental conditions are spatially heterogeneous?

$$\frac{\partial B_1}{\partial t} = \nabla \cdot \left(d_1(x) \left(1 - \frac{B_1 + B_2}{k}\right) \nabla B_1 \right) + r_1(x) B_1 \left(1 - \frac{B_1 + B_2}{k}\right) - c_{12} B_1 B_2,$$

$$\frac{\partial B_2}{\partial t} = \nabla \cdot \left(d_2(x) \left(1 - \frac{B_1 + B_2}{k}\right) \nabla B_2 \right) + r_2(x) B_2 \left(1 - \frac{B_1 + B_2}{k}\right) - c_{21} B_1 B_2.$$

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?

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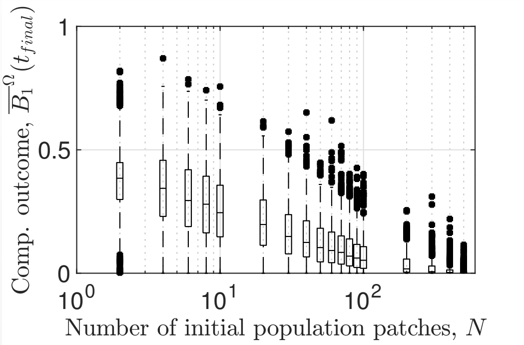

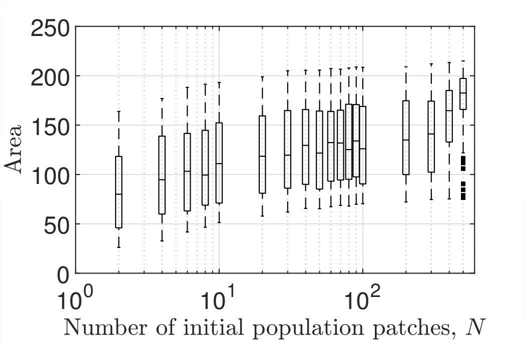

A: Low founder density determines variability in competitive outcome but spatial heterogeneities determine variability in footprint.

Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions for competitive outcome?

Predictions of competitive outcome in heterogeneous landscapes

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

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

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

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

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

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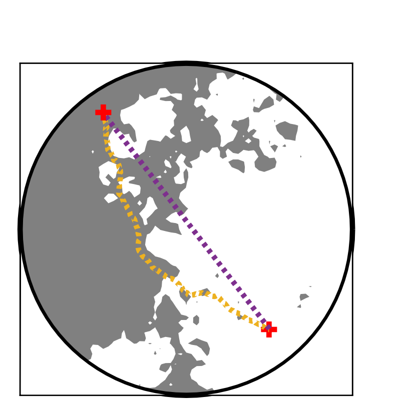

Predictions of competitive outcome in heterogeneous landscapes

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Voronoi tessellation of whole domain:

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

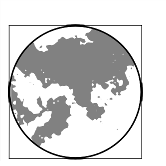
where $\mathcal{B}_i := \{\mathrm{x} \in \{\mathrm{x_1}, \dots \mathrm{x_N}\} : B_i(\mathrm{x}, 0) > 0\}, i = 1, 2.$

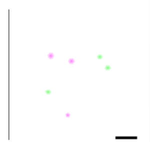
Restrict to area expected to be occupied by time t:

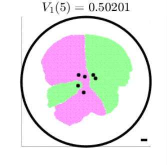
$$\Delta_{B_i}(t) := \left\{ \mathrm{x} \in \Delta_{B_i}^{\Omega} : \min_{\mathrm{y} \in \mathcal{B}_i} t_{\mathrm{FP}}(\mathrm{x}, \mathrm{y}) \leq t \right\}, \quad i = 1, 2.$$

Voronoi index:

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







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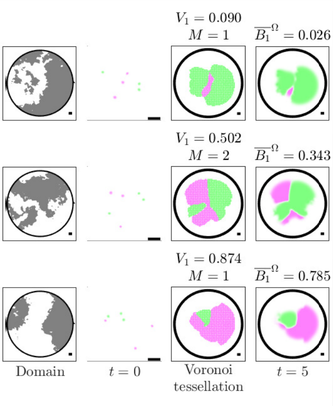

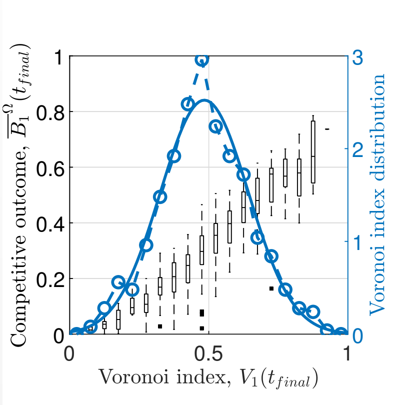

Conclusions

- Large variability in competitive outcome occurs for biofilms inoculated at low founder density, induced by the random positions of founder cells within the inoculum.
- Large variability in biofilm footprint occurs in spatially heterogeneous environments.
- Competitive outcome can be predicted based on founder cell locations and information on the spatial environment.
- Predictions hold true even if kin discrimination occurs ⇒ "Race for space" is more important than antagonistic actions at low 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.

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- David Stevenson
- Tetyana Sukhodub

References

Slides are available on my website.

`http://lukaseigentler.github.io`

- Eigentler, L., Stanley-Wall, N. R. and Davidson, F. A.: 'A theoretical framework for multi-species range expansion in spatially heterogeneous landscapes'. *BioRxiv preprint* (2021).
- 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'. *BioRxiv preprint* (2021).