A Bio-energetic Modeling and Simulation of Myxobacteria Life-Cycle

Björn Birnir

Department of Mathematics
and
Center for Complex and Nonlinear Science
University of California, Santa Barbara

Notre Dame Oct. 1, 2008

Graduate Student and Collaborators

- The graduate student who is doing all the simulations is Melisa Hendrata 
- We also collaborate with an experimental group at UCLA, Wenyuan Shi  and his postodoc Renata Lux

Outline

Cell Characteristics

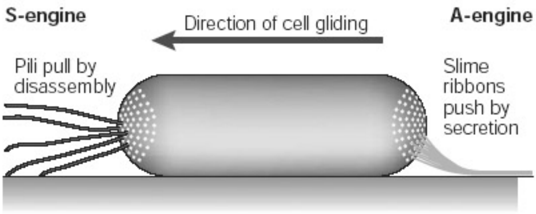
- Social behavior → complex multicellular organization
- Motility engines:
  - A(adventurous)-motility: slime secretion
  - S(social)-motility: pili

Cell Characteristics

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

Cell Characteristics

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

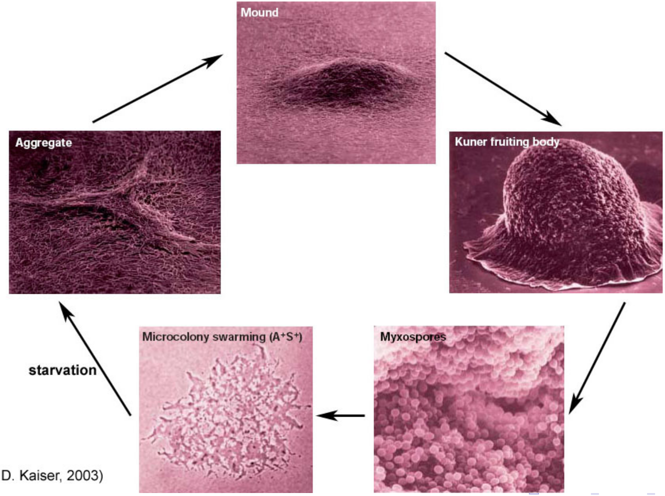


(Ref: D. Kaiser, 2003)

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)

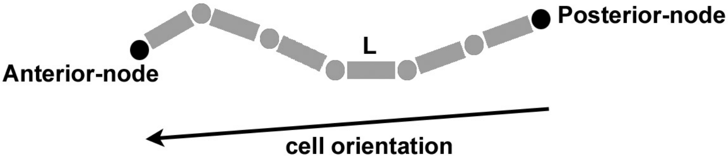
Lattice vs. Off-Lattice model

- 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)

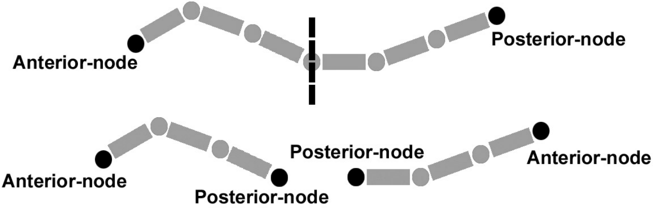
Cell Representation

- 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

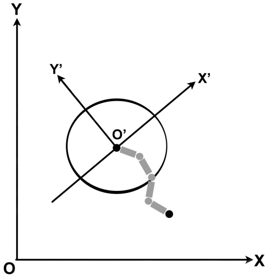


General Assumptions

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

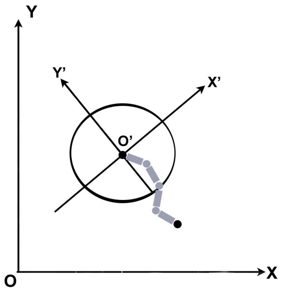
Modeling A-motility

- 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



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

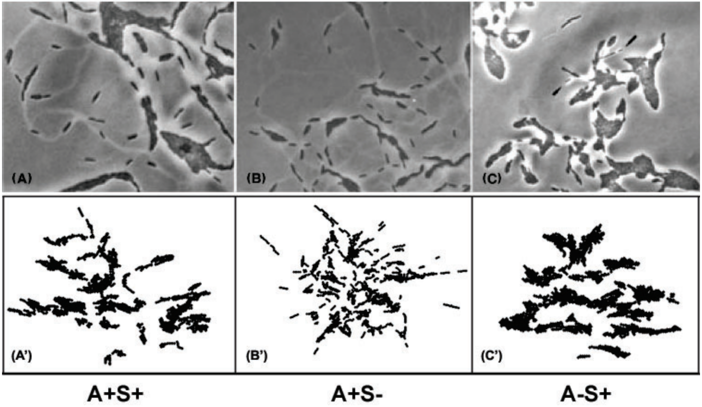
$$\frac{dN}{dt} = \frac{cN(N_{\max} - N)}{N_{\max}} \tag{1}$$

A+S+

A-S+

A+S-

Comparison with Experiments



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

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 stage of fruiting body formation

(Ref: S. Kooijman, 2000)

DEB Model

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

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

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)

Non-dimensionalization

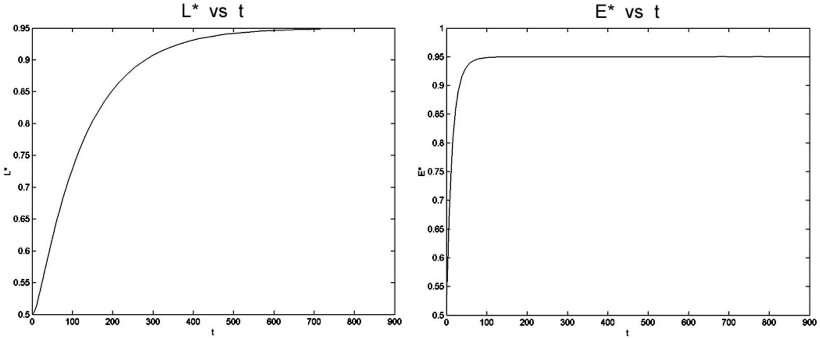
Let

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

Then

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

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



Experimental data:

Doubling time = 3 hours ($\sim$ 900 time steps)

Cell length = 2-12 μm

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

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

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

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

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