

Aggregate Formation in Myxobacteria

Yi Jiang jiang@lanl.gov

Fruiting body formation in bacteria occurs in response to adverse conditions and is critical for species survival. Complex morphogenesis must be robust despite internal and external noise. Myxobacteria, a social swarming bacteria, are one such example. When starved, myxobacteria undergo a process of alignment, rippling, streaming and aggregation that culminates in the three-dimensional fruiting body (Fig. 1).

Canonically, models for bacteria (e.g. *E. Coli* and *B. subtilis*) and amoebae (e.g. *Dictyostelium discoideum*) aggregation have been based on attractive chemotaxis, a long range cell interaction that shares many features of chemical reaction-diffusion dynamics. Initialization of chemotactic signals plays an important role in the initial position of aggregates. Cells following the maximal chemical gradient navigate towards aggregates that are large and near. In myxobacteria, however, aggregates form without the aid of chemotactic cues. Yet myxobacteria travel large distances to enter an aggregate. How do the myxobacteria cells know where to go to form aggregates of optimal size? Understanding the aggregate formation in myxobacteria will shed new light into collective bacterial motion.

During aggregation, myxobacteria cells are elongated with a 7:1 length to width ratio. They move on surfaces by gliding along their long axis. Fruiting body development are controlled by the C-signal morphogen, which is exchanged at cell poles by cell-cell contact (hence the name C-signaling). Different levels of C-signal, encoded by the *csgA* gene, induce the different stages of fruiting body formation. The expression of *csgA* is regulated by two feedback loops in the signal transduction pathway. Each time a cell receives the C-signal it increases expression of *csgA*.

Based on these observations, we designed a lattice cell model [1], in which cell interactions are contact-mediated. The local rules demand that

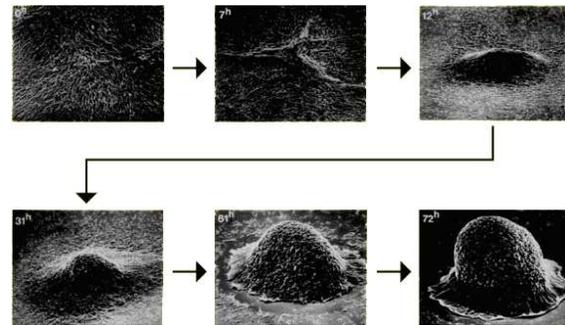


Figure 1. Snapshots of the life-cycle of *Myxococcus xanthus*.

cells turn preferentially in directions that increase their level of C-signal. Cells move on a hexagonal lattice with unit velocities (*or channels*) in each of the six directions. We model identical rod-shaped cells as 3×21 rectangles, corresponding to a cell size of $1 \times 7 \mu\text{m}$. Each cell is represented as: (1) a single lattice node as the cell's center in the xy plane, (2) an occupied channel designating cell's velocity, and (3) a local neighborhood defining the physical size and shape of the cell. This cell representation is computationally efficient, yet approximates aggregates more closely than point-like cells. Cells may turn stochastically 60 degrees clock-wise or counter-clockwise, or stay in its current direction, but favors directions that maximize the overlap of the C-signal exchange neighborhood at the poles of a cell with that of its neighboring cells. All cells then move synchronously one node in the direction of their velocity by updating the positions of their centers.

Our simulations show that cells aggregate in two distinctive stages. First, initially randomly distributed cells condense into small stationary aggregates (Fig. 2 (a)). These aggregate centers grow by absorbing immediately surrounding cells. Next, some adjacent stationary aggregates merge and form long, thin streams which extend and shrink dynamically on their own or in response to interactions with other aggregates (Fig. 2 (b)). These streams are transient and eventually disappear, leaving behind a new set of larger, denser stationary aggregates which are stable over time (Fig. 2 (c)). These results agree with exper-

Aggregate Formation in Myxobacteria

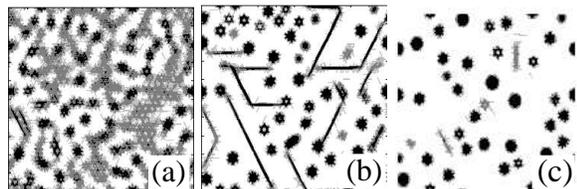


Figure 2. Aggregation stages on a 500×500 lattice, corresponding to an area of 2.8cm^2 . Local cell density at (a) 200, (b) 900, and (c) 25,000 timesteps. The darker shade of gray corresponds to higher cell density. Small aggregates form first at random positions; some of them interact and form long streams, which disappear and leave behind larger, denser and more stable aggregates.

imental observations and explain how some aggregates can 'mysteriously' disappear while their neighbors grow (when the streams are below the resolution of the observation). The simulated aggregates also reproduce the unique structures of several fruiting bodies.

We measure the areas and densities of every stationary aggregate which appeared over the course of two large simulations. They all fall within a narrow range in the area-density phase diagram, indicating that for an aggregate of a given cell number, it has a fixed structure, its area and density is prescribed within a narrow region, which we call an attractor region. As this attractor region covers continuous space rather than disconnected, the different aggregate structures can continuously transform from one to another.

We perform several tests to analyze the stability of this attractor region. Different initial random cell distributions result in statistically the same aggregates. When we slowly add cells to an aggregate, it "walks" in the phase space within the attractor region to larger area and density. When we put two aggregates together, making an artificial aggregate with double area but the same density, the aggregate settles back into the attractor region rather quickly. These tests show that this attractor region is stable with respect to the external noise (initial condition and our perturbation).

We have also devised a deterministic version of the model, describing the cell turning probability

by a function that is equivalent to averaging over a large number of stochastic cell turning events (similar to converting a lattice gas model to a lattice Boltzmann model). Both models evolve very similarly, indicating that the aggregation dynamics are not sensitive to internal noise that originates from the stochastic nature of the cell's turning process. There are, however, a few important differences between these two models. One difference is that streams in the deterministic model are fewer and smaller. Another difference is that streams are shorter-lived, and the deterministic simulation reaches a steady state much faster. These differences have a critical effect on the way aggregates reorganize: with the internal noise, aggregates can reach much larger sizes. This is not surprising because noise slows the process of stream contraction so that streams persist longer and span a greater area, which enables more aggregates to interact and form larger, more stable aggregates. In other words, the presence of some internal noise is required to efficient streaming. It is as if the cells must make short-term mistakes for the formation of unstable transients that ultimately results in more efficient aggregation.

To summarize, our lattice cell model is based on a very simple local rule in which cells align by turning preferentially to make end to end contact, mimicking C-signaling in myxobacteria that drives myxobacteria aggregation. The model reveals a novel two-stage process of aggregation mediated by transient streams. Noise in individual cell behavior increase the effects of streams and results in larger, more stable aggregates.

Acknowledgements

This work is in collaboration with Prof. M. Alber and M. Kiskowski at University of Notre Dame, and is partially funded by DOE under contract W-7405-ENG-36.

Los Alamos Report LA-UR-03-8696.

References

- [1] M. Alber, M. Kiskowski and Y. Jiang, *Two-Stage Aggregation Formation via Streams in Myxobacteria*, preprint, to appear in Phys. Rev. Lett. 2004.