

A Dynamical Systems Simulation of Myxobacteria Life-Cycle Regulated by Dynamic Energy Budget (DEB) Theory

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Graduate Student and Collaborators

- The graduate student who is doing all the simulations is



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- We also collaborate with an experimental group at UCLA,



Wenyuan Shi

and his postdoc Renata Lux

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Cell Characteristics

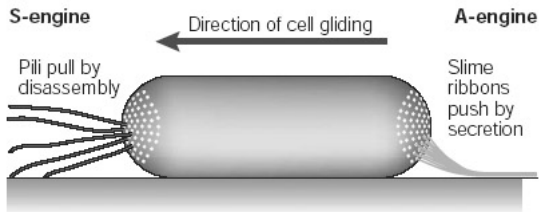
- Social behavior → complex multicellular organization
- Motility engines:
 - A(adventurous)-motility: slime secretion
 - S(social)-motility: pili

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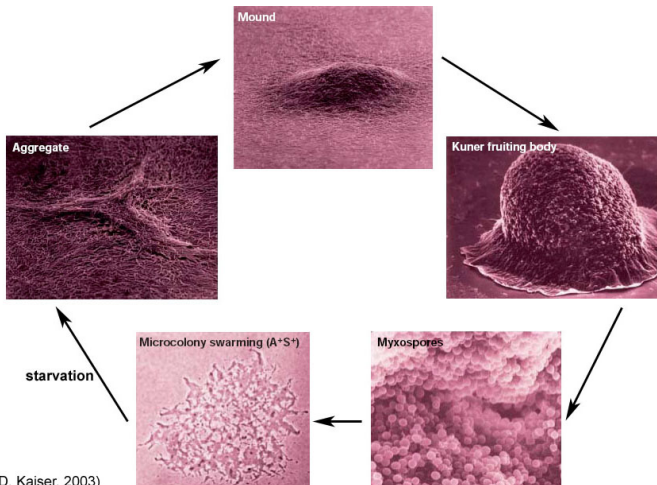


(Ref: D. Kaiser, 2003)

Myxobacteria strains:

- Motile: A+S+ (wild-type), A+S-, A-S+
- Nonmotile: A-S-

Myxobacteria life cycle



(Ref. D. Kaiser, 2003)

Fruiting body formation

- non-chemotaxis
- controlled by C-signal morphogen
- direct cell-cell local interaction

(Ref: S. Kim and D. Kaiser, 1990)

Lattice vs. Off-Lattice model

- LGCA (Lattice Gas Cellular Automaton) model
 - uses hexagonal lattice
 - geometric constraint
- Off-Lattice model
 - free movement in space
 - reduce geometric constraint

(Ref: Y. Wu et al., 2006)

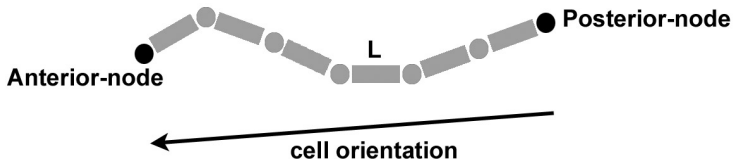
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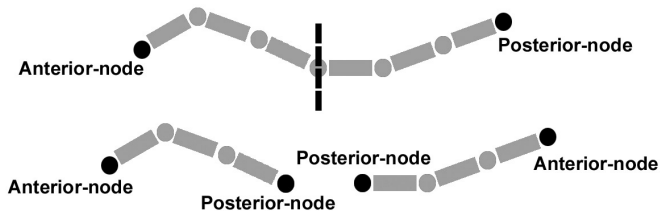
Cell Representation

- string of 4 to 7 nodes, connected by segment
- cell orientation
- polarity reversal



Cell Division

- cell waits until it has fully grown before dividing
- cell divides in the middle
- length of new cells is half of original cell

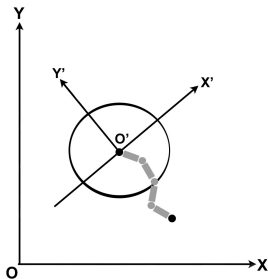


General Assumptions

- cell movement is directed by anterior node
- cell moves with a fixed step length
- collision handling mechanism: align or stop

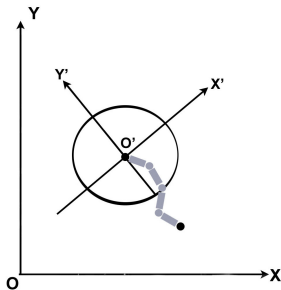
Modeling A-motility

- searching circle
- turn at acute angle to follow slime trail
- need to consider cell density



Modeling S-motility

- searching area around the anterior node
- cell moves towards the most crowded quadrant



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Off-Lattice Model

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The Local Order Simulation

A and S-motility

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Simulating C-signaling

A+S+

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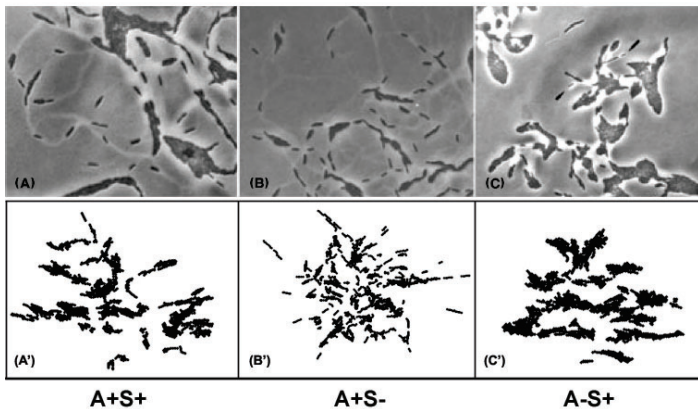
A and S-motility

Modeling C-signaling

Simulating C-signaling

A+S-

Comparison with Experiments



(Ref: C. Wolgemuth et al., 2002)

Modeling C-signaling

- C-signaling occurs when two cells are in end-to-end contact
- cell turns to direction that increases the level of C-signaling
- C-signaling triggers locking between cells
- N is number of C-signal molecules on the cell surface

$$\frac{dN}{dt} = \frac{cN(N_{\max} - N)}{N_{\max}} \quad (1)$$

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C-signaling

Dynamic Energy Budget

- describes how cells acquire and utilize energy for maintenance, growth and division
- uses κ -rule: a fixed fraction κ of energy flowing out of reserves is used for maintenance and growth, and the rest for reproduction
- trigger mechanism from the swarming stage to the streaming stage and the stages of fruiting body formation

(Ref: S. Kooijman, 2000)

DEB Model

$$\frac{dL}{dt} = \frac{\dot{\nu} (E/E_m) - (L/L_m)}{3g + (E/E_m)} \quad (2)$$

$$\frac{dE}{dt} = \frac{A_m}{L} \left(f - \frac{E}{E_m} \right) \quad (3)$$

where

$$f = \frac{X}{K + X}, \quad \dot{\nu} = \frac{A_m}{E_m}, \quad g = \frac{G}{\kappa E_m} \quad (4)$$

E = stored energy density, L = length, X = food density,

κ = fraction of utilized energy spent on maintenance and growth,

K = saturation coefficient, G = energy costs for a unit increase in size,

E_m = max storage energy, L_m = max length, A_m = max assimilation rate

(Ref: R. Nisbet et al. and S. Kooijman, 2000)

The Internal Energy

- The internal energy E in the DEB theory models the level of Adenosine Triphosphate (ATP)
- ATP is a complex molecule that is considered as primary energy currency in all organisms
- ATP powers all activities of the cell, such as cell growth, locomotion, DNA replication and cell division (binary fission)
- ATP is the carrier and regulation-storage unit of energy

Non-dimensionalization

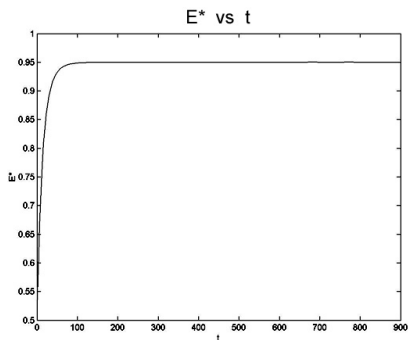
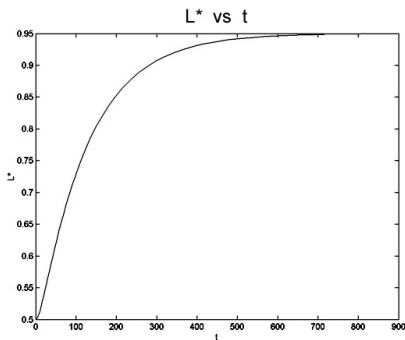
Let

$$L^* = \frac{L}{L_m}, \quad E^* = \frac{E}{E_m} \quad (5)$$

Then

$$\frac{dL^*}{dt} = \frac{\dot{\nu}}{3L_m} \frac{(E^* - L^*)}{(g + E^*)} \quad (6)$$

$$\frac{dE^*}{dt} = \frac{\dot{\nu}}{L^* L_m} (f - E^*) \quad (7)$$



Experimental data:

Doubling time = 3 hours (~ 900 time steps)

Cell length = 2-12 μm

Estimated parameters: $f = 0.95$, $\nu = 0.25$, $g = 0.5$

Fruiting Body Formation

Summary

- A interacting particle model of myxobacteria simulates the different swarming patterns of three strains of bacteria
- A dynamic energy budget (DEB) model controls the reproduction (splitting) of the bacteria and triggers the transition from swarming into the starvation phase
- In the starvation phase DEB, with the addition of C-signaling, controls the different stages of the fruiting body formations culminating in sporulation

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The Scaling: Superindividual \rightarrow Individual

- The interaction particle system can be written as

$$\Delta x = v\Delta t + \epsilon^* dB_t \quad (8)$$

- Hence, the following scaling relationship hold between various parameters:

$$\Delta t \sim \Delta x \sim \epsilon^* \sim r_s \sim r_p \quad (9)$$

- We want to find the scaling parameter α . The density in a computational square of size Δx is $\rho = \frac{n}{\Delta x^2}$.

The Number of Superindividuals

- The total number of superindividuals is $n_T = \frac{nA}{\Delta x^2}$ and the number of cells each superindividual represents is

$$\beta = \frac{N}{n_T} = \frac{N\Delta x^2}{nA} \quad (10)$$

- Thus the number of particles in a computational square is

$$n = \frac{N\Delta x^2}{\beta A} \quad (11)$$

Fixed number of particles n in a square

- Let Δx_0 and β_0 denote the spatial resolution and the number of cells in represented by a superindividual (or individual if $\beta_0 = 1$) in a reference simulation, respectively.
- Since n is constant, (11) gives us the relationship

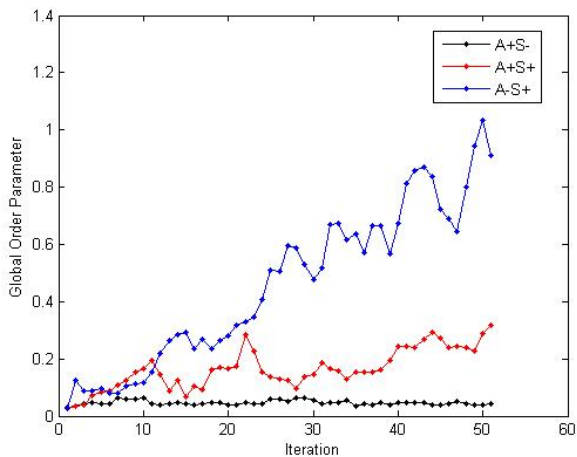
$$\frac{N\Delta x^2}{\beta A} = \frac{N\Delta x_0^2}{\beta_0 A},$$

which implies $\Delta x = \sqrt{\beta/\beta_0}\Delta x_0$

- The scaling factor is

$$\alpha = \sqrt{\beta/\beta_0}$$

The Order Parameter



A+S-

