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<http://lukaseigentler.github.io>

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

QSEB Seminar

24/04/2024

*Lukas Eigentler*

*joint with Margarita Kalamara, Graeme Ball, Nicola R. Stanley-Wall,  
Fordyce A. Davidson (all Dundee), Cait E. MacPhee (Edinburgh)*

# My research

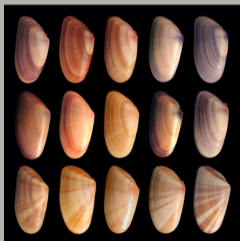
## Vegetation patterns in semi-arid ecosystems

in collaboration with [Jonathan A. Sherratt](#) and [Mattia Senti](#)



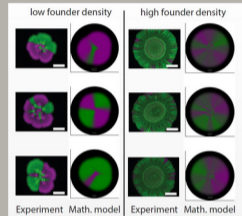
## Evolution and maintenance of individual variation

in collaboration with [Klaus Reinhold](#) and [David W. Kikuchi](#)



## Competition and cooperation in bacterial biofilms

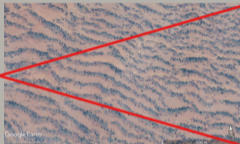
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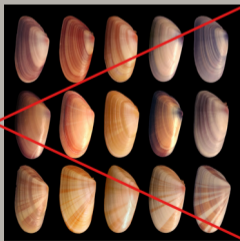
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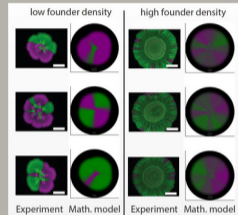
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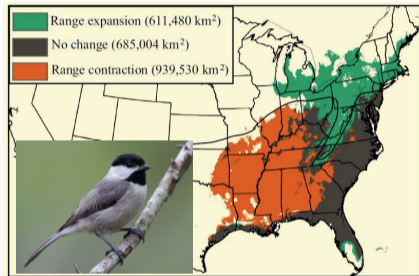
## Competition and cooperation in bacterial biofilms

in collaboration with [Margarita Kalamara](#), [Thibault Rosazza](#), [Graeme Ball](#), [Cait E. MacPhee](#), [Nicola R. Stanley-Wall](#) and [Fordyce A. Davidson](#)



# 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**, ...

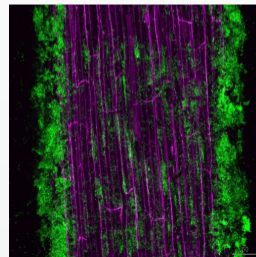
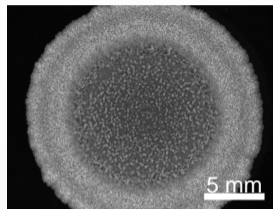


Range expansion of Carolina chickadee (*Poecile carolinensis*)<sup>1</sup>

<sup>1</sup>McQuillan, M. A. and Rice, A. M.: *Ecology and Evolution* 5.21 (2015)

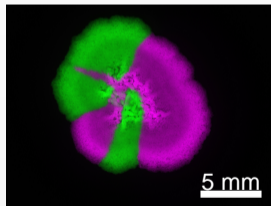
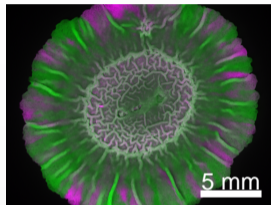
# Biofilms

- 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

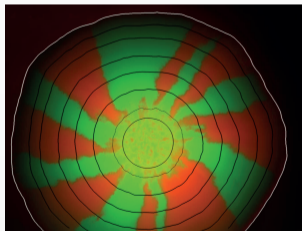
- Competition in biofilms is underpinned by kin discrimination.
- Many mechanisms of kin discrimination require spatial co-location of strains.
- Take a step back: **need to understand the role of spatial structure first.**



# Colony biofilms

Spatial structure in biofilms is typically studied through the **colony biofilm model**<sup>a</sup>:

- Genetic drift induces spatial segregation.<sup>b</sup>



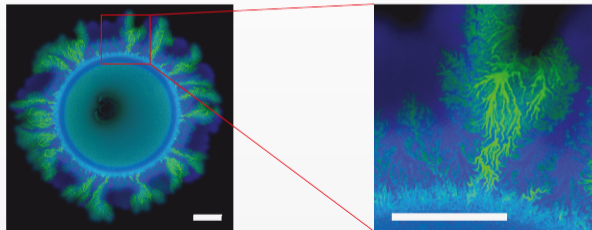
<sup>a</sup>Eigentler, L. et al.: *Open Biol.* 12.220294 (2022).

<sup>b</sup>Hallatschek, O. et al.: *PNAS* 104.50 (2007).

# Colony biofilms

Spatial structure in biofilms is typically studied through the **colony biofilm model**<sup>a</sup>:

- Syntrophic relationships induce dendritic patterns.<sup>b</sup>



<sup>a</sup>Eigentler, L. et al.: *Open Biol.* 12.220294 (2022).

<sup>b</sup>Goldschmidt, F. et al.: *The ISME Journal* 11.9 (2017).

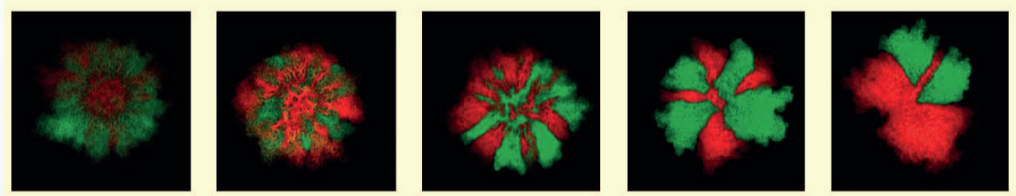


# Colony biofilms

Spatial structure in biofilms is typically studied through the **colony biofilm model**<sup>a</sup>:

- Reduction in initial population density induces spatial segregation.<sup>b</sup>

————— decreasing initial population density —————>

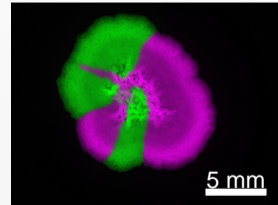
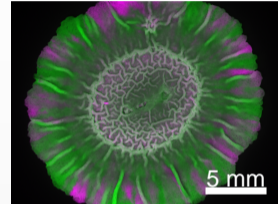


<sup>a</sup>Eigentler, L. et al.: *Open Biol.* 12.220294 (2022).

<sup>b</sup>van Gestel, J. et al.: *ISME J.* 8.10 (2014).

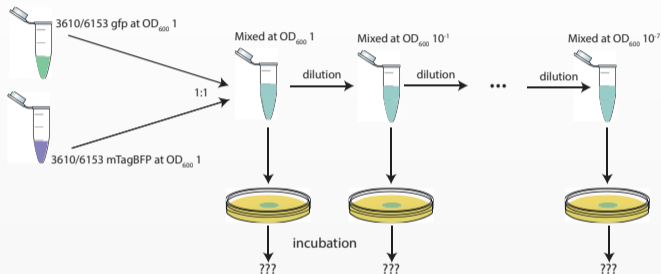
# Competition within biofilms

- Questions: How does spatial structure arise in biofilms with low initial population density and how does it affect competitive interactions?
- Spatial structure is best studied using **isogenic strains**: all other competitive mechanisms (e.g. kin discrimination) are excluded from the model system by design.
- $\Rightarrow$  Then extend to strain combinations with antagonistic interactions.



# Methods

## Experimental assay:



## Tested for

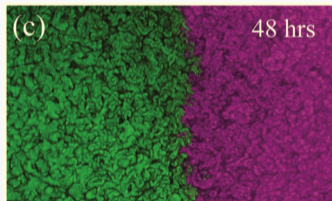
- *B. subtilis* NCIB3610 (“standard” lab strain).
- *B. subtilis* NRS6153 (isolated from garden soil in Tayport, Fife, UK).

# Methods

Mathematical model for isogenic strain pair:

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

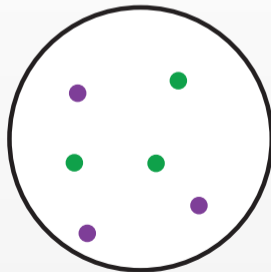
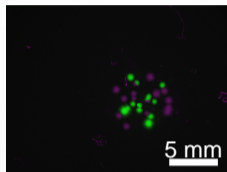
- Circular domain  $\Omega = \{x \in \mathbb{R}^2 : \|x\| \leq R\}$ .
- Logistic growth
- Diffusion with density-dependent diffusion coefficient, motivated by experimental observation that initially separated colonies abut rather than merge<sup>2</sup>.



<sup>2</sup>Matoz-Fernandez, D. et al.: *Soft Matter* 16.13 (2020)

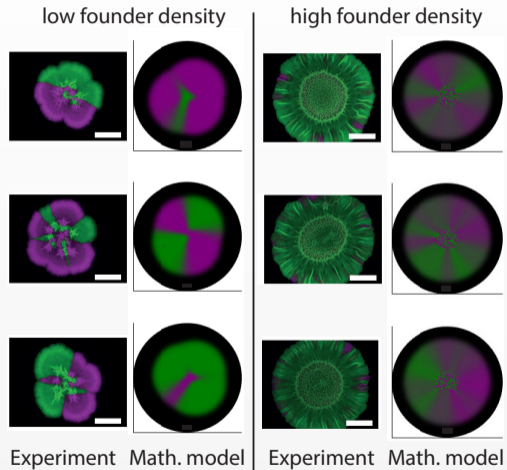
# Initial conditions

- 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.**



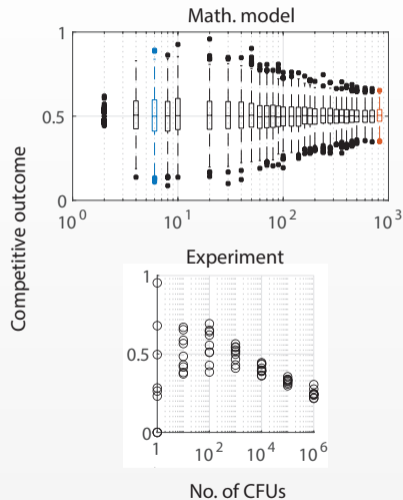
# Variability in competitive outcome

- 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.



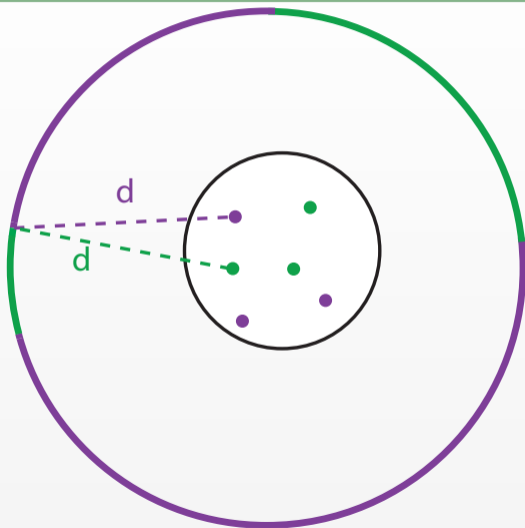
# Variability in competitive outcome

- 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

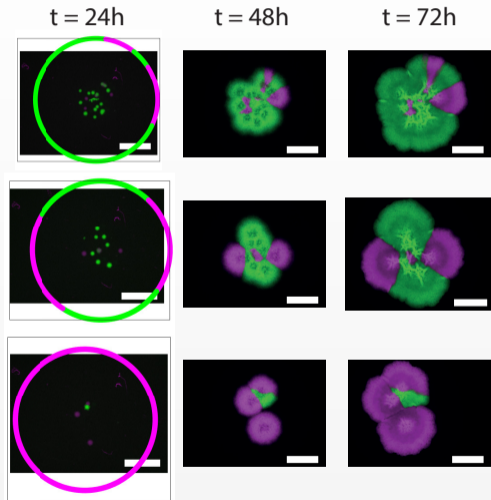
- Hypothesis: only initial patches that can drive the biofilm's radial expansion contribute to outcome density.
- We define a quantity that, based on the initial cell locations, **measures a strain's "access to free space"**





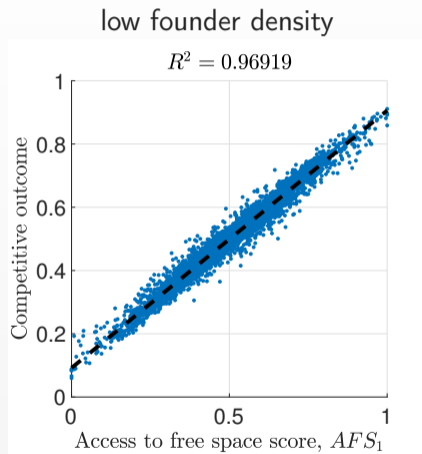
# Disentangling variability

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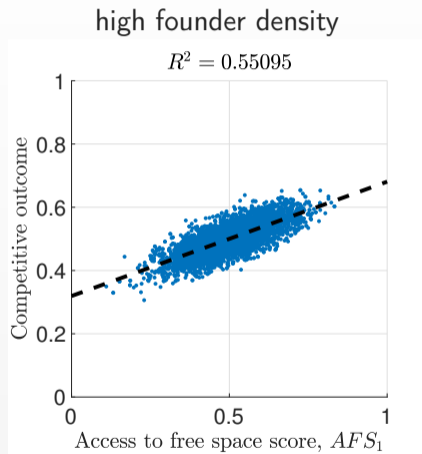
## Access to free space predicts outcome

- 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

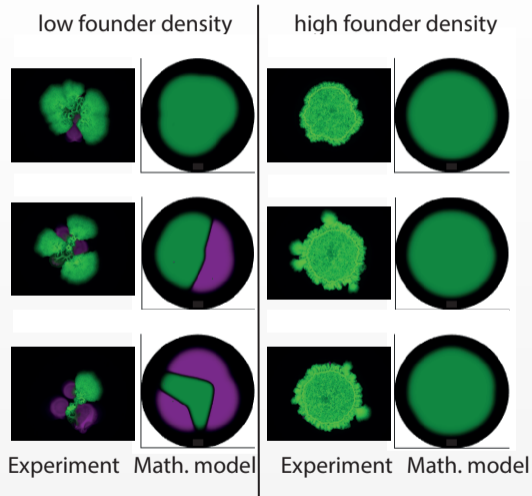
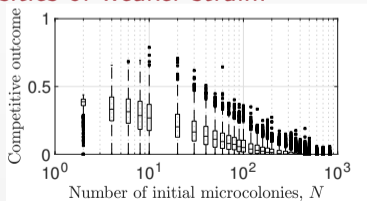
- Do these results also hold if **strains are non-isogenic and interact through local antagonisms?**

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

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

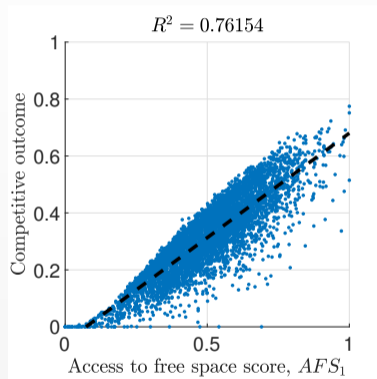
# Non-isogenic strains

- 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.



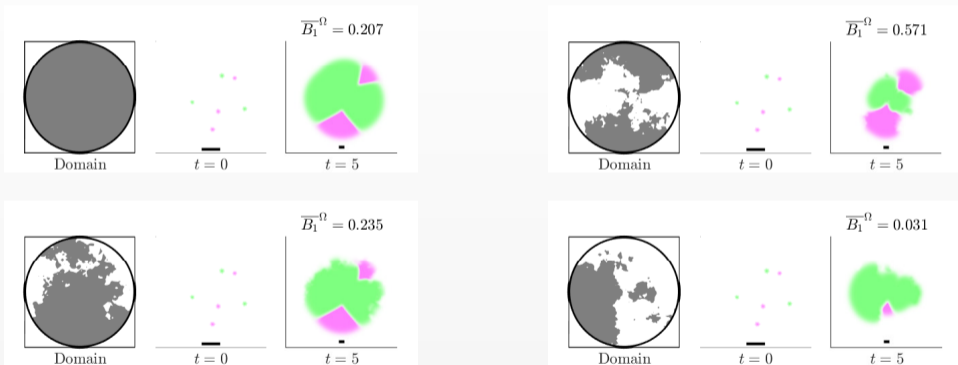
## Impact of spatial heterogeneity

Q: What if environmental conditions are spatially heterogeneous?

$$\frac{\partial B_1}{\partial t} = \nabla \cdot \left( d_1(\mathbf{x}) \left( 1 - \frac{B_1 + B_2}{k} \right) \nabla B_1 \right) + r_1(\mathbf{x}) B_1 \left( 1 - \frac{B_1 + B_2}{k} \right) - c_{12} B_1 B_2,$$
$$\frac{\partial B_2}{\partial t} = \nabla \cdot \left( d_2(\mathbf{x}) \left( 1 - \frac{B_1 + B_2}{k} \right) \nabla B_2 \right) + r_2(\mathbf{x}) B_2 \left( 1 - \frac{B_1 + B_2}{k} \right) - c_{21} B_1 B_2.$$

# 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.



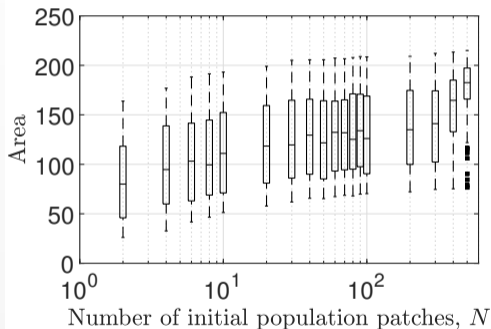
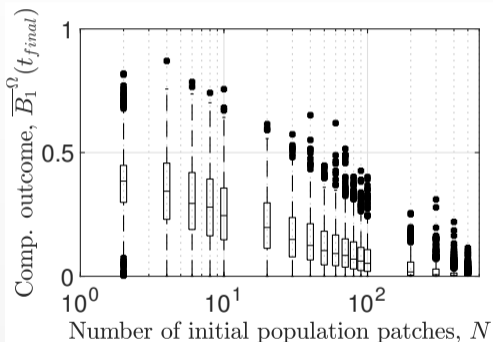
## Impact of spatial heterogeneity

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

## 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 but spatial heterogeneities determine variability in footprint.

# Predictions of competitive outcome in heterogeneous landscapes

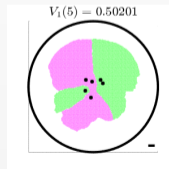
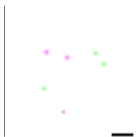
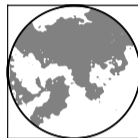
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Q: Can we still make predictions of competitive outcome?

# Predictions of competitive outcome in heterogeneous landscapes

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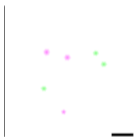
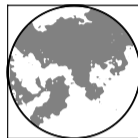
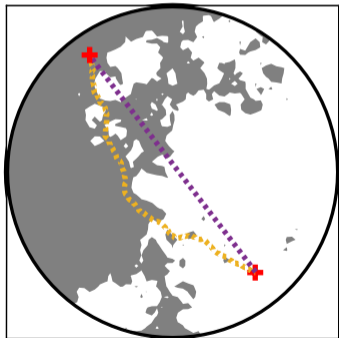
A: Yes, using **Voronoi tessellations based on an appropriate metric.**



# Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions of competitive outcome?

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



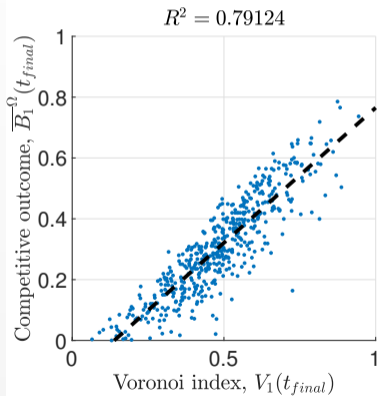
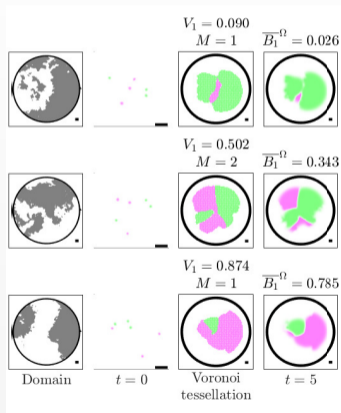
$$V_1(5) = 0.50201$$



# 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

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- 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  $\Rightarrow$  “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.

# Acknowledgements

## Collaborators:

- Margarita Kalamara (Univ. of Dundee)
- Graeme Ball (Univ. of Dundee)
- Cait E. MacPhee (Univ. of Edinburgh)
- Nicola R. Stanley-Wall (Univ. of Dundee)
- Fordyce A. Davidson (Univ. of Dundee)

## Funding:



**Biotechnology and  
Biological Sciences  
Research Council**



**University  
of Dundee**



# References

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Slides are available on my website.

<http://lukaseigentler.github.io>

- [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.

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Additional slides

# Predictions of competitive outcome in heterogeneous landscapes

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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  $\mathcal{P}(x, y) := \{P = p([0, 1]) \subset \Omega, \text{ where } p : [0, 1] \rightarrow \Omega : p \in \mathcal{C}^1 \text{ a.e., } p(0) = x, p(1) = y\}$  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

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

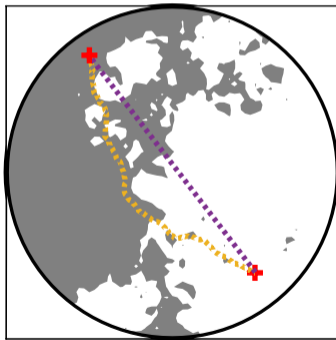
where  $0 \leq c(x) < \infty$  represents the propagation speed along the path  $P$ . We define the *front propagation metric* from  $x$  to  $y$  as

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

# Predictions of competitive outcome in heterogeneous landscapes

Q: Can we still make predictions of competitive outcome?

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**.

Voronoi tessellation of whole domain:

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

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

Restrict to area expected to be occupied by time  $t$ :

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

Voronoi index:

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

