Bacterial chemotaxis in nutrient replete environments

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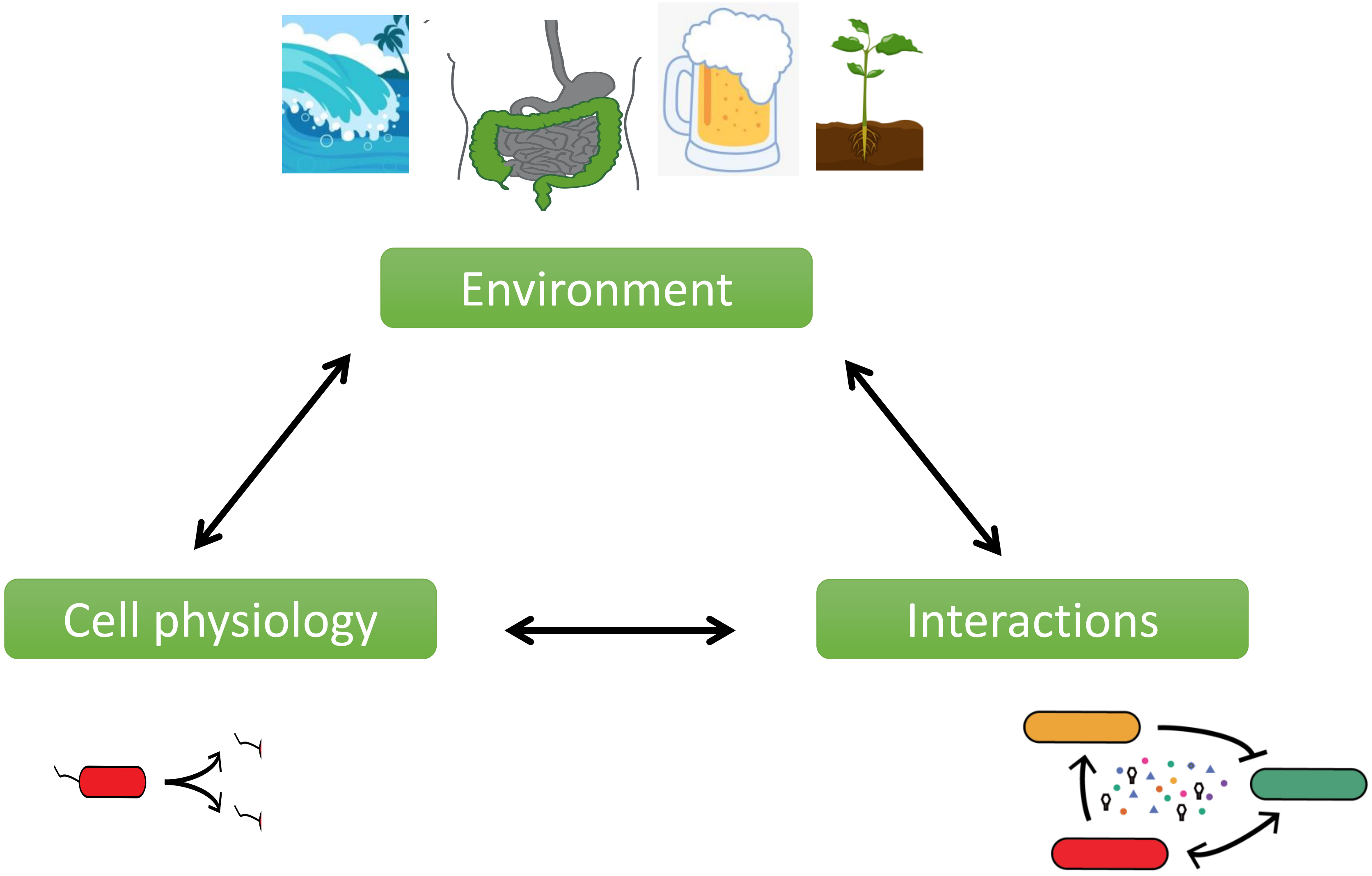
November 2019

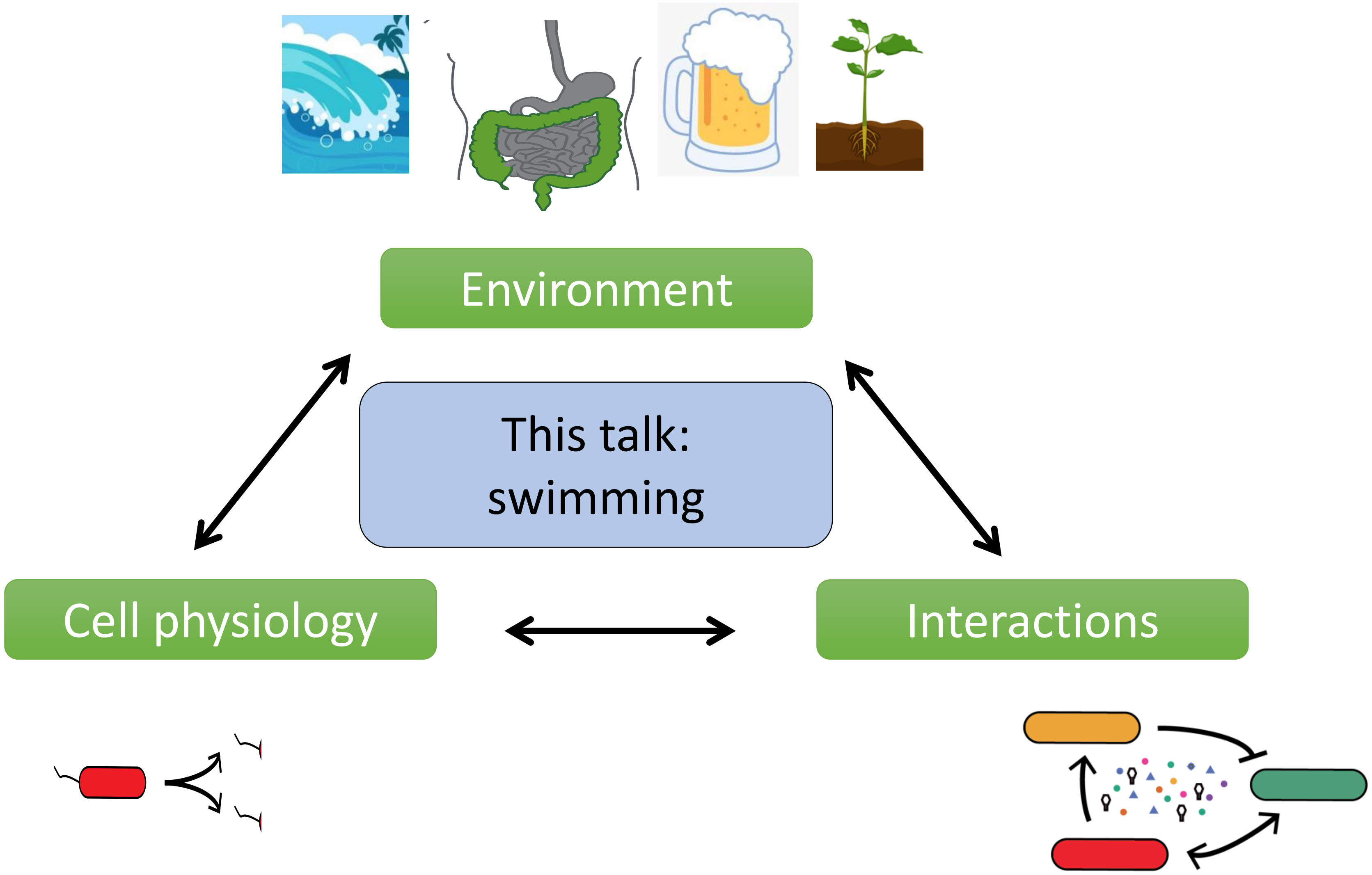
www.bacterialphysiology.com

Postdoc positions available!

Microbes and their communities



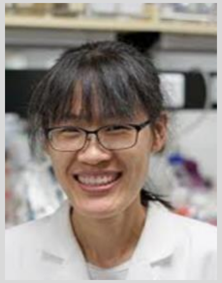
Microbes and their communities



Acknowledgements

Chemotaxis

Tomo Honda
UCSD



Weirong Liu
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Massimo Vergassola
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Mini-gut (UCSD)

Alex Groisman

Igor Segota

Zhongge Zhang

Alex Yang

Edgar Gutierrez

John Sauls

Bacterial physiology

Rohan Balakrishnan (UCSD)

Dany Incarnato (RUG)

Bert Poolman (RUG)

Evolution of cooperation

Erwin Frey (LMU)

Heinrich Jung (LMU)

Gut growth

Markus Arnoldini (ETH)

Luis Rubio San Millan (EEZ Granada)

Biofilms

Alberto Reinders (Basel)

Urs Jenal (Basel)

Funding

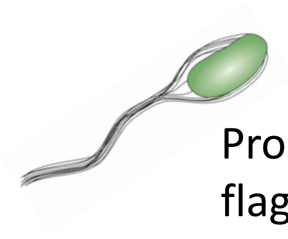
Leopoldina Nationale Akademie der Wissenschaften

Bill & Melinda Gates foundation

NIH National Institutes of Health

Bacterial chemotaxis: sensing and movement along gradients

Bacteria swim

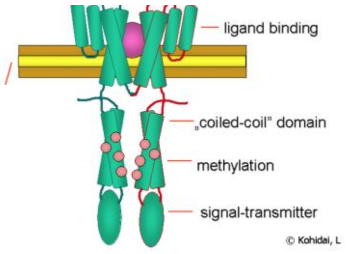


Propulsion by flagella-rotation

Bacteria sense

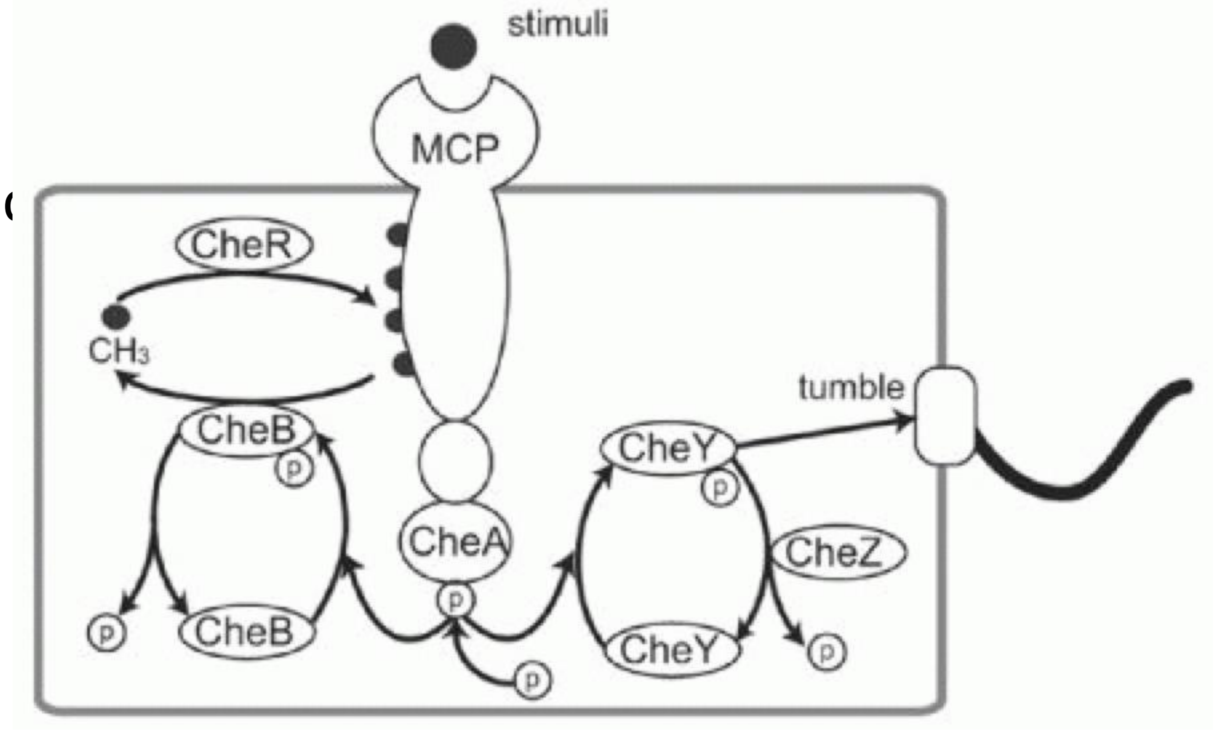
For E.coli:

- amino acids
- oxygen
- carbohydrates
- …



aspartate receptor

Bac

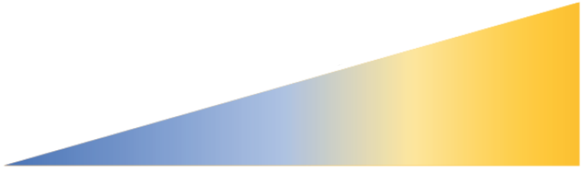


Chemotaxis

What is the physiological role? Advantage of chemotaxis for bacterial cells and populations?

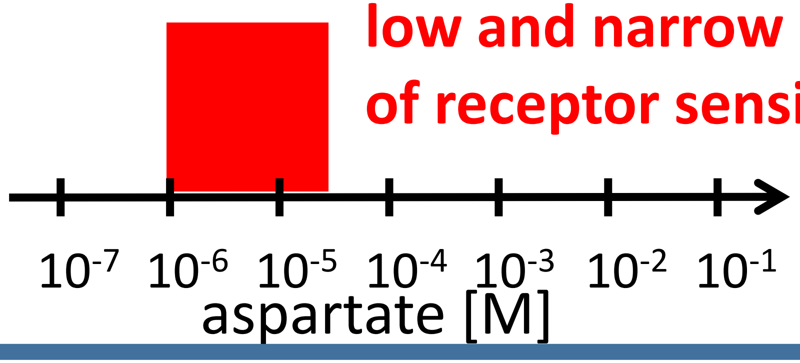
Chemotaxis is occuring on the population level

Environment sets gradients ⟷ Population sets gradients



attractants (AA, sugars, oxygen) are consumed

Consider aspartate:



low and narrow range of receptor sensitivity

\+

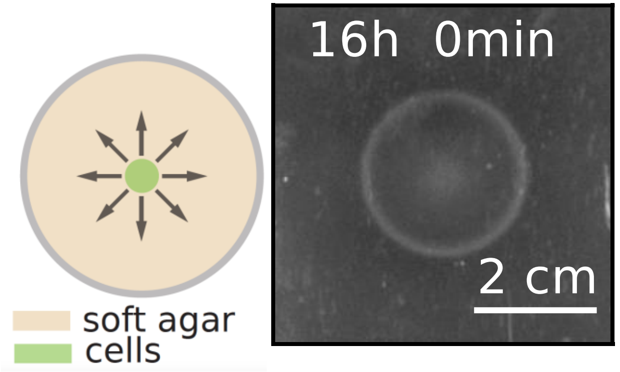
high uptake rate

1/1000th of volume occupied by bacteria (OD 1): Detectable range consumed within ~second

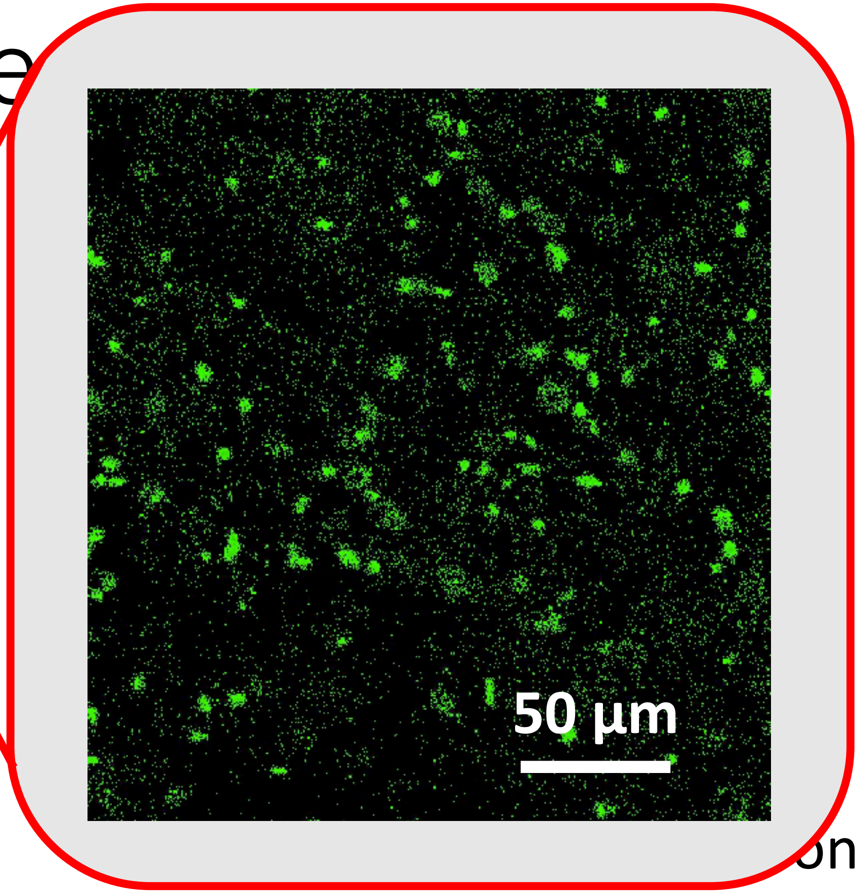
→ Bacteria shape the gradients they sense

Colony expansion of che

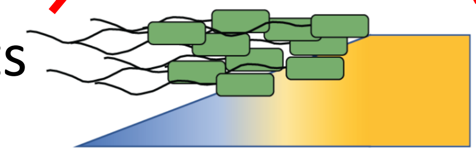
observation in soft-agar: “ring-assay”



E.Coli K-12; growth condition: glycerol +



Chemotaxis along gradients



onditions / physiological state of cells

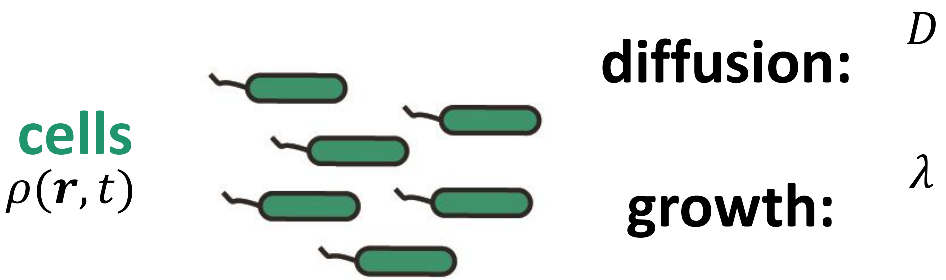
Many experimental and theoretical studies

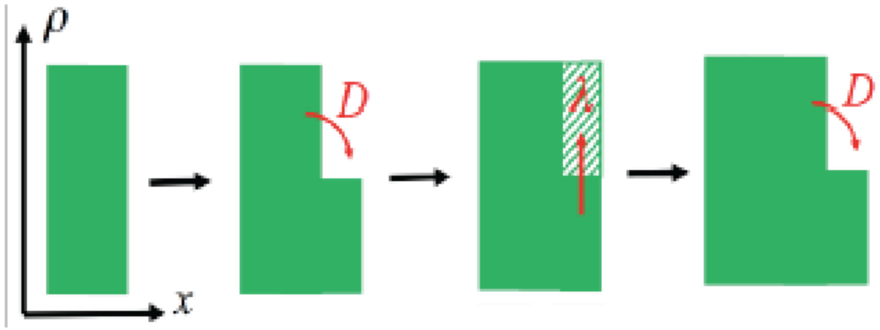
[Keller & Segel, 1971][Lauffenburger, 1984][Jiang et al 2010] [Saragosti et al, 2011] [Koster et al 2012] [Waite et al 2016][Baym et al 2016][Yi & Dean, 2016][Fraebell et al. 2017] [Brenner et al, 1998][Saragosti et al, 2010]

Let’s understand a simpler scenario first: population expansion without chemotaxis

Modeling expansion without chemotaxis

- No attractant: undirected run and tumbling
- Cell growth

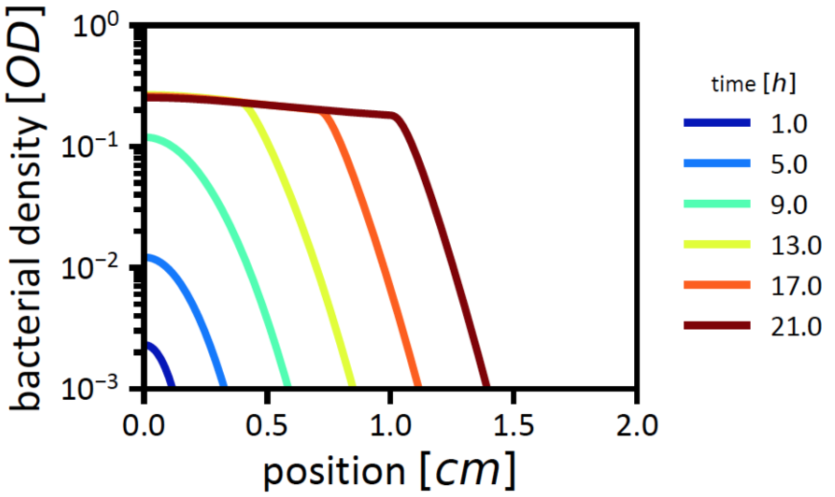




Fisher-Kolmogorov dynamics

$$\partial_t \rho = D\Delta\rho + \lambda\rho(\rho_{max} - \rho)$$

Model predictions:



expansion speed: $u_{FK} = 2\sqrt{D \cdot \lambda}$

slope expansion front: $k = \sqrt{\frac{D}{\lambda}}$

[Fisher 1937, Kolmogorov et al, 1937]

[Andow et al, 1990, Hallatschek et al, 2007, Korolev et al 2012, Gandhi et al 2016] and others

Can we confirm Fisher-Kolmogorov dynamics for swimming bacteria?

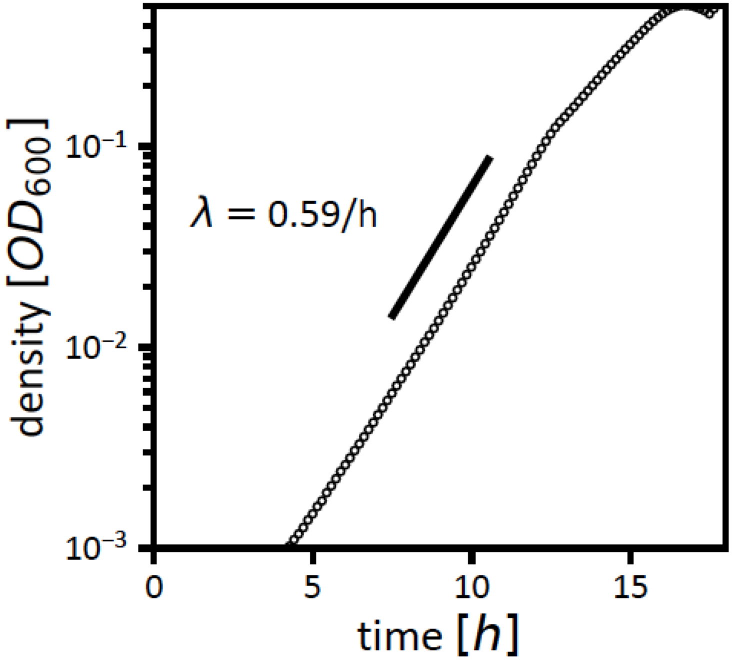
Experimentally: growth in glycerol (not an attractant)

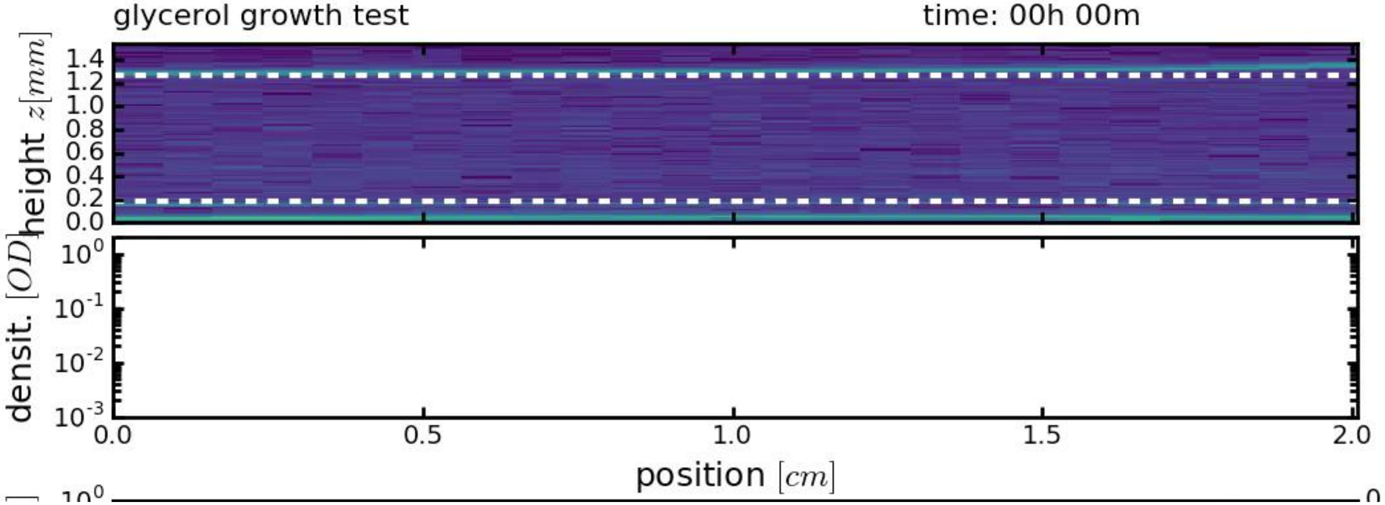
Need to measure cellular diffusion and growth to test predictions

expansion speed: $$u_{FK} = 2\sqrt{D \cdot \lambda}$$

slope expansion front: $$k = \sqrt{\frac{D}{\lambda}}$$

Determine growth rate



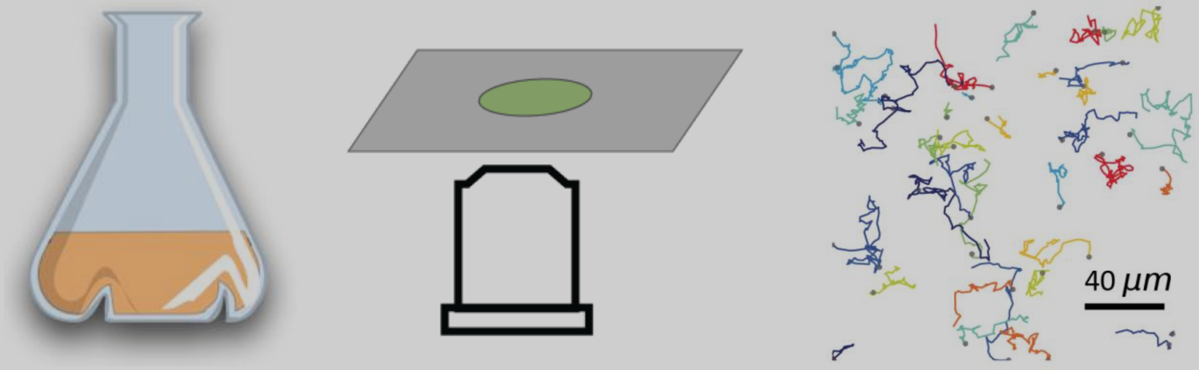


condition: glycerol, no attractant

→ Growth rate λ : 0.59 1/h

Side remark: Growing cells swim

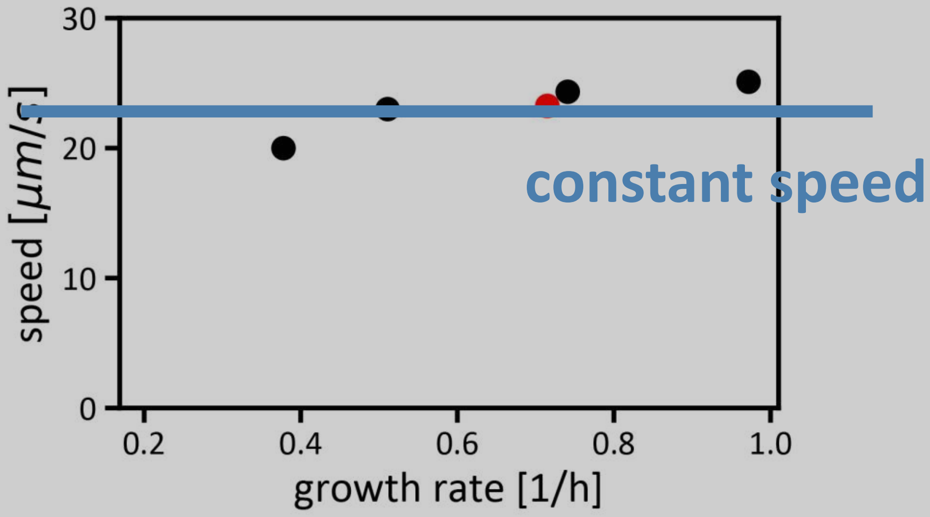
Measure swimming speeds for different conditions



batch culture

microscopy

trajectory analysis

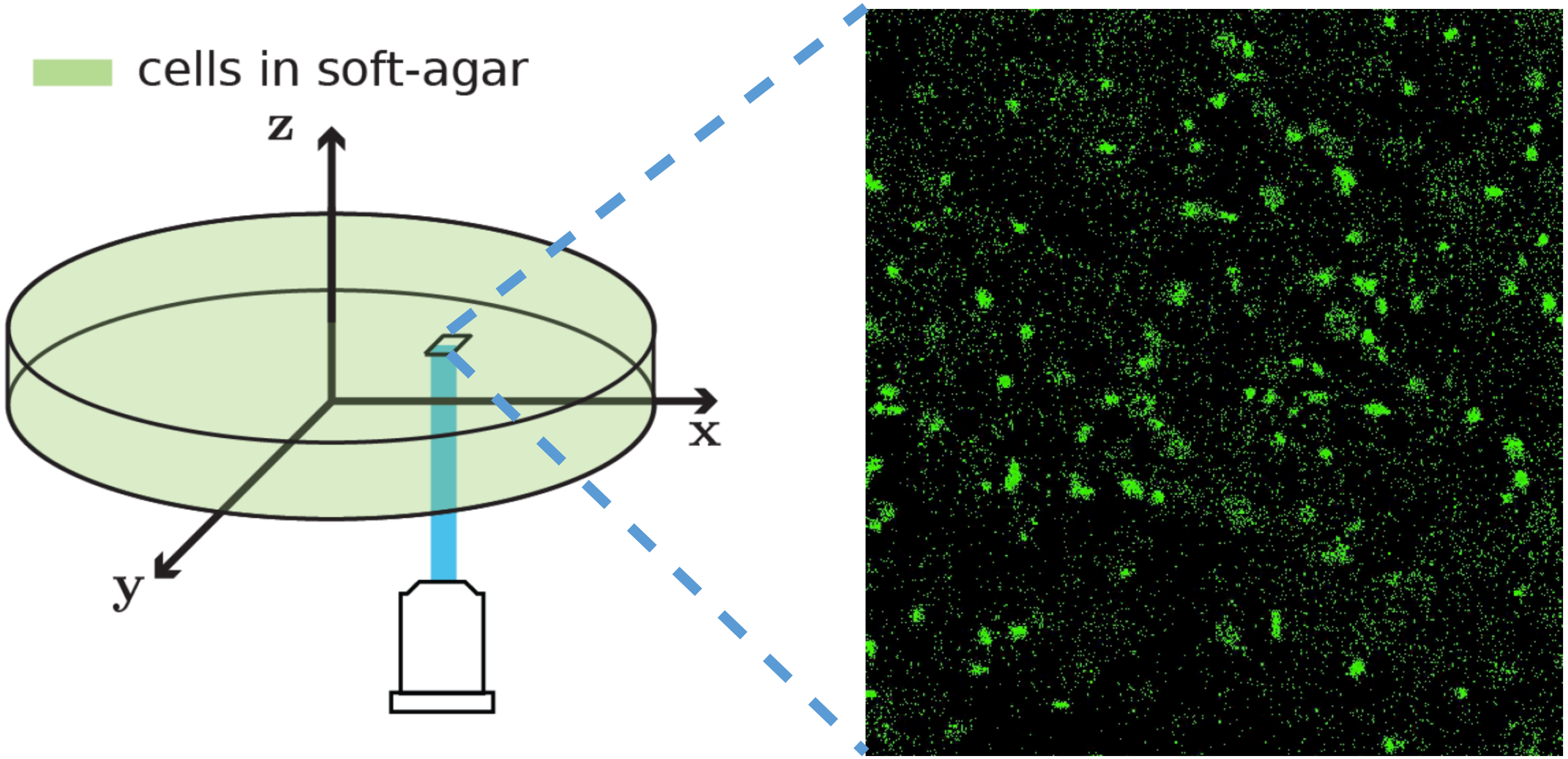


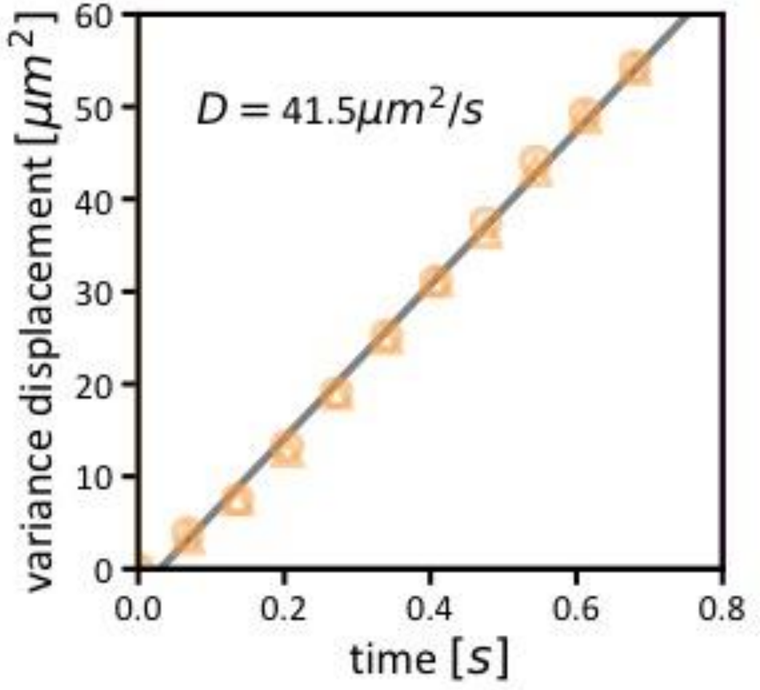
→ **Growing cells swim with constant speed, independent of exact growth condition**

→ Active regulation of swimming behavior

Determine effective diffusion: direct measurement in soft-agar

200 x 200 µm



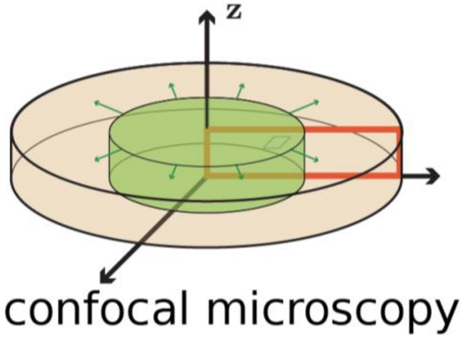


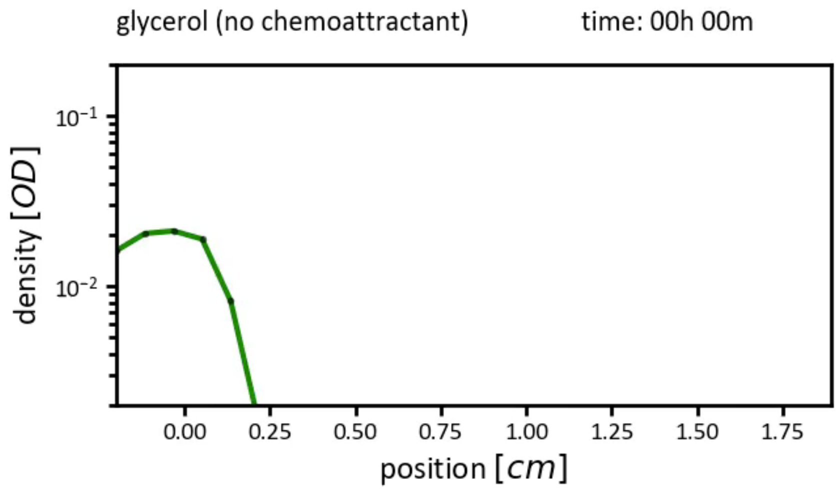
→ Diffusion D : 42 µm²/s

growth in glycerol

Observed expansion without chemotaxis follows Fisher-Kolmogorov dynamics

Observing expansion

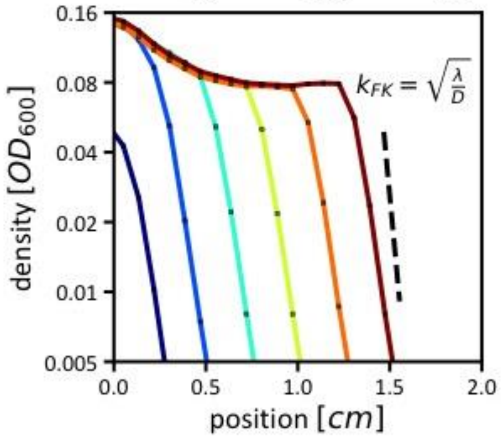


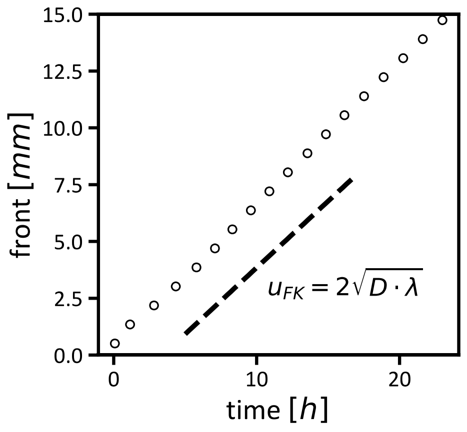


quite fast expansion 0.9 mm/h

Colony of non-motile cells: 0.1 mm/h

Comparison with theoretical prediction





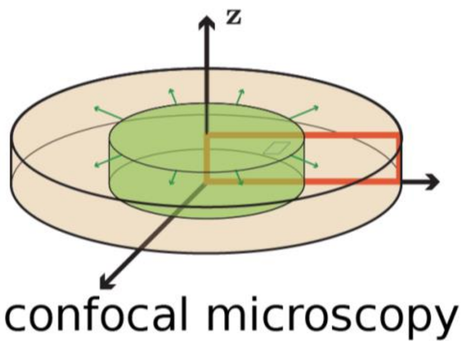
Fisher-Kolmogorov describes expansion

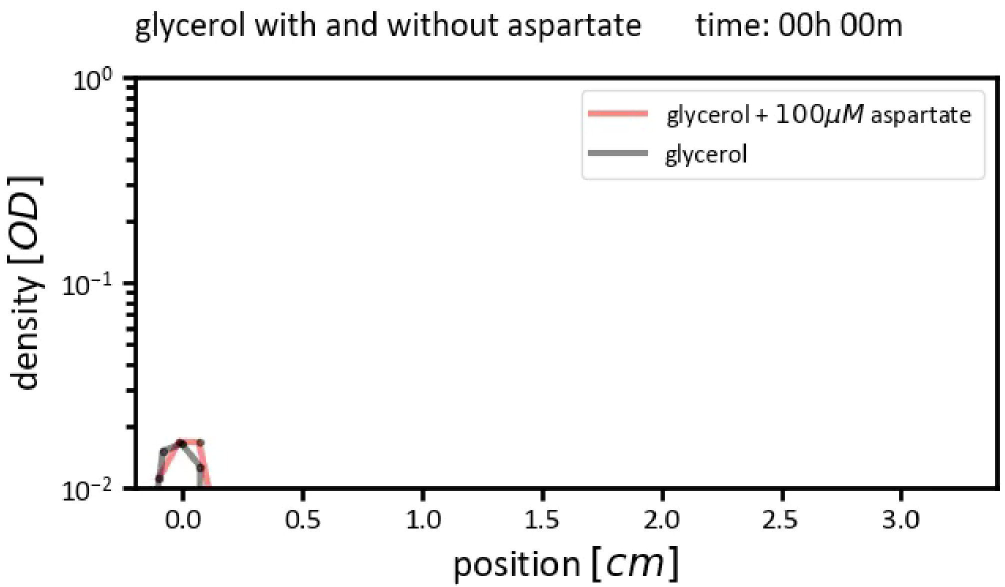
Back to chemotaxis

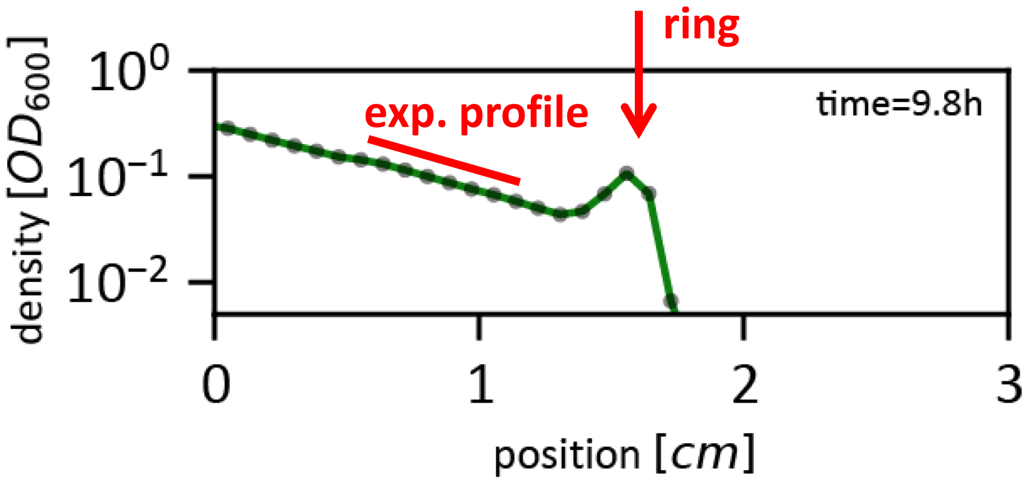
Experimentally: glycerol + aspartate

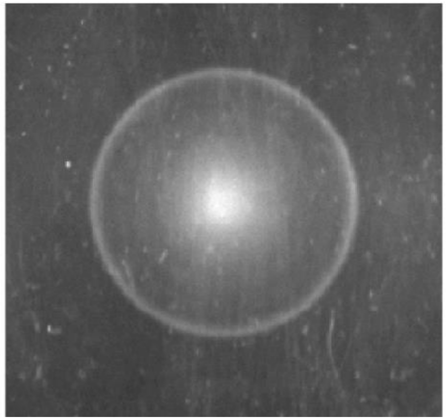
Expansion with chemotaxis: ring and exponential trailing profile

Observing expansion









fast expansion:
3.7 mm/h

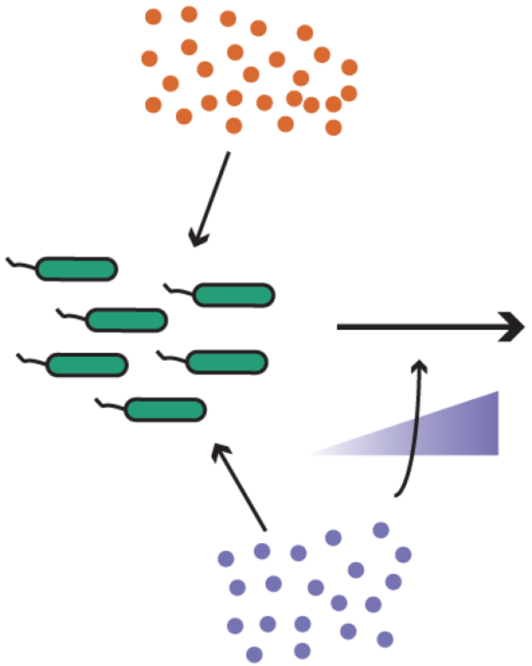
FK: 0.9 mm/h
Colony: 0.1 mm/h

A new model to describe chemotactic expansion

nutrients $n(\boldsymbol{r},t)$

cells $\rho(\boldsymbol{r},t)$

attractant $a(\boldsymbol{r},t)$



$$\partial_t n = -\frac{\lambda(n,a)}{Y}\rho + D_{\mathrm{n}}\Delta n$$

$$\partial_t \rho = -\nabla[\,\boldsymbol{v}\rho] + D\Delta\rho + \lambda(n,a)\rho$$

$$\boldsymbol{v} = \chi_0 \nabla \log\left[\frac{1 + {}^{a}/_{a_-}}{1 + {}^{a}/_{a_+}}\right] \approx \chi_0 \frac{\nabla a}{a}$$

in sensible range

$$\partial_t a = -\mu\rho + D_a \Delta a$$

Crucial modifications of previous models:

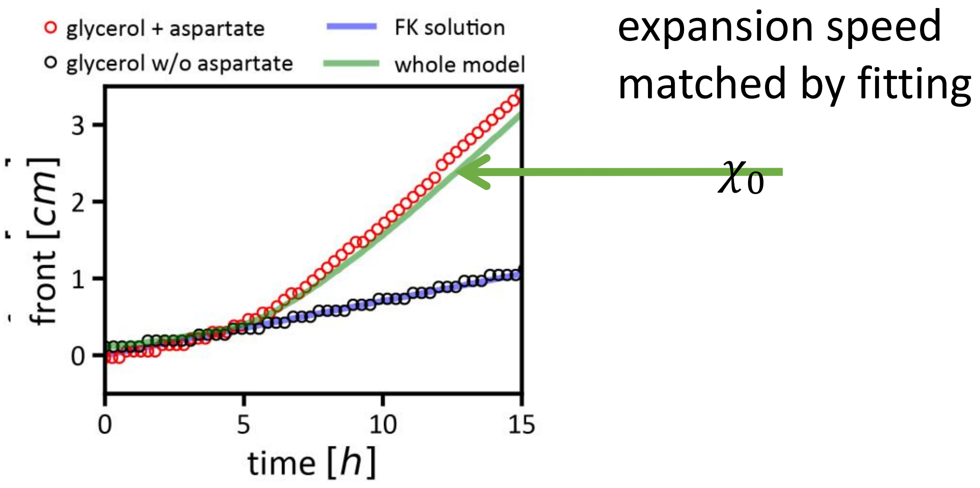
- Includes cell growth
- Separation between nutrient and attractant field

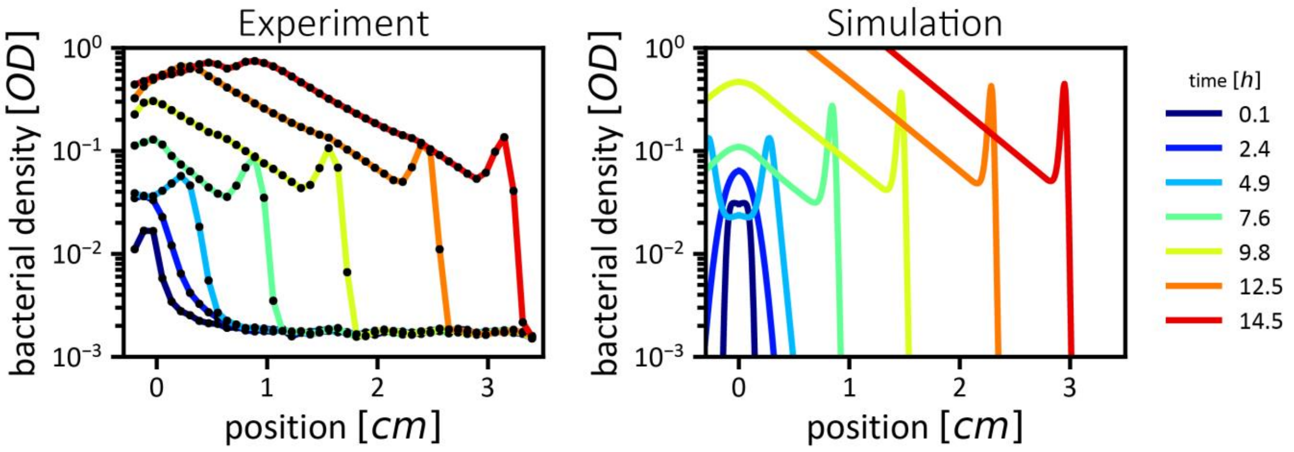
Only one fitting parameter:

χ_0

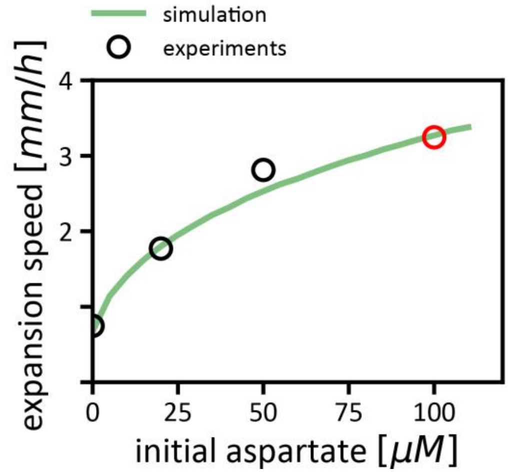
Model predicts expansion dynamics

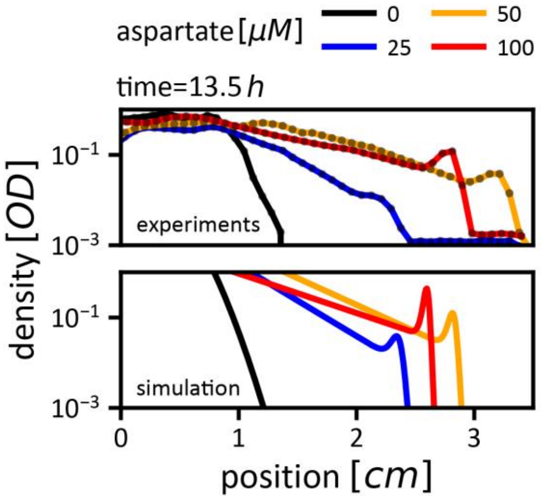
Reference condition: glycerol + aspartate



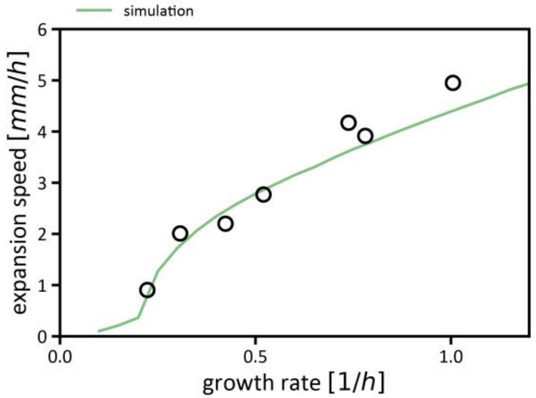


Change in chemoattractant concentration

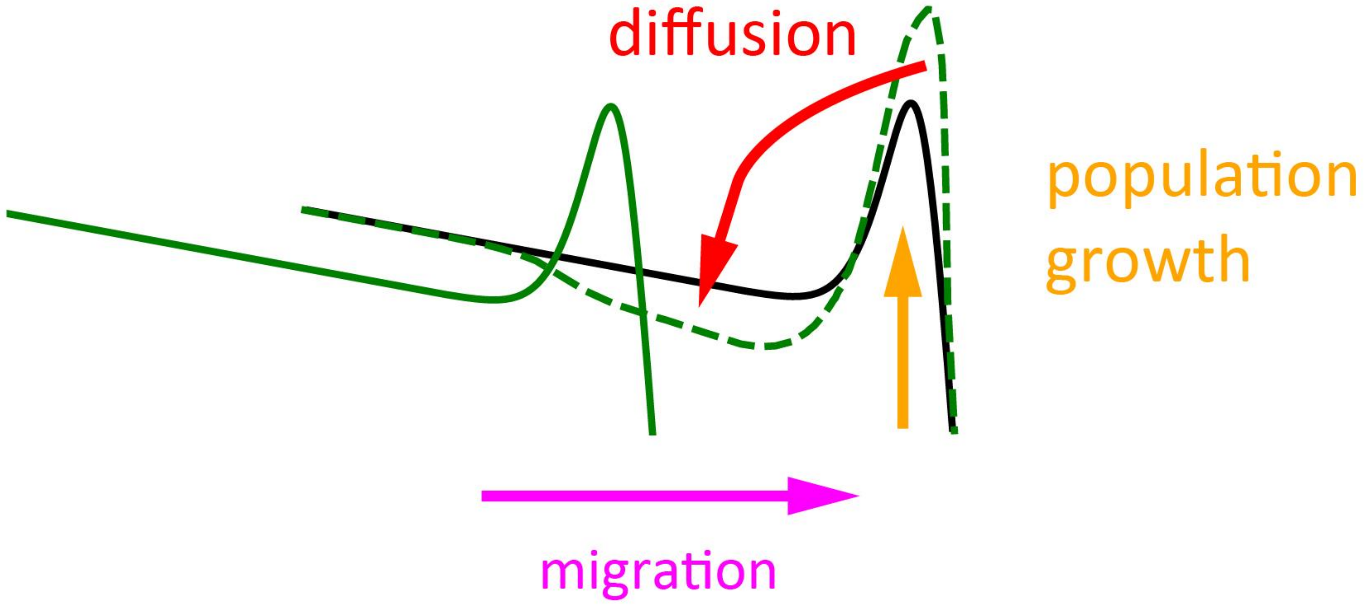




Change in growth rate

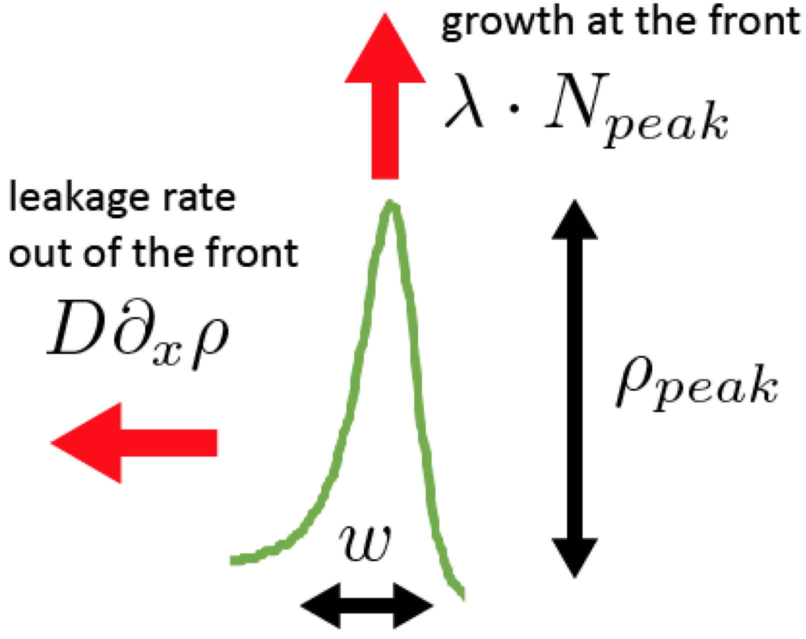


Mode of expansion dynamics



- Growth at front is balanced by diffusion to the back.
- This leads to an efficient seeding of the trailing region
- Growth at the trailing region leads to an exponentially increasing profile

A scaling theory of chemotactic expansion

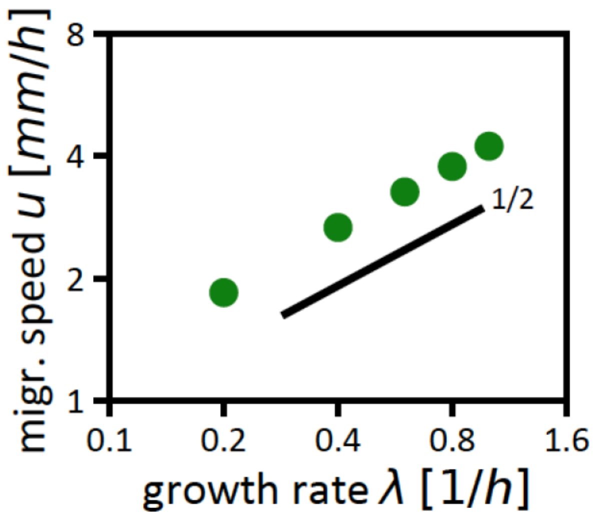


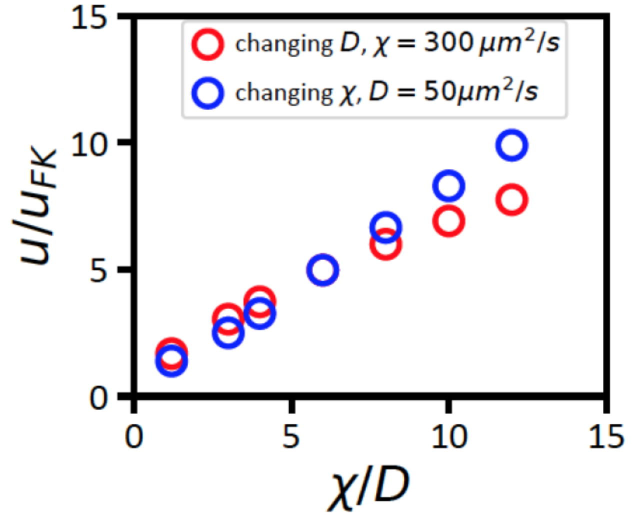
$$N_{peak} \sim \rho_{peak} \cdot w$$

$$\lambda \cdot N_{peak} \sim D \cdot \rho_{peak} / w$$

$$u \sim \chi / w$$

$$u \sim (\chi/D)\sqrt{D \cdot \lambda}$$

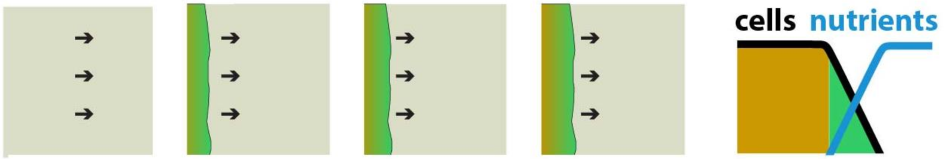




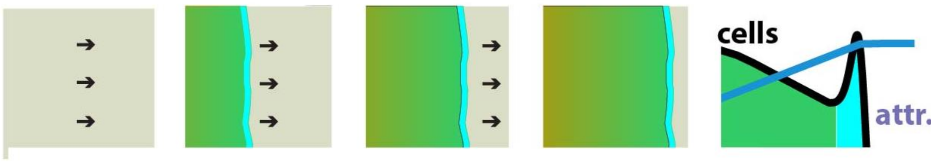
→ Chemotactic range expansion boost expansion speed

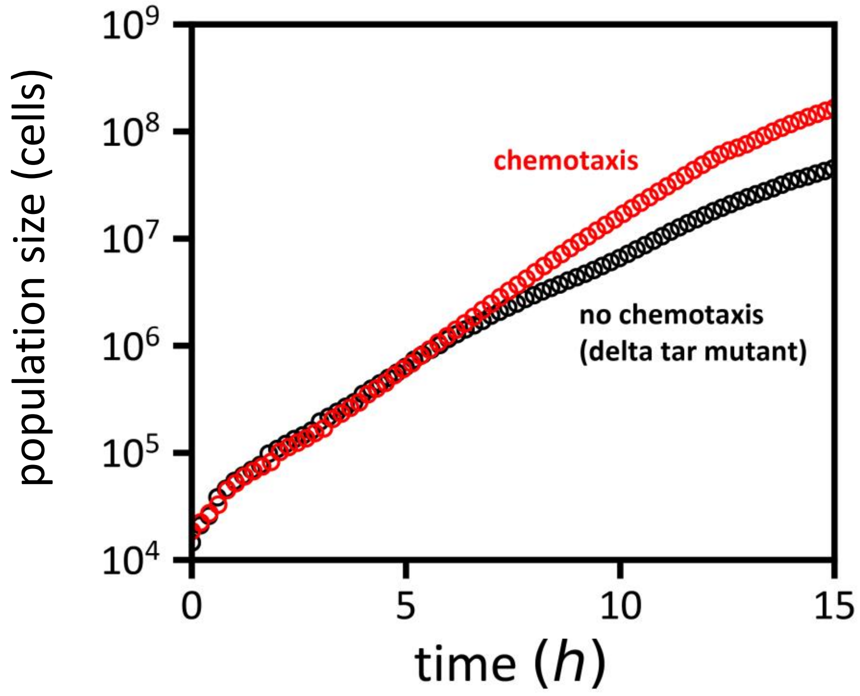
Summary: Chemotaxis as growth strategy to thrive in nutrient-replete environments

unguided range expansion (FK)



navigated range expansion (chemotaxis)





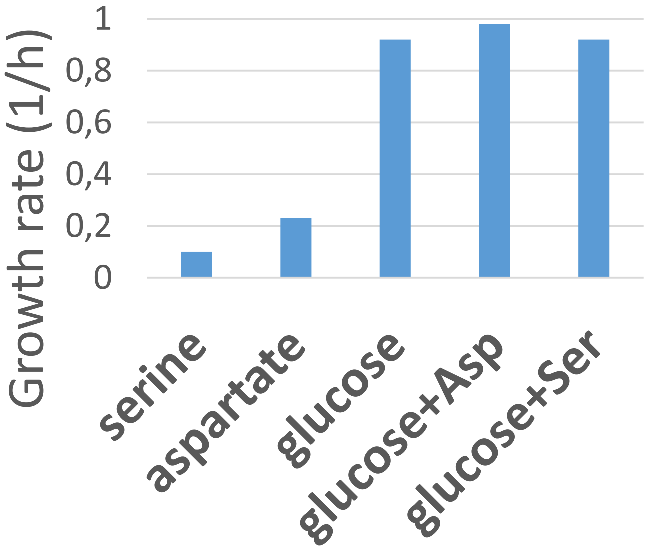
Chemotaxis leads to fast expansion via self-generated gradients and is an efficient strategy to grow in nutrient replete environments

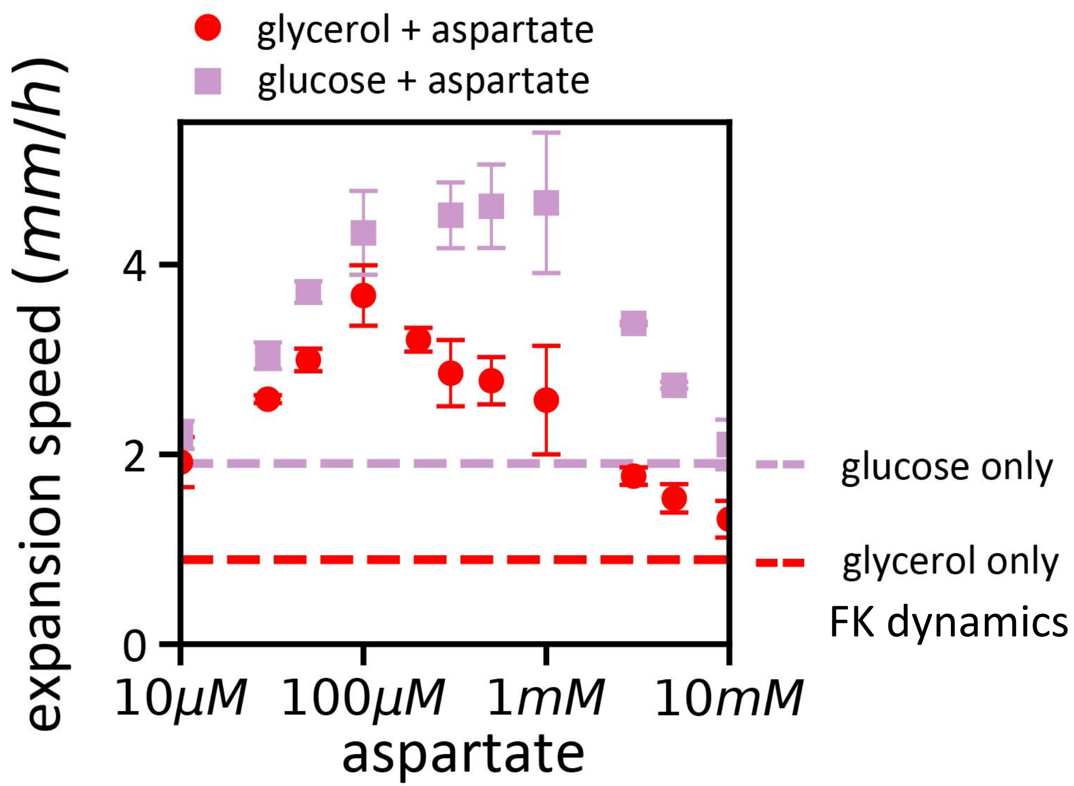
Non-nutritious attractants as cues for navigated range expansion

- A nutrient alone which can be sensed is only weakly increasing expansion speed:

$$u \sim \sqrt{\chi \cdot \lambda}$$

- Separation of nutrient and attractant speeds up migration: $u \sim \chi \cdot \sqrt{\lambda}$
- Good attractants are not good nutrients but rather cues to boost range expansion.





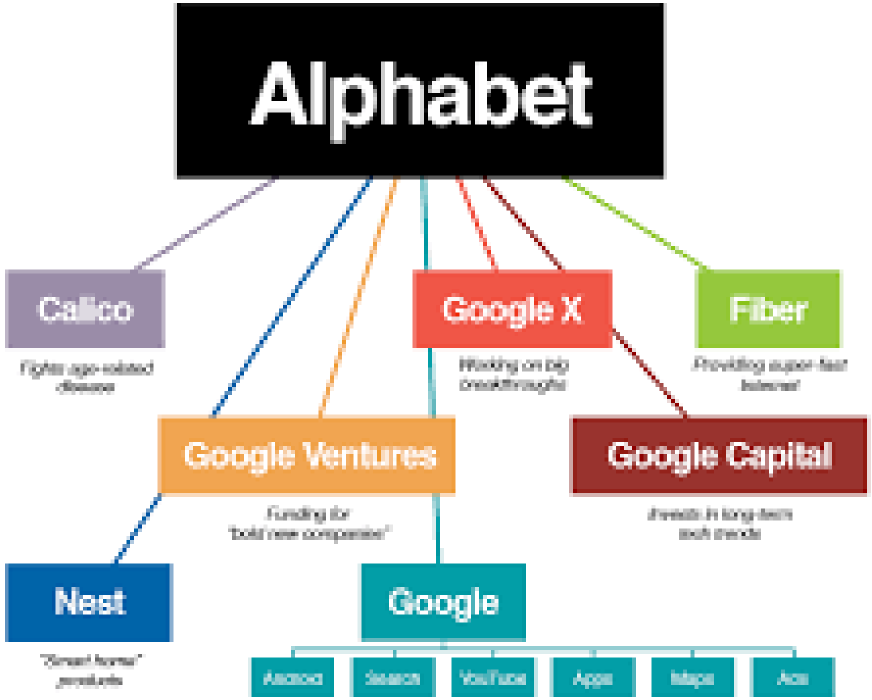
Cremer, Honda, Tang, Wong-Ng, Vergassola, Hwa. Nature (2019)

Oversimplified summary

Canonical hypothesis: nutrient foraging during starvation

Alternative (non-exclusive) hypothesis:

range expansion <u>during good growth conditions</u> (diversification)



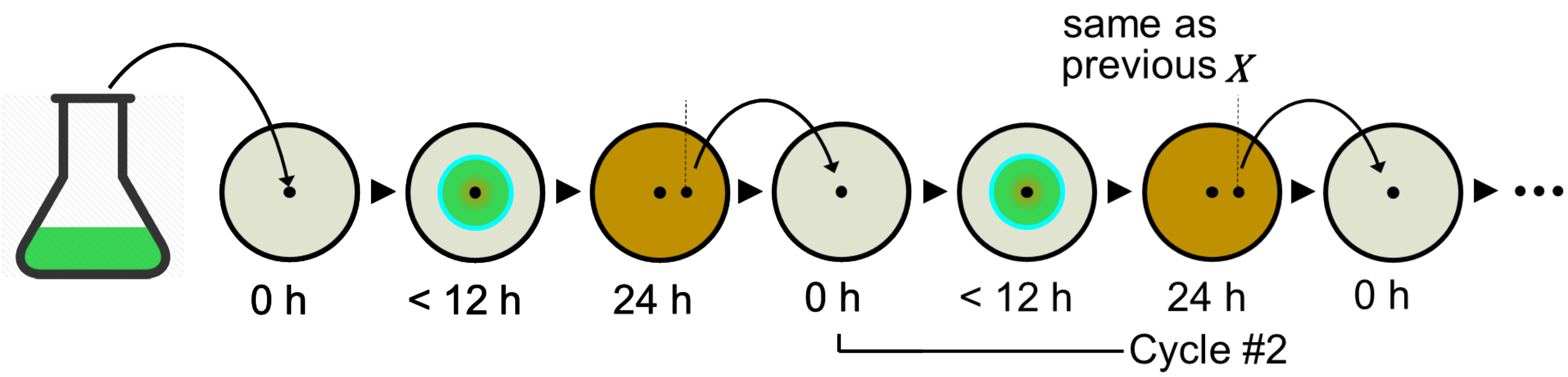
Is there an optimal swimming speed and expansion behavior?

If expansion via chemotaxis increases population growth:

Why are cells not expanding even faster?

Evolutionary study of swimming behavior

Introduce space dependent selection



Liu, Cremer, Li, Hwa, Liu. Nature (2019)

Evolutionary study of swimming behavior

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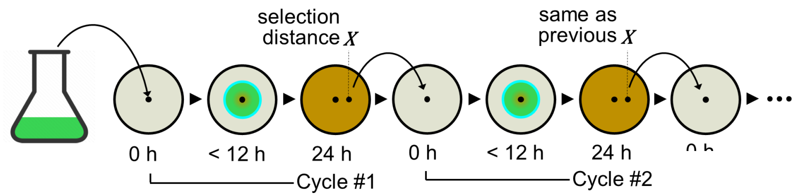
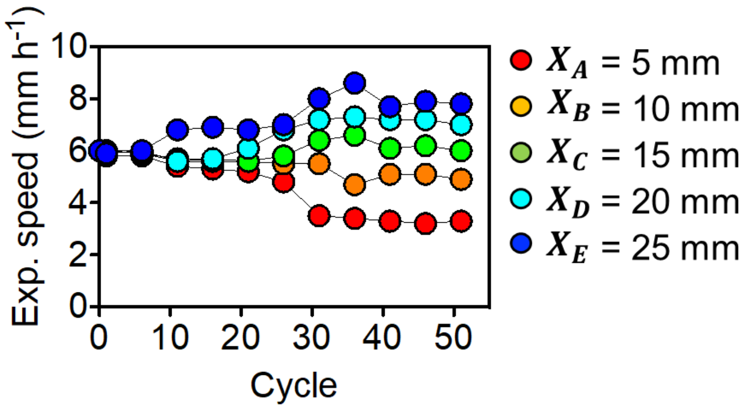


Evolution depends on selection distance



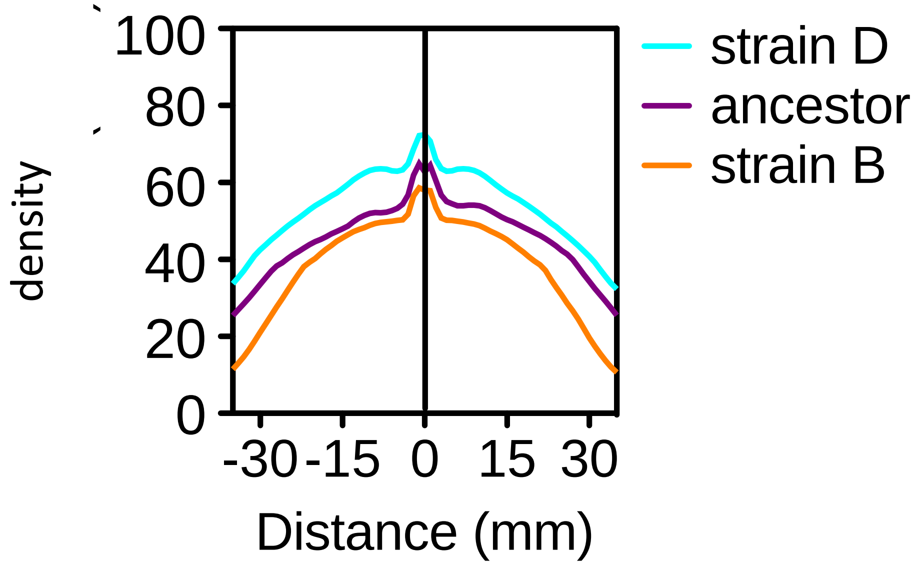
Fast swimming is not always good: optimal swimming depends on typical habitat size cells encounter

Liu, Cremer, Li, Hwa, Liu. Nature (2019)

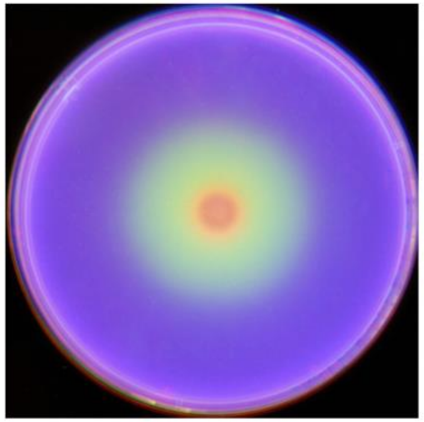
Competition drives local abundance and selection dynamics

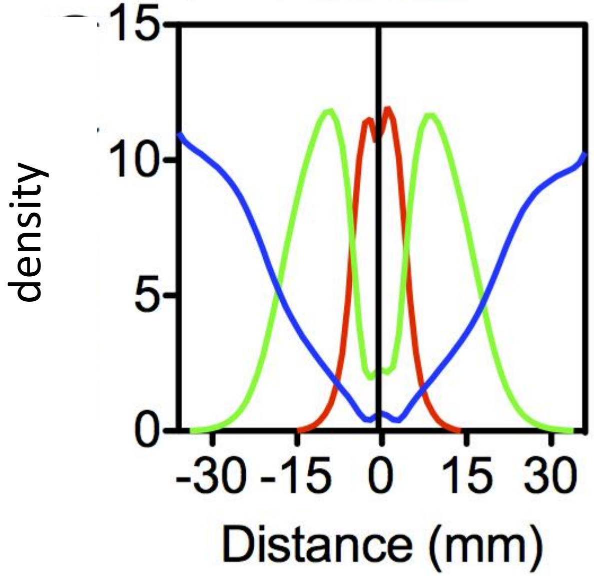
Separate expansion

	strain	ES (mm/h)	GR (1/h)
fast	str. D	7.02	1.96
	anc.	5.92	1.98
slow	str. B	4.32	1.92

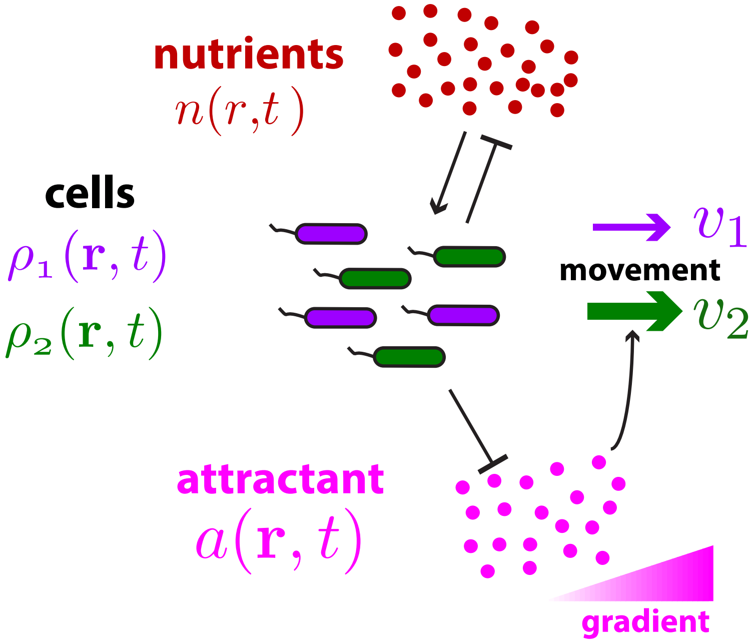


Direct competition





Modeling dynamics



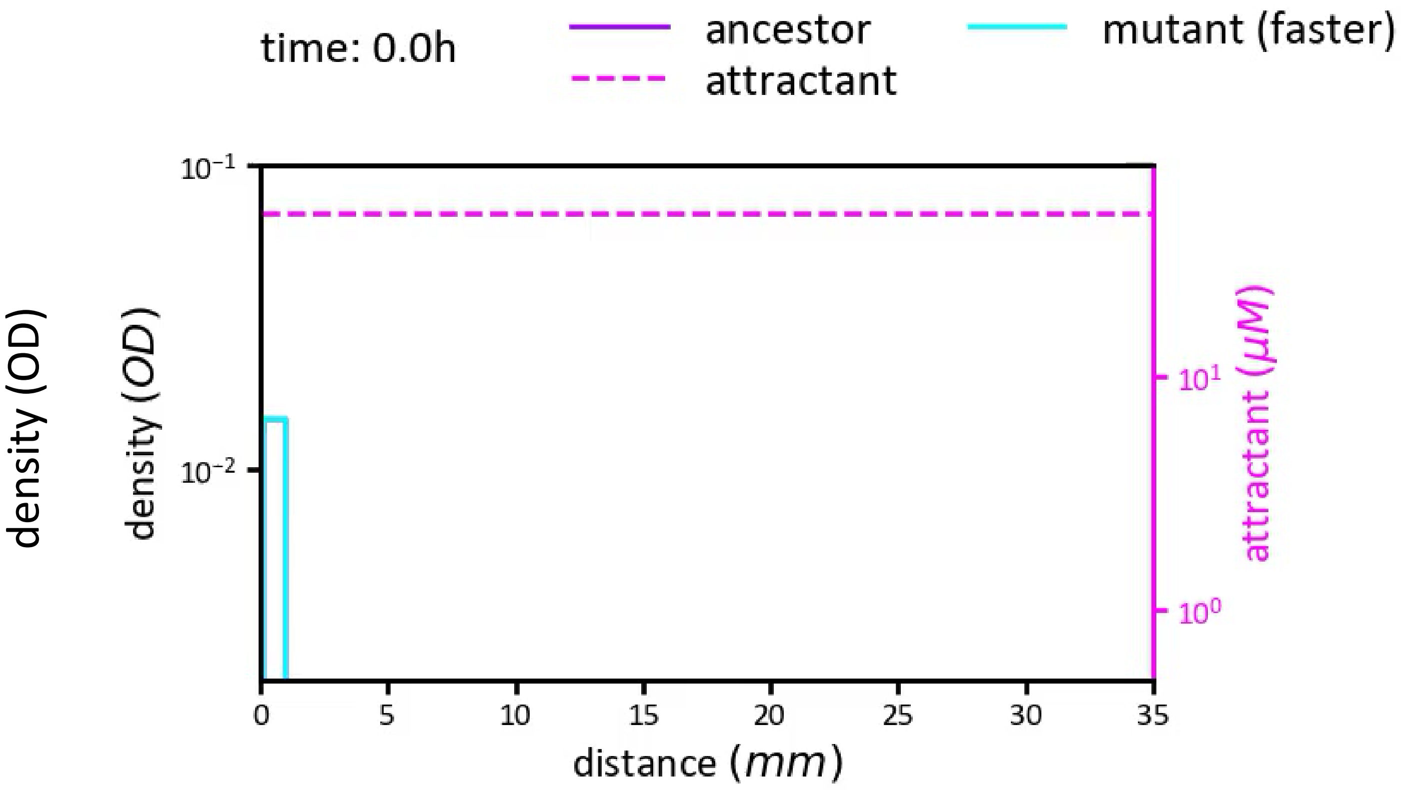
$$\partial_t \rho_1 = D_1 \Delta \rho_1 - \nabla \cdot (v_1\, \rho_1) + \lambda(n) \cdot \rho_1$$

$$\partial_t \rho_2 = D_2 \Delta \rho_2 - \nabla \cdot (v_2\, \rho_2) + \lambda(n) \cdot \rho_2$$

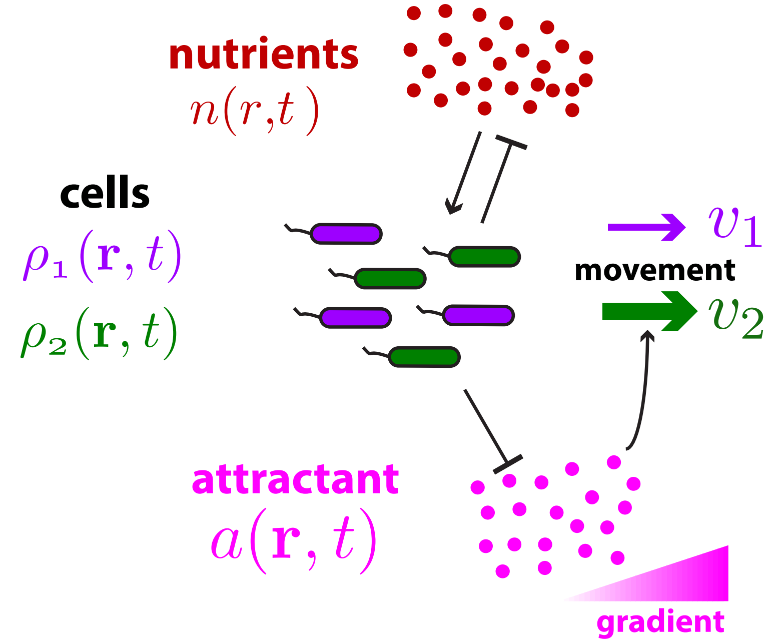
$$v_{1,2} = c_{1,2}\, \nabla \log \left(\frac{1 + a/K_I}{1 + a/K_A} \right)$$

$$\partial_t a = D_0 \Delta a - \mu(a) \cdot (\rho_1 + \rho_2)$$

$$\partial_t n = D_0 \Delta n - \lambda(n) \cdot (\rho_1 + \rho_2)/Y_n$$



Modeling dynamics



$$\partial_t \rho_1 = D_1 \Delta \rho_1 - \nabla \cdot (v_1\, \rho_1) + \lambda(n) \cdot \rho_1$$

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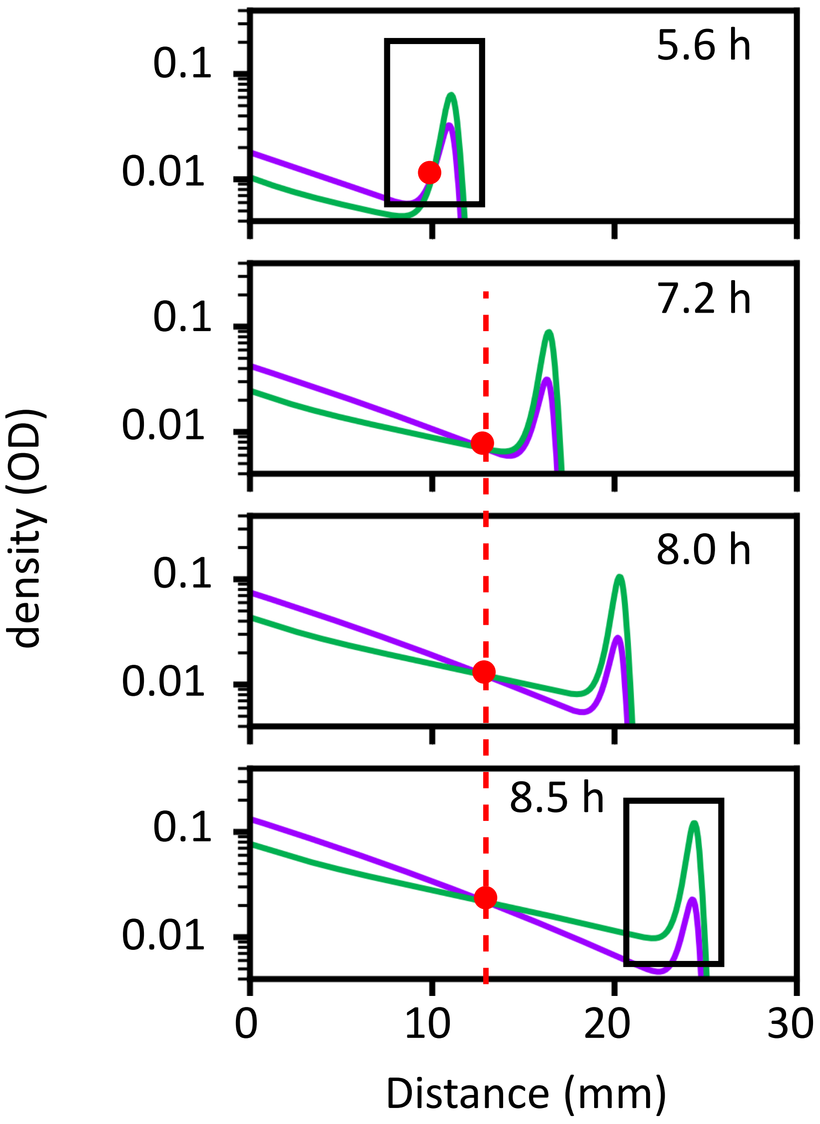
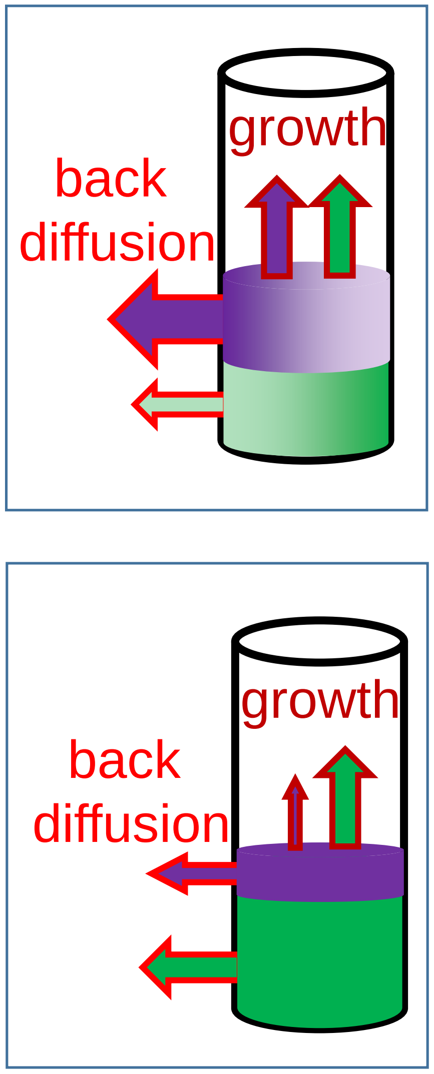
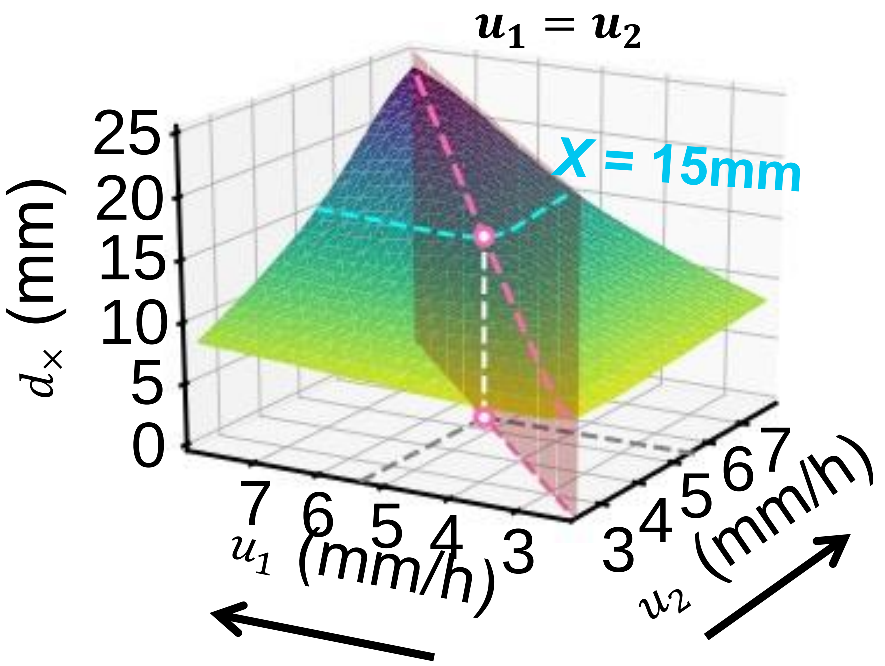
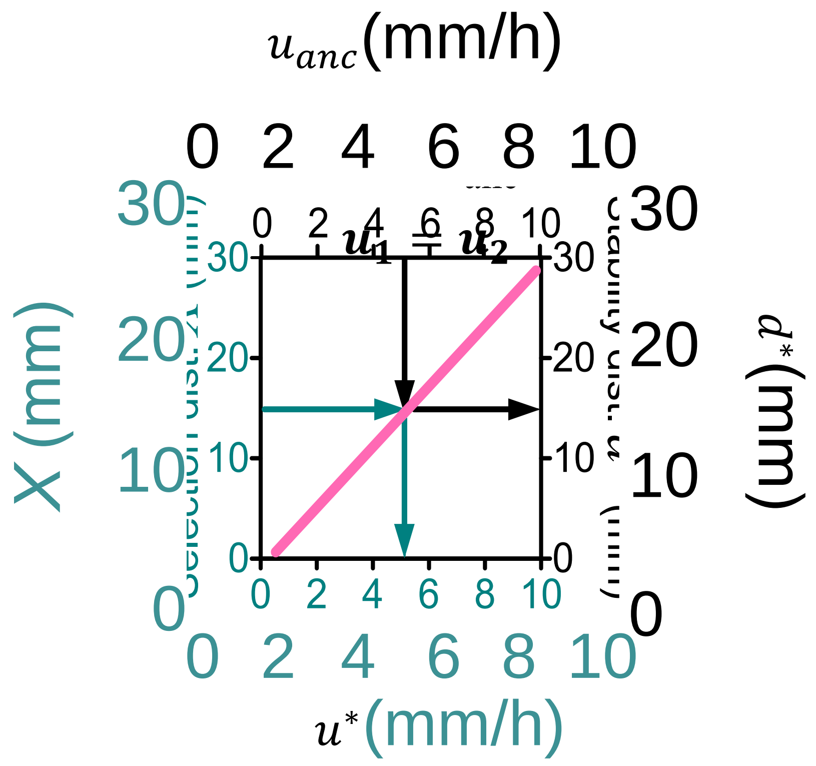




Stable attractor of evolution

analyzing different expansion speeds





predicted stable attractor:

$$u^*(X) \propto X \cdot \lambda.$$

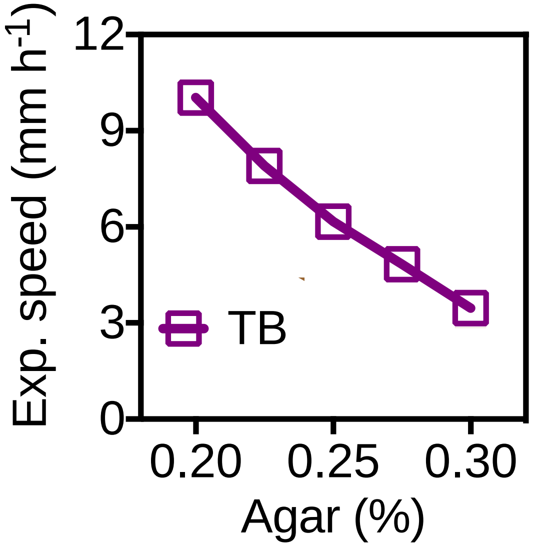
stable expansion speed **position** **growth-rate**

Test model prediction

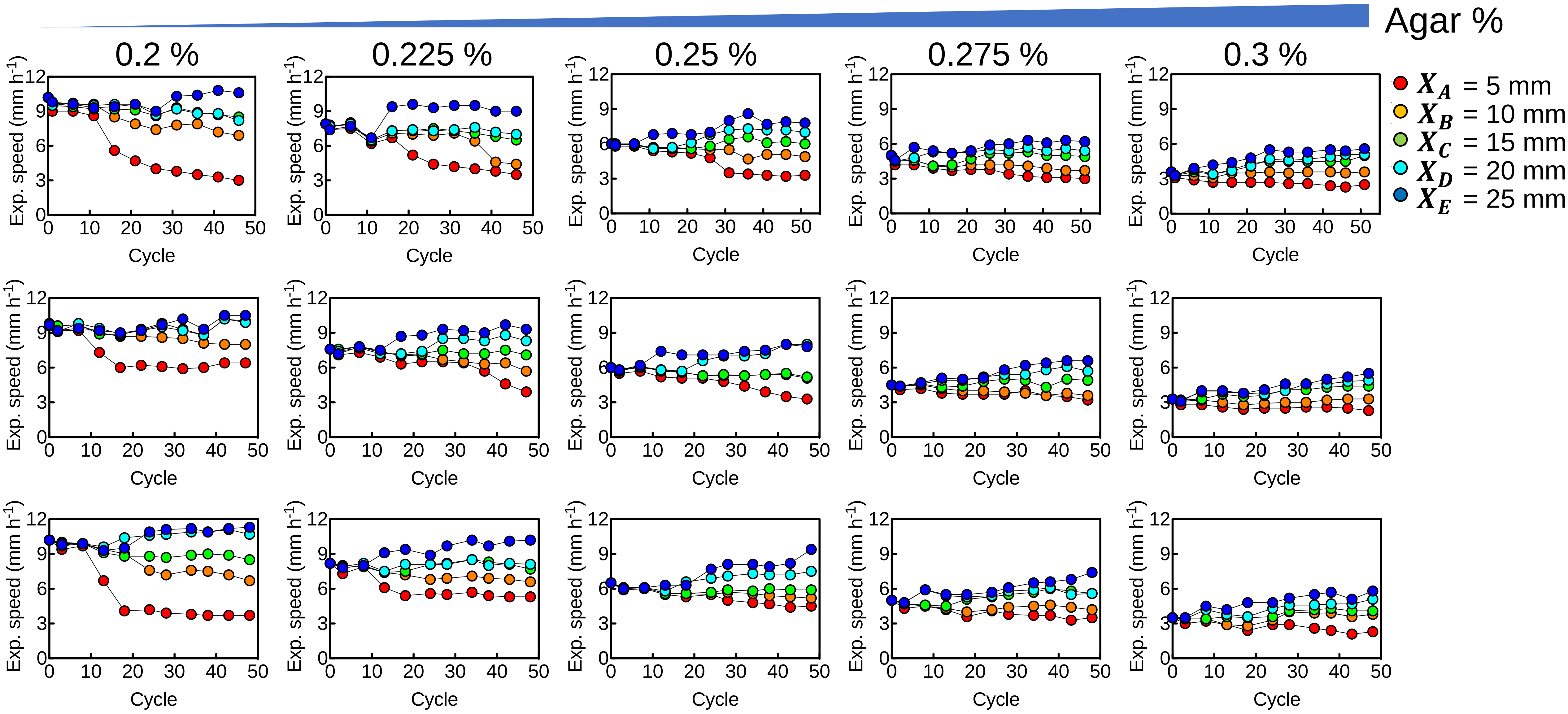
predicted stable attractor:

$$u^*(X) \propto X \cdot \lambda.$$

stable expansion speed **position** **growth-rate**



Evolution in different agar concentrations



Test model prediction

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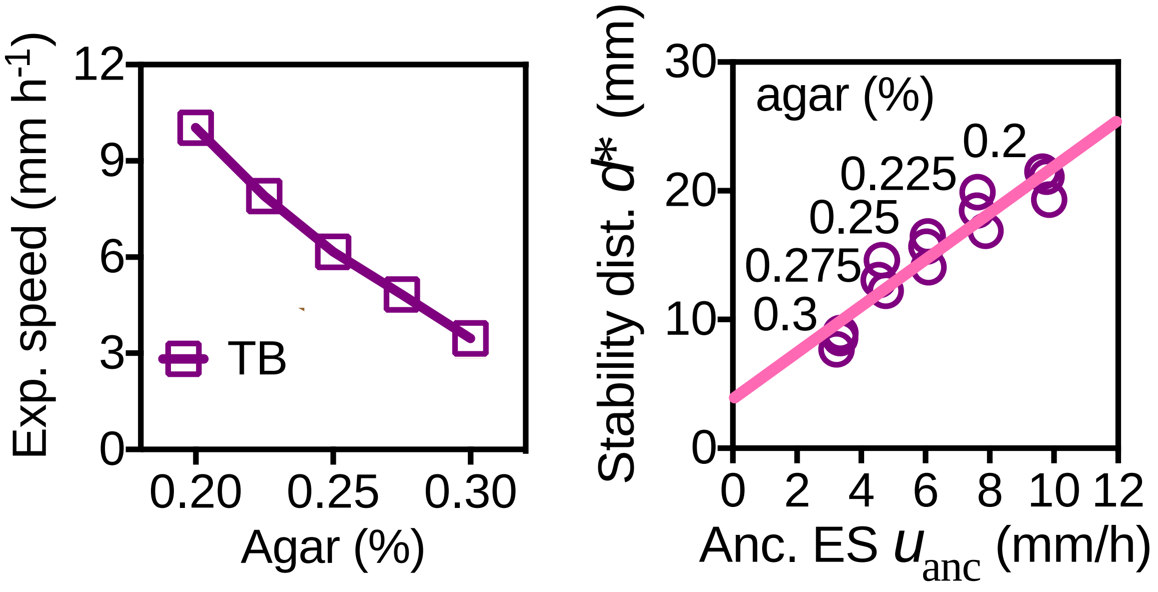
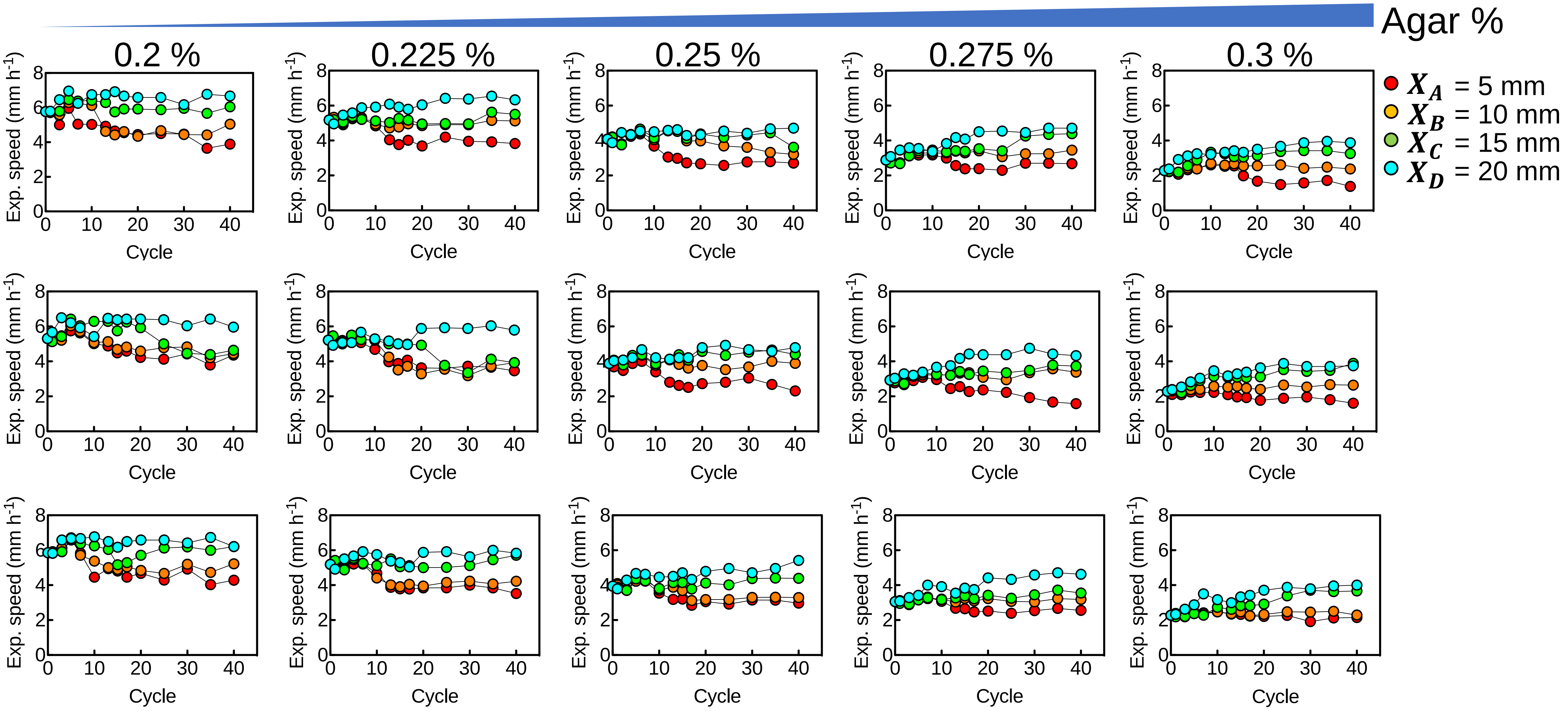
stable expansion speed **position** **growth-rate**



Evolution in Casamino acids (slower growth)

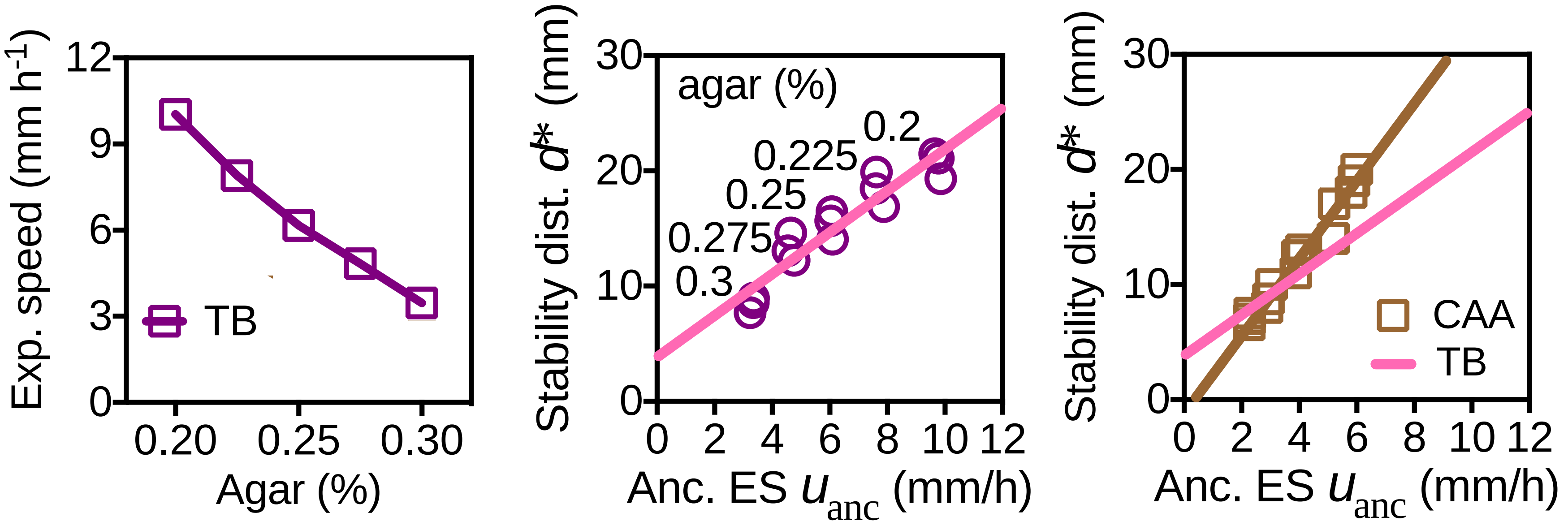


Test model prediction

predicted stable attractor:

$$u^*(X) \propto X \cdot \lambda.$$

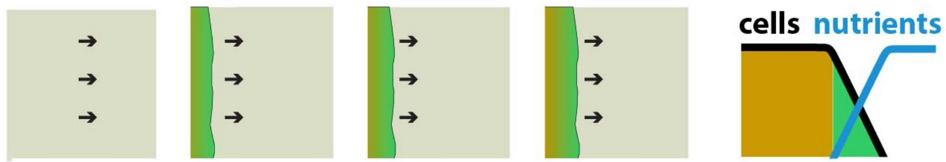
stable expansion speed **position** **growth-rate**



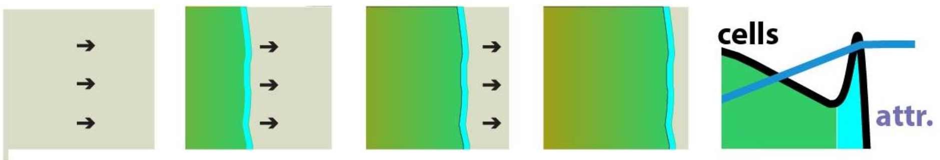
Summary: Chemotaxis as growth strategy to thrive in nutrient-replete environments

Consumption of non-nutritious attractants leads to fast expansion and is an effective strategy to boost colonization into nutrient replete environments

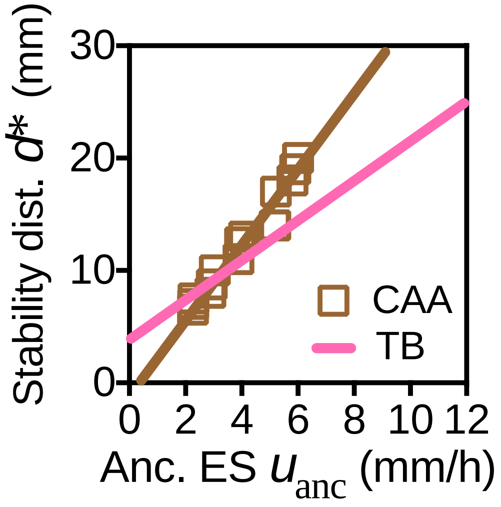
unguided range expansion (FK)



navigated range expansion (chemotaxis)



Competition leads to an optimal expansion speed which depends on habitat size



$$u^*(X) \propto X \cdot \lambda$$

stable expansion speed **size** **growth-rate**

Cremer, Honda, Tang, Wong-Ng, Vergassola, Hwa. Nature (2019)

Liu, Cremer, Li, Hwa, Liu. Nature (2019)

Thank you for your attention!

Postdoc positions available. Contact me for further details.